

Contents

About the Authors — VII

Preface — IX

List of Symbols — XV

1 Introduction — 1

- 1.1 Crystallization in the Chemical Processing Industries — 1
- 1.2 Crystallization as a Multiscale Design Problem — 3
- 1.3 An Integrative Approach to Crystallization Process Design — 4
- 1.4 Organization of the Book — 6

2 Basics of Solid–Liquid Equilibrium Phase Behavior — 9

- 2.1 Solid–Liquid Equilibrium — 9
 - 2.1.1 Melting point and solubility — 9
 - 2.1.2 Phase diagram and Gibbs phase rule — 10
- 2.2 Molecular Systems — 11
 - 2.2.1 Single component systems — 11
 - 2.2.2 Binary systems — 12
 - 2.2.3 Ternary systems — 19
 - 2.2.4 Quaternary systems — 24
 - 2.2.5 Multicomponent systems — 28
 - 2.2.6 Reactive systems — 35
- 2.3 Electrolyte Systems — 39
 - 2.3.1 Acid–base systems — 42
 - 2.3.2 Conjugate salt systems — 44
 - 2.3.3 Multicomponent salt system — 48
- 2.4 Summary — 51

3 Thermodynamic-Based Conceptual Design of Crystallization Processes — 57

- 3.1 Movements in Composition Space — 57
 - 3.1.1 Lever rule — 58
 - 3.1.2 Representation of basic operations on SLE phase diagram — 60
- 3.2 Maximum Recovery of a Pure Solid — 62
- 3.3 Crystallization of Desirable Product — 73
- 3.4 Complete Dissolution — 79
- 3.5 Summary — 83

4	Synthesis of Crystallization-Based Separation Processes — 89
4.1	Crystallization as a Separation Process — 89
4.2	Bypassing the Thermodynamic Boundary — 89
4.2.1	Ternary system — 89
4.2.2	Quaternary system — 97
4.2.3	Multicomponent system — 100
4.2.4	Conjugate salt system — 102
4.3	Effect of Solvent — 109
4.3.1	Solvent selection — 109
4.3.2	Solvent switching — 111
4.4	Hybrid Separation Process — 113
4.5	Summary — 120
5	Crystallization Processes Involving More Complex Phase Behaviors — 126
5.1	Adductive Crystallization — 126
5.1.1	SLE phase behavior involving adduct — 126
5.1.2	Process synthesis — 127
5.2	Chiral Resolution by Crystallization — 131
5.2.1	SLE phase behavior of chiral systems — 132
5.2.2	Process synthesis — 134
5.2.3	Hybrid process for chiral resolution — 138
5.3	Solid Solution Crystallization — 141
5.3.1	SLE phase behavior of solid solution systems — 141
5.3.2	Process synthesis — 142
5.4	Amino Acid and Protein Crystallization — 149
5.4.1	SLE phase behavior of amino acid systems — 149
5.4.2	Process synthesis — 151
5.5	Antisolvent Crystallization — 156
5.5.1	Solid–liquid–liquid equilibrium phase behavior — 156
5.5.2	Process synthesis — 159
5.6	Supercritical Fluid Crystallization — 162
5.6.1	Solid–fluid equilibrium phase behavior — 162
5.6.2	Process synthesis — 166
5.7	Summary — 170
6	Impact of Kinetics and Mass Transfer on Crystallization — 176
6.1	Kinetic Effects in Crystallization Process — 176
6.1.1	Supersaturation — 176
6.1.2	Nucleation and growth models — 177
6.2	Actual Process Path — 179
6.3	Preferential Crystallization — 181

6.4	Kinetically Controlled Reactive Crystallization —	184
6.5	Polymorphic Crystallization —	190
6.5.1	SLE phase behavior of polymorphic systems —	191
6.5.2	Process synthesis —	193
6.6	Summary —	202
7	Management of Particle Size Distribution and Impurities in Crystallization Processes —	207
7.1	Crystallizer Model —	207
7.1.1	Population balance —	207
7.1.2	Solutions of population balance equations —	210
7.2	Particle Size Distribution Management —	211
7.2.1	PSD manipulation in batch crystallization —	211
7.2.2	PSD targeting in continuous crystallization —	220
7.2.3	Scale-up consideration in PSD management —	225
7.3	Impurity Management —	227
7.3.1	Control of inclusion impurities —	228
7.3.2	Removal of inclusion impurities by melt crystallization —	233
7.3.3	Crystallization downstream processing system —	238
7.3.4	Simultaneous washing and melt crystallization —	244
7.4	Summary —	247
8	Determination of Solid–Liquid Equilibrium Phase Behavior and Crystallization Kinetics —	253
8.1	Strategy for SLE Phase Behavior Determination —	253
8.2	Modeling of SLE Phase Behavior —	254
8.2.1	Solubility equation and solubility product equation —	255
8.2.2	Activity coefficient models —	260
8.2.3	Equation of state models —	260
8.3	Prediction of Solid–Liquid Equilibrium Phase Behavior —	264
8.3.1	Group contribution methods —	264
8.3.2	Quantum chemistry methods —	270
8.4	Experimental Determination of SLE Phase Behavior —	270
8.4.1	Thermal method for obtaining SLE data —	271
8.4.2	Synthetic method for obtaining SLE data —	276
8.4.3	Analytical method for obtaining SLE data —	279
8.4.4	Fitting of model parameters —	280
8.4.5	Boundary verification —	287
8.5	Experimental Determination of Crystallization Kinetics —	292
8.6	Summary —	294

XIV — Contents

9 Concluding Remarks — 300

9.1 A Hierarchical, Multiscale, Integrative Approach — **300**

9.2 Outlook — **303**

Appendix: Solutions to Selected Exercise Problems — 307

References — 331

Index — 347