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Stochastic Global Model for the Prediction of the Asymptotic CSDs Using Antisolvent Crystallization Processes

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A stochastic global formulation for the description of antisolvent mediated crystal growth processes is discussed based on the Fokker-Planck equation (FPE). The obtained global model is used to define an operating map of the crystallization process, where asymptotic iso-mean and iso-variance curves are reported in an antisolvent flowrate – temperature plane. Using the obtained asymptotic operational map, three different CSDs have been predicted and compared, both in asymptotic and then dynamic conditions, using experimental results.

1. Introduction

Antisolvent crystallization has been modeled for many systems using the traditional population balance modeling approach (Woo et al., 2006; Zhou et al., 2006; Nowee et al., 2008a/b; Sheikhzadeh et al., 2008; Trifkovic et al., 2008). As an alternative, it was recently shown (Grosso et al., 2010; Cogoni et al., 2012), that it is possible to describe a crystallization process by means of a stochastic approach, which allows the obtainment of the Crystal Size Distribution (CSD) evolution with respect to time using the Fokker-Planck equation, FPE. Further, this type of representation leads to simpler models and allow for the analytical solution to describe the CSD over time in antisolvent crystallization operations (Tronci et al., 2011; Cogoni et al., 2012). Furthermore, in order to use the model over the whole operational range proper relationships between the parameters of the model and the two process variables, namely antisolvent flowrate and temperature, has been developed. This is also extremely important when using the model in a model-based control configuration. From the explicit relationships, between FPE parameters and process variables, was possible to define operating maps, reporting the mean and the variance of crystals in asymptotic conditions, in a temperature-flowrate plane. This represents an useful way to study the feasibility to obtain a certain product in terms of mean size of crystals and variance and, eventually to visualize multiplicities of the asymptotic conditions, aiming to obtain the same product using less antisolvent and minimizing the energy consumption. Results are provided through investigations in the nonisothermal antisolvent crystallization of sodium chloride (NaCl), which solubility is practically independent of temperature.

2. Experimental work

The experiments were performed in a bench scale crystallizer, where only purified water, reagent grade sodium chloride (99.5 %) and ethanol, 190 proof, were used.

The experimental rig is comprised of a 1 L jacketed reactor connected to a Thermo Scientific® cooling/heating bath circulator that provides to keep constant the temperature inside the reactor by an embedded PID controller and a thermocouple wired inside the reactor. The antisolvent is added using a Masterflex® peristaltic pump calibrated for each experiment. The crystal size distribution is determined from the pictures of the samples taken from the reactor using a digital camera mounted in a stereo-microscope and then processed by means of sizing computer software (Amscope®).

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At the start-up condition, the crystallizer is loaded with an aqueous solution of NaCl made up of 34 g of NaCl dissolved in 100 g of water. The temperature is kept constant throughout the run, using three different values for the temperature, respectively 10 °C, 20 °C, and 30 °C. The ethanol was added to the aqueous NaCl solution using a calibrated peristaltic pump using a constant flowrate, the same for all the temperatures considered, equal to 2.25 ml/min. Along the operation, 8 ml samples were taken in an infrequent fashion. Samples were then vacuum filtered over filter paper and then dried into an oven, at least for 24 hours, with a constant temperature of 50 °C for further visual inspection (Grosso et. al., 2010).

3. Stochastic modelling approach

The crystallization process has been modelled using the approaches proposed previously (Galan et al., 2009; Grosso et al., 2010, 2011), where the growth of crystal size L is assumed to be governed by a deterministic and a stochastic term:

$$\frac{dL}{dt} = Lg(L;\theta) + L\eta(t) \tag{1}$$

In Eq. (1) g($L;\ \theta$) represents the deterministic contribution to the growth rate of L, defined as a Gompertz model (Cogoni et al., 2012), θ is the vector parameter defined in the model and $L\eta(t)$ is the a random component linearly depending on crystal size, and $\eta(t)$ is the Langevin force. It is further assumed that:

$$\begin{aligned} &E[\eta(t)] = 0 \\ &E[\eta(t)\eta(t')] = 2\Lambda\delta(t-t') \end{aligned} \tag{2}$$

Where Λ is the intensity of the Langevin force, which has been assumed as constant and equal to $\sqrt{D}$, where D is the diffusivity parameter of the FPE. Dividing both terms of Equation (1) by L, the Langevin equation becomes:

$$\frac{dy}{dt} = r\left(1 - \frac{y}{K}\right) + \eta(t) \tag{3}$$

Where y is defined as $y = \ln L$.
The Probability Density Function (PDF) related to the y random variable can then be described by the following linear Fokker-Planck equation with linear coefficients:

$$\frac{\partial\psi(y,t)}{\partial t} = D\frac{\partial^2\psi(y,t)}{\partial y^2} - \frac{\partial}{\partial y}\left[r\left(1 - \frac{y}{K}\right)\psi(y,t)\right] \qquad t \geq 0, y \in \Re \tag{4}$$

And the initial condition for $t = t_0$ is assumed as a normal distribution:

$$\psi(y,t_0) = \frac{1}{\sigma_0\sqrt{2\pi}}\exp\left[-\frac{(y-\mu_0)^2}{2\sigma_0^2}\right] \tag{5}$$

where μ_0 and σ_0 are, respectively, the initial mean size of crystals (logarithmic scale) and the initial standard deviation at $t = t_0$.
The linear FPE expression designed with the Equation 4, the PDF preserves its Gaussian shape at any time (Cogoni et al., 2012), thus the distribution is described by its first two moments, the mean, μ(t), and the variance, σ^2(t):

$$\psi(y,t) = N(\mu(t),\sigma^2(t)) \tag{6}$$

Respectively given by:

$$\mu(t) = K\left[1 - \left(1 - \frac{\mu_0}{K}\right)e^{-\frac{r}{K}(t-t_0)}\right] \tag{7}$$

$$\sigma^2(t) = \sigma_0^2 e^{-2\frac{r}{K}(t-t_0)} + \frac{DK}{r}\left[1 - e^{-2\frac{r}{K}(t-t_0)}\right] \tag{8}$$

Where in stationary state conditions they become:

$$\mu_{SS} = K \tag{9}$$

$$\sigma_{SS}^2 = \frac{DK}{r} \tag{10}$$

In order to transform from logarithmic to linear scale the following expressions have been used:

$$\mu_{Lin}(t) = \exp\left(\mu_{\ln}(t) + \frac{\sigma_{\ln}^2(t)}{2}\right) \tag{11}$$

$$\sigma_{Lin}^2(t) = \left[\exp\left(\sigma_{\ln}^2(t)\right) - 1\right]\exp\left(2\mu_{\ln}(t) + \sigma_{\ln}^2(t)\right) \tag{12}$$

4. Stochastic global model

The stochastic global model has been developed using a polynomial dependency between the operating conditions and the three FPE parameters, respectively *r*, *K*, and *D.* Considering the behaviour and the number of the three parameters along the manipulated variables, the exponent for the temperature and the antisolvent flowrate dependency has been considered only equal to 1 or 2.

The best model obtained using the Akaike Index Criterion is reported below:

$$\begin{aligned} r_i(q,T) &= \gamma_{i,0r} + \gamma_{i,1r}q + \gamma_{i,2r}T \\ K_i(q,T) &= \gamma_{i,0K} + \gamma_{i,1K}q^2 + \gamma_{i,2K}T^2 \qquad i = 1, 2 \\ D_i(q,T) &= \gamma_{i,0D} + \gamma_{i,1D}q^2 + \gamma_{i,2D}T \end{aligned} \tag{13}$$

The coefficients of expressions (13) were estimated using the Maximum Likelihood Method (MLM), using a set of nine experimental runs, combining three temperatures and three antisolvent flowrates, respectively T = [10, 20, 30] °C and q = [0.7, 1.5, 3.0] ml/min. The coefficients obtained have been reported on Table 1. The following behaviour can be treasured: (i) r_i increases with antisolvent flowrate and decreases with temperature; (ii) K_i decreases with antisolvent flowrate and increases with temperature and (iii) D_i increases with antisolvent flowrate and decreases with temperature. In fact, increasing antisolvent flow rate leads to higher nucleation rates (r increases), but reduces the average asymptotic crystal size (K decreases). Temperature has an opposite effect as already discussed3 in the non-isothermal antisolvent crystallization of sodium chloride (NaCl). Higher values of temperature, decreases *r* and reduces the driven force for nucleation and favours crystal growth (*K* increases). The operating conditions that favour nucleation determine a higher dispersion of the PSD, and this aspect has been correctly reconstructed by the behaviour of coefficient *D*.

Table 1: Values of the model parameters describing the dependence of (r, K, D) on antisolvent flowrate and temperature.

$\gamma_{i,0r}$	5.7639
$\gamma_{i,1r}$	2.8342
$\gamma_{i,2r}$	-0.1584
$\gamma_{i,0K}$	4.8593
$\gamma_{i,1K}$	-0.0244
$\gamma_{i,2K}$	2.0 E-4
$\gamma_{i,0D}$	0.3864
$\gamma_{i,1D}$	0.0287
$\gamma_{i,2D}$	-0.0094

5. Operational map

The obtained stochastic global model can be used to define the operating conditions of the crystallization process, leading to the desired mean and variance of the crystal size distribution. In order to have a functioning tool for designing the proper crystallization runs, a map can be constructed where asymptotic iso-mean and iso-variance curves are reported in an antisolvent flowrate – temperature plane, in linear scale.

First the global model has been validated for different operating conditions, in particular, we have considered three temperatures, 10 °C, 20 °C and 30 °C, using a constant antisolvent flowrate, equal to 2.25 ml/min.

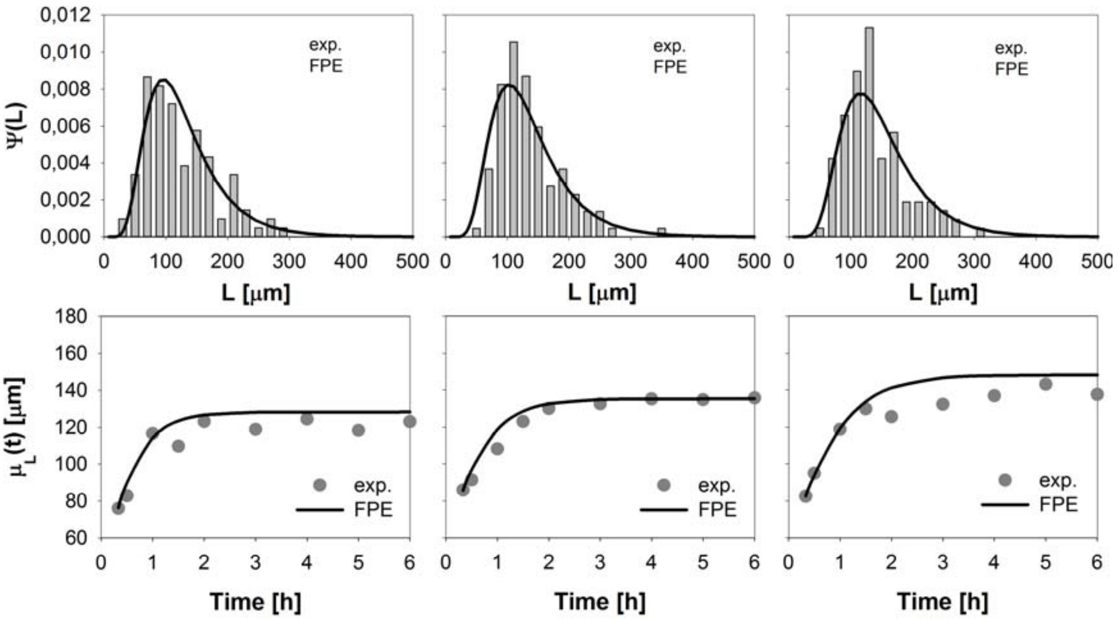

Figure 1: First row: asymptotic CSDs (line) predicted, (histogram) experimental. Second row: time evolution of the mean size of crystals (circle) experimental data and (line) predicted. The results are reported increasing the temperature from the left to the right.

The comparison between the experimental data and the predictions shows a good fitting for the stochastic global model for all the three condition selected, see Figure 1. From the results obtained it is possible to affirm that the global model, although the simplicity of the model used and the simple polynomial relation to correlate the FPE parameters to the operating conditions, has a good performance also in conditions different from the ones used for calibration.

Observing the operating map, Figure 2, was also possible to identify multiple asymptotic conditions, leading to obtain a specific product, considering the mean and the variance, using different antisolvent feedrates and temperatures. In order to study this fact we have reported the results obtained, in terms of asymptotic CSDs, for the two set of operating conditions, the two circles in Figure 2. This result is coherent with the opposite effects that antisolvent flowrate and temperature have on the crystallization process: high asymptotic crystal size can be reached with low *q* and high *T*, but the same result can be obtained increasing q and, at the same time, decreasing *T*.

Once again we can affirm that the global model has a good fitting of the experimental data, confirming also the multiplicity of the asymptotic conditions observed from Figure 3. From an operating point of view, we can now identify a region, from the operating map illustrate in Figure 2, in which the same CSDs can be obtain with a higher consumption of antisolvent and with a higher temperature.

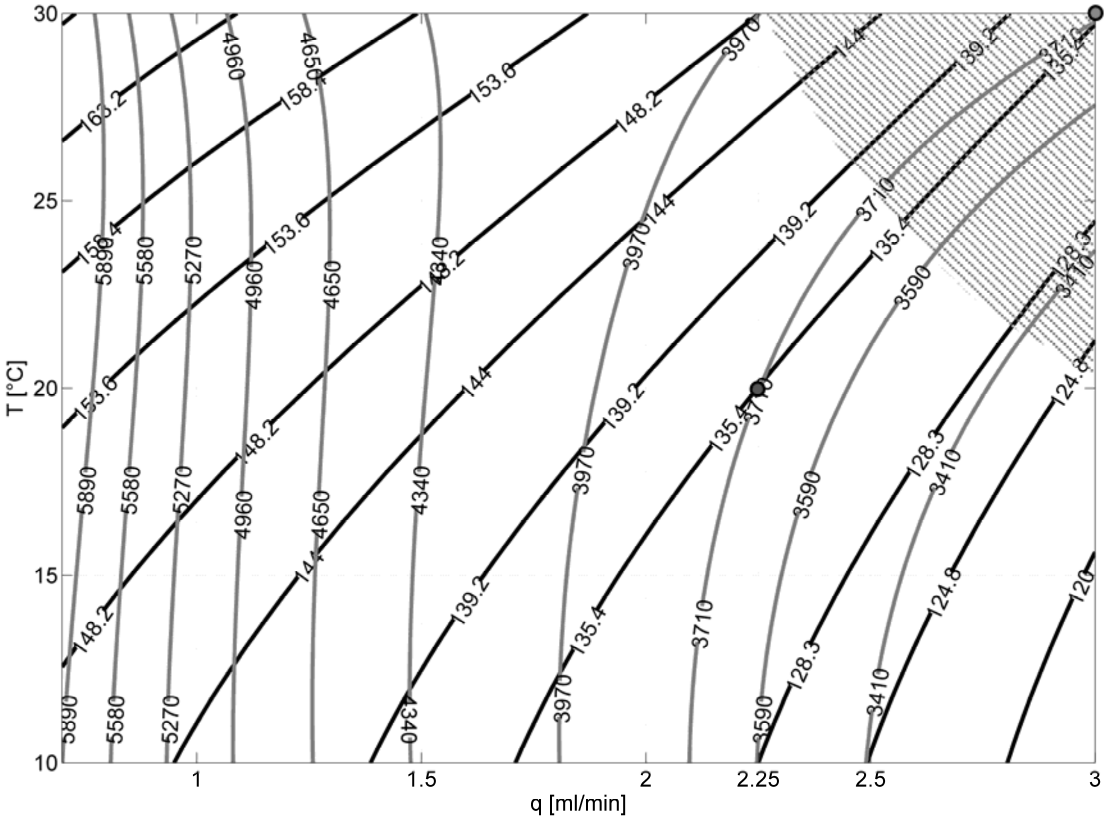

Figure 2: Iso-means - iso-variances map, reported in function of T and q, for the linear FPE in linear scale. The black lines represent the means and the grey lines the variances. The two dark grey dots in the map represent a multiple asymptotic CSD. The patterned area represents a region of multiplicity.

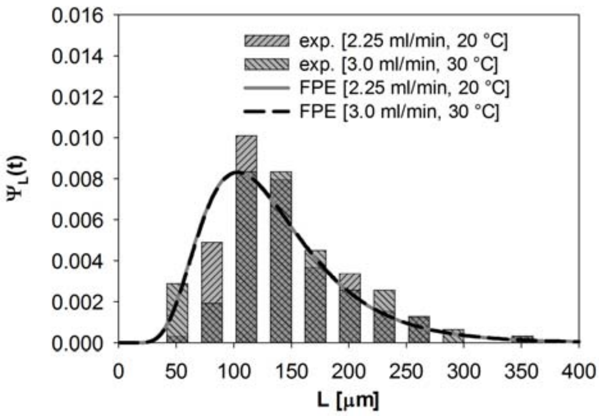

Figure 3: Asymptotic CSDs obtained in the multiple asymptotic CSDs, previously showed in Figure 2, compared to the prediction made with the operating maps.

6. Conclusions

The crystallization aided antisolvent process has been here described using the Fokker-Planck approach, including the dependencies on the manipulated inputs, which are the antisolvent flowrate and temperature. The obtained global model has been used to define an operative map, where the first two moments of the predicted CSD, such as variance and mean size of crystals, have been plotted with respect to the operating conditions (temperature and antisolvent flowrate). This representation allows studying the feasibility to obtain a specific product, in particular considering a given mean size and variance of the CSDs, but also identify if the same product can be obtained considering a lower antisolvent feedrate and minimizing the energy consumptions, by observing the multiplicities of the asymptotic conditions. All the results have been experimentally validated considering the asymptotic CSDs and the dynamic of the mean size of crystals, showing a good prediction of the system considered.

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