

Contents

Preface *XI*

Nomenclature *XIII*

Part I Basic Concepts and Principles 1

1 Introduction 3

- 1.1 Background and Scope 3
- 1.2 Dimensions and Units 4
- 1.3 Intensive and Extensive Properties 6
- 1.4 Equilibria and Rates 6
- 1.5 Batch versus Continuous Operation 8
- 1.6 Material Balance 8
- 1.7 Energy Balance 9
- References 11

2 Elements of Physical Transfer Processes 13

- 2.1 Introduction 13
- 2.2 Heat Conduction and Molecular Diffusion 13
- 2.3 Fluid Flow and Momentum Transfer 14
- 2.4 Laminar versus Turbulent Flow 18
- 2.5 Transfer Phenomena in Turbulent Flow 21
- 2.6 Film Coefficients of Heat and Mass Transfer 22
- References 25

3 Chemical and Biochemical Kinetics 27

- 3.1 Introduction 27
- 3.2 Fundamental Reaction Kinetics 27
 - 3.2.1 Rates of Chemical Reaction 27
 - 3.2.1.1 Elementary Reaction and Equilibrium 28
 - 3.2.1.2 Temperature Dependence of Reaction Rate Constant k 29
 - 3.2.1.3 Rate Equations for First- and Second-Order Reactions 30
 - 3.2.2 Rates of Enzyme Reactions 34
 - 3.2.2.1 Kinetics of Enzyme Reaction 35

3.2.2.2	Evaluation of Kinetic Parameters in Enzyme Reactions	37
3.2.2.3	Inhibition and Regulation of Enzyme Reactions	39
	References	45
4	Cell Kinetics	47
4.1	Introduction	47
4.2	Cell Growth	47
4.3	Growth Phases in Batch Culture	49
4.4	Factors Affecting Rates of Cell Growth	50
4.5	Cell Growth in Batch Fermentors and Continuous Stirred-Tank Fermentors (CSTF)	52
4.5.1	Batch Fermentor	52
4.5.2	Continuous Stirred-Tank Fermentor	54
	References	55
Part II	Unit Operations and Apparatus for Bio-Systems	59
5	Heat Transfer	59
5.1	Introduction	59
5.2	Overall Coefficients U and Film Coefficients h	59
5.3	Mean Temperature Difference	62
5.4	Estimation of Film Coefficients h	64
5.4.1	Forced Flow of Fluids Through Tubes (Conduits)	64
5.4.2	Forced Flow of Fluids Across a Tube Bank	66
5.4.3	Liquids in Jacketed or Coiled Vessels	67
5.4.4	Condensing Vapors and Boiling Liquids	68
5.5	Estimation of Overall Coefficients U	68
	References	71
6	Mass Transfer	73
6.1	Introduction	73
6.2	Overall Coefficients κ and Film Coefficients k of Mass Transfer	73
6.3	Types of Mass Transfer Equipment	77
6.3.1	Packed Column	77
6.3.2	Plate Column	79
6.3.3	Spray Column	79
6.3.4	Bubble Column	79
6.3.5	Packed (Fixed)-Bed Column	80
6.3.6	Other Separation Methods	80
6.4	Models for Mass Transfer at the Interface	80
6.4.1	Stagnant Film Model	80
6.4.2	Penetration Model	81
6.4.3	Surface Renewal Model	81
6.5	Liquid-Phase Mass Transfer with Chemical Reactions	82

6.6	Correlations for Film Coefficients of Mass Transfer	84
6.6.1	Single-Phase Mass Transfer Inside or Outside Tubes	84
6.6.2	Single-Phase Mass Transfer in Packed Beds	85
6.6.3	J -Factor	86
6.7	Performance of Packed Columns	87
6.7.1	Limiting Gas and Liquid Velocities	87
6.7.2	Definitions of Volumetric Coefficients and HTUs	88
6.7.3	Mass Transfer Rates and Effective Interfacial Areas	91
	References	95
7	Bioreactors	97
7.1	Introduction	97
7.2	Some Fundamental Concepts	98
7.2.1	Batch and Continuous Reactors	98
7.2.2	Effects of Mixing on Reactor Performance	99
7.2.2.1	Uniformly Mixed Batch Reactor	99
7.2.2.2	Continuous Stirred-Tank Reactor (CSTR)	99
7.2.2.3	Plug Flow Reactor (PFR)	100
7.2.2.4	Comparison of Fractional Conversions by CSTR and PFR	101
7.2.3	Effects of Mass Transfer Around and Within Catalyst or Enzymatic Particles on the Apparent Reaction Rates	101
7.2.3.1	Liquid Film Resistance Controlling	102
7.2.3.2	Effects of Diffusion Within Catalyst Particles	103
7.2.3.3	Effects of Diffusion Within Immobilized Enzyme Particles	105
7.3	Bubbling Gas-Liquid Reactors	107
7.3.1	Gas Holdup	107
7.3.2	Interfacial Area	107
7.3.3	Mass Transfer Coefficients	108
7.3.3.1	Definitions	109
7.3.3.2	Measurements of $k_L a$	109
7.4	Mechanically Stirred Tanks	112
7.4.1	General	112
7.4.2	Power Requirements of Stirred Tanks	113
7.4.2.1	Ungassed Liquids	114
7.4.2.2	Gas-Sparged Liquids	115
7.4.3	$k_L a$ in Gas-Sparged Stirred Tanks	116
7.4.4	Liquid Mixing in Stirred Tanks	118
7.4.5	Suspending of Solid Particles in Liquid in Stirred Tanks	120
7.5	Gas Dispersion in Stirred Tanks	120
7.6	Bubble Columns	120
7.6.1	General	121
7.6.2	Performance of Bubble Columns	121
7.6.2.1	Gas Holdup	122
7.6.2.2	$k_L a$	122
7.6.2.3	Bubble Size	122

7.6.2.4	Interfacial Area a	123
7.6.2.5	k_L	123
7.6.2.6	Other Correlations for $k_L a$	123
7.6.2.7	$k_L a$ and Gas Holdup for Suspensions and Emulsions	123
7.7	Airlift Reactors	125
7.7.1	IL Airlifts	125
7.7.2	EL Airlifts	125
7.8	Packed-Bed Reactors	127
7.9	Microreactors [29]	127
	References	131
8	Membrane Processes	133
8.1	Introduction	133
8.2	Dialysis	134
8.3	Ultrafiltration	135
8.4	Microfiltration	138
8.5	Reverse Osmosis	139
8.6	Membrane Modules	141
8.6.1	Flat Membrane	141
8.6.2	Spiral Membrane	142
8.6.3	Tubular Membrane	142
8.6.4	Hollow-Fiber Membrane	142
	References	143
9	Cell-Liquid Separation and Cell Disruption	145
9.1	Introduction	145
9.2	Conventional Filtration	146
9.3	Microfiltration	147
9.4	Centrifugation	148
9.5	Cell Disruption	151
	References	153
10	Sterilization	155
10.1	Introduction	155
10.2	Kinetics of the Thermal Death of Cells	155
10.3	Batch Heat Sterilization of Culture Media	156
10.4	Continuous Heat Sterilization of Culture Media	158
10.5	Sterilizing Filtration	162
	References	164
11	Adsorption and Chromatography	165
11.1	Introduction	165
11.2	Equilibria in Adsorption	165
11.2.1	Linear Equilibrium	165
11.2.2	Adsorption Isotherms of Langmuir-Type and Freundlich-Type	166

11.3	Rates of Adsorption into Adsorbent Particles	167
11.4	Single- and Multi-Stage Operations for Adsorption	168
11.5	Adsorption in Fixed Beds	170
11.5.1	Fixed-Bed Operation	170
11.5.2	Estimation of the Break Point	171
11.6	Separation by Chromatography	174
11.6.1	Chromatography for Bioseparation	174
11.6.2	General Theories on Chromatography	176
11.6.2.1	Equilibrium Model	176
11.6.2.2	Stage Model	177
11.6.2.3	Rate Model	178
11.6.3	Resolution Between Two Elution Curves	178
11.6.4	Gel Chromatography	179
11.6.5	Affinity Chromatography	181
	References	183

Part III Practical Aspects in Bioengineering 187

12	Fermentor Engineering	187
12.1	Introduction	187
12.2	Stirrer Power Requirements for Non-Newtonian Liquids	189
12.3	Heat Transfer in Fermentors	191
12.4	Gas-Liquid Mass Transfer in Fermentors	193
12.4.1	Special Factors Affecting $k_L a$	194
12.4.1.1	Effects of Electrolytes	194
12.4.1.2	Enhancement Factor	194
12.4.1.3	Presence of Cells	194
12.4.1.4	Effects of Antifoam Agents and Surfactants	195
12.4.1.5	$k_L a$ in Emulsions	195
12.4.1.6	$k_L a$ in Non-Newtonian Liquids	197
12.4.2	Desorption of Carbon Dioxide	198
12.5	Criteria for Scaling-Up Fermentors	199
12.6	Modes of Fermentor Operation	202
12.6.1	Batch Operation	202
12.6.2	Fed-Batch Operation	203
12.6.3	Continuous Operation	204
12.6.4	Operation of Enzyme Reactors	206
12.7	Fermentors for Animal Cell Culture	207
	References	209
13	Downstream Operations in Bioprocesses	211
13.1	Introduction	211
13.2	Separation of Microorganisms by Filtration and Microfiltration	213
13.2.1	Dead-End Filtration	214

13.2.2	Cross-Flow Filtration	216
13.3	Separation by Chromatography	218
13.3.1	Factors Affecting the Performance of Chromatography Columns	218
13.3.1.1	Velocity of Mobile Phase and Diffusivities of Solutes	218
13.3.1.2	Radius of Packed Particles	219
13.3.1.3	Sample Volume Injected	220
13.3.1.4	Column Diameter	220
13.3.2	Scale-Up of Chromatography Columns	221
13.4	Separation in Fixed Beds	222
13.5	Sanitation in Downstream Processes	224
	References	209

14 Medical Devices 227

14.1	Introduction	227
14.2	Blood and Its Circulation	227
14.2.1	Blood and Its Components	227
14.2.2	Blood Circulation	228
14.3	Oxygenation of Blood	230
14.3.1	Use of Blood Oxygenators	230
14.3.2	Oxygen in Blood	231
14.3.3	Carbon Dioxide in Blood	233
14.3.4	Types of Blood Oxygenator	234
14.3.5	Oxygen Transfer Rates in Blood Oxygenators	235
14.3.5.1	Laminar Blood Flow	236
14.3.5.2	Turbulent Blood Flow	236
14.3.6	Carbon Dioxide Transfer Rates in Blood Oxygenators	242
14.4	Artificial Kidney	242
14.4.1	Human Kidney Functions	243
14.4.2	Artificial Kidneys	245
14.4.2.1	Hemodialyzer	245
14.4.2.2	Hemofiltration	246
14.4.2.3	Peritoneal Dialysis	246
14.4.3	Mass Transfer in Hemodialyzers (cf. Section 8.2)	247
14.5	Bioartificial Liver	251
14.5.1	Human Liver	251
14.5.2	Bioartificial Liver Devices	251
	References	254

Appendix 255

Index 257