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On Multiple Nucleation Bursts During Solution Crystallization in Pure and Impure Solvant.

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ABSTRACT.

It is widely accepted that during batch cooling crystallization processes, uncontrolled cooling can produce multiple nucleation events which have a detrimental effects on the Crystal Sizes Distributions (CSD). Controlling the CSD therefore requires mastering nucleation during the whole batch development: this is the starting point of many studies devoted to temperature control during industrial crystallization operations. When nucleation phenomena take place throughout the batch process; the time allocated to every crystal to grow is widespread, which enlarges the width of final CSD. Successive nucleation phenomena are referred below to as "Multiple Nucleation Bursts (MNB)". Oscillatory Supersaturation Dynamics (OSD) are sometimes assumed to accompany the trend of multiple nucleation bursts and it is suggested in the following that MNBs should not be misread as oscillatory supersaturation profiles.

Experimental results obtained during the crystallization of ammonium oxalate in the presence of impurities (NiSO₄) are presented to support and illustrate OSDs crystallizations which, even though they are often presented as a basic pattern of uncontrolled batch crystallization systems, were never observed before. A PBE simulation model based on Kubota-Mullin's pinning mechanism is developed to represent the observed oscillations of supersaturation. The latter are shown to be rather likely when inhibiting impurities are present in solution, but it is suggested that oscillations of supersaturation are unlikely in pure solvents. These latter two results shed some new light on the need of controlling temperature during batch cooling crystallization processes.

Introduction

The course of supersaturation during cooling solution crystallization is known to considerably affect the final CSD (Crystal Size Distribution) and the crystal habits. This is the reason why significant benefits are expected from the open-loop or closed-loop control of industrial batch crystallizers and, in particular from the optimization of supersaturation profiles. However, it is clear that few such input variables can be used to control supersaturation in the case of batch crystallization operation. Among the available control variables, the crystallizer temperature is clearly the most straightforward way of manipulating supersaturation trajectories in order to improve final crystal properties such as the CSD. The closed-loop control of industrial crystallizers, or at least the open-loop optimization of operating conditions –i.e., tracking of temperature profiles, addition of small amounts of habit modifiers, seeding or fines dissolving policies- were early investigated as possible means of ensuring some mastery over the final CSD of industrial batch crystallization $^{1.4}$. One of the earliest studies of batch cooling crystallization control was published by Griffiths⁵ who suggested methods for controlling the product CSD⁶⁻⁸. As schematically shown in Figure 1a, inappropriate cooling policies were shown to lead to the onset of repeated and detrimental nucleation "showers". More generally, the basic pattern in Fig.1a indicates that at any one time when supersaturation is allowed to exceed the limit of metastable zone an important burst of nuclei should be produced. From this observation Griffiths⁵ proposed the four following principles: 1. Within the

deposition of fresh nuclei may occur in contact with cooling surfaces of the crystallizer, so that loss of control of the crystallization process will occur, 3. Fresh nuclei can be produced by attrition, 4. Departure from the metastable region will produce immediately a "shower" consisting of a very

metastable zone a nucleation range exists where no fresh nuclei will be formed, 2. Formation and

large number of nuclei. This is why Griffiths proposed that if the supersaturation could be maintained at some "optimal" level inside the metastable zone, an improved final product CSD would be obtained. The principle of appropriate supersaturation trajectory is illustrated in Fig.1b ; many papers were thus devoted to the design of advanced temperature control schemes.

Roughly speaking two main approaches can be distinguished:

- Optimal control strategies are aimed at optimizing the competition between nucleation and growth processes through the tracking of the "pseudo-optimal" temperature set-point trajectories. The resulting supersaturation profiles are expected to yield optimized CSDs (e.g. maximized average particle sizes, reduced number of fines, minimized width of the final size distribution, etc)

- Advanced closed loop control approaches are based on direct or indirect in-line measurements of the CSD, or of any property related to the quality of the particles. The measurements are then used for feedback control purposes: appropriate process inputs are manipulated in order to keep some desired CSD parameters under control.

The assumption that Fig. (1) is representative of operating compromises which have to be taken into account for obtaining suitable final number of crystals and correct CSD, without increasing excessively the batch duration, is at the heart of most advanced control studies devoted to batch crystallization processes. It is assumed that undesirable late nucleation can be avoided, or at least controlled, thanks to appropriate and efficient feedback temperature tracking strategies. Now, with industrial processes in view, it is the goal of this paper to shed some light on the physical meaning of "multiple nucleation bursts". More precisely, an effort is made below to situate the problem of possible nucleation bursts in the industrial context of crystallization in real media. Even though multiple nucleation burst happen, it is claimed, on the one hand, that concentration trajectories like in Fig.1a cannot happen in pure solvents (i.e. it is highly implausible that supersaturation increases

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might follow the first nucleation peak). On the other hand, it is suggested that the presence of impurities can lead to the dynamic situation illustrated in Fig.1a and, indeed, allow multiple nucleation bursts to take place (i.e., in the sense of Fig.1a).



Figure 1. Schematic representation of the effect of excessive cooling rate on the development of cooling crystallization, after Griffiths^{5,13} (a) Uncontrolled cooling (b) Controlled cooling leading to limited nucleation events during the crystallization process (i.e., the supersaturation is kept inside the metastable zone so that the final CSD is expected to be improved).

The following points are thus addressed in this paper:

The dynamics presented in Fig.1a was neither irrefutably explained nor proved in the literature, and no convincing experimental results are actually published that would demonstrate the onset of repeated supersaturation bumps during uncontrolled cooling crystallization operations. In fact, to the best of our knowledge, concentration profiles like the one shown in Fig.1a were never reported in the case of batch operations, while the existence of multiple nucleation bursts leading to oscillatory behaviors of crystallizers was clearly established and thoroughly analyzed in the case of

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continuous processes ⁹⁻¹². It is suggested below that supersaturation oscillations are implausible when pure solvents are used, even when multiple nucleation events take place. A clear distinction will thus be made in the following between Multiple Nucleation Bursts (MNB) and supersaturation oscillations which, for the sake of clarity, will be referred below to as OSD (Oscillatory Supersaturation Peaks). The first case refers to the onset of primary nucleation followed by secondary nucleation burst(s). The second case refers to the possibility of supersaturation to increase several times during the batch process, consistently with Fig.1a, thus leading to several nucleation showers. Through simulation study, supersaturation oscillations are shown be unlikely (if not impossible) when the crystallization operation is performed in pure solvent (i.e. in a rather "academic" experimental context.)

As opposed to the ideal case of pure solvents, experimental and theoretical results are presented below to demonstrate that even at relatively low cooling rates and low impurity concentrations, unsteady-state inhibition effects of impurities can lead to multiple supersaturation oscillations, within the meaning defined above.

Impurities and industrial batch cooling crystallization processes.

It is obvious that the industrial practice of crystallization cannot avoid undesirable impurities to be generated during the many chemical reactions preceding the crystallization steps. It is also well-known that even minute amounts of impurities in the initial solution can affect tremendously the development of crystallization operations and the quality of the solid product. Through complex effects on nucleation, growth and aggregation mechanisms, process impurities affect the quality of the final particles: size distribution, shapes, polymorphic state, cristallinity, etc.¹⁵⁻¹⁸. Yet, almost all academic modeling and control papers deal with pure solute/solvent systems: this restriction raises

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an essential question as to whether the results of such works are fully relevant for industrial applications.

In many cases, dissolved impurities induce significant reductions of the rates of basic crystallization phenomena, notably crystal nucleation and growth. However, increases of the corresponding rates were also reported¹⁷⁻¹⁹. Among other phenomena, a noticeable reported effect of impurities is the reduction of growth rates leading to supersaturation thresholds at the end of crystallization operations: below the supersaturation threshold the growth of crystals seems to be stopped.

In order to get more relevant and in-depth data on the development of crystallization processes in the presence of impurities, new sensing technologies are highly valuable because they can provide continuous *in situ* data on both the continuous and the dispersed phases. During the past decade, infrared spectroscopy (IR), near infrared spectroscopy (NIR), and Raman spectroscopy were developed for monitoring the solute concentration during crystallization processes. As in- line sensors these techniques can provide reliable and accurate measurements of solute concentration, and consequently on both supersaturation and solids content. This is how the acquisition of supersaturation measurements during the present work provided new information about the existence of oscillatory concentration trajectories. Indeed, in-line refined experimental information was obviously unavailable when the pioneering control works and the textbooks quoted above were published ⁽¹⁻¹³⁾.

Modeling the effect of impurities on the crystal growth rates.

According to McCabe's hypothesis, the rate of crystal growth G(t) is usually assumed not to depend on the particle size, but essentially on supersaturation which can be defined as the relative supersaturation $\sigma(t)$ or supersaturation ratio $\beta(t)$, which both are adimensional variables:

$$\sigma(t) = \frac{C(t) - C^*(T(t))}{C^*(T(t))}$$
(1)

$$\beta(t) = \frac{C(t)}{C^*(T(t))} \tag{2}$$

where C^* is the solubility and C(t) is the actual solute concentration.

Many primary and secondary nucleation models are available in the literature. The following expression is used in the sequel to describe primary nucleation during unseeded processes (see e.g. $Myerson^7$). In the following, parameters A_{hom} and B_{hom} will be assumed not to depend on temperature:

$$R_{N1}(t) = A_{hom} \cdot \exp\left(-\frac{B_{hom}}{T^3 \left[\log\beta(t)\right]^2}\right)$$
(3)

Secondary nucleation is often observed during batch solution crystallization process, it is usually assumed to be made easier by increasing amounts of solid in suspension. In fact, several complex mechanisms can be referred to as "secondary nucleation". Again, for the sake of simplicity, the simple following phenomenological equation will be used in the sequel:

$$R_{N2}(t) = A_{SN} C_S(t)^k \sigma(t)^j$$
(4)

Despite its lack of clear physical meaning, Eq.(4) accounts for the impact on the generation of new particles of the solid already generated in suspension

The following simplified equation is often used to represent the growth rate of crystals which, for the sake of simplicity, are assumed here to be characterized by a single size parameter L:

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$$G_0(t) = \frac{dL}{dt} = k_g \,\,\mathbf{\sigma}(t)^i \tag{5}$$

Index o refers to the crystal growth rate in pure solvent. G_0 is thus considered as the "reference" growth rate of ammonium oxalate determined from batch experiments performed in pure water.

In Eq.(5), exponent i depends on the growth mechanism(s) involved. In practice, consistently with "standard" theoretical models, most published values of i are found to vary between 1 and 2 (i.e, diffusion controlled or integration controlled crystal growth, BCF growth model, etc.)

When compared to the growth of crystals in pure solvent, the time-averaged advancement velocity of a step in impure solvent can be hindered by the adsorption of impurity species on the growing crystal surface. During the crystal growth, kink sites can be blocked by foreign species that cannot easily incorporate the crystal lattice. To allow further advancement, the growth-step has to circumvent the adsorbed impurity, which obviously reduces the overall growth rate. Models describing such so-called "pinning mechanism" were early described in the literature²⁰ and many experimental observations of the mechanism were reported, notably thanks to the use of advanced imaging techniques such as AFM (Atomic Force Microscopy)²¹⁻²³. Kubota-Mullin's model was proposed to describe the pinning mechanism through the expression of the following ratio Γ between the step velocities in pure (u₀) and impure (u) solvents²⁴:

$$\Gamma = \frac{u}{u_0} \approx \frac{G}{G_0} = 1 - \left[\frac{\gamma a}{k_B T \sigma L}\right] \theta^* = 1 - \alpha \theta^* = 1 - \frac{\omega}{T \sigma} \theta^*$$
(6)

 γ is the edge free energy, a is the size of the growth unit, k_B is the Boltzmann constant and θ^* is the steady-state coverage fraction of active growing crystal surface by adsorbed impurities. α , is a global parameter accounting for the efficiency of impurities to hinder the crystal growth.

As Eq.(6) shows, α does not only depend on relevant properties of the solid, but also on supersaturation and temperature. Several approaches can be used to compute the equilibrium coverage fraction θ^* but a simple way of describing the equilibrium coverage of the growing crystal surface is to have recourse to Langmuir adsorption theory ^{19,24,25}, as follows:

$$\theta^* = \frac{KC_i}{1 + KC_i} \tag{7}$$

where K is Langmuir's adsorption constant and C_i is the concentration of impurity.

It was shown that the dynamics of adsorption of impurity species on the crystal surface cannot always be neglected. This is the reason why, as a first phenomenological approximation, the transient behavior of the coverage process (i.e., the time variations of θ) was suggested by Kubota ¹⁹ to obey the following first-order phenomenological dynamics where τ is a time constant:

$$\theta = \theta^* (1 - \exp(-t/\tau)) \tag{8}$$

Assuming that the crystal growth rate is proportional to the step velocity (i.e., $\Gamma \approx G/G_0$) it finally turns out that in the presence of impurities *G* depends on both time and supersaturation. Combining expressions (5) to (8) leads to the following expression (9) where ν is the time at which the crystal surface is set in contact with the dissolved impurity.

In the industrial practice, impurities might be introduced fortuitously in the mother liquor or as undesired initial products of secondary chemical reactions. In this latter case, the impurities are present from the beginning of the crystallization process. The nucleation events (i.e. primary homogeneous or heterogeneous and further secondary nucleation) occur in the presence of these latter impurities and this is the reason why, in the sequel, v is supposed to coincide with the nucleation time. The growth rate of crystals generated in the presence of impurities is thus expressed as follows:

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$$G(t) = G_0(t) \left[1 - \alpha \frac{KC_i}{1 + KC_i} \left(1 - exp\left(-\frac{(t - \mathbf{v})}{\tau}\right) \right) \right]$$

$$= k_g \sigma(t)^i \left[1 - \alpha \frac{KC_i}{1 + KC_i} \left(1 - exp\left(-\frac{(t - \mathbf{v})}{\tau}\right) \right) \right]$$
(9)

Applying the impurity adsorption model to Population Balance Equations (PBE) increases the dimension of the problem because the time (t- v) spent by the crystals in contact with impurities should now be accounted for. Indeed, even though they are exposed to the same supersaturation, two crystals present in suspension at time t do not necessarily exhibit the same growth rate because their coverage by the impurity specie(s) differs. This is why a method of characteristics allowing solving the Population Balance Equations (PBE) accounting for both times t and v was proposed ²⁶. To accounts for the time spent by the distributed crystals in the presence of impurities, the usual variables involved by population density functions, L and t, are completed by time v. As already mentioned, v will be here considered to be the nucleation time of particles. The following system (10-13) describes PBEs for unseeded crystallization occurring in impure solvent; where v is the time of nucleation of particles evolving on the same characteristic curve. More details about the numerical resolution technique can be found elsewhere²⁶.

$$\left[\frac{\partial\phi(L,t,\nu)}{\partial t} + G(t,\nu)\frac{\partial\phi(L,t,\nu)}{\partial L} = 0\right]$$
(10)

$$\phi(L,0,\mathbf{v}) = 0 \tag{11}$$

$$\phi(0,t,\mathbf{v}) = \frac{A_N(t)}{G(t,\mathbf{v})}\delta(t-\mathbf{v}) \tag{12}$$

Experimental design

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The experimental setup was presented in previous papers²⁷⁻²⁸. Batch cooling unseeded crystallization of ammonium oxalate (AO) was performed in water with and without the presence of impurities. The initial and final batch temperatures were 42°C and 10°C, respectively and the following cooling rates were applied: R = dT/dt = -2;-5;-7;-10;-20;-25 and -30°C/h. The choice of dissolved Nickel Sulfate as model-impurity was essentially motivated by the availability of published data concerning the effect of Ni²⁺ ions on the growth rate of AO in water ^{14,17}.

In situ measurements of supersaturation were performed using the Matrix FTIR spectrometer manufactured by Bruker, equipped with an immersion ATR diamond probe. The probe was connected to the spectrometer through fiber optic. More details about the overall experimental design, including the calibration procedure, can be found in ref.²⁷. The experiments were first focused on the investigation of the nucleation and growth kinetics of Ammonium Oxalate monohydrate in pure water. The kinetic parameters of the crystallization system were identified and published; these parameters will be used as reference data in the sequel²⁷⁻²⁸.

Primary and secondary nucleation in pure solvents

Experimental data on the crystallization of ammonium oxalate (AO) in pure water.

The initial AO concentration was $C_0 = 0.1$ kg/kg water for a crystallizer volume of 2,5 L. The stirring rate was set constant to 300 rpm. As expected, increasing cooling rates widen the apparent metastable zone width. "Apparent" means here that, even though primary particles are supposed to be generated as soon as the initial solute concentration exceeds the solubility (according to Eq.(3)), significant bifurcation of the concentration trajectory (i.e., sufficient solids formation) requires supersaturation to reach a minimal value. Both measured and simulated supersaturation profiles were presented in a previous paper devoted to the modeling of the pure AO/water system²⁷. However an example of typical solute concentration trajectory is displayed in Fig.2 (Run 5)

Crystallization of ammonium oxalate in the presence of impurities (Nickel Sulfate).

Batch cooling crystallization of ammonium oxalate was performed with the same operating conditions as previously, but three different amounts of nickel sulfate were dissolved prior to starting the cooling process. The weight fractions of dissolved Nickel sulfate were the following:

 C_i = $10^{\text{-3}}$; 5 $10^{\text{-4}}\,$ and 2 $10^{\text{-4}}\,$ kg NiSO₄/kg solution.

As during the experiments in pure water, varying constant cooling rates were applied during the batch processes. As one can see in Fig. 2, the apparent width of metastable zone is significantly enlarged when impurities are present in solution. Runs 5, 6 and 7 were performed with the same cooling policy but with or without impurities: the related measured supersaturation profiles exhibit major differences. The solute consumption in the presence of impurities (e.g., $C_{NiSO4}=10^{-3}$ kg/kg for Run n°6) becomes significant when the relative supersaturation $\sigma=0.62$ is reached, while $\sigma=0.16$ corresponds to the "limit of metastable zone" in pure solvent (Run n°5). Moreover, the concentration profile obtained in the presence of impurities suggests that two successive nucleation bursts occurred during the batch operation.

In order to simulate the crystallization in the presence of impurities, system (10-12) was solved using the method of characteristics mentioned above. The unsteady-state adsorption of impurity molecules at the crystal surface was described using Eqs.(7-9). The steady-state version of Kubota Mullin's model was first applied to simulate Run n°6, but this first approach did not allow reproducing the two bumps shown by the experimental data. A rather satisfactory (yet imperfect) model representing the two observed supersaturation "bumps" was obtained with the unsteady-state version of the pinning model after setting significant values of the time constant τ =800 s (as defined by Eq.(9)). Transient features of the impurity adsorption process were therefore necessary to represent the two successive

supersaturation bumps observed in Figs.4 and 5 at 27.5 and 23°C. The inhibition parameters used for the simulation of Run 6 were estimated after minimizing the difference between the model prediction of concentration and the measurements. As an example, the following estimates are related to the simulated profiles displayed in Figs.2-4:

K = 550 kg solution/kg NiSO₄ ;
$$\tau$$
= 800 s ; $\omega = \left[\frac{\gamma a}{k_B L}\right] = 1080 K$ (14)

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where ω was assumed constant and set according to eq.(6), such that:

$$\Gamma = \frac{G}{G_0} = 1 - \left[\frac{\gamma a}{k_B T \sigma L}\right] \theta^* = 1 - \left[\frac{\omega}{T \sigma}\right] \theta^* = 1 - \alpha \theta^*$$
(15)

As one can see in Fig. 2-4, the simulation of solute concentration profiles in impure media was rather satisfactory until the final period of the batch process (i.e., until the final stage where the suspension was left at 20°C under stirring to return to its equilibrium state). Indeed, during the final stage, the solute concentration is significantly overestimated by the model (see Fig. 3a and 4). The final supersaturation threshold is therefore overestimated by Kubota-Mullin's model.

Fig.3b shows that two successive nucleation bursts leading to two distinct supersaturation bumps are predicted by the inhibition model. Such behavior can be attributed to insufficient crystal growth rate together with delayed inhibition effects: the delay allows sufficient crystal growth right after the nucleation of "young crystals" so that, as a first step, the rate of solute consumption is sufficient to allow returning towards the equilibrium. Afterwards, before reaching the solubility, the same crystals get more and more inhibited so that, again, the supersaturation is allowed to increase until the onset of a new nucleation burst.

Figure 4 displays an additional example of experimental and simulated supersaturation profiles obtained in the presence of impurities. During Run 7, the cooling rate was the same as during Run 6 but the concentration of impurity was halved. The simulation is rather satisfactory but, again, the final period of the batch cooling process is rather poorly described by the model. This latter problem deserved deeper investigation and will be the object of a forthcoming paper. In particular, the assumption of supersaturation threshold in the presence of impurities has to be more thoroughly examined. Indeed, the in situ video monitoring of the suspension revealed that the crystals grown in the presence of impurities exhibit irregular, rough and broken shapes. As a result of breakage

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phenomena, the generation of new clean surfaces might explain the ability of the final crystal population to grow more easily than predicted by Kubota-Mullin's model.



Figure 2. Comparison between the supersaturation profiles measured during experiments performed with the same operating conditions ($dT/dt=-30^{\circ}C/h$ and $C_{init}=0.1$ kg/kg), in pure water (Run 5) and with 10^{-3} kg/kg water of dissolved Nickel Sulfate (Run 6). Dotted lines = ATR FTIR concentration measurements; Solid line = Simulated concentration profile.



Figure 3. PBE simulation of Run 6 (see also Fig. 2). (a) Simulated (Solid line) and Measured (Dotted line) degree of supersaturation β against time. (b) Simulation of the primary nucleation rate vs. Temperature.

Due to its weaknesses at the end of the crystallization, the ability of the PBE model to allow drawing conclusions on the dynamic behavior of impure solution crystallization processes can of course be questioned. However, as outlined above, the objective of this study is more to demonstrate the relationship between the onset of supersaturation oscillations and dissolved impurities, than to represent accurately the development of the batch cooling process. With this aim in view, many simulations based on the parameters estimated previously were performed to analyze the oscillatory behavior of batch crystallizers operating with impurities.



Figure 4. Cooling crystallization of AO monhydrate with $C_i = 5.10^4$ NiSO₄ and dT/dt=-30 °C(Run 7). Simulated and measured degree of supersaturation $\beta = C/C^*$ vs. time.

Simulation of multiple nucleation bursts during cooling crystallization.

Crystallization of ammonium oxalate in pure water.

To the best of our knowledge, supersaturation oscillations were neither experimentally, nor theoretically demonstrated in the case of batch cooling crystallization processes performed in pure solvents. Roughly speaking it can be argued that when high cooling rates are applied during crystallization in pure media, because of the highly-nonlinear features of the nucleation kinetics, the delayed onset of nucleation leads to substantial nucleation showers: it is well-known that increasing cooling rates widen the width of metastable zone. Such a large number of particles is thus generated that even assuming further low crystal growth rate, supersaturation is consumed by further crystal growth. Supersaturation increases after primary nucleation would therefore remain unlikely. On the other hand, when primary nucleation occurs at low cooling rate (i.e. lower level of supersaturation), further solute consumption remains moderate, but, due to the low level of supersaturation production, subsequent increases of supersaturation are unlikely and further supersaturation bumps remain implausible.

Simulation of crystallizations in pure solvent exhibiting primary and secondary nucleation

The in situ video monitoring of crystallization operations performed in pure solvent suggested that nucleation takes place as a sustained process during the whole batch operation. Consistently with this observation, significant secondary nucleation was the only way of explaining both the measured supersaturation trajectory and the final CSD of the batch process²⁷.

Starting from the basic kinetic framework defined by Eqs.(3-5) and PBEs (10-12), the possibility of obtaining multiple supersaturation bumps with varying kinetic parameters was evaluated for a wide range of values. The reference values of the parameters involved by eqs.(3-5) (see Table 1) were taken from the paper above mentioned. Such a selection, at first, could seem very questionable because the growth rate of ammonium oxalate is known to be very high: increases of supersaturation after the first (single or double) nucleation burst are almost impossible, even at excessive cooling rates. This is the reason why many possible kinetic scenarios were evaluated during the simulation study. 200000 simulations of cooling crystallization operations were thus performed with random nucleation and growth parameters computed inside the bounds presented in Table 1. In order to reduce the

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dimension of the parametric space, exponents j and k in Eq.(4) were kept constant during the simulations. The evaluation through simulation of the kinetic parameters displayed in Table 1 was intended to show if the basic kinetic framework set above enables the onset of supersaturation bumps, in particular for systems exhibiting much lower growth rates than the growth rate of ammonium oxalate. For all simulations, the cooling procedure was starting from 47°C until 10°C with a constant cooling rate of -30°C/h. The system was then kept at 10°C for one hour. The dissolved solute concentration was initially set equal to 0.1 kg of solute/kg solvent, which corresponds to an initially undersaturated solution.

Table 1. Set of random kinetic parameters used for simulating 2.10^5 batch cooling crystallization operations in pure solvent. The reference values were taken from ref. 27. The low bound ε (arbitrarily small value) was set to avoid numerical indeterminacy.

Kinetic parameters	A _{hom} (#.m ⁻³ .s ⁻¹) Eq.(3)	B _{hom} (-) Eq.(3)	A _{SN} Eq.(4)	k Eq.(4)	j Eq.(4)	kg (m.s ⁻¹) Eq.(5)
Reference values	6.7 10 ⁷	7.05 10 ⁶	1.4 10 ⁹	1.77	1.36	2.7 10 ⁻⁵
Parameter Bounds	[ε to100]x A _{hom,ref}	[ε to 5] x B _{hom,ref}	[ϵ to 100] x $A_{SN,ref}$	constant	constant	[ɛ to 5] x k _{g,ref}

Figure 5 shows a scatter plot of the values of the four kinetic parameters varied during the study: the coverage of the domains given in Table 1 is really dense, including many values of the growth rate constant lower than the constant estimated for the crystallization of pure ammonium oxalate (see Fig.5d). None of the simulated crystallization was found to exhibit multiple supersaturation bumps, while about 5.7 % of the computed nucleation profiles showed double nucleation peaks. Actually, with the kinetic scheme under investigation, primary and secondary nucleation peaks

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were always found to be overlapping, but each of the two distinct nucleation processes can be prevailing. Fig.6 illustrates four typical nucleation scenarios where double nucleation peaks were reproduced in simulation. The corresponding kinetic data are presented in Table 2. It can be seen that the dominating nucleation process (in terms of particle number) might be either primary or secondary nucleation (see Fig.6, curves 4 and 3, respectively), and that the two distinct mechanisms can also produce similar numbers of particles and appear as almost indiscernible (see e.g. Fig.6, curve 1). The simulated CSDs corresponding to the runs presented in Fig.6 are displayed in Fig.7. The model predicts rather broad CSDs, except in the case of the simulation run n°1 which represents a rather delayed onset of primary nucleation burst (i.e. very large metastable zone width).

As far as supersaturation bumps are concerned, even in the case of double nucleation peaks, no simulation led to supersaturation increase(s) after the first single or double nucleation burst. The kinetic scheme studied in this paper therefore suggests that double nucleation peaks cannot lead to supersaturation oscillations looking like the pattern presented in Fig.1a. Indeed, Fig.6 (top) illustrates the fact that, whatever the kinetic parameter values, supersaturation is always monotonically decreasing after its first maximum. Even though the very large set of simulations performed does not constitute a true mathematical proof, it seems reasonable to infer that supersaturation bumps cannot take place for the kinetic framework set in the present study.

Simulation N°	$\begin{array}{c} A_{hom} \\ (\#.m^{-3}.s^{-1}) \\ Eq.(3) \end{array}$	B _{hom} (-) Eq.(3)	A _{SN} Eq.(4)	k Eq.(4)	j Eq.(4)	k _g (m.s ⁻¹) Eq.(5)
1	$1.98 \ 10^{10}$	2.255 10 ⁷	2.27 10 ⁶	1.35	1.86	0.29 10 ⁻⁶
2	5.2 10 ⁸	1.3 10 ⁷	6.15 10 ⁵	1.35	1.86	62 10 ⁻⁶
3	9.85 10 ⁸	7.10 10 ⁶	8.205 10 ⁷	1.35	1.86	5.75 10 ⁻⁶
4	3.29 10 ⁸	$1.81 \ 10^{6}$	3.73 10 ⁸	1.35	1.86	41.96 10 ⁻⁶

Table 2. Kinetic parameters values used for the simulations presented in Figs. 6 and 7.



Figure 5. Scatter plot of 20000 kinetic parameter random values used for simulating batch cooling crystallization operations governed by kinetic Eqs.(3-5) performed in pure solvent. (1-2) Values of primary and secondary nucleation parameters vs. corresponding value of A_{hom} (3-4) Values of the growth rate constant k_g . (**I**) Reference data taken from Table 1; (.) Whole set of simulated data ; (•) Simulation parameters leading to double nucleation peaks.



Figure 6. (Top) Simulated supersaturation profiles obtained after the simulation runs displayed in Table 2, and corresponding overall nucleation rates profiles (Bottom).



Figure 7. Simulated final CSD related to the simulation runs displayed Fig.6.

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Crystallization in the presence of impurities inducing transient inhibiting effects.

As outlined above, the simulations assuming pure solute/systems did not result in multiple supersaturation peaks. Contrary to these simulations, the measured concentration profiles and the related simulation results obtained in impure solvent looked like the general pattern summarized in Fig.1. This observation suggests that the oscillatory behavior underlined by Griffith might be due to unsteady-state pinning mechanisms induced by the presence of impurities.

Again, simulations were performed to evaluate the dynamic behavior of the crystallization process assuming unsteady-state adsorption of impurities. Various static and dynamic features of the adsorption process were thus simulated. The reference kinetic data were the same as in the previous paragraph. 100000 simulations were carried out with random values of the crystallization kinetic parameters and of the parameters related to the pinning mechanism: K, τ and ω In order to reduce the dimension of the investigated parametric space, the two parameters of primary nucleation were set constant and equal to the reference values given in Table 1 and, as previously, the two exponents j and k (Eq.4) were unchanged. Among the many "successful" random simulations, all the dynamic results exhibiting at least 3 supersaturation bumps were selected to illustrate the OSD case in point: about 15% of the simulated systems finally exhibited 3 or more supersaturation bumps. Three Typical examples of OSD are displayed in Fig.8, and the related final CSDs are presented in Fig.9. The parameters used for these 3 simulations are given in Table 3. As expected, due to the successive nucleation showers caused by the oscillations of supersaturation, the CSD is clearly multimodal and dispersed. Among others, run n°1 shows an example of simulation obtained with slow growth rate (i.e. low value of k_{g}), run n°2 corresponds to a crystallization assuming no secondary nucleation (A_{SN}=0). R un n°3 was performed simulating low adsorption time constant. The role of τ will be discussed in more details below.



Figure 8. Examples of random simulations of OSD dynamics performed with constant cooling rate $dT/dt=-30^{\circ}C/h$. Numbers 1 to 3 refer to the data given in Table 3.



Figure 9. Final CSDs obtained after the three simulations presented in Fig.8.

Crystal Growth & Design

A scatter plot of 1400 parameter values leading to OSD dynamics is presented in Fig.10. It appears that whatever the kinetic parameters used for the simulation, no OSD can be reproduced when the inhibition time constants is set below a threshold value of about 200 s. More to the point, simulating OSD dynamics turned out to be impossible assuming steady-state impurity adsorption (i.e. τ =0). In some way this observation strengthens Kubota and coworkers's model of unsteady-state adsorption dynamics.

The data displayed in Fig.10 show other interesting information. Many very small values of the secondary nucleation parameters A_{SN} gave rise to OSDs. The fact that secondary nucleation is not necessary to reproduce supersaturation oscillations was confirmed by additional simulations performed with A_{SN} =0. This point deserves to be underlined because, as explained above, the onset of secondary nucleation was the only way of simulating multiple nucleation bursts in the case of "standard" crystallization models developed in the absence of impurities. The repartition of the parameters displayed in Fig.10 shows also that OSDs can happen for any value of the growth rate constant and of the steady-state coverage parameter θ^* . However, concerning the latter variable, it can be seen that increasing values of the coverage factor decrease the likelihood of observing OSDs.

To our knowledge, the physical meaning of the dynamics of the adsorption of impurity species on the crystal surface is not clearly explained. Actually, the time constant τ was set rather as a phenomenological first order dynamical trend suggested by experimental observation than as a clear physical parameter. Kubota et al ^{18,30}. estimated τ =3700 s from experimental data on the growth of ammonium sulfate ³⁰. From a physical viewpoint such large value of τ is somewhat questionable because one can reasonably think that after a one hour period of growth process any impurity stuck on the crystal surface would entirely be covered by a new layer of crystallized solid. According to Kubota, the time constant is expected to increase with increasing supersaturation³⁰ but only a few experimental data have actually been published on the unsteady-state growth. This is why the simulations presented

here assume constant values of τ . In the absence of further studies, it seems reasonable to state that parameter τ cannot fully be considered as a true adsorption time constant but rather as an adjustment parameter accounting for dynamic inhibition phenomena.



Figure 10. Random parameter values leading to OSD crystallizations. The simulations were performed with identical primary nucleation parameters and constant cooling rate dT/dt=-30°C/h.

As far as experimental supersaturation trajectories are concerned, the PBE simulation of AO inhibited crystallization experiments was finally rather successful. However Eqs. (6) to (9) turned out to be unable to "predict" realistic particles size. Fitting the simulation results to the measured solute concentration profiles leads to predict much smaller particles than the real experimental ones. Such mismatch puts into question the relevancy of Kubota-Mullin's pinning model. This is the reason why several refinements were further brought to the PBE model which finally allowed reproducing the measured solute concentration profile simulation profile simultaneously with realistic particle sizes.

Such refinements are not essential to the present study and, in order not to extend too much this paper, the improvements of the PBE model will be reported in a forthcoming paper. At this point, it is worthy of noting however that even though satisfactory simulation results were obtained for every experimental condition, no comprehensive model describing the whole set of experimental data could be developed.

Table 3. Kinetic parameter values used for the simulations presented in Figs. 8 and 9.

Simulation	$K_g (m.s^{-1})$	A_{SN}	K.C _i (-)	τ (s)	ω (K)
N°	Eq. (5)	Eq. (4)	Eq. (7)	Eq. (8)	Eq. (6)
1	7.5 10 ⁻⁷	1.52 10 ⁹	0.62	1097	530.5
2	$1.74 10^{-4}$	0	0.114	1040	850.3
3	1.54 10 ⁻⁵	6.3510 ⁷	0.502	288	413.4

Conclusions

Controlling the crystal size distribution during industrial batch cooling crystallization operations requires keeping the phenomena of particle generation under control. Such an objective can partly be achieved thanks to optimal open-loop and/or advanced closed-loop control of temperature trajectories because temperature is the straightest practical means of controlling supersaturation against time. Though many studies were devoted to temperature control of crystallization processes during the past 50 years, the advanced control of CSD in batch crystallization remains an open problem. Control difficulties arise essentially from the specific and complex features of crystallization processes: the infinite dimension of the control target (i.e. the CSD), the non-linear and coupled features of the nucleation and growth kinetics involved and the lack of efficient input control variables. This is the reason why controlled cooling is a rather poor means of manipulating the CSD. Moreover it is clear that undesirable nucleation phenomena are irreversible and cannot be corrected by any cooling strategy: the final particle size is unavoidably determined by every particle generated throughout the batch process. Anyway, above all, late nucleation bursts should be avoided: "late crystals" often remain tiny as they lack of time and substance to achieve their growth, and therefore impair the quality of the product.

Among the many papers devoted to the open-loop or feedback closed-loop control of supersaturation, it is usually assumed that uncontrolled cooling rates can trigger undesirable multiple nucleation bursts. This paper does not claim that the idea of avoiding multiple nucleation bursts using appropriate cooling strategies is wrong. Indeed, the production of secondary nuclei (referred above to as Multiple Nucleation Bursts, MNB) occurs continuously during industrial batch crystallization even when no significant nucleation showers can be observed. From this latter point of view, it was clearly demonstrated in the past that improvements of the final CSD could be obtained thanks to supersaturation control. The point here is rather to shed a new light on the "historical" pattern of

Crystal Growth & Design

multiple nucleation showers recalled in Fig.1: we simply put forward the idea that oscillations of the supersaturation trajectory (referred in the text to as Oscillatory Supersaturation Dynamics, OSD) are rather unlikely when the crystallization is performed in pure solvent, while they are clearly favored by the presence of inhibiting impurities.

Specific OSD profiles were suggested by new experimental results demonstrating atypical supersaturation oscillatory profiles obtained in the presence of impurities. The experimental context of the related study was briefly described in this paper, but the goal here was not to report the whole set of experimental and modeling data obtained in this context. Only two typical experimental results are presented above to support the modeling approach developed to relate the effect of impurities on the development of batch crystallization operations. The proposed dynamic PBE model of cooling crystallization in the presence of impurities was extensively evaluated to assess the possibility of simulating OSDs. A wide simulation study based on Kubota-Mullin's pinning model (KMM) was performed with random values of the nucleation, growth and inhibition parameters. The simulations showed that inhibiting effects of impurities allow reproducing easily OSDs situations. For example, more than 15% of the random KMM simulations performed led to OSDs with 3 or more supersaturation bumps. It was also outlined that the latter are never "predicted" through "standard" random PBE simulation assuming basic primary and secondary nucleation mechanisms in pure solvents. It was therefore proposed that oscillations of the supersaturation profile can only occur in the context of impure crystallization systems, even though the performed simulations do not provide substantive evidence.

From a more practical viewpoint, a major conclusion can be drawn from these observations. Indeed, impurities are obviously present in industrial crystallization slurries so that future studies should take into account inhibition effects in the design of relevant and robust feedback control policies. Such innovative field of research might be highly valuable for industrial applications and, to the best of our knowledge, was never extensively addressed in the past. In particular, academic

studies performed in pure solvents cannot easily be considered as relevant and efficient in bringing appropriate solutions to real complex industrial control problems. In other words, improving the mastery over the final CSD requires, in the future, to get beyond the stage of pure crystallization systems and to cope with the challenge of understanding and modeling more realistic crystallization phenomena in impure industrial solvents.

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Nomenclature.

а	Size of growth unit	(6)	m ²
A_{hom}	Primary nucleation parameter	(3)	#.kg ⁻¹ .s ⁻¹
A_{SN}	Secondary nucleation parameter	(4)	#.kg ⁻¹ .s ⁻¹
\mathbf{B}_{hom}	Primary nucleation parameter	(3)	-
С	Solute concentration		kg solute/kg suspension
C_{s}	Concentration of solid in suspension	(4)	kg/kg
C*	Solubility		kg solute/kg suspension
C_i	Impurity concentration	(7)	kg/kg solution
G	Growth rate	(5)	m/s
G_{o}	Growth rate in pure solvant	(6)	m/s
i	Exponent of supersaturation in G	(5)	-
j	Exponent of supersaturation in $R_{\mbox{\tiny N2}}$	(4)	-
k	Exponent of the concentration of solid in R_{N2}	(4)	-
k_{g}	Growth rate constant	(5)	m/s
К	Langmuir adsorption constant	(7)	kg solution/kg impurity
L	Average distance between the active site		m
R_{N1}	Primary nucleation rate	(3)	#.kg ⁻¹ .s ⁻¹
R_{N2}	Secondary nucleation rate	(4)	#.kg ⁻¹ .s ⁻¹
Т	Temperature	(3)	К
u	Step velocity in the presence of impurities	(6)	m/s
α	Inhibiting impurity efficiency	(6)	-
β	Degree of supersaturation	(2)	-
γ	Edge free energy	(6)	J/m
$\delta(\tau)$	Dirac function		
ø	Number density function	(10-12)	#.kg ⁻¹ .m ⁻¹
θ	Coverage fraction	(6)	-
$\theta *$	Equilibrium Coverage fraction	(6)	-
ν	Time of contact of crystals with dissolved impurities		S
	(nucleation time in the present study)		
τ	Adsorption time constant (unsteady-state pinning	(8)	S
	mechanism)		
ω	Constant parameter (=γa/k _B L)	(6)	К
σ	Relative supersaturation	(1)	-

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Figures Captions

Figure 1. Schematic representation of the effect of excessive cooling rate on the development of cooling crystallization, after Griffiths^{5,13} (a) Uncontrolled cooling (b) Control cooling driven inside the metastable zone computed so as to minimize nucleation events.

Figure 2. Comparison between the supersaturation profiles measured during experiments performed with the same operating conditions ($dT/dt=-30^{\circ}C/h$ and $C_{init.}=0.1$ kg/kg), in pure water (Run 5) and with 10^{-3} kg/kg water of dissolved Nickel Sulfate (Run 6). Dotted lines = ATR FTIR concentration measurements; Solid line = Simulated concentration profile.

Figure 3. PBE simulation of Run 6 (see also Fig. 2). (a) Simulated (Solid line) and Measured (Dotted line) degree of supersaturation β against time. (b) Simulation of the primary nucleation rate vs. Temperature.

Figure 4. Run 7: Cooling crystallization of AO monhydrate with $C_i = 5.10^{-4}$ NiSO₄ and dT/dt=-30 °C. Simulated and measured degree of supersaturation $\beta = C/C^*$ vs. time.

Figure 5. Scatter plot of 20000 kinetic parameter random values used for simulating batch cooling crystallization operations governed by kinetic Eqs.(3-5) performed in pure solvent. (1-2) Values of primary and secondary nucleation parameters vs. corresponding value of A_{hom} (3-4) Values of the growth rate constant k_{g} . (**■**) Reference data taken from Table 1; (.) Whole set of simulated data ; (.) Simulation parameters leading to double nucleation peaks.

Figure 6. (Top) Simulated supersaturation profiles obtained after the simulation runs displayed in

Table 2, and corresponding overall nucleation rates profiles (Bottom).

Figure 7. Simulated final CSD related to the simulation runs displayed Fig.6.

Figure 8. Examples of random simulations of OSD dynamics performed with constant cooling rate dT/dt=-30°C/h. Numbers 1 to 3 refer to the data given in Table 3.

Figure 9. Final CSDs obtained after the three simulations presented in Fig.8.

Figure 10. Random parameter values leading to OSD crystallizations. The simulations were performed with identical primary nucleation parameters and constant cooling rate $dT/dt=-30^{\circ}C/h$.

Tables captions

Table 1. Set of random kinetic parameters used for simulating 2.10^5 batch cooling crystallization operations in pure solvent. The reference values were taken from ref. 27. The low bound (arbitrarily small value) was set to avoid numerical indeterminacy.

Table 2. Kinetic parameters values used for the simulations presented in Figs. 6 and 7.

Table 3. Kinetic parameter values used for the simulations presented in Figs. 8 and 9.



Figure 1. Schematic representation of the effect of excessive cooling rate on the development of cooling crystallization, after Griffiths^{5,13} (a) Uncontrolled cooling (b) Controlled cooling leading to limited nucleation events during the crystallization process (i.e., the supersaturation is kept inside the metastable zone so that the final CSD is expected to be improved).

519x264mm (72 x 72 DPI)





Figure 2. Comparison between the supersaturation profiles measured during experiments performed with the same operating conditions ($dT/dt=-30^{\circ}C/h$ and $C_{init.}=0.1$ kg/kg), in pure water (Run 5) and with 10^{-3} kg/kg water of dissolved Nickel Sulfate (Run 6). Dotted lines = ATR FTIR concentration measurements; Solid line = Simulated concentration profile. 567x358mm (72 x 72 DPI)



Figure 3. PBE simulation of Run 6 (see also Fig. 2). (a) Simulated (Solid line) and Measured (Dotted line) degree of supersaturation β against time. (b) Simulation of the primary nucleation rate vs. Temperature. 653x328mm (72 x 72 DPI)



Figure 4. Cooling crystallization of AO monhydrate with C_i= 5.10^{-4} NiSO4 and dT/dt=-30 °C(Run 7). Simulated and measured degree of supersaturation β = C/C* vs. time. 627×463 mm (72 x 72 DPI)







Figure 6. (Top) Simulated supersaturation profiles obtained after the simulation runs displayed in Table 2, and corresponding overall nucleation rates profiles (Bottom).

365x282mm (72 x 72 DPI)



Figure 7. Simulated final CSD related to the simulation runs displayed Fig.6. 777x243mm (72 x 72 DPI)



Figure 8. Examples of random simulations of OSD dynamics performed with constant cooling rate dT/dt=-30°C/h. Numbers 1 to 3 refer to the data given in Table 3. 639x509mm (72 x 72 DPI)



606x346mm (72 x 72 DPI)

x 10⁻⁴