Evidence for a chemical clock in oscillatory formation of UiO-66

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Chemical clocks are often used as exciting classroom experiments, where an induction time is followed by rapidly changing colours that expose oscillating concentration patterns. This type of reaction belongs to a class of nonlinear chemical kinetics also linked to chaos, wave propagation and Turing patterns. Despite its vastness in occurrence and applicability, the clock reaction is only well understood for liquid-state processes. Here we report a chemical clock reaction, in which a solidifying entity, metal–organic framework UiO-66, displays oscillations in crystal dimension and number, as shown by X-ray scattering. In rationalizing this result, we introduce a computational approach, the metal–organic molecular orbital methodology, to pinpoint interaction between the tectonic building blocks that construct the metal–organic framework material. In this way, we show that hydrochloric acid plays the role of autocatalyst, bridging separate processes of condensation and crystallization.

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A chemical clock is a particular type of chemical reaction that is frequently applied in chemistry education. The precise definition of a chemical clock is cause for some debate, but it is generally accepted that the reaction possesses an induction time after which a sudden and marked change in concentration of the reactant and product species ensues. A reaction based on hydrogen peroxide, iodide and thiosulfate is popular:

\[ \text{H}_2\text{O}_2 + 2\text{I}^- + 2\text{H}^+ \rightarrow \text{I}_2 + 2\text{H}_2\text{O} \]  
(1)

\[ 2\text{S}_2\text{O}_3^{2-} + \text{I}_2 \rightarrow \text{S}_4\text{O}_6^{3-} + 2\text{I}^- \]  
(2)

The first reaction is slow, the second one fast. As a result of the difference in reaction rates and the fact concentrations of the autocatalytic redox-pair iodide/iodine are coupled in nonlinear kinetics, the iodine concentration is seen to shoot up after an initial lag time after which it oscillates to equilibrium. Iodide is not consumed in the overall reaction and serves as autocatalyst. If starch is added, the oscillations can be followed by corresponding changes in the solution colour. This makes it a popular classroom reaction. In broad context, clock reactions correspond to changes in the solution colour. This makes it a very useful tool in chemistry education. For example, Howse et al. fabricated in this way a device capable of producing 20 mW kg\(^{-1}\) of power. These are solution-driven oscillations in the solid state. A particularly exciting development is the use of chemical actuation to fabricate a synthetic muscle. It is possible to use a clock reaction to produce oscillatory pH or temperature trajectories that drive a muscle-like mechanical response from a polymeric material. For example, Howse et al. fabricated in this way a device capable of producing 20 mW kg\(^{-1}\) of power. These are solution-driven oscillations in the solid state, but 'direct' oscillatory behaviour exists in conversion and temperature during certain polymerization reactions. Clock reactions involving phase transitions, in which for instance precipitating or crystallizing particle dimensions oscillate during the course of reaction, have never been shown to exist, despite nonlinear dynamics suspected to govern several important condensation processes, such as the hardening of cement.

In crystal engineering studies—the design and synthesis of functional crystalline structures based on a bottom-up approach from smaller building blocks—scientists have shown remarkable chemical mechanisms to prelude and govern synthesis of metal–organic framework (MOF) crystals. MOFs are porous materials consisting of metal clusters that are linked to each other by organic bridging ligands. MOFs carry, arguably more than any other type of material, the potential to fulfill crystal engineering, for the cluster and ligand connectivity, and properties, can be to certain extent controlled. This control is limited, much because of the unpredictability of coordination chemistry around the tectonic building blocks of MOFs. One example is a report by Farha et al. on the synthesis of the ultra-stable and highly popular MOF UiO-66, which is based on hexanuclear zirconium/hafnium oxoclusters, and terephthalate. The authors showed that the addition of hydrochloric acid (HCl) considerably speeds up the synthesis. This is surprising, because HCl is formed during the synthesis, which (based on naive grounds) would suggest that its neutralization, rather than addition would lead to improvement in synthesis by favourably shifting the equilibrium towards the formation of the MOF. The only scenario, in which HCl is formed in situ, while being kinetically beneficial matters the scenario of HCl being autocatalytic, fulfilling a similar role to iodide in reactions 1 and 2, and possibly sparking spectacular phenomena during the formation of UiO-66.

Using a combination of in situ synchrotron X-ray scattering and a quantum chemical methodology, we herein show that HCl is indeed autocatalytic; as a consequence, the formation of UiO-66 involves a clock reaction with a lag time followed by an oscillatory wave front in crystal dimensions.

**Results**

**X-ray scattering.** *In situ* small- and wide-angle X-ray scattering (SAXS/WAXS) is well suited to follow crystallization and condensation processes. If synchrotron radiation is used, time-resolved data of high resolution can be obtained on multiple length scales of self-assembly. The small-angle camera follows events on the colloidal (2–50 nm) length scale, permitting time-resolved analysis of the solidifying entity, while the wide-angle camera follows the evolution of Bragg peaks in case of evolution of a crystalline compound. Important, and of great use in this work, is the possibility to deconvolute condensation from crystallization by respectively analysing SAXS versus WAXS data.

The SAXS/WAXS measurements were carried out at the X9 beamline at the National Synchrotron Light Source (NSLS), Brookhaven, NY, USA. SAXS data were processed to obtain temporal information on the following integral parameters:

- Porod volume, \(V_p (\text{nm}^3)\): volume of the particle.
- Radius of gyration \(R_g (\text{nm})\): root mean square average of all distances from the particle boundary to its centre of mass.
- Number density \(N/V (\cdot)\): the number of particles per unit volume, in arbitrary units. Only the trend is followed.
- Porod surface-to-volume \(S/V (\text{nm}^{-1})\): specific surface area of the precipitating particle.
- During the experiments, WAXS was used to follow:
  - Extent of crystallization \(\alpha (\cdot)\): extent parameter obtained via Bragg peak evolution. In this case focused on the most dominant reflection of UiO-66 at \(q = 0.5 \text{ nm}^{-1}\).

Figure 1 displays the time derivative of the calculated Porod volume, \(V'_p\) (or \(dV_p/dt\)), versus time. \(V'_p\) is used as a parameter for the particle growth rate. With Zr in blue and Hf in red, the evolution is displayed for the slower syntheses; \(\frac{1}{2}\) eq. HCl at 100 °C and 1 eq. HCl at 80 °C (eq. concerns a defined equivalent of HCl specified in the Methods section). We see that after a certain induction time and rapid condensation thereafter, the particle size oscillates to final values, that is, the derivative in Fig. 1 oscillates to zero. Oscillations were, in fact, found for the trends of all integral parameters (Supplementary Figs 10–14), and fully reproducible over several numbers of experiments. There is a difference between Zr and Hf in terms of dependence of maximum growth rate on temperature and HCl concentration. For Zr, decreasing the temperature by 20 °C and doubling the amount of HCl leads to a decrease of this maximum, whereas for Hf, there is only a small change and it follows the opposite direction. In further analysing the patterns, we found the evolution of the Porod volume to mimic the response of an underdamped harmonic oscillator. All trends, with exception of the fastest syntheses at 120 °C or 2 eq. of HCl, could be well fitted to \(V(t)=\exp[-\gamma t] \cdot a \cdot \cos(\omega t - \phi)\), where \(\gamma (\text{min}^{-1})\) is the damping coefficient, \(\omega (\text{min}^{-1})\) the frequency and \(a (\cdot)\) and \(\phi (\text{min}^{-1})\) amplitude and offset constants, respectively (see Supplementary Methods and Supplementary Fig. 1 for a more detailed explanation). What follows directly from our mathematical analysis is that syntheses involving higher temperatures and/or higher concentrations of HCl have their oscillations more effectively damped, and induction times are decreased. This is expected for a chemical clock: increasing the concentration of the autocatalytic species, generally, carries the same effect as increasing the temperature: the rate of the overall reaction goes up. It is interesting to check the response of oscillation frequency \(\omega\) to changes in temperature and HCl concentration for both metals, by comparing it to the natural
frequency $\omega_0$, which is the frequency of the undamped system. In doing so, Supplementary Fig. 9, we see that Zr-based UiO-66 reacts more strongly to an increase of temperature and HCl concentration with respect to Hf, and its oscillations are more easily damped. So, there are differences between Zr and Hf. This, and certainly Hf’s sluggish behaviour with respect to Zr, is not new in coordination chemistry and has been observed before20.

Let us go back to the oscillations of all integral parameters; we remark that the final, equilibrium values for particle dimensions ($V_p$, $R_g$, $S/V$) in synthesis were found to be independent of temperature and or HCl concentration, consistent with scanning electron microscope analysis on the UiO-66 crystals by Farha and colleagues19. Notably, no oscillatory behaviour was observed for the extent of crystallization $x$ obtained from the WAXS data, which is in line with observations by Ragon et al.21 in a study on formation of UiO-66 with in situ synchrotron X-ray diffraction. Moreover, the start of bulk crystallization was in all cases seen to carry a small delay, while proceeding gradually with respect to the process of condensation. This indicates that the condensed coordination polymer is briefly amorphous before rearranging towards a crystalline structure.

It is now important to explain the induction time and ensuing oscillatory behaviour, which is something expected for clock reactions, such as the clock reaction discussed in the introduction. In that reaction, iodide served as autocatalytic species serving an overall reaction without being consumed. The only species in the synthesis of UiO-66 that could carry such a role is HCl. A starting point in explaining the influence of HCl lies in the observation that as-synthesized UiO-66 contains four $\mu_3$-OH ligands, next to four $\mu_3$-O ligands. This is striking, because the $\mu_3$-OH ligand is known to be highly Brønsted acidic. Indeed, in the case of UiO-66, it has been used to play either an active role in acid catalysis22, or be prone to exchange for other monovalent moieties in targeted functionalization of the inorganic node23. These ligands are thus expected to materialize in rather acidic local environments, which implies that HCl might be actively protonating the inorganic cluster during the synthesis of UiO-66. This by itself does not explain the clock-like phenomenon, for which HCl needs to be released by the crystallizing solid during the oscillations. But since we know that only four out of eight bridging oxygen ligands are protonated in the final framework for charge-balancing reasons, this would imply that in the short

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**Figure 1 | Particle growth rates.** Time-resolved plot of particle growth rate, as monitored by $V'_p$ (nm$^3$ min$^{-1}$) for zirconium (blue) and hafnium (red) based UiO-66, at the conditions of ½ eq. HCl and 100 °C, and 1 eq. HCl and 80 °C.

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period during which the solid is amorphous, the number of protonated oxygen ligands could exceed the number of four. Thus, the question is whether protonated inorganic clusters may be vital during UiO-66 synthesis. In fact, this would not be a major surprise, for the decoration of building blocks by small moieties to promote MOF topologies is commonplace. For instance, we have shown by quantum chemical calculations before that the addition of an amine group to terephthalate is important for the ligand's ability to coordinate to the μ₃-O-centred Al₃ tectonic unit that builds NH₃-Material Institute Lavoisier (MIL)-101(Al)15. Despite confirmation of experiment by computation, this, and analogous cases, have remained unexplained from the perspective of chemical theory, for calculations have merely focused on quantitative determination of energies instead of qualitative understanding14.

As Kohn–Sham density functional theory (DFT) is a molecular orbital (MO) method, it is insightful to picture the metal–organic bond as an MO interaction between an inorganic and an organic fragment, the nature of which we will try to unravel physically. We introduce the metal–organic MO (MOMO) analysis, which we believe will be of general use in providing chemically intuitive interpretation of DFT computation on MOF self-assembly. Herein, it is employed to investigate metal–organic interaction as function of degree of protonation of the inorganic unit.

**Density functional calculations.** All calculations were carried out with Amsterdam density functional (ADF) at the ZORA-Becke-Lee-Yang-Parr (BLYP)-D3(BJ)/TZ2P level of the generalized gradient approximation (GGA) of Kohn–Sham DFT24–26, where ZORA stands for zeroth-order regular approximation, used to take relativistic effects into account, expected to be particularly important for calculations involving hafnium27,28. More details are given in the Methods section. In this first use of the MOMO method, a fragment of 12 geometrically optimized formate ligands. We then note that in many cases the orbital interactions between the two fragments involve more than two fragment orbitals, which makes it rather challenging to construct a simple MO picture that provides a good qualitative picture of the influence of protonation on the metal–organic bond formation. However, if one only considers the interactions involving the inorganic fragments with zero and eight protons, one does not only consider the extremes that span the range of study, but also the interactions in which both interacting fragments carry O₈ symmetry. This considerably facilitates the analysis: the use of group theory indicates that solely considering the high symmetries A₁g, A₂p, A₃u, thus three MO diagrams per

![Figure 2](image-url)  
**Figure 2** | Activation strain model and degree of covalency. (a) Implementation of the activation-strain model and energy decomposition analysis (EDA), in which the [formato]₁₂ fragment reacts with 18 isoelectronic M₆O₈Hₓ (x = 0–8) fragments. ζ represents the reaction coordinate. The fragments deform towards their final state in the framework, and this metal–organic interaction is decomposed into energetic terms for electrostatic interaction, orbital interaction and Pauli repulsion. (b) Degree of covalency defined as ΔE_rel/ΔV_elstat as calculated for the 18 fragment interactions (nine for zirconium and nine for hafnium based UiO-66).
The highly protonated clusters then engage in metal–organic bond formation in step 2 and fast condensation of the solid coordination polymer ensues. The solid is not fully crystalline at this brief stage, and the situation is metastable. Reorganization however, evidenced by SAXS versus WAXS comparison, is swift: the crystalline UiO-66 lattice is formed and the oxido bridges deprotonate, leaving the scaffold charge-neutralized (step 3). This process of bulk crystallization within the solid state deserves some notion. By virtue of established laws in solid-state chemistry, such rapid transition requires a large degree of chemical inheritance between parent and resulting solid, that is, involving no substantial bond breakage and reformation. Thus, in line with works by Cheetham, we expect the solid to exist as amorphous MOF, chemically cognate to UiO-66, but with protonated oxido bridges countered by chloride ions in solution.

The drive behind the process of crystallization is in all likelihood caused by lattice enthalpy, similar to what we observed before in the crystal-to-crystal transformation of the preparation of the precursor solution and concerns the water-promoted hydrolysis of ZrCl₄ and formation of zirconyl chloride species, which are known to form multinuclear species in solution, such as [Zr₃(O₂Cl)₈]³⁺. The rearrangement of such clusters into the hexanuclear UiO-66 building block follows an unknown path, but what is certain is that the pathway to condensation must be both water and acid catalysed, since in the appearance of μ₃-O(H) bridges, O’s remain largely protonated. This is indeed observed by the groups of Serre and Farha.

The analysis of the metal–organic bonding thus indicates that while bonds are spatially similar, covalency—as we measured overlap, which remains similar if not slightly decreasing for the eight proton inorganic clusters with respect to their zero proton analogues.

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In calculation of the integral parameters, the Guinier regime for the calculation of $R_g$ was for all data sets based on the scattering vector range of $q = (0.07–0.15)$, the Porod regime was in all cases $q = (3.2…4)$. The number density is based on both the Guinier and Porod regime.

All data sets were background subtracted, azimuthally integrated and normalized for beam intensity to yield time-resolved one-dimensional data that was processed to obtain temporal information on the following integral parameters: radius of gyration $R_g$ (nm),

$$I(q) = \Delta n^2 \exp \left( -\frac{qR_g^2}{3} \right)$$

Porod volume $V_p$ (nm$^3$)

$$V_p = -2\pi^2 \cdot I(q)\frac{Q}{q^4}$$

Porod surface-to-volume $S/V$ (nm$^{-1}$)

$$S/V = \pi \times \lim_{q \to 0} I(q)q^4/Q$$

and number density $N/V$ ("")

$$N/V \propto \frac{Q^2}{I(q = 0)}$$

Where forward scattering, $I(q = 0)$ was calculated using (3) to extrapolate $q$ to 0.

Extent of crystallization $x$ was derived from the most intense Bragg peak in UiO-66, at $q = 0.5$ nm$^{-1}$. Supplementary Figures 3–8 show the in situ collected diffraction data.

**DFT calculations**. All standard calculations were performed using the ADF program27,28,37,38, using the BLYP functional. The numerical integration was performed using the procedure developed by Boerfinger, te Velde and Barends39,40. The MOs were expanded in a large uncontracted set of Slater type orbitals containing diffuse functions, which is of triple-$\zeta$ quality for all atoms and was augmented with two sets of polarization functions (TZ2P). The core shells of all atoms were treated by the frozen-core approximation41. All energies and geometries were calculated using the GGA of DFT at the BLYP level42,43. GGA proceeds from the local density approximation, where exchange is described by Slater’s $X_a$ potential and correlation is treated in the Vosko–Wilk–Nusair parametrization44, which is augmented with nonlocal corrections to exchange due to Becke45 and correlation due to Perdew46 added self-consistently47. For all calculations, relativistic effects were accounted for by ZORA48 and dispersion by Grimme’s correction, D349. The (small) contribution from dispersion, relativistic effects and exchange correlation was added self-consistently to the DFT result. The results of these calculations are available in the Supplementary Information.

The MOMO approach is based on the activation-strain model, elaborated on elsewhere32,49–51. Activation-strain model was only applied to the organic fragment, since the unprotonated inorganic fragment is not stable upon geometry optimization. To verify that formate ligands are representative in calculation, an additional (exchanges with Porod invariant $Q$

$$Q = \int_0^\infty 4 \cdot \pi \cdot I \cdot q^4 \cdot dq$$

**Methods**

**Synthesis**. An in-house developed SAXS/WAXS cell (Supplementary Figs 2 and 3), further described elsewhere16, was used for the experiments. For a typical solution, 0.75 mmol terephthalic acid (134 mg), 0.54 mmol anhydrous ZrCl$_4$/HClO$_4$ (125/172 mg), 1 ml HCl (37%) and 15 ml dried dimethylformamide (DMF) were mixed and injected in the synchrotron cell. A measure of 1 ml stands for 1 eq. of HCl in the text, added to the starting solution.

**SAXS/WAXS measurements**. Time-resolved SAXS/WAXS experiments were performed at the X9 beamline at the NSLS at Brookhaven National Laboratory (New York, USA). The undulator-based X9 beamline at the NSLS applied a marCCD SAXS detector and photonic science WAXS detector. The wavelength was in all cases 0.879 Å, and the sample-to-detector distance was 3.099 and 0.4500 m for the SAXS and WAXS camera, respectively. In the cell, the synthesis solution was loaded between two mica windows separated by polytetrafluoroethylene (PTFE) spacers (1.5 mm thickness). The depth of the solution probed by X-rays in measurement was ca. 75 mm. The beam-spot size was 20 by 20 μm. Heating was provided by four cartridge electrical resistances and temperature was controlled at the external wall of the PTFE inserts with a temperature controller.
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Author contributions
M.G.G. designed the project, led the synchrotron SAXS experiments, performed the DFT calculations, worked on the analogy to the undamped harmonic oscillator and wrote the manuscript. M.F.L. performed the fittings to the underdamped harmonic oscillator model and co-performed the SAXS experiments. J.G. co-performed the SAXS experiments. F.M.B. provided feedback on...
the MOMO method and is co-developer of the ADF software. All authors were involved in discussion of the results.

Additional information

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