Atomic-resolution transmission electron microscopy of electron beam-sensitive crystalline materials

Daliang Zhang,1* Yihan Zhu,2⊥ Lingmei Liu,2 Xiangrong Ying,2 Chia-En Hsiung,2 Rachid Sougrat,1 Kun Li,1* and Yu Han2,3*

1 King Abdullah University of Science and Technology (KAUST), Imaging and Characterization Core Lab, Thuwal 23955-6900, Saudi Arabia.
2 King Abdullah University of Science and Technology (KAUST), Advanced Membranes and Porous Materials Center, Physical Sciences and Engineering Division, Thuwal 23955-6900, Saudi Arabia.
3 King Abdullah University of Science and Technology (KAUST), KAUST Catalysis Center, Physical Sciences and Engineering Division, Thuwal 23955-6900, Saudi Arabia.
⊥ Current address: Department of Chemical Engineering, Zhejiang University of Technology, Hangzhou 310014, China PR.
*Corresponding author. Email: daliang.zhang@kaust.edu.sa; kun.li@kaust.edu.sa; yu.han@kaust.edu.sa

Abstract: High-resolution imaging of electron beam-sensitive materials is one of the most difficult applications of transmission electron microscopy (TEM). The challenges are manifold, including the acquisition of images with extremely low beam doses, the time-constrained search for crystal zone axes, the precise image alignment, and the accurate determination of the defocus value. We develop a suite of methods to fulfill these requirements and acquire atomic-resolution TEM images of several metal organic frameworks that are generally recognized as highly sensitive to electron beams. The high image resolution allows us to identify individual metal atomic columns, various types of surface termination, and benzene rings in the organic linkers. We also apply our methods to other electron beam-sensitive materials, including the organic-inorganic hybrid perovskite CH3NH3PbBr3.

One Sentence Summary: We describe a suite of methods for high-resolution transmission electron microscopy imaging of beam-sensitive materials.
Main Text: Understanding the fundamental structure-property relationships in functional materials is the essence of materials science. High-resolution TEM (HRTEM) is a powerful tool for structure characterization (1). However, there are a wide range of materials that are easily damaged by the electron beams (2-5). Metal organic frameworks (MOFs), which have designable porous structures and fascinating properties (6-8), represent a typical example of electron beam-sensitive materials. During the few attempts to image MOFs using HRTEM, only the primary channels could be resolved by the limited resolution as a result of beam damage (2, 9-11).

The mechanisms of beam damage are complex and vary with the material, primarily including knock-on damage, heating effects, and radiolysis (3, 4, 12). One means of alleviating beam damage is to reduce the energy of electron beam. HRTEM with low accelerating voltages has successfully imaged carbon nanotube and graphene (13-15). However, the use of low-energy electrons results in poor image resolution and a short penetration depth, and only prevents knock-on damage. Similarly, the use of cryo-TEM only lessens the heating damage to a certain degree (11). An alternative, in-principle more general solution to this issue is to acquire the HRTEM images with a sufficiently low electron dose to capture the structure before damage occurs. Although this idea is straightforward, it is difficult to realize because it requires an extremely sensitive camera to record acceptable images with only a few electrons per pixel. Conventional cameras cannot produce images with a sufficient signal-to-noise ratio under such low dose conditions.

Direct-detection electron-counting (DDEC) cameras have an unprecedentedly high detective quantum efficiency and enable HRTEM at ultralow electron doses (16, 17). Taking advantage of this, structural biologists have boosted the voxel resolution for protein structures using cryo-TEM (18). In the field of materials science, however, the potential of DDEC cameras in HRTEM imaging of electron beam-sensitive materials remains largely unexplored, due to some practical obstacles. First, unlike the single-particle cryo-TEM that reconstructs a protein structure from randomly oriented particles, for crystalline materials images should be acquired along specific directions, i.e., along the zone axes of the lattice. With beam-sensitive specimens, the process of finding a zone axis must be accomplished very quickly to minimize the beam irradiation. Second, the electron-counting mode is capable of producing successive short-exposure images, but the images must be precisely aligned to fully restore the high resolution information. Third, it is impossible to acquire a focus series of a beam-sensitive material, even when using a DDEC camera,
and thus the interpretation of the image is difficult unless an accurate defocus value can be determined. We reported the use of a DDEC camera to image a MOF material (ZIF-8) with an ultralow electron dose, in which the zone-axis image was obtained by sampling a large number of randomly oriented crystals (19). However, this is an inefficient trial-and-error process and success is not guaranteed. In this work, we develop a suite of methods to overcome these obstacles, advancing the HRTEM of beam-sensitive materials to a nearly routine process.

To design the quantitative HRTEM conditions for MOFs, we first evaluated their stabilities under a 300 KV-accelerated electron beam. The results reveal they began to lose their crystallinity when the cumulative electron dose reached 10-20 e⁻ Å⁻², as determined by the fading of the electron diffraction (ED) spots (fig. S1). These values set the upper limits of the cumulative electron dose for both locating a zone axis and the subsequent image acquisition. In our experiments, we used a DDEC camera to acquire images at a reasonably high magnification of 55,000 to achieve atomic resolution (pixel size: 0.57 Å × 0.57 Å) with electron doses of 2-4 e⁻ per pixel (6-12 e⁻ Å⁻²). Therefore, the maximum electron dose that can be used to find a zone axis is less than 10 e⁻ Å⁻².

The conventional, manual method for aligning a zone axis does not meet this threshold, because it requires time-consuming, iterative toggles between the diffraction and imaging modes, often causing the total electron dose to reach hundreds of electrons per Å².

We developed a simple program to achieve a direct, one-step alignment of the zone axis (figs. S2 and S3). When the electron beam incidence deviates from a zone axis by an angle φ, the zero-order Laue zone of the lattice intersects with the Ewald sphere, forming an arc in the ED that is part of the Laue circle. The radius of the Laue circle is approximately equal to sin(φ)*(1/λ), where λ is the wavelength of the beam. Our program first identifies a Laue circle by analyzing the distribution of reflections from an off-axis ED pattern. Different from an earlier software of automatic zone axis alignment (20) that estimates the crystal orientation by evaluating the intensities of reflections, our program determines the Laue circle from the positions of reflections to avoid the influence of structure factors or dynamic effects. Once the Laue circle is identified, φ is determined by its radius and λ. The program then decomposes φ into two components, φα and φβ, which correspond to two tilting angles around the α-tilt and β-tilt axes of the double-tilt TEM holder, based on the predetermined directions of the two tilting axes. By applying the program-calculated tilting angles φα and φβ, we can directly tilt the crystal from the initial orientation to
align with the zone axis. The whole process requires the acquisition of only two EDs, one for determining the Laue circle and the other for confirming the on-axis orientation; the electron beam is blanked in between while the program does its calculations, and the total dose consumed is far below $1 \text{ e}^-/\text{Å}^2$. This method requires that the initial crystal orientation is close to a zone axis ($-5^\circ < \varphi < 5^\circ$); otherwise, there are very few reflections observed in ED, making the identification of a Laue circle difficult. In practice, the probability of seeing a Laue circle is $>10\%$ in randomly oriented powder samples.

HRTEM of electron beam-sensitive materials often suffers from a beam-induced specimen motion that results in blurred images. When using a DDEC camera, this issue can be overcome by breaking the total exposure into a stack of successive short-exposure images (frames), on the condition that the drift between frames can be precisely corrected by image alignment. In principle, the exposure of each frame should be as short as possible to minimize specimen motion and statistical errors from the detector. However, beam-sensitive materials require low electron dose rate to avoid structural damage, and consequently, short exposure times result in very noisy frames with poor signal to noise that cannot be aligned using the common methods based on feature matching or phase correlation. To increase the signal to noise, several successive frames can be merged into one, which is equal to using longer exposure and thus detrimental to image resolution, especially when the specimen motion is severe. Image filters can also increase the signal to noise to facilitate image alignment, but the existing filters do not work well with high noise levels (fig. S4).

A general principle of image alignment is to decompose a real-space image into components of different spatial frequencies in the reciprocal space by Fourier transform (FT). Image drift can be determined from the ‘phases’ variation in the FTs. The difficulty in aligning noisy images lies in the poor signal to noise that affects the accuracy of phase determination. We hypothesize that the impact of noise can be minimized by selectively analyzing pixels in the FT with strong amplitudes, because phase determination of weak pixels is more easily influenced by noise and prone to errors. On the basis of this hypothesis, we developed an “amplitude filter” to confine the phase analysis to ‘reliable’ strong-amplitude pixels (figs. S5 and S6).

Unlike the common methods that deal with the weak signals of individual frames, the “amplitude filter” starts by integrating the FTs of all the frames in an image stack to pinpoint the
strong-amplitude pixels. The workflow is illustrated in Fig. 1 using an HRTEM image stack of MOF UiO-66 (21). With extremely low dose (0.033 e/\text{pixel}) (Fig. 1A), even the reflections are difficult to identify in the FT of each frame (Fig. 1B). We summed the FT amplitude components from all of the frames in the stack, as the reflections have invariable coordinates in the FTs, irrespective of image drift. As shown in Fig. 1C, the “hidden” reflections emerged in the summed FT amplitude pattern (we call it ‘amplitude pattern’ because it does not contain phase information). We filtered out background and weak pixels that have amplitudes lower than a set threshold from the amplitude pattern. The “amplitudes” of the remaining pixels were combined with the “phases” from the original FT of each frame to generate a series of modified FTs (Fig. 1D), followed by inverse FTs to generate a series of filtered images (Fig. 1E). Finally, the image drift was calculated using iterative cross-correlation based on the filtered images (Fig. 1F), and this information was used to align the original images in the stack. The drift-corrected, summed image shows rich high-resolution structural details, as evidenced by the appearance of the 1.4 Å reflection in the FT (Fig. 1G). By contrast, the cross-correlation without our “amplitude filter” could not correctly align this image stack until it is 1×1×10 binned, which led to a marked reduction in image resolution in the direction of the image drift (Fig. 1H). The result of merging all of the frames without drift correction is shown in Fig. 1I for comparison.

We are now able to study various MOFs with TEM along different zone axes, and to restore high-resolution information from the obtained images. Results from MOF UiO-66 are presented in Fig. 2. The successful acquisition of HRTEM images from four zone axes, <001>, <011>, <111>, and <013>, demonstrates the effectiveness of our method for zone axis alignment. FTs of these images show that the information transfer is < 2 Å in all directions (Fig. 2), confirming the efficacy of our method for image alignment.

The contrast in HRTEM images varies with the specimen thickness and defocus, making a single image difficult to interpret directly. A common practice in HRTEM is to acquire a series of images with different defocuses for structure reconstruction (22, 23). But this method is not suitable for MOFs because it is impossible to acquire multiple images without causing structural damage, even when using the low-dose conditions. On the other hand, the very low framework density of MOFs greatly decreases their effective scattering thickness; therefore, we can safely apply the weak-phase object approximation to MOFs for a wide range of thicknesses up to ~ 100
nm. Therefore, a single image can be made more interpretable by correcting the “contrast inversion” caused by the contrast transfer function (CTF) of the objective lens, if the absolute defocus of the image is known (24). Here we propose that we can take advantage of the “instability” of MOFs to determine the defocus. Specifically, after an HRTEM image is captured, we prolong the beam irradiation to deliberately destroy the crystalline structure, and acquire a focus series of this amorphized area (fig. S7). Using established methods (22), we can determine the absolute defocus value of each image in the series and, thus, that of the HRTEM image of MOF for CTF correction.

The success of our methodology has been demonstrated in a case study, in which an HRTEM image of UiO-66 along the <011> axis was acquired, aligned, and CTF-corrected using the methods described above. The sample was heated at 300 °C under vacuum for 10 h to remove the solvent/guest molecules before HRTEM. The imaged area contains a truncated octahedral crystal with an ultra-thin piece of crystal protruding from its lower right corner (Fig. 3A). In the CTF-corrected and denoised image (Fig. 3B and fig. S8), triangular channels encompassed by three metal clusters and three 1,4-benzenedicarboxylic acids (BDC) are identified, and atomic columns of Zr are distinguished within the Zr6O8 clusters, in good agreement with the crystal structure of UiO-66. The benzene rings with face-on configurations in the BDC linkers are resolved (Fig. 3B and fig. S8). In addition to the bulk structure, our image reveals detailed local structures. At the truncation surface of the octahedral crystal that corresponds to the fast-growing {100} planes, the crystal growth steps are identified as a number of small {100} and {111} facets (Fig. 3C). Furthermore, the high resolution allows us to investigate the surface termination of this crystal. In the CTF-corrected image, the outermost layer of Zr clusters have dark contrast and can be identified at the crystal surfaces, where the organic linkers are hardly visible because of the weak contrast associated with the low atomic numbers. We performed real-space averaging along the crystal surface to enhance the signal to noise (fig. S9). The results reveal the coexistence of ligand-free (metal-exposing) and ligand-capped surfaces: the major exposed {111} surface terminates with BDC linkers (Fig. 3D); in contrast, the small truncation surface (growth steps) expose Zr clusters at the kink positions between {100} and {111} facets (Fig. 3E).

It has been speculated that upon heating to 300 °C, the octahedral ZrO4(OH)4 clusters in UiO-66 undergo dehydroxylation forming distorted Zr6O6 clusters (25). In a <110> projection, this distortion gives rise to increased Zr-Zr distances along the in-plane <110> direction (fig. S10).
However, the random orientation of this distortion makes it difficult to verify by conventional characterizations. Using HRTEM, we observed the subtle structural change in UiO-66 associated with dehydroxylation (figs. S11 to S13). As revealed in the images, the as-synthesized UiO-66 contains only one type of Zr cluster with uniform Zr-Zr distances of 3.34 Å, whereas the heated UiO-66 contains two types of Zr clusters; one is same as the cluster in the as-synthesized sample and the other has larger Zr-Zr distances of 3.89 Å (Fig. 3, F and G, and fig. S12). This result supports speculation that the Zr clusters in UiO-66 become distorted upon heating (25). The appearance of a small number of undistorted clusters (Zr-Zr: 3.34 Å) in the heated UiO-66 (fig. S13) was likely caused by partial re-hydroxylation during the TEM sample preparation process. We note that the exact values of the Zr-Zr distance measured using HRTEM are not very accurate due to the pixel size limitations.

HRTEM images of MOFs ZIF-8 and HKUST-1 (26) and a germanosilicate zeolite are presented in figs. S14 and S15, which show good matching with the corresponding crystal structures after CTF-correction. We also successfully acquired HRTEM images of the organic-inorganic hybrid perovskite CH$_3$NH$_3$PbBr$_3$, which has emerged as an optoelectronic material and is known to be very sensitive to electron beams. The hybrid perovskites show anomalous I-V hysteresis in photovoltaic applications (27). Ferroelectric effect (28) and ion migration (29) have been posited to be likely causes for the hysteresis. Our image reveals that CH$_3$NH$_3$PbBr$_3$ crystals contain ordered nanometer-sized domains with off-centered CH$_3$NH$_3$ cations that have differing orientations. In the two typical domains highlighted in Fig. 4, the CH$_3$NH$_3$ cations exhibit normal and parallel configurations (relative to the projection direction), giving rise to in-plane and out-of-plane electric dipoles, respectively. This observation implies the ferroelectric order in this material.

In summary, we developed a suite of methodologies that enable atomic-resolution TEM imaging of electron beam-sensitive crystalline materials, which have traditionally been considered unsuitable for TEM characterization. With this capability, we are able to observe the local structures of MOFs and other fragile materials, significantly expanding the range of applications for HRTEM. It is worth noting that our method for zone axis alignment not only reduces the electron dose, but also enhances the precision of alignment. Its application is not limited to beam-sensitive materials; it is particularly useful for aligning nanosized crystals. Likewise, our method
for image alignment can be generally applied to various noisy images with periodic features. This study facilitates investigations in a wide variety of “unstable” materials using HRTEM.

References and Notes


Acknowledgments: We thank M. Pan and O. Terasaki for helpful discussions. This work was supported by King Abdullah University of Science and Technology through Competitive Research Grant (URF/1/2570-01) and Center Competitive Funding (FCC/1/1972-19). All data are reported in the main text and supplementary materials. Raw and processed images presented in this paper can be obtained from the corresponding authors upon reasonable request. D. Z., Y. Z., K. L., and Y. H. are inventors on United States Provisional patent applications (62/490,967 and 62/490,968) submitted by King Abdullah University of Science and Technology that cover the methods for crystal zone axis alignment and image alignment.

Supplementary Materials:
Materials and Methods
Figures S1-S16
Table S1
References (31-41)
Fig. 1. Alignment of an image stack using the “amplitude filter”. (A) A single frame and (B) the corresponding FT in an HRTEM image stack (120 frames in total) acquired for UiO-66 along the <011> zone axis. (C) The FT amplitude pattern formed by summing up the FT amplitude component of all frames. (D) Modified FT of a single frame by adopting filtered amplitudes from (C). (E) An amplitude-filtered single frame that is produced by inverse FT of (D). (F) The image-drift profile determined from filtered frames. (G) The drift-corrected image based on (F). (H) The drift-corrected image by cross-correlation, where the image stack is 1×1×10 binned to enhance the signal to noise. (I) Uncorrected image formed by directly summing up all the frames. In (G)-(I), the corresponding FTs are shown as insets; the half circles represent the frequency of 2 Å. In (G), a local area is zoomed in to highlight the observed 14 -4 4 reflection (d = 1.4 Å).
Fig. 2. HRTEM images of UiO-66 acquired from different zone axes: (A) <001>, (B) <011>, (C) <111> and (D) <013>. The top, middle, and bottom rows show raw images, denoised images and FTs of the raw images, respectively. The half circles in the FTs represent 2 Å. In all directions, there are reflections observed beyond the circle, indicating that the information transfer is less than 2 Å. As an example, the 10 -6 6 reflection (d = 1.6 Å) is highlighted in (B).
**Fig. 3.** **HRTEM of thermally treated UiO-66.** (A) Drift-corrected HRTEM image of a truncated octahedral UiO-66 crystal and an ultra-thin piece of crystal with the same <011> orientation. (B) CTF-corrected denoised image from the ultra-thin crystal (area 2 in (A)), showing triangular channels, individual Zr atomic columns, and the BDC linkers. The benzene rings in the BDC linkers are indicated by the arrows. Overlays are simulated projected potential maps and a projected structural model of UiO-66 for comparison. (C) A truncation surface (area 1 in (A)), showing crystal growth steps involving small {100} facets and {111} facets (labeled in blue and yellow, respectively). The white arrows indicate “kink” positions between {100} and {111} facets. (D) Ligand-terminated {111} surface: (left) structural model; (middle) processed HRTEM image by real-space averaging of 5 motifs from area 3 in (A); (right) the averaged image displayed in the rainbow colors to increase the visibility of the ligand contrast. (E) Ligand-free (metal-terminated) {100}/{111} kink: (left) structural model; (middle) processed HRTEM image by real-space averaging of 7 motifs from area 1 in (A); (right) the averaged image displayed in the rainbow colors. (F and G) The structure model (left) and the processed HRTEM image (right) of the (F) hydroxylated and (G) dehydroxylated Zr clusters featuring different Zr-Zr distances. The image processing details are shown in fig. S13.
Fig. 4. HRTEM of organic-inorganic hybrid perovskite CH$_3$NH$_3$PbBr$_3$. (A) CTF-corrected denoised HRTEM image. The raw image is shown in fig. S16. The squares highlight two ordered domains with off-centered CH$_3$NH$_3$ cations that have differing orientations. (B and C) The structural model (left) (30) and the simulated projected potential map (right) of CH$_3$NH$_3$PbBr$_3$ with different CH$_3$NH$_3$ orientations, corresponding to region 1 and 2 in (A), respectively. In (B) and (C), the off-centered CH$_3$NH$_3$ cations exhibit normal and parallel configurations (relative to the projection direction), giving rise to in-plane and out-of-plane electric dipoles, respectively.
Supplementary Materials for

Atomic-resolution transmission electron microscopy of electron beam-sensitive crystalline materials

Daliang Zhang,* Yihan Zhu, Lingmei Liu, Xiangrong Ying, Chia-En Hsiung, Rachid Sougrat, Kun Li,* and Yu Han*

Correspondence to: daliang.zhang@kaust.edu.sa; kun.li@kaust.edu.sa; yu.han@kaust.edu.sa

This PDF file includes:

Materials and Methods
Table S1
Figs. S1 to S16
Materials and Methods

Materials

The electron beam-sensitive materials investigated in this work include MOF UiO-66, MOF ZIF-8, MOF HKUST-1, a UTL germanosilicate zeolite, and an organic-inorganic hybrid perovskite (CH$_3$NH$_3$PbBr$_3$); these materials were synthesized using the previously reported protocols (31-35).

UiO-66, ZIF-8, and CH$_3$NH$_3$PbBr$_3$ were synthesized in the form of nano-sized crystals, and therefore they were directly imaged by HRTEM without the need of special specimen preparation. HKUST-1 and the UTL zeolite both consist of micron-sized crystals that are too large for HRTEM. To prepare their HRTEM specimen, we used an ultra-microtome to cut HKUST-1 crystal into thin slices, and used an agate mortar to crush UTL crystals into small fragments.

The dehydroxylated UiO-66 sample was prepared by heating the as-synthesized UiO-66 at 300 °C under vacuum ($10^{-6}$ Torr) for 10 h, which led to complete removal of the solvent/guest molecules from the microporous channels.
Stability evaluation under electron beams

To evaluate the stability of a MOF under electron beam (300 KV) irradiation, we acquired a time series of selected-area electron diffraction (SAED) patterns (20 patterns in total; 3 sec exposure for each; 5.3 sec pause between two exposures) to monitor the structural degradation. The pre-specimen electron beam shutter of the CCD camera was disabled during the experiment. The electron dose was calibrated using the counting mode of the DDEC (Gatan K2) camera. The results from a UiO-66 crystals (the last eight patterns in the series) are shown in Fig. S1.

**Fig. S1.** SAED patterns of a UiO-66 crystal acquired successively at a dose rate of 0.11 e⁻ /Å²/s. The cumulative electron dose is labeled in each pattern. The (0 0 10) reflection with a d-spacing of ~ 2.1 Å is marked with circles, which starts to fade when the cumulative dose reaches about 17 e⁻/Å². The TEM image of the crystal is presented in the lower right corner.
Alignment of zone axis

Our method for zone axis alignment is demonstrated on a real example (the alignment of the <011> zone axis of UiO-66 from an off-axis orientation).

Figure S2 illustrates how we determine the Laue circle from the initial SAED pattern. First, we identify the reflection peaks in the SAED pattern (Figs. S2a and S2b) using the algorithm described by Wan et al. (36). We then delineate the Laue circle by fitting the positions of the peaks, and denote its center as \( O_L \) (Fig. S2c).

Figure S3 illustrates the correlation between the Laue circle and the tilting angles for zone axis alignment, in which points O, \( O_E \), and \( O_L \) refer to the origin of the reciprocal lattice (the position of the direct beam), the center of the Ewald sphere, and the center of the Laue circle, respectively, and the directions \( O_E \rightarrow O \) and \( O_E \rightarrow O_L \) correspond to the beam incidence and the zone axis, respectively. The alignment from ‘off-axis’ (Fig. S3a) to ‘on-axis’ (Fig. S3b) is equivalent to moving \( O_L \) towards O until they coincide. To achieve the one-step alignment, we need to know the exact directions of the \( \alpha \)- and \( \beta \)-axes of the double-tilt holder to decompose the deviation angle (between the zone axis and the beam incidence) into two components, \( \phi_\alpha \) and \( \phi_\beta \), which correspond to two tilting angles around the \( \alpha \)- and \( \beta \)-axes (Fig. S3c). Therefore, we pre-calibrated the directions of the \( \alpha \)-tilt and \( \beta \)-tilt axes and the tilting accuracy of the double-tilt holder using a standard single-crystalline sample. With the directions of two tilting axes known and the assistance of an auxiliary line segment \( O_L' - O_L \)’, which is parallel to the \( \beta \)-axis and intersects the \( \alpha \)-axis at \( O_L' \), it can be easily understood that the angles \( \angle O_L - O_E - O_L' \) and \( \angle O_L' - O_E - O \) correspond to \( \phi_\alpha \) and \( \phi_\beta \), respectively (Fig. S3c). Given that the lengths of \( O_E - O \), \( O_L' - O_L \), and \( O_L' - O \) are known or measurable and that \( O_E - O \) is perpendicular to the Laue circle, the two angles (\( \phi_\alpha \) and \( \phi_\beta \)) can be determined by the law of cosines.

In this particular case (Fig. S2), \( \phi_\alpha \) and \( \phi_\beta \) were calculated to be -1.79° and -0.31°, respectively. We input the calculated values of \( \phi_\alpha \) and \( \phi_\beta \) into our program to direct the double-tilt holder to tilt accordingly by using scripting control. Then, we switched the electron beam on, centered the specimen, and acquired the second SAED pattern. The result showed that the zone axis was well aligned (Fig. S2d).

In our experiments, the program-controlled tilting is accomplished by using DigitalMicrograph scripting (Gatan) on a Titan Cube transmission electron microscope (FEI). The actual tilt angles of the stage that have been calibrated using a standard sample can be read out with an accuracy of 0.01°. However, the stage control is less precise. It is common to have ± 0.02° deviation between the input angle value and the value read out after the tilting operation. Occasionally, the error can be as large as ± 0.05°, due to the mechanical imperfectness of the stage. In practice, the precision of zone axis alignment mainly depends on how accurately the Laue circle is estimated. When the initial crystal orientation is close to a zone axis with a deviation angle smaller than 2°, nearly perfect alignment can be achieved with one or two tilting operations.
Fig. S2. (a) The initial SAED pattern taken from UiO-66 close to the <011> zone axis. (b) Reflection peaks with intensities stronger than 5% of the intensity of the center peak are identified. (c) The Laue circle is delineated by fitting the positions of the reflection peaks; the center of the circle is denoted as $O_L$. (d) The SAED pattern obtained after applying the program-derived tilting angles, showing a perfect zone-axis alignment.
**Fig. S3.** Illustration of the one-step zone-axis alignment principle. (a) The off-axis condition, at which the reflections in the ED pattern form an arc that is part of the Laue circle. \( O_L \) is the center of the Laue circle, \( O \) is the origin of the reciprocal lattice, \( O_E \) is the center of the Ewald sphere, and \( \varphi \) is the angle between the zone axis and the incidence of the electron beam. (b) The on-axis condition at which the Laue circle disappears and the zone axis coincides with the incidence of the electron beam. (c) Illustration of how the alignment process (from (a) to (b)) can be achieved by tilting the specimen along the \( \alpha \)- and \( \beta \)-tile axes. The tilting angles are calculated based on the position of \( O_L \) and the pre-determined directions of the \( \alpha \)- and \( \beta \)-tile axes.
Amplitude Filter and image alignment

To align each individual extremely noisy frame in the image stack, we developed an Amplitude Filter. We describe its working principle as follows. For an image stack that contains \( n \) frames \( (f_1(x, y), f_2(x, y), \ldots, f_n(x, y)) \), the Fourier Transform (FT) of one individual frame \( f_i(x, y) \) is:

\[
F_i(u, v) = \iint f_i(x, y) e^{-2\pi i (ux + vy)} \, dx \, dy
\]

or, in the polar form, it is:

\[
F_i(u, v) = |F_i(u, v)| e^{-i\Phi(u, v)}
\]

where \( |F_i(u, v)| \) is the “amplitude” and \( \Phi(u, v) \) is the “phase” of \( F_i(u, v) \).

The FT amplitude components from all of the frames in the stack can be summed to form an Amplitude Pattern, which is denoted as:

\[
F_A(u, v) = \sum_{i=1}^{n} |F_i(u, v)|
\]

The function of our Amplitude Filter is to pinpoint pixels in the Amplitude Pattern whose intensities are stronger than a specified threshold value \( I_t \), to produce a Filtered Pattern. The threshold value can be a value in the following range:

\[
I_t > 2 \times I_{mean} - I_{min}
\]

where \( I_{mean} \) and \( I_{min} \) are the mean value and the minimum value among all the pixels in the FT.

A Filtered Pattern is:

\[
H(u, v) = \begin{cases} 
  I_{uv} - I_t & \text{if } I_{uv} \geq I_t \\
  0 & \text{if } I_{uv} < I_t
\end{cases}
\]

where \( I_{uv} \) is the intensity value at point \((u, v)\) in the Amplitude Pattern \( F_A(u, v) \).

\( H(u, v) \) is then used to replace the “amplitude” component, \( |F_i(u, v)| \), in the FTs of all the frames. That is, the modified FT pattern \( G_i(u, v) \) of a frame \( f_i(x, y) \) is generated by combining \( H(u, v) \) as the amplitude component and \( \Phi(u, v) \) as the phase component:

\[
G_i(u, v) = H(u, v) e^{-i\Phi(u,v)}
\]

Finally, inverse Fourier Transform is performed on \( G_i(u, v) \) to generate a filtered image \( g_i(x, y) \):

\[
g_i(x, y) = \iint G_i(u, v) e^{2\pi i (ux + vy)} \, du \, dv
\]
In the image stack shown in Fig. 1, each frame has a mean count value as low as $0.033 \times 10^{-6}$/pixel, meaning that only ~4% pixels are nonzero. Due to the very limited information in each low-dose single frame, these conventional filters cannot produce useful features for the subsequent alignment (Fig. S4). As a consequence, attempts to use these filters to facilitate the alignment of single frames all failed. In contrast, our Amplitude Filter is capable of filtering these frames to enable the subsequent alignment, and its workflow that mainly contains three steps is illustrated in Fig. S5.

Step 1. The generation of an “Amplitude Pattern”

The FT amplitude components of all frames are summed to generate an Amplitude Pattern (equation 3).

Step 2. The generation of a “Filtered Pattern”

In our method, the threshold value is chosen based on the intensity histogram of the “Amplitude Pattern”. For example, the histogram in Fig. S6a is calculated from Fig. 1c. As background pixels dominate an Amplitude Pattern, the most probable distribution of intensity (the intensive peak in Fig. S6a) corresponds to the background and its center can be approximated to the mean value ($I_{\text{mean}}$) of all pixels in the pattern. We consider the intensity range of the background as $I_{\text{mean}} \pm (I_{\text{mean}} - I_{\text{min}})$ (Fig. S6b), and therefore set the threshold ($I_t$) with a value above $(2 \times I_{\text{mean}} - I_{\text{min}})$ to filter out the background (equation 4). In practice, we usually set the threshold to be $I_t = 2 \times I_{\text{mean}}$ to filter out most weak reflections as well (Fig. S6b). Using the threshold, a Filtered Pattern is calculated by equation (5).

Step 3. The generation of filtered frames

After the amplitude component in FT results of all the frames are replaced by the Filtered Pattern (equation 6), inverse Fourier transform is performed to these revised FTs to produce filtered images (equation 7).

Because the filtered frame, $g_i(x, y)$, contains periodic lattice, the determination of drifts can work only for motions within a periodic unit. Therefore, cross-correlation calculations require the use of a neighboring frame instead of a fixed frame as a reference, considering that the drift between two neighboring frames unlikely exceeds the unit cell length. In this circumstance, we need to determine the drift motions through iterative cross-correlation. A typical iteration cycle includes a drift determination operation and a drift correction operation of the entire image stack. Assuming that the drift correction determination includes $m$ circles and that the drift determined for frame $i$ (relative to frame 1) at iterative circle $k$ is $r_{ik} = [\Delta x_{ik}, \Delta y_{ik}]$, the overall drift (relative to frame 1) for frame $i$, $r_i$, is:

$$r_i = \sum_{k=1}^{m} [\Delta x_{ik}, \Delta y_{ik}].$$  

We performed sub-pixel cross-correlation calculations and corrections via Digital Micrograph (Gatan) software. Experience showed that we could usually obtain convincing results in ten cycles.
Fig. S4. (a) One frame extracted from the image stack shown in Fig. 1. Commonly used image filters, including (b) Sobel filter, (c) Laplace filter, (d) Hanning-window, (e) low-pass filter and (f) High-pass filter, are applied to this frame in which ~96% of the pixels are blank. The results show that these conventional filters cannot produce useful features for the subsequent alignment.
**Fig. S5.** A flow chart of the Amplitude Filter that contains three steps: (1) the generation of an amplitude pattern, (2) the generation of a filtered pattern, and (3) the modification of FTs and inverse FTs to generate filtered images. The image stack used here is the same as the one shown in Fig. 1, and it contains 120 inter-frames. Filtered images shown here are cropped images (128×128) from the center of original Filter images from frame 1, frame 10 and frame 120, respectively.
Fig. S6. (a) Intensity histogram of the Amplitude Pattern shown in Fig. 1c, in which we separate the background region and signal region by an intensity cutoff at $2 \times I_{\text{mean}} - I_{\text{min}}$. (b) An enlarged view of the signal region, showing the general threshold used in this report ($2 \times I_{\text{mean}}$).
HRTEM imaging and simulations

TEM experiments were performed on a Cs-corrected FEI Titan transmission electron microscope operated at 300 kV. Spherical aberration was corrected to be in a range of ± 5 µm. Specimen searching, zone axis alignment and pre-focusing were conducted at 13,000× magnification with a dose rate of ~ 0.03 e/Å²/s.

Selected Area Electron Diffraction (SAED) patterns were collected using a Gatan Ultra-scan CCD camera. The acquisition parameters were set to a frame size of 512×512 (binning 4) and an exposure time of 1~5 seconds. In most of the cases, beam-stop was not applied.

HRTEM images were acquired by a Gatan K2 direct-detection camera in the electron-counting mode with the Dose Fractionation function. Detailed experimental conditions for HRTEM imaging of different specimens are listed in Table S1.

We simulated projected potentials using the QSTEM software (37). In the simulations, we set the point spread function width to 1.6 Å for UiO-66, 2.0 Å for HKUST-1, 2.0 Å for ZIF-8, and 1.5 Å for the hybrid perovskite.

The conditions of defocus and astigmatism are determined by comparing the experimental FT pattern of amorphous “crystals” with the simulated pattern calculated by the software “CtfExplorer” (38). The phase inversions caused by Contrast Transfer Function (CTF) are corrected by home-developed code scripted in Digital Micrograph (Gatan). The amplitude component is not included in the CTF correction.

### Table S1. Imaging conditions of the studied specimens

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Mag.</th>
<th>Pixel size (Å)</th>
<th>Total exp. (s)</th>
<th>No. of frames</th>
<th>Frame exp. (s)</th>
<th>Dose rate (e/Å²/s)</th>
<th>Total dose (e/Å²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dehydroxylated UiO-66</td>
<td>55k</td>
<td>0.57</td>
<td>6</td>
<td>120</td>
<td>0.05</td>
<td>~2</td>
<td>~12</td>
</tr>
<tr>
<td>As-synthesized UiO-66</td>
<td>55k</td>
<td>0.57</td>
<td>6</td>
<td>120</td>
<td>0.05</td>
<td>~2</td>
<td>~12</td>
</tr>
<tr>
<td>HKUST-1</td>
<td>44k</td>
<td>0.71</td>
<td>3</td>
<td>120</td>
<td>0.025</td>
<td>~2</td>
<td>~6</td>
</tr>
<tr>
<td>ZIF-8</td>
<td>55k</td>
<td>0.57</td>
<td>6</td>
<td>120</td>
<td>0.05</td>
<td>~0.8</td>
<td>~5</td>
</tr>
<tr>
<td>Hybrid-Perovskite</td>
<td>55k</td>
<td>0.57</td>
<td>3</td>
<td>30</td>
<td>0.1</td>
<td>~3.7</td>
<td>~11</td>
</tr>
</tbody>
</table>
**Fig. S7.** (a) A typical HRTEM image acquired using the methods we described in the manuscript. (b) An image of the same area acquired at exactly same conditions as (a) but after a prolonged illumination by the electron beam to amorphize the specimen. The crystalline and amorphous natures of the two images are reflected by the FTs (insets). (c) Selected images from a defocus series of the same area after amorphization, from which defocus values at different astigmatism axes, averaged defocus values, and focus steps are determined by established methods (22). (d) A 2-D CTF plot (without considering the Envelop function) simulated according to the determined defocus is overlaid on the FT pattern in (a). (e) The CTF-corrected image based on the determined CTF function.
**Fig. S8.** (a) The drift-corrected raw image cropped from region 2 of Fig. 3a. (b) CTF-corrected (a); the CTF-correction process is shown in Fig. S7. (c) Denoised (b) using an Average Background Subtraction Filter (ABSF) filter. (d) Denoised (b) using a Wiener filter. (e) Enlarged rotated image of marked region in (c) with visible benzene rings highlighted by red arrows. The ABSF and Wiener filters were developed by D.R.G. Mitchell (39, 40). In our studies, we always applied the two filters for the same image to avoid potential artifacts introduced by a specific filter.
Fig. S9. Real-spacing averaging along the ligand-capping (upper) and ligand-free (lower) surfaces. The selected “motifs” are labelled in the images, and cropped as individual images (the top row); the cropped images are further aligned by cross-correlation and then averaged to produce the “averaged” images.
Fig. S10. Hydroxylated and dehydroxylated Zr clusters. (a) Structural models of the Zr₆O₄(OH)₄ cluster in the as-synthesized (hydroxylated) UiO-66: (left) a stick-and-ball model with Zr, O and H labelled; (right) a model with O and H omitted to highlight the Zr₆ octahedron. (b) Structural models of the distorted Zr₆O₆ cluster in the thermally treated (dehydroxylated) UiO-66 (25). (c) Projection views of the Zr₆ octahedron in (a). (d) Projection views of the distorted Zr₆ octahedron in (b). In (c) and (d), the <001> projection views help to visualize the distortion, while the <011> projection views are directly related to the HRTEM images discussed in Fig. 3 and Figs. S11-S13. We follow the assumption made in the previous study that during the hydroxylation, the four in-plane Zr atoms maintain a square shape, that is, the distorted Zr₆ cluster is a squeezed octahedron in shape (25). As such, the symmetry of the Zr₆ octahedron is reduced from Oh (m-3m) to D₄h (4mmm) (Fig. S10a-b). In the <011> projection, the distorted Zr₆ clusters generally have longer Zr-Zr distances along the in-plane <011> direction regardless of the distortion direction, than the undistorted cluster (Fig. S10c-d).
**Fig. S11.** HRTEM image of the as-synthesized (hydroxylated) UiO-66. (a) The drift-corrected raw image taken along the <011> zone axis with the corresponding FT pattern (inset). (b) CTF-corrected image of (a). Inset is a filtered image (using the ABSF filter) from the marked area overlaid with Zr₆ octahedron models, in which the two neighboring Zr columns along the in-plane <011> direction of each cluster are well-resolved. The unit cell parameters determined from HRTEM are \( a = 20.671 \text{Å} \) for the as-synthesized UiO-66 and \( a= 20.650 \text{Å} \) for the thermally treated UiO-66, respectively. These values are close to those reported in the literature (20.7551Å and 20.7004 Å) (25). The unit cell parameters calculated from the 00l reflections are consistent with those calculated from the \( hh0 \) reflections (< 1% deviation for both samples).
Fig. S12. (a and b) Side-by-side comparison of the as-synthesized (a) and the thermally treated (b) UiO-66, based on CTF-corrected, ABSF-filtered HRTEM images along the <011> incidence and intensity profiles of two marked areas, each including 10 Zr-Zr pairs. The intensity profiles are plotted using the averaged values of four vertically adjacent pixels. (c) A selected area from (b) to highlight two types of Zr-Zr distances (3.34 Å and 3.89 Å) coexisting in adjacent regions in the thermally treated UiO-66. This is in contrast to the case of the as-synthesized UiO-66, which contains only one type of Zr-Zr distance (3.34 Å). (d) Summary of the measurement results in (a) and (b).

“Number of pixels” refers to the number of pixels between two Zr atoms (within a cluster) in the image, whose positions are defined by the pixel with the lowest intensity in a peak; “Distance” refers to the Zr-Zr distances that were calculated from the number of pixels and a common pixel size value, 0.5563 Å/pixel. We attribute the larger Zr-Zr distance observed in the thermally treated UiO-66 to the distortion of Zr cluster by dehydroxylation (25). Measurement errors from image distortion can be excluded as a possible cause of the observed differences between the two samples, given that (i) the measured Zr-Zr distances in the as-synthesized UiO-66 are exclusively 3.34 Å (6 pixels) and (ii) various Zr-Zr distances are observed among adjacent clusters in the thermally treated UiO-66. In addition, some Zr atoms in the image of the thermally treated UiO-66 look horizontally elongated (e.g., Zr-Zr pairs 14 and 15 in Fig. S12c), whereas no elongation phenomenon is observed in the as-synthesized UiO-66. These results are consistent with the models shown in Fig. S10d that Zr atoms are not perfectly aligned in certain orientations, and thus, consistent with the speculation that Zr clusters become distorted upon thermal treatment.
Fig. S13. (a) CTF-corrected, ABSF-filtered HRTEM image of the thermally treated UiO-66, in which 200 clusters at the thin crystal edge are classified into two categories, “Oval” and “Square”, based on the measured Zr-Zr distances (3.34 and 3.89 Å, respectively). (b and c) Real-space average images using (b) 77 “Oval” clusters and (c) 123 “Square” clusters as motifs, respectively, and structural models of Zr₄O₄(OH)₄ and Zr₆O₆. (d) Horizontal intensity profiles of the selected areas in (b) and (c), confirming the difference in Zr-Zr distance between the two categories. The difference in Zr-Zr distance between the two types of clusters corresponds to the size of only one pixel in our HRTEM image (0.5563 Å/pixel). Due to the limitation of the pixel size, the measured values of the Zr-Zr distances and their difference is not very precise. However, the “one-pixel difference” appears reproducibly in images between the as-synthesized and the thermally treated UiO-66, and is therefore considered reliable.
Fig. S14. HRTEM images of MOFs ZIF-8 and HKUST-1. (a) Drift-corrected HRTEM image and (b) cropped, CTF-corrected and Wiener-filtered image of MOF ZIF-8 taken along the <001> axis. (c) Drift-corrected HRTEM image and (d) cropped, CTF-corrected and Wiener-filtered image of MOF HKUST-1 taken along the <011> axis. Insets of (a) and (c) are the FTs of the corresponding images in which white dashed circles refer to an information transfer of 2 Å. Insets of (b) and (d) are the simulated projected potential maps of the corresponding structures with a point spread function width of 2 Å with embedded structural models.
**Fig. S15.** HRTEM of a UTL germanosilicate zeolite. (a) Drift-corrected HRTEM image taken along the [101] zone axis.Insets are the corresponding FT (lower) and the structure projection model (upper). Dashed circle in the FT refers to an information transfer of 2 Å. (b) A cropped image from the marked area in (a). (c) A Wiener-filtered image from (b).Germanosilicate zeolites are considered sensitive to electron beams. In our experiment, however, we found that the UTL zeolite was remarkably more stable under electron beams, as compared to MOFs and the hybrid perovskite.During the preparation of our manuscript, we were aware that HRTEM of the UTL germanosilicate zeolite has been reported recently (41), meaning that it is manageable by conventional low-dose TEM technique. Therefore, unlike the cases of other materials reported in this work (UiO-66, ZIF-8, HKUST-1, and hybrid perovskite CH$_3$NH$_3$PbBr$_3$), the image shown above is *not* the first ever HRTEM image of this material.
Fig. S16. HRTEM of organic-inorganic hybrid perovskite CH$_3$NH$_3$PbBr$_3$. (a) Drift-corrected HRTEM image. Inset is the corresponding FT with a dashed circle representing 2 Å. (b) A cropped image from the marked region in (a). (c) CTF-corrected image from (b) based on a defocus value of -255 nm. (d) ABSF-filtered and (e) Wiener-filtered images from (c).