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DISCUSSIONS

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Growing crystals by design: general discussion

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Wenhao Sun opened the discussion of the paper by Kristen Fichthorn: Kristen, I really enjoyed reading your paper (**https://doi.org/10.1039/d1fd00091h**). To me, it suggests a theoretical pathway to computing the kinetic Wulff shape, which often is not the same as the thermodynamic Wulff shape. Unfortunately, as you show, your calculation is very expensive. I'm wondering if there are any heuristics or faster ways to reach a kinetic Wulff shape, perhaps from DFT-computable parameters?

Kristen Fichthorn responded: Kinetics is so system-dependent. I'm not certain there is an easy universal approach to the kinetic Wulff shape. In this work, we used DFT-computable parameters to get at linear-facet growth rates (though we did not explicitly mention this in the current paper, we did mention it in the past[1,2]). This could be done with considerable computational expense. Is there a faster way? In a past study, we could show (with the support of experiments) that it was the case that one facet was completely covered by a self-assembled monolayer of capping agent, while the other major facet present during growth did not have surfactant for the same solution-phase chemical potential. From there, we could conclude that solution-phase ion adsorption occurred only on the one facet, but not on the other, leading to certain experimentally observed kinetic shapes.[3,4] These DFT calculations were relatively easy, but the result was not "automatic".

[1] J. Kim, J. Cui and K. A. Fichthorn, *ACS Nano*, 2021, **15**, 18279–18288.
[2] X. Qi, Z. Chen, T. Yan and K. A. Fichthorn, *ACS Nano*, 2019, **13**, 4647–4656.
[3] M. J. Kim, S. Alvarez, Z. Chen, K. A. Fichthorn and B. J. Wiley, *J. Am. Chem. Soc.*, 2018, **140**, 14740–14746.
[4] K. A. Fichthorn and Z. Chen, *J. Vac. Sci. Technol. A*, 2020, **38**, 023210.

Wenhao Sun added: I just had a thought about the kinetic Wulff shape; different facets ought to have different solubility, we should be able to compute this. The chemical potential is $\mu = \mathrm{d}G/\mathrm{d}N$, and the surface energy is $\gamma = \mathrm{d}G/\mathrm{d}A$. So we can do a chain rule kind of thing: $\mu = \mathrm{d}G/\mathrm{d}A \times \mathrm{d}A/\mathrm{d}N$. In other words, the chemical potential (and thereby the solubility of the surface) is $\mu = \gamma \times$ [surface area of a monomer]. Perhaps using this, we could find an atomistic description based on the crystal structure for conditions where the flux of atoms from one surface to another (based on their different solubilities) results in a nanoparticle morphology that diverges from the thermodynamic Wulff shape… but I have to think about this more.

Kristen Fichthorn responded: So, it is true that differences in chemical potential provide a thermodynamic driving force for certain kinetic crystal shapes. However, I believe a formalism such as the one you propose would need more – a kinetic coefficient or knowledge of a mechanism. It would be great if we could totally predict kinetics from thermodynamics – catalysis might not be so much of a challenge in this case, for example. However, away from equilibrium, kinetics rules and there are so many different mechanisms with so many different rates. Uncovering these mechanisms and their ramifications will lead to much research for many, many years to come.

Christine Kirschhock commented: Your model suggests an intergrowth between ccp and hcp is necessary to explain the observed plate growth. This can be analysed by diffraction, determining the degree of stacking faults, for example using DIFFaX. Has this been attempted? Your model also should allow to deduce the faulting parameters, which then could be compared with the experimental observations.

Kristen Fichthorn answered: We could predict the stacking fault density based on our calculations and it would be interesting to compare this to experimental results. However, to our knowledge, the experiments have not been attempted.

Ruel Cedeno asked: What specific property of the iodine ion could rationalize its ability to favor the anisotropic growth of thin Cu plates (ionic radius, polarizability)? Do you observe chemisorption or orbital overlap between Cu and I or is it purely physisorption? Finally, do these findings extend to other halogen ions (*e.g.* bromide, chloride)?

Kristen Fichthorn replied: Iodine chemisorbs to the Cu surface – it binds quite strongly. From our analysis, probably the main factor for how iodine affects diffusion is its size. It restricts Cu binding on tightly packed Cu(111) to a greater degree than on more loosely packed Cu(100). As for Br and Cl, we studied the interaction of Cl with the Cu surfaces quite extensively: though the chemical interaction of Cl with the Cu surfaces is stronger than I, it turns out that the hydration free energy drives stronger I binding on Cu.[1] Also, interestingly, Cl binding drives faster diffusion on Cu(100) than on Cu(111) – opposite to what we find here.[2]

1 M. J. Kim, M. A. Cruz, Z. Chen, M. Brown, K. A. Fichthorn and B. J. Wiley, *Chem. Mater.*, 2021, **33**, 881–891.
2 J. Kim, J. Cui and K. A. Fichthorn, *ACS Nano*, 2021, **15**, 18279–18288.

Jutta Rogal queried: What happens to the iodine as the system grows? Does the coverage remain the same and if so where do the additional iodine atoms come from? And if the system grows another Cu layer, is it grown underneath the iodine adlayer?

Kristen Fichthorn answered: Cu atoms bind underneath iodine on the {100} facets, which leads to iodine naturally floating above the surface as the layer grows. On the {111} facets, Cu atoms bind in the same layer with I at low coverages. While the exact growth mechanism is less clear on the {111} facets, our calculations show that an intermixed Cu–I layer is less favored energetically than a layer in which I resides on top of Cu. These results (which we have not published) also suggest that an I layer floats on top of Cu as Cu atoms accumulate on the {111} facets.

Christian Kuttner commented: Your findings appear to be similar to the growth of gold nanoplates, nanotriangles, and nanoprisms. There are two types of mechanisms in the literature, namely, “plate-like” and “face-blocking” growth.[1] You showed the first one which relies on stacking faults. However, the alternative “face-blocking” relies on additional surfactant molecules and their selective adsorption at the most favourable facets. How do you see the competition between the two mechanisms? But I guess including anisotropy in the surface chemistry, *e.g.*, due to different surfactant densities at specific facets, would make the simulations too complex, right?

1 C. Kuttner, M. Mayer, M. Dulle, A. Moscoso, J. M. López-Romero, S. Förster, A. Fery, J. Pérez-Juste and R. Contreras-Cáceres, *ACS Appl. Mater. Interfaces*, 2018, **10**(13), 11152–11163.

Kristen Fichthorn responded: So, in our first paper on this topic,[1] we determined that under the conditions most relevant to experiments, the Cu surfaces are devoid of HDA capping agent. In that work, we did consider the co-adsorption of HDA and I – that calculation is highly do-able. In fact, we were able to demonstrate that the “face-blocking” (or probably more correctly “side-blocking”) mechanism likely underlies the growth of Cu nanowires, as our first-principles calculations showed the side facets of penta-twinned Cu nanowires were covered with HDA and Cl, but the ends contained only Cl.[2]

1 M. J. Kim, M. A. Cruz, Z. Chen, M. Brown, K. A. Fichthorn and B. J. Wiley, *Chem. Mater.*, 2021, **33**, 881–891.

2 M. J. Kim, S. Alvarez, Z. Chen, K. A. Fichthorn and B. J. Wiley, *J. Am. Chem. Soc.*, 2018, **140**, 14740–14746.

Alan Hare asked: I guess you can exclude chloride from the iodide system in theory; but are you considering a possible chloride impurity? If so, and if this impurity occurs experimentally in “the real world”, how might this affect the design outcome?

Kristen Fichthorn responded: In a study preceding the one presented here,[1] we considered possible co-adsorption of Cl and I on Cu(100) and Cu(111). Those calculations indicated there was no co-adsorption – the system either contained adsorbed Cl or adsorbed I, both with possible HDA coverage. However, first-principles calculations are limited by the size of the unit cell we can consider, so we cannot rule out the possibility of dilute impurities of any kind: Cl, defects, *etc.* Actually, experiments did indicate that dilute Cl was needed for plates to form, but the exact role of Cl was unclear. It is possible that Cl affected nucleation of the nanoplate seeds. Another possibility is this: our "ball stacking analog experiments" indicated higher index facets occur at the nanoplate sides during growth. We did not probe I adsorption and diffusion or Cl co-adsorption on those surfaces – we just assumed I was the main player and that adsorption was as strong and as slow as on the {100} facets. At any rate, the role of Cl in plate nucleation and/or growth is unclear.

1 M. J. Kim, M. A. Cruz, Z. Chen, M. Brown, K. A. Fichthorn and B. J. Wiley, *Chem. Mater.*, 2021, **33**, 881–891.

Matteo Salvalaglio asked: How did you enumerate the states used to define your Markov chain model? Do you have recommendations on strategies for the construction of kinetic models like your Markov chain from atomistic simulation data?

Kristen Fichthorn replied: One of the reasons we can successfully apply our model to this system (as well as to similar systems, where we applied it in the past[1,2]) is because the Cu plate structure is highly anisotropic, suggesting little Cu accumulation on the {111} facets. We are, in essence, using these calculations to predict how wide the plates will grow before adding another layer of height. In this case, the number of states is equal to the number of sites for a Cu atom to bind on the basal facet. For our initial configurations, we simply assume that a Cu atom is equally likely to bind to each of the N sites available to it.

If we accounted for accumulation on the {111} facets, the Markov chain calculations would rapidly become untenable, as there are too many permutations, which would lead to an intractable number of states. In this more difficult case, we have advocated combining absorbing Markov chain calculations with kinetic Monte Carlo, in an approach we call Local Superbasin Kinetic Monte Carlo.[3] In this approach, one can identify and treat groups of states connected by small barriers into superbasins – one can calculate the net exit time from such groups, as well as where the exits are likely to occur. This approach can greatly accelerate kinetic Monte Carlo simulations.

As far as building models, one needs to have a map of all relevant states of the system, as well as the rates of all important kinetic processes that take the system between various states. From there, one constructs the Markov matrix, as well as the transient and recurrent matrices. The procedure has been discussed in the literature.[3,4]

1 X. Qi, Z. Chen, T. Yan and K. A. Fichthorn, *ACS Nano*, 2019, **13**, 4647–4656.
2 J. Kim, J. Cui and K. A. Fichthorn, *ACS Nano*, 2021, **15**, 18279–18288.
3 K. A. Fichthorn and Y. Lin, *J. Chem. Phys.*, 2013, **138**, 164104.
4 B. Puchala, M. L. Falk and K. Garikipati, *J. Chem. Phys.*, 2010, **132**, 134104.

Wenhao Sun further commented: I had another idea for the kinetic Wulff shape. Different surfaces should have different solubility. If you have different solubilities, then the local concentration in the immediate vicinity of the two surfaces would be different. By Fick's first law, this would result in a flux of atoms from one surface to another. Perhaps this could be the origin of a kinetic Wulff shape…

Kristen Fichthorn replied: I believe your proposed mechanism could occur in certain systems. However here, the metal atoms bind so strongly that they stick where they hit. It could be that certain surfactants or capping agents can alter the rates at which the atoms reach certain surfaces, but it seems unlikely the solubility mechanism would apply to these metal systems.

Sten O. Nilsson Lill opened a general discussion of the paper by Colin Freeman: Based on your results, would you suggest to always include defects as a control experiment and study the effects when investigating heterogeneous nucleation with MD-simulations? Surface defects could for example, be randomly generated to see any major impacts.

Colin Freeman responded: This depends on the effect being examined. Certainly if you are trying to understand the rate of nucleation, the site of nucleation or the very early stages of nucleation, then including defects could be very important as these will govern ion concentrations and potential early clustering.

Jincheng Tong asked: The examples you present show the cracks that can induce nucleation, however they are very big (even in the micrometre scale), it is more likely these cracks are like edges of the substrate that can change nucleation dynamics. Do you have any idea if there is any case study that shows the atomic scale defects can change crystallization dynamics? Or do you think using a mixture of SAMs with different chain lengths that is able to form a non-flat surface, may have a similar effect on nucleation?

Colin Freeman answered: The experimental examples shown do involve larger defects. These are long but will not be micrometres in width, but are still larger than the atomic scale. Observing atomic sized defects in a surface is very difficult and therefore it is hard to identify examples where these scale defects have been shown to be significant. The results we present which highlight an enhanced concentration gradient at a defect may be applicable to larger defects as well, depending on their specific features. There has been a lot of work in the literature on building different patterned SAM systems using microcontact printing and examining crystallisation on these (see ref. 1 for example). These can produce patterns of crystal formation on the scale of tens of microns or less.

1 J. Aizenberg, *Adv. Mater.*, 2004, **16**, 1295–1302.

Ruel Cedeno asked: Since both the solvent and the solute ions can selectively cluster around the active defect sites, what is the ratio of the effective local concentration with respect to the bulk concentration? What are its implications on nucleation modelling where the bulk concentration is used for the driving force term?

Colin Freeman answered: Where we have used larger numbers of ions (bulk 0.41 M and 0.69 M) we can see significantly increased numbers of ions close to the defect (Fig. 10; 17 and 18 in the ESI of our article, **https://doi.org/10.1039/d1fd00082a**) – 3–5 times as many as would be expected for an equilibrium distribution of ions through the whole solution. Converting this to an effective concentration would, however, require a definition of a volume around the defect, as these simulations have a fixed number of ions present in the simulation box rather than a bulk fixed concentration (as in a constant chemical potential simulation). So the ratio obtained from the simulation is not the true local/bulk ratio. However, the difference between local and bulk concentration is certainly large and would affect both the surface free energy of the cluster and the kinetics of attachment of solute ions.

Christian Kuttner queried: If defects can promote nucleation, would it be reasonable to assume that defects can also suppress nucleation in special cases?

Colin Freeman replied: In the work we have performed we would suggest that defects can be either inactive (in which case they have little to no effect on the localised concentration of the nucleating species) or active (where they help concentrate the nucleating species). It is possible that a defect could actively lower the local concentration around it, but this would not suppress nucleation as this would cause very little effect on the overall concentration across the whole surface or at the active defect sites. It would also be possible for a defect to destabilise a growing nucleus by increasing its interfacial energy.

Perhaps the most important factor would be the concentration of defects. If the concentration of defects is low, then it is possible to grow clusters large enough to exceed the critical size without depleting the solute concentration of the local solution too much. If the concentration of defects is very high, then large numbers of sub-critical clusters may be produced, greatly depleting the solution concentration near the interface and producing diffusion-limited control.

Aaron R. Finney commented: Equilibrium molecular dynamics simulations are performed and, as already mentioned, the supersaturation at the surface and in the bulk (far from the surface in the simulations) is the same and the thermodynamic driving force for nucleation is the same too. An increased concentration of ions locally in the active defects could lead to a reduction of the kinetic barriers for nucleation, but then the very slow diffusion of ions could mean that translation and rotation of ions to adopt a crystalline lattice arrangement is potentially hindered. How do the authors reconcile these two effects? Furthermore, could the clustering of ions in defects facilitate nucleation in other ways *e.g.*, by leading to increased short-range ordering of ions and removal of water?

Colin Freeman responded: We are suggesting that the increased concentration of ions around the defect could lead to an increased number of “attempts” to cross the nucleation barrier which makes nucleation more probable at these points. The long range diffusion of these ions in these regions is lower but we have not seen evidence that their basic mobility is reduced (*i.e.*, they still rotate, vibrate and librate quickly) but we have not examined this in detail. We think we are seeing a more general reduction in their configurational freedom (as has been observed for other molecules/ions at surfaces, *e.g.* ref. 1). We have not seen any evidence to suggest that nucleation is being enhanced with increased short range order or a removal of water but these effects are certainly possibilities and would merit further investigation.

1 C. L. Freeman and J. H. Harding, *J. Phys. Chem. C*, 2014, **118**, 1506–1514.

Joonsoo Kim opened a general discussion of the paper by Peter Vekilov: Are there any other hypotheses trying to find a relationship between attaching a unit's symmetry and overall crystal symmetry?

Peter Vekilov responded: A common assumption in a large segment of the crystallization literature has been that the structural motifs of the crystal represent the solute species that associate to the kinks,[1–5] which would imply that crystal symmetry elements arise in the solution prior to crystallization. The inconsistencies of this assumption have been pointed out before our work (**https://doi.org/10.1039/d1fd00080b**), and it cannot explain how crystal forms with distinct structural motifs arise in the same solution. The elementary acts of incorporation into kinks, however, have only been directly visualized for relatively few crystals, mostly of large protein molecules.[6–22] Given these constraints to directly identify the growth unit, the promotion of the solute oligomers to the rank of the incorporating species had remained largely unchallenged until our recent results.

1 S. A. Kulkarni, E. S. McGarrity, H. Meekes and J. H. ter Horst, *Chem. Commun.*, 2012, **48**, 4983–4985.
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5 J. Chen and B. L. Trout, *J. Phys. Chem. B*, 2008, **112**, 7794–7802.
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7 S.-T. Yau, B. R. Thomas, O. Galkin, O. Gliko and P. G. Vekilov, *Proteins: Struct., Funct., Genet.*, 2001, **43**, 343–352.
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9 S.-T. Yau, B. R. Thomas and P. G. Vekilov, *J. Crystal Growth*, 2001, **232**, 188–194.
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11 M. Sleutel, C. Vanhee, C. V. de Weerdt, K. Decanniere, D. Maes and L. W. R. Willaert, *Cryst. Growth Des.*, 2008, **8**, 1173–1180.
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13 M. Sleutel, J. Lutsko, A. E. S. Van Driessche, M. A. Durán-Olivencia and D. Maes, *Nat. Commun.*, 2014, **5**, 5598.
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Ian Ford commented: The non-linear dependence of the step velocity on bulk concentration might indicate that the surface concentration of the depositing species is not equal to the bulk concentration. We have shown that this can emerge in a recent analysis of data on calcite growth: the observed critical step length of a screw dislocation source is consistent with a reduction in supersaturation due to diffusion through the boundary layer. Please refer to poster P45 at this meeting, or ref. 1. Do you think that this might explain your non-linear kinetics?

1 R. Darkins, I. J. McPherson, I. J. Ford, D. M. Duffy and P. R. Unwin, *Cryst. Growth Des.*, 2022, **22**, 982–986.

Peter Vekilov replied: The deviations from linearity due to depletion of the surface supersaturation at low solution flow rates depend on the surface kinetics, as highlighted in my previous answer above to Professor Ian Ford. The kinetics of step growth for both olanzapine and etioporphyrin I are sufficiently slow that diffusion supplies a sufficient feed of solute even in the absence of forced convection (our measurements were carried out in unstirred solutions). More importantly, insufficient solute supply to the steps enforces a sublinear correlation between the step velocity and the solute concentrations as the surface depletion is more severe at high supersaturations, at which the steps grow faster and consume more solute. The observed correlation with both olanzapine and etioporphyrin I are superlinear and I argue that they have nothing to do with insufficient solute supply to the steps.

Matthew Bennett said: Crystal growth is not easy. Do you think that studies like this, that do not provide the full answer/theory, close the gaps of the unknown, helping general understanding of the basics?

Peter Vekilov responded: I do not think that anyone would disagree with the statement that crystal growth is very complex. This is also the main message of our paper, that efforts to identify the solute unit that incorporates into the crystal cannot use shortcuts that only consider the crystal structure or the solution speciation. We present a method to identify the crystal growth unit that starts with measurements of the chemical kinetics at the kinks. We then demonstrate that a reliable identification of the molecular species that associates to the kinks requires a combined study of all three elements of crystal growth, the state of the solute in the solution, the kinetics of incorporation, and the crystal structure, by synergistic application of both experiment and high-power computer modeling. I strongly disagree that the denunciation of shortcuts retrogresses our understanding of crystal growth. On the contrary, I would argue that the proposed method to identify the crystal growth unit is a major step towards closing the knowledge gaps and promoting the understanding of crystal growth basics. Besides its fundamental implications, results due to our method may find immediate use in computer models of anisotropic crystal growth rates aimed to predict and control crystal sizes and morphologies for numerous technological applications.

Wenhao Sun commented: I really enjoyed your paper, showing that one surface grows due to monomer attachment, and the other results from dimer attachment. If you can control the ratio of dimers in solution, can the ratio of the growth rates of different surfaces be tailored?

Peter Vekilov answered: What an excellent idea! If an additive is found that binds preferentially to either dimers or monomers, it would shift the dimerization equilibrium, the ratio of monomers to dimers, and the relative rates of growth of the faces, which incorporate exclusively either monomers or dimers. This approach appears to be a potentially powerful tool for crystal habit control by modifying the solution properties of the solute, rather than by selective interactions with the anisotropic crystal faces, as pursued in most current strategies.

Wenhao Sun asked: So, Peter, you made a comment that different surfaces cannot have different solubility. I just wanted to address that with a thought-experiment. Suppose you have some material with very anisotropic surface energies. (001) is high energy and (100) is low energy. If you make two fake, non-equilibrium, very flat nanoparticles with the same number of atoms in each; one nanoparticle that exposes (001) and the other that exposes (100), you would have two nanoparticles with different solubility, right? This is based on Gibbs–Thomson or Ostwald–Freundlich arguments on the solubility.

So if you divide through both nanoparticles by the number of atoms (which is the same between the two nanoparticles), you would arrive at the conclusion that the differences in solubility arise from the differences in solubility of the surfaces. If you have different solubilities, then the local concentration in the immediate vicinity of the two surfaces would be different. This would result in a flux of atoms from one surface to another. Perhaps this could be the origin of a kinetic Wulff shape…

Peter Vekilov replied: The solubility is the concentration of a solution in equilibrium with a crystal. For large crystals, the exchange of molecules with the adjacent solution occurs exclusively at the kinks. The crystal edges at any temperature higher than 0 K are rounded and represent rough crystal surfaces rich in kinks. The kinks are defined as surface sites where a molecule has exactly half of the bonds that it would have in the crystal bulk. Thus, the free energy of a molecule binding to a kink is the same for kinks on all crystal faces; this is true for both centrosymmetric and polar crystal structures. Accordingly, solubility measurements based on observations of the step dynamics (steps neither grow nor dissolve at the solubility) yield solubilities which are identical across all facets and equal to the value measured in bulk crystallization experiments (**https://doi.org/10.1039/d1fd00080b**).[1–5] Thus, for large crystals the solubility is fully independent of the surface free energies of the facets which are clearly distinct.

Going back to your question, if {111} facets have higher surface free energy than {100} facets (I slightly modified your argument since you could not fully facet crystals with either {100} or {001} facets) crystals terminated exclusively by {111} facets would have higher total free energy and dissolve in a nearly equilibrated solution in the presence of crystals fully faceted by {100} faces, if they are sufficiently small. If both facets are present on the same small crystal at near-equilibrium, the sizes of the {111} and {100} facets will adjust by growth or dissolution until their ratios comply with the Wulff rule.

How small is sufficiently small? The answer is hidden in the Gibbs–Thomson relation, which for 3D crystals attains the form

$$\frac{c_{eR}}{c_e} = \exp\frac{2\Omega\gamma}{Rk_BT}$$

Here c_{eR} is the solubility of a crystal of size R, c_e is the solubility of a very large crystal, Ω is the molecular volume, k_BT is the thermal energy, and γ is the surface free energy. The Gibbs–Thomson relation argues that for crystals with small R, facets with distinct γ will equilibrate with solutions of different c_{eR}. The crucial governing parameter here is the capillary length

$$\frac{2\Omega\gamma}{k_BT}$$

which is typically a few nanometers. Thus for R greater than the capillary length, the factor in the exponential function on the right-hand side will be vanishingly small and $c_{eR} \cong c_e$. The small solubility differences between facets of moderate sizes, about 1 μm, is the reason why equilibrium shapes dictated by the Wulff construction, take several years to reach.[6,7]

1 M. Warzecha, L. Verma, B. F. Johnston, J. C. Palmer, A. J. Florence and P. G. Vekilov, *Nat. Chem.*, 2020, **12**, 914–920.
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Ivo B. Rietveld remarked: It is very interesting that you can show the different growth rate dependencies for two different surfaces (010 and 001) in the case of etioporphyrin crystals, as the 010 surface growth rate appears to depend on the molecular concentration, while the 001 surface depends on the dimer concentration.

How have you been able to experimentally distinguish between the growth dynamics of the two surfaces?

Peter Vekilov responded: The cross section of the etioporphyrin I crystals is nearly square. As a result, some of the crystals deposited on a substrate exhibit (010) facets, whereas others show (001) facets. This is in contrast to olanzapine crystals, which are shaped as plates along the (001) plane and always land on substrates with the (002) face facing upwards and exposed to AFM observation. The presence of a (101) face in the crystal morphology of etioporphyrin I enforces distinct shapes, a parallelogram for the (010) face and trapeze for the (001) face, which we use to identify the face monitored by AFM.

Jan Sefcik commented: There are two reasons for differences between solute concentration in the bulk solution and at the solution–solid interface: the first is due to diffusion limitations, which would lead to solute being attached to the interface of a growing crystal faster than it can be replenished by diffusion from the bulk solution, so the interfacial concentration would be lower than that in the bulk; the second is due to a local dispersion force field of the interface, where the interfacial concentration would be higher than that in the bulk.[1] In the second case, the interfacial concentration enhancement would be in thermodynamic equilibrium with the bulk solution, so the solute activity (and its chemical potential) would be the same as in the bulk. However, local concentration and ordering could be very different, which could facilitate non-classical/two-step nucleation pathways in the interfacial region. Also, dimer concentrations may be very different at the interface compared to the bulk solution.

1 D. McKechnie, S. Anker, S. Zahid, P. A. Mulheran, J. Sefcik and K. Johnston, *J. Phys. Chem. Lett.*, 2020, **11**, 2263–2271.

Peter Vekilov replied: This paper by McKechnie *et al.* suggests that glycine accumulates at the interface between an aqueous solution and mineral oil and this accumulation may boost heterogeneous nucleation of glycine crystals at the oil–water interface. I have no problem with that finding, even though I would prefer some experimental evidence in support. My own personal experience suggests that any such interfacial effects would be strongly dependent on the solute and the substance on the other side of the interface. Not all solutes will accumulate at a particular interface and if a solute accumulates at one interface, it will not necessarily adsorb on all others. Now, the suggestion appears to be that a similar accumulation of solute would occur at the interface of a solute with its own crystal and support nucleation of new crystallites at the interface with a growing larger crystal; the nucleated crystallites then incorporate into the large crystal, converting the growth mode to non-classical. The first part of this scenario appears trivial: solute adsorbed in the surface of a growing crystal diffuses along the surface and feeds the crystal growth, this represents the surface diffusion pathway, one of the two classical mechanisms of crystal growth. The adsorbed solute may form two-dimensional nuclei that initiate new crystal layers, another part of the classical crystal growth mechanisms put forth by Stranski and Kaischew in the 1930s.[1–3] Can the absorbed solute form 3D nuclei of new crystals? Highly unlikely in the absence of additional factors. The critical radius of 3D nuclei is two-fold larger than that of 2D nuclei, which contributes to a nucleation barrier for 3D nucleation several-fold higher than that for 2D nucleation. The nucleation barrier enters the nucleation rate law in the exponent, so that a several-fold higher barrier would suggest that 3D nucleation pretty much never happens. There may be scenarios that help 3D nucleation. They include elastic strain of the top crystal layers strong enough to shift the applicable rules from those of homoepitaxy (*i.e.*, crystal growth) to those of heteroepitaxy. Another type of event that may support 3D nucleation is the adsorption of larger foreign molecules at the crystal surface that favorably interact with a 3D nucleus of the solute. Recent liquid-phase TEM observations reveal the nucleation of crystallites not at the interface of a larger growing crystal, but at a certain distance from it. A lot is still not clear about the mechanism of this nucleation, current models appear to focus on solvent structuring that may stretch up to 1 nm from the crystal surface.

1 I. N. Stranski and R. Kaischew, *Z. Phys. Chem.*, 1934, **B26**, 114–116.
2 R. Kaischew, *Z. Phys.*, 1936, **102**, 684–690.
3 R. Kaischew and I. N. Stranski, *Z. Phys. Chem.*, 1937, **B35**, 427–432.

Ian Ford said: Finite element modelling of the deposition of calcite onto a surface in a typical flow cell has shown that the growth rate can be reasonably independent of flow rate and yet the supersaturation at the surface can still differ substantially from that in the bulk. Please see poster P45 at this meeting or ref. 1. Increasing the flow rate is not an entirely reliable way to exercise control over the surface conditions.

1 R. Darkins, I. J. McPherson, I. J. Ford, D. M. Duffy and P. R. Unwin, *Cryst. Growth Des.*, 2022, **22**, 982–986.

Peter Vekilov responded: This cited paper presents an ingenious way to evaluate the supersaturation on the surface of a calcite crystal growing in a typical Bruker Nasoscope AFM fluid cell.[1] The proposed method relies on the critical step length that can be measured by AFM. Indeed, the paper shows that the surface supersaturation is lower than that in the bulk. Notably, the flow rates analysed in the paper were low – up to 100 ml per hour. For a cell with 0.5 ml volume and about 1 cm length, this flow rate corresponds to a linear rate of about 0.5 mm s^{-1}. Other studies of the coupling of solute convective-diffusive transport and crystal interfacial kinetics employ flow rates from several cm s^{-1} (ref. 2) to m s^{-1}.[3] No wonder at such slow flow rates the boundary layer thickness δ is significant and the surface supersaturation, low. Classical analyses by Chernov[4,5] demonstrate that the ratio of the surface to the bulk supersaturations is

$$\frac{\sigma_s}{\sigma_b} = \left(1 + \frac{\delta h \beta}{Dl}\right)^{-1}$$

where h and l are the step height and step separation, respectively, β is the step kinetic coefficient, and D is the solute diffusivity. The presence of β in this relation highlights that the ratio

$$\frac{\sigma_s}{\sigma_b}$$

reflects the coupling of the solute supply to the incorporation kinetics and is not fully governed by the solution flow; faster β require lower δ, reached at higher flow rate, for σ_s to approach σ_b. Furthermore, for β of order 1 mm s^{-1}, D of order 10^{-5} cm^2 s^{-1}, and $h/l \approx 10^{-2}$ (roughly representative of calcite step kinetics 6), $\sigma_s \approx \sigma_b$ if $\delta < 10$ μm. The lowest δ analysed in Darkins *et al.*[1] is about 120 μm. It appears that there is no contradiction between the results of the beautiful study by Darkins *et al.*[1] and classical understating of how solute transport couples with the dynamics at the kinks.

1 R. Darkins, I. J. McPherson, I. J. Ford, D. M. Duffy and P. R. Unwin, *Cryst. Growth Des.*, 2022, **22**, 982–986.
2 M. Sleutel, A. E. S. Van Driessche, W. Pan, E. K. Reichel, D. Maes and P. G. Vekilov, *J. Phys. Chem. Lett.*, 2012, 1258–1263.
3 N. A. Booth, A. A. Chernov and P. G. Vekilov, *J. Crystal Growth*, 2002, **237–239**, 1818–1824.
4 A. A. Chernov, *Sov. Phys. Uspekhi*, 1961, **4**, 116–148.
5 A. A. Chernov, *Modern Crystallography III, Crystal Growth*, Springer, Berlin, 1984.
6 H. H. Teng, P. M. Dove, C. A. Orme and J. J. De Yoreo, *Science*, 1998, **282**, 724–727.

Marta K. Dudek asked: In MD simulations, were conformations in monomers different to those of dimers and in crystals, and do you know how they relate to gas phase (or solution phase) global minimum conformations?

Peter Vekilov answered: The constituent monomers in a dimer were allowed all translational, rotational, and molecular degrees of freedom on the pathway from fully separated monomers to monomers in a stable dimer. So, yes, the simulations did consider all possible dimer configurations.[1] We never considered etioporphyrin I in a gas phase, I am not sure if it can melt and evaporate without decaying first.

[1] L. Verma, M. Warzecha, R. Chakrabarti, V. G. Hadjiev, J. C. Palmer and P. G. Vekilov, *Isr. J. Chem.*, 2021, **61**, 818–827.

Kevin Roberts commented: The transformation from the creation of intermolecular structures with short range order within the solution state and at the solution-mediated crystal growth interface, to that of the 3D periodic structures needed for the development of the bulk crystallographic structures, have a rate-limiting growth processes defined by the creation of stoichiometric periodic bonding chains (PBCs). As an example, the crystal structure of the dicarboxylic acid adipic acid $HOOC(CH_2)_4COOH$, has infinite chains of hydrogen-bonded carboxylic acid dimers which are PBCs and hence provide strong stoichiometric growth-promoting interactions. In contrast, the closely related monocarboxylic acid caproic acid ($H_3C(CH_2)_4COOH$) has a single ended molecular structure resulting in a PBC comprising of a combination of carboxylic acid hydrogen-bonded dimers (strong) and van der Waals interactions (weaker) which when combined have lower growth-promoting capability due to the weak link between the alkyl chain's terminal methyl groups. The latter are much weaker than the former and therefore are rate limiting to growth. I was wondering as to which of these two cases fit the compound you presented in your paper?

Peter Vekilov answered: As stated in our paper in this issue (**https://doi.org/10.1039/d1fd00080b**), crystal symmetry combines point symmetry elements, such as an inversion center, mirror planes, and rotation axes, typical of finite-size objects, with translation. Translational symmetry dictates exact rules for how a molecule in a crystal orients and positions with respect to any other crystal molecule. It arises during crystallization. The origin of point symmetry elements, however, is far less understood. The results that we present elucidate the origin of point symmetry, a subject of intense controversy in the literature. We show that in some cases molecular dimers that carry the structure of a unit in the crystal lattice may form in the solution and incorporate in the crystal as a whole. Clearly, the periodic bond chains that you allude to would form as the preformed dimer incorporates in the crystal lattice. Our results also argue that the formation of the PBCs is not the rate limiting step, which determines whether the crystal grows by incorporation of monomers, which are much more abundant in the solution, or of the minority monomers. We show that the preference for growth by dimers is dictated not by the faster (than that of monomers) incorporation of dimers at kinks, but rather by the greater energy of adsorption of the dimers on the terraces between steps. Owing to the energetically-favorable adsorption of dimers, the surface layer is enriched with dimers, and growth by incorporation of dimers is much faster than that by incorporation of monomers.[1]

[1] M. Warzecha, L. Verma, B. F. Johnston, J. C. Palmer, A. J. Florence and P. G. Vekilov, *Nat. Chem.*, 2020, **12**, 914–920.

Rachel Pooley asked: In the case of etioporphyrin I, you stated that from the measured kinetics of terrace growth, that the incorporating species on the (010) face are monomeric and on the (001) face the kinetics are consistent with a bimolecular reaction, corresponding to dimeric growth units. However, AFM scans as presented in Fig. 8 in your paper show step heights on the (001) face of EtpI of both double *and* single height, corresponding to dimeric and monomeric growth, respectively. There is also no significant difference between the growth rates of the double and single height steps. This suggests that monomeric growth must have some role to play in the growth of the (001) face. Conversely, in Fig. 9 of your article you present an analysis of the shape of the (001) surface, and present a hypothesis that " …monomers may be trapped in the dimples at the step edge and erect growth-incompetent configurations, whereas dimers, which fit seamlessly into the dimples, provide continuous growth." How can the observation of single height steps on the (001) face, growing at a comparable rate to the double height steps, be consistent with this assertion that the face is only growing by dimer inclusion and that monomeric species form a "growth incompetent configuration"?

Peter Vekilov responded: The structure of etioporphyrin I crystals (Fig. 4c in our article, **https://doi.org/10.1039/d1fd00080b**) suggests that a scenario, by which the step heights on the (001) and the (010) faces are equal to a dimension of solute dimers, would require a dimer structured as two monomers positioned next to one another in a single plane and with a minimal number of contacts. This is not the structure of the dimer predicted by all-atom MD simulations.[1] As expected, the etioporphyrin I dimer comprises two monomers positioned in two roughly parallel planes, an orientation, which maximizes the number and the strength of contacts between the two monomers. Furthermore, double height steps arise due to the dynamics of adjacent steps, some of which move slightly faster than others and catch up with them. In turn, the double height steps decay into single height steps. These observed behaviors imply that there are no fundamental differences between the mechanism of incorporation of solute molecules into steps of distinct height. Then the equal velocities of double and single height steps are evidence for step growth by direct incorporation of solute molecules and not by surface diffusion, as argued in the text of our article (**https://doi.org/10.1039/d1fd00080b**). Lastly, if we had a mixed mechanism of growth by incorporation of both monomers and dimers, the correlation between the step velocity and the solute concentration would be a power between one and two. It is, in fact, strictly quadratic on the (001) face and strictly linear on the (010) face.

1 L. Verma, M. Warzecha, R. Chakrabarti, V. G. Hadjiev, J. C. Palmer and P. G. Vekilov, *Israel J. Chem.*, 2021, **61**, 818–827.

Damien Thompson queried: Can you explain more about how your model predicts oligomer geometries in solution? Does solvent structuring around olanzapine play a role in stabilising the dimer? What solvent effect and/or olanzapine conformational effects block formation of higher-order structures, such as trimer, tetramer *etc.*?

Peter Vekilov responded: In the MD simulations, the two monomers on the way to forming a dimer were allowed all translational, rotational, and molecular degrees of freedom. We evaluated the free energies of all possible dimer conformations. We identified the conformation that is characterized with the lowest free energy. For olanzapine, the dimer configuration that occupies the minimum of the mean free force potential between the two monomers is identical to that in the crystals.[1] We never considered higher order oligomers. The similarity of the computer Raman spectra to those measured at higher olanzapine concentrations suggests that higher order oligomers are poorly represented in the solution. The simulations explicitly accounted for all atoms of two solvents, 1 : 1 water : ethanol mixture and chloroform. The similarity between the dimer structures predicted for these two relatively different solvents suggests that at least for olanzapine, the solvent properties exert small effects on the dimer structure.

[1] M. Warzecha, L. Verma, B. F. Johnston, J. C. Palmer, A. J. Florence and P. G. Vekilov, *Nat. Chem.*, 2020, **12**, 914–920.

Sten O. Nilsson Lill said: In your Raman DFT-models of olanzapine, it seems you didn't include water or solvent which are present in the experiment and also in the final crystal. Do you expect any impact on the results for the models by solvent inclusion or does it only affect higher wavenumbers?

Peter Vekilov replied: The models did consider the effects of the solvents.[1] We generated Raman spectra of olanzapine dissolved in ethanol and water and chloroform using COSMO (COnductor-like Screening MOdel)2 and the DMol3 module in Materials Studio. COSMO treats each solvent as a continuum with a permittivity ε surrounding the solute molecules outside of a molecular cavity.[2] COSMO derives the polarization charges of the continuum, caused by the polarity of the solute, from a scaled-conductor approximation. The computed and measured spectra of olanzapine in a water–ethanol mixture and in chloroform are similar, suggesting that the solvent effects are not very strong.

[1] M. Warzecha, L. Verma, B. F. Johnston, J. C. Palmer, A. J. Florence and P. G. Vekilov, *Nat. Chem.*, 2020, **12**, 914–920.
[2] A. Klamt and G. Schüürmann, *J. Chem. Soc., Perkin Trans. 2*, 1993, 799–805.

Adam Hill asked: Would you expect different results if you selected a solvent that specifically breaks up the observed dimers (*e.g.*, by forming strong aromatic interactions or strong hydrogen bonds with the monomers)? If so, could the differences (or similarities) in crystal growth behaviour in different solvents be used to further prove the reliance of the growth mechanism on preformed solute dimers or monomers?

Peter Vekilov answered: Absolutely. We in fact tried this experiment with olanzapine. An anhydrous form IV of olanzapine crystals, grown in a polymer dispersion, was found, in which olanzapine molecules are not arranged in dimers.[1] We wanted to study the growth mechanism of this form and the solute properties in the solution from which they grow, as a crucial benchmark for our studies. Unfortunately, our extensive efforts failed to produce stable crystals of olanzapine form IV. Differential calorimetry scans of the generated solids indicate the presence of crystals with a melting temperature equal to that of form IV. These crystals converted to the stable anhydrous form I, before we could record the powder X-ray diffraction pattern or the Raman spectra.

1 S. Askin, J. K. Cockcroft, L. S. Price, A. D. Gonçalves, M. Zhao, D. A. Tocher, G. R. Williams, S. Gaisford and D. Q. M. Craig, *Cryst. Growth Des.*, 2019, **19**, 2751–2757.

Kristen Fichthorn opened the discussion of the paper by Jeffrey Rimer: Polymers added to nanoparticle suspensions can cause depletion forces that induce aggregation of the nanoparticles. Do you think this could play a role in the systems you are studying?

Jeffrey Rimer replied: This is an excellent point. We do not believe that depletion forces are playing a large role in the observed aggregation of silica nanoparticles. This argument is based on the fact that we surveyed a number of different polymers and only observed this effect with one (PDDA). If depletion forces were acting upon silica nanoparticles, we would anticipate a more general phenomenon; however, we cannot rule out the potential that depletion forces have a small contribution. According to our hypothesis, we posit the concentration of (alumino)silicate nutrient species in the interstitial spaces of aggregated particles is higher than that of the bulk solution, which could facilitate faster rates of zeolite nucleation and crystal growth. Further experiments are required to identify what role (if any) depletion forces play in the observed aggregation of precursors with the addition of PDDA.

Christine Kirschhock said: Many authors suggest zeolite nucleation and growth is mediated by the liquid phase. Do you suspect the concentrations and speciation within the confined liquid in the pockets you create is different compared to the bulk liquid? May such an assumption explain your observations?

Jeffrey Rimer answered: This is an excellent question. The short answer is that we are not certain if there will be differences in the speciation of soluble (alumino) silicates between the bulk and pockets. Our expectation is that the confined volume could have a different level of supersaturation, which could, with the aid of polymers encapsulated within these spaces, direct the formation of distinct (alumino)silicate species. It is possible that these species could be a driving force that accelerates zeolite nucleation. This hypothesis is also qualitatively consistent with our observations for the effects of alkali infusion in amorphous precursors, which we discuss in a previous publication.[1]

1 H. Dai, J. Claret, E. L. Kunkes, V. Vattipalli, N. Linares, C. Huang, M. Fiji, J. García-Martinez, A. Moini and J. D. Rimer, *Angew. Chem., Int. Ed.*, 2022, **61**, e202117742.

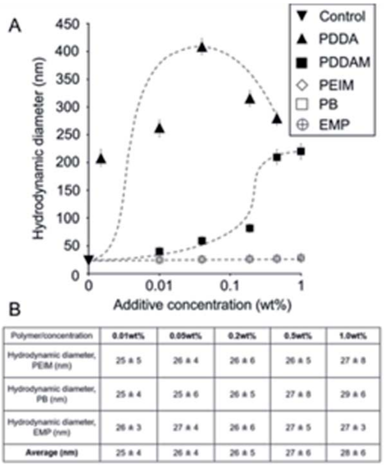
Michael Anderson commented: The driving force in zeolite crystallisation is driven by the difference in free energy between the gel and the zeolite (for a gel preparation). This will in large part be given by the Qn species in the gel which can be measured by ^{29}Si solid-state NMR? Is this something that you did?

Jeffrey Rimer replied: This is an excellent question. In our previous publication,[1] we performed ^{29}Si solid-state NMR on the fully crystalline samples instead of partially-crystalline materials to reveal if there is any pronounced effect of PDDA concentration on the final product. Characterization of partially crystalline solids extracted from syntheses using Si NMR is non-trivial and often leads to significant peak broadening. To this end, we used UV-Raman spectra to examine partially crystalline solids removed at different times of hydrothermal treatment. These measurements revealed a much faster (and progressive) development of peaks associated with 4- and 6-membered rings of the CHA framework structure when PDDA is present. The use of UV-Raman was a surrogate for powder XRD with the latter providing more accurate assessment of structure development to estimate the time of nucleation. We unfortunately do not have Si NMR data to gain more insight into the progressive changes in Qn species, but this information would indeed be very useful to determine how PDDA influences crystallization in ways that cannot be easily discerned by other techniques.

1 H. Dai, J. Claret, E. L. Kunkes, V. Vattipalli, N. Linares, C. Huang, M. Fiji, J. García-Martinez, A. Moini and J. D. Rimer, *Angew. Chem., Int. Ed.*, 2022, **61**, e202117742.

Marta K. Dudek asked: What do you think is the molecular mechanism of polymer-related enhancement in crystallization of zeolites? Or more specifically, why do you think PDDA polymer works and others not so much?

Jeffrey Rimer replied: We appreciate this question. The unique behavior of PDDA relative to the other polymers examined in this study is not well understood. PDDA induces bridging flocculation of precursors within a narrow range of polymer concentration, which accelerates nucleation. We also observe that PDDA can promote the precipitation of soluble silicates from light-scattering experiments. In our previous publication,[1] identical DLS studies were performed in solutions with pseudo monomer EMP and polymers PB, PDDAM, and PEIM. These studies were conducted over a range of modifier concentrations. The results showed that only one other additive (*i.e.* PDDAM) induced moderate particle aggregation (to a lesser extent than PDDA) at a concentration above the critical concentration of PDDA (please see Fig. S19, showing the comparison of PDDA and PDDAM reproduced from the supporting information of our previous work[1]). The other additives showed no appreciable change in the hydrodynamic diameter of dispersed colloidal silica particles. This indicates a uniqueness for PDDA; however, this cannot be solely associated with the quaternary ammonium functional group since other polymers possess the same functionality. We surmise that the structure of PDDA enables configurational degrees of freedom that facilitate the bridging of two or more colloidal particles. The mechanism for this mode of action is elusive, and would likely require more detailed investigation (*e.g.* molecular modelling) to elucidate the unique behavior of PDDA compared to other polyquats.



Polymer/concentration	0.01wt%	0.05wt%	0.2wt%	0.5wt%	1.0wt%
Hydrodynamic diameter, PEIM (nm)	25 ± 5	26 ± 4	26 ± 6	26 ± 5	27 ± 8
Hydrodynamic diameter, PB (nm)	25 ± 4	25 ± 6	26 ± 5	27 ± 8	29 ± 6
Hydrodynamic diameter, EMP (nm)	26 ± 3	27 ± 4	26 ± 6	27 ± 5	27 ± 3
Average (nm)	25 ± 4	26 ± 4	26 ± 5	27 ± 6	28 ± 6

Figure S19. (A) DLS measurements of colloidal silica particle size with different concentrations of polymer (PDDAM, PB, and PEIM) or monomer (EMP). Solutions were prepared with a diluted SSZ-13 synthesis gel composition in the absence of the Al source using the molar composition 1 SiO_2: 1 NaOH: 1760 H_2O: 0.1TMAda. Error bars span two standard deviations and dashed lines are interpolations to guide the eye. (B) Table for the overlapping data (PEIM, PB, and EMP) in panel (A) that exhibit no appreciable change in hydrodynamic diameter with increasing modifier concentration.

1 H. Dai, J. Claret, E. L. Kunkes, V. Vattipalli, N. Linares, C. Huang, M. Fiji, J. García-Martinez, A. Moini and J. D. Rimer, *Angew. Chem., Int. Ed.*, 2022, **61**, e202117742.

Christian Kuttner commented: I wonder if the molecular weight of PDDA plays a role in the formation and volume of the interstitial volume. The molecular weight of 150 kDa is quite high. What do you expect to happen when you reduce the molecular weight of PDDA chains?

Jeffrey Rimer responded: This is an excellent question. In our previous paper,[1] we tested the effect of PDDA molecular weight on the SSZ-13 crystallization time; however, we did not focus on smaller molecular weight, but rather compared three cases: monomer, 150 kDa PDDA, and 450 kDa PDDA. For the monomer and higher molecular weight polymer, the crystallization time was longer than that of the nominal case (150 kDa PDDA). As shown in our current manuscript (**https://doi.org/10.1039/d1fd00096a**), the monomer also results in a longer crystallization time than the optimal concentration of PDDA (150 kDa). It is uncertain if the crystallization time can be reduced even further by selecting a polymer in the range 50–100 kDa molecular weight. To our knowledge, these materials are not commercially available, but this question does pose an interesting topic for future investigation.

1 H. Dai, J. Claret, E. L. Kunkes, V. Vattipalli, N. Linares, C. Huang, M. Fiji, J. García-Martinez, A. Moini and J. D. Rimer, *Angew. Chem., Int. Ed.*, 2022, **61**, e202117742.

Jan Sefcik asked: Aluminium has to be present for the synthesis of zeolites; what would be a way to find out where aluminium is and what it does? It is well known that aluminium also plays an important role in aluminosilicate speciation in the liquid phase.[1,2] Are there models available that can capture the effects of alkali cations on aluminosilicate speciation to provide insight on how zeolite solubility and liquid phase supersaturation depends on liquid phase composition and specific cations?

1 J. Šefčík and A. V. McCormick, *Microporous Mater.*, 1997, **10**, 173–179.
2 J. Šefčík and A. V. McCormick, *Chem. Eng. Sci.*, 1999, **54**, 3513–3519.

Jeffrey Rimer responded: Experimentally it is possible to track the evolution of Al and aluminosilicate species using solution Al NMR. Elemental analysis by EDX or ICP of samples extracted at periodic times can also be used to track changes in Al concentration between solution and solid phases during zeolite synthesis. In the solid state, the scenario is more complicated and techniques such as EXAFS and pair distribution function (PDF) analysis can be used to investigate the local environment of Al species in the solid phase. Theoretically, models such as the one described in ref. 1 can also be used to assess changes in Al distribution. We were able to find a DFT[1] study and a mathematical model[2] that examined the effects of alkali cations on Al speciation in synthesis solutions.

1 J. D. Gale, A. L. Rohl, H. R. Watling and G. M. Parkinson, *J. Phys. Chem. B*, 1998, **102**(50), 10372–10382.
2 J. Provis and J. Van Deventer, *Chem. Eng. Sci.*, 2007, **62** (9), 2318–2329.

Ivo B. Rietveld opened the discussion of the paper by Mollie Trueman: The software that you have presented (**https://doi.org/10.1039/d1fd00097g**) is very interesting and it seems to me that it could also be used for teaching students crystallisation, or at least to help students understand the connection between a molecule and its crystal formation.

Could you tell me on which platforms this software can run? How many resources are needed to calculate the crystal growth (is it possible to run it on a laptop for example). What is your opinion about using the software within a teaching program for university students on crystallisation?

And my last question is because the presentation was mainly on modelling the crystallisation of zeolites, to what level is the software suitable to model crystallisation of molecular species (drug molecules for example)?

Mollie Trueman answered: The software is cross platform and has been tested on Linux, Windows and MacOS systems. It can operated either through the command line or through a graphical user interface (which is also cross platform). Simple simulations can be easily run using laptops. I think teaching would be a great application of CrystalGrower. I think it could be useful in explaining concepts such as the role of screw dislocations in crystal growth and the link between inter-molecular bonds and crystal shape. We would be happy to hear from you if you have any ideas on how this could be used in teaching! In terms of modelling crystallisation of molecular species, this is something we handle using individual molecules as growth units. When we look at zeolites, we assume each of the covalent interactions formed is of the same strength, which provides us a starting point for our interaction strength. Finding the interaction strength in molecular crystals is more challenging, since it usually involves a larger number of interactions with variable strength. We attempt to fit these to experimental data, but the larger the number of interactions, the more difficult this process becomes. We're working with theoretical groups to develop methods which we hope will allow for prediction of interaction strengths in these systems.

Adam Hill queried: Could you comment on what systems this approach to disorder could be extended? Could you model the morphological effect of substitutional defects in systems such as solid solutions?

Mollie Trueman answered: This approach for modelling disorder could be adapted to substitutional defects fairly easily. In order to handle stacking faults we had to encode a system which allowed multiple growth units to compete for the same growth site. This could easily be adapted to a system containing substitutional defects.

Michael Anderson asked: Are you able to use the CrystalGrower software to look at dendritic growth by incorporating diffusion limitations?

Mollie Trueman responded: Currently this is not possible in the software since we simplify the solution phase to be parameterised by a single value (the $\Delta\mu$ parameter). This simplification allows us to run simulations to micron sizes but restricts us from handling situations where mass transfer plays a role in determining crystal shape. In order to handle dendritic growth we would need to reconsider how we handle the liquid phase, and this is something we would be keen to explore in future work.

Jutta Rogal asked: In KMC simulations, if you have the correct rate constants for the processes, you recover the appropriate timescale; considering the approximations that you make for the attachment/detachment probabilities, is the timescale in your simulations sensible and how does it compare to experimental timescales?

Follow up: if you are fitting the probabilities to, for example, match experimental growth rates, how confident are you that you capture all important processes?

Mollie Trueman said: Timescales recovered agree fairly well under most growth conditions, but under conditions of high supersaturation agreement is poor. We do not believe we fully capture all important processes, for example we neglect mass transfer in the solution phase and do not account for non-classical processes. Whilst we do not believe these factors are likely to have a major impact on the systems studied in this paper we do hope to incorporate these factors into our model in later work.

Ruel Cedeno queried: In the CrystalGrower program, what experimental data are required as input to the model? Do you fix which facets appear in the final form? How does the model account for the different growth rates of each facet (anisotropy)?

Mollie Trueman responded: We do not fix which facets appear in the final form. The input consists of a connected net of growth units and interactions, which are then used to simulate crystal growth using a classical Kossel-style model. The difficulty lies in identifying sensible values to use as interaction strengths in the net, since these contain components from bonds formed within the crystal structure as well as an offset which corresponds to desolvation of the growth unit. Here we use experimental data to help us arrive at values which agree with what we see experimentally and can be used in further simulations.

Christine Kirschhock asked: You indicated that the normal approach to CrystalGrower depends on a cif file which extracts the topology. However, zeolites can create intergrowth, which cannot be described by a single periodic crystal structure. Examples are zeolite beta and zeolite W. Especially in the case of zeolite W, the MER/PHI intergrowth also leads to combination of tiles of the two parent topologies, using half tiles of the two frameworks. How do you implement this difficulty in your modelling?

Mollie Trueman replied: In previous work from our research group, we have used AFM to study the surfaces of zeolites and other porous materials and found that step heights at surfaces correlate to complete cages.[1,2] This suggests these cage-like units represent sensible growth units for growth simulations. In our methodology, partitioning of zeolite crystal structures into these closed cages can be achieved through an interface with the software ToposPro,[3] which applies a natural tiling algorithm to identify closed cage structures. In the case of intergrown phases, this methodology falls apart since each structure has its own set of cages and these often do not tesselate with one another. In the structures discussed in this work, and in the case of the PHI/MER system, growth units must be selected carefully such that they are common to both of the intergrowing crystal phases, such as the half tiles you describe for zeolite W. Currently we do not have an automated way to identify such units, and it is necessary to manually produce input files for CrystalGrower in order to simulate growth in these cases.

1 P. Cubillas and M. W. Anderson, in *Zeolites and Catalysis*, Wiley-VCH Verlag GmbH and Co. KGaA, Weinheim, Germany, 2010, pp. 1–55.
2 R. Brent, P. Cubillas, S. M. Stevens, K. E. Jelfs, A. Umemura, J. T. Gebbie, B. Slater, O. Terasaki, M. A. Holden and M. W. Anderson, *J. Am. Chem. Soc.*, 2010, **132**, 13858–13868.
3 V. A. Blatov, A. P. Shevchenko and D. M. Proserpio, *Cryst. Growth Des.*, 2014, **14**, 3576–3586.

Jeffrey Rimer commented: Given that many zeolite mechanisms involve multiple growth units, particularly the dominance of nonclassical pathways where oligomers or particles can play a role in synergy with monomers, is the CrystalGrower software capable of modelling different growth units or multiple pathways simultaneously? Is it possible to speculate on how the results would potentially be altered by inclusion of more complex growth units?

Mollie Trueman commented in reply: I think this is a really important question and currently this is not something we can consider easily in our growth model. Given the growing evidence that particle attachment plays a role in the growth of zeolites (and other materials) it's clearly an important omission and something we need to consider incorporating in future work. Incorporating non-classical pathways into simulations would likely require reassessing how we handle the solution phase in simulations. Currently we use the simplification that the growth solution has a single, homogeneous driving force for attachment at all points on the surface. Although this simplification lowers the computational load and allows us to explore how the surface might look at larger length scales than typical computational methods, it compromises accuracy. Attempts to incorporate non-classical pathways, could potentially involve adding local regions of high supersaturation at surfaces to mimic particle attachment (although whether this would accurately describe the growth pathway is unclear). To speculate how this might influence results, these local regions of high supersaturation could lead to higher rates of 2d nucleation which would in turn result in a higher level of defects formed at the points where growth fronts meet one another. If these pathways were active on some facets, but not others, this may enhance the 'zoning' effect we see, where growth off certain facets gives rise to regions of the crystal with higher levels of defects. Whilst I think this would be an interesting avenue to explore, I feel we need greater understanding of how crystal growth by particle attachment occurs to accurately include this pathway in our model, and to fully understand how non-classical growth modes influence the resulting crystal.

Connor Hewson asked: Do you think this modelling software could be capable of accurately determining the BET surface area of large macromolecules like zeolites? Especially when large surface area materials are hard to define experimentally.

Mollie Trueman answered: The simulations we run can predict the presence of defects and mesoporosity – both of which will have consequences for the BET surface area in the materials. Whilst this may allow us to predict trends in how we would expect the BET surface areas to vary, we do not believe we are at a point where this data can be used to predict surface areas accurately. This is due in part to difficulties in defining these values experimentally, but also to the high sensitivity of these values to experimental conditions.

Fiona Meldrum suggested: Have you considered analysing your crystals using a high resolution tomography technique such as X-ray ptychography? Resolutions of 10 nm can be achieved on optimal samples as large at 10 microns.

Mollie Trueman replied: This is something we are looking into and hope to do in the future! We're hoping to use either X-ray or electron tomography to map the mesoporosity in zeolite beta crystals.

Alan Hare commented: It may be foolhardy of me to take silica out of a discussion about aluminosilicate crystals(!) … but as the rôle of aluminal species did not seem crystal clear, I thought I would comment as to some that might be active. Delegates at the *Faraday Discussions* meeting at UCL in 2007 will recall Akihiro Wakisaka's presentation[1] of the mass spectrometric experiment, electrospray ionisation (or ESI), which shed light on alkali metal chloride nucleation.

Later, inspired by this paper, I was able to reinterpret mass-to-charge ratio values (m/z) arising out of aluminium salt solutions. Admittedly with silica absent, the experiment in nitrate and chloride solutions[2] revealed a variety of aluminium(III) cations, including a monomer, dimer (several dimers, in fact), trimer, tetramer and pentamer.[3] While ambiguity of the m/z value mitigated

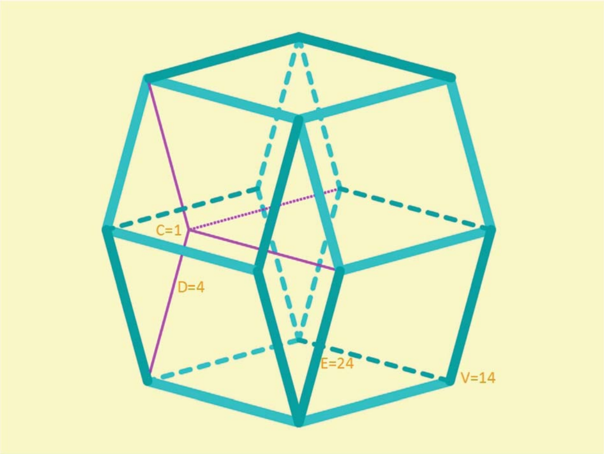


Fig. 1 A rhombic dodecahedron. A dodecahedron of the Biliński kind comprises four golden rhombohedra, two prolate and two oblate. With cations at its vertices (one internal), the Keggin structure may be formulated as a special case that can be identified with an Al_{13}^{3+} tridecamer in which the central aluminate tetrahedron $[AlO_4]^{5-}$ is caged. Like the cube – and unlike the sphere – the Biliński is a 3-d space-filler. When Aristotle allegedly mistook the tetrahedron (which like the cube is a Platonic solid) for a space-filler, could he have foreseen what Stanko Biliński first recognised only as recently as 1960?

against identification of a cyclic hexamer, its existence was not disproved. But neither was a linear hexamer prominent, nor indeed any likely $Al_nO_p(OH)_q(OH_2)_r^{(3n-2p-q)+}$ oligomer with $n > 6$ below $n = 13$. The pentamer and one particular dimer may be of interest: $Al_5O_4(OH)_6(OH_2)_2^{+}$ and $Al_2(OH)_4(OH_2)_2^{2+}$, respectively (each of these species was identified unambiguously, and both appeared to be tetrahedral). The former species may attach four of the latter – the OH^- or $[Al(OH)_4]^-$ ion seemingly playing an important role in the process – giving rise to a tridecameric polycation $[AlO_p(OH)_{4-p}][Al_3(OH)_{6+x}(OH_2)_{3-x}]_4^{(11-p-4x)+}$ such as the tripositive $[Al_3(OH)_8(OH_2)]_4[Al(OH)_4]^{3+}$ ($p = 0$, $x = 2$) or $AlO_4[Al_3(OH)_7(OH_2)_2]_4^{3+}$ ($p = 4$, $x = 1$). The tetrahedral structure of the tridecamer (see Fig. 1 attached, below) could stabilise octahedral trimer chains, offering plenty of space for choride or nitrate anions to surround it. This would explain its long-term persistence reported in quasi-amorphous alumina[2] and its inhibition in the sulfate case. Of course, this is not to say that these species will necessarily populate an aluminosilicate system. But it is not beyond all credibility to suggest that, prior to formation of the zeolite framework, one or two of the smaller cations – monomer, dimer or trimer, perhaps – could play a part in its nucleation.

1 A. Wakisaka, *Faraday Discuss.*, 2007, **136**, 299–308.
2 T. Urabe and M. Tanaka, *Rapid Commun. Mass Spectrom.*, 2011, **25**, 2933–2942.
3 A. S. Hare, *RSC Adv.*, 2016, **6**, 86540–86559; Correction, 2017, **7**, 7694.

Conflicts of interest

There are no conflicts to declare.