

Contents

Preface	XV
List of Contributors	XXI

Part I Chemical and Other Processing Systems 1

1	Dynamic Process Modeling: Combining Models and Experimental Data to Solve Industrial Problems	3
	<i>M. Matzopoulos</i>	3
1.1	Introduction	3
1.1.1	Mathematical Formulation	4
1.1.2	Modeling Software	5
1.2	Dynamic Process Modeling – Background and Basics	5
1.2.1	Predictive Process Models	6
1.2.2	Dynamic Process Modeling	6
1.2.3	Key Considerations for Dynamic Process Models	7
1.2.4	Modeling of Operating Procedures	9
1.2.5	Key Modeling Concepts	10
1.2.5.1	First-Principles Modeling	10
1.2.5.2	Multiscale Modeling	10
1.2.5.3	Equation-Based Modeling Tools	11
1.2.5.4	Distributed Systems Modeling	12
1.2.5.5	Multiple Activities from the Same Model	13
1.2.5.6	Simulation vs. Modeling	13
1.3	A Model-Based Engineering Approach	14
1.3.1	High-Fidelity Predictive Models	14
1.3.2	Model-Targeted Experimentation	16
1.3.3	Constructing High-Fidelity Predictive Models – A Step-by-Step Approach	16
1.3.4	Incorporating Hydrodynamics Using Hybrid Modeling Techniques	22
1.3.5	Applying the High-Fidelity Predictive Model	22

1.4	An Example: Multitubular Reactor Design	23
1.4.1	Multitubular Reactors – The Challenge	24
1.4.2	The Process	25
1.4.3	The Solution	25
1.4.4	Detailed Design Results	29
1.4.5	Discussion	30
1.5	Conclusions	31
2	Dynamic Multiscale Modeling – An Application to Granulation Processes	35
	<i>G.D. Ingram and I.T. Cameron</i>	35
2.1	Introduction	35
2.2	Granulation	36
2.2.1	The Operation and Its Significance	36
2.2.2	Equipment, Phenomena, and Mechanisms	37
2.2.3	The Need for and Challenges of Modeling Granulation	39
2.3	Multiscale Modeling of Process Systems	41
2.3.1	Characteristics of Multiscale Models	41
2.3.2	Approaches to Multiscale Modeling	43
2.4	Scales of Interest in Granulation	45
2.4.1	Overview	45
2.4.2	Primary Particle Scale	47
2.4.3	Granule Scale	48
2.4.4	Granule Bed Scale	48
2.4.5	Vessel Scale	49
2.4.6	Circuit Scale	50
2.5	Applications of Dynamic Multiscale Modeling to Granulation	52
2.5.1	Overview	52
2.5.2	Fault Diagnosis for Continuous Drum Granulation	55
2.5.3	Three-Dimensional Multiscale Modeling of Batch Drum Granulation	56
2.5.4	DEM-PBE Modeling of Batch High-Shear Granulation	58
2.5.5	DEM-PBE Modeling of Continuous Drum Granulation	59
2.6	Conclusions	61
3	Modeling of Polymerization Processes	67
	<i>B.S. Amaro and E.N. Pistikopoulos</i>	67
3.1	Introduction	67
3.2	Free-Radical Homopolymerization	68
3.2.1	Kinetic Modeling	68
3.2.2	Diffusion-Controlled Reactions	69
3.2.2.1	Fickian Description of Reactant Diffusion	71
3.2.2.2	Free-Volume Theory	72

3.2.2.3	Chain Length Dependent Rate Coefficients	73
3.2.2.4	Combination of the Free-Volume Theory and Chain Length Dependent Rate Coefficients	75
3.2.2.5	Fully Empirical Models	76
3.3	Free-Radical Multicomponent Polymerization	77
3.3.1	Overview	77
3.3.2	Pseudo-Homopolymerization Approximation	78
3.3.3	Polymer Composition	80
3.4	Modeling of Polymer Molecular Properties	80
3.4.1	Molecular Weight Distribution	80
3.5	A Practical Approach – SAN Bulk Polymerization	90
3.5.1	Model	90
3.5.1.1	Kinetic Diagram	90
3.5.1.2	Mass Balances	91
3.5.1.3	Diffusion Limitations	92
3.5.1.4	Pseudo-Homopolymerization Approximation	94
3.5.2	Illustrative Results	95
3.6	Conclusions	97
4	Modeling and Control of Proton Exchange Membrane Fuel Cells	105
	<i>C. Panos, K. Kouramas, M.C. Georgiadis and E.N. Pistikopoulos</i>	<i>105</i>
4.1	Introduction	105
4.2	Literature Review	108
4.3	Motivation	109
4.3.1	Reactant Flow Management	112
4.3.2	Heat and Temperature Management	112
4.3.3	Water Management	113
4.4	PEM Fuel Cell Mathematical Model	113
4.4.1	Cathode	114
4.4.2	Anode	117
4.4.3	Anode Recirculation	119
4.4.4	Fuel Cell Outlet	120
4.4.5	Membrane Hydration Model	120
4.4.6	Electrochemistry	122
4.4.7	Thermodynamic Balance	123
4.4.8	Air Compressor and DC Motor Model	125
4.4.9	DC Motor	126
4.4.10	Cooling System	127
4.5	Reduced Order Model	128
4.6	Concluding Remarks	132
5	Modeling of Pressure Swing Adsorption Processes	137
	<i>E.S. Kikkinides, D. Nikolic and M.C. Georgiadis</i>	<i>137</i>
5.1	Introduction	137

5.2	Model Formulation	144
5.2.1	Adsorbent Bed Models	144
5.2.2	Single-Bed Adsorber	145
5.2.3	Adsorption Layer Model	146
5.2.3.1	General Balance Equations	146
5.2.3.2	Mass Balance	147
5.2.3.3	Heat Balance	147
5.2.3.4	Momentum Balance	148
5.2.3.5	Equation of State	148
5.2.3.6	Thermophysical Properties	148
5.2.3.7	Axial Dispersion	148
5.2.3.8	Transport Properties	149
5.2.3.9	Boundary Conditions	149
5.2.4	Adsorbent Particle Model	150
5.2.4.1	General Mass Balance Equations	150
5.2.4.2	Local Equilibrium	151
5.2.4.3	Linear Driving Force (LDF)	152
5.2.4.4	Surface Diffusion	152
5.2.4.5	Pore Diffusion	153
5.2.4.6	Gas–Solid Phase Equilibrium Isotherms	154
5.2.5	Gas Valve Model	157
5.2.6	The Multibed PSA Model	158
5.2.7	The State Transition Network Approach	158
5.2.8	Numerical Solution	162
5.3	Case-Study Applications	163
5.3.1	Simulation Run I	165
5.3.2	Simulation Run II	165
5.3.3	Simulation Run III	166
5.4	Conclusions	167
6	A Framework for the Modeling of Reactive Separations	173
	<i>E.Y. Kenig</i>	173
6.1	Introduction	173
6.2	Reactive Separations	174
6.3	Classification of Modeling Methods	176
6.4	Fluid-Dynamic Approach	178
6.5	Hydrodynamic Analogy Approach	183
6.6	Rate-Based Approach	188
6.7	Parameter Estimation and Virtual Experiments	193
6.8	Benefits of the Complementary Modeling	196
6.9	Concluding Remarks	199

7	Efficient Reduced Order Dynamic Modeling of Complex Reactive and Multiphase Separation Processes Using Orthogonal Collocation on Finite Elements	203
	<i>P. Seferlis, T. Damartzis and N. Dalaouti</i>	203
7.1	Introduction	203
7.2	NEQ/OCFE Model Formulation	205
7.2.1	Conventional and Reactive Absorption and Distillation	207
7.2.2	Multiphase Reactive Distillation	213
7.3	Adaptive NEQ/OCFE for Enhanced Performance	218
7.4	Dynamic Simulation Results	220
7.4.1	Reactive Absorption of NO_x	220
7.4.1.1	Process Description	220
7.4.1.2	Dynamic Simulation Results	223
7.4.2	Ethyl Acetate Production via Reactive Distillation	225
7.4.2.1	Process Description	225
7.4.2.2	Dynamic Simulation Results	227
7.4.3	Butyl Acetate Production via Reactive Multiphase Distillation	231
7.4.3.1	Process Description	231
7.4.3.2	Dynamic Simulation Results	232
7.5	Epilog	234
8	Modeling of Crystallization Processes	239
	<i>A. Abbas, J. Romagnoli and D. Widenski</i>	239
8.1	Introduction	239
8.2	Background	240
8.2.1	Crystallization Methods	241
8.2.1.1	Recrystallization Methods	241
8.2.2	Driving Force	242
8.3	Solubility Predictions	243
8.3.1	Empirical Approach	243
8.3.2	Correlative Thermodynamic	244
8.3.3	Predictive Thermodynamic	244
8.3.3.1	Jouyban–Acree Model	245
8.3.3.2	MOSCED Model	245
8.3.3.3	NRTL-SAC Model	246
8.3.3.4	UNIFAC Model	247
8.3.3.5	Solubility and Activity Coefficient Relationship	247
8.3.4	Solubility Examples	247
8.3.5	Solution Concentration Measurement Process Analytical Tools	250
8.4	Crystallization Mechanisms	251
8.4.1	Nucleation	251
8.4.1.1	Modeling Nucleation	252
8.4.2	Growth and Dissolution	254
8.4.3	Agglomeration and Aggregation	255

8.4.4	Attrition	255
8.5	Population, Mass, and Energy Balances	256
8.5.1	Population Balance	256
8.5.2	Solution Methods	257
8.5.2.1	Method of Moments	257
8.5.2.2	Discretization Method	258
8.5.3	Mass and Energy Balances	264
8.6	Crystal Characterization	264
8.6.1	Crystal Shape	264
8.6.2	Crystal Size	265
8.6.3	Crystal Distribution	265
8.6.4	Particle Measurement Process Analytical Tools	266
8.7	Solution Environment and Model Application	266
8.7.1	Simulation Environment	266
8.7.2	Experimental Design	267
8.7.3	Parameter Estimation	268
8.7.4	Validation	269
8.8	Optimization	270
8.8.1	Example 1: Antisolvent Feedrate Optimization	270
8.8.2	Example 2: Optimal Seeding in Cooling Crystallization	274
8.9	Future Outlook	276

9 Modeling Multistage Flash Desalination Process – Current Status and Future Development 287

I.M. Mujtaba 287

9.1	Introduction	287
9.2	Issues in MSF Desalination Process	289
9.3	State-of-the-Art in Steady-State Modeling of MSF Desalination Process	292
9.3.1	Scale Formation Modeling	299
9.3.1.1	Estimation of Dynamic Brine Heater Fouling Profile	301
9.3.1.2	Modeling the Effect of NCGs	301
9.3.1.3	Modeling of Environmental Impact	302
9.4	State-of-the-Art in Dynamic Modeling of MSF Desalination Process	303
9.5	Case Study	308
9.5.1	Steady-State Operation	308
9.5.2	Dynamic Operation	311
9.6	Future Challenges	312
9.6.1	Process Modeling	312
9.6.2	Steady-State and Dynamic Simulation	313
9.6.3	Tackling Environmental Issues	313
9.6.4	Process Optimization	314
9.7	Conclusions	315

Part II Biological, Bio-Processing and Biomedical Systems 319

10	Dynamic Models of Disease Progression: Toward a Multiscale Model of Systemic Inflammation in Humans	321
	<i>J.D. Scheff, P.T. Foteinou, S.E. Calvano, S.F. Lowry and I.P. Androulakis</i>	321
10.1	Introduction	321
10.2	Background	322
10.2.1	<i>In-Silico</i> Modeling of Inflammation	323
10.2.2	Multiscale Models of Human Endotoxemia	325
10.2.3	Data Collection	327
10.3	Methods	328
10.3.1	Developing a Multilevel Human Inflammation Model	328
10.3.1.1	Identification of the Essential Transcriptional Responses	328
10.3.1.2	Modeling Inflammation at the Cellular Level	330
10.3.1.3	Modeling Inflammation at the Systemic Level	335
10.3.1.4	Modeling Neuroendocrine–Immune System Interactions	336
10.3.1.5	Modeling the Effect of Endotoxin Injury on Heart Rate Variability	338
10.4	Results	340
10.4.1	Transcriptional Analysis and Major Response Elements	340
10.4.2	Elements of a Multilevel Human Inflammation Model	343
10.4.3	Estimation of Relevant Model Parameters	345
10.4.4	Qualitative Assessment of the Model	347
10.4.4.1	Implications of Increased Insult	348
10.4.4.2	Modes of Dysregulation of the Inflammatory Response	349
10.4.4.3	The Emergence of Memory Effects	353
10.4.4.4	Evaluation of Stress Hormone Infusion in Modulating the Inflammatory Response	354
10.5	Conclusions	360
11	Dynamic Modeling and Simulation for Robust Control of Distributed Processes and Bioprocesses	369
	<i>A.A. Alonso, M.R. García and C. Vilas</i>	369
11.1	Introduction	369
11.2	Model Reduction of DPS: Theoretical Background	372
11.2.1	Model Reduction in the Context of the Finite Element Method	374
11.2.1.1	Proper Orthogonal Decomposition	376
11.2.1.2	Laplacian Spectral Decomposition	377
11.3	Model Reduction in Identification of Bioprocesses	377
11.3.1	Illustrative Example: Production of Gluconic Acid in a Tubular Reactor	378
11.3.2	Observer Validation	379

11.4	Model Reduction in Control Applications	383
11.4.0.1	Model Equations	384
11.4.1	Robust Control of Tubular Reactors	386
11.4.1.1	Controller Synthesis	389
11.4.1.2	Robust Control with a Finite Number of Actuators	392
11.4.2	Real-Time Optimization: Multimodel Predictive Control	394
11.4.2.1	Optimization Problem	395
11.4.2.2	The Online Strategy	396
11.5	Conclusions	397
12	Model Development and Analysis of Mammalian Cell Culture Systems	403
	<i>A. Kiparissides, M. Koutinas, E.N. Pistikopoulos and A. Mantalaris</i>	403
12.1	Introduction	403
12.2	Review of Mathematical Models of Mammalian Cell Culture Systems	406
12.3	Motivation	410
12.4	Dynamic Modeling of Biological Systems – An Illustrative Example	413
12.4.1	First Principles Model Derivation	415
12.4.2	Model Analysis	421
12.4.3	Design of Experiments and Model Validation	432
12.5	Concluding Remarks	435
13	Dynamic Model Building Using Optimal Identification Strategies, with Applications in Bioprocess Engineering	441
	<i>E. Balsa-Canto, J.R. Banga and M.R. García</i>	441
13.1	Introduction	441
13.2	Parameter Estimation: Problem Formulation	443
13.2.1	Mathematical Model Formulation	444
13.2.2	Experimental Scheme and Experimental Data	444
13.2.3	Cost Function	445
13.2.4	Numerical Methods: Single Shooting vs. Multiple Shooting	446
13.3	Identifiability	447
13.4	Optimal Experimental Design	449
13.4.1	Numerical Methods: The Control Vector Parameterization Approach	450
13.5	Nonlinear Programming Solvers	450
13.6	Illustrative Examples	453
13.6.1	Modeling of the Microbial Growth	453
13.6.2	Modeling the Production of Gluconic Acid in a Fed-Batch Reactor	457
13.7	Overview	463

14	Multiscale Modeling of Transport Phenomena in Plant-Based Foods	469
	<i>Q.T. Ho, P. Verboven, B.E. Verlinden, E. Herremans and B.M. Nicolai</i>	469
14.1	Introduction	469
14.2	Length Scales of Biological Materials	470
14.3	Multiscale Modeling of Transport Phenomena	472
14.3.1	Mass Transport Fundamentals	472
14.3.2	Multiscale Transport Phenomena	474
14.3.2.1	Macroscale Approach	474
14.3.2.2	Microscale Approach	474
14.3.2.3	Kinetic Modeling	475
14.3.2.4	Multiscale Model	476
14.4	Numerical Solution	476
14.4.1	Geometrical Model	476
14.4.2	Discretization	478
14.5	Case Study: Application of Multiscale Gas Exchange in Fruit	480
14.5.1	Macroscale Model	480
14.5.2	Microscale Model	482
14.5.3	O ₂ Transport Model	482
14.5.4	CO ₂ Transport Model (Lumped CO ₂ Transport Model)	483
14.6	Conclusions and Outlook	485
15	Synthetic Biology: Dynamic Modeling and Construction of Cell Systems	493
	<i>T.T. Marquez-Lago and M.A. Marchisio</i>	493
15.1	Introduction	493
15.2	Constructing a Model with Parts	494
15.2.1	General Nomenclature	494
15.2.1.1	Parts and Devices	494
15.2.1.2	Common Signal Carriers	496
15.2.1.3	Pools and Fluxes	497
15.2.2	Part Models	500
15.2.2.1	Promoters	500
15.2.2.2	Ribosome-Binding Sites	504
15.2.2.3	Coding Regions	508
15.2.2.4	Noncoding DNA	509
15.2.2.5	Small RNA	511
15.2.2.6	Terminator	511
15.2.3	Introducing Parts and Fluxes into Deterministic Equations	512
15.3	Modeling Regimes and Simulation Techniques	518
15.3.1	Deterministic or Stochastic Modeling?	519
15.3.1.1	Deterministic Regime	519
15.3.1.2	Stochastic Regime	520

15.3.2	Stochastic Simulation Algorithms	522
15.3.2.1	Exact Algorithms	522
15.3.2.2	Coarse-Grained Methods	527
15.4	Application	532
15.4.1	The Repressilator	533
15.5	Conclusions	541

16	Identification of Physiological Models of Type 1 Diabetes Mellitus by Model-Based Design of Experiments	545
	<i>F. Galvanin, M. Barolo, S. Macchietto and F. Bezzo</i>	545
16.1	Introduction	546
16.1.1	Glucose Concentration Control Issues	547
16.2	Introducing Physiological Models	548
16.3	Identifying a Physiological Model: The Need for Experiment Design	548
16.4	Standard Clinical Tests	550
16.5	A Compartmental Model of Glucose Homeostasis	551
16.6	Model Identifiability Issues	552
16.6.1	A Discussion on the Identifiability of the Hovorka Model	554
16.7	Design of Experiments Under Constraints for Physiological Models	556
16.7.1	Design Procedure	558
16.8	Design of Experimental Protocols	560
16.8.1	Modified OGTT (mOGTT)	561
16.8.1.1	Effect of the Number of Samples	562
16.9	Dealing with Uncertainty	563
16.9.1	Online Model-Based Redesign of Experiments	565
16.9.2	Model-Based Design of Experiment with Backoff (MBDoE-B)	566
16.9.2.1	Backoff Application	567
16.9.3	Effect of a Structural Difference Between a Model and a Subject	569
16.10	Conclusions	572

Index	583
--------------	------------