Ostwald Ripening, Chiral Crystallization, and the Common-Ancestor Effect

Julyan H. E. Cartwright,[1] Oreste Piro,[2] and Idan Tuval[3]
[1]*Laboratorio de Estudios Cristalográficos, CSIC, E-18100 Armilla, Granada, Spain*
[2]*Institut Mediterrani d'Estudis Avançats, CSIC-UIB, E-07071 Palma de Mallorca, Spain*
[3]*DAMTP, Centre for Mathematical Sciences, University of Cambridge, Cambridge CB3 0WA, United Kingdom*
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We introduce an agent-based model for advection-mediated chiral autocatalysis in which we take into account dissolution-crystallization processes through Ostwald ripening. We demonstrate that the latter phenomenon is the key to explaining previously puzzling experimental results whereby complete chiral symmetry breaking is attained from an initially unbiased mixture of seed crystals. We show that this homochirality is achieved by what has been termed the common-ancestor effect: Ostwald ripening removes competing lineages, leaving only one common ancestor for the entire system.

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Many chemical compounds, including the vast majority of those that figure in the biochemistry of living organisms, exist in two mirror-image versions: They are, in Kelvin's coinage, chiral [1]. While abiotic chemical reactions typically produce statistically equal amounts of each enantiomer, or handed version of a molecule, one of the most marked attributes of living matter is that it is composed of only one of the possible enantiomers of each of its component molecules; it is homochiral. A principal concern of studies into the origin of life has been to understand the source of this symmetry breaking. Moreover, it is of interest to the pharmaceutical industry to be able to produce a given enantiomer of a particular compound, as the different enantiomers have varying biological effects, and, on occasion, one may be beneficial but the other harmful; such was the case with the thalidomide disaster.

A striking example of chiral symmetry breaking of some relevance to the above was first observed by Kondepudi and co-workers [2]: If one stirs the container of certain chiral chemical compounds crystallizing from solution or from the melt, one of the two enantiomers predominates, although without stirring, both are formed in equal proportions. In previous work [3], we constructed a minimal model for chirality selection in crystallization by building upon the work of Metcalfe and Ottino on nonlinear autocatalytic processes in flows [4], to which we added a simple but realistic model for the physics of crystal nucleation and growth. We explained the mechanism on the microscale of the symmetry breaking in chiral crystallization in terms of the growth of tiny whisker crystals on the surfaces of the larger crystals and the ease with which they could be broken off to form further crystal nuclei, and we showed simulations producing large but not complete symmetry breaking. These reproduced the results of experiments starting without seed crystals and finishing with a large, but not complete, preponderance of one of the two chiralities [2]. More recently, however, experiments of Viedma have shown how total symmetry breaking—complete chiral purity—can be achieved [5]: These begin with many seed crystals of both chiralities but end with all crystals possessing a single chirality; none remain of the opposite chirality. In these, in contrast to the earlier experiments, there is vigorous agitation with glass beads within the container during crystallization.

Here, using an agent-based approach, we construct a model that explains these new experimental results. We incorporate the microscopic dynamics of crystallization as behavior rules of the individual crystals—the agents—in interaction with an advective medium. In the internal dynamics of the agents, we introduce Ostwald ripening [6]. Ostwald ripening is a ubiquitous phenomenon of coarsening occurring in the late stages of phase separation and domain growth processes. In crystallization, it is the process in which large crystals grow at the expense of smaller ones that shrink and ultimately disappear or denucleate. The classical physical model of Ostwald ripening, the Lifshitz-Slyozov-Wagner theory [7,8], predicts that the crystal size distribution should evolve asymptotically to a unique scaling form in the limit when the dense phase volume fraction tends to zero. Here we are not so much interested in the distribution of sizes but in the interplay between the dynamics of Ostwald ripening and chiral crystallization. Thus, we are fundamentally concerned with denucleation; this is the critical aspect of Ostwald ripening in chiral crystallization, as only through the disappearance of small crystals can we achieve chiral purity. Beyond explaining the specific experiment detailed above, our results demonstrate that Ostwald ripening is a general nonlinear dynamical process capable of driving symmetry breaking to completion and that this operates through what has been termed the common-ancestor effect [9]: the removal of competing lineages to leave just one common ancestor for the entire system.

We model chaotic journal-bearing flow, the time-periodic Stokes flow of a viscous incompressible Newtonian fluid in the gap between two eccentric cylinders. This is a well-known, experimentally realizable system with an analytical solution for the stream function [10]. The fact that a chaotic flow can easily be generated by rotating the cylinders in a time-periodic fashion makes it a convenient prototype for studying mixing phenomena. The geometry of the flow domain is characterized by two dimensionless parameters: the ratio of the radii of the inner and outer cylinders R_i/R_o and the dimensionless eccentricity $e = D/R_o$, where D is the distance between the centers of two cylinders. A periodic flow is induced by rotating the cylinders using a discontinuous two-step protocol: During the first half-period, the outer cylinder is rotated while the inner remains stationary; in the second, the outer cylinder is fixed and the inner one rotates. In the Stokes approximation, the fluid motion is completely determined by the rotation angles of the cylinders. Thus, the flow protocol can be described by two further dimensionless parameters: the rotation angle Θ of the outer cylinder and the ratio $\Omega = \Omega_i/\Omega_o$ of the rotation angle of the inner cylinder to that of the outer. In all of our simulations, we set the geometric parameters to $R_i/R_o = 1/3$ and $e = 0.3$ and the ratio of the rotation angles to $\Omega = -3.0$.

Into this flow we insert an agent-based model for chiral crystallization from an achiral solution. This implies incorporating the physics of the three stages in this phase transition: crystal nucleation, growth, and ripening. First, crystal nucleation requires overcoming a certain energy barrier [11], whose height is a function of the concentration of the solution; a supersaturated solution, concentrated beyond its saturation point, is a system metastable to nucleation. Nucleation from the solution is termed primary nucleation, while, with a solid surface already present, less energy is required to surmount the barrier, and, thus, the presence of one crystal facilitates the production of others; this is termed secondary nucleation. In chiral crystallization, primary nucleation produces nuclei of either chirality, while secondary nucleation gives nuclei of the same chirality as the mother crystal. Next, crystal growth proceeds by the incorporation of growth units (molecules, ions, atoms, etc.) from the solute into the crystal, thereby depleting the surrounding solution of solute. In chiral crystallization, secondary nucleation and growth couple to amplify small initial fluctuations in the concentrations of the enantiomers. The mechanism, suggested by Frank [12], has a nonlinear dynamics, a form of autocatalysis in which each enantiomer catalyzes its own production while suppressing that of its mirror image. Last, the physics driving Ostwald ripening is the minimization of the interfacial energy of the system—expressed by the Gibbs-Thomson equation [11]—by reducing the total interfacial area. Smaller particles have greater surface energy, so are more soluble. Hence, coarsening occurs via smaller crystals dissolving and the liberated solute being incorporated into larger crystals. On a molecular level, growth units transfer from smaller crystals to larger crystals through the medium of the solution. This mass transfer via the intervening medium is what drives all systems that display Ostwald ripening. However, in a stirred system such as this, transport is dominated by convection rather than by diffusion; in contrast to the more commonly studied regime, this is Ostwald ripening at a high Péclet number.

We simulate this physics with a minimal agent-based model. A large number n of solute particles S are initially distributed uniformly throughout the domain and are advected passively, that is, without affecting the underlying flow. We allow a certain probability of a solute particle nucleating into a primary crystal. For this, we define the primary nucleation flux p as the fraction of primary crystals produced per period of the flow. We consider crystals $C_{k,i}$ as agents having an internal state—a chirality k, either L (laevo) or D (dextro), and a size, represented by an integer i—and subject to behavior rules that modify this state according to the environmental conditions. Primary nuclei are randomly assigned one of the two chiralities, and the crystal size is set to one in the process $S \rightarrow C_{k,1}$. When a crystal $C_{k,i}$ of size i comes within a distance δ of a solute particle S, the crystal adsorbs the solute and increases its size by one in the growth process $C_{k,i} + S \rightarrow C_{k,i+1}$. On the other hand, when a crystal passes through a region of sufficiently high shear, a number of secondary nuclei break off from it, and the size of the mother crystal diminishes accordingly. Secondary nucleation depends on the shear stress σ in the flow and, therefore, on the parameters that define the flow itself. We need to set the minimum shear stress σ_0 needed to break a secondary nucleus from a mother crystal. However, as we are allowing ourselves to vary Θ, we can renormalize σ_0 to unity. The secondary nuclei produced have the same chirality as their parent, following the rule $C_{k,i} \rightarrow C_{k,i-s} + sC_{k,1}$, where the number of secondary nuclei $s = \min[\mathrm{integer}(\sigma/\sigma_0), i-1]$ is proportional to the local shear stress and is bounded to be less than the size of the crystal itself. They are placed randomly within a circle of radius δ from the mother crystal. Last, we assume that the smallest crystals—those of size 1—can dissolve into the achiral solute phase through Ostwald ripening: $C_{k,1} \rightarrow S$. This allows the recycling of crystallites when they reach the achiral molecular level. The model has two further parameters: η_T, the number of times we check for interactions per period of the flow (but the results are independent of this once it is large enough), and the interaction distance δ. We can relate the choice of this microscopic length scale to macroscopic quantities; we take $\delta = 2^{3/2}n^{-1/2}$, which corresponds to the mean distance between solute particles. If we varied δ, we would explore the limits of dilute and densely packed systems, but in all simulations here these parameters are set to $n = 7000$, $\eta_T = 1000$, and $\delta = 0.03$. In summary, once we fix all of the geometrical and computational parameters, our model depends only on two parameters: the rotation angle Θ and the primary nucleation flux p. In the simulations herein, we have explored $\Theta \in [\pi/2, 15\pi]$ with $p = 0.05$; in earlier work without Ostwald ripening, we explored $p \in [0.01, 0.5]$ [3]. We have described the model in the context of crystal growth from solution to correspond with the experiments of Kondepudi *et al.* [2] and Viedma [5] on sodium chlorate crystallization. But it can also be applied to chiral symmetry breaking in the context of crystal growth from the melt, such as in the work on 1,1′-binaphthyl crystallization [3,13,14].

In order to analyze the effect of Ostwald ripening on the symmetry-breaking events that take place during stirred chiral crystallization, we compare the time evolution of the enantiomeric excess in three different situations. The enantiomeric excess is defined as $\varepsilon = (N_D - N_L)/(N_D + N_L)$, where N_D and N_L are the numbers of crystals of each enantiomer, and it provides a good measure to quantify the symmetry breaking. We display in Fig. 1 results obtained in the following three cases: first, a modified Metcalfe-Ottino model in the presence of primary nucleation, second, our model of chiral autocatalysis through secondary nucleation, and, finally, our model in the presence of Ostwald ripening. In the first case, primary nucleation is the dominant effect, as is made obvious by the low value of the enantiomeric excess. In contrast, with secondary nucleation this increases to a range in which symmetry breaking is clearly acting; secondary nucleation is sufficient to achieve high values of the enantiomeric excess even at large supersaturation. Nevertheless, these high values are still far from chiral purity. The addition of a denucleation process dramatically changes the results; in the presence of both secondary nucleation and Ostwald ripening, homochirality is now easily achieved. This is revealed by ε saturating to a value very close to 1.

This overwhelming asymptotic dominance of one of the species can be enhanced even more dramatically by increasing the chaoticity of the flow. This is exhibited in Fig. 2, where the limiting enantiomeric excess is plotted against the total rotation angle per cycle, which is the parameter that controls the chaotic character of the flow and thereby the secondary nucleation rate. For both the model with and that without Ostwald ripening, the enantiomeric excess after a fixed number of periods increases as we increase the secondary nucleation rate. But, while in the absence of a coarsening process ε saturates at an intermediate value, with Ostwald ripening it practically reaches one—complete chiral purity—when the chaos of the flow is strong enough. Notice that Fig. 1 shows the evolution of the enantiomeric excess for a fixed value of the total rotation angle Θ of 3π, which is at the borderline of complete homochirality. Nevertheless, for this value of Θ, we already have $\varepsilon = 0.98$, to be compared with 0.73 obtained in the case without Ostwald ripening.

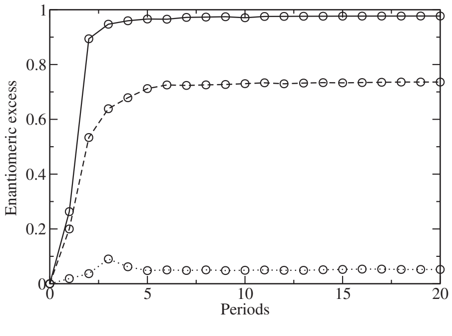

FIG. 1. Enantiomeric excess ε against the number of flow periods for fixed $\Theta = 3\pi$ provides a comparison of three models for chiral symmetry breaking in crystallization in the case of a high primary nucleation rate: with solely primary nucleation (dotted line), with secondary nucleation included (dashed line), and finally with the addition of Ostwald ripening (solid line).

It is a remarkable fact that the reported evolution of the enantiomeric excess is similar even if large numbers of both enantiomers are initially present in the system. Instead of starting the simulation from an initial condition without crystals present and letting the crystals appear through primary nucleation, we now model the recent experiments of Viedma [5], wherein the initial condition is a mixture of approximately equal numbers of crystals of both chiralities. In Fig. 3, we show that, after a few periods of the flow, one or the other chirality completely monopolizes the system, as was found to occur in these experiments.

It is clear that, in the system without Ostwald ripening, since a crystal cannot disappear once it has formed, the chiral mixture present at the finish is derived from the crystals independently nucleated in the initial phase, when the supersaturation allowed primary nucleation to take place. We could imagine, if there were just one primary nucleation event, an entire experiment dominated by the chirality of a single mother crystal, leading to complete homochirality. This phenomenon does not occur in the simulations we present here of the model without Ostwald ripening; to produce it, we have to either decrease the domain size or increase the mixing, as we demonstrated in our earlier work [3] (see Fig. 2 therein). However, upon including Ostwald ripening, it is much easier to achieve homochirality. Indeed, Viedma [5] notes that there is strong crystal recycling—that is, Ostwald ripening—in his experiments whose outcome is homochirality. But he states that this achievement of complete chiral purity is "incompatible with the hypothesis of an initial single chiral phase or 'mother crystal'." In fact, the reverse is true: Figure 4 demonstrates that Ostwald ripening coupled to the nonlinear growth dynamics removes competing lineages from the system and allows just one to monopolize it, so that, by the time that ten flow periods have passed in Fig. 4, only one crystal lineage remains.

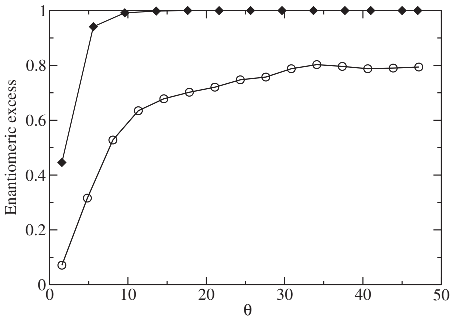

FIG. 2. Enantiomeric excess ε for different values of the total rotation angle $\Theta \in [\pi/2, 15\pi]$, both with (solid diamonds) and without (open circles) Ostwald ripening.

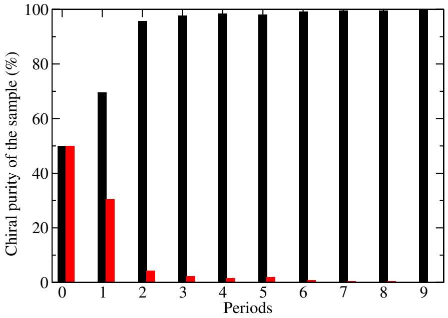

FIG. 3 (color online). Initially symmetric mixtures of D and L crystals show total symmetry breaking and chiral purity after a few flow periods in the presence of Ostwald ripening. The homochirality is L or D randomly.

We began by remarking upon the emergence of homochirality in living organisms. Cairns-Smith dubbed this the common-ancestor effect [9] and introduced a thought experiment to explain it consisting of 100 balls in a box. The binary version of his experiment uses two colors of balls; at each step, we throw away at random half of the balls and duplicate those that remain. He points out that, after some time, all of the balls in the box will be of the same color. It is clear that such a random-culling model will produce homochirality, which was Cairns-Smith's point in introducing it. However, Ostwald ripening coupled to the Frank dynamics is a much more efficacious process for producing the common-ancestor effect, the achievement of homochirality in crystallization, and, in general, the attainment of complete symmetry breaking in systems in which it operates. The counterintuitive result is that, through the removal of competing lineages, Ostwald ripening produces more efficiently what we previously dubbed an ancestral Eve [3], a common ancestor for the entire system.

Ostwald ripening occurs in phase transitions with both solid and liquid precipitates—in crystallization, in emulsions, in foams, etc.—but the notion of an object possessing a greater amount of some attribute growing at the expense of one having less of the same has a nonlinear dynamics that can be seen operating in many fields. Beyond physics, it can profitably be applied to biological, economic, and social systems. For example, the process of the rich getting richer and the poor getting poorer that occurs in some economic systems is also Ostwald ripening, as in sociology is rural depopulation. As in chiral crystallization, Ostwald ripening may couple to further nonlinear dynamics to produce counterintuitive results. We should, however, take care to distinguish Ostwald ripening from other phenomena. It should be differentiated from coalescence; in phase transitions in physics, Ostwald ripening involves feeding a larger particle at the expense of a smaller one by molecular diffusion through the continuous phase. Coalescence, sometimes termed Smoluchowski ripening or coagulation, is a different mechanism by which particles grow by fusing together. Similarly, we can conceive of both Ostwald ripening and coalescence in an economic system: A small company can go bust and its business be picked up by its larger competitors (Ostwald ripening), or it can be taken over by a larger competitor (coalescence). Nor is Ostwald ripening merely random culling but the removal of the very smallest from the system to allow those larger than them to grow. The concept is clearly rather general, and awareness of it very ancient, as we find it mentioned, for example, in Christian scripture: "For unto every one that hath shall be given, and he shall have abundance: but from him that hath not shall be taken away even that which he hath" [15].

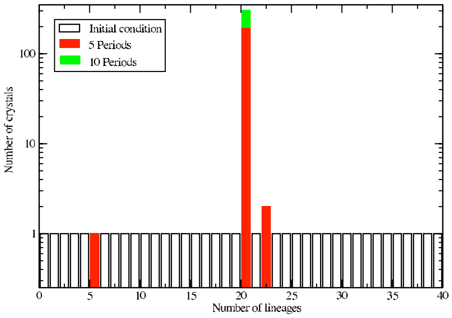

FIG. 4 (color online). The evolution of lineages from different primary nucleation events; with Ostwald ripening, competing lineages die out to leave just one common ancestor.

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[1] Lord Kelvin, *Baltimore Lectures on Molecular Dynamics and the Wave Theory of Light* (Cambridge University Press, Cambridge, England, 1904).
[2] D. K. Kondepudi, R. J. Kaufman, and N. Singh, Science **250**, 975 (1990).
[3] J. H. E. Cartwright, J. M. García-Ruiz, O. Piro, C. I. Sainz-Díaz, and I. Tuval, Phys. Rev. Lett. **93**, 035502 (2004).
[4] G. Metcalfe and J. M. Ottino, Phys. Rev. Lett. **72**, 2875 (1994).
[5] C. Viedma, Phys. Rev. Lett. **94**, 065504 (2005).
[6] W. Ostwald, Z. Phys. Chem., Stochiom. Verwandtschaftsl. **34**, 495 (1900).
[7] I. M. Lifshitz and V. V. Slyozov, J. Phys. Chem. Solids **19**, 35 (1961).
[8] C. Wagner, Z. Elektrochem. **65**, 581 (1961).
[9] A. G. Cairns-Smith, Chemistry in Britain **22**, 559 (1986).
[10] J. M. Ottino, *The Kinematics of Mixing: Stretching, Chaos, and Transport* (Cambridge University Press, Cambridge, England, 1989).
[11] J. M. García-Ruiz, J. Struct. Biol. **142**, 22 (2003).
[12] F. C. Frank, Biochim. Biophys. Acta **11**, 459 (1953).
[13] D. K. Kondepudi, J. Laudadio, and K. Asakura, J. Am. Chem. Soc. **121**, 1448 (1999).
[14] C. I. Sainz-Díaz, A. P. Martín-Islán, and J. H. E. Cartwright, J. Phys. Chem. B **109**, 18 758 (2005).
[15] *The Holy Bible*, authorized King James version (1611), Matthew 25:29.