Copyright is owned by the Author of the thesis. Permission is given for a copy to be downloaded by an individual for the purpose of research and private study only. The thesis may not be reproduced elsewhere without the permission of the Author.

# EVAPORATIVE CRYSTALLIZATION OF ALPHA-LACTOSE MONOHYDRATE

A thesis presented in partial fulfilment of the requirements for the degree of

Doctor of Philosophy

In

Chemical Engineering

at Massey University, Manawatu New Zealand.

Shailesh Ghanashyam Agrawal

2012

Dedicated to

Rasikbihari...

#### **Abstract**

Evaporative crystallization has been used by Fonterra Cooperative Group (New Zealand) for producing lactose. It represents an important step during lactose manufacturing where control over crystal size can be obtained, a critical parameter governing the yield and end use. The art of operating these crystallizers has been developed by observation and not from scientific principles. This project was undertaken to understand the mechanisms controlling the crystal size in evaporative crystallizers.

A review of the existing literature showed that secondary nucleation is the major source of nuclei in industrial crystallizers. Based on the review, attrition, contact and fluid shear induced nucleation were identified as the probable secondary nucleation mechanisms in the studied system. Experimental investigation on each of the three mechanisms was carried out separately on a laboratory scale.

It was found that the crystal size had the most significant effect on attrition, followed by impeller speed, which together implies that the crystal collision energy intensity is the dominant factor producing new fragments. Contact nucleation was also found to be controlled by crystal-impeller collisions. It was found that at the studied supersaturation there exists a minimum kinetic energy of contact below which secondary nucleation would not occur. This threshold value was used as the basis to assess the contribution of various mechanisms at the industrial scale. Shear nucleation was found to be independent of shear above 5000 s<sup>-1</sup>.

A mathematical model describing the operation of the industrial crystallizer was formulated. Sensitivity analysis was conducted by simulating the model for a range of operational and kinetic parameter values. It was found that the crystal size is affected most by secondary nucleation. The volume weighted mean size approximately halved with a 5.5 times increase in the secondary nucleation rate.

The model was refined to accommodate size dependent growth rate and growth rate dispersion. The kinetic parameters were fitted to match the measured size distribution from the industrial crystallizer. A range of simulations were conducted for various theoretical and empirical models and compared to that of plant measurements. Based on the results it was proposed that the majority of secondary nucleation is expected to occur in the pump and the boiling zone.

#### **Acknowledgement**

It's not easy to move to an alien country to do a PhD. So my first thank to New Zealand and its people for making me feel comfortable and for being my home for close to four years. I will then like to thank my main supervisor, Prof. Tony Paterson for giving me the opportunity to work under him. Thanks Tony for showing constant faith in my abilities and being there whenever I needed advice, academic or personal. This PhD would not be possible without your guidance and encouragement.

Big thanks to my co-supervisors: Dr. Jeremy McLeod, Prof. Jim Jones and Prof. John Bronlund. Thanks Jeremy for proposing this PhD and getting me started into Fonterra during your last few days with them. Thanks for attending my weekly meeting from USA and taking a keen interest in the project. Jim, I learnt a lot about technical writing from you. I would be happy if I could become half as good as you. John, thanks for helping me with my model. That one small session with you on Matlab got me going!

My sincere thanks to my mentors at Fonterra: Tony Styles and Raymond Joe. It is not easy to carry out experimental studies in an industrial environment. Raymond, thanks for making sure that I have all the resources to complete my trials at Kapuni. Tony thanks for arranging the work contract with Fonterra for the last six months of the project when I ran out of funding. My special thanks to Karl Goble, who was the go to person during my stay at Kapuni; whether it be collecting data from the plant or for discussing my mathematical model or simply someone to talk to regarding the project. Karl, you have got the most amazing collection of theses and references on crystallization!! Thank you to Sharon, Michelle and all others at the Kapuni site who made my stay there enjoyable.

Financial security is a critical factor for any PhD student. Therefore, I will like to thank the Foundation for Research Science and Technology, Government of New Zealand for providing me with the scholarship to able me to undertake this project. I

would also like to thank Fonterra from the bottom of my heart for sponsoring my conference trips and university fees.

I spent most of my PhD study in Taranaki. So I will like to thank all the people who made my stay enjoyable at Hawera and helped me at some stage or other: The Turuturu cricket team and its members, Chandu Bhana and his family, Daniel Hovell and Jimmy. The cricket matches over the weekend were fun and allowed to take my mind off the PhD for little bit. Chandu, thanks for inviting us to your home and the volleyball games on Mondays. Thank you to Daniel and Jimmy for being great flat mates and providing an environment where I could return to in the evenings and relax. Daniel, I will always remember the round the mountain relay which I ran for your team. It was a great experience! Thanks.

I also need to thank people who helped me during my stay at Massey and in Palmy. First of all I will like to thank the PhD students at SEAT in the sustainable processing cluster: Horng, Ihli, Georg, Konrad, Fitri, for making my PhD experience memorable. My thanks to intern students: Amandine, Amit and Yohannes, for being part of my PhD journey at different stages. Thanks to Ann-Marie, Bruce, Anthony and John for helping me in different ways in my experimental work. Thanks to Gayle and Linda for sorting out all the administrative and financial issues during the length of my PhD.

My sincere thanks to Rajesh for being my first point of contact and helping me settle in New Zealand. Thanks to Mallesh for being a wonderful flatmate during my second term in Palmy. I will also like to thank Nilesh to whom I approached whenever I needed some advice. I will like to express my gratitude towards my friends in the badminton group for all the fun I had while playing with them. Palash, I still hope to beat you some day in singles! Special thanks to Ken Mercer for taking me on the most beautiful journeys and giving me an opportunity to see the real NZ. Ken, I will never forget our three day hiking trip to Nelson Lakes National Park!!

I now like to say thank and pay obeisance to my parents for their constant emotional and spiritual support. I cannot express in words my gratitude towards them for the sacrifices they have made. To my brother Saket, thanks for your belief in me. I also

express gratefulness to all my in-laws, especially parents-in-law for their kind words and love.

My hearty thanks to the most special person who became the part of my life during the latter half of my PhD: my wife Sneha. I need to first say sorry to you that you missed the festivities and occasions which are very special for a newly married Indian girl because I dragged you half away across the world to a completely new country. Thanks for all the love and support. Your smiling face is the biggest energy booster for me!!

### **Table of Contents**

ABS	STRACT		I
ACKNOWLEDGEMENT			
LIS	T OF FIGUR	ES	XI
CH	APTER 1	PROJECT OVERVIEW	1
CH	APTER 2	CRYSTALLIZATION THEORY	5
2.1	Nucleation		5
2.2	Growth		7
2.3	Lactose		9
2.4	Industrial Cry	stallizer	10
2	.4.1 Forced (	Circulation Evaporative Crystallizers	14
2.5	Modelling		15
2	2.5.1 Method of Moments (MOM)		
2	.5.2 Discreti	zation	19
2.6	Conclusions		20
СН	APTER 3	LITERATURE REVIEW ON SECONDARY NU	JCLEATION21
3.1	Collision Ind	uced Secondary Nucleation	24
3	.1.1 Attrition	ı	24
3	.1.2 Contact	Nucleation	26
3.2	Shear Second	ary Nucleation	29
3.3	Secondary N	ucleation Studies on Lactose	33
3.4	Conclusions		35

CHAPT	ER 4 EXPERIMENTS ON SECONDARY NUCLEATION	37
4.1 Attı	ition	37
4.1.1	Theory	38
4.1.2	Materials and Methods	43
4.1.3	Results and Discussions	44
4.1.4	Conclusions	51
4.2 Con	tact Nucleation	52
4.2.1	Theory	52
4.2.2	Crystal-impeller Contacts	53
4.2.3	Crystal-crystal Contacts	55
4.2.4	Experimental	57
4.2.5	Results and Discussions	60
4.2.6	Conclusions	68
4.3 She	ar Nucleation	69
4.3.1	Results and Discussions	73
4.3.2	Conclusions	74
СНАРТ	ER 5 MODEL DEVELOPMENT AND SENSITIVITY ANALYSIS	75
5.1 Ma	thematical Model Development	75
5.1.1	Mass Balance	76
5.1.2	Population Balance	79
5.1.3	Growth and Nucleation Kinetics	81
5.1.4	Lactose Solubility	82
5.1.5	Lactose Mutarotation Kinetics	82
5.2 A B	rief Review on Lactose Crystallization Kinetics	83
5.2.1	Growth	83
5.2.2	Secondary Nucleation	84
5.2.3	Primary Nucleation	86
5.3 Sim	ulation and Sensitivity Analysis	87
5.3.1	Effect of Growth Rate	88
5.3.2	Effect of Primary Nucleation	92
5.3.3	Effect of Secondary Nucleation	97
5.3.4	Effect of Evaporation Rate	101

5	.3.5	Effect of Residence Time	104
5	.3.6	Effect of Temperature	108
5.4	Sum	mary and Conclusions	111
CH.	APTI	ER 6 INDUSTRIAL CRYSTALLIZER	113
6.1	Hyd	rodynamics	113
6.2	Plan	t Data and Parameter Estimation	119
6	.2.1	Sampling and analysis	119
6	.2.2	Results	121
6	.2.3	MSMPR Analysis	125
6	.2.4	Simulation and Parameter Estimation	132
6.3	Sim	ulations using Mechanistic Models for Secondary Nucleation	142
6	.3.1	Attrition	142
6	6.3.2 Contact Nucleation due to Crystal-Impeller Collisions		147
6	.3.3	Contact Nucleation due to Crystal-crystal Collisions	151
6	.3.4	Plant trials	159
6.4	Con	clusions	162
CH.	APTI	ER 7 PROJECT REVIEW	163
NO	MEN	CLATURE	167
RE	FERE	ENCES	171
AP	PENI	DIX I	I
AP	PENI	DIX II	V
AP	PENI	DIX III	VII
AP	PENI	DIX IV	XVII

### **List of Figures**

Figure 1-1. Framework for describing the crystallizer behaviour
Figure 2-1. Solubility diagram, supersaturation generation and crystallization kinetics [adapted from Mersmann (2001b) and Jones (2002)]. Anti-solvents lower the solubility of the solute. On anti-solvent addition (refered to as dilution in the figure) the excessive solute (defined by the anit-solvent solubility curve) precipitates out Chemical reaction leading to high concentrations of the new generated species car also trigger precipitation.
Figure 2-2. Nucleation mechanisms [adapted from Randolph & Larson (1988)]
Figure 2-3. Plot of crystal growth rate, G, vs. solution velocity (or slurry mixing) showing the mechanism governing crystal growth (Genck, 2003)
Figure 2-4. Effect of agitation speed on lactose growth rate at a supersasturation of 5.23 g per 100 g of water at 30°C (McLeod, 2007)
Figure 2-5. α-lactose tomahawk morphology [reproduced from van Kreveld & Michaels (1965)]
Figure 2-6. Mean crystal size produced by different industrial crystallizers as a function of residence time and nucleation rate [reproduced from Wöhlk, Hofmann, & de Jong (1991)
Figure 2-7. Forced circulation evaporative crystallizer [reproduced from Bennet (2002)]
Figure 2-8. DTB crystallizer [reproduced from Bennet (2002)]13
Figure 2-9. Fluidized bed crystallizer [reproduced from Bennet (2002)]13
Figure 2-10. Feedback interactions between various factors effecting crystallization [adapted from Randolph & Larson (1988)]
Figure 2-11. Semi logarithmic plot of population density versus crystal size for ar MSMPR continuous crystallizer
Figure 3-1. Secondary nucleation classifications as applicable to an industrial crystallizer.
Figure 3-2. Contact nucleation photomicroscopic cell [reproduced from Garside, et al., (1979)]
Figure 3-3. Growth rate comparison of lactose under different experimental conditions. ▲ present data from Shi, et al., (1989) for a photomicroscopic cell, × present data from Shi, et al., (1990) for a CSTR (continuous stirred tank reactor) Temperature ranged from 30-60 °C. Residence time for CSTR studies varied from 4.6-52 minutes and growth rates determined by MSMPR population balance

technique. In the photomicroscopy study, growth of a population of nuclei was followed in a single experiment for 30-500 minutes, with mean growth rate plotted. 29
Figure 3-4. Secondary nucleation studies on lactose. A: Spontaneous nucleation line/Supersolubility curve (Hunziker, 1949); B: Solubility curve; C: Forced crystallization (Hunziker, 1949) [refers to the optimum viscosity (a function of temperature) and supersaturation at which the solution was seeded and held under vigorous agitation for 60 minutes]; D:Critical supersaturation for growth (Shi, et al., 1989); E: SNT (Butler, 1998); F: Forced secondary nucleation (Shi, et al., 1989) and G:Nuclei first detection curve (Wong, Bund, Connelly, & Hartel, 2011)
Figure 4-1. Different attrition mechanisms [adapted from Barbosa-Cánovas, Ortega-Rivas, Juliano, & Yan (2005)]
Figure 4-2. Effect of different dominant attrition mechanisms on the CSD with time [reproduced from Malave-Lopez & Peleg (1986)]
Figure 4-3. Particle size distributions and difference plots for a range of attrition outcomes
Figure 4-4. Normalized frequency CSD for a single HHH run. The trial name represents high levels of crystal size, impeller speed and concentration
Figure 4-5. Cumulative size distribution at 0 and 60 minutes for selected experimental runs. The legend gives high/low levels of particle size, impeller speed and particle concentration respectively. The data shown is the average of four replicates46
Figure 4-6. Differential attrition index (standard error bars, $n=4$ ) measured between time, $t=0$ and $t$ . Trial names represent high, medium and low levels of crystal size, impeller speed and concentration
Figure 4-7. Importance of seed pretreatment for fines. The beaker on the left contained untreated settled seed crystals and would have led to an over-estimation of secondary nucleation, while that on the right are the washed seeds
Figure 4-8. Secondary nucleation versus time (Supersaturation: 10.7 g of $\alpha$ -LMH per 100 g of water / Seed size: 357 $\mu$ m / Seed loading: 2% (w/w) / Impeller speed: 550 rpm). Standard deviation error bars for 4 replicates are shown
Figure 4-9. Effect of seed loading on secondary nucleation rate at constant supersaturation (8.4g $\alpha$ –LMH per 100 g water) for different combinations of seed size and impeller speed. Standard deviation error bars for 4 replicates are shown64
Figure 4-10. Effect of seed loading on secondary nucleation from kinetic energy and contact frequency perspective at constant supersaturation (8.4 g of α-LMH per 100 g water)
Figure 4-11. Secondary nucleation at constant seed loading of $2\%$ (w/w) at 10.7 and 6.7 s.s. (g $\alpha$ -LMH per 100 g water) from a kinetic energy and frequency of contacts perspective. Standard deviation error bars based on 4 replicates are shown. The 8

kinetic energies correspond to the same combinations of impeller speed and crystal size as shown in Figure 4-9
Figure 4-12. Experimental setup for shear secondary nucleation
Figure 4-13. Shear secondary nucleation: Effect of shear rate and supersaturation. The primary nucleation trials contain no immobilized lactose crystals. Supersaturations are g of $\alpha$ -LMH per 100 g of water
Figure 5-1. A generalized schematic of an evaporative crystallizer
Figure 5-2. Growth studies on lactose
Figure 5-3. Secondary nucleation studies on lactose85
Figure 5-4. Lactose primary nucleation rate (McLeod, 2007)
Figure 5-5. Effect of growth rate kinetics on a), dissolved lactose; b), supersaturation; c), slurry density; d), crystal concentration; e), mean diameter; f), instantaneous growth rate; and g), coefficient of variation. Solid line represent profiles obtained by using growth parameters of Shi, et al.,(1990) and the broken line uses that of McLeod (2007)
Figure 5-6. Effect of primary nucleation rate constant on a), dissolved lactose; b), supersaturation; c), slurry density; d), crystal concentration e), instantaneous primary nucleation rate; f), mean diameter and g), coefficient of variation96
Figure 5-7. Effect of secondary nucleation rate constant on a), dissolved lactose; b), supersaturation; c), slurry density; d), crystal concentration; e), instantaneous secondary nucleation rate; f), mean diameter; and g), coefficient of variation 100
Figure 5-8. Effect of evaporation rate on a), dissolved lactose; b), supersaturation; c), slurry density; d), crystal concentration; e), mean diameter; and f), coefficient of variation
Figure 5-9. Effect of residence time on a), dissolved lactose; b), supersaturation; c), slurry density; d), crystal concentration; e), mean diameter; and f), coefficient of variation.
Figure 5-10. Effect of temperature of operation (constant for an evaporative crystallizer) on a), dissolved lactose; b), supersaturation; c), slurry density; d), crystal concentration; e), mean diameter; and f), coefficient of variation
Figure 6-1. Fluid dynamics scale in a crystallizer, x represents crystal (reproduced from Rielly & Marquis (2001))
Figure 6-2. Compartment model for a forced circulation evaporative crystallizer (reproduced from Kramer, et al. (2000))
Figure 6-3. Prediction of the height at which boiling starts inside the calandria tubes of the Kapuni FC evaporative crystallizer116

Figure 6-4. Slurry velocity in the boiling zone in the calandria tubes of the Kapuni FC evaporative crystallizer
Figure 6-5. Compartmental model for the Kapuni FC evaporative crystallizer117
Figure 6-6. Supersaturation decay transient profile in absence of evaporation i.e. no supersaturation generation, for prediction of $t_{\Delta c,1/2}$
Figure 6-7. Residence time profile of the Kapuni FC evaporative crystallizer during the three sampling trials
Figure 6-8. Dissolved solids profile of the Kapuni FC evaporative crystallizer for the three sampling runs (MA: moisture analyzer and HRM: Handheld refractometer). 122
Figure 6-9. Total solids profile of the Kapuni FC evaporative crystallizer for the three sampling runs (measured using the Metler Toledo moisture analyzer)122
Figure 6-10. Crystalline solids content profile of the Kapuni FC evaporative crystallizer for the three sampling runs (calculated from mass balance using total solids and dissolved solids)
Figure 6-11. Crystal size distribution profile of the Kapuni FC evaporative crystallizer for the three sampling runs a) Trial 1 b) Trial 2 c) Trial 3. 0 minute indicates the 124
Figure 6-12. Volume weighted mean diameter profiles of the Kapuni FC evaporative crystallizer for the three sampling runs
Figure 6-13. Population density curve for lactose crystals obtained from the Kapuni FC evaporative crystallizer under steady state
Figure 6-14. Size dependent growth rate fitted to the population density curve in Figure 6-13
Figure 6-15. Size dependent growth rate versus crystal size. Fitted values of the parameters $a$ , $c$ and $G_e$ for the Mydlarz model are 0.0059, 0.0091 and 1.82 $\mu$ m min <sup>-1</sup> , respectively.
Figure 6-16. Various growth rate dispersion models fitted to plant population density.
Figure 6-17. Probability density distribution for various growth rate dispersion models (value of the fitted parameters is listed in Table 6-1)
Figure 6-18. Effect of grid size on simulation results
Figure 6-19. Dissolved lactose profile for Kapuni FC evaporative crystallizer for fitted growth, primary nucleation and secondary nucleation rate constants. The broken and continuous lines represent the model prediction during the semi-batch and the continuous mode respectively

Figure 6-20. Total solids profile for Kapuni FC evaporative crystallizer for fitted growth, primary nucleation and secondary nucleation rate constants. The broken and continuous lines represent the model prediction during the semi-batch and the continuous mode respectively
Figure 6-21. Crystal concentration profile for Kapuni FC evaporative crystallizer for fitted growth, primary nucleation and secondary nucleation rate constants. The broken and continuous lines represent the model prediction during the semi-batch and the continuous mode respectively.
Figure 6-22. Volume weighted mean diameter profile for Kapuni FC evaporative crystallizer for fitted growth, primary nucleation and secondary nucleation rate constants. The broken and continuous lines represent the model prediction during the semi-batch and the continuous mode respectively. The line through the measured data points is drawn as a visual guide to compare with the model prediction
Figure 6-23. Steady state population density distribution for Kapuni FC evaporative crystallizer predicted by the model using optimized fitted parameters
Figure 6-24. Dry crystal sieve analysis representative of the CSD dynamics of the Kapuni FC evaporative crystallizer
Figure 6-25. Dissolved lactose profile for size independent growth
Figure 6-26. Volume weighted mean diameter profile for size independent growth
Figure 6-27. Population density curve for size independent growth140
Figure 6-28. Dissolved lactose profile using method of moments and parameters estimated by SIG (size independent growth)
Figure 6-29. Volume weighted mean diameter profile calculated using the method of moments
Figure 6-30. Effect of impeller blade discretization on simulation results
Figure 6-31. Dissolved lactose concentration profile with attrition (calculated by Mersmann model) as the source of secondary nucleation. Markers depict measured values.
Figure 6-32. Volume weighted mean diameter profile with attrition (calculated by Mersmann model) as the only source of secondary nucleation. Markers depict measured values.
Figure 6-33. Crystals withdrawn from the crystallizer at steady state
Figure 6-34. Secondary nucleation at constant seed loading of 2% (w/w) at 10.7 and 6.7 s.s. (g α-LMH per 100 g water) from a kinetic energy and frequency of contacts perspective

Figure 6-35. Plot of ln of the intercept of the lines fitted in Figure 4-11 versus the ln of the supersaturations to determine $K_N$ and $b$ in Equation 4-12
Figure 6-36. Dissolved lactose concentration profile with crystal-impeller contact nucleation at the operational circulation pump speed as the source of secondary nucleation. Markers depict measured values
Figure 6-37. Volume weighted mean diameter profile with crystal-impeller contact nucleation at the standard operating circulation pump speed as the source of secondary nucleation. Markers depict measured values
Figure 6-38. Solid liquid suspension (redrawn from (Eskin et al., 2004))151
Figure 6-39. Variation of flow quality with the tube height in the calandria of the Kapuni FC evaporative crystallizer
Figure 6-40. The refractive index (dissolved solids in wt %) trends for the plant trial conducted at two temperatures. The figure on the left gives trend for the lower and to the right for the higher temperature.
Figure 6-41. Observed crystal size distribution during unplanned one off trial. Blue line depicts the CSD with the lower feed concentration. Normal feed resumed around midday. Green and red lines depict CSD after approximately 3 and 4 hours of resumption of normal feed

## **List of Tables**

Table 2-1 Various Moments of Density Distribution and Mean Crystal Sizes19
Table 3-1 Selected Data from Sung, et al., (1973) showing the Generation of Secondary Nuclei for Magnesium Sulphate at Different Levels of Mixing and Supersaturations
Table 3-2 Data from Wang, M.L., et al., (1981) in Terms of Shear Rates at a Constant Absolute Supersaturation for Citric Acid (16.6 gm per 100gm of water)
Table 3-3 Secondary Nucleation Studies in Literature on Lactose
Table 4-1 Factors Varied during the Attrition experiments. H = High, M= medium, L = Low
Table 4-2 Experimental Design Matrix (Size:Speed:Concentration)
Table 4-3 Comparison of Calculated and Experimental Volumetric Attrition Ratios.  To Remove the Effect of Concentration) the Mid Values for the Bands HH*, HL*,  LH* and LL* After 60 Minutes are Used
Table 4-4 Run Time (t) for Different Trials Conducted for Each Experiment with Two Impeller Speeds of 400 and 550 rpm, and Four Particle Sizes of 106-212, 212-300, 300-425 and 425-600 Microns
Table 4-5 Values of Different Parameters for Impeller-Crystal Contact Induced Secondary Nucleation
Table 4-6 Values of Different Hydrodynamic Parameters for Crystal-Crystal Contact for Different Impeller Speeds62
Table 4-7 Inter-Particle Mean Space and the Kinetic Energy of Contact for Crystal-Crystal Contacts
Table 4-8 Straight Line Fits Through the Data Points of Figure 4-9 And Kinetic Energy of Collisions for Various Combinations of Seed Size and Impeller Speed64
Table 4-9 Comparison of the Experimental and Theoretical Slopes of the Secondary Nucleation Rate Line
Table 5-1 Secondary Nucleation Studies on Lactose
Table 5-2 Values and Range of Parameters Studied During Simulation
Table 5-3 Values of the Crystallizer Outputs at Steady State at the Maximum and Minimum Values of the Various Kinetic and Operation Parameters Simulated 112

Table 6-1 Growth Rate Dispersion Models	130
Table 6-2 Kinetic Parameters Estimated from Size Dependent and Growth Models	-
Table 6-3 Values of Critical Parameters for Crystal-Crystal Circulation Loop Pipe	
Table 6-4 Values of Critical Parameters for Crystal-Crystal Calandria Pipes	

#### **List of Equations**

Equation 2-1 Population balance equation	.16
Equation 2-2 Population balance equation for a batch process	.16
Equation 2-3 Population balance equation for a continuous process	.16
Equation 2-4 Population density for a steady state continuous process	.17
Equation 2-5 Nucleation rate calculation for MSMPR crystallizer	.17
Equation 2-6 Discretized Method of lines for solving population balance equation	.20
Equation 4-1 Secondary nucleation: empirical model	.37
Equation 4-2 Difference function for a frequency distribution	.40
Equation 4-3 Differential attrition index definition	.40
Equation 4-4 Volumetric attrition rate due to impeller-crystal collisions	.48
Equation 4-5 Volumetric attrition rate due to crystal-crystal collisions	.48
Equation 4-6 Volumetric crystal hold up	.49
Equation 4-7 Volumetric attrition rate due to crystal-crystal collisions in terms crystal size and concentration	
Equation 4-8 Relationship between target efficiency and crystal size	.49
Equation 4-9 Volumetric attrition rate in terms of crystal size	.49
Equation 4-10 Volumetric attrition rate ratio for a given impeller	.50
Equation 4-11 Volumetric attrition rate ratio approximation by DAI slope ratio	.50
Equation 4-12 Collision secondary nucleation	.52
Equation 4-13 Kinetic energy of impeller-crystal collision	.53
Equation 4-14 Mass of a single crystal	.53
Equation 4-15 Crystal-impeller collision velocity	.53
Equation 4-16 Kinetic energy of contact for impeller-crystal collisions	.54
Equation 4-17 Impeller-crystal collision frequency	.54

Equation 4-18 Target efficiency as a function of Stokes number	54
Equation 4-19 Stokes number	54
Equation 4-20 Contact nucleation due to impeller-crystal collisions	55
Equation 4-21 Kinetic energy of crystal-crystal collision	55
Equation 4-22 Inter-particle space in a slurry suspension	55
Equation 4-23 Crystal-crystal collision velocity	55
Equation 4-24 Length of smallest eddy	56
Equation 4-25 Energy dissipation rate in an agitated system	56
Equation 4-26 Reynolds number for an agitated system	56
Equation 4-27 Crystal-crystal collision frequency	56
Equation 4-28 Total crystal volume in Malvern presentation unit	58
Equation 4-29 Crystal volume per ml of the sample	59
Equation 4-30 Number of crystals in size bin (i)	59
Equation 4-31 Total number of crystals across all size bins	59
Equation 4-32 Theoretical ratio of the slopes of fitted lines in Figure 4-9	65
Equation 4-33 Approximate impeller-crystal collision frequency	66
Equation 4-34 Wall shear stress for a flow through a rough tube	69
Equation 4-35 Shear rate at the wall	69
Equation 4-36 Pressure drop for a flow inside a tube	70
Equation 4-37 Wall shear stress for a flow through a rough tube	70
Equation 4-38 Shear rate at the tube wall in terms of pressure drop across the tube	70
Equation 4-39 Pressure drop in a U-tube manometer	70
Equation 5-1 Solute balance over crystallizer	76
Equation 5-2 Semi-batch solute balance	77
Equation 5-3 Dissolved lactose concentration differential for semi-batch mode	77
Equation 5-4 Overall mass balance	77

Equation 5-5 Condition for constant operation. Volumetric rate of feed equal to volumetric rate of water removal
Equation 5-6 Dissolved lactose concentration differential for continuous mode78
Equation 5-7 Mean residence time
Equation 5-8 Zeroth moment derivative
Equation 5-9 First moment derivative
Equation 5-10 Second moment derivative
Equation 5-11 Third moment derivative79
Equation 5-12 Fourth moment derivative
Equation 5-13 Coefficient of variation of a size distribution
Equation 5-14 Slurry voidage
Equation 5-15 Rate of change of slurry voidage
Equation 5-16 Volume weighted mean diameter
Equation 5-17 Crystal content of the slurry80
Equation 5-18 Total solids in the slurry80
Equation 5-19 Slurry density-total solids relationship
Equation 5-20 Primary nucleation rate
Equation 5-21 Secondary nucleation rate
Equation 5-22 Growth rate
Equation 5-23 Equilibrium α-lactose solubility
Equation 5-24 Correction factor for α-LMH82
Equation 5-25 Equilibrium lactose solubility
Equation 5-26 Total dissolved lactose
Equation 5-27 Mutarotation rate constant
Equation 5-28 Dissolved α-lactose concentration
Equation 5-29 Equilibrium mutarotation rate constant as a function of temperature83
Equation 5-30 Relationship between residence time and mean particle size

Equation 6-1 Converting volumetric distribution to population density distribution 125
Equation 6-2 Size dependent growth rate
Equation 6-3 Population density with size dependent growth rate
Equation 6-4 Growth rate from population density distribution
Equation 6-5 Cumulative size distribution with growth rate distribution130
Equation 6-6 Converting cumulative number distribution to frequency distribution 131
Equation 6-7 Analytical solution for inverse gamma distribution function
Equation 6-8 Secondary nucleation rate due to attrition
Equation 6-9 Collision secondary nucleation
Equation 6-10 Modified Equation 4-20 for secondary nucleation due impeller-crystal collisions
Equation 6-11 Determination of collision nucleation rate constant and supersaturation dependence
Equation 6-12 Stokes number
Equation 6-13 Particle relaxation time
Equation 6-14 Turbulent eddy life time
Equation 6-15 Turbulent kinetic energy
Equation 6-16 Energy dissipation rate in a pipe flow
Equation 6-17 Shear velocity
Equation 6-18 Wall shear stress
Equation 6-19 Crystal RMS velocity
Equation 6-20 Constant in Equation 6-19
Equation 6-21 Crystal-crystal collision frequency
Equation 6-22 Kinetic energy of crystal-crystal contact