Unraveling Structure and Dynamics in Porous Frameworks via Advanced In Situ Characterization Techniques

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Dynamic metal–organic frameworks (MOFs) represent a subgroup of frameworks featuring unique performance, as they are capable of adapting their pore size and/or the orientation of framework constituents in response to specific guest molecules such as gases or solutes and often outperform their rigid analogues in gas storage, sensing, or separation. In this review, the authors focus on recent methodical developments of advanced in situ diffraction and spectroscopic techniques for comprehensive characterization of porous frameworks. Examples for advanced instrumentation are highlighted for in situ nuclear magnetic resonance, electron paramagnetic resonance, and optical spectroscopies as well as X-ray and neutron diffraction. Several examples of high-resolution transmission electron microscopy (HRTEM) on MOFs are shown because HRTEM is an emerging technique for the characterization of time-resolved structural dynamics in MOFs. These methods shed light on structural features and phase transitions of the host, its spin state, electronic structure, specific host–guest and guest–guest interactions, preferable adsorption sites, and bonding situation in the framework, focusing on the most prominent recent case studies. The synergistic development of novel in situ characterization methods and exploration of well-defined model framework systems are crucial to advance the understanding of dynamic processes in porous materials in future.

1. Introduction

Metal-organic frameworks (MOFs) are crystalline porous solids, discovered in the 1990s,[3] constructed from metal ions or clusters and organic ligands using modular building principle[2] forming porous frameworks with targeted pore size and accessibility. Record values of surface areas and pore volumes[3] render MOFs as prospective materials for gas storage[4] and separation.[5] A wide range of functionalization of MOF structures allows to test them in various catalytic reactions,[6] sensor materials[7] and even electronic devices.[8] However, one of the unique features of MOFs, which is not (or only to a very limited degree) accessible in other porous solids, is structural flexibility as a response to external stimuli, such as guest molecules, electromagnetic irradiation, temperature or hydrostatic pressure.[9] The structural switchability was initially only considered as an interesting fundamental phenomenon and is currently generally understood from both theoretical and experimental standpoints.[10] Nowadays, flexible MOFs are even discussed for some very specific applications. One of the prospective fields of application for flexible MOFs is gas storage. Long and co-workers demonstrated significantly increased storage capacity in a methane gas tank using a “gate pressure” MOF Co(1,4-benzenedipyrrozolate (bdp) as a working material.[11] Kundu et al. pointed out the role of the crystallite size of Matériaux de l’Institut Lavoisier (MIL)-53(Al) on effective methane storage capacity.[12] Kitagawa and co-workers showed the selective CO adsorption in the flexible MOF from CO/N₂ mixture.[13] MOF-carbon composites were demonstrated as threshold sensors,[14] they are also discussed as a self-folding surfaces etc.[15] The state of the art in rational design, thermodynamics and factors affecting switchability has been reviewed to a certain extent.[9]

Shortly after discovery of MOFs in the late 1990s, two groups from Japan reported on coordination polymers showing hystereses in physisorption isotherms which were different from typical capillary condensation in mesoporous solids. Li and Kaneko heated the previously reported coordination polymer with composition Cu(bpy)2(BF₄)2(H₂O)₂·bpy (bpy: 4,4’-bipyridine), which resulted in the formation of the new 2D layered structure Cu(bpy)₄(BF₄)₂, today known as ELM-11 (ELM states for elastic layer material).[16] Typical “gate pressure” hystereses...
were observed in nitrogen (77 K), argon (87 K), and CO₂ (273 K) physisorption experiments. In parallel to this study, Kitagawa and co-workers synthesized a Cu(II)-based coordination polymer with the composition Cu₃(pzdc)₃(dpyg) (pzdc: pyrazine-2,3-dicarboxylate; dpyg: 1,2-di(4-pyridyl)-glycol), which undergoes a phase transition upon solvent removal.[17] Physisorption of methanol vapor at 25 °C results in a hysteresis between adsorption and desorption branches of the isotherm. Shortly after Frey and co-workers reported a 3D coordination polymer based on the (Cr(III)–O–)ₙ chains interconnected by terephthalates, also known as MIL-53(Cr).[18] This 3D polymer shows a microporous channels in the crystal structure and reversible crystal-to-crystal transition in the thermo-powder X-ray diffraction (PXRD) experiment. Later, reversible contraction, further denotes as “breathing” was observed in this material during adsorption of carbon dioxide and water.[19] Shortly after discovery of flexibility in MOFs, Kitagawa and co-workers introduced the classification of the porous coordination polymers regarding to removal of guest molecules from the pores, according to which, MOFs showing reversible structural changes belong to the third generation and also denoted as “soft porous crystals.”[9b] Physisorption isotherms and corresponding phase transitions of archetypical switchable MOFs MIL-53(Al), Co(bdp), ELM-11, and Dresden University of Technology (DUT)-8(Ni) are shown in Figure 1.

However, a key challenge for a deeper exploration of dynamic phenomena is the detailed characterization of all intermediate MOF structures traversed during operation in order to understand the mechanism of structural transition, host–guest, guest–guest interactions as well as energetic of the transitions. Despite theory is making great progress to predict such intermediate states there are still open questions in modeling dynamic phenomena and selective host guest interactions. Hence, experimental observations are crucial to develop reliable predictive modeling schemes in future. The latter implies the necessity to measure physical characteristics such as diffractograms, nuclear magnetic resonance (NMR), electron paramagnetic resonance (EPR), or optical spectra under defined conditions, namely, defined pressure and temperature, electric and/or magnetic field or hydrostatic pressure ideally time resolved, and further denoted as in situ. Such an approach requires specially adapted cells, as most of them are not commercially available. For a deeper analysis of flexibility phenomena the development of in situ cells for analyses under specified working conditions is a crucial scientific task. Only newly this rather expanding research field motivated equipment suppliers to start some commercialization of these developments and propose automated solutions for in situ measurements.

In the following, we review the recent developments in advanced in situ instrumentation for the characterization of dynamic MOFs, in particular switchable MOFs by EPR, NMR, and optical spectroscopies, which shed a light on electronic state of the metal ions, host–guest and guest–guest interactions in MOFs, but also monitor the changes in the bonding situation in different phases. Development of in situ instrumentations for X-ray and neutron diffraction techniques is reviewed since both directly follow the structural changes and positions of adsorbed molecules in the pores. The typical instrumentations accessing various conditions and techniques, which provides...
unique information on flexibility and most prospective results, obtained using these instruments are described.

2. In Situ NMR Techniques

2.1. General Remarks

2.1.1. NMR Spectroscopy: A Versatile Tool for MOF Characterization

Nuclear magnetic resonance spectroscopy is increasingly applied for MOF characterization.[21] Based on the detection of NMR-active nuclei such as $^1$H, $^{13}$C, $^{15}$N, $^{31}$P, and many others, this method allows not only the characterization of the MOF lattice but also studies of adsorbed molecules inside the pore system without the need of long-range (crystalline) order. In general, two fundamentally different NMR methods can be distinguished, namely liquid-state (solution-state) and solid-state NMR spectroscopy.[22] Liquid-state NMR spectra of sufficiently small molecules dissolved in isotropic solvents usually exhibit well-resolved spectra due to the fast and isotropic reorientation of the molecules. This makes structure-sensitive parameters like isotropic chemical shifts, $J$-couplings or nuclear Overhauser effect (NOE) contacts easily accessible. Liquid-state NMR spectroscopy is, therefore, routinely applied to characterize the linker molecules before MOF synthesis, but also for in situ synthesis reaction monitoring (see below). In contrast, solid-state NMR experiments usually require the application of line-narrowing techniques in order to suppress or at least reduce the influence of spatially anisotropic line broadening interactions such as the chemical shift anisotropy, magnetic dipole–dipole interaction, electric quadrupole interaction (for spins of quantum number $I > \frac{1}{2}$), and others. The most popular line narrowing technique is magic angle spinning (MAS).[23] Its application results in well-resolved solid-state NMR spectra as is demonstrated in Figure 2. Adsorbed guest molecules inside the pore system often exhibit a relatively high mobility resulting in narrow signals even without MAS—in contrast to nuclei located in the MOF lattice. This is an important point with respect to in situ NMR spectroscopic studies because in situ techniques are not always compatible with MAS (see below).

2.1.2. Advantages of NMR Spectroscopy and Its Information Content

One fundamental property of NMR spectroscopy is that it does not require crystalline order because it relies on the exploitation of short-range interactions, typically at a range below one nanometer. The information content of NMR spectroscopy is thus complementary to diffraction techniques. NMR therefore also allows studying disordered adsorbed molecules inside the pore system as well as their interactions with the MOF lattice (host–guest interactions).[21]

Advantages of NMR spectroscopy related to its information content are the following:

i. NMR is a quantitative method, i.e., the signal intensity is proportional to the number of spins in the detected sample.
volume. Intensities of different signals are thus directly comparable with each other—in contrast to optical spectroscopy.

ii NMR spectra reveal structure information based on measured parameters such as chemical shifts, $J$-couplings and—in solid-state NMR spectra—distance dependent or spatially anisotropic parameters like dipolar couplings, chemical shift anisotropies, and electric field gradient tensors.\(^{[22,23b]}\) Especially the distance-dependent dipolar couplings are a valuable source of structure information in solid-state NMR spectroscopy. They can be exploited selectively by advanced techniques such as the rotational echo double resonance (REDOR)\(^{[24]}\) experiment.

iii NMR spectroscopy provides information on dynamic processes like thermal motions of molecules including diffusion, exchange processes and others. Various time scales are accessible by appropriate NMR spectroscopic experiments. For exchange processes, the critical exchange rate $k_{\text{crit}} = \Delta \omega$ is determined by the frequency distance between the NMR signals of the involved states A and B in units of the angular frequency, $\Delta \omega = 2\pi|\nu_A - \nu_B|$. Processes fast at this time scale can be investigated, e.g., by line shape or relaxation time analysis. Slow processes are detectable for example by 2D exchange spectroscopy (2D EXSY).\(^{[25]}\) Diffusion coefficients can be measured by the so-called pulsed field gradient (PFG) NMR technique.\(^{[26]}\)

The major drawback of NMR spectroscopy is a relatively low sensitivity compared with other techniques like optical spectroscopy. In order to overcome this problem, various approaches are developed. On the one hand, superconducting magnets with increasingly strong magnetic fields are constructed. The maximum available magnetic field corresponds to 1 GHz $^1H$ resonance frequency at the moment; 1.2 GHz will be feasible soon. Other approaches are tackling the sensitivity problem by increasing the spin polarization of nuclei beyond the value expected in thermal equilibrium at the given magnetic field strength. These so-called hyperpolarization techniques include experiments such as dynamic nuclear polarization (DNP),\(^{[27]}\) parahydrogen-induced polarization (PHIP),\(^{[28]}\) spin-exchange optical pumping (SEOP),\(^{[29]}\) and others.

### 2.2. Experimental Techniques for In Situ NMR Spectroscopy

#### 2.2.1. Techniques for Monitoring Materials Synthesis and Functionalization

NMR spectroscopy offers great possibilities for in situ monitoring of materials synthesis reactions as a function of time, temperature, and pressure by the identification and quantitative evaluation of characteristic signals caused by educts, reaction intermediates, products, and side products.\(^{[30]}\) Mobile species can be detected by liquid-state NMR whereas the study of the formed solid materials requires MAS NMR spectroscopy. A first in situ MAS NMR study of zeolite crystallization was published by Shi et al.\(^{[31]}\) Pioneering work to develop liquid-state NMR for in situ monitoring of aluminophosphate formation was done by Taulelle and co-workers.\(^{[32]}\) In such experiments, special sample containers are required for both, liquid-state and solid-state NMR spectroscopy allowing to adjust temperature and pressure to synthesis-relevant high values. Standard MAS NMR probes routinely allow measurements at temperatures...
between ≈120 and 370 K and commonly used MAS rotors (cf. Figure 2) do not allow high pressures because the rotor caps are not sealed and pressure safe.

Increasing efforts are thus made in order to construct special solid-state NMR probes allowing MAS NMR studies at high temperatures and pressures. Hu et al. [30d] developed a sealed rotor system for MAS NMR studies up to 520 K and 100 bar (cf. Figure 3). If such high pressures are unnecessary, even higher temperatures are nowadays accessible, e.g., by using hf-heated rotor insets.[33]

An elegant combination of liquid- and solid-state NMR spectroscopy on identical samples under MAS is provided by the so-called combined liquid- and solid-state in situ crystallization (CLASSIC) approach.[34] The crystallization of m-aminobenzoic acid was monitored in situ as a function of time by subsequently changing the pulse sequence used for signal detection between a) single pulse $^{13}C$ excitation (direct excitation) at short recycle delay without $^1H$ decoupling and b) $^1H$–$^{13}C$ cross-polarization (CP). Excitation scheme (a) delivers the liquid-state NMR spectrum and (b) the solid-state NMR spectrum because the CP experiment only works in the presence of dipolar interactions which are averaged to zero in isotropic liquids. That means, CLASSIC experiments allow to record the liquid-state and solid-state NMR spectra in an interleaved, time resolved fashion.

It should be noted in this context that solid-state NMR experiments will become increasingly powerful in the future by the combination with the aforementioned hyperpolarization methods, especially DNP. This technique was already successfully applied to study MOFs as well as the functionalizations of MOFs. First experiments were performed on N-functionalized MIL-68.[35] The obtained signal enhancement enabled the acquisition of high-quality 1D $^{13}C$ solid-state NMR spectra, 2D $^1H$–$^{13}C$ dipolar HETCOR and 1D $^{15}N$ solid-state NMR spectra with natural isotopic abundance in experiment times on the order of minutes. Other authors for example investigated $^{11}C$–$^{27}Al$ proximities in MIL-100(Al) by DNP enhanced solid-state NMR methods[35d] as well as platinum dispersed in MOFs[35b] using DNP-enhanced wideline $^{195}Pt$ NMR spectroscopy.

### 2.2.2. Techniques for Adsorption Studies

Adsorption is the enrichment of molecules from a gas or liquid at the surface of a solid. Porous materials like zeolites or MOFs usually provide a high adsorption capacity due to their huge internal surface area. The adsorption capacity of a material furthermore depends on the surface chemistry as well as temperature and pressure. It is highly desirable to perform NMR studies of adsorption phenomena on activated samples under controlled thermodynamic conditions. Two fundamentally different approaches for such in situ NMR studies should be distinguished:

- **i** Experiments at constant loading. Such samples are loaded with a defined number of molecules or atoms and sealed afterward. Temperature variation then causes pressure changes inside the sealed samples because the equilibrium between surface-adsorbed phase and gas phase is temperature-dependent. Determination of the exact pressure inside the sample is then difficult.
- **ii** Experiments at constant pressure. Temperature variation under constant pressure or pressure variation under constant temperature will cause changes in the number of adsorbed species after equilibration, but both thermodynamic variables, pressure and temperature, are kept under external control.

An advantage of the first approach (i) is that sealed samples can be inserted into an MAS rotor providing improved spectral resolution. NMR studies on loaded and sealed samples with and without MAS have a long tradition in surface NMR spectroscopy. Probes such as $^{129}Xe$, $^{13}CO$, $^{13}CO_2$, acetonitrile, and many others were already used to study host–guest interactions with the surface of various materials like zeolites and related compounds, porous carbon materials, etc.[36]

Approach (ii) is hardly compatible with MAS because it requires the connection of the sample with an outside gas reservoir or a gas outlet to allow for equilibration after...
temperature variation. On the other hand, approach (ii) allows to record in situ NMR spectra under comparable conditions as used for the measurement of volumetric or gravimetric adsorption/desorption isotherms. This enables the correlation of volumetric adsorption experiments with in situ NMR data. A corresponding experimental setup\cite{37} is shown in Figure 4.

Increasing interest is devoted to adsorption processes taking place in electrochemical devices, for example on electrodes under the influence of external electric fields. The understanding of such electroadsorption processes is crucial, e.g., for the development of fast energy storage devices of high capacity such as supercapacitors. Pioneering work was performed by Grey and co-workers.\cite{38} to develop in situ NMR techniques capable of monitoring electroadsorption processes under the influence of electric fields (cf. Figure 5). This type of apparatus was meanwhile applied, e.g., to study various devices as well as for in situ reaction monitoring of electrocatalytic reactions.\cite{38a–c} Since conductive MOFs are envisioned as potent electrode materials, such experiments may become important for investigations on MOF-based electrodes in future research.

2.3. In Situ NMR Studies of MOFs

MOFs are promising candidates for gas storage due to their huge internal surface area which strongly exceeds the internal surface of zeolites. Adsorption of CO$_2$ is currently of special importance because CO$_2$ capture and storage is an environmentally important problem. MOFs are considered as potent materials for gas storage and separation applications, e.g., removal of CO$_2$ from other gases like methane. Consequently, various in situ $^{13}$C NMR spectroscopic investigations of CO$_2$ adsorbed on MOFs were reported over the past years.\cite{39} Kong et al.\cite{39b} studied the interaction of CO$_2$ with the open Mg sites in Mg-MOF-74—giving rise to exceptional CO$_2$ capture properties. Adsorbed CO$_2$ molecules exhibit a line shape characteristic for chemical shift anisotropy but of reduced width compared to rigid CO$_2$. It was concluded that the motional state should be described by jump processes between different open metal sites giving rise to partial averaging of the chemical shift anisotropy. The interaction of CO$_2$ with MOFs and the motional state of the adsorbed molecules was further analyzed in various subsequent publications.\cite{39c-h}

In situ high-pressure $^{13}$C NMR spectroscopy was recently applied in order to demonstrate the enhanced selectivity of flexible versus rigid MOFs for the case of CO$_2$ adsorption from CO$_2$/CH$_4$ mixtures.\cite{39i}

The adsorption of natural gas (methane) by MOFs is another issue of great practical relevance because natural gas is considered as a promising carrier for mobile applications. Yan et al.\cite{40} used a combination of $^2$H solid-state NMR spectroscopy and neutron powder diffraction (NPD) of methane-loaded samples to study methane adsorption by members of the so-called “Manchester framework material” (MFM) family. It could be shown that their favorable properties are due to the combination of optimal linker dynamics, pore size and geometry, as well as favorable binding sites.

In situ $^{129}$Xe NMR spectroscopy is another frequently used method to characterize host-guest interactions and dynamic phenomena in MOFs. Xenon has a long tradition as a probe in surface NMR spectroscopy.\cite{36a–c} MOFs are also discussed for uses in noble gas mixtures separations, e.g., for Xe/Kr mixture separation. Usually, the $^{129}$Xe chemical

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**Figure 4.** High-pressure in situ NMR apparatus for gas adsorption studies (here: connected to a xenon cylinder for in situ $^{129}$Xe NMR studies). Reproduced with permission.\cite{37} Copyright 2011, American Chemical Society.

**Figure 5.** In situ NMR probe for studies of electrochemical devices under applied voltage as developed by Grey et al. and scheme showing the principle of the sample design.
shift of adsorbed xenon is interpreted in such experiments. It can be written as
\[ \delta = \delta_s + \delta_{\text{Xe-Xe}}(\rho_{\text{Xe}}, T) \]  

The term \( \delta_s \) represents all contributions caused by interactions between xenon atoms and the different surface sites of the pore system. The term \( \delta_{\text{Xe-Xe}} \) is caused by interactions among adsorbed xenon atoms and depends on the density of xenon \( \rho_{\text{Xe}} \) and the temperature.\[^{36a-c}\] That means, the \(^{129}\text{Xe} \) NMR chemical shift of adsorbed xenon encodes information on the structure and surface chemistry as well as on Xe–Xe interactions. Its accurate interpretation requires chemical shift calculations for specific interactions between xenon and preferred adsorption sites as well as weighted averaging along the path of the xenon atoms in the pore system, i.e., molecular dynamics (MD) simulations.\[^{41}\] Empirical correlations can often be established between the average pore size and the xenon chemical shift for systems of comparable surface chemistry.\[^{42}\] Due to its favorable properties, \(^{129}\text{Xe} \) NMR spectroscopy also finds increasing use to study MOFs.\[^{43}\] Notably, the \(^{129}\text{Xe} \) chemical shift is also highly sensitive to collective structure changes (“switching transitions”) in so-called flexible MOFs as is demonstrated for DUT-50 in Figure 6.\[^{43c}\]  

3. In Situ Optical Spectroscopy  
3.1. General Remarks  
Optical spectroscopy relies on the interaction between electromagnetic radiation and matter.\[^{45}\] Optical transitions can be observed either in absorption or emission. Absorption spectra can be measured either in transmission or reflectance mode. Transmission spectra can be quantified using the Lambert–Beer law, i.e., by measuring the extinction \( E = \varepsilon \cdot c \cdot d \) where \( c \) denotes the concentration and \( d \) the path length of light passing through the sample. Furthermore, the measured extinction \( E \) is proportional to the specific molar extinction coefficient \( \varepsilon \). It depends on the wavelength and the analyte under study. Quantification thus requires the calibration of individual lines—in contrast to NMR spectroscopy. Reflectance spectra are measured on nontransparent samples such as many solids or aqueous solutions in the infrared (IR) frequency range. 

Advantages of optical spectroscopy are the following:  

i. Optical methods are inherently very sensitive. They can thus be used to detect even spurious sample amounts or contaminations.  
ii. The sensitivity of optical spectroscopy can be even increased by the application of special techniques such as surface-enhanced Raman scattering (SERS) or tip-enhanced Raman scattering (TERS).  
iii. Optical spectroscopy contains structural information. Examples are characteristic vibrations observed in IR/Raman spectroscopy which allow the identification of certain functional groups as well as the detection of interactions between such functional groups and adsorbed molecules (guests).  
iv. Due to its inherently high sensitivity and based on fast detection schemes such as rapid-scan Fourier transform (FT) or step-scan FT spectroscopy, time-dependent processes like adsorption or reaction kinetics can be monitored with a time resolution down to about ten milliseconds. This enables efficient reaction monitoring including the identification of reaction intermediates.

Figure 6. In situ \(^{129}\text{Xe} \) NMR of DUT-50. Left: In situ \(^{129}\text{Xe} \) NMR spectra measured at various pressures at 200 K. The boiling pressure \( p_0 \) amounts to \( \approx 5 \) bar at this temperature. Right: Adsorption-induced structural transitions of DUT-50 between the open pore (op) and closed pore (cp) state in DUT-50. Note the chemical shift jump of \( \approx 100 \) ppm caused by pore contraction causing negative gas adsorption (NGA). This counterintuitive phenomenon is accompanied by a partial release of previously adsorbed species.\[^{10b,44}\] Reproduced with permission.\[^{43c}\] Copyright 2019, American Chemical Society.
3.2. Experimental Techniques for In Situ Optical Spectroscopy

In situ optical spectroscopy on porous materials/heterogeneous catalysts like zeolites, MOFs or others can be carried out in transmission or reflectance mode. Due to the strong absorption, transmission experiments must be carried out on sufficiently thin samples. Since the materials are usually present as powders, they must be processed into mechanically stable thin layers. This can be done either by embedding into a matrix, usually by processing the sample into a KBr pellet or by mechanically pressing the powder without any matrix into a self-supported layer. The KBr pellets are mechanically more stable, but the matrix can influence the behavior of the sample in the in situ experiment, e.g., by limiting transport and accessibility. Therefore, many in situ studies are performed in reflectance mode. Reflectance spectra can be measured by the attenuated total reflection (ATR), the diffuse reflectance Fourier transform IR (DRIFTS), or the reflection–absorption (RAIRS) technique. Figure 7 provides a schematic overview about these different IR absorption techniques. Note that the quantification of reflectance spectra in general requires corrections accounting for the problem of limited light penetration depth. For example, diffuse reflectance spectra are usually transformed into so-called Kubelka–Munk units.

Various experimental setups have been developed over the past decades in order to allow in situ optical spectroscopy under relevant conditions. Numerous instrument developments resulted in the design of in situ cells allowing gas adsorption studies as well as reaction monitoring on heterogeneous catalysts at variable temperature and pressure. An example in situ DRIFTS cell allowing high-temperature high-pressure studies even under continuous flow is given in Figure 8. In situ Raman spectroscopic approaches for heterogeneous catalysts as well as catalytic reactions nowadays often rely on resonance Raman (RR) techniques. Techniques like the aforementioned SERS and TERS are also often applied to increase the sensitivity as well as selectivity in detecting catalytically active sites/components of the samples. It should be mentioned that even phase transitions induced by mechanical pressure can be studied by in situ optical spectroscopy using so-called diamond anvil cells customized for in situ Raman or FTIR. A more detailed overview about the various experimental setups for in situ Raman spectroscopy can for example be found in ref. 52.

3.3. In Situ Optical Spectroscopy of MOFs

Increasing interest is devoted to the development of in situ techniques for monitoring the synthesis/formation of MOFs (cf. also Section 2.3). Embrechts et al. used time resolved in situ ATR FTIR spectroscopy in order to elucidate the formation of MIL-53(Al). It was possible to identify different intermediates, i.e., to follow the different synthesis steps. A prenucleation building unit (PNBU) consisting of one linker molecule and one Al atom could for example be identified. Furthermore, the assembly of PNBU’s to MIL-53(Al), the decomposition of...
dimethylformamide into formic acid and dimethylammonium in solution as well as the precipitation of the crystallites was observed. These observations highlight the great potential of in situ optical spectroscopy to monitor MOF synthesis procedures.

Various publications describe the use of in situ IR and Raman spectroscopy to study gas adsorption by MOFs. This includes for example investigations of the interaction between MOFs and H₂, CH₄, and N₂, CO₂, NO₂, and SO₂. \(^{[57]}\) Figure 9 demonstrates monitoring of SO₂ adsorption by NOTT-202a using in situ DRIFTS spectroscopy at various pressures. Water cluster confinement and the dissociation of H₂O on coordinatively unsaturated metal ions in MOF-74 could be investigated by in situ IR spectroscopy. \(^{[58]}\) In situ Raman spectroscopy allowed to study the catalytic oxidation of carbon monoxide by MOF-cobalt oxide composite catalysts. \(^{[59]}\) The catalytic hydrogenation of hydrocarbons by Pd nanoparticles inside the MOF Universitetet i Oslo (UiO)-67 was monitored by IR spectroscopy. \(^{[60]}\)

The effect of mechanical pressure applied by a diamond anvil cell upon a MOF was studied by in situ Raman and FTIR spectroscopy. \(^{[61]}\) The compound was found to be chemically stable up to 13 GPa but exhibited an irreversible structural transition at 2 GPa.

4. In Situ EPR Techniques

4.1. EPR Spectroscopy

Electron paramagnetic resonance spectroscopy has been developed into the major investigation technique for the investigation of paramagnetic species, which do naturally occur in many
systems and play an important role in material sciences, chemistry, and biology. Transition metal ions (TMI) such as Ti^{4+}, V^{4+}, Cu^{2+}, Mn^{2+}, Fe^{3+}, and Co^{2+} and rare-earth ions (REI) such as Gd^{3+} and Eu^{3+} are major groups of paramagnetic species that form important constituents of metal-organic framework compounds. Other groups of paramagnetic species that become more and more relevant for research on MOFs are organic and inorganic free radicals as well as photoexcited triple states. As a local probe, EPR spectroscopy reveals the nature, concentration, and electronic state of a paramagnetic species as well as its coordination symmetry and can provide unique information about its coordination environment. EPR techniques can be applied to single crystals, polycrystalline and amorphous samples as well as liquid and frozen solutions. Today, EPR spectroscopy compromises continuous wave (cw) EPR and a variety of pulse EPR experiments that are described in several textbooks. EPR deals with the interaction of electromagnetic radiation with inherent magnetic moments within the sample, but in contrast to NMR with those of the unpaired electron spins. EPR employs electromagnetic radiation in the microwave (mw) frequency range. Among those, X-band experiments, corresponding to mw frequencies of about ν_{mw} = 9.5 GHz, are still most commonly used in practice. As the resulting interaction energies are in the order of ~0.04 meV, the energy entry into the sample is low and the method is non-destructive. But unlike NMR both cw and pulse experiments are common in EPR spectroscopy. In situ experiments have so far only been built using cw EPR spectroscopy.

The ground state energies of a paramagnetic species with electron spin S and l interacting nuclei with nuclear spins I_{k} in a magnetically diluted system and consequently its EPR spectrum can be described by the spin Hamiltonian

\[ H = \frac{\beta B g S}{\hbar} \cdot \vec{S} \cdot \vec{D} + \sum_{k=1}^{I} \frac{\beta g S}{\hbar} I_{k} + \sum_{i=1}^{S} \frac{\beta g S}{\hbar} \cdot \vec{A} \cdot \vec{I} + \sum_{i=1}^{S} \frac{\beta Q}{\hbar} \cdot \vec{I} \cdot \vec{I}_{i} \]

(2)

given in angular frequency units, where \( \hbar = h/2\pi \) with the Planck’s quantum of action \( h \). \( \beta_g \) and \( \beta_q \) are the Bohr and nuclear magneton, respectively. The electron Zeeman interaction in the first term with the external magnetic field \( B_0 \) and the electron g tensor comprises the spin–orbit coupling effect and contains information about the coordination symmetry, ground state, and its energy spacing to excited states of the paramagnetic center. The second term applies to spin systems with \( S > 1/2 \) and describes the zero-field splitting (ZFS) which originates from the electron–electron dipole–dipole interaction and the spin–orbit coupling. The traceless ZFS tensor \( D \) contains again important information about the coordination symmetry and in addition about bond angles and bond distances. The hyperfine (HF) interactions between the electron spins and all interacting nuclear spins described by the respective HF interaction tensors \( A_k \) are collected in the third term. The HF interaction tensor of the central nucleus of the paramagnetic center contains again information about its coordination symmetry and ground state. Otherwise, the so-called super hyperfine (SHF) interaction tensors \( A_k \) of the ligand nuclear spins interacting with the electron spin provide access to the distances between electron and nuclear spins and the spin density distribution across the coordinating ligands.

The fourth and fifth term in Equation (1) describe the nuclear Zeeman and nuclear quadrupole (NQ) interactions with the corresponding nuclear g-factors \( g_k \) and NQ interaction tensors \( Q_k \) of the various coupled nuclear spins. In general, only the first three terms in Equation (1) are relevant for cw EPR spectroscopy whereby in case of the HF interactions only HF splittings are resolved from the central nucleus and from the first coordination sphere. The nuclear Zeeman and NQ interaction together with SHF couplings are detectable by pulse EPR techniques such as electron nuclear double resonance (ENDOR) and electron spin echo envelope modulation (ESEEM) spectroscopy. It is worth to emphasize that a thorough and reliable determination of the geometrical and electronic structure of a paramagnetic centers from its spin Hamiltonian parameters measured by EPR requires a quantum chemical analysis of the interaction tensors \( g, D, A_k, Q_k \) in Equation (2) by using for instance density functional theory (DFT) calculations.

4.2. Instrumentation and Application Potential of In Situ EPR Spectroscopy in MOF Research

4.2.1. Application Potential

In situ (cw) EPR spectroscopy has been already established and coupled to optical spectroscopies (operando EPR) mainly for the investigation of the valence state of TMIs during catalytic reactions over zeolites and various metal oxide surfaces. In these experimental setups the designed in situ EPR cells work with a continuous gas flow at temperatures up to 813 K which contains the reactants and can be coupled to a gas chromatograph for product analysis.

However, in current research on MOFs the exploration of adsorption phenomena in MOF materials with flexible frameworks that feature gate pressure and breathing effects and photocatalytic activities are in the center of interest. Based on the interactions relevant for EPR spectroscopy and described by the spin Hamiltonian in Equation (1) four possible scenarios for the investigation of MOF materials at a local molecular level by in situ cw EPR spectroscopy can be envisaged (Figure 10).

Three scenarios, the adsorption of a diamagnetic adsorbate molecule on the coordinatively unsaturated (CUS) binding site of a paramagnetic framework TMI or REI (scenario I), the dynamics of a paramagnetic adsorbate molecule and its binding at a CUS of a diamagnetic framework TMI or REI (scenario II), and the modification of the coordination geometry of paramagnetic TMI or REI during an adsorption controlled gate pressure or breathing framework transformation (scenario III), will lead to distinct changes in the EPR interaction tensors \( g, A_k \), and \( D \) or EPR linewidth parameters. Changes of these spin Hamiltonian parameters in turn lead to characteristic modifications of the EPR spectra, which can be followed in an in situ experiment. In that way the adsorption at specific framework sites and structural changes of the MOF framework at the metal ions can be directly addressed on a molecular level by in situ EPR experiments as a local probe technique. Scenario IV requires light illumination of the sample during the EPR experiment to generate a photoelectron that can reduce a framework TM.
or REI.[74] As a result, a paramagnetic valence state is either produced or quenched due to the light exposure of the MOF sample, which can be easily tracked by EPR signal intensity measurements. Alternatively, free radical species generated by light illumination of MOF materials[73a] could be likewise investigated by in situ EPR spectroscopy. It is worth noting that the photoexcitation of triple states in MOF materials appears to be a further attractive and promising research field, which has so far only been exploited sparsely.[64]

4.2.2. Instrumentation

So far the vast majority of in situ EPR cells for investigations of catalytic reactions over metal oxide surfaces in a continuous gas flow[68c,75] and of adsorption processes in MOFs under a static pressure[72a,c,d] were constructed for X-band frequencies with one notable exemption working at Q-band frequencies (34 GHz).[76] Today state of the art X-band EPR spectrometers provide a realistic sensitivity limit of about $10^{13}$ spins cm$^{-3}$ even in case of TMI species in polycrystalline samples[77] which seems to be fully sufficient for most EPR applications in MOF research.

For the specific application case of gas adsorption studies of MOF materials the in situ cell should allow for measurements with controllable static gas pressures between 1 mbar and 1000 mbar at low leakage rates and variable temperatures. Here, temperatures ranging from room temperature down to $T = 10$ K are desirable to detect also TMI or REI species with short spin lattice relaxation times such as for instance Co$^{2+}$, Ti$^{3+}$ Ce$^{3+}$, and Yb$^{3+}$. The size of the X-band EPR cavities allow for easy housing of a hose to provide and maintain a static gas pressure. A typical and straightforward experimental setup for such in situ EPR experiments at X-band frequencies is illustrated in Figure 11.

It relies on a commercial cylindrical EPR cavity and He flow cryostat.[72d] Alternatively, rectangular cavities such as TE$_{102}$ and TE$_{104}$ can be used as well and the He flow cryostat can be substituted by a N$_2$ flow cryostat for measurements above room temperature. The setup in Figure 11 allows in situ EPR measurements in a temperature range $5 \leq T \leq 473$ K. The quartz glass sample tube fixed to the cryostat and cavity is attached via an aluminum-made home-built adapter to a stainless steel hose, which in turn connects directly to a 190 mL gas reservoir. The latter is filled from a gas storage volume by a high precession dosage valve at the desired gas pressure. Capacitive pressure gauges covering a pressure range from $p = 0.1$ mbar to $p = 1330$ mbar allow a precise pressure measurements independent of the type of gas. The whole gas loading station except the home-built sample tube adapter is made of DN 10 ISO-KF vacuum components to ensure low leakage rates that are here in the order of $0.05$ mbar h$^{-1}$ at $p = 10$ mbar.[72d] Such low leakage rates are essential because long equilibrium times up to 20 min are typically expected in in situ EPR adsorption studies of gate pressure and breathing MOF materials[72a] such as those of the DUT-8 family, pillared layered MOFs, and MIL-53(Al).[9b] These equilibrium times are basically determining the temporal resolution of the in situ EPR adsorption experiments.

For optical excitation of the sample, the cavities and the cryostat provide access for external light sources during the experiment. Such EPR investigations with light illumination are already established standard techniques in photosynthesis[78] and semiconductor[79] research and therefore their technical aspects are not considered further here.

4.3. Selected Applications of In Situ EPR Spectroscopy in MOF Research

4.3.1. Gas Adsorption Studies of Flexible MOFs

The mixed-metal pillared-layered MOF Zn$_{1.9}$Cu$_{0.1}$(2,5-bis(2-methoxyethoxy)-1,4-benzenedicarboxylate, dabco-1,4-diazabicyclo[2.2.2]octane (BME-bdc)$_2$(dabco) belongs to the family of
so-called soft porous crystals (SPCs) that are flexible and those frameworks exhibit reversal framework phase transitions from a closed or narrow pore (np) phase to an expanded open or large pore (lp) phase.\textsuperscript{86}\ The related swelling and shrinking behavior of the framework is known as so-called breathing behavior.\textsuperscript{86,90} In situ EPR spectroscopy of Cu\textsuperscript{2+} ions with $S = \frac{1}{2}$ is a very suitable probe to monitor the np $\leftrightarrow$ lp phase transition on local molecular level for the SPC material Zn$_{1.9}$Cu$_{0.1}$(BME-bdc)$_2$(dabco) during CO$_2$ adsorption as the coordination geometry of the paramagnetic cupric ions changes during the np $\leftrightarrow$ lp transition and the Cu\textsuperscript{2+} g and $A_{\text{Cu}}^{\text{g}}$ tensors are very sensitive with respect to these small deformations of Cu-Zn paddle wheels.\textsuperscript{72,28} Indeed the $g_{zz}$ principal value of the Cu\textsuperscript{2+} g tensor decreases from $g_{zz} = 2.632$ to 2.355 whereas the $A_{\text{Cu}}^{\text{g}}$ principal value of the tensor $A_{\text{Cu}}$ increases from 398 to 418 MHz upon the CO$_2$ adsorption induced np $\leftrightarrow$ lp transition indicating an enhanced equatorial ligand field at the cupric ion in the lp phase. Figure 12 illustrates the spectral changes observed in the in situ EPR experiments during CO$_2$ adsorption and subsequent desorption.

Obviously the Cu\textsuperscript{2+} species $A_{\text{II}}$ from the np phase transforms into a species $A_{\text{II}}$ belonging to the lp phase with increasing CO$_2$ pressure where a coexistence of both species is observed for a broad intermediate pressure range (Figure 13a,b). The back transformation from A$_{\text{II}}$ to A$_{\text{I}}$ is observed for the CO$_2$ desorption (Figure 13c,d). The weights $I_1$ and $I_2$ of the species $A_{\text{I}}$ and $A_{\text{II}}$ for the various CO$_2$ pressures were derived from spectral simulations of the in situ EPR spectra and the relative amount $n_{\text{II}}$ of the lp phase species $A_{\text{II}}$ was determined according to\textsuperscript{72a}

$$n_{\text{II}} = \frac{I_1}{I_1 + I_2}$$ \hspace{1cm} (3)

The CO$_2$ pressure dependence of $n_{\text{II}}$ is illustrated in Figure 13. The parameter $n_{\text{II}}$ can be considered as a measure for the volume fraction of the lp phase in the Zn$_{1.9}$Cu$_{0.1}$(BME-bdc)$_2$(dabco) sample. A comparable pressure dependence with substantial hysteresis effects was deduced from a powder X-ray diffraction study.\textsuperscript{86} Therefore, the Cu\textsuperscript{2+} in situ EPR spectra nicely monitors the reversible np $\leftrightarrow$ lp phase transition of this MOF upon CO$_2$ adsorption and desorption on a local molecular scale.

MIL-53(Al) is another flexible MOF that exhibit breathing behavior with a reversible np $\leftrightarrow$ lp phase transition induced either by temperature variation or adsorption of various gases.\textsuperscript{69,72} Nević et al.\textsuperscript{72,b,c} applied in situ EPR spectroscopy to explore the adsorption of air, N$_2$, and O$_2$ over vanadium doped MIL-53(Al). Here, V$^{4+}$ ions incorporate as paramagnetic VO$^{4+}$ species with $S = \frac{3}{2}$ at Al$^{3+}$ framework sites and can serve as local paramagnetic probes to monitor the reversible np $\leftrightarrow$ lp phase transition.\textsuperscript{81} Figure 14 illustrates the effects of increasing O$_2$ gas adsorption pressure on the room temperature V$^{4+}$ in situ X-band EPR spectra for the lp phase and the dehydrated narrow pore (np-d) phase of MIL-53(Al).\textsuperscript{72b} Only the spectra of the lp phase are affected by the O$_2$ adsorption where a constant increase in line width and decrease in signal amplitude with rising oxygen pressure is observed due to an exchange interaction between the VO$^{4+}$ units and the paramagnetic O$_2$ molecules. Therefore, oxygen can only enter the pores in the lp phase of MIL-53(Al) whereas its pores of the np-d phase are closed for O$_2$ up to pressures of 1 bar. The lp $\leftrightarrow$ np phase transition of MIL-53(Al) during adsorption of CO$_2$\textsuperscript{69a,82} at pressures below 1 bar could be directly observed by in situ EPR spectroscopy for Cr$^{3+}$ doped sample with the apparatus depicted in Figure 11. Here paramagnetic high spin Cr$^{3+}$ ions with $S = 3/2$ substitute likewise Al$^{3+}$ framework ions and form sensitive probes to monitor the structure of the metal-oxygen octahedrons of the MIL-53(Al) framework via the chromium ZFS interaction. In case of MIL-53(Al) the lp $\leftrightarrow$ np phase transition triggered by the adsorption of CO$_2$ is accompanied by a lowering of the symmetry of the Cr$^{3+}$ ZFS interaction tensor D from axial to rhombic symmetry\textsuperscript{83} leading to characteristic changes in the in situ EPR spectra of the chromium ions (Figure 15a). Again, the relative amount $n_{\text{np}}$ of the Cr$^{3+}$ species in the lp phase (Figure 15b) is obtained by the weights of the Cr$^{3+}$ subspectra from the lp and np phase as determined by spectral simulations of the overall Cr$^{3+}$ in situ EPR spectra.

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The parameter \( n_{np} \) can be considered as a measure for the volume fraction of the np phase during the \( \text{CO}_2 \) adsorption and monitors the \( \text{lp} \rightarrow \text{np} \) transition of MIL-53(Al) in good agreement with theoretical predictions.\(^{[82]}\)

### 4.3.2. Photocatalysis

Emerging photocatalytic applications of MOFs for water splitting and \( \text{CO}_2 \) reduction renders EPR spectroscopy as a valuable technique to achieve a deeper understanding of redox reactions and charge transfer mechanisms involved.\(^{[6e,84]}\) In the exploration of photocatalytic reactions in MOFs most in situ EPR investigations focus so far on paramagnetic \( \text{Ti}^{3+} \) ions with \( S = \frac{1}{2} \) that are formed from diamagnetic \( \text{Ti}^{4+} \) by photo-generated electrons and subsequent charge transfer to titanium.\(^{[71,73]}\) In an exemplary

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**Figure 12.** \( \text{Cu}^{2+} \) X-band in situ EPR spectra of activated \( \text{Zn}_{1.9}\text{Cu}_{0.1}(\text{BME-bdc})_2(\text{dabco}) \) recorded at \( T = 195 \) K during a,b) \( \text{CO}_2 \) adsorption and c,d) subsequent \( \text{CO}_2 \) desorption at the listed gas pressures. Panels (a–d) show the \( g_{zz} \) and \( g_{yy} \) spectral ranges of the corresponding \( \text{Cu}^{2+} \) EPR powder patterns. Reproduced with permission.\(^{[72d]}\) Copyright 2019, American Chemical Society.

**Figure 13.** a) Relative amount \( n_{II} \) of the in situ measured EPR signal of the \( \text{Cu}^{2+} \) species \( A_{II} \) in the lp phase \( \text{Zn}_{1.9}\text{Cu}_{0.1}(\text{BME-bdc})_2(\text{dabco}) \) as estimated from spectral simulations versus \( \text{CO}_2 \) pressure at \( T = 195 \) K and b) illustration of the movement of the \( \text{Cu}^{2+} \) ion in the Cu/Zn mixed-metal paddle wheel unit of this MOF upon \( \text{CO}_2 \) adsorption. Reproduced with permission.\(^{[72d]}\) Copyright 2019, American Chemical Society.
work Horiuchi et al. investigated the light-promoted photocatalytic production of hydrogen in Ti-MIL-125-NH$_2$ MOF with 2-amino-1,4-benzenedicarboxylate (BDC-NH$_2$) linkers.\[71\] In situ EPR experiments of an evacuated Ti-MIL-125-NH$_2$/triethanolamine solution revealed the formation of the typical EPR signals of Ti$^{3+}$ ions (Figure 16) with $g$ tensor principal values $g_{xx} = 1.980$, $g_{yy} = 1.953$, and $g_{zz} = 1.889$ under visible light illumination at wavelengths $\lambda > 420$ nm at $T = 77$ K whereas no Ti$^{3+}$ was observed in the dark. Subsequent exposure to air leads to reoxidation of Ti$^{3+}$ to Ti$^{4+}$ and the disappearance of the Ti$^{3+}$ EPR signal. In case of the Ti-MIL-125 MOF without amino-functionalized linkers no signal of Ti$^{3+}$ ions could be generated by visible light illumination at any wavelength. Thus, the in situ EPR experiments confirmed convincingly a model of the reaction mechanism where the BDC-NH$_2$ linkers adsorb visible light and their excited states transfer electrons to the conduction band of the photocatalytically active titanium-oxo clusters resulting in the observed paramagnetic Ti$^{3+}$ species.\[71\]

5. In Situ X-Ray and Neutron Diffraction Techniques

Since the majority of MOFs are crystalline solids, application of X-ray and neutron diffraction techniques at controlled conditions namely gas atmospheres at defined pressures and temperatures, hydrostatic pressures, allows to study processes of crystallization, pore filling, switching and mechanical stability. Therefore, development of advanced in situ diffraction techniques is crucial for understanding of the key properties of MOFs at conditions, which are as close as possible to potential applications and real working conditions. The history of development of in situ diffraction techniques starts several years after discovery of X-ray diffraction experiment of iron at 1000 °C.\[85\] Since that time, in situ diffraction techniques developed remarkably, which is reflected in numerous books and reviews.\[86\] Most of them were developed at large scale facilities, providing much higher beam intensity and flexibility. Many instruments are even dedicated to one or several in situ techniques.

Discovery of MOFs 20 years ago stimulated the development of new or adapting of existing techniques for this material class. Since temperature-dependent PXRD became a widespread and available characterization technique\[86g\] for analyzing phase transitions and thermal stability of MOFs, we do not further discuss this established technique here. Developments of in situ crystallization and combined adsorption/diffraction techniques are also reviewed and can be accessed elsewhere.\[87\]

Recent achievements on the characterization of guest-loaded mostly rigid MOF materials via synchrotron PXRD, single

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**Figure 14.** Room temperature X-band in situ EPR experiments of O$_2$ adsorption over V-doped activated MIL-53(Al). a) V$^{4+}$ EPR spectra of MIL-53(Al) in its lp phase as a function of O$_2$ pressure. EPR linewidths as deduced from spectral simulations and c) signal amplitudes in dependence on O$_2$ pressure. d) V$^{4+}$ EPR spectra of MIL-53(Al) in its dehydrated np-d phase as function of O$_2$ pressure. The insets in (a) and (d) display the full V$^{4+}$ EPR spectra. Reproduced with permission.\[72b\] Copyright 2017, Royal Society of Chemistry.

**Figure 15.** Room temperature X-band in situ EPR experiments of CO$_2$ adsorption over Cr$^{3+}$-doped activated MIL-53(Al). a) Cr$^{3+}$ EPR spectra during CO$_2$ adsorption. b) Relative amount $n_{np}$ of the in situ measured EPR signal of the Cr$^{3+}$ species in the np phase.
crystal diffraction, NPD, inelastic neutron scattering, quasielastic neutron scattering, small angle X-ray scattering, IR, and NMR techniques were reviewed by Easun et al.\textsuperscript{[38]} Instead in the following we discuss advanced techniques for monitoring stimuli induced switchability in dynamic frameworks and the specific demands in controlling stimulus related thermodynamic parameters and the acquisition of high quality data.

5.1. In Situ X-ray Diffraction

5.1.1. In Situ PXRD/Gas Sorption

In many cases, the only way to follow the phase transition is to conduct the PXRD experiment in the conditions, identical to those observed in ex situ experiment. In other words, one should conduct the corresponding experiment in the X-ray beam and measure PXRD patterns at conditions of interest. This is a challenging task and in most of the cases needs special measurement cells, which on the one hand completely reflect the conditions, used in ex situ experiments and on the other hand are transparent for X-rays and allow to conduct PXRD measurements. Since temperature and adsorption of guest molecules were observed to trigger the structural transitions in MOFs and in situ cells for thermo-PXRD are broadly available even for laboratory instruments, the development of in situ cells for parallelized gas adsorption and powder X-ray diffraction became the highest priority in the community. The first prototypes of such in situ cells were developed at synchrotrons, since typically monochromatic radiation with high flux and brilliance is needed for collection of high-resolution PXRD data.

Technically such setups are usually based on a glass capillary, filled with MOF powder and connected to a gas handling system. The temperature is ensured by nitrogen cryostream. The sample in the capillary can be easily degassed and the required gas pressure can be introduced at the target temperature, simulating the points in adsorption isotherm.

Most of diffraction beamlines have nowadays such kind of gas cells in different modifications for in operando characterization of catalysts. Typically such kind of cells can be pressurized up to 100 bar and work perfectly at temperatures close to ambient. Small dimensions of the setup allows to collect high-resolution PXRD data, which often allows ab initio solution of crystal structures. However, at temperatures of 250 K and lower, ice formation on the outer capillary surface can occur at longer experimental exposure times. Temperatures lower than 100 K are also not accessible for this setup. Swiss–Norwegian beamline\textsuperscript{[89]} and BM25-SpLine\textsuperscript{[90]} (ESRF), 111\textsuperscript{[91]} (Diamond), BL02B2 and RIKEN\textsuperscript{[92]} (Spring8), powder diffraction beamline\textsuperscript{[93]} (ANSTO), and 17-BM-B\textsuperscript{[94]} (APS) at synchrotrons provide beamline\textsuperscript{[89]} and BM25-SpLine \textsuperscript{[90]} (ESRF), I11 \textsuperscript{[91]} (Diamond), BL02B2 and RIKEN \textsuperscript{[92]} (Spring8), powder diffraction beamline \textsuperscript{[93]} (ANSTO), and 17-BM-B \textsuperscript{[94]} (APS) at synchrotrons provide such in situ gas cells for their users. Adsorption induced phase transitions in MIL-53 series, ELM-11, coordination polymer (CPL)-1, and Co(bdp) were studied using capillary-based gas cells.

Extensive tests of a comparable type of capillary cell at KMC-2 beamline of BESSY-II synchrotron in Berlin revealed extended spatial temperature variation and huge gradients in such kind of cells.\textsuperscript{[87b]} Therefore, only a small region in the capillary reflects the targeted point on the isotherm consequently leading to erroneous results if the X-ray beam is focused not in the centrum of the nitrogen stream. The problem with ice formation was solved only after several iterations by using advanced isolation of the capillary space. However, the tiny amount of the sample in capillary generally does not allow to measure adsorption isotherms in situ using volumetric techniques.

An alternative setup, which allows to overcome the shortcuts with sample amount and temperature stability is based on an adsorption chamber, mounted on a closed cycle cryostat and covered with a beryllium dome.\textsuperscript{[95]} The adsorption chamber allows to allocate a reasonable amount of the sample, sufficient for volumetric registration of the adsorption. Therefore, the chamber is connected to a manometric adsorption instrument. The cell shows excellent thermal stability and well reproduces adsorption isotherms, measured via commercial volumetric equipment. Closed cycle helium cryostat reach temperatures ranging from 20 to 450 K, which is sufficient for both degassing of the sample as well as in situ adsorption measurements at low temperature. High-quality PXRD patterns could be measured at the selected points of the isotherm in transmission geometry using 2D area detectors, which improves the intensity statistics and compensates the static positioning of the sample in the beam. The only drawbacks of the setup, compared to capillary, are lower resolution and limited pressure range of 0–1 bar (Figure 17). However, the instrumentation allows measuring high quality PXRD patterns further used for characterization of flexible MOFs and subsequent structural analysis via Rietveld refinement.

As a further development Bon et al. designed a cell for in situ PXRD during vapor and mixture gas adsorption (Figure 17). The main challenge in this case was to avoid the condensation of overcooled fluids in the gas supply lines. A sophisticated combination of the thermal management of the cell and heatable gas lines allowed to nicely reproduce ex situ measured isotherms. Current developments aim to introduce a combination of chemical and electromagnetic stimuli simultaneously and...
monitor photocatalytic processes or photon-induced switchability by PXRD.

High intensity and brilliance of the synchrotron beam is in most cases essential for collecting high-resolution PXRD data for ab initio structure solution and refinement of unknown intermediate phases. However, often an access to synchrotron facilities is limited. This stimulated the development of laboratory in situ PXRD equipment for controlled gas atmospheres. Krautscheid and co-workers equipped a STOE STADI P diffractometer with a capillary-based cell, connected to the gas handling system and used it for study of the structural flexibility in the Cu-based MOF during adsorption of $n$-butane and $iso$-butane at 298 K. This fruitful cooperation between Rigaku and MicrotracBEL companies resulted in the development of the first commercial gas cell for in situ PXRD during gas adsorption, allowing in house experiments in a wide range of temperatures using all noncorrosive gases as external stimuli.

Kitagawa and co-workers reported the first experiment on parallelized gas adsorption and PXRD in 2002. They studied the adsorption of oxygen on CPL-1 framework with a composition $Cu_2(pzdc)_2(pz)$$_n$ ($pzdc$: pyrazine-2,3-dicarboxylate; $pz$: pyrazine) at the constant pressure of 80 kPa in the temperature range 90–300 K and even found the position of oxygen molecules in the channels by Rietveld analysis. Later, Bon et al. applied a combination of in situ PXRD and X-ray absorption techniques in order to shed light on the “gate opening” in $Ni_2(2,6$-naphthalenedicarboxylate ((ndc))$_2$ 1,4-diazabicyclo(2,2,2)octane (dabco), also known as DUT-8(Ni). The crystal structure of the “closed pore” (cp) was solved and refined using combination of single crystal and powder diffraction techniques and in situ measured EXAFS spectra proved the strong deformation of the Ni-paddle wheel, also explained by the color change upon transition. Adopting up to 250% of the volume change between open and closed states, DUT-8(Ni) is a record holder in terms of breathing amplitude among all switchable MOFs, in which switching induced by gas molecules. Furthermore, in situ PXRD played a key role in the discovery of a new counterintuitive phenomenon of “Negative Gas Adsorption” (NGA), observed for the first time during the adsorption of methane on DUT-49 at 111 K (Figure 18).

The technique was also effectively used in studies of crystal size dependencies in DUT-49 as well as for characterization of NGA transitions in newly discovered frameworks. In summary, in situ PXRD measured during adsorption of gases is nowadays a key enabling technique for the characterization of stimuli responsive frameworks. This technique has newly become available at several beamlines at high technical level and starts to become accessible as a laboratory tool. The latter is a prerequisite for analyzing and tailoring the targeted conditions for dynamic porous materials and essential for analyzing the breathing and gating mechanisms in new generations of flexible framework materials.

Figure 17. Instrumentation for in situ PXRD/adsorption: a) in situ cell for low-pressure gas adsorption, b) in situ cell for high-pressure gas adsorption, and c) in situ cell for vapor adsorption.
5.1.2. In Situ Single Crystal Diffraction at Controlled Conditions

Although combination of PXRD and adsorption allows to follow the structural transition in bulk and generally requires a powder sample, which is often straightforward in preparation and handling, the solution of the crystal structures from PXRD data is still challenging and even not always possible due to low symmetry of the contracted and intermediate phases or insufficient quality of the data. In such cases, in situ diffraction experiments on single crystals under controlled pressure/temperature conditions shows clear advantages compared with PXRD. From the technical point of view, in situ single crystal diffraction (SCD) experiments do not require complicated setups and as a rule performed in the glass or quartz capillary. The capillary is either fire-sealed in a constant gas atmosphere or mounted on the simple gas dosing system. Since SCD experiments require free rotation of the sample and also take longer time in comparison with PXRD, gas dosing during the experiment is not essential. However, reports on in situ SCD experiments on flexible MOFs are rather rare because of the following challenges: i) not all switchable MOFs are available as single crystals, suitable for SCD; ii) due to the extended strain during the switching, most of the single crystals deteriorate into smaller separated domains after switching and is not suitable for further SCD experiments; iii) the preparation of the single crystals under controlled gas atmospheres is not straightforward. Despite these limitations, several reports on in situ SCD can be found in the literature.

The first report on in situ SCD studies of solvent desorption from a 2D flexible framework with a composition $M(bpy)_{1.5}(NO_3)_2 \cdot \text{guest}$ ($M$: Co, Ni, Zn; bpy: 4,4′-bipyridine) was published by Halder and Kepert in 2005. The framework is an assembly of chiral bilayers of opposite handedness and is resistant to guest molecules removal at 100 °C. Authors monitored desorption of ethanol, methanol, acetonitrile, dichloromethane and tetrahydrofuran by in situ SCD and concluded that there is no evidence for partial ordering of guests in the channels in the partially adsorbed phases. Flexibility, observed during the solvent removal reflected the energies of guest sorption apparently being comparable to those of the various framework distortions observed. However, solvent molecules could be modeled for full-loaded crystals with further analysis of weak specific interactions. Several years later, Miller et al. studied the single crystals of rigid scandium terephthalate framework $Sc_2(O_2CC_6H_4CO_2)_3$ depending on the loading of CO$_2$ (235 K), H$_2$ (80 K), CH$_4$ (230 K), and C$_2$H$_6$ (230 K). Authors observed the symmetry change from $Fddd$ to $C_2/c$ in the case of CO$_2$ and H$_2$ adsorption, while only for CO$_2$ the guest molecules were refined unambiguously. Hydrocarbons were located in the pores with low occupancies and high displacement parameters. For the first time, Kitagawa and co-workers observed the switching of the flexible structure of triple interpenetrated pillared layer MOF with composition $[Zn_2L_2P]_n$ ($L = 1,4$-bis(4-pyridyl)benzene; $P = 2,3$-difluoro-1,4-bis(4-pyridyl)benzene). Desorption of guest molecules from the frameworks, followed by SCD, shows the strong deformation of the Zn-paddle wheel in the first step, involving degassing of the sample at room
temperature, followed by partial decomposition of the paddle wheel and change of the coordination geometry of Zn$^{2+}$ at higher temperature. A great progress in the development of in situ SCD was achieved by Barbour and co-workers, who published a series of excellent studies on in situ SCD during the gas loading using the high-pressure capillary-based cell, adapted for SCD studies.\textsuperscript{[107]} Initially, the model system of interpenetrated pillared-layer MOF Zn$_2$(bdc)$_2$(bpy) was studied under various CO$_2$ pressures and the position of the CO$_2$ in the channels could be determined in the structure refinement.\textsuperscript{[107]} In the following study, authors combined in situ SCD and in situ PXRD during adsorption of CO$_2$ for a study of switching mechanism and preferable adsorption sites in Cd-MOF with fourfold interpenetration and diamondoid (dia) topology.\textsuperscript{[108]} SCD experiments on the degassed single crystal and crystals in a pressurized cell with 15, 20, and 40 bar of CO$_2$ elucidated preferable binding sites of gas molecules and followed the transition of the host framework (Figure 19).

Similar studies were performed on the first porous halogen-bonded framework.\textsuperscript{[109]} Interestingly, in the case of [Zn(tp)(1,2,3-tz)$_x$DMF]$_n$ (tp = terephthalate, 1,2,3-tz = 1,2,3-triazolate), subjected to SCD studies under CO$_2$ high-pressure loadings, authors clearly show the limitation of the technique in some particular cases.\textsuperscript{[110]} Thus, degassed and loaded with 2 bar CO$_2$ crystals remain as intact single crystals, while further increasing of CO$_2$ pressure to 20 and 50 bar leads to loss of integrity and disintegration of the crystal. Therefore, in situ PXRD was applied for the analysis of the structures at higher CO$_2$ loadings. In the following report, authors perform in situ SCD loading experiments with ethane at 6.4, 12, and 20 bar loaded in [Zn(tp)(1,2,3-tz)·xDMF]$_n$.\textsuperscript{[111]} Successful data collection could be done at two pressure points and the structure at 20 bar was derived from in situ PXRD. The authors could not determine exact positions of the ethane in the pore, which explained by weaker interactions compared to CO$_2$. In order to get a direct proof of unprecedented selectivity of the fluorinated frameworks [Ni(NbOF$_5$)(pyrazine)]$_n$ and [Ni(AlF$_5$(OH$_2$)(pyrazine)]$_n$, also known as King Abdullah University of Science & Technology (KAUST)-7 and KAUST-8, to SO$_2$, Eddaoudi and co-workers designed in situ SCD experiments.\textsuperscript{[112]} Fortunately, authors could clearly determine the position of the SO$_2$ in the microchannels of the framework and define all interactions (Figure 20).

In a recent study on specific interactions of fluids with open metal sites of Co$_2$(dobdc) (dobdc$^{4-} = 2,5$-dioxido$^{-}$1,4-benzenedicarboxylate), known as coordination polymer of Oslo (CPO)-27(Co) or MOF-74(Co) framework, Long and co-workers obtained a direct evidence of the interaction of fluids with open metal sites from in situ SCD of CO, CO$_2$, N$_2$, O$_2$, CH$_4$, Ar, and P$_4$-loaded crystals at different temperatures.\textsuperscript{[113]} As it has been

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**Figure 19.** Structural dynamic and localization of guest molecules in switchable Cd-MOF: a) Cd–Cd distances, bond angles, and dihedral angles of the miba ligand and the coordination environment of the Cd(II) atoms of a) 1a and b) 1b. c) Perspective along the c axis view of the 3D framework of 1a showing 1D channels. d) Perspective view along the c axis of the 3D structure of 1b. b) Crystal structure of 1b-40 bar(R) from PXRD refinement showing a,b) preferential binding sites for CO$_2$ uptake (sites I, II, and III), and c) 3D framework of 1b-40 bar(R) from PXRD refinement with guest CO$_2$ molecules in the channels. Reproduced with permission.\textsuperscript{[108]} Copyright 2018, American Chemical Society.
shown, SCD data, measured under controlled gas atmosphere provides irrefutable evidence on the location of gas molecules in the pores and specific host–guest interactions. The main limitations are accessibility of single crystals of switchable MOFs and technical know-how on the preparation of gas-loaded capillaries.

5.1.3. In Situ PXRD/Hydrostatic Pressure

Mechanical response of MOFs is a crucial indicator, providing information on the framework rigidity.[114] Quantitative information is deduced for elastic as well as inelastic transformations. The frameworks mechanical stability can be theoretically estimated by applying Born stability criteria and pressure versus volume equations of state in MD simulations.[10c,e,115] However, for flexible frameworks theoretical values of inelastic transition pressures are ranging from 10 to 100 MPa which are hardly accessible by experimental standard techniques normally operating at higher pressures, i.e., GPa. One of the suitable techniques, widely used for analysis of mechanical response is mercury porosimetry, initially developed for characterization of macroporous solids.[116] This technique is extremely useful for determination of the compressibility of the desolvated MOFs and allows to directly measure the pressure and reversibility of phase transitions from open pore to contracted pore phase. It should be mentioned that for flexible MOFs with cp phase as thermodynamically stable one, for example DUT-8(Ni) large crystallites, ELM-11, this technique cannot be applicable. However, these experiments provide only volume change information but do not provide detailed structural information on the framework under pressure. This can be done only if SCD or PXRD experiment could be done in parallel. With mercury as pressure-transmitting fluid such experiments are not possible because of toxicity and high absorption coefficient of mercury even for hard X-rays. Therefore, in situ PXRD or SCD experiments should be conducted in order to monitor the pathway and prove the reversibility of phase transitions. Such experiments could be conducted in diamond anvil cells (DACs), as already introduced in Section 3.2.[51] The DACs for X-ray diffraction have cone surfaces for diffracted beam and can be used for both powder and single crystal samples. Tungsten gasket

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**Figure 20.** In situ visualization of SO₂ in host frameworks. Intermolecular host–guest interactions in SO₂-loaded crystal structures of a,c) KAUST-7 and b,d) KAUST-8. Reproduced with permission.[112] Copyright 2019, Springer Nature.
is usually used between the anvils in order to reduce the low-angle scattering. In case of microporous MOFs, perfluorinated silicon oils are usually used as pressure transmitting media, since they do not penetrate the pore and stays X-ray amorphous in the target pressure range. As a rule, the pressure in the cell can be estimated from the shift of the fluorescence line of the ruby single crystal, which should be introduced in the cell together with the sample. Since high-pressure experiments in DACs are conducted between two diamond crystals, only diffraction experiments in transmission geometry are possible, which restrict experimenters on X-ray tubes with Mo or Ag anodes in the lab or hard synchrotron X-rays. High-pressure crystallography on MOFs was pioneered by Cheetham and co-workers by experimental study of single crystal of ZIF-8 framework in DAC.[117] Authors used methanol–ethanol mixture as pressure transmitting fluid and observed the phase transition to the high-pressure phase at 1.47 GPa for the first time (Figure 21). Later the mechanism of ligand flipping was also proved by in situ PXRD/gas adsorption experiments and molecular simulations.[118]

Hodday et al. extended these studies on ZIF-65 and ZIF-90, also with sod topology, but showing smaller pore apertures because of bulky functional groups, influencing degree of ligand flipping.[119] The challenging high-pressure experiments using N\textsubscript{2}, O\textsubscript{2}, Ar and CH\textsubscript{4} as hydrostatic fluids were conducted by the same authors and elucidated the adsorption induced high-pressure breathing of ZIF-8 from both experimental and simulation standpoints.[120] Exact positions of the gas molecules at high pressures could be unambiguously determined on atomistic scale and their interaction energies with framework were estimated (Figure 22).

Later, Bennett et al. conducted similar studies on ZIF-4 single crystal and powder in DAC and discovered reversible pressure-induced amorphization and glass formation of the framework, which became a start of a novel research field, namely MOF glasses.[121] Cheetham and Moggach summarized the progress on the mechanical properties and high-pressure crystallography of MOFs in two review articles.[122] Mechanical properties of MIL-53 family were studied by Yot et al. Since MIL-47, MIL-53 and M-fumarates (M–Al, Ga) structures can be synthesized only in the form of powder, in situ PXRD at high pressure was performed to analyze their mechanical properties. In the case of MIL-47, which does not show adsorption induced breathing, authors obtained a hysteresis in the mercury intrusion experiment, which indirectly pointed out on the reversible structural contraction. The latter was proven by in situ high-pressure PXRD showing reversible contraction at 340 MPa, from which the energy barrier to be overcome by the work of applied pressure and force the $lp \rightarrow np$ transition determined as 7.6 kJ mol$^{-1}$ (Figure 23). This value was substantiated by molecular simulations, predicting 10 kJ mol$^{-1}$ for the transition.[123] In contrast to MIL-47, MIL-53(Al) showed completely different behavior in both mercury porosimetry and DAC experiments, namely an irreversible phase transition to $np$ phase at 19 MPa.[124] Beyond the fundamental interest, such kind of research defines materials for potential application as shock absorbers or nanosprings. Following studies revealed the mechanical properties of UiO-66, MIL-125 and aluminum fumarate.[125]

It should be pointed out that pressure estimation technique using ruby fluorescence is originally developed for high-pressure studies of inorganic compound showing phase transition in GPa range and hits the lower limits in the case of soft porous crystals. As a possible solution, Kieslich and co-workers used an in situ cell, developed at I15 beamline of Diamond light source.[126] This cell uses a different transducing mechanism and is pressurized with water. The material is mounted in the plastic capillary and sealed in oil as pressure transmission medium. The pressure range 0–400 MPa as well as pressure steps of 3 MPa ideally fit to the target pressure range of dynamic framework materials. Experiments, conducted on UiO-66 with variable defects concentration revealed a decreasing resistance toward amorphization with increasing defect concentration in a series of the samples.[127]

In summary, high-pressure crystallography provides information on the mechanical response of porous materials which is complementary to gas adsorption in situ studies and also allows following the complete pathway of the structural evolution for bi-stable frameworks, which is sometimes not accessible for combined X-ray diffraction and gas adsorption studies.

5.2. In Situ Neutron Diffraction/Gas Sorption Studies

In contrast to X-rays, elastic interaction of neutrons with condensed matter occurs at atomic nuclei and therefore the scattering power is strongly dependent on individual nuclei properties like scattering length and cross section, and therefore randomly distributed over periodic table and even between the isotopes of the same element.[128] For example, hydrogen isotopes $^1$H and $^2$H (D) have completely different coherent scattering lengths of $-3.7406$ and $6.671$ fm and absorption cross sections of $0.3326$ and $0.000519$ barn.[129] The values for deuterium

**Figure 21.** Optical images of a single crystal of ZIF-8 a) at ambient pressure and b) at 1.47 GPa (ZIF-8-II) in a diamond-anvil cell. Void analysis, as carried out in the program MERCURY, of a) ZIF-8 at ambient pressure and b) ZIF-8-II at 1.47 GPa as viewed down the body diagonal. Reproduced with permission.[117] Copyright 2018, Wiley-VCH.
Figure 22. Experimentally derived unit cell of ZIF-8-HP with N₂ and O₂ adsorption sites: a) adsorbed N₂ molecules at 3.25 GPa; b) adsorbed O₂ molecules at 1.20 GPa (in (a) and (b) guest shown as ellipsoids (50% probability) and each color represents symmetry-independent adsorption sites); c) 6MR window with sites O₂-1 and O₂-6; d) 4MR window with sites O₂-3 and O₂-4; e) 6MR window with O₂-2 and O₂-5 showing O₂(1)-O₂(2)-C₃ angle of 130°; f) 6MR window with N₂-2 and N₂-5, showing N₂(1)-N₂(2)-C₃ angle of 150°. Reproduced with permission. [120] Copyright 2018, Springer Nature.

Figure 23. High-pressure study on MIL-47: a) cumulative volume of intruded mercury in a two-cycle intrusion–extrusion as a function of the applied pressure obtained for the MIL-47⁴⁺ sample; b) X-ray diffraction patterns of the MIL-47⁴⁺ as a function of the applied pressure. Compression a) 0.1 MPa, b) 51.1 MPa, c) 90.1 MPa, d) 147.1 MPa, e) 178.1 MPa, f) 340.1 MPa and decompression g) 3.1 MPa. Reproduced with permission. [123] Copyright 2012, Royal Society of Chemistry.
are close to that for carbon, nitrogen and even some metals, the contribution to elastic neutron scattering is significant and can be used for determination of deuterium containing fluids in the pores in case these are ordered. In contrast, hydrogen \(^1\text{H}\) is mostly contributing to inelastic scattering events and therefore not desired in the neutron diffraction studies neither in the material investigated nor in the interacting fluid.  

Experiments on high-resolution powder neutron diffraction are usually performed on a dedicated instrument, installed at neutron reactors or spallation sources. In terms of instrumentation, generally aluminum or vanadium cans varying in diameter can be used. Since neutron beams cannot be focused and the fluxes are much lower in comparison to synchrotron X-rays, usually larger sample amounts and longer measurement times are required for NPD pattern acquisition with reasonable statistics.

Since MOFs were initially considered for gas storage applications, most experiments on in situ neutron diffraction were performed with in situ loading of deuterated versions of fuel-relevant gases, namely hydrogen and methane in order to study the preferable adsorption sites and help to develop MOFs with enhanced storage performance.

The pioneering work on the in situ NPD study of deuterium adsorption in Hong Kong University of Technology (HKUST)-1 was published by Kepert and co-workers in 2006. Authors measured NPD patterns of degassed framework and four different \(D_2\) loadings with 0.5, 1.0, 1.5, and 2.0 \(D_2\) molecules per paddle wheel and were able to locate the preferable adsorption sites from the difference Fourier map (Figure 24).

In case of methane, Kaskel and co-workers explored the methane storage mechanism in HKUST-1 using in situ NPD. Using the same algorithm, authors could determine the preferable adsorption sites from NPDs, measured in situ from three different loadings of 8, 104, and 176 \(CD_4\) molecules per unit cell. Further works on in situ NPD during adsorption of \(D_2\) and \(CD_4\) published until 2016, are summarized in a recent book chapter.

At later stage, further in situ NPD/\(D_2\) and \(CD_4\) adsorption were reported by the group of Long confirming the high volumetric adsorption capacity of \(CD_4\) in HKUST-1 and later revealing the hydrogen storage properties in isoreticular MOF-74 frameworks.

Bloch and co-workers performed an extended study on methane storage in porous coordination cages. It should be admitted that the guest molecules that can be used for in situ NPD experiments are not limited to \(D_2\) and \(CD_4\). Thus, Chen and co-workers used in situ NPD in order to explain an exceptional adsorption selectivity of the “gate pressure” MOF ELM-12 to \(C_2H_2\) over \(C_2H_4\). Two preferable sites were derived from the Rietveld refinement: i) two \(C_2D_2\) molecules are restricted in the pore center, and each \(C_2D_2\) is bound by two \(CF_3SO_3^-\) anions from different nets through cooperative C–D/O H-bonding (2.43 and 2.44 Å (Figure 25b)); ii) the \(C_2D_2\) molecule shows slightly weaker binding affinity as implied by its lower occupancy, with a C–D/F H-bonding from 2.29 to 3.31 Å (Figure 25c). Experiment proved that exceptional selectivity to \(C_2H_2\) in ELM-12 is attributed to its optimal pore sizes and polar functional moieties for binding \(C_2H_2\).

A similar in situ NPD study with \(C_2D_2\) was conducted by Schröder and co-workers on the nitro-functionalized MFM-102-NO\(_2\) framework showing increased acetylene capacity. Crystallographic studies proved a counterintuitive binding between electron-rich \(C_2H_2\) molecules and electron withdrawing –NO\(_2\) groups in the MOF, MFM-102-NO\(_2\). Using the same experimental protocol, oxygen binding to unsaturated metal centers of CPO-27 series was explored by Dietzel and co-workers. Raising levels of atmospheric \(CO_2\) motivated Long and co-workers to search for the optimal materials for \(CO_2\) capture. In situ NPD on a series of sodalite type frameworks with composition \([\text{M}_4\text{Cl}]_3(\text{BTT})_8\)\(^{3-}\) (\(\text{M} = \text{Cr}, \text{Mn}, \text{Fe}, \text{Co}, \text{Ni}, \text{Cu}, \text{and Cd}; \text{BTT}\) = 1,3,5-benzenetristetrazolate), loaded with \(CO_2\), provided an information of the adsorption sites, well reflecting molecular simulation data, which additionally supported experimental results. A series of in situ NPD experiments was conducted on a mesoporous MOF, DUT-49 and their isoreticular networks, showing a novel counterintuitive phenomenon named “negative gas adsorption” (NGA). In situ NPD in this case gives important information on the pore filling mechanism in these frameworks with trimodal pore size distribution and its impact on NGA.

**Figure 24.** In situ NPD on HKUST-1 upon \(D_2\) loading: a) NPD data for \(\text{Cu}_3(\text{BTC})_2\) with adsorbed \(D_2\); b) \(D_2\) in \(\text{Cu}_3(\text{BTC})_2\) shown along the [001], left, and [111], right, directions; c) \(D_2\) sites in \(\text{Cu}_3(\text{BTC})_2\): axial Cu site (left); view along [111] in the 5 Å small pore with 3.5 Å side windows (middle); and view along [100] showing the 9 Å pore. Reproduced with permission. Copyright 2006, American Chemical Society.
mesoporous nature and high methane capacity of these solids, the validity of Rietveld refinement of in situ NPD data were supported by ab initio Monte Carlo simulations of adsorption isotherms. An excellent agreement of the pore filling diagrams confirm the experimentally derived pore filling mechanism in these isoreticular frameworks (Figure 26).[10b] Certainly this

![Image](image_url)

**Figure 25.** a,c) Rietveld refinement of the NPD ELM-12 ⊃ 2.5C₂D₂ at 298 K (Cu, green; C, gray; O, red; S, yellow; F, light blue). b,d) The two preferential binding sites for C₂D₂ adsorption (sites I and II) in ELM-12. Reproduced with permission.[135] Copyright 2017, Royal Society of Chemistry.

![Image](image_url)

**Figure 26.** Methane distribution in DUT-49. a) Simulated (red circles) and experimental (open symbols) methane adsorption isotherm of DUT-49 at 111 K including points at which NPD patterns were recorded (blue diamonds). b) Structure of DUT-49 with increasing population of pores with methane upon pressure increase, including on the left trimodal pore system: octahedral (oct, orange), tetrahedral (tet, blue), cuboctahedral (cub, green). Experimentally refined methane positions in light pink, simulated methane density in pink. c) Visualization of DUT-49 unit cell at selected loadings which correspond to experimentally investigated pressure. d) Illustration of methane-filled pores of DUT-49 unit cell in the region of NGA viewed along (100) direction (top), (110) direction (middle), and (111) direction (bottom). Reproduced with permission.[10b] Copyright 2019, Springer Nature.
localized picture should not be overinterpreted as the molecules rapidly exchange between various pores and adsorption sites even at 111 K. This rapid exchange of gas atoms or molecules also leads to a single signal in $^{129}$Xe NMR spectra of Xe loaded DUT-49op (Figure 6).

In summary neutron diffraction, measured under in situ conditions gives detailed structural insights and is mostly suited to identify preferable adsorption sites and clarification of the adsorption mechanism in MOFs. The main limitations are accessibility of neutron facilities, corresponding in situ instrumentation as well as deuterated fluids for experiments.

6. In Situ Transmission Electron Microscopy on MOFs

Transmission electron microscopy (TEM) is an advanced technique for characterization of materials using high energy focused electron beam in a nanometer regime. Max Knoll and Ernst Ruska developed the technique in 1931 and the first commercial microscope was produced in 1939. Since that time, the technique is constantly developing further in the sense of improvement of electron sources, optics, detectors and sample environments. In 1986, Ernst Ruska was awarded a Nobel...
prize in Physics for his invention. At the present, numerous textbooks and monographs are available on the physical principles and fundamentals of TEM,[139] but also more sophisticated STEM[140] and diffraction techniques.[141] Several monographs are also devoted to in situ environmental cells, allowing to image materials at variable conditions.[142] For a long period, the main objects for TEM investigations were only purely inorganic materials, which could survive under high-intensive electron beam, as the latter destroys organic, metal-organic and biological samples within a second. Therefore, the technique was preferentially used for observation growing of nanoparticles,[143] catalytic reactions,[144] surface processes,[145] and liquid chemical reactions.[146] Special stages are designed for imaging of micro- and nano-electronic devices.[147]

The first application of TEM on MOFs was devoted to imaging of the metal nanoparticles in the MOF pores, usually synthesized for catalytic applications. Fischer and co-workers published pioneering papers on the imaging of Ru and Pd nanoparticles in MOF-5 pores (Figure 27).[148]

Implementation of Ru and Pd nanoparticles with size ranging from 1 to 5 nm could be unambiguously proven by TEM imaging and diffraction patterns.

Studies incorporating nanoparticles in MOFs with larger pores subsequently followed. Senker and co-workers successfully synthesized the composite Pt@MOF-177 for room temperature hydrogen storage and oxidative catalysis.[149] It should be admitted that all the above-mentioned examples proved only the size of nanoparticles, their dispersion and crystallinity. However, since the MOF host contains organic building blocks, which are extremely sensitive to the electron beam, the integrity of the framework could not be proven in any of these articles. In order to image MOF-5 nanocrystals Wiktor et al. decreased the acceleration voltage from 200 to 80 kV and used liquid nitrogen to cool down the sample stage. These conditions allow to achieve high-resolution images of MOF-5 on atomic scale and also obtain Bragg diffraction, which unambiguously confirms the integrity of the MOF under TEM conditions for the first time (Figure 28).[150]

Figure 29. Left: A) Crystal structure of MOF-74. DOT link is joined by a metal oxide SBU to make the 3D MOF-74 structure with 1D hexagonal channels. B) Chemical structure of organic links used in the synthesis of a series of nine IRMOFs; Right: I) HRSEM image of a crystal of IRMOF-74-VII. J,K) HRTEM images of IRMOF-74-VII and -IX, respectively. Insets: The corresponding FFT diffraction patterns of the dashed square area in the original images. Reproduced with permission.[151] Copyright 2012, American Association for the Advancement of Science.
Later, Yaghi and co-workers published groundbreaking papers on TEM imaging of MOF-74 family materials\textsuperscript{[151]} in the case of MOF-74 type materials, hexagonal channels were clearly imaged and corresponding diffraction patterns were obtained. The crystal structure of this material, containing overgrown 200 nm large crystallites was derived from 3D electron diffraction tomography and also high-resolution TEM images were obtained (Figure 29).

Covalent organic frameworks (COFs) are crystalline organic polymers that usually can be obtained as nanocrystalline powders. Therefore, ab initio structure solution using powder X-ray diffraction data is in most cases impossible without proper structural model. Since COFs are pure organic materials, their stability in the electron beam is even lower than in MOFs. However, Terasaki and co-workers successfully obtained high resolution transmission electron microscopy (HRTEM) images and diffraction patterns of COF-505\textsuperscript{[152]} by using the low-dose technique with beam density less than 500 electrons (nm\(^2\) s\(^{-1}\)) (Figure 30). In these breakthrough studies, low-dose TEM technique opened an access to HRTEM imaging and even structure solution of extremely sensitive MOFs and COFs.

In the review article on TEM on electron-beam sensitive crystalline materials, Han analyzed factors, influencing material damage in the electron beam and techniques, developed to avoid the material damage, namely low-energy electron beam and cryo-TEM.\textsuperscript{[153]} The role of direct-detection electron-counting (DDEC) cameras was highlighted because of their high detector quantum efficiency and enable HRTEM at ultralow electron doses that significantly reduces the beam damage in the beam-sensitive materials. Moreover, in this paper, Han and co-authors reported a routine procedure for MOF imaging with HRTEM, which is a breakthrough in the field. Authors empirically determined a maximal cumulative electron dose for MOFs as 10 to 20 e\(^{-}\) Å\(^{-2}\) and propose to acquire the images with electron doses of 2–4 e\(^{-}\) per pixel and with that keep the maximum electron dose within 10 e\(^{-}\) Å\(^{-2}\). Using the developed algorithm, both original and thermally treated UiO-66 could be imaged at atomic resolution (Figure 31). Image resolution even allowed to differentiate the difference in Zr···Zr distance in hydrated and dehydrated clusters.

In the following works authors could image even defects and their evolution in UiO-66 structure,\textsuperscript{[154]} but also directly “see” the single molecular magnet molecules in the MOF pores\textsuperscript{[155]} or directly look into the mesopores of MIL-101(Cr) structure.\textsuperscript{[156]}

Although a number of publications are reported on in situ liquid and solid-gas cells for TEM, these were not yet applied on the beam-sensitive nanoporous materials. Obviously, the combination of ultralow-dose technique, which is complicated on itself with environmental conditions like pressure, adsorption etc. is complicated from experimental point of view and is still not well-developed. However, it is to be expected that after developing ultralow dose methods further, development and application of in situ conditions in the TEM will deliver the next level of precise in situ analysis techniques even for dynamic phenomena probably very soon.

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Figure 30. Morphology and electron microscopy studies of COF-505. A) Crystallites aggregated on a crystalline sphere observed by SEM. B) TEM image of a single sub-millimeter crystal used for 3D-EDT. C) 2D projection of the reconstructed reciprocal lattice of COF-505 obtained at 298 K from a set of 3D-EDT data. D) HRTEM image of COF-505 taken with the [1-10] incidence. E) 2D projected potential map obtained by imposing pgg plane group symmetry on Figure 1D. F) Reconstructed 3D electrostatic potential map (threshold, 0.8). G) Indexed PXRD pattern of the activated sample of COF-505 (black) and the Pawley fitting (red) from the modeled structure. Reproduced with permission.\textsuperscript{[152]} Copyright 2016, American Association for the Advancement of Science.
7. Conclusions

In summary, advanced analytic in situ techniques give unique insights into novel dynamic phenomena in the field of switchable MOFs and open our eyes for intermediates under working conditions and their relevance for understanding switchability mechanisms. A wide range of in situ spectroscopic and diffraction techniques has been developed in recent years for the characterization of MOFs under defined conditions, inducing such structural switching during the adsorption of gas molecules, hydrostatic pressure, or temperature. While combined powder X-ray diffraction during gas adsorption or hydrostatic pressure are currently widely used for characterization of switching phenomena, mostly for analyzing the framework structural changes, single crystal and powder neutron diffraction under gas loading provide detailed insights into guest localization but are rather less frequently used either because of experimental complexity or accessibility of the suitable facilities. NMR and EPR spectra, measured upon gas sorption provide unique information on the weak interactions within the framework in both open and contracted states, physical states of the fluid and its mobility in the pore system as well as spin states of the framework metal ions and their changes upon switching. However, despite being accessible in the laboratory so far only few groups apply these techniques on MOFs, probably due to complexity of the technique, the lack of commercial measurement cells and sometimes nontrivial interpretation of the spectra.

In our view further development of advanced characterization techniques, which allow a closer “view” and analysis of the pore filling processes, phase transitions and fluid mobility will significantly advance the understanding of dynamic phenomena in frameworks in future. A fundamental understanding is a key requirement for applying dynamic materials in energy related applications such as gas storage and separation.

A crucial need for future development is the access of temporal information at various time scales. Hence, the next generation of in situ techniques will provide a new view on the time-dependent characteristics of dynamic framework materials. It is to be expected that the further development of in situ TEM methods (diffraction and imaging) will provide such information of paramount importance for the development of dynamic porous materials in near future.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords

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