

## Contents

<b>Chapter 1. What are the Challenges for the Control of Bioprocesses?</b> . . . .	11
Denis DOCHAIN	
1.1. Introduction . . . . .	11
1.2. Specific problems of bioprocess control . . . . .	12
1.3. A schematic view of monitoring and control of a bioprocess . . . . .	12
1.4. Modeling and identification of bioprocesses: some key ideas . . . . .	13
1.5. Software sensors: tools for bioprocess monitoring . . . . .	14
1.6. Bioprocess control: basic concepts and advanced control . . . . .	15
1.7. Bioprocess monitoring: the central issue . . . . .	15
1.8. Conclusions . . . . .	16
1.9. Bibliography . . . . .	16
<b>Chapter 2. Dynamic Models of Biochemical Processes: Properties of Models</b> . . . . .	17
Olivier BERNARD and Isabelle QUEINNEC	
2.1. Introduction . . . . .	17
2.2. Description of biochemical processes . . . . .	18
2.2.1. Micro-organisms and their use . . . . .	18
2.2.2. Types of bioreactors . . . . .	19
2.2.3. Three operating modes . . . . .	19
2.3. Mass balance modeling . . . . .	21
2.3.1. Introduction . . . . .	21
2.3.2. Reaction scheme . . . . .	21
2.3.3. Choice of reactions and variables . . . . .	23
2.3.4. Example 1 . . . . .	23
2.4. Mass balance models . . . . .	24
2.4.1. Introduction . . . . .	24
2.4.2. Example 2 . . . . .	24
2.4.3. Example 3 . . . . .	25

2.4.4. Matrix representation . . . . .	25
2.4.4.1. Example 2 (continuation) . . . . .	26
2.4.4.2. Example 1 (continuation) . . . . .	26
2.4.5. Gaseous flow . . . . .	27
2.4.6. Electroneutrality and affinity constants . . . . .	27
2.4.7. Example 1 (continuation) . . . . .	28
2.4.8. Conclusion . . . . .	29
2.5. Kinetics . . . . .	30
2.5.1. Introduction . . . . .	30
2.5.2. Mathematical constraints . . . . .	30
2.5.2.1. Positivity of variables . . . . .	30
2.5.2.2. Variables necessary for the reaction . . . . .	31
2.5.2.3. Example 1 (continuation) . . . . .	31
2.5.2.4. Phenomenological knowledge . . . . .	31
2.5.3. Specific growth rate . . . . .	32
2.5.4. Representation of kinetics by means of a neural network . . . . .	34
2.6. Validation of the model . . . . .	35
2.6.1. Introduction . . . . .	35
2.6.2. Validation of the reaction scheme . . . . .	35
2.6.2.1. Mathematical principle . . . . .	35
2.6.2.2. Example 4 . . . . .	36
2.6.3. Qualitative validation of model . . . . .	37
2.6.4. Global validation of the model . . . . .	39
2.7. Properties of the models . . . . .	39
2.7.1. Boundedness and positivity of variables . . . . .	39
2.7.2. Equilibrium points and local behavior . . . . .	40
2.7.2.1. Introduction . . . . .	40
2.8. Conclusion . . . . .	42
2.9. Bibliography . . . . .	43
<b>Chapter 3. Identification of Bioprocess Models . . . . .</b>	<b>47</b>
Denis DOCHAIN and Peter VANROLLEGHEM	
3.1. Introduction . . . . .	47
3.2. Structural identifiability . . . . .	48
3.2.1. Development in Taylor series . . . . .	49
3.2.2. Generating series . . . . .	50
3.2.3. Examples for the application of the methods of development in series . . . . .	50
3.2.4. Some observations on the methods for testing structural identifiability . . . . .	51
3.3. Practical identifiability . . . . .	52
3.3.1. Theoretical framework . . . . .	52
3.3.2. Confidence interval of the estimated parameters . . . . .	54

3.3.3. Sensitivity functions . . . . .	55
3.4. Optimum experiment design for parameter estimation (OED/PE) . . . .	57
3.4.1. Introduction . . . . .	57
3.4.2. Theoretical basis for the OED/PE . . . . .	59
3.4.3. Examples . . . . .	61
3.5. Estimation algorithms . . . . .	63
3.5.1. Choice of two datasets . . . . .	63
3.5.2. Elements of parameter estimation: least squares estimation in the linear case . . . . .	64
3.5.3. Overview of the parameter estimation algorithms . . . . .	65
3.6. A case study: identification of parameters for a process modeled for anaerobic digestion . . . . .	68
3.6.1. The model . . . . .	69
3.6.2. Experiment design . . . . .	70
3.6.3. Choice of data for calibration and validation . . . . .	70
3.6.4. Parameter identification . . . . .	71
3.6.5. Analysis of the results . . . . .	75
3.7. Bibliography . . . . .	75
<b>Chapter 4. State Estimation for Bioprocesses . . . . .</b>	<b>79</b>
Olivier BERNARD and Jean-Luc GOUZÉ	
4.1. Introduction . . . . .	79
4.2. Notions on system observability . . . . .	80
4.2.1. System observability: definitions . . . . .	80
4.2.2. General definition of an observer . . . . .	81
4.2.3. How to manage the uncertainties in the model or in the output . .	83
4.3. Observers for linear systems . . . . .	84
4.3.1. Luenberger observer . . . . .	85
4.3.2. The linear case up to an output injection . . . . .	86
4.3.3. Local observation of a nonlinear system around an equilibrium point . . . . .	86
4.3.4. PI observer . . . . .	87
4.3.5. Kalman filter . . . . .	87
4.3.6. The extended Kalman filter . . . . .	89
4.4. High gain observers . . . . .	89
4.4.1. Definitions, hypotheses . . . . .	89
4.4.2. Change of variable . . . . .	90
4.4.3. Fixed gain observer . . . . .	91
4.4.4. Variable gain observers (Kalman-like observer) . . . . .	91
4.4.5. Example: growth of micro-algae . . . . .	92
4.5. Observers for mass balance-based systems . . . . .	94
4.5.1. Introduction . . . . .	94
4.5.2. Definitions, hypotheses . . . . .	96

4.5.3. The asymptotic observer . . . . .	96
4.5.4. Example . . . . .	98
4.5.5. Improvements . . . . .	99
4.6. Interval observers . . . . .	101
4.6.1. Principle . . . . .	102
4.6.2. The linear case up to an output injection . . . . .	103
4.6.3. Interval estimator for an activated sludge process . . . . .	105
4.6.4. Bundle of observers . . . . .	107
4.7. Conclusion . . . . .	110
4.8. Appendix: a comparison theorem . . . . .	111
4.9. Bibliography . . . . .	112
<b>Chapter 5. Recursive Parameter Estimation . . . . .</b>	<b>115</b>
Denis DOCHAIN	
5.1. Introduction . . . . .	115
5.2. Parameter estimation based on the structure of the observer . . . . .	116
5.2.1. Example: culture of animal cells . . . . .	116
5.2.2. Estimator based on the structure of the observer . . . . .	117
5.2.3. Example: culture of animal cells (continued) . . . . .	119
5.2.4. Calibration of the estimator based on the structure of the observer: theory . . . . .	119
5.2.5. Calibration of the estimator based on the structure of the observer: application to the culture of animal cells . . . . .	124
5.2.6. Experimental results . . . . .	127
5.3. Recursive least squares estimator . . . . .	129
5.4. Adaptive state observer . . . . .	133
5.4.1. Generalization . . . . .	138
5.5. Conclusions . . . . .	140
5.6. Bibliography . . . . .	141
<b>Chapter 6. Basic Concepts of Bioprocess Control . . . . .</b>	<b>143</b>
Denis DOCHAIN and Jérôme HARMAND	
6.1. Introduction . . . . .	143
6.2. Bioprocess control: basic concepts . . . . .	144
6.2.1. Biological system dynamics . . . . .	144
6.2.2. Sources of uncertainties and disturbances of biological systems . . . . .	146
6.3. Stability of biological processes . . . . .	147
6.3.1. Basic concept of the stability of a dynamic system . . . . .	147
6.3.2. Equilibrium point . . . . .	148
6.3.3. Stability analysis . . . . .	149
6.4. Basic concepts of biological process control . . . . .	150
6.4.1. Regulation and tracking control . . . . .	150
6.4.2. Strategy selection: direct and indirect control . . . . .	151

6.4.3. Selection of synthesis method . . . . .	152
6.5. Synthesis of biological process control laws . . . . .	153
6.5.1. Representation of systems . . . . .	153
6.5.2. Structure of control laws . . . . .	154
6.6. Advanced control laws . . . . .	160
6.6.1. A nonlinear PI controller . . . . .	160
6.6.2. Robust control . . . . .	162
6.7. Specific approaches . . . . .	165
6.7.1. Pulse control: a dialog with bacteria . . . . .	165
6.7.2. Overall process optimization: towards integrating the control objectives in the initial stage of bioprocess design . . . . .	167
6.8. Conclusions and perspectives . . . . .	170
6.9. Bibliography . . . . .	170
<b>Chapter 7. Adaptive Linearizing Control and Extremum-Seeking Control of Bioprocesses . . . . .</b>	<b>173</b>
Denis DOCHAIN, Martin GUAY, Michel PERRIER and Mariana TITICA	
7.1. Introduction . . . . .	173
7.2. Adaptive linearizing control of bioprocesses . . . . .	174
7.2.1. Design of the adaptive linearizing controller . . . . .	174
7.2.2. Example 1: anaerobic digestion . . . . .	176
7.2.2.1. Model order reduction . . . . .	177
7.2.2.2. Adaptive linearizing control design . . . . .	179
7.2.3. Example 2: activated sludge process . . . . .	183
7.3. Adaptive extremum-seeking control of bioprocesses . . . . .	188
7.3.1. Fed-batch reactor model . . . . .	189
7.3.2. Estimation and controller design . . . . .	191
7.3.2.1. Estimation equation for the gaseous outflow rate $y$ . . . . .	191
7.3.2.2. Design of the adaptive extremum-seeking controller . . . . .	192
7.3.2.3. Stability and convergence analysis . . . . .	195
7.3.2.4. A note on dither signal design . . . . .	196
7.3.3. Simulation results . . . . .	197
7.4. Appendix: analysis of the parameter convergence . . . . .	202
7.5. Bibliography . . . . .	207
<b>Chapter 8. Tools for Fault Detection and Diagnosis . . . . .</b>	<b>211</b>
Jean-Philippe STEYER, Antoine GÉNOVÉSI and Jérôme HARMAND	
8.1. Introduction . . . . .	211
8.2. General definitions . . . . .	212
8.2.1. Terminology . . . . .	212
8.2.2. Fault types . . . . .	213
8.3. Fault detection and diagnosis . . . . .	214
8.3.1. Methods based directly on signals . . . . .	215

8.3.1.1. Hardware redundancy . . . . .	215
8.3.1.2. Specific sensors . . . . .	216
8.3.1.3. Comparison of thresholds . . . . .	217
8.3.1.4. Spectral analysis . . . . .	217
8.3.1.5. Statistical approaches . . . . .	218
8.3.2. Model-based methods . . . . .	218
8.3.2.1. Parity space . . . . .	219
8.3.2.2. Observers . . . . .	220
8.3.2.3. Parametric estimation . . . . .	221
8.3.3. Methods based on expertise . . . . .	222
8.3.3.1. AI models . . . . .	223
8.3.3.2. Artificial neural networks . . . . .	224
8.3.3.3. Fuzzy inference systems . . . . .	225
8.3.4. Choice and combined use of diverse methods . . . . .	227
8.4. Application to biological processes . . . . .	227
8.4.1. “Simple” biological processes . . . . .	228
8.4.2. Wastewater treatment processes . . . . .	229
8.5. Conclusion . . . . .	231
8.6. Bibliography . . . . .	232
<b>List of Authors . . . . .</b>	<b>239</b>
<b>Index . . . . .</b>	<b>241</b>