

Electronic Supplementary Information (ESI)

Crystal surface defects as possible origins of cocrystal dissociation

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1. Experimental section

Samples were analysed using a Nanoscope Multimode AFM (Veeco Instruments, Cambridge, UK). Samples were imaged in air under ambient conditions using intermittent contact mode with a J scanner (180 μm^2 maximum scan size), together with MikroMasch NSC15 SPM probes which had a typical force constant of 40 Nm^{-1} and tip radius of 10 nm (MikroMasch, 2008). The tapping force which was applied to the probe while imaging was kept to a minimum to prevent the tip from damaging the sample surface. The typical scan area was 5 μm^2 (resolution of 256 lines), recorded at a scan rate of 1 Hz per line. Images were processed using Nanoscope Analysis v1.40 and a first order flattening correction was applied.

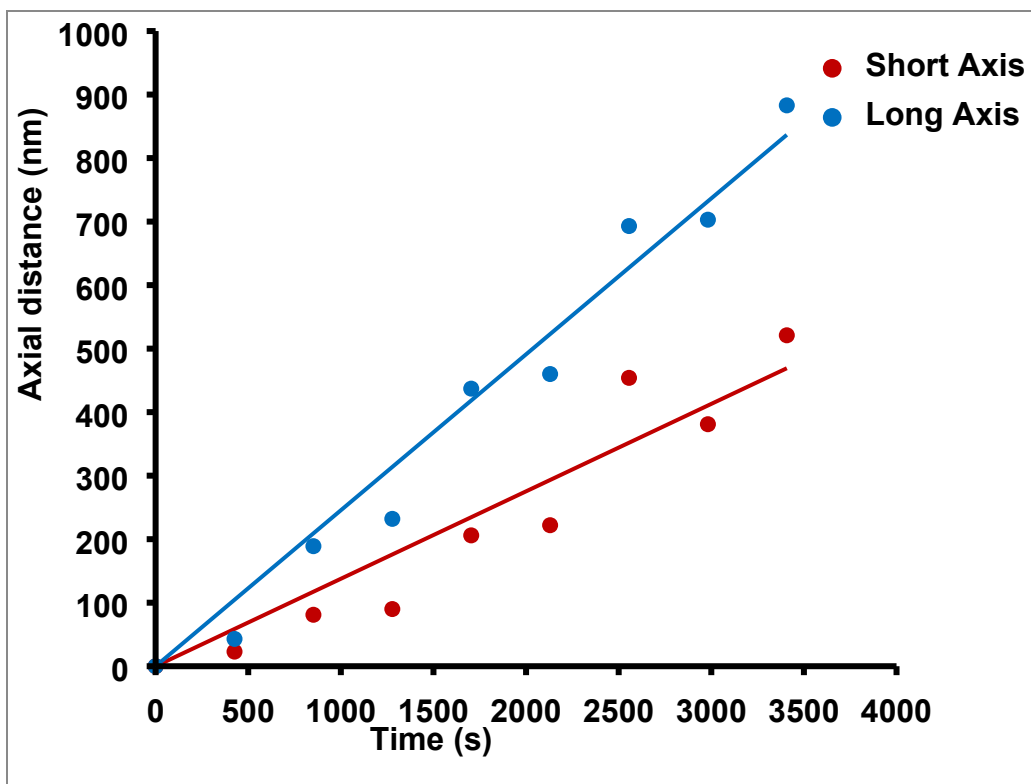


Figure S1. Axial distance (nm, y-axis) vs. time (s, x-axis) during molecular diffusion across the four faces with different rate at 0 % RH.

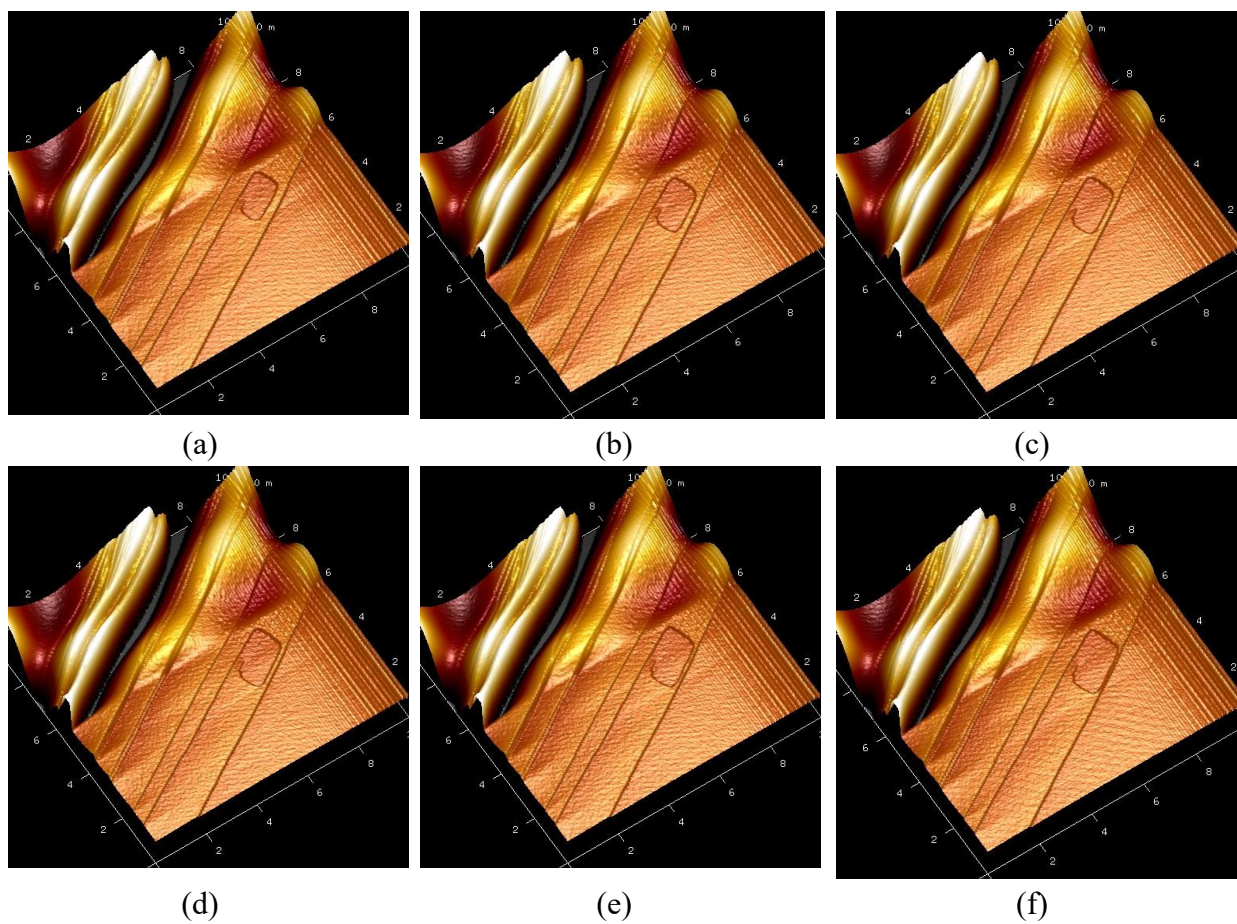


Figure S2. IC-AFM height images of Form II (Area 1) at 40% humidity. Screw dislocation inducing molecular diffusion can be observed as the rectangular groove across the surface.

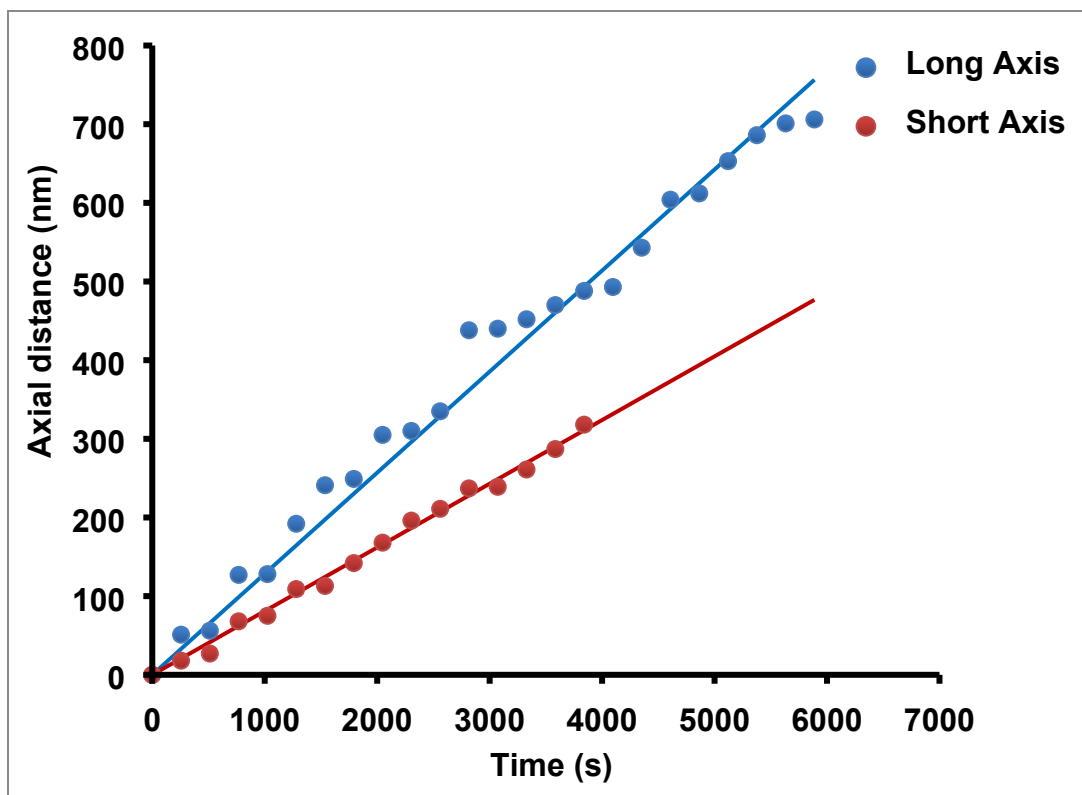


Figure S3. Axial distance (nm, y-axis) vs. time (s, x-axis) during molecular diffusion across the four faces with different rate (Area 1) at 40% humidity.

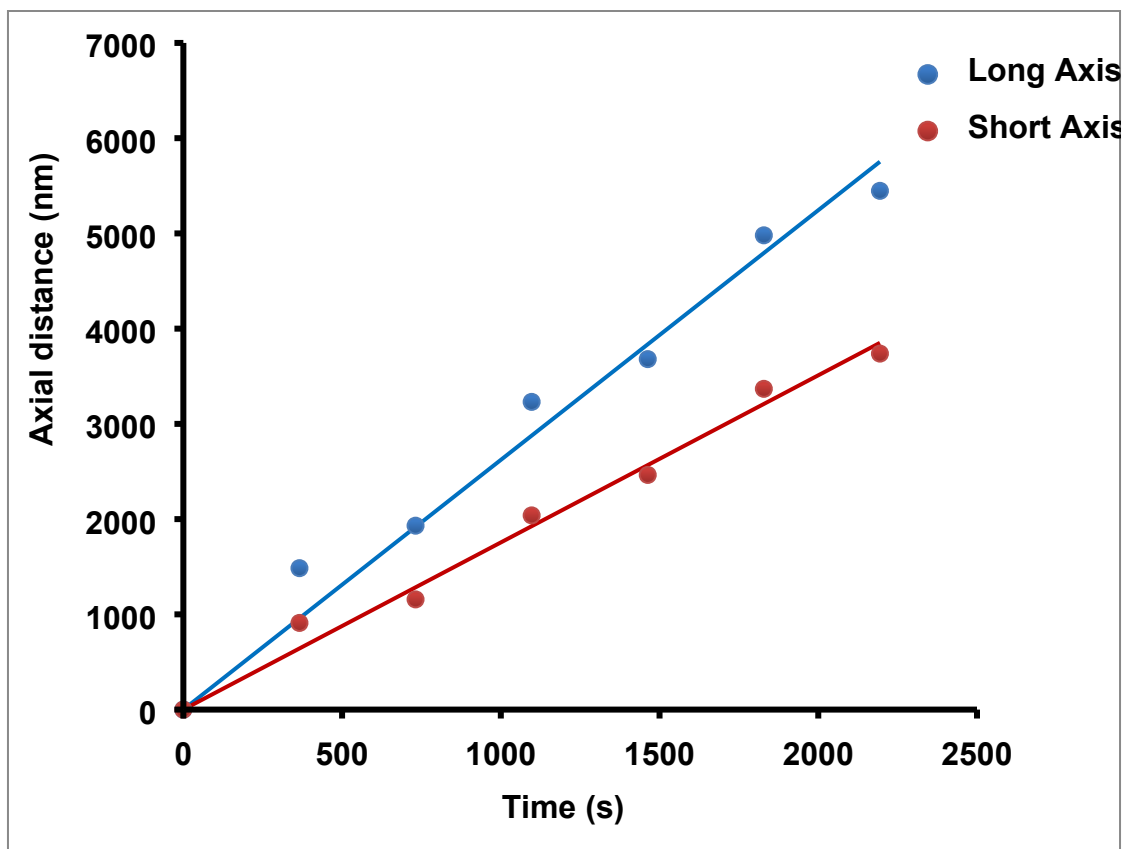


Figure S4. Axial distance (nm, y-axis) vs. time (s, x-axis) during crystal growth across the four faces with different growth rate (Area 3) at 40% RH.

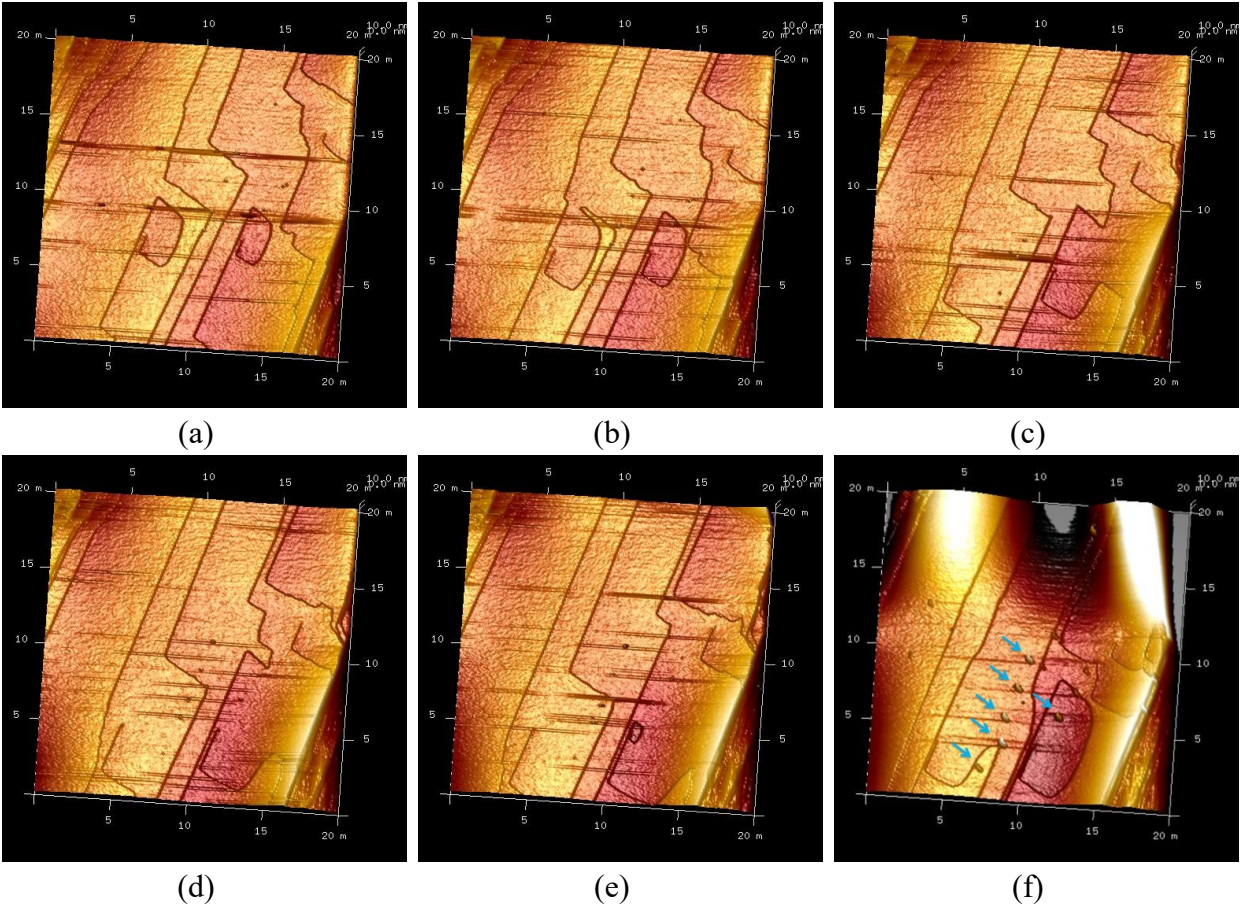


Figure S5. IC-AFM height images of Form II (Area 4) at 70% RH show two screw dislocation sites. White protrusions observed in image (f) are deposition of caffeine hydrate needles (blue cursor) on crystal surface based on our previous report.^{1,2}

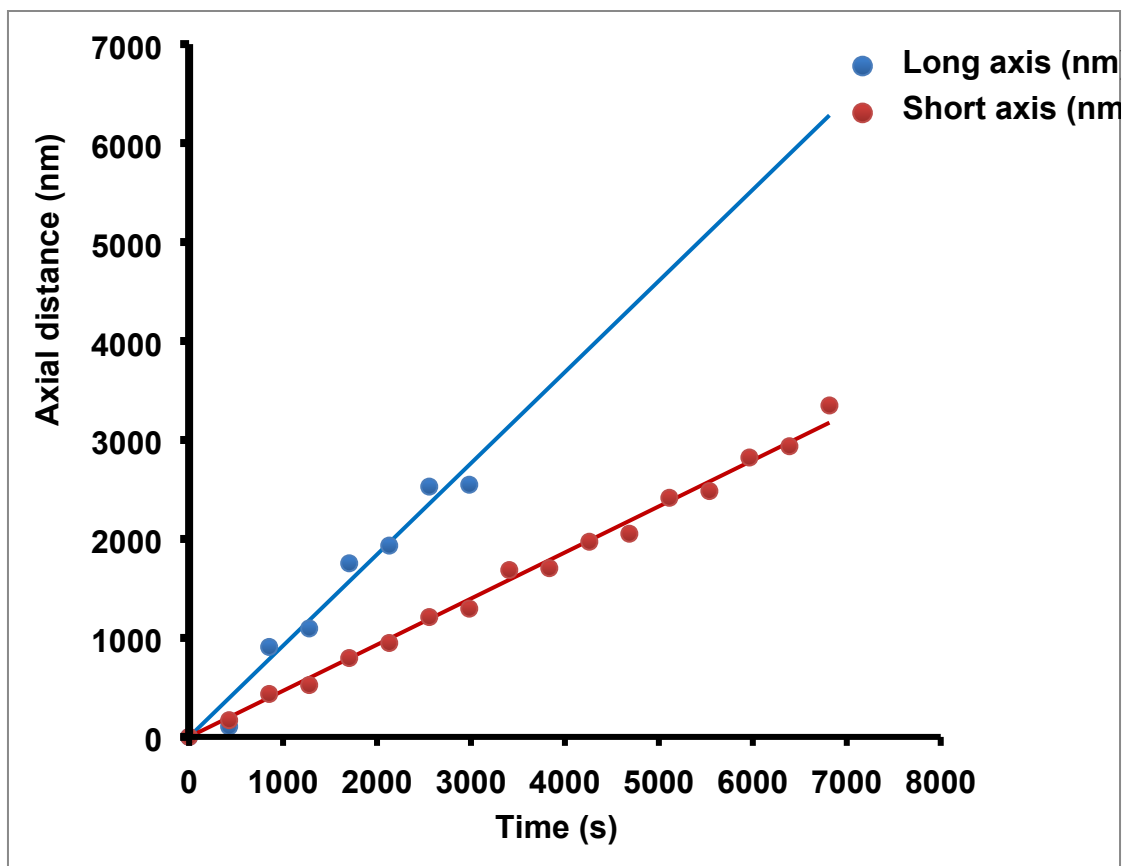


Figure S6. Axial distance (nm, y-axis) vs. time (s, x-axis) during molecular diffusion across the four faces (Area 4) with different rate at 70% RH (Upper layer, 1st unit).

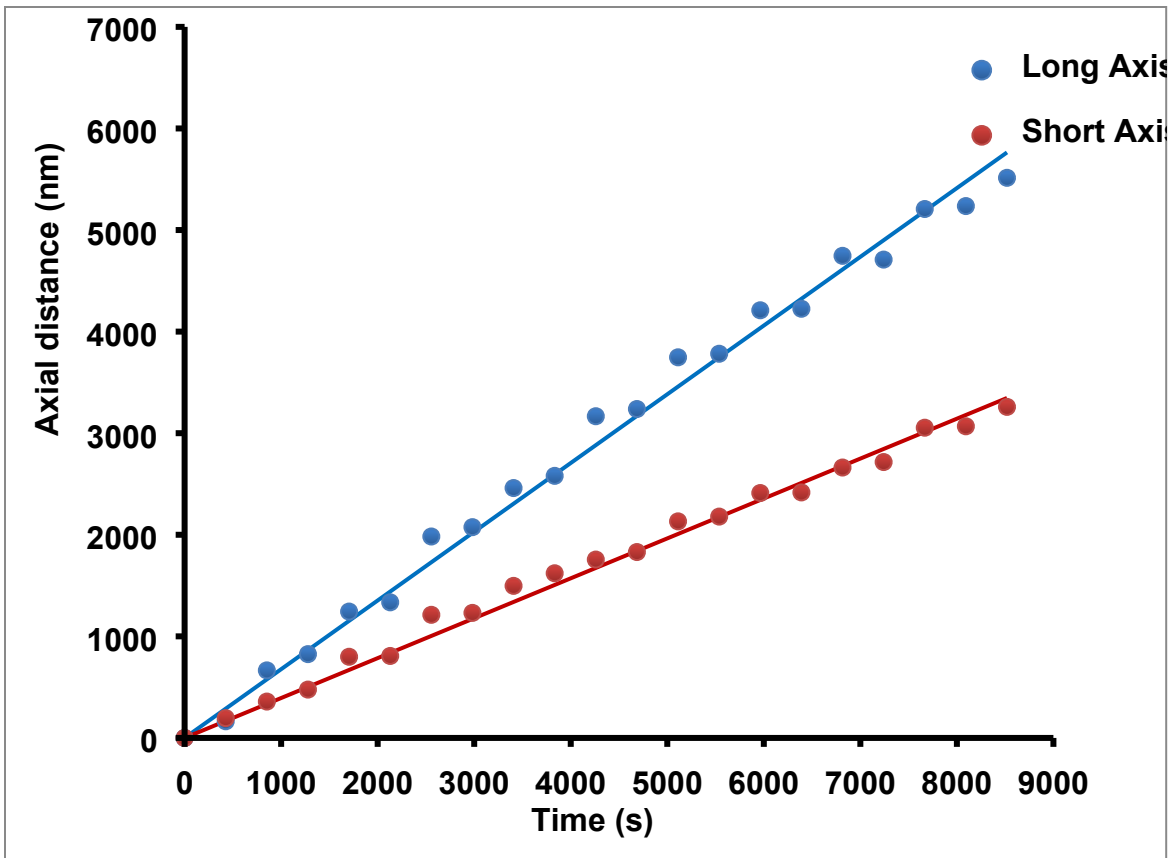


Figure S7. Axial distance (nm, y-axis) vs. time (s, x-axis) during molecular diffusion across the four faces with different rate at 70% RH (Upper layer, 2nd unit beneath the 1st unit).

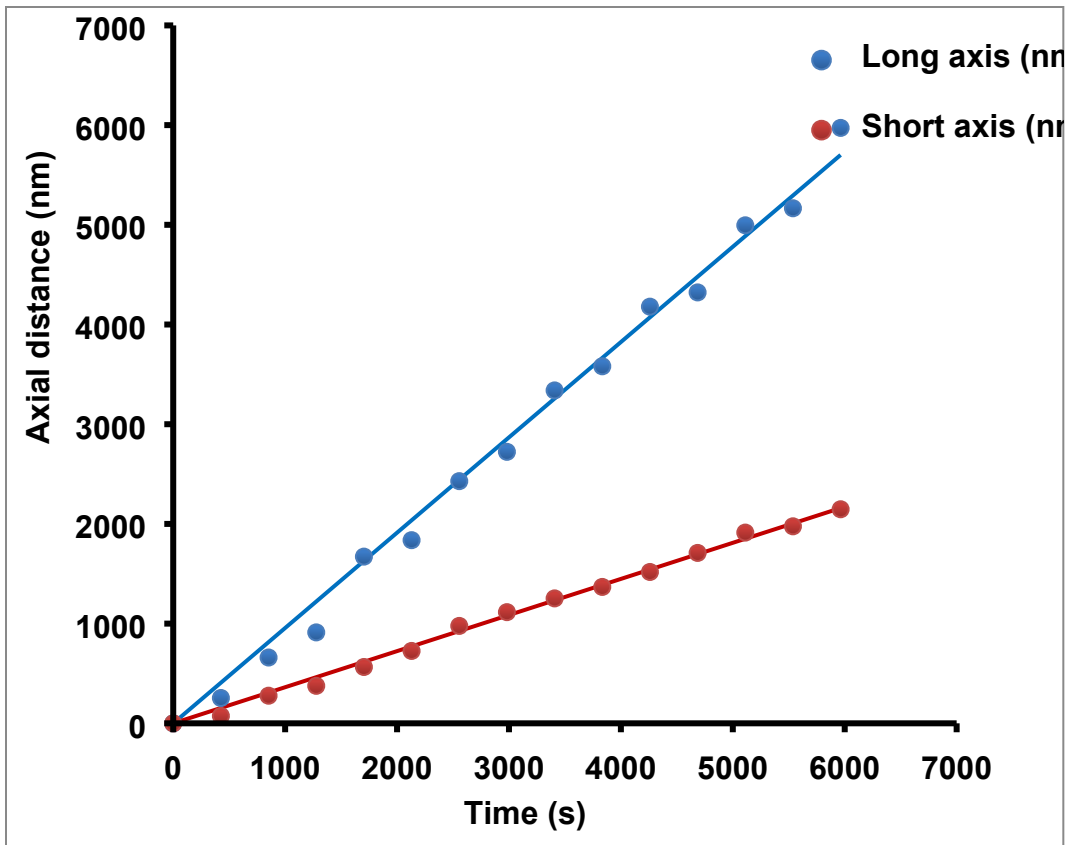


Figure S8. Axial distance (nm, y-axis) vs. time (s, x-axis) during molecular diffusion across the four faces with different rate at 70% RH (lower layer, 1st unit).

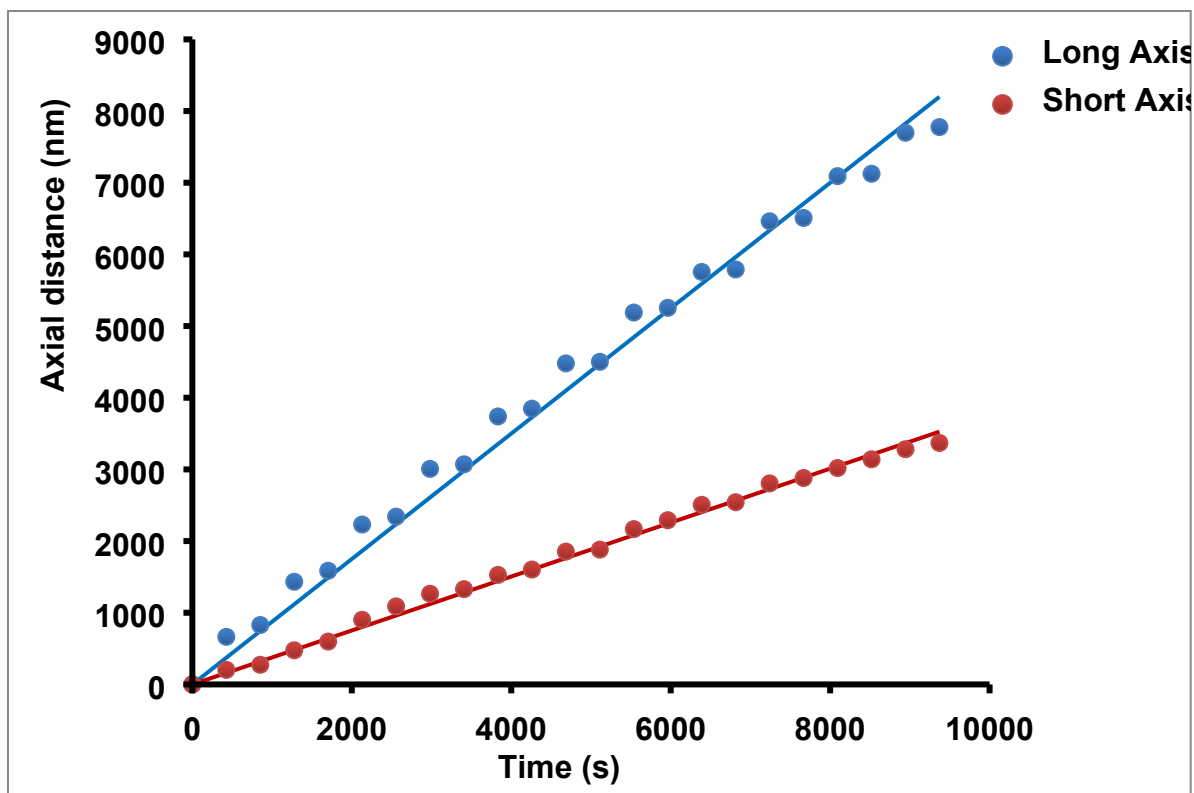


Figure S9. Axial distance (nm, y-axis) vs. time (s, x-axis) during molecular diffusion across the four faces with different rate at 70% RH (lower layer, 2nd unit beneath the 1st unit).

Reference

1. R. Thakuria, M. D. Eddleston, E. H. H. Chow, L. J. Taylor, B. J. Aldous, J. F. Krzyzaniak and W. Jones, *CrystEngComm*, 2016, **18**, 5296-5301.
2. R. Thakuria, M. Arhangelskis, M. D. Eddleston, E. H. H. Chow, K. K. Sarmah, B. J. Aldous, J. F. Krzyzaniak and W. Jones, *Org. Process Res. Dev.*, 2019, **23**, 845-851.