New Insights into Nucleation through Chiral Crystallization

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The use of sodium chlorate crystallization as a tool for probing nucleation has shed new light in our understanding of secondary nucleation, and has raised a number of questions regarding processes perceived as primary nucleation.

Sodium chlorate is a compound whose individual ions are achiral. However, its crystals produced from an aqueous solution belong to a chiral cubic group. As a result, two types of crystals with enantiomeric lattices can be grown, identified as L- or D-. This property makes sodium chlorate an interesting tool for studying nucleation processes, both primary and secondary.

In secondary nucleation, that is, new nuclei breeding from a seed crystal of the crystallizing compound, one would expect that nuclei resulting by microattrition (by collision or the shearing action of the agitated liquid) from the parent seed would be of the same chirality as the seed. This would be, as referred by physicists, a case of chiral symmetry breaking and it would be useful in a process separating chiral compounds by preferential crystallization. However, in a series of seeded experiments using a crystal of $NaClO_3$ of known chirality as a seed, our group has observed that a wide range of conditions exist in which nuclei of both chiralities were obtained. The first results were published in 1972 (Denk and Botsaris, 1972a,b). More detailed data were reported in our recent article (Qian and Botsaris, 1998) together with an explanation based on our model of secondary nucleation termed Embryo Coagulation Secondary Nucleation (ECSN) (see also Qian and Botsaris, 1997). These experiments clarified the process of secondary nucleation indicating that the origin of secondary nuclei is not always the parent seed, but, in many cases, the supersaturated solution around the seed. In the latter case, since embryos of both chiralities exist in the solution, nuclei of both chiralities may be produced. In brief, in secondary nucleation one would expect chiral symmetry *breaking* crystallization, yet in many cases chiral *symmetry* crystallization is observed. The inverse can be stated for the primary nucleation. One would expect chiral symmetry crystallization; instead, chiral symmetry breaking is observed. This article deals with this phenomenon in primary, nonseeded nucleation.

Nonseeded Nucleation from a Supersaturated Solution of $NaClO_3$

In primary nucleation no seeding is involved and the new nuclei appear when the supersaturation exceeds a critical value. According to the classical nucleation models, the nuclei result from the growth of embryos that exist in the supersaturated solution. Since embryos of both chiralities exist in a supersaturated solution of $NaClO_3$—presumably in equal numbers—a spontaneous nucleation process would produce a mixture of D- and L- crystals. Actually, one would expect their ratio to approach 1:1 if a large number of crystals are produced. Experiments, however, have indicated that although in unstirred solutions ratios fluctuating around 1:1 are obtained, in stirred solutions the ratios are close to 1:0 or 0:1.

First, there are the data we obtained from a stirred nonseeded supersaturated solution of $NaClO_3$ and reported in Qian and Botsaris (1998). The solution was cooled until a large number of nuclei were generated. The crystals were collected and their chirality of each individual crystal was determined by its rotation of linearly polarized light. The results showed that each crystallization generated crystals of one chirality, either all D- or all L-. Then, there are the experiments reported by Kontepudi et al. (1990, 1993, 1995). There, the crystallization occurred also in nonseeded $NaClO_3$ solutions, in which, however, the supersaturation was generated by evaporation. The crystals produced were, in excess of 99%, of one chirality, either D- or L-. This unexpected chiral symmetry breaking generated considerable interest not only among the crystallization people working in nucleation modeling or chiral separations, but also among scientists studying the phenomenon of chiral symmetry breaking which has occurred in nature in the case of biological molecules such as amino-acids that exist in nature only in one chiral form.

One approach focused on the hydrodynamics of the stirred solution. Metcalfe and Ottino (1994) modeled the above nucleation experiments as an autocatalytic reaction scheme

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combined with chaotic mixing. The scheme consists of a pair of autocatalytic reactions involving white (W) (representing the solute), red (R) and green (G) particles

$$W + G = 2G \tag{1a}$$

$$W + R = 2R \tag{1b}$$

Although the simulation showed that many initial conditions resulted in states in which over 90% of the colored particles were of the same color, red or green, the scheme actually does not represent the physical reality of the nucleation process. In nucleation a solute molecule added to a cluster will simply increase the size of the cluster, and it will not create a second cluster. In addition, in an independent process each cluster will breed a large number of secondary nuclei, which are of the same "color" as the parent cluster if traditional contact nucleation is the predominant mechanism, or of both "colors" if ECSN predominates. We believe that the physical nucleation model is sufficient by itself to provide an explanation for the production of one-chirality crystals. It should be noted that Martin et al. (1996) have also concluded that "hydrodynamic *convection* plays little or no role in producing high chirality pure states."

Kondepudi et al. (1990, 1993, 1995) have outlined an explanation for the production of one-chirality crystals based on the physical nucleation model. They recognized that an explanation should involve the following elements:

- A single parent crystal, which is the first to be created by the primary nucleation, breeds all the other crystals;
- The other crystals are created by contact secondary nucleation;
- Subsequent primary nuclei, after the first, for some reason are not able to participate in secondary nucleation. For this reason, Kontepudi introduced the idea that a parent crystal can breed secondary nuclei only when it reaches a minimum size.

The idea of a single primary nucleation event is the most crucial for the explanation. This can be tested by conducting a crystallization process in such a way that many local nucleation centers may be created simultaneously. In this case primary nuclei of both chiralities would be created and progeny crystals of both chiralities will result. This is exactly the test our experimental investigation conducted and the results are reported below.

Results and Discussion

Experimental investigation

In all the experiments bubbling of air through a supersaturated solution was used as a means to achieve multiple nucleation centers. As the bubbles rise, water evaporates and a higher solute concentration and supersaturation is achieved locally at the bubble-liquid interface. At the same time, the cooling effect of the evaporation also increases the supersaturation close to the liquid surface as it lowers the temperature of the surface.

The produced crystals were counted and their chirality was determined by placing them between two polarizers and observing the direction of the rotation of the polarized light.

Table 1. Nuclei Chirality in Spontaneous Nucleation with and without Air Bubbling in Agitated Solution

Air Bubbling	ΔT (°C)	% D	% L	CEE
No	10.0	100	0	−1.00
	13.2	0	100	+1.00
	14.0	100	0	−1.00
	14.2	0	100	+1.00
	15.3	0	100	+1.00
Yes				
Run I	12.0	51	49	−0.02
Run II	12.0	38	62	+0.24
Run III	12.0	16	84	+0.68

Two series of bubbling experiments were conducted. In the first series, air was bubbled through a solution supercooled to a temperature close to the critical supercooling. In the second, the supercooling was low (3°C) such that the solution was not nucleating without bubbling.

Table 1 contains first data from a previous work (Qian and Botsaris, 1998) obtained by spontaneous (nonseeded) nucleation of agitated supersaturated solutions of supercoolings ranging between 10° and 15.3°C. The data show that crystals of a single chirality were obtained in each case. The data can be expressed also in terms of a parameter, the crystal enantiomeric excess

$$CEE = (N_L - N_D)/(N_L + N_D)$$

where N_L and N_D are the numbers of L- and D- crystals, respectively. In the above data CEE has the value of either +1 or −1.

Spontaneous nucleation at 12°C supercooling was repeated with the addition of air bubbling. The experimental conditions were the following: Approximately 600 mL of a solution of sodium chlorate supersaturated at 35°C were placed in a 1,000 mL crystallizer. The solution was heated under agitation to 45°C, kept there for about 2 h, cooled at a rate of 5°C per h to 35°C and then at a rate of 2.5°C down to 23°C. At this point, the agitation (190 rpm) was stopped and air bubbling (10 L/min) through a bubble cap began. When crystals were formed, the bubbling was stopped and the agitation was restarted until several hundreds of nuclei appeared at which point the agitation was stopped.

The results from the air-bubbling experiments I, II, and III, shown also in Table 1, clearly indicate that crystals of both chiralities are formed in each run. The CEE deviates from the absolute value of one towards the value of zero (the latter is the value of CEE for the case of 50-50 mixture of crystal of both chiralities). This can be attributed to the fact that in this case numerous nucleation centers are created, and primary crystals of random chirality are produced. As a result, progenies of both chiralities are generated. What is interesting is that in I and II the CEE is closer to zero than to 1 or −1; a case of almost chiral symmetry. In Run III, however, it was observed that during the cooling of the solution under agitation, at 10.5°C, and before air bubbling, a crystal was formed under the propeller. The chirality of this crystal was later determined, and it was found to be L-. One

Table 2. Comparison of Nuclei Chirality in Spontaneous Nucleation by Air Bubbling vs. Seeded Nucleation without Bubbling at the Same Supercooling

Agitation	ΔT (°C)	% D	% L	CEE
No				
Air bubbling				
Run IVa	3.0	24	76	+0.52
Run IVb	3.0	76	24	−0.52
Run V	3.0	53	47	−0.06
Run VI	3.0	53	47	−0.06
Seeded (D seed)	3.0	99.7	0.3	−0.994
	3.0	92	8	−0.84
	3.0	100	0	−1.00
Yes				
Air bubbling				
Run VII	3.0	54	46	−0.08
Run VIII	3.0	59	41	−0.18
Seeded (D seed)	3.0	100	0	−1.00
	3.0	100	0	−1.00

would expect the chirality of the progeny crystals to be biased towards the L- and the results show that indeed it is (84% L-).

Experiments were conducted also at a supercooling of 3°C. At that supercooling, no spontaneous nucleation occurs. The air bubbling, however, creates locally areas of higher supercooling, and thus nucleation is initiated in the nonseeded solution. The results from Runs IV to VIII for both agitated and nonagitated solutions are presented in Table 2. For comparison, previous data with seeded crystallization at the same supercooling (see Qian and Botsaris, 1998) are also shown. As explained in that article, the overwhelming majority of the secondary nuclei are of the same chirality as the seed: absolute value of CEE close to 1. In contrast in the air bubbling experiments nuclei of both chiralities are observed. Actually, the CEE in most of the cases approaches zero. Air bubbling corresponds to the case in which a large number of random-chirality seeds is introduced.

The above results confirm our thesis that when multiple centers of primary nucleation are involved, the bred secondary nuclei are of both chiralities. Therefore, experimental support for Kondepudi's model (Kondepudi et al., 1993) has been provided. This model suggests that in the case of the spontaneous nucleation which generated crystals of almost one chirality, the crystals are generated from a single primary crystal, a single progenitor. This single crystal can breed in an agitated solution by contact secondary nucleation a very large number of secondary nuclei.

If one considers the classical model of nucleation kinetics that postulates an exponential dependence of nucleation rate on supersaturation, the generation of only a single crystal at a certain point of time is not an improbable event. When the supersaturation of a solution is increased, either by cooling or by evaporation, the nucleation rate is initially extremely low. As the supersaturation increases, it is possible at a certain point of time or at a certain locality to nucleate just a single crystal. A valid question may arise, nevertheless: as the cooling or evaporation continues, why are additional primary nuclei not created? One answer may be, as Kondepudi has recognized (Kondepudi et al., 1993) that, at that high supersaturation, the secondary nucleation from the single parent seed is such a catastrophic event and produces such a large number of nuclei that the supersaturation drops to levels not supporting further primary nucleation. An additional hypothesis advanced by Kondepudi is that other primary nuclei are subsequently produced, but their size will be smaller than the first crystal. A minimum crystal size is required for secondary nucleation. That size is achieved first by the initial crystal that provides all the progenies.

In conclusion, our experiments with spontaneous crystallization by air bubbling support the idea of a single progenitor in cases of spontaneous nucleation by cooling. This also points out that in many processes that are perceived as cases of primary nucleation, only one crystal is actually generated primarily and all the others are bred from it by secondary nucleation.

Acknowledgments

The authors gratefully acknowledge the support of National Science Foundation for this project through grant CTS-9316096.

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Manuscript received June 29, 1998, and revision received Sept. 28, 1998.