

国外化学经典教材系列（影印版）

6

生物反应工程原理

**Bioreaction Engineering Principles
(3rd Edition)**

John Villadsen, Jens Nielsen and Gunnar Lidén

原著第3版



科学出版社

国外化学经典教材系列(影印版) 6

Bioreaction Engineering Principles

(3rd Edition)

生物反应工程原理

(原著第3版)

John Villadsen

Jens Nielsen

Gunnar Lidén

科学出版社

北京

图字：01-2012-0171

Reprint from English language edition:

Bioreaction Engineering Principles

by John Villadsen, Jens Nielsen and Gunnar Lidén

Copyright © 2011, Springer US

Springer US is a part of Springer Science+Business Media

All Rights Reserved

This reprint has been authorized by Springer Science & Business Media for distribution in China Mainland only and not for export therefrom.

本影印版由施普林格科学商业媒体授权仅在中国大陆境内发行,不得出口。

图书在版编目(CIP)数据

生物反应工程原理 = Bioreaction Engineering Principles: 第3版: 英文/
(丹麦)维拉森(Villadsen, J.)等编著. —影印本. —北京: 科学出版社, 2012
国外化学经典教材系列 6
ISBN 978-7-03-033298-1

I. ①生… II. ①维… III. ①生物工程: 化学工程-高等学校-教材-英文
IV. ①Q81②Q939.97

中国版本图书馆CIP数据核字(2012)第001014号

责任编辑: 周 强 / 责任印制: 钱玉芬 / 封面设计: 耕者设计室

科学出版社出版

北京东黄城根北街16号

邮政编码: 100717

<http://www.sciencep.com>

骏杰印刷厂印刷

科学出版社发行 各地新华书店经销

*

2012年1月第一版 开本: B5(720×1000)

2012年1月第一次印刷 印张: 37

字数: 741 000

定价: 128.00元

(如有印装质量问题, 我社负责调换)

Preface

In early 2009, we were approached by Springer Verlag, the company that had absorbed Kluwer Academic/Plenum Publishers. The second edition of our textbook “*Bioreaction Engineering Principles*” was now sold out, and we were asked to prepare a third edition.

With very little hesitation we accepted the offer.

Since 2003 the book has been used as course-book, in European universities and also in North and South America, in the Far East, and in Australia. We wished not only to revise the text, but also to write a book that would appeal to students at the best universities, at least until 2020. In short courses given at major Biotech companies we have also found that some of the material in the previous editions could be used right away to give the companies a better understanding of their processes and to propose better design of their reactors. This acceptance of the book by the industrial community prompted us to include even more examples relevant for design of processes and equipment in the industry. The changes that have been made since the second edition are outlined in the first, introductory chapter of the present edition.

Our initial enthusiasm to embark on a complete revision of the text was mollified by the duties imposed on two of us (J.N. and G.L.) in handling large research groups and with the concomitant administration. One of us (J.V.) had much more time available in his function as senior professor, and he became the main responsible person for the work during the almost 2 years since the start of the project. But we are all happy with the result of our common efforts – “*Tous pour un, un pour tous.*”

Some chapters have been read and commented by our colleagues. Special thanks are owed to Prof. John Woodley for commenting on Chaps. 2 and 3, and to Prof. Alvin Nienow for long discussions concerning the right way to present Chap. 11. The former Ph.D. students, Drs. Mikkel Nordkvist and Thomas Grotkjær have kindly given comments to many of the chapters.

We also thank Ph.D. student Saeed Sheykshoae at Chalmers University who redrew many of the figures in the last rush before finishing the manuscript. Ph.D. student Jacob Brix at DTU has often assisted J.V. with his extensive knowledge of “how to handle the many tricks of Word.”

Lyngby, Denmark
Gothenburg, Sweden
Lund, Sweden

John Villadsen
Jens Nielsen
Gunnar Lidén

List of Symbols

Symbols that are defined and used only within a particular Example, Note, or Problem are not listed. It should be noted that a few symbols are used for different purposes in different chapters. For this reason, more than one definition may apply for a given symbol.

a	Cell age (h)
a	Specific interfacial area (m^2 per m^3 of medium)
a_d	Specific interfacial area (m^2 per m^3 of gas–liquid dispersion)
a_{cell}	Specific cell surface area (m^2 per gram dry weight)
A	Matrix of stoichiometric coefficients for substrates, introduced in (7.2)
$b(y)$	Breakage frequency (h^{-1})
B	Matrix of stoichiometric coefficients for metabolic products, introduced in (7.2)
c_i	Concentration of the i th chemical compound (kg m^{-3})
c_i^*	Saturation concentration of the i th chemical compound (kg m^{-3})
c	Vector of concentrations (kg m^{-3})
C_{ij}	Concentration control coefficient of the j th intermediate with respect to the activity of the i th enzyme
C_i^j	Flux control coefficient with respect to the activity of the i th enzyme
C*	Matrix containing the control coefficients defined in (6.34)
d_b	Bubble diameter (m)
δ_f	Thickness of liquid film (m)
d_{mean}	Mean bubble diameter (m)
d_{mem}	Lipid membrane thickness (m)
d_s	Stirrer diameter (m)
d_{Sauter}	Mean Sauter bubble diameter (m), given by (10.18)
D	Dilution rate (h^{-1}), given by (3.1)
D_{max}	Maximum dilution rate (h^{-1})
D_{mem}	Diffusion coefficient in a lipid membrane ($\text{m}^2 \text{s}^{-1}$)
D_{eff}	Effective diffusion coefficient ($\text{m}^2 \text{s}^{-1}$)

D_i	Diffusion coefficient of the i th chemical compound ($\text{m}^2 \text{s}^{-1}$)
e_0	Enzyme concentration (g enzyme L^{-1})
E_g	Activation energy of the growth process in (7.28)
E	Mixing efficiency, defined in (11.1)
\mathbf{E}	Elemental matrix for all compounds
\mathbf{E}_c	Elemental matrix for calculated compounds
\mathbf{E}_m	Elemental matrix for measured compounds
$f(\mathbf{y}, t)$	Distribution function for cells with property \mathbf{y} in the population (8.1)
\mathbf{F}	Variance-covariance matrix
g	Gravity (m s^{-2})
G	Gibbs free energy (kJ mol^{-1})
G^0	Gibbs free energy at standard conditions (kJ mol^{-1})
ΔG_{ci}	Gibbs free energy of combustion of the i th reaction component (kJ mol^{-1})
ΔG_d	Gibbs free energy of denaturation (kJ mol^{-1}) (7.29)
ΔG_{ci}^0	Gibbs free energy of combustion of the i th reaction component at standard conditions (kJ mol^{-1})
ΔG_f^0	Gibbs free energy of formation at standard conditions (kJ mol^{-1})
Gr	Grashof number, defined in Table 10.6
h	Test function, given by (3.54)
$h(\mathbf{y})$	Net rate of formation of cells with property \mathbf{y} upon cell division (cells h^{-1})
$h^+(\mathbf{y})$	Rate of formation of cells with property \mathbf{y} upon cell division (cells h^{-1})
$h^-(\mathbf{y})$	Rate of disappearance of cells with property \mathbf{y} upon cell division (cells h^{-1})
H_A	Henry's constant for compound A (atm L mol^{-1})
ΔH_{ci}	Enthalpy of combustion of the i th reaction component (kJ mol^{-1})
ΔH_f^0	Enthalpy of formation (kJ mol^{-1})
\mathbf{I}	Identity matrix (diagonal matrix with 1 in the diagonal)
\mathbf{J}	Jacobian matrix (9.102)
k_0	Enzyme activity (g substrate $[\text{g enzyme}]^{-1} \text{h}^{-1}$)
k_i	Rate constant (e.g., $\text{kg kg}^{-1} \text{h}^{-1}$)
k_g	Mass transfer coefficient for gas film (e.g., $\text{mol atm}^{-1} \text{s}^{-1} \text{m}^{-2}$)
k_l	Mass transfer coefficient for a liquid film surrounding a gas bubble (m s^{-1})
$k_l a$	Volumetric mass transfer coefficient (s^{-1})
k_s	Mass transfer coefficient for a liquid film surrounding a solid particle (m s^{-1})
K_a	Acid dissociation constant (mol L^{-1})
K_1	Overall mass transfer coefficient for gas-liquid mass transfer (m s^{-1})
K	Partition coefficient
K_{eq}	Equilibrium constant
K_m	Michaelis constant (g L^{-1}) (6.1)
m	Amount of biomass (kg)

m_{ATP}	Maintenance-associated ATP consumption (moles ATP $[\text{kg DW}]^{-1} \text{h}^{-1}$)
m_s	Maintenance-associated specific substrate consumption ($\text{kg} [\text{kg DW}]^{-1} \text{h}^{-1}$)
$M_n(t)$	The n th moment of a one-dimensional distribution function, given by (8.9)
n	Number of cells per unit volume (cells m^{-3}) (8.1)
N	Stirring speed (s^{-1})
N_A	Aeration number, defined in (11.14)
N_f	Flow number, defined in (11.6)
N_p	Power number, defined in (11.10)
p	Extracellular metabolic product concentration (kg m^{-3})
p_A	Partial pressure of compound A (e.g., atm.)
$p(\mathbf{y}, \mathbf{y}^*, t)$	Partitioning function (8.5)
P	Dimensionless metabolic product concentration
P	Permeability coefficient (m s^{-1})
P	Power input to a bioreactor (W)
P_g	Power input to a bioreactor at gassed conditions (W)
\mathbf{P}	Variance-covariance matrix for the residuals, given by (3.48)
Pe	Peclet number, defined in Table 10.6
q_A^t	Volumetric rate of transfer of A from gas to liquid ($\text{mol L}^{-1} \text{h}^{-1}$)
q_x	Volumetric rate of formation of biomass ($\text{kg DW m}^{-3} \text{h}^{-1}$)
\mathbf{q}	Volumetric rate vector ($\text{kg m}^{-3} \text{h}^{-1}$)
\mathbf{q}^t	Vector of volumetric mass transfer rates ($\text{kg m}^{-3} \text{h}^{-1}$)
Q	Number of morphological forms
Q	Heat of reaction (kJ mol^{-1})
Q_r	Fraction of repressor-free operators, given by (7.47)
Q_2	Fraction of promoters being activated, given by (7.53)
Q_3	Fraction of promoters, which form complexes with RNA polymerase, in (7.55)
r_i	Specific reaction rate for species i ($\text{kg} [\text{kg DW}]^{-1} \text{h}^{-1}$)
r	Enzymatic reaction rate (Chap. 6) ($\text{g substrate L}^{-1} \text{h}^{-1}$)
r_{ATP}	Specific ATP synthesis rate (moles of ATP $[\text{kg DW}]^{-1} \text{h}^{-1}$)
\mathbf{r}	Specific reaction rate vector ($\text{kg} [\text{kg DW}]^{-1} \text{h}^{-1}$)
\mathbf{r}_s	Specific substrate formation rate vector ($\text{kg} [\text{kg DW}]^{-1} \text{h}^{-1}$)
\mathbf{r}_p	Specific product formation rate vector ($\text{kg} [\text{kg DW}]^{-1} \text{h}^{-1}$)
\mathbf{r}_x	Specific formation rate vector of biomass constituents ($\text{kg} [\text{kg DW}]^{-1} \text{h}^{-1}$)
$\mathbf{r}(\mathbf{y}, t)$	Vector containing the rates of change of properties, in (8.2)
R	Gas constant ($=8.314 \text{ J K}^{-1} \text{ mol}^{-1}$)
R	Recirculation factor (Sect. 9.1.4)
\mathbf{R}	Redundancy matrix, given by (3.41)
\mathbf{R}_r	Reduced redundancy matrix

Re	Reynolds number, defined in Table 10.6
s	Extracellular substrate concentration (kg m^{-3})
\mathbf{s}	Extracellular substrate concentration vector (kg m^{-3})
s_f	Substrate concentration in the feed to the bioreactor (kg m^{-3})
S	Dimensionless substrate concentration
ΔS	Entropy change ($\text{kJ mol}^{-1} \text{K}^{-1}$)
Sc	Schmidt number, defined in Table 10.6
Sh	Sherwood number, defined in Table 10.6
t	Time (h)
t_c	Circulation time (s) (11.7)
t_m	Mixing time (s) (11.3)
T	Temperature (K)
\mathbf{T}	Matrix in (5.11). \mathbf{T}^T , the transform of \mathbf{T} , is the stoichiometric matrix
\mathbf{T}_1	Matrix corresponding to calculated fluxes (5.12)
\mathbf{T}_2	Matrix corresponding to measured rates (5.12)
u_b	Bubble rise velocity (m s^{-1})
u_i	Cybernetic variable, given by (7.36)
u_s	Superficial gas velocity (m s^{-1})
\mathbf{u}	Vector containing the specific rates of the metamorphosis reaction ($\text{kg kg}^{-1} \text{h}^{-1}$)
v	Liquid flow ($\text{m}^3 \text{h}^{-1}$)
v_e	Liquid effluent flow from the reactor ($\text{m}^3 \text{h}^{-1}$)
v_f	Liquid feed to the reactor ($\text{m}^3 \text{h}^{-1}$)
v_g	Gas flow ($\text{m}^3 \text{h}^{-1}$)
v_i	Flux of internal reaction i in metabolic network ($\text{kg} [\text{kg DW}]^{-1} \text{h}^{-1}$)
v_{pump}	Impeller induced flow ($\text{m}^3 \text{s}^{-1}$) (11.6)
\mathbf{v}	Flux vector, i.e., vector of specific intracellular reaction rates ($\text{kg} [\text{kg DW}]^{-1} \text{h}^{-1}$)
V	Volume (m^3)
V_d	Total volume of gas-liquid dispersion (m^3) (10.16)
V_g	Dispersed gas volume (m^3) (10.16)
V_l	Liquid volume (m^3)
V_y	Total property space (8.2)
w_i	Cybernetic variable, given by (7.47)
x	Biomass concentration (kg m^{-3})
X	Dimensionless biomass concentration
X_i	Concentration of the i th intracellular component ($\text{kg} [\text{kg DW}]^{-1}$)
\mathbf{X}	Vector of concentrations of intracellular biomass components ($\text{kg} [\text{kg DW}]^{-1}$)
\mathbf{y}	Property state vector
Y_{ij}	Yield coefficient of j from i ($\text{kg } j$ per kg of i or C-mol of j per kg of i)
$Y_{x\text{ATP}}$	ATP consumption for biomass formation (moles of ATP $[\text{kg DW}]^{-1}$)
Z_i	Concentration of the i th morphological form ($\text{kg} [\text{kg DW}]^{-1}$)

Greek Letters

α_{ji}	Stoichiometric coefficients for substrate i in intracellular reaction j
β_{ji}	Stoichiometric coefficient for metabolic product i in intracellular reaction j
$\dot{\gamma}$	Shear rate (s^{-1})
γ_{ji}	Stoichiometric coefficient for intracellular component i in intracellular reaction j
$\dot{\gamma}$	Shear rate (s^{-1}), defined in (11.24)
Γ	Matrices containing the stoichiometric coefficients for intracellular biomass components
δ	Vector of measurement errors in (3.43)
Δ	Matrix for stoichiometric coefficients for morphological forms
ε	Gas holdup (m^3 of gas per m^3 of gas–liquid dispersion)
ε	Porosity of a pellet
ε_{ji}	Elasticity coefficients, defined in (6.27)
$\mathbf{\varepsilon}$	Vector of residuals in (3.46)
\mathbf{E}	Matrix containing the elasticity coefficients
η	Dynamic viscosity ($\text{kg m}^{-1} \text{s}^{-1}$)
η	Internal effectiveness factor, defined in (9) of Note 6.2
π_i	Partial pressure of compound i (atm)
θ	Dimensionless time
κ_i	Degree of reduction of the i th compound
μ	Specific growth rate of biomass (h^{-1})
μ_{\max}	Maximum specific growth rate (h^{-1})
μ_q	Specific growth rate for the q th morphological form ($\text{kg DW} [\text{kg DW}]^{-1} \text{h}^{-1}$)
ρ_{cell}	Cell density ($\text{kg wet biomass} [\text{m}^{-3} \text{cell}]$)
ρ_l	Liquid density (kg m^{-3})
σ	Surface tension (N m^{-1})
σ^2	Variance
τ	Space time in reactor (h)
τ	Shear stress (N m^{-2}), defined in (11.25)
τ_p	Tortousity factor, used in (6.23)
Φ_n	Thiele modulus for reaction of order n (2) and (5) in Note 6.2
Φ_{gen}	Generalized Thiele modulus, Note 6.2
$\psi(X)$	Distribution function of cells (8.8)

Abbreviations

AcCoA	Acetyl co-enzyme A
ADP	Adenosine diphosphate
AMP	Adenosine monophosphate
ATP	Adenosine triphosphate
CoA	Coenzyme A
DHAP	Dihydroxy acetone phosphate
DNA	Deoxyribonucleic acid
E_c	Energy charge
EMP	Embden–Meyerhof–Parnas
FAD	Flavin adenine dinucleotide (oxidized form)
FADH	Flavin adenine dinucleotide (reduced form)
FDA	Food and Drug Administration
F6P	Fructose-6-phosphate
F1,6P	Fructose 1,6 diphosphate
GAP	Glyceraldehyde triphosphate
2 PG	2-phosphoglycerate
3 PG	3-phosphoglycerate
1,3 DPG	1,3 diphosphoglycerate
GTP	Guanosine triphosphate
G6P	Glucose-6-phosphate
HAc	Acetic acid
HLac	Lactic acid
LAB	Lactic acid bacteria
MCA	Metabolic control analysis
MFA	Metabolic Flux Analysis
NAD ⁺	Nicotinamide adenine dinucleotide (oxidized form)
NADH	Nicotinamide adenine dinucleotide (reduced form)
NADP ⁺	Nicotinamide adenine dinucleotide phosphate (oxidized form)
NADPH	Nicotinamide adenine dinucleotide phosphate (reduced form)
PEP	Phosphoenol pyruvate
PP	Pentose phosphate
PSS	Protein synthesizing system
PTS	Phosphotransferase system
PYR	Pyruvate
P/O ratio	Number of molecules of ATP formed per atom of oxygen used in the oxidative phosphorylation
RNA	Ribonucleic acid
mRNA	Messenger RNA

rRNA	Ribosomal RNA
tRNA	Transfer RNA
RQ	Respiratory quotient
R5P	Ribose-5-phosphate
TCA	Tricarboxylic acid
UQ	Ubiquinone

Contents

1	What Is This Book About?	1
1.1	Note on Nomenclature	5
2	Chemicals from Metabolic Pathways	7
2.1	The Biorefinery	8
2.1.1	Ethanol Production	9
2.1.2	Production of Platform Chemicals in the Biorefinery	14
2.2	The Chemistry of Metabolic Pathways	17
2.2.1	The Currencies of Gibbs Free Energy and of Reducing Power	18
2.2.2	Glycolysis	22
2.2.3	Fermentative Metabolism: Oxidation of NADH in Anaerobic Processes	26
2.2.4	The TCA Cycle: Provider of Building Blocks and NADH/FADH ₂	30
2.2.5	Production of ATP by Oxidative Phosphorylation	33
2.2.6	The Pentose Phosphate Pathway: A Multipurpose Metabolic Network	36
2.2.7	Summary of the Primary Metabolism of Glucose	38
2.3	Examples of Industrial Production of Chemicals by Bioprocesses	41
2.3.1	Amino Acids	42
2.3.2	Antibiotics	45
2.3.3	Secreted Proteins	49
2.4	Design of Biotech Processes: Criteria for Commercial Success	50
2.4.1	Strain Design and Selection	51
2.4.2	Criteria for Design and Optimization of a Fermentation Process	52
2.4.3	Strain Improvement	54

2.5	The Prospects of the Biorefinery	56
	Problems	58
	References	60
3	Elemental and Redox Balances	63
3.1	The Continuous, Stirred Tank Reactor	65
3.1.1	Mass Balances for an Ideal, Steady-State Continuous Tank Reactor	69
3.2	Yield Coefficients.....	71
3.3	Black Box Stoichiometries	76
3.4	Degree of Reduction Balances.....	78
3.4.1	Consistency Test of Experimental Data	86
3.4.2	Redox Balances Used in the Design of Bioremediation Processes	92
3.5	Systematic Analysis of Black Box Stoichiometries	96
3.6	Identification of Gross Measurement Errors	100
	Problems	110
	References	117
4	Thermodynamics of Bioreactions	119
4.1	Chemical Equilibrium and Thermodynamic State Functions	120
4.1.1	Changes in Free Energy and Enthalpy	120
4.1.2	Free Energy Changes in Bioreactions	124
4.1.3	Combustion: A Change in Reference State	128
4.2	Heat of Reaction	129
4.2.1	Nonequilibrium Thermodynamics	135
4.2.2	Free Energy Reclaimed by Oxidation in the Electron Transfer Chain.....	137
4.2.3	Production of ATP Mediated by $F_0 - F_1$ ATP Synthase.....	142
	Problems	145
	References	149
5	Biochemical Reaction Networks.....	151
5.1	Basic Concepts	152
5.1.1	Metabolic Network with Diverging Branches	157
5.1.2	A Formal, Matrix-Based Description of Metabolic Networks	166
5.2	Growth Energetics.....	172
5.2.1	Consumption of ATP for Cellular Maintenance	172
5.2.2	Energetics of Anaerobic Processes.....	175
5.2.3	Energetics of Aerobic Processes	180

5.3	Flux Analysis in Large Metabolic Networks	184
5.3.1	Expressing the Rate of Biomass Formation	186
5.3.2	The Network Structure and the Use of Measurable Rates	187
5.3.3	The Use of Labeled Substrates	199
	Problems	206
	References	212
6	Enzyme Kinetics and Metabolic Control Analysis.....	215
6.1	Enzyme Kinetics Derived from the Model of Michaelis–Menten.....	217
6.2	More Complicated Enzyme Kinetics	221
6.2.1	Variants of Michaelis–Menten Kinetics.....	222
6.2.2	Cooperativity and Allosteric Enzymes	227
6.3	Biocatalysis in Practice	232
6.3.1	Laboratory Studies in Preparation for an Industrial Production Process	233
6.3.2	Immobilized Enzymes and Diffusion Resistance	238
6.3.3	Choice of Reactor Type	243
6.4	Metabolic Control Analysis	244
6.4.1	Definition of Control Coefficients for Linear Pathways ...	245
6.4.2	Using Connectivity Theorems to Calculate Control Coefficients	249
6.4.3	The Influence of Effectors.....	257
6.4.4	Approximate Methods for Determination of the C_i^j	258
	Problems	265
	References	268
7	Growth Kinetics of Cell Cultures	271
7.1	Model Structure and Complexity.....	272
7.2	A General Structure for Kinetic Models	275
7.2.1	Specification of Reaction Stoichiometries	275
7.2.2	Reaction Rates	277
7.2.3	Dynamic Mass Balances.....	278
7.3	Unstructured Growth Kinetics	279
7.3.1	The Monod Model.....	280
7.3.2	Multiple Reaction Models.....	289
7.3.3	The Influence of Temperature and pH.....	297
7.4	Simple Structured Models	300
7.4.1	Compartment Models	301
7.4.2	Cybernetic Models	311
7.5	Derivation of Expression for Fraction of Repressor-free Operators	315

7.6	Morphologically Structured Models	327
7.6.1	Oscillating Yeast Cultures.....	331
7.6.2	Growth of Filamentous Microorganisms.....	334
7.7	Transport Through the Cell Membrane.....	341
7.7.1	Facilitated Transport, Exemplified by Eukaryotic Glucoside Permeases.....	342
7.7.2	Active Transport.....	345
	Problems	348
	References	353
8	Population Balance Equations.....	359
	Problems	378
	References	381
9	Design of Fermentation Processes	383
9.1	Steady-State Operation of the STR	386
9.1.1	The Standard CSTR with $v_f = v_e = v$	387
9.1.2	Productivity in the Standard CSTR	390
9.1.3	Productivity in a Set of Coupled, Standard CSTR's	394
9.1.4	Biomass Recirculation	399
9.1.5	Steady-State CSTR with Substrates Extracted from a Gas Phase.....	405
9.2	The STR Operated as a Batch or as a Fed-Batch Reactor	407
9.2.1	The Batch Reactor.....	408
9.2.2	The Fed-Batch Reactor	411
9.3	Non-steady-State Operation of the CSTR.....	419
9.3.1	Relations Between Cultivation Variables During Transients.....	419
9.3.2	The State Vector $[s, x, p]$ in a Transient CSTR Experiment	422
9.3.3	Pulse Addition of Substrate to a CSTR. Stability of the Steady State.....	425
9.3.4	Several Microorganisms Coinhabit the CSTR	429
9.3.5	The CSTR Used to Study Fast Transients	436
9.4	The Plug Flow Reactor.....	439
9.4.1	A CSTR Followed by a PFR.....	441
9.4.2	Loop Reactors.....	443
	Problems	448
	References	458
10	Gas-Liquid Mass Transfer.....	459
10.1	The Physical Processes Involved in Gas to Liquid Mass Transfer.....	460
10.1.1	Description of Mass Transfer Using k_1a	462

10.1.2	Models for k_1	465
10.1.3	Models for the Interfacial Area, and for Bubble Size ...	466
10.2	Empirical Correlations for k_1a	474
10.3	Experimental Techniques for Measurement of O_2 Transfer	482
10.3.1	The Direct Method.....	482
10.3.2	The Dynamic Method	484
10.3.3	The Sulfite Method	485
10.3.4	The Hydrogen Peroxide Method.....	486
10.3.5	k_1a Obtained by Comparison with the Mass Transfer Coefficient of Other Gases.....	488
	Problems	490
	References	495
11	Scale-Up of Bioprocesses	497
11.1	Mixing in Bioreactors.....	498
11.1.1	Characterization of Mixing Efficiency	499
11.1.2	Experimental Determination of Mixing Time	502
11.1.3	Mixing Systems and Their Power Consumption	505
11.1.4	Power Input and Mixing for High Viscosity Media	514
11.1.5	Rotating Jet Heads: An Alternative to Traditional Mixers	520
11.2	Scale-Up Issues for Large Industrial Bioreactors	527
11.2.1	Modeling the Large Reactor Through Studies in Small Scale	527
11.2.2	Scale-Up in Practice: The Desirable and the Compromises.....	535
	Problems	541
	References	545
	Index	547