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Modelling of crystallization process and optimization of the cooling strategy

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Abstract−To obtain a uniform and large crystal in seeded batch cooling crystallization, the cooling strategy is very important. In this study, an optimal cooling strategy is obtained through simulation and compared to linear and natural cooling strategies. A model for a crystallization process in a batch reactor is constructed by using population balance equation and material balance for solution concentration, and a prediction model for meta-stable limit is formulated by the dynamic meta-stable limit approach. Based on this model, an optimal cooling strategy is obtained using genetic algorithm with the objective function of minimizing the unwanted nucleation and maximizing the crystal growth rate. From the simulation results, the product from the optimal cooling strategy showed uniform and large crystal size distribution while products from the other two strategies contained significant amount of fine particles.

Key words: Optimal Cooling, Batch Crystallization, Meta-stable Zone, Genetic Algorithm

INTRODUCTION

The crystallization process is an important unit operation in modern industry both as a separation and purification technique. With the rapid growth of the biochemical and pharmaceutical industries, the importance of crystallization has been recognized even more. Crystallization is a convenient separation technique, because this process often yields high purities easily and mostly cheaper in energy consumption than other techniques. The importance of a well-controlled crystallization process is emphasized in the pharmaceutical and fine chemical industries where the properties of the product highly depend on the operating conditions of crystallization process. Especially, the product purity can be significantly enhanced as the particle size increases through crystallization at the final stage of the production process [1]. The effort to obtain large crystals has been increased significantly over the past decades [2]. However, the mechanism and kinetics of crystallization still seem to be an art rather than science. A good part of research interest is focused on the modelling of the crystallization process by different mathematical techniques, because the accuracy of the process model will result in an improved profit of the industrial crystallization. The most important objectives of the crystallization process are the yield and purity, but equally important are the morphology and size of crystals. Among these, the control of crystal size distribution (CDS) is the main target in industrial cooling crystallizations. For controlling the CSD of product, the most crucial manipulated variable is the temperature profile of the cooling crystallizer. Depending on the cooling strategy, the CSD is influenced significantly. Thus, it is very important to understand the effect of temperature on nucleation and growth kinetics [3].

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In crystallization, it is desirable that the CSD of the final product should be narrow and the average size as large as possible. To obtain good quality of product through crystallization, the nucleation has to be suppressed while the rate of crystal growth should be maximized so that the seeds grow as fast as possible while the generation of nuclei is minimized. Thus, the suppression of undesired ancillary nucleation after the seed crystals are fed or generated is a crucial factor to achieve the desired CSD. For this purpose, the solution is required to be carefully maintained within the meta-stable zone, which refers to the region where spontaneous nucleation is believed to be unlikely [4]. Many research efforts have been exerted in the investigation of meta-stable zone. Nonetheless, its definition has still some vagueness and the models to estimate the meta-stable limit (MSL) have not been matured enough to be used in practical operation. Recently, a new method to predict the MSL based on the dynamic interpretation [5]. Even though there are many important factors affecting the MSL behavior, the cooling rate is the most frequently used manipulated variable to control the CSD in industrial crystallization. Most common form of the MSL prediction is the power law of the cooling rate as suggested by Nývlt [6]. Their method regarded the MSL as a static function of cooling rate. However, their method failed to explain the MSL behaviors in different cooling strategies. For example, if the cooling stops after a constant cooling in meta-stable zone, their model predicts the generation of nucleation at the moment when the cooling stops. This is clearly different from reality. Thus, the new dynamic approach can be used to predict the meta-stable limit and to optimize the operating condition of the crystallizer for desirable product quality. If a reliable prediction of MZW is available in real-time, one may push the solution temperature to the point where the driving force for crystal growth is maximized while not violating the MSL so that the nucleation can be inhibited. In cooling crystallization, the optimal operation strategy should be close to MSL as possible and this strategy can

be obtained by formulating a constrained optimization problem. The objective function can be chosen as a function of the third moments of the CSD, which represents the average crystal size and combining the closeness to MSL. If the solution temperature does not violate the MSL during the operation, the nucleation will be minimized and the CSD of product will be maintained as the shape of seed CSD with grown average size.

In this study, a model for the cooling crystallization process is constructed by using the population balance model with dynamic meta-stable limit prediction. Then, the optimal cooling strategy is obtained by using the genetic algorithm as an optimization method in order to maximize the crystal growth rate while suppressing the nucleation so that the final product CSD is as narrow as possible. In the simulation of the crystallization process, the cooling rate has upper and lower bound as constraints as in real processes. The operation time and the final temperature are set to be identical in all types of the cooling strategies in order to compare results of various cooling strategy. The obtained cooling strategy can be applied to the industrial crystallizer for desirable product. If there are some discrepancies in actual application for optimal operation due to modelling error, then the optimal cooling strategy has to be recalculated after reducing the weight for the closeness to MSL in the objective function so that the possibility of nucleation can be reduced.

MODEL FOR BATCH COOLING CRYSTALLIZATION

1. Dynamic Model of Meta-stable Limit

The states of solution for crystallization can be classified by three regions in the phenomenological point of view. A stable region exists in the unsaturated condition that more solute can be dissolved. Labile region exists in the supersaturated condition that both nucleation generation and crystal growth can occur in the solution. The meta-stable region also exists in the supersaturated condition but only crystal growth is possible and nucleation will not occur spontaneously. The concept of the labile and the meta-stable supersaturation was first introduced by Wilhelm Ostwald in 1897 [4]. For maximizing crystal growth while inhibiting the nucleation, the meta-stable limit has to be determined as exact as possible and the operating condition should be maintained in the meta-stable region. Many researches on predicting the meta-stable limit have been published over a long period of time. However, the exact definition of MSL is still not clear and its prediction is not accurate. Among traditional approaches, Nývlt in the 1970's and 1980's proposed that the meta-stable zone width, $\Delta T_{max}(c)$, depended on the cooling rate directly as follows:

$$\Delta T_{max}=ku^{p} \tag{1}$$

where, u is the cooling rate of the solution, and the two parameters, k and p, are dependent on the saturation concentration. This static model in that meta-stable limit location varies only with cooling rates has been widely accepted and used for the definition of meta-stable limit in industrial crystallization. Despite the acute prediction for the linear cooling case, the prediction results could not explain the observations from the cases of variable cooling rate. For example, when the cooling rate is turned to zero while the solution temperature is lower than the saturation temperature, it yields $\Delta T_{max}=0$ since u=0. It implies that some nucleated crystals appear at the moment of stopping cooling. In reality, crystal particles would be observed after some period of time from the instant when the cooling stops. Also, when solution is cooled with constant cooling rate from a steady state, this approach predicted that the meta-stable limit width becomes nonzero from zero immediately. It is unnatural to assume that a physical property changes in step manner in reality. Therefore, it is more natural to postulate that the meta-stable limit changed gradually separated from the saturation curve. To explain the dynamic behavior of meta-stable limit, following 1st-order dynamic model was proposed [5].

$$\tau\frac{\Delta T_{max}(t)}{dt}+\Delta T_{max}(t)=ku(t)^{p} \tag{2}$$

This model has a 1st-order dynamics of meta-stable limit width with nonlinear input to the rate of driving force inducing supersaturation. Three parameters, k, p, and τ depend on saturation concentration.

2. Model of Batch Crystallizer

To simplify the mathematical model, a few assumptions are employed: that the solution is well-mixed, crystal breakage and agglomeration are negligible, the density of the crystals as well as the surface and volume shape factors are independent of the temperature, crystals are born at zero size and heat transfer in the solution is neglected. With these assumptions, the population balance equation (PBE) for crystallization is obtained as in the following form.

$$\frac{\partial f(L,t)}{\partial t}=-\frac{\partial[G(L,t)\cdot f(L,t)]}{\partial L} \tag{3}$$

where f denotes the population density of crystals, t is the time, L is the size of the crystals, and G represents the growth rate. The overall growth rate is given by

$$G=k_g(T,L)\cdot\Delta c^{g} \tag{4}$$

where Δc is the driving force which is the difference between the solution concentration, c, and the saturation concentration c^*. The kinetic growth rate constant, k_g is given by relation below and the parameters can be obtained from the experiments. The parameters are dependent on temperature and length of the crystals:

$$k_g(T,L)=k_0\exp\left(\frac{-E_g}{RT}\right)(1+k_1L)^{k_2} \tag{5}$$

The driving force is decided by the solution concentration and the solution concentration varies as the nucleation and growth of crystal proceed. The changes of environment for crystal formation should be modelled by the material balance. The rate of changes in solution concentration is entirely dependent of the rate of change in crystal mass.

$$\frac{dc}{dt}=-\rho\cdot k_v\frac{d\mu_3}{dt} \tag{6}$$

where μ_3 is the third moment of the CSD which is defined as

$$\mu_3=\int_0^{\infty} n\cdot L^2 dL \tag{7}$$

and k_v is the shape factor of crystals. To calculate the saturation concentration an experimental equation reported by Choi and Kim [7] is used, which is given by the following equation as a function of temperature.

$$c^* = Ce_1 + Ce_2 \cdot T \quad (8)$$

The nucleation rate, N, can have diverse forms, but the most widely used empirical equation is given by

$$N = k_b(T) \cdot \Delta c_{max}^{\beta}(T) \quad (9)$$

This equation has a very similar form as that of the growth rate. Then, the model for batch cooling crystallization can be constructed by one PDE and one ODE which are the PBE and the material balance in the solution, respectively. Both equations depend on time and indirectly on temperature and crystal size. These equations have to be solved simultaneously. However, it is difficult and computationally expensive to solve these equations. Therefore, an additional solution technique can be exploited. Hu et al. [8] have reported a simple solution for PBE in a combination of discretization and method of characteristics. This method provides an effective method to reduce the PBE to a set of algebraic equations. In this method the population density of crystals is expressed as following equation:

$$f(L_i, t_{j+1}) \approx \frac{f(L_i, t_j)}{1 + \left.\frac{\partial G(L,t)}{\partial L}\right|_{L=L_i} \Delta t} \quad (10)$$

and $L_{i,j+1}$ is given by

$$L_{i,j+1} \approx G(L_{i,j}, t_j)\Delta t + L_{i,j} \quad (11)$$

These equations can be easily solved along with the ordinary differential mass balance equation.

OPTIMIZATION BASED ON GENETIC ALGORITHM

Since the nature of the problem to find the optimal cooling curve in this study is very nonlinear and possesses many local optima, ordinary optimization methods such as sequential quadratic programming cannot obtain the solution. Thus, it requires an optimization technique that can find the global optimum. In this study, the genetic algorithm (GA) is employed for finding the optimal cooling strategy. The genetic algorithm was first suggested by John Holland, who developed the idea and the framework in the late 1960s and the early 1970s [8]. The GA is a search technique hat can be used to find exact or approximate solutions to optimization and search problems. It is categorized as global search heuristics. Also, it is a particular class of evolutionary algorithms that use techniques inspired by evolutionary biology such as inheritance, mutation, selection, and crossover. Among many optimization approaches, GA is a popular method in various chemical engineering problems because it has some advantages over the other methods. The GA has flexibility and robustness as a global search method, and it does not require gradient information and makes relatively few assumptions about the problem being solved. Also, it can deal with highly nonlinear problems and non-differentiable functions as well as functions with multiple local optima. The concept of this technique can be summarized as follows. The initial population of possible solutions to the problem is selected in a domain of independent variables, Ω randomly or by some strategy. Each candidate solution, which is called a chromosome, has its own set of variables that describe the solution. Each individual is evaluated by the objective function, and the value of function is called the fitness of the individual. Based on the fitness function values, the whole population is sorted and some of them are selected according to the fitness of its individuals, which is called the fittest survival. Some individuals who are randomly selected from survived individuals mate with each other by crossover for a new generation and some are mutated randomly for finding a global optimum. Then, the new population, which consists of old and new generation, is again going through the same selection procedure using the fittest survival strategy. Commonly, the algorithm terminates when either a maximum number of generations has been reached and/or a fitness level has reached to a desired value. To formulate the problem of this study all of the real-valued genes in the chromosome represent cooling rates of each time interval, and the allowable cooling rate is automatically satisfied by limiting the gene code within the bounds.

In this study, the optimization problems are related to the quality of product CSD. The important objectives are to suppress nucleation and to maximize the crystal mean size. So the objective function can be formulated as follows:

$$\min_{u(t)} \left(\mu_3^n + w\frac{1}{\mu_3^s} \right)$$
$$\text{subject to } 0 \le u(t) \le 50 \quad (12)$$

where μ_3^n and μ_3^s are the third moments of the CSD of crystal formed by nucleation and the crystal growing from the seeds, respectively. To avoid heating and violating the allowable cooling rate, the cooling rate is limited from 0 to 50 °C/hr. For the comparisons of various types of cooling strategies, the operation time and termination temperature sets to be identical. Even the cooling profile is a continuous function of time; the full time span of the operation is divided into 50 sections in order to apply the GA. The higher value for the number of sections would not make much difference in the objective function. Thus, the number of sections has been decided based on the calculation efficiency and computational efficiency.

RESULT AND DISCUSSIONS

The optimal cooling strategy is obtained by the GA for the objective function and constraints given in Eq. (12). To evaluate the effectiveness of the optimal cooling curve, two other cooling strategies, which are the linear and natural cooling methods, are considered. The simulation results of the linear, natural and optimal cooling curves are shown in Figs. 1-3, respectively. For fair comparison, the initial and final temperatures, batch time, seed size and amount of seeds are fixed at the same values for all cases. In Fig. 1, the linear cooling strategy is applied. The cooling starts at 60 °C and the solution is cooled down so that the final temperature 24 °C at 1.5 hr linearly. In this case, the solution temperature and the meta-stable limit cross each other in the middle of the operation, at which the nucleation occurs. Even though two lines cross back later so that the nucleation stops, the generated nuclei will grow and the final CSD contains large number of fine particles. In Fig. 2, the natural cooling strategy is applied. The natural cooling strategy has higher cooling rate at the initial period and lower cooling rate at the later period, which is determined by the temperature difference between the solution and constant cooling medium temperatures. In this case also, there is a region that the solution temperature is lower than the meta-stable limit and fine particles are generated. Thus,

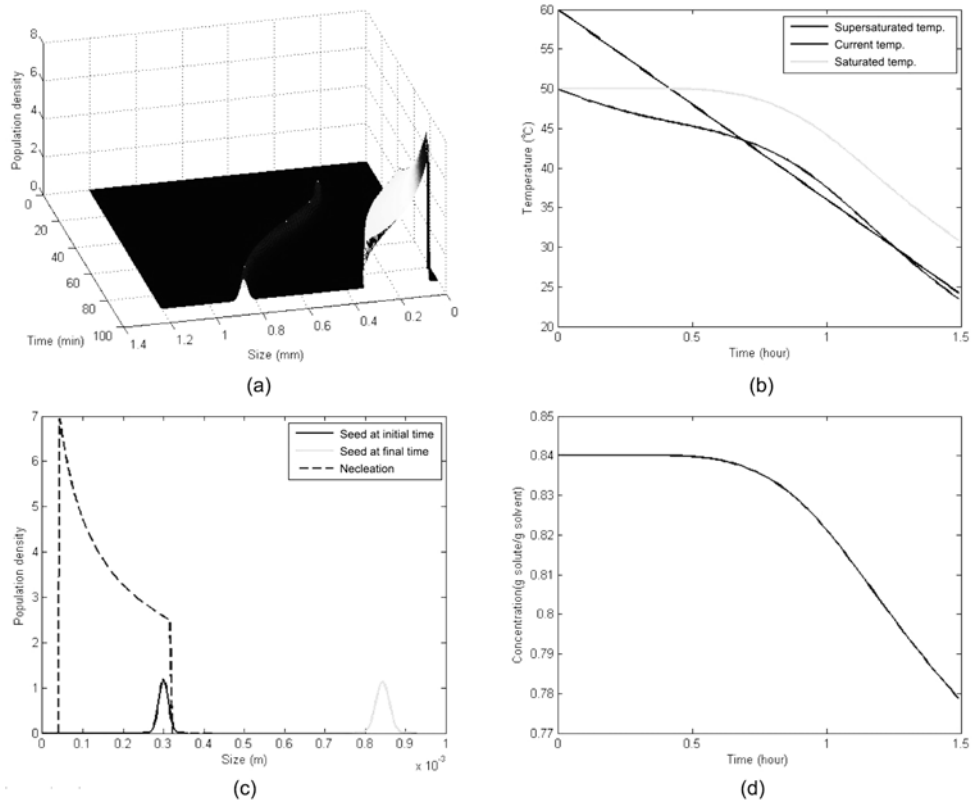

Fig. 1. Simulation results for the linear cooling curve (a) Evolution of CSD, (b) The linear cooling curve and metastable limit, (c) Seed and newly formed crystal size distribution, (d) Solution concentration profile.

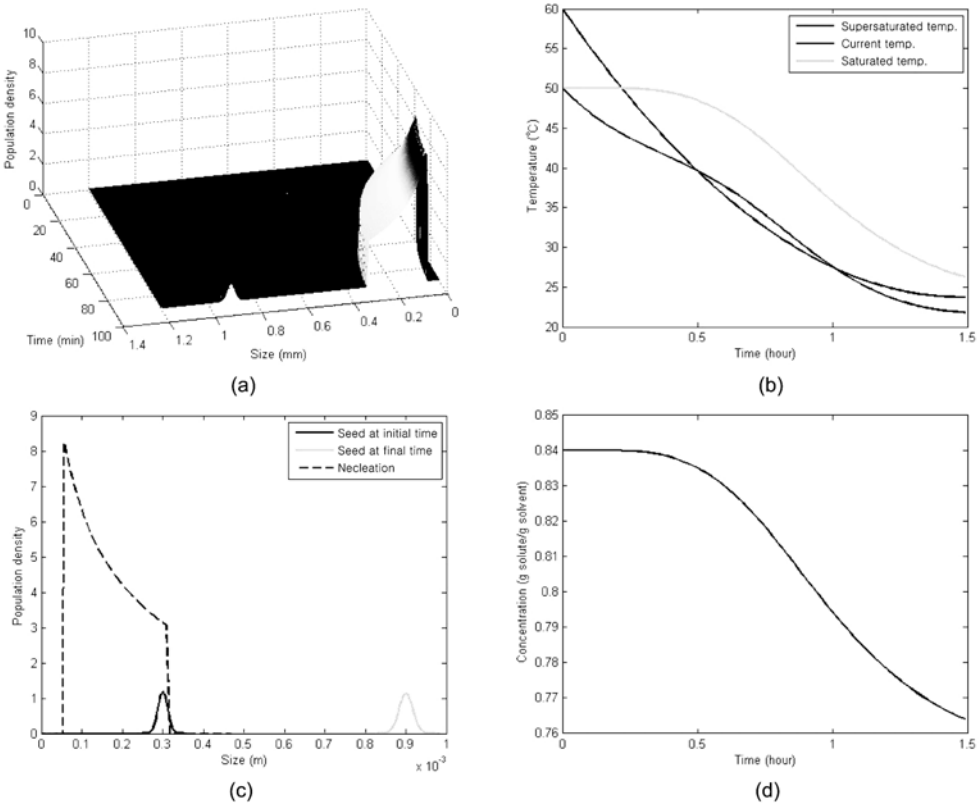

Fig. 2. Simulation results for the natural cooling curve (a) Evolution of CSD, (b) The natural cooling curve and metastable limit, (c) Seed and newly formed crystal size distribution, (d) Solution concentration profile.

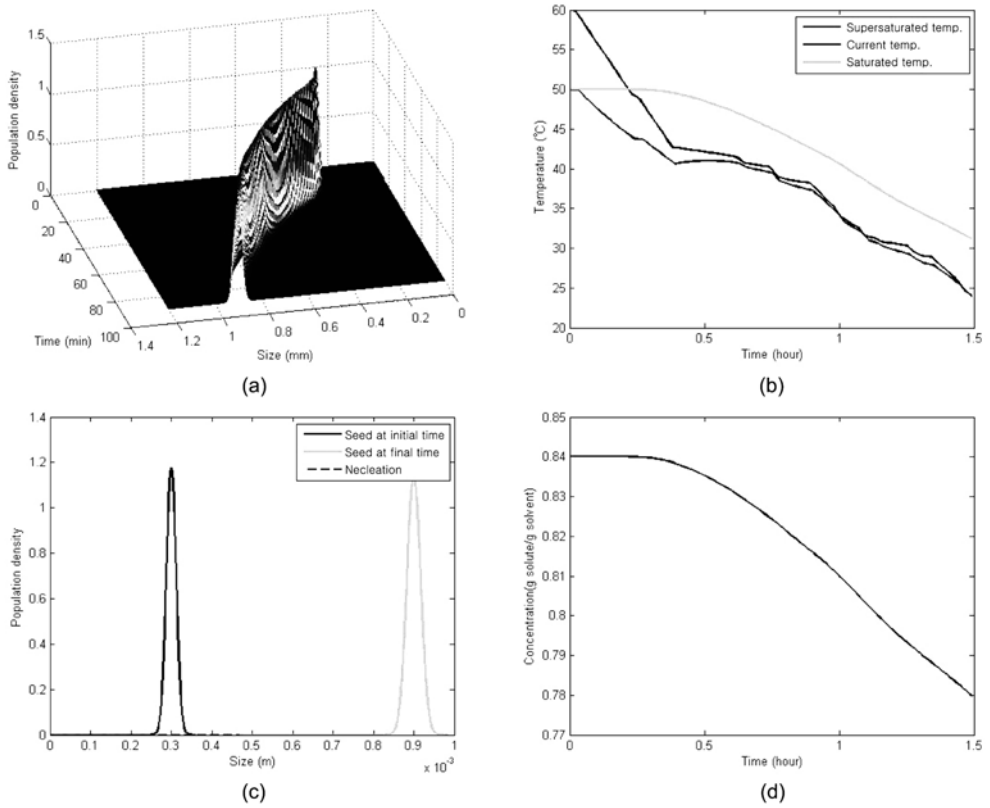

Fig. 3. Simulation results for the optimal cooling curve (a) Evolution of CSD, (b) The optimal cooling curve and metastable limit, (c) Seed and newly formed crystal size distribution, (d) Solution concentration profile.

the final CSD has undesirable shape as the linear cooling case. The average size of the particles for natural cooling case is larger than that of linear cooling case, but the population density for nucleated particles is higher. In Fig. 3, the optimal cooling strategy obtained from the optimization solution is adopted. Since there is no violation of the meta-stable limit in the optimal cooling curve, the nucleation does not occur. The product from the optimized process has very uniform distribution as seed particles and the average crystal size is larger than the other two cases.

Through the simulation study, the effectiveness of the optimal cooling strategy has been verified. Since the product particle contains a reduced amount of fine particles, the cake resistance will be reduced and this will lead to facilitate the post-processes such as filtering, washing, drying etc. If the model contains errors, the obtained optimal cooling strategy may not be of great help in a real situation. In that case, a different type of objective function can be chosen. The most important objective in this operation is to prohibit the unwanted nucleation and maximize the growth rate if possible. The increased uncertainty of the model will increase the risk of unwanted nucleation. To reduce the risk, the concept of closeness of the solution temperature to meta-stable limit can be incorporated into the objective function. With the wider gap between those values on the closeness, it will lead to conservative operation so that the risk of nucleation is reduced at the cost of slower growth rate.

CONCLUSIONS

In this study, an optimal cooling strategy is obtained through simulation and compared to linear and natural cooling strategies. A model for a crystallization process in a batch reactor is constructed by using a population balance equation and material balance for solution concentration, and the prediction model for meta-stable limit is formulated using the dynamic meta-stable limit approach. Based on this model, an optimal cooling strategy is obtained by using the genetic algorithm with the objective function of minimizing the unwanted nucleation and maximizing the crystal growth rate. From the simulation results, the product from the optimal cooling strategy showed uniform and large crystal size distribution, while products from the other two strategies contained a significant amount of fine particles. For further study, it is necessary to verify the optimal cooling strategy with the experimental results and consider the seed effects and operation time for improving productivity.

NOMENCLATURE

ΔC_{max} : maximum allowable super-saturation, solute kg/solvent kg
k : parameter for meta-stable limit dynamics
p : kinetic order of cooling rate for meta-stable limit dynamics
ΔT_{max} : maximum allowable undercooling [°C]
t : time [sec]
t : time constant for meta-stable limit dynamics [hr]
u : cooling rate [°C/hr]
k_b : nucleation rate constant, crystal number/kg*min
k_g : growth rate constant [m/min]
k_v : volume shape factor
L : crystal size, as length [m]

N : overall nucleation rate, crystal number/kg*min
f : population density
T : temperature [°C]
ΔC : super-saturation, kg solute/kg solvent
β : power of nucleation rate
μ_3 : third moment of the crystal size distribution
ρ : density of crystals [g/m^3]

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