

PHYSICAL CHEMISTRY

Did life grind to a start?

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Many solids can adopt two mirror-image crystal forms, and often grow as mixtures of both. A curious mechanism of crystal growth might explain why some mixtures convert into one form when subjected to grinding.

If Alice had been a biochemist, she would have found an even more unfamiliar world on the far side of the looking-glass. In principle, the molecules of life can adopt two mirror-image forms (often described as left- and right-handed), which from a chemical perspective are equally likely to exist. Yet all biological molecules on Earth adopt a single handedness, even though their reflections in Alice's looking-glass world should function just as well. Did the machinery of early life impose the observed bias, or was the development of life favoured by a pre-existing pool of single-handed molecules? And if the latter is true, how could this pool have formed?

One explanation could be that a fundamental physical bias exists that generates an excess of a particular molecular handedness. Proposed theories invoke the weak nuclear force, or the action of 'circularly' polarized light somewhere in the Universe. But these influences would be far too weak to explain the existence of a single molecular form. So, if a pool of single-handed molecules existed on prebiotic Earth, it must have developed from a mixture containing almost equal numbers of mirror-image forms where the excess of the major form was amplified dramatically. Reporting in the *Journal of the American Chemical Society*¹, and at a meeting at the Nordic Institute for Theoretical Physics in Stockholm², Noorduin *et al.* describe a remarkably simple

system for the spontaneous amplification of molecular handedness — stirring a slurry of crystals in the presence of glass beads.

More than 50 years ago, the theoretical physicist Charles Frank addressed the existence of single-handed biomolecules in what became a much-cited paper³. He commented: "I have long supposed that this was no problem on the basis of a supposition that the initial production of life is a rare event." He went on to prove mathematically that, in a system containing

entities that both copy themselves and destroy their mirror images, an initial random event that provides a tiny excess of one hand would necessarily lead to the exclusive occurrence of that form, even if mirror-image versions could also form randomly. He concluded: "A laboratory demonstration may not be impossible." This seminal paper was Frank's sole contribution to biology — he is better known for his insights concerning the mechanisms of crystal growth. He might have been gratified to learn that his own field is supplying increasingly convincing laboratory demonstrations to support his biological model.

The first such demonstration came in 1990 with the report⁴ that a highly concentrated solution of sodium chlorate (whose dissolved molecules have no handedness) deposits crystals of a single mirror-image form on cooling, if stirred. This phenomenon was soon understood to involve the random formation of a single crystal of arbitrary handedness, from which seed crystals of the same handedness were broken off by the stirrer^{5,6}. A feature of this 'secondary nucleation' mechanism is that only crystals larger than a certain critical size will grow; smaller crystals dissolve, because a higher proportion of their molecules occupy unstable positions at the crystal surface. The critical size is inversely related to the concentration of the solution. Because the initial fortuitous growth of crystals of one handedness reduces the concentration of the surrounding solution, the formation of mirror-image crystals that are large enough to grow becomes impossible.

To obtain single-handed crystals of sodium chlorate by secondary nucleation, a single seed crystal is required, and the solution must begin in a so-called supersaturated state, which is far from equilibrium. But in 2005, it was discovered that single-handed crystals of sodium chlorate could be obtained from a slurry of mixed mirror-image crystals in a saturated solution⁷ (a system near to equilibrium). If there was an excess of one crystal form in the solid material, simply stirring the slurry resulted in complete conversion of the crystals to the dominant form, even if the initial excess was only a few per cent. The secret of this success was to add glass beads, which continually grind the crystals during stirring. As the starting conditions in this system are so different from those required for secondary nucleation, the mechanism must be different.

Noorduin *et al.*¹ now show that the grinding method works for a different compound — an amino-acid derivative. This may not seem like big news, but there is a crucial distinction from the previous work. Unlike sodium chlorate, the amino-acid derivative retains its handedness in solution,



Figure 1 | Molecules through the looking-glass. The molecules of life in Alice's looking-glass world would be mirror images of those in ours, and should work just as well. So why don't they exist?

although the mirror-image molecules do inter-convert slowly when the solution is basic. For this reason, a base was required, as well as glass beads, to obtain single-handed crystals in the new system. But for the conversion to work, a seemingly unlikely condition must prevail: the concentration of molecules dissolved from the smaller component of the solid must be greater than that of molecules from the larger component.

The mechanism underlying this remarkable behaviour is unknown. Noorduin *et al.*¹ propose that 'Ostwald ripening' — the growth of large crystals at the expense of smaller ones — might be a crucial factor. Alternatively, a theory⁸ proposed to explain the conversion of sodium chlorate crystals to a single-handed form might also apply here. This theory concerns tiny crystal fragments chipped from the larger, growing crystals — fragments that are small enough to be subcritical (and thus expected to dissolve), but large enough to retain their handedness. Chipping off such fragments artificially accelerates the dissolution of the larger crystals. But the acceleration is reduced if the fragments are rescued from dissolving by merging with larger crystals of the same hand.

If this explanation is correct, then subcritical fragments that can be incorporated into the dominant population of crystals have more chance of being saved from dissolving than their mirror images (for which fewer rescuing crystals exist). For the dominant crystals, this selective reincorporation is particularly effective at reducing the portion of their dissolution that is induced by grinding. Abrasion therefore speeds up the net dissolution of the minor population of crystals; once dissolved, their molecules convert into their mirror-image form, thereby feeding the growth of the major population of crystals. This process also satisfies the curious requirement for the concentration of the dissolved molecules from the minor population of crystals to be higher than that of the dissolved molecules from the major population of crystals.

Crystals from the smaller population eventually convert completely into the same form as the larger population, in a process that actually accelerates as the conversion proceeds (unlike most spontaneous transformations). The conversion is entropically unfavourable, but grinding supplies the energy needed to overcome this obstacle.

Were Frank alive today, he would be delighted by these observations, because the crystallization fits his model for amplification of a single-handed entity: the major crystals catalyse their own production by capturing fragments destined for dissolution; and they catalyse the destruction of their mirror image by capturing more molecules from solution than they contribute to it.

It is impossible to say whether grinding of crystals in a prebiotic world, perhaps by wave-tossed sand, might have supplied single-

handed molecules to support early life. Nevertheless, Noorduin and colleagues¹ might have provided dramatic evidence to support the idea that substantial clusters of molecules can be incorporated intact into existing crystals. Their report suggests new opportunities for manufacturers of pigments or pharmaceuticals who must prepare solids in only one of several possible crystal forms. Furthermore, grinding is arguably the first original method for isolating single-handed crystals from a mixture of mirror-image forms since Pasteur used tweezers to effect such a separation in 1848. ■

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