"BABES–BOLYAI" UNIVERSITY,

CLUJ-NAPOCA

Faculty of Chemistry and Chemical Engineering

Botond Szilagyi

MODEL BASED ANALYSIS AND CONTROL OF COOLING CRYSTALLIZERS

Abstract

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Chapter 1. Motivation and main objectives

The crystallization is a widely applied separation, purification and particle formation method in chemistry as well as in chemical and pharmaceutical industry [1]. Moreover, it has numerous applications in food industry, heavy chemical industry and petrochemical industries too. According to estimates around 80 % of chemical industrial end-products involve powder ingredients [2]. In chemical research the aim of crystallization may be the X-Ray Diffraction (XRD) analysis whose result is proven to depend on crystal size and shape. The protein crystallization represents increased interests as the drug design methods often make use of it. The state-of-the art heat storage systems use the latent heat of crystallization as a straightforward manner of energy accumulation [3]. Nano-sized materials are also crystallized and the quick spread of plastics also generated significant research in polymer crystallization. The crystallization serves the microelectronic industry by offering the possibility of silicone production. The possibility of growing pure crystals of controlled size distribution with reduced energy demand made the crystallization the most important separation tool in sugar industry [4]. Nevertheless, the crystallization might appear as a natural accompanying phenomenon of heat and mass transfer processes. Such an example might be the fouling, undesired salt deposition in the heat exchangers or the methane hydrate formation in oil industry [5].

Crystallization operations are carried out in batch, continuous batch and tubular crystallizers as well [6]. The choice between the continuous or batch operation generally depend on the scale of production: the benefits of optimal continuous operation are inevitable if the requirements are high enough but for smaller quantities, as generally happen in the pharmaceutical industry, the batch crystallization may be more favorable. Nevertheless, in the last years the Food and Drug Administration (FDA) is urging the adaptation of continuous technologies into food and pharmaceutical industries too [7].

Regardless of operation mode, the key concern in any industrial process is to improve the quality of final product and to maximize the production efficiency while taking into account various ecological and economical aspects [8]. One of main challenges in modern particulate science is the robust and reproductive control of crystal size distribution as it significantly affects the downstream operation (filtration, drying, granulation, transportation) and some of relevant macroscopic properties of the powder (porosity, dissolution rate, specific surface etc.). Significant time was spent on analysis and control of crystallization processes from both theoretical and experimental sides [9]. Despite of the fact that crystallization is one of the oldest unit operations there is a disproportionate number of problems associated with its deep understanding and control. These uncertainties the results of the complex competitive-consecutive process dynamics, the significant effects of hydrodynamics and the lack of understanding the exact mechanisms of nucleation and crystal growth [10].

The problem of analyzing and controlling the CSD was investigated majorly for monodimensional (e.g. sphere or cube) crystals but the behavior of higher dimensional crystal shapes during the crystallization was not in research focus for long years [11]. The explanation lies in the fact that tracking higher dimensional crystal size distributions became possible in the

last decades with the most advanced tools of microscopes and image processing tools [12]. However, multidimensional population balance models were proposed and discussed which, among of other applications, is able to describe de temporal evolution of multi-dimensional crystal shape, these instruments predominately were applied to support the experimental results [13]. Nevertheless, some publication emerged detailed model based system analysis, only a few of them refers to multi-dimensional case [14]. The state-of-the art shape control generally reduces to mean aspect ratio and mean size control or tracks a (model based) pre-defined concentration or temperature profile [15].

The overall aim of this work was to develop single and multivariable population balance model-based analysis and control approaches for cooling crystallization processes. The main focus is on manipulation possibilities of the CSD. The following objectives were posed:

- To identify gaps in our actual knowledge in cooling crystallization and to develop mathematical models for the given system.
- To develop solution methods for fast and accurate solution of extended multivariable population balance equations.
- To carry out parametric analysis with the simulations in focus of factors influencing the CSD.
- To apply high performance computing in control-oriented solution (Finite Volume Method - FVM) of population balances exploring the compute capacities of the GPU.
- To create a MatLab based function, which enables the simple solution of PBE-s.
- To develop a Graphical User Interface (GUI) for the MatLab based program which, enables the interactive, simple simulation of crystallization processes.
- To develop a NMPC strategy for batch crystallization which uses state-of-the-art process analytical technologies (FBRM and PVM). Demonstrate the control system performance and robustness via numerical simulations.
- To gather experimental data and validate a mathematical model.
- To implement the NMPC, running with the validated mathematical model for ascorbic acid crystallization from water and
- To validate a bidimensional mathematical model based on concentration and chord length distribution data

Chapter 2 - Literature survey

The crystal formation - crystallization occurs when the atoms or molecules of a substance are locating systematically in a well-defined crystal lattice. A solid state crystal can be formed by solidification of a melt, by vapor deposition (either chemical or physical), by a solution crystallization *etc*. Solid state crystallization processes are also known when the atoms of a disordered (amorphous) solid are forming a crystal or one crystal structure is transforming to another one in solid state. In this context the crystallization, as a rule, involves at least two distinct phases. These phases, in the case of solution crystallization are in two distinct state of matter - solid and liquid. This thesis axes in the topic of solution crystallization.

The crystallization itself is a natural stabilization process of thermodynamically un-stable systems. This instability is a result of supersaturation state: a solution is supersaturated if the actual solute concentration exceeds the saturation concentration under the given thermodynamic conditions (temperature, ionic force, solution composition *etc*.). There are a several ways of superaturation generation but the most important is the cooling, which uses the simple principle that the solubility (generally) decreases with the temperature.

Next to the solubility line, one more additional curve can be defined in the temperature – concentration phase diagram: the metastable limit, as Figure 1 illustrates. It seen that the metastable concentration limit is higher than the solubility. Above the metastable limit the solution is labile, which entails spontaneous crystallization. In metastable zone, however, the situation is more interesting: in this zone the growth of existing crystals occurs but the nucleation, the formation of new crystals is prohibited. In contrast with the solubility line, which is constant, the metastable limit depends on operating conditions such as the cooling rate. As the nucleation occurs above the metastable limit this is often referred as nucleation curve.

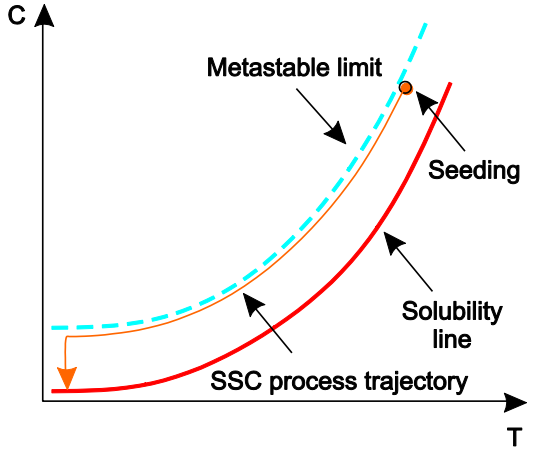

Figure 1. General trajectory of a batch crystallization process in the c-T phase diagram

The crystallization generally is conducted within the metastable zone, as the Figure 1 presents: the two, industrially applied feedback control strategies, finally, applies this principle. (i) the supersaturation control (SSC) works based on concentration measurement and is aimed to maintain desired supersaturation level [9]. (ii) the direct nucleation control (DNC) measures the

relative particle number and by repeated heating-cooling (fines dissolution-growth) cycles it keeps the crystal number in desired level [16] thus it keeps the system in the metastable zone.

The more advanced, model based controllers uses the so-called process models to predict the system behavior [17], whose idea is to find the temperature profile, based on process simulations, which will lead exactly to the desired product [18], as the Figure 2 illustrates. It was showed that employing process models in the calculation of temperature profile improves the quality of control: either from economical (e.g. shorter batch time) or technological (e.g. improved crystal size distribution, not requiring milling or coagulation) point of view [19].

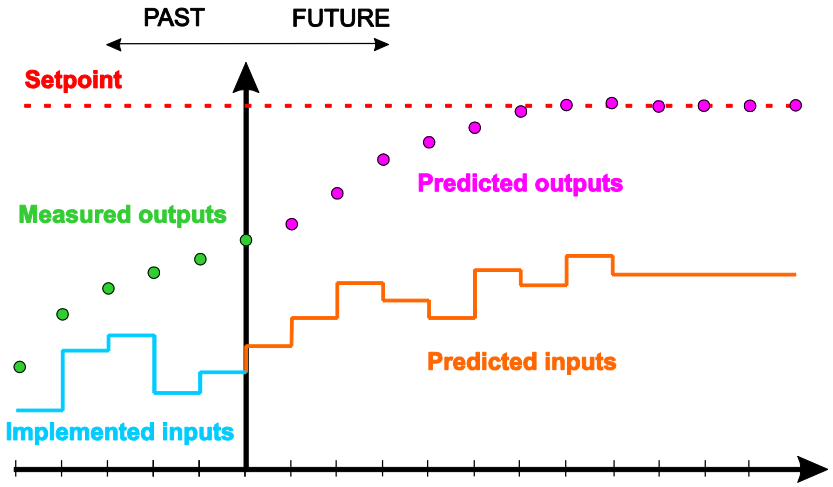

Figure 2. Schematic representation of the working principle of the model based controllers

The model based controllers involves, generally, population balance models, which describes the temporal evolution of crystal size distribution [20]. Is a general situation that the solution of these model equations, due to their hyperbolic nature, is more complicated than the deduction for the given system [21]. The moment based method [22] and the finite volume methods [23] are promising techniques for crystallization simulation. One of these is employed in the overwhelming majority model based control systems.

For robust crystallizer operation state estimators are required [24]. The state estimator, as it name already suggests, it aimed to estimate the (un-measurable) system states for the model based controller. For instance the population balance based simulation is used to calculate the optimal temperature profile (NMP control). The crystal size (distribution) is required in the actual time moment, as an initial condition of process simulation, but this cannot be directly measured with real time measuring tools. Thus, a numerical apparatus is required, which, by using the available measurements (e.g. concentration) estimates the actual crystal size distribution. Various state estimators are applied in crystallization control from the famous Kalman filters [25], through the Luenberger observers [26] to moving horizon estimators [27].

Despite of the significant (and continuously growing) process engineering efforts of last two decades, the model based crystallizer analysis and control has still numerous open challenges and issues. The model methods are more and more accepted tools in the pharmaceutical industry as well.

Chapter 3. Modeling the cooling crystallizers

The batch crystallization is still widely applied in fine chemical and pharmaceutical industries where the crystal shape and solution crystallization has significant role. The morphological PBE is, as a rule, multidimensional, which is able to reconstruct the shape of crystals at any moment of simulation. The simplest crystal shape is two dimensional [28]. With this restriction the rod-like and the plate-like crystals can be approximated, thus the simplest morphological PBM's are ready to describe the crystallization of rod-like and plate-like crystals [29]. Next to the PBE the mass balance is required to close the crystallizer model. Energy balance is necessary only if assuming natural cooling, otherwise (for linear cooling or temperature control) the temperature is a known variable, thus is not modeled.

The two dimensional particle is characterized with two so-called internal properties, which are in this case the two characteristic sizes (L_1 and L_2). These can be the length and width of the crystal. Then, the crystal population is characterized by a bi-dimensional size density function $n(L_1,L_2,t)$, which gives the number of crystals within the $(L_1, L_{1+}dL_1)\times(L_2, L_{2+}dL_2)$ size domain in t time moment. A typical 2D CSD is presented in Figure 3.

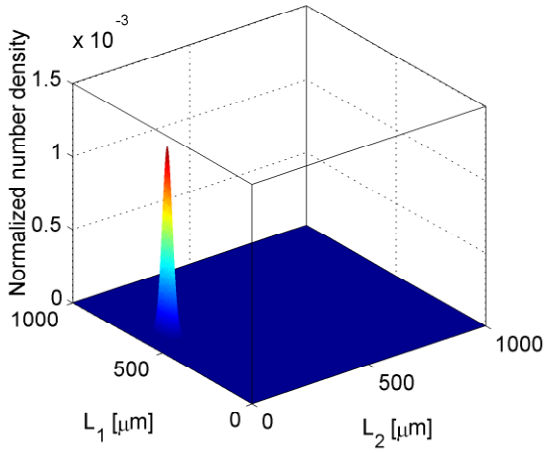

Figure 3. A typical 2D crystal size distribution

The 2D PBE governs the temporal evolution of the 2D CSD under the influence of various crystallization mechanisms (nucleation, growth, dissolution, breakage *etc*.). The 2D PBE is a two dimensional hyperbolic partial differential equation, which might involve integral terms if secondary crystallization mechanisms (such as agglomeration or breakage) are also modeled. The solution of these equations might cause difficulties as only limited number of numerical algorithms is suitable, and those generally have increased computational burden.

The 2D method of moments is a model reduction technique, which calculates the moments of the distribution by applying the moment transformation rule on the original PBE [30]:

$$\mu_{l,m}(t) = \int_0^{\infty}\int_0^{\infty} L_1^l L_2^m n(L_1, L_2, t) dL_1 dL_2, \quad l, m = 0,1,2... \tag{1}$$

Solving the generated moment equation system is generally carried out by numerical approximations to avoid the closure problem [31]. Using the calculated moments the mean crystal sizes and aspect ratio can easily be calculated:

$$\langle L_1 \rangle = \frac{\mu_{1,0}}{\mu_{0,0}}; \langle L_2 \rangle = \frac{\mu_{0,1}}{\mu_{0,0}}; A.R. = \frac{\langle L_1 \rangle}{\langle L_2 \rangle} = \frac{\mu_{1,0}}{\mu_{0,1}} \tag{2}$$

In some practical cases the mean particulate properties are enough to know and in these situations the quadrature moment of method is applicable, which has two very useful properties: it is applicable on complex, extended PBE's and its computational burden is decreased.

In the process control is sometimes required to manipulate the CSD, not only the mean crystal sizes. In these situations is required to use a PBE solution technique, which calculates the full CSD. Such a method is the high resolution finite volume method, which is accurate in terms of CSD and it has reduced computational cost compared to the classical FVM, if same accuracy requirements are posed, however, still much larger than of the moment based methods. The HR-FVM is a discretization based technique: it discretizes the continuous size distribution function (see Figure 4) and for each size bin generates an individual equation [32].

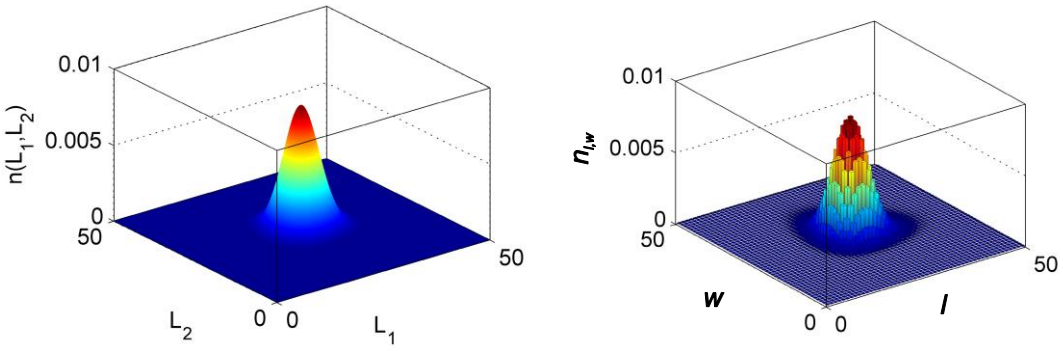

Figure 4. Illustrative two dimensional finite volume discretization

According to the Figure, 4 the approximation becomes more accurate if the mesh is finer. However this generates more equations, which needs to be solved. In the present thesis a novel implementation is developed for the HR-FVM, which utilizes the graphical processing unit (GPU) to solve the (parallel) HR-FVM equations. The GPU has massively parallel hardware architecture, equipped with hundreds or thousands of individual compute units. A typical CPU-GPU core comparison is presented in Figure 5.

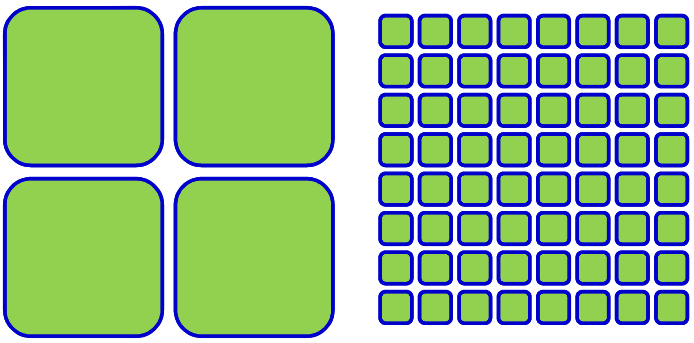

Figure 5. Comparison of a typical CPU (with four, fast cores) and GPU (with hundreds of slower cores) architectures

In the hybrid implementation the GPU is used to solve the parallel operations (such as integral calculations, HR-FVM equations and size dependent growth rate calculations) and the CPU for the serial parts of the algorithm (time stepping, mass balance calculation *etc*.). The code is compiled to *.mex* file, which is callable from the MatLab. The flow-sheet of this *.mex* file is presented in Figure 6. The main difficulty in the implementation is that the data existing in the on-board GPU memory is not visible for the CPU and *vice-versa*, thus the data need to be copied to the respective computing unit before attempting to execute the calculations. Next to the serial programming issues the parallel-specific questions, such as race conditions or thread synchronization needs to be handled.

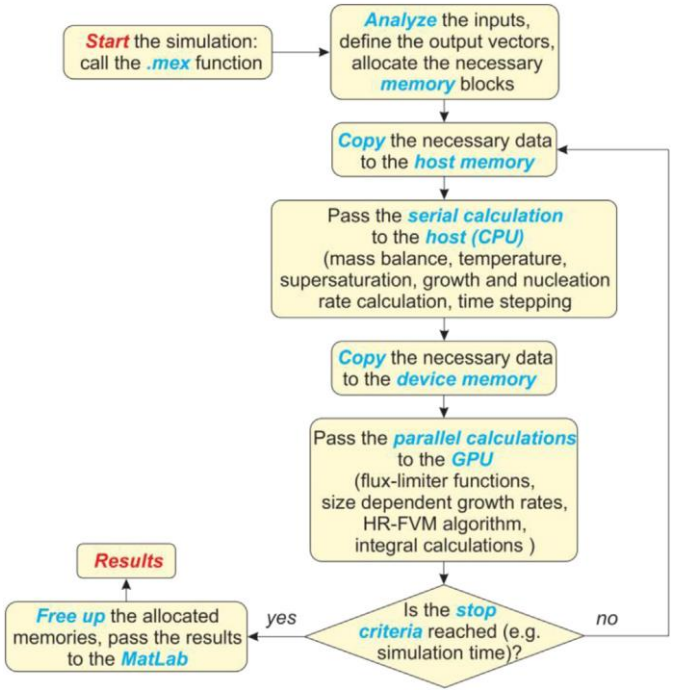

Figure 6. The working principle of the hybrid CPU-GPU implementation of HR-FVM solution

Nevertheless, *not all 2D* models are a *morphological* population balance. In this thesis a 2D model is developed for heat effects: in this case the first internal property of the crystals is the linear crystal size and the second the crystal temperature. Thus, the distribution of crystals temperature is taken into account, in contrast with the generally applied homogeneous temperature field approximation. This model enables the investigation of influence of un-measurable temperature distribution on the size distribution. The temperature and concentration conditions around of a particle being in supersaturated solution (growing crystal) are represented in Figure 7.

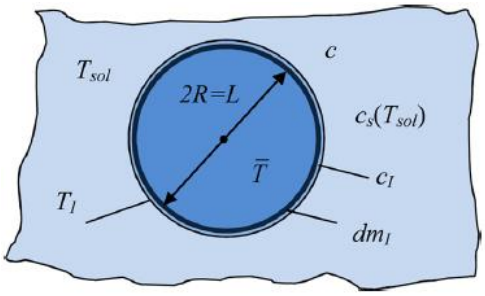

Figure 7. Thermal and concentration conditions during the crystal growth

In the model-predictive control simpler (1D) models were applied, as the main purpose of this part was the development of an MPC system, which uses the Chord Length Distribution (CLD), a distributional data routinely measured but very rarely used for quantitative purposes, strictly in of-line applications. A soft-sensor was developed, which, in fact, is the first principle simulation of the FBRM (Focused Beam Reflectance Measurement, measuring the CLD) which enables the CSD→CLD simulation thus enables the direct comparison of measured CLD with the simulation results. The method has negligible real time computational expense.

Chapter 4. Numerical analysis of cooling crystallizers

In this section simulation results are presented analyzing the behavior of continuous and discontinuous cooling crystallizers based on the models discussed in the previous chapter.

4.1. Batch cooling crystallization of plate-like crystals

The plate-like crystal shape appears amongst of pharmaceutical industry relevant organic materials but only a few paper deals with their simulation. In the simulations seeded crystallization was considered with secondary nucleation and growth(s) mechanisms. In the simulations it was showed that the seeding temperature (the temperature, at which the seeds are added, proportional with the degree of sub-cooling) has the most powerful effect on the product shape. According to the simulation results presented in Figure 8, the cooling rate has considerably weaker influence on the product shape than the seeding temperature. Manipulating the seeding temperature the product aspect ratio varies between 2 and 4. Truly, in real systems the seeding temperature depends cannot exceed the nucleation curve as above of this spontaneous primary nucleation occurs.

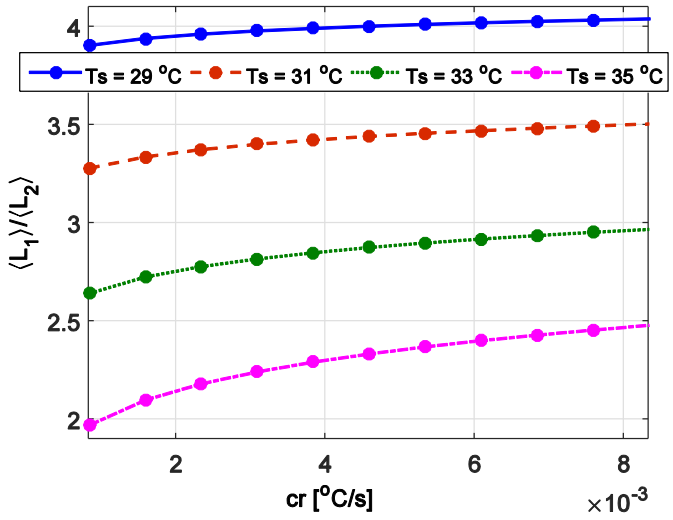

Figure 8. Influence of linear cooling rate and seed addition temperature on the product crystal shape (aspect-ratio) [33]

4.2. Crystallization of high aspect ratio crystals

Numerous paper and research showed that numerous organic and inorganic material form high aspect ratio rod-like crystal. These crystals are naturally sensitive to breakage along their length. In the thesis the crystallization of rod-like crystals is analyzed in continuous crystallizer

assuming primary nucleation, size dependent growth and size dependent breakage. The novelty in this model is that employs the quadrature method of moments solution method (an own implementation), which permits the direct application of nonlinear growth and breakage models. The simulation results revealed an interesting and unexpected inverse effect: according to the results, the increasing breakage rate might lead to decrease in crystal number (Figure 9), if the crystal production rate is governed by the nucleation but the breakage rate is also significant. This inverse effect illustrates well that the nonlinear sub-processes (nucleation, growth and breakage) are linked to each-other strongly by the supersaturation and the crystal size distribution.

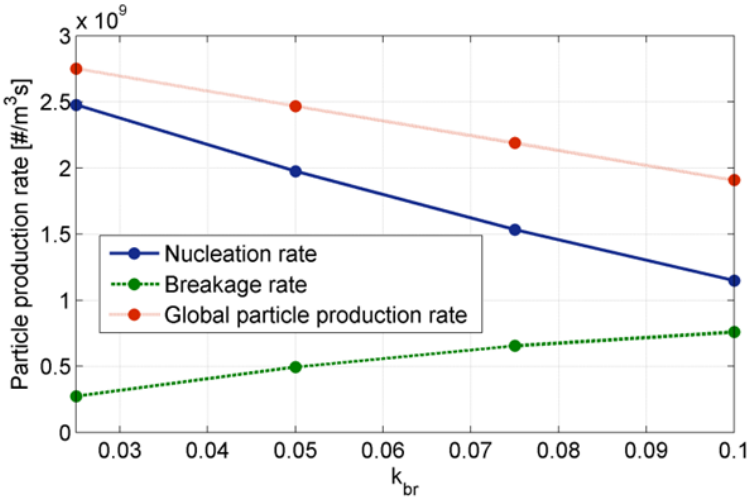

Figure 9. Steady state particle production rate in the function of breakage rate constant [28]

4.3. Modeling the solution crystallization with heat effects

The effect of crystallization heat is a relative un-cared aspect of the crystallization from both experimental and modeling part. The heat of crystallization is released on the surface of growing crystals which leads to temperature difference between the crystal and solution. The generally applied models uses homogeneous temperature field approximation: assumes that the heat of crystallization is absorbed by the whole suspension. To check the validity of this approximation we developed a 2D population balance model which distinguishes the particle and solution temperature handling the particle temperature as a meso-scale property of crystals population. The batch crystallization model includes the primary and secondary nucleation, crystal growth and crystal-solution heat transfer. The primary nucleation is assumed to occur at solution temperature while the secondary nucleation and crystal growth, being sub-processes associated to the crystal surface, are assumed to occur at the temperature (and corresponding supersaturation) of the crystal. The simulation results revealed that the simplified 1D model applying the widely used homogeneous temperature field approximation presents up to 10 % deviation from the results of the (thermally) more detailed 2D model. According to the results

the 2D simulation results goes to the 1D results as the particle-solution heat transfer coefficient goes to infinite. This is expected as in this case the temperature distribution becomes degenerated, which, according to the mathematical derivation, simplifies the 2D model to the corresponding 1D PBM.

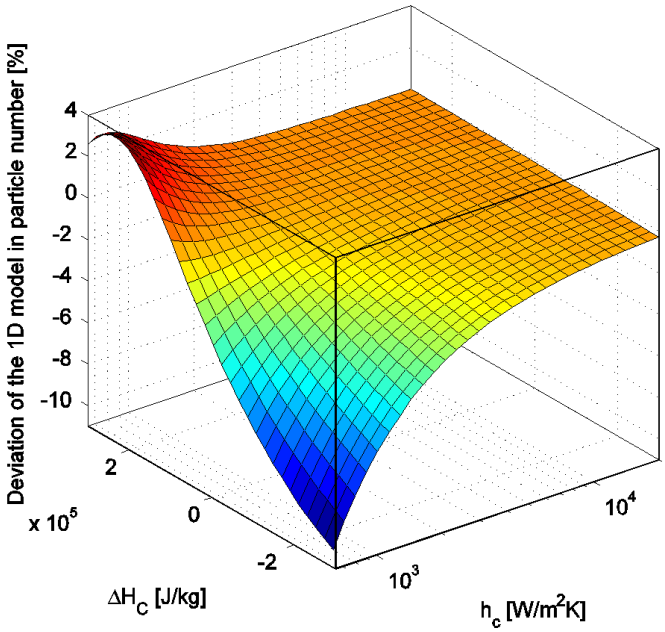

Figure 10. Deviations of crystals number predicted by the 1D model from 2D model results as a function of crystallization heat and crystals-solution heat transfer coefficient [34]

4.4. GPU acceleration for high resolution finite volume PBE solution

The real time controller application requires that the model is solved with orders of magnitude faster than the real process. Despite of the advantages of FVM, it has increased computational burden which is a power-law function of problem dimensionality. For this reason several attempts were made to improve the computational efficiency. The majority of these methods employ supercomputers involving multiple CPU's. However, from industrial point of view this is not desired, due to the increased cost of these computers.

The GPU's are low-to mid-cost devices, being suitable for the execution of heavy, parallel calculations. They have been used for accelerating massive scientific calculations in almost all area of science and technology. In the field of crystallization several works were published discussing mainly the GPU acceleration of Monte Carlo methods. Surprisingly, GPU's were not used yet for the acceleration of HR-FVM PBE solution.

Figure 11 presents the effects of mesh size on solution time and accuracy. It seems that for the cruder mesh (N = 300/2 μm discretization) the error is almost 1 % and it decreases quickly with the mesh size. The N = 1500 mesh size (0.375 μm) presents a local minima in the error curve thus it is a good trade-off between the accuracy and computational burden. The CUDA .mex : .mex speed up increases with the mesh size from 5 to 18 and the .mex : MatLab is

decreasing. The MatLab simulations were not carried out due to the extremely high computational time. It seen that the run time, which for a 2D PBE is quadratic function of mesh size, with N = 1500 division required 18000 seconds (~5 hours). According to the investigations the advantage of CUDA .mex over the .mex function is higher for the computationally more expensive calculations. The CUDA .mex, in contrast, required one and a half minute.

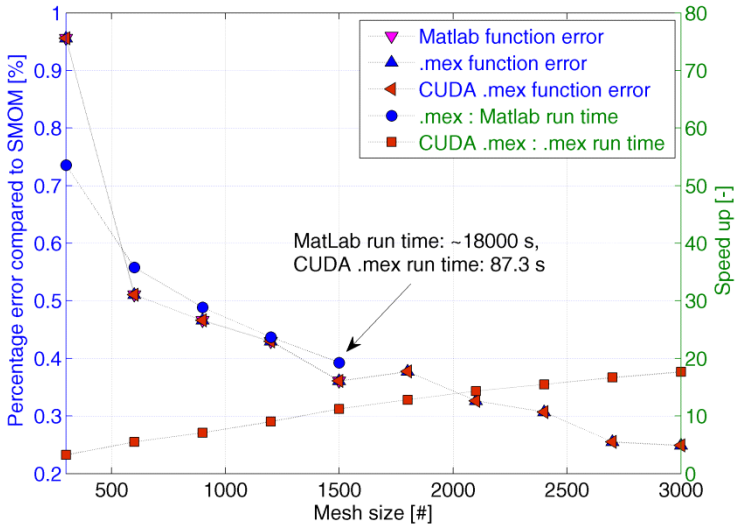

Figure 11. Dependence of acceleration ratio and accuracy on mesh size [35]

4.5. The CrySiV tool

The CrySiV, acronym of the Crystallization Simulation and Visualization Tool is a numerical instrument for simulating solution crystallization problems. The CrySiV is based on the functions presented in the previous section, thus employs the high resolution finite volume method to solve the 1D and 2D PBE. The motivation of starting the development of a generic platform which can easily be shared with the crystallization community was the unexpected and surprisingly high performance of the combined CPU-GPU implementation. The main advantages of the first distributed CrySiV version over the currently available crystallization simulators are the ability of simulating 2D PBEs, the GPU acceleration and the embedded dissolution model.
The CrySiV has two parts, for two well-separated target users:

- A MatLab based function. This has similar calling methodology as the internal MatLab functions. The MatLab based function is designated for process engineering purposes: for simulation/parameter estimation, optimization and control. The fact that the CrySiV has no optimization and control functionality, by using the CrySiV function in combination with the optimization and control toolboxes of the MatLab, this can hardly be an obstacle for process engineers.

- MatLab based Graphical User Interface (GUI). The GUI was created for visualization purposes and is aimed to make the simulation more interactive and user friendly

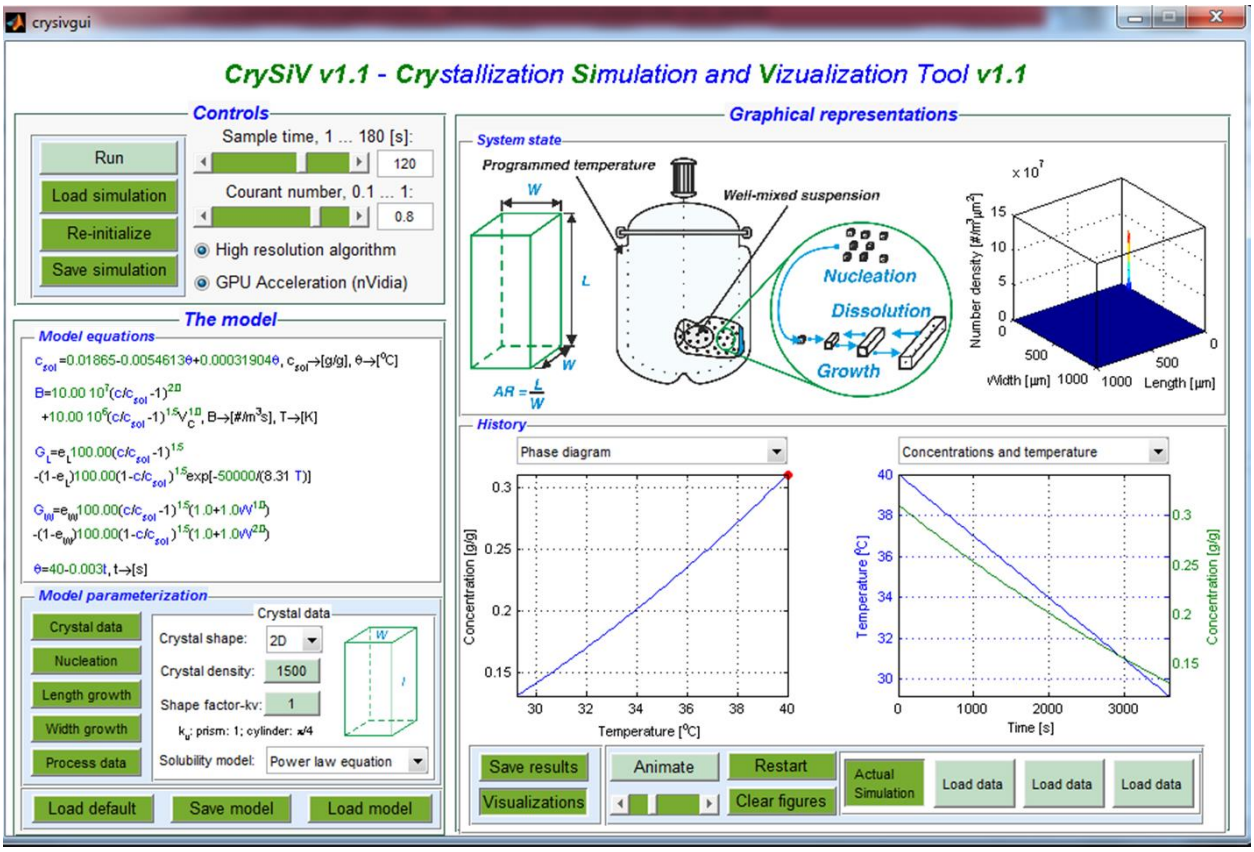

Figure 12. The graphical user interface of the CrySiV v1.1

4.6. FBRM and PVM soft sensors

To illustrate the functioning of the developed projection based CSD→CLD, ARD transformation, in this section simulations are carried out for 2D prism shaped crystals. Note that the transformation can also be used for 1D cube like crystals with the $L_1 = L_2$ restriction. The CSD→CLD transformation is a heavily investigated but still open topic in the crystallization science as is the basic requirement of using the routinely measured CLD (by FBRM) for qualitative purposes. The Aspect Ratio Distribution (ARD) is extracted from the images captured with an in-line imaging tools (for instance with PVM-Process Vision and Microscopy) by the means of image analysis.

Let us consider a bivariate uncorrelated log-normal distribution with L_1 = 600 μm, L_2 = 100 μm mean sizes and σ_{L1} = 500 μm, σ_{L2} = 200 μm dispersions. The simulated CLD and ARD for the bivariate crystal population presented in Figure 3 is presented in Figure 13. In the CLD plot it can be seen the characteristic bimodal distribution of high aspect ratio crystals. The chord

lengths are 100 and 700 μm and the maximums are located at around 400 and 550 μm. In the ARD plot there is a strong maximum at 1.5 but aspect ratios are expected up to 10.5, what is strange as the real mean aspect ratio is 6. This can be explained with the combined effects of dispersion of crystal size distribution and the distorting effects of 2D projections.

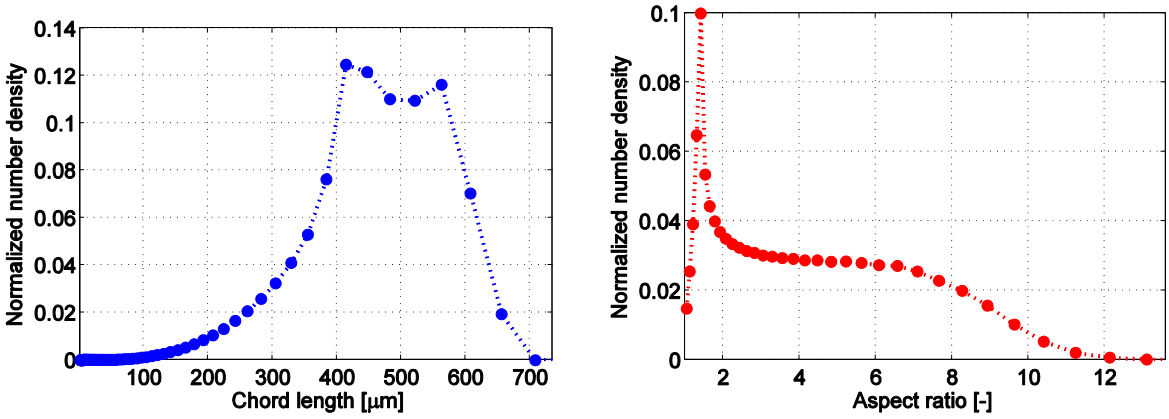

Figure 13. Simulated CLD and ARD

Chapter 5. Optimal control of cooling crystallizers

In this chapter of the thesis model based kinetic estimation studies, control system development and model predictive control experiments are presented.

5.1. CLD based NMPC + RHE algorithm. Simulation results

The objective of this part of the thesis is to develop a shrinking horizon NMPC for the product CSD in fixed batch time cooling crystallizer. The control strategy involves a MHE whose estimation horizon is growing with the actual process time (receding horizon estimator RHE) and uses the measured concentration and CLD. To deal with the parametric PMM the RHE has the role, next to the estimation of un-measurable system states, to continuously improve the model quality by re-adjusting the kinetic parameters. In NMPC calculations an accelerated direct single shooting dynamic optimization strategy is applied which reduces the calculation time to the range of industrial sampling time. To avoid the structural PMMs (deviations from the ”Plant” caused by numerical inaccuracies) fine mesh is applied in the PBM solution. The calculations are finished within industrial sampling time (2-3 minutes).

Figure 14 presents the open loop temperature profile and the NMPC/RHE performance. The *Plant optimum* is the optimal temperature profile calculated by CSD based optimization with the *Plant parameters*. This strategy directly operates on CSD and the correct kinetic parameters are involved, this is the *Optimal profile* from the point of view of product quality. However, the CSD cannot be measured with on-line real time tools. Amongst the possible CLDs (weighting degree) the non-weighted (NW) CLD is the most suitable for control application. The *NW CLD based optimum* curve has been calculated involving the correct (plant) kinetic parameters based on the simulated CLDs. As it seems, this curve is above of the CSD based optimal temperature profile. The kinetic parameters used in simulations might differ from the actual plant kinetics (case of parametric plant-model mismatch). This situation is demonstrated by carrying out a CLD based optimization involving the *Model parameters*. This temperature trajectory is the *NW CLD based model profile*. This profile totally differs from both Plant parameter simulations: at the beginning a strong cooling is applied which is followed by a long, slow cooling period. The initial kinetic parameters of NMPC system might be different from the actual parameters. The *NW CLD based RHE+NMPC* is a control simulation, started with the *Model parameters* but the RHE continuously re-adjusts them. According to the figure, very good agreement exists between the NMPC run and the CLD based optimal temperature profile. The CSDs realized by these two cooling profiles practically overlaps. The CLD based optimization carried out with the Model parameters leads to the worst, bimodal CSD. These results indicate the robustness of RHE/NMPC combination against parametric PMM, ensured by the efficient state estimator.

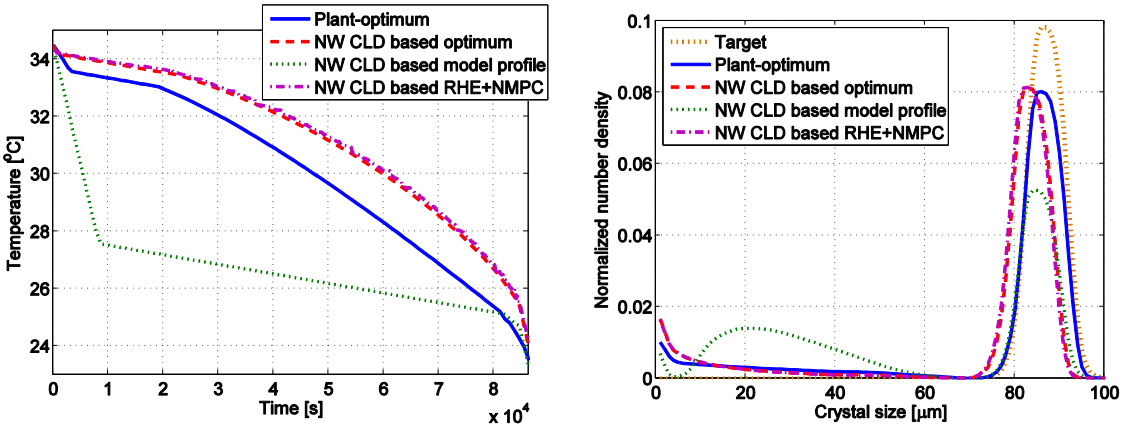

Figure 14. Open loop optimal temperature profiles and the RHE/NMPC control and the realized CSDs by the temperature profiles

5.2. Batch cooling crystallization of L-ascorbic acid from aqueous solution: process analytical technology based kinetic and control studies

Despite of the fact that the crystallization modeling and control is intensively investigated area of modern particulate science and technology and the L-ascorbic acid (vitamin C) is produced in high quantities, only a few paper deals with the vitamin C crystallization. In the literature the shape and size variations were monitored using state-of-the-art PAT tools assuming two dimensional shape during the seeded batch crystallization from water. The solubility, nucleation and growth kinetics have been investigated for alcohol water systems by others but the kinetic equations of these investigations can hardly be incorporated into the traditional PB based crystallizer models. In a theoretical investigation it was showed that the shape of L-ascorbic acid is not constant but it exhibits complex habit during the crystallization. However, a control oriented study on L-ascorbic acid crystallization not appeared yet. In this section the CLD based NMPC system is applied for the L-ascorbic acid crystallization. Naturally, beforehand of the NMPC run the kinetic parameters of seeded batch crystallization of L-ascorbic acid were determined by fitting the 1D model on concentration and CLD data of four experiments.

The surface of Figure 15 illustrates the temporal variation of the CLD as well as the target CLD. It seems well that at the end of the batch the target CLD is very well approached. Although, in the upper view of the same surface seems well that the maximal variation of the CLDs are recorded in the slow cooling region, where the supersaturation was high and the fine seeds were growing, in diameter, quickly. On this view is also suggested that, when the final, faster cooling occurs, the CLs slightly decreased.

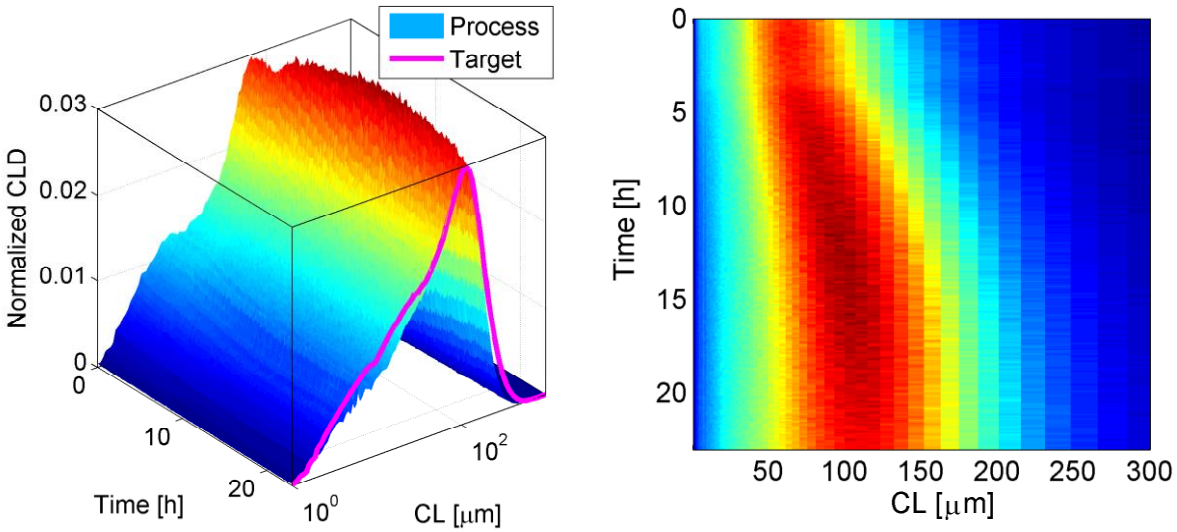

Figure 15. Variation of CLD during the N-MPC batch and upper view of the CLD variation surface

It worth noting that the target is the real CLD of the crystals which the N-MPC is supposed to produce, measured with the same FBRM under the same conditions as the used in the control experiment. This is very advantageous as the potential errors of CSD→CLD transformations are completely omitted from the point of view of process control and it might manifest only in the quality of intermediate kinetic parameters.

5.3. Parameter estimation of rod-like succinic acid crystallization

The understanding of formation of crystal shape during the solution crystallization is a major challenge in modern crystallization science, which would made possible the rational and efficient simultaneous manipulation of the size and shape. The high aspect ratio crystals were already analyzed in this work, which have the very advantageous property that their agglomeration, generally, is negligible and by choosing well the impeller type and revolution speed the breakage rate can also minimized. Thus, the nucleation, growth and dissolution are the mechanisms whose rate needs to be estimated. Consequently the rod like crystals seems to be ideal candidates for calibration of 2D morphological population balance models, based on quantities recorded by commercially available PAT tools.

It is known that the dissolution might considerably improve the system flexibility and help considerably in reaching the target distribution due to fines dissolution. In the 2D case, next to the fines dissolution, the dissolution might lead to modifications in crystal shape due to the different growth/dissolution supersaturation exponents of different crystal facets. Thus, in the design of experiment cooling-heating stages of different rate were applied to generate results which are suitable for the estimation of nucleation, growth and dissolution kinetics.

Figure 16 presents a temperature profile which involves multiple cooling-heating stages, aimed to improve the estimation quality. The variation of experimental CLD is also depicted and it seems well that the first cooling generates a high small fraction, which dissolves in the first dissolution stage and starting from the second cooling considerably larger crystals are produced. It seems that every heating stage brings the CL's in larger domains, which confirms the supposition that the supersaturation dependencies of the dissolution and growth rates differs.

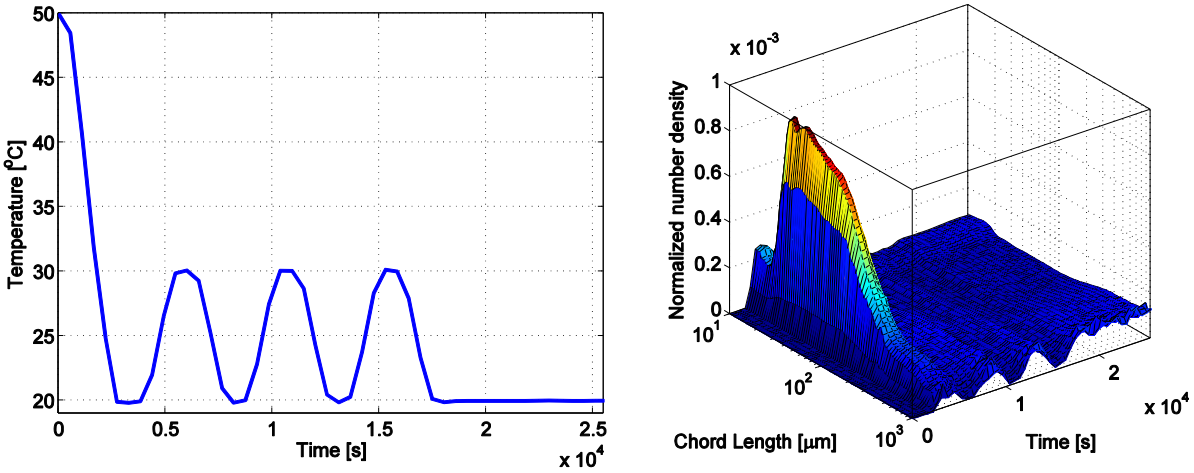

Figure 16. A temperature profile applied in 2D estimation experiment with multiple heating-cooling stages and the variation of CLD under the action of this temperature profile

Figure 17 presents the simulated and measured concentrations during the batch of Figure 16. It can be observed that the agreement is very good between the values. It seems that the concentrations correlate with the applied temperature, what is caused by the temperature dependency of solubility. As a consequence, the concentration plot suggests that in this case fast growth and dissolution kinetics are present as the actual concentrations follows fairly the temperature, which indicates that the actual concentration is near to the solubility at all time.

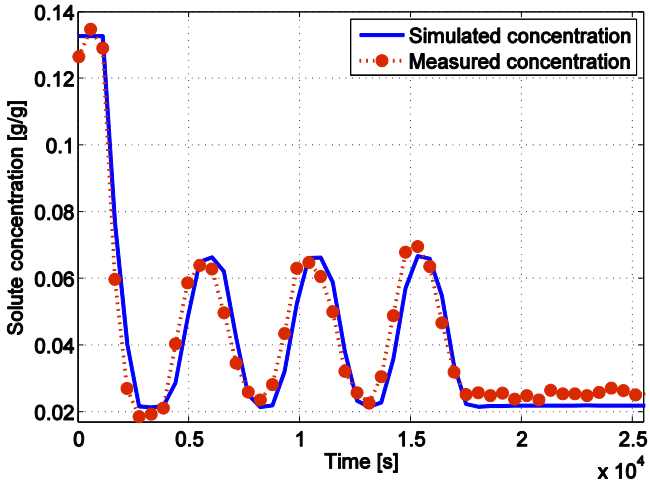

Figure 17. Variation of simulated and measured concentrations during the temperature profile of Figure 16

Conclusions

The central topic of this PhD work was the model based analysis and control of cooling crystallizers. In the model based analysis part novel crystallizer models, involving morphological population balances for plate-like and rod like crystals and a 2D model for the crystal size-temperature binary population were developed. The simulations carried out based on these population balance based models were aimed to help in the deeper understanding of complex crystallization processes. All investigation gave some unexpected results, which were explained by the complex inter-correlation of crystallization sub-processes with each other through the supersaturation and crystal size distribution. A GPU assisted implementation of the HR-FVM method was proposed, which opens new doors in the applicability of multidimensional full population balances.

The model based control part utilizes 1D population balances but a novel CSD→CLD transformation, standing on physical basis was developed. The transformation is developed for 2D prism-like crystals, whose limiting case is the 1D cube shape. This enables the application of FBRM provided CLD in the process control, which is routinely collected during the experiments but only rarely used for quantitative purposes. The NMPC, coupled with an RHE state estimator ensured robust functioning in the simulations. The developed control system was tested in the batch crystallization of L-ascorbic acid. It presented good control behavior and produced considerably better CSD than the corresponding linear cooling. In this chapter the crystallization kinetics of the 2D prism-like succinic acid was estimated based on batch experiments (concentration and CLD data).

Selected bibliography

[1] A. Mersmann, *Crystallization Technology Handbook*. Marcel Dekker Inc., New York, Basel, 2001.

[2] P. D. Christofides, N. El-Farra, M. Li, and P. Mhaskar, "Model-based control of particulate processes," *Chem. Eng. Sci.*, vol. 63, no. 5, pp. 1156–1172, 2008.

[3] X. Wang, M. Dennis, and L. Hou, "Clathrate hydrate technology for cold storage in air conditioning systems," *Renew. Sustain. Energy Rev.*, vol. 36, pp. 34–51, Aug. 2014.

[4] M. Grabowski, J. Klemeš, K. Urbaniec, G. Vaccari, and X. . Zhu, "Minimum energy consumption in sugar production by cooling crystallisation of concentrated raw juice," *Appl. Therm. Eng.*, vol. 21, no. 13–14, pp. 1319–1329, Oct. 2001.

[5] A. Melchuna, A. Cameirao, J.-M. Herri, and P. Glenat, "Topological modeling of methane hydrate crystallization from low to high water cut emulsion systems," *Fluid Phase Equilib.*, Nov. 2015.

[6] A. S. Myerson, *Handbook of Industrial Crystallization*. Elsevier, 2002.

[7] S. L. Lee, T. F. O'Connor, X. Yang, C. N. Cruz, S. Chatterjee, R. D. Madurawe, C. M. V Moore, L. X. Yu, and J. Woodcock, "Modernizing Pharmaceutical Manufacturing: from Batch to Continuous Production," *J. Pharm. Innov.*, vol. 10, no. 3, pp. 191–199, 2015.

[8] L. Y. Ng, N. G. Chemmangattuvalappil, and D. K. S. Ng, "A Multiobjective Optimization-Based Approach for Optimal Chemical Product Design," *Ind. Eng. Chem. Res.*, vol. 53, no. 44, pp. 17429–17444, 2014.

[9] Z. K. Nagy and R. D. Braatz, "Advances and New Directions in Crystallization Control," *Annu. Rev. Chem. Biomol. Eng.*, vol. 3, no. 1, pp. 55–75, 2012.

[10] J. De Yoreo, "Crystal nucleation: more than one pathway.," *Nat. Mater.*, vol. 12, pp. 284–5, 2013.

[11] A. Randolph and M. Larson, *Theory of particulate processes, analysis and techniques of continuous crystallization*. Salt Lake City: Academic Press, 1988.

[12] Z. K. Nagy, G. Fevotte, H. Kramer, and L. L. Simon, "Recent advances in the monitoring, modelling and control of crystallization systems," *Chem. Eng. Res. Des.*, vol. 91, no. 10, pp. 1903–1922, Oct. 2013.

[13] C. Y. Ma and X. Z. Wang, "Model identification of crystal facet growth kinetics in morphological population balance modeling of l-glutamic acid crystallization and experimental validation," *Chem. Eng. Sci.*, vol. 70, pp. 22–30, 2012.

[14] D. Acevedo, Y. Tandy, and Z. K. Nagy, "Multiobjective Optimization of an Unseeded Batch Cooling Crystallizer for Shape and Size Manipulation," *Ind. Eng. Chem. Res.*, vol. 54, no. 7, pp. 2156–2166, Feb. 2015.

[15] C. Y. Ma and X. Z. Wang, "Closed-loop control of crystal shape in cooling crystallization of l-glutamic acid," *J. Process Control*, vol. 22, no. 1, pp. 72–81, Jan. 2012.

[16] M. R. Abu Bakar, Z. K. Nagy, A. N. Saleemi, and C. D. Rielly, "The impact of direct nucleation control on crystal size distribution in pharmaceutical crystallization processes," *Cryst. Growth Des.*, vol. 9, no. 3, pp. 1378–1384, 2009.

[17] P. S. Agachi, M. V. Cristea, Z. K. Nagy, and A. Imre-Lucaci, *Model based control: case studies in process engineering*. John Wiley & Sons, 2007.

[18] Z. K. Nagy, "Model based robust control approach for batch crystallization product design," *Comput. Chem. Eng.*, vol. 33, no. 10, pp. 1685–1691, 2009.

[19] M. W. Hermanto, M.-S. Chiu, and R. D. Braatz, "Nonlinear model predictive control for the polymorphic transformation of L-glutamic acid crystals," *AIChE J.*, vol. 55, no. 10, pp. 2631–2645, Oct. 2009.

[20] H. M. Hulburt and S. Katz, "Some problems in particle technology. A statistical mechanical formulation," *Chem. Eng. Sci.*, vol. 19, pp. 555–574, 1964.

[21] A. Mesbah, H. J. M. Kramer, A. E. M. Huesman, and P. M. J. Van den Hof, "A control oriented study on the numerical solution of the population balance equation for crystallization processes," *Chem. Eng. Sci.*, vol. 64, no. 20, pp. 4262–4277, Oct. 2009.

[22] D. L. Marchisio, J. T. Pikturna, R. O. Fox, R. D. Vigil, and A. A. Barresi, "Quadrature method of moments for population-balance equations," *AIChE Journal*, vol. 49, no. 5. pp. 1266–1276, 2003.

[23] R. Gunawan, I. Fusman, and R. D. Braatz, "High resolution algorithms for multidimensional population balance equations," *AIChE J.*, vol. 50, no. 11, pp. 2738–2749, 2004.

[24] A. Mesbah, A. E. M. Huesman, H. J. M. Kramer, and P. M. J. Van den Hof, "A comparison of nonlinear observers for output feedback model-based control of seeded batch crystallization processes," *J. Process Control*, vol. 21, no. 4, pp. 652–666, Apr. 2011.

[25] R. E. Kalman, "A New Approach to Linear Filtering and Prediction Problems," *J. Basic Eng.*, vol. 82, no. 1, p. 35, 1960.

[26] D. G. Luenberger, "Observers for Multivariable Systems," *IEEE Trans. Automat. Contr.*, vol. 11, no. 2, pp. 190–197, 1966.

[27] J. S. Il Kwon, M. Nayhouse, G. Orkoulas, D. Ni, and P. D. Christofides, “A method for handling batch-to-batch parametric drift using moving horizon estimation: Application to run-to-run MPC of batch crystallization,” *Chem. Eng. Sci.*, vol. 127, pp. 210–119, 2015.

[28] B. Szilágyi, P. Ş. Agachi, and B. G. Lakatos, “Numerical analysis of crystallization of high aspect ratio crystals with breakage,” *Powder Technol.*, vol. 283, pp. 152–162, 2015.

[29] H. Briesen, “Simulation of crystal size and shape by means of a reduced two-dimensional population balance model,” in *Chemical Engineering Science*, 2006, vol. 61, no. 1, pp. 104–112.

[30] B. G. Lakatos, “Moment method for multidimensional population balance models,” in *Proc. 4th Int. Conf. Population Balance Modelling*, 2010, pp. 885–903.

[31] D. L. Wright, D. L. Wright, R. McGraw, R. McGraw, D. E. Rosner, and D. E. Rosner, “Bivariate Extension of the Quadrature Method of Moments for Modeling Simultaneous Coagulation and Sintering of Particle Populations.,” *J. Colloid Interface Sci.*, vol. 236, no. 2, pp. 242–251, 2001.

[32] R. J. LeVeque, *Finite volume methods for hyperbolic problems*, vol. 31. Cambridge university press, 2002.

[33] B. Szilágyi and B. Lakatos, “Batch Cooling Crystallization of Plate-like Crystals: A Simulation Study,” *Period. Polytech. Chem. Eng.*, vol. 59, no. 2, pp. 151–158, 2015.

[34] B. G. Lakatos and B. Szilagyi, “Modeling Crystallization from Solution with Heat Effects,” *Cryst. Growth Des.*, vol. 15, no. 12, pp. 5726–5737, 2015.

[35] B. Szilágyi and Z. K. Nagy, “Graphical Processing Unit (GPU) Acceleration for Numerical Solution of Population Balance Models Using High Resolution Finite Volume Algorithm,” *Comput. Chem. Eng.*, 2016.