

Edited by Toshiomi Yoshida

Applied Bioengineering

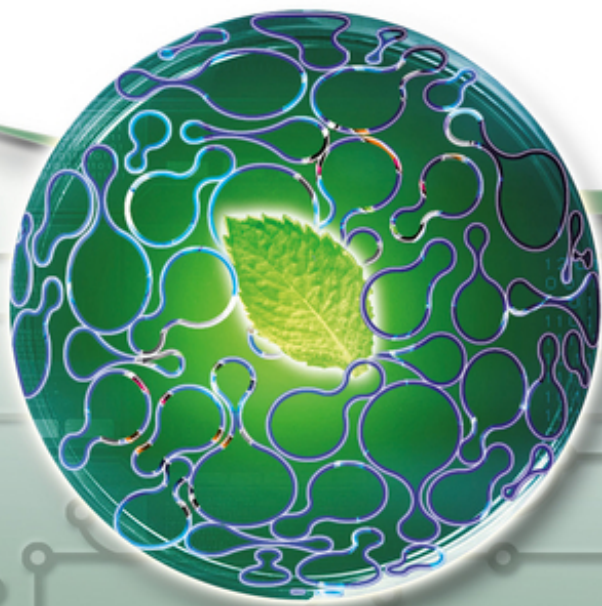
Innovations and Future Directions

Volume 5

Series Editors:

S. Y. Lee, J. Nielsen,

G. Stephanopoulos



Edited by
Toshiomi Yoshida

Applied Bioengineering

Related Titles

Buchholz, K., Kasche, V., Bornscheuer, U.T.

Biocatalysts and Enzyme Technology

2 Edition

2012

Print ISBN: 978-3-527-32989-2

Meyer, H., Schmidhalter, D.R. (eds.)

Industrial Scale Suspension Culture of Living Cells

2014

Print ISBN: 978-3-527-33547-3

Behme, S.

Manufacturing of Pharmaceutical Proteins From Technology to Economy 2 Edition

2015

Print ISBN: 978-3-527-33766-8

Further Volumes of the "Advanced Biotechnology" Series:

Published:

Villadsen, J. (ed.)

Fundamental Bioengineering

2016

Print ISBN: 978-3-527-33674-6

Love, J. Ch. (ed.)

Micro- and Nanosystems for Biotechnology

2016

Print ISBN: 978-3-527-33281-6

Coming soon:

Wittmann, Ch., Liao, J.C. (eds.)

Industrial Biotechnology Microorganisms 2 Volumes

2017

Print ISBN: 978-3-527-34075-0

Wittmann, Ch., and Liao, J. C. (eds.)

Industrial Biotechnology Products and Processes

2017

Print ISBN: 978-3-527-34181-8

Planned:

Systems Biology

J. Nielsen & S. Hohmann (Chalmers University, Sweden)

Emerging Areas in Bioengineering

H. N. Chang (KAIST, South Korea)

Edited by Toshiomi Yoshida

Applied Bioengineering

Innovations and Future Directions

WILEY-VCH
Verlag GmbH & Co. KGaA

Volume Editor

Toshiomi Yoshida

Osaka University
International Center for Biotechnology
2-1 Yamada-oka
Suita-shi
565-0871 Osaka
Japan

Series Editors

Sang Yup Lee

KAIST
373-1; Guseong-Dong
291 Daehak-ro, Yuseong-gu
305-701 Daejeon
South Korea

Jens Nielsen

Chalmers University
Department of Chemical and Biological
Engineering
Kemivägen 10
412 96 Göteborg
Sweden

Gregory Stephanopoulos

Massachusetts Institute of Technology
Department of Chemical Engineering
77 Massachusetts Avenue
Cambridge MA 02139
USA

All books published by **Wiley-VCH** are carefully produced. Nevertheless, authors, editors, and publisher do not warrant the information contained in these books, including this book, to be free of errors. Readers are advised to keep in mind that statements, data, illustrations, procedural details or other items may inadvertently be inaccurate.

Library of Congress Card No.: applied for

British Library Cataloguing-in-Publication Data

A catalogue record for this book is available from the British Library.

Bibliographic information published by the Deutsche Nationalbibliothek

The Deutsche Nationalbibliothek lists this publication in the Deutsche Nationalbibliografie; detailed bibliographic data are available on the Internet at <<http://dnb.d-nb.de>>.

© 2017 Wiley-VCH Verlag GmbH & Co. KGaA, Boschstr. 12, 69469 Weinheim, Germany

All rights reserved (including those of translation into other languages). No part of this book may be reproduced in any form – by photoprinting, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Registered names, trademarks, etc. used in this book, even when not specifically marked as such, are not to be considered unprotected by law.

Print ISBN: 978-3-527-34075-0

ePDF ISBN: 978-3-527-80058-2

ePub ISBN: 978-3-527-80060-5

Mobi ISBN: 978-3-527-80061-2

oBook ISBN: 978-3-527-80059-9

Cover Design Adam Design, Weinheim, Germany

Typesetting SPi Global, Chennai, India

Printing and Binding

Printed on acid-free paper

Contents

List of Contributors XIX

1	Introduction	1
	<i>Toshiomi Yoshida</i>	
1.1	Introduction	1
1.2	Enzyme Technology	2
1.3	Microbial Process Engineering	2
1.3.1	Bioreactor Development	2
1.3.2	Measurement and Monitoring	3
1.3.3	Modeling and Control	4
1.3.4	Solid-State Fermentation	4
1.4	Plant Cell Culture	5
1.5	Animal Cell Culture	5
1.6	Environmental Bioengineering	6
1.7	Composition of the Volume	7
	References	7
	Part I Enzyme Technology	11
2	Enzyme Technology: History and Current Trends	13
	<i>Klaus Buchholz and Uwe T. Bornscheuer</i>	
2.1	The Early Period up to 1890	13
2.1.1	Observations and Empirical Results	13
2.1.2	Theoretical Approaches	14
2.2	The Period from 1890 to 1940	16
2.2.1	Scientific Progress	16
2.2.2	Theoretical Developments	17
2.2.3	Technological Developments	18
2.3	A New Biocatalyst Concept – Immobilized Enzymes	19
2.3.1	Fundamental Research	19
2.3.2	Examples of Industrial Development: The Case of Penicillin Amidase (PA) – Penicillin Hydrolysis and Derivatives	20

2.3.3	Examples of Industrial Development: The Case of Sugar Isomerization	23
2.4	Expanding Enzyme Application after the 1950s	24
2.5	Recombinant Technology – A New Era in Biocatalysis and Enzyme Technology	27
2.5.1	New Enzymes – A Key to Genetic Engineering	27
2.5.2	Analytical and Diagnostic Enzymes	29
2.5.3	Expanding Market of Industrial Enzymes	31
2.6	Current Strategies for Biocatalyst Search and Tailor Design	32
2.6.1	Enzyme Discovery from the Metagenome or Protein Databases	32
2.6.2	Protein Engineering of Enzymes	34
2.6.3	Enzyme Cascade Reactions	35
2.6.4	Metabolic Engineering	37
2.7	Summary and Conclusions	39
	Acknowledgment	40
	Abbreviations	40
	References	40
3	Molecular Engineering of Enzymes	47
	<i>Maria Elena Ortiz-Soto and Jürgen Seibel</i>	
3.1	Introduction	47
3.2	Protein Engineering: An Expanding Toolbox	48
3.2.1	From Sequence to Fold and Function	49
3.2.2	Improving Enzyme Properties by Rational Design and Directed Evolution	49
3.2.3	Designing Smart Libraries	51
3.2.4	<i>In Vivo</i> Continuous Directed Evolution	54
3.2.5	Diversification of Enzyme Functionalities by Recombination	55
3.3	High-Throughput Screening Systems	56
3.4	Engineered Enzymes for Improved Stability and Asymmetric Catalysis	58
3.4.1	Stability	58
3.4.1.1	Cellulases	59
3.4.1.2	Lipases	60
3.4.2	Asymmetric Biocatalysis	62
3.5	<i>De Novo</i> Design of Catalysts: Novel Activities within Common Scaffolds	65
3.6	Conclusions	69
	References	69
4	Biocatalytic Process Development	81
	<i>John M. Woodley</i>	
4.1	A Structured Approach to Biocatalytic Process Development	83
4.2	Process Metrics	83
4.2.1	Reaction Yield	84

4.2.2	Productivity	85
4.2.3	Biocatalyst Yield	85
4.2.4	Product Concentration	86
4.3	Technologies for Implementation of Biocatalytic Processes	87
4.3.1	Biocatalyst Engineering	87
4.3.1.1	Protein and Genetic Engineering	87
4.3.1.2	Biocatalyst Immobilization	87
4.3.2	Reaction Engineering	88
4.3.2.1	Reactant Supply	89
4.3.2.2	Product Removal	89
4.3.2.3	Two-Phase Systems	90
4.4	Industrial Development Examples	91
4.4.1	Development of a Biocatalytic Route to Atorvastatin (Developed by Codexis Inc., USA)	91
4.4.2	Development of a Biocatalytic Route to Sitagliptin (Developed by Codexis Inc., USA and Merck and Co., USA)	92
4.5	Future Outlook	95
4.6	Concluding Remarks	96
	References	96
5	Development of Enzymatic Reactions in Miniaturized Reactors	99
	<i>Takeshi Honda, Hiroshi Yamaguchi, and Masaya Miyazaki</i>	
5.1	Introduction	99
5.2	Fundamental Techniques for Enzyme Immobilization	100
5.2.1	Enzyme Immobilization by Adsorption	101
5.2.1.1	Monoliths and Particles	109
5.2.1.2	Synthetic Polymer Membranes and Papers	109
5.2.1.3	Adsorption to Channel Walls	109
5.2.2	Enzyme Immobilization by Entrapment	110
5.2.2.1	Silica-Based Matrices	111
5.2.2.2	Non-Silica-based Matrices	117
5.2.3	Enzyme Immobilization by Affinity Labeling	119
5.2.3.1	His-Tag/Ni-NTA System	119
5.2.3.2	GST-Tag/Glutathione System	125
5.2.3.3	Avidin/Biotin System	125
5.2.3.4	DNA Hybridization System	126
5.2.3.5	Other Techniques Using Nucleotides for Enzyme Immobilization	126
5.2.4	Enzyme Immobilization by Covalent Linking	127
5.2.4.1	Immobilization to Solid Supports	127
5.2.4.2	Direct Immobilization to a Channel Wall	142
5.2.4.3	Enzyme Polymerization	146
5.2.5	Enzyme Immobilization by Other Techniques Using Organisms	149

5.2.6	Application of Immobilized Enzymes in Microfluidics	149
5.3	Novel Techniques for Enzyme Immobilization	150
5.3.1	Polyketone Polymer: Enzyme Immobilization by Hydrogen Bonds	151
5.3.2	Thermoresponsive Hydrogels	151
5.3.3	Immobilization Methods Using Azide Chemistry	152
5.3.3.1	Staudinger Ligation	152
5.3.3.2	Click Chemistry	152
5.3.4	Graphene-Based Nanomaterial as an Immobilization Support	153
5.3.5	Immobilization Methods Using Proteins Modified with Solid-Support-Binding Modules	154
5.4	Conclusions and Future Perspectives	155
	Abbreviations	156
	References	157

Part II Microbial Process Engineering 167

6	Bioreactor Development and Process Analytical Technology	169
	<i>Toshiomi Yoshida</i>	
6.1	Introduction	169
6.2	Bioreactor Development	170
6.2.1	Parallel Bioreactor Systems for High-Throughput Processing	171
6.2.1.1	Microtiter Plate Systems	172
6.2.1.2	Stirred-Tank Reactor Systems	178
6.2.1.3	Microfluidic Microbioreactor Systems	184
6.2.1.4	Bubble Column Systems	188
6.2.1.5	Comparison of Various Parallel-Use Micro-/Mini-Bioreactor System	189
6.2.2	Single-Use Disposable Bioreactor Systems	193
6.2.2.1	Features of Single-Use Bioreactors	194
6.2.2.2	Sensors and Monitoring	194
6.2.2.3	Single-Use Bioreactors in Practical Use	195
6.3	Monitoring and Process Analytical Technology	196
6.3.1	Monitoring and State Recognition	196
6.3.1.1	Sensors for Monitoring Bioprocesses	196
6.3.1.2	Spectrometry	199
6.3.2	Process Analytical Technology (PAT)	200
6.3.2.1	PAT Tools	201
6.3.2.2	PAT Implementations	202
6.4	Conclusion	203
	Abbreviations	204
	References	204

7	Omics-Integrated Approach for Metabolic State Analysis of Microbial Processes 213
	<i>Hiroshi Shimizu, Chikara Furusawa, Takashi Hirasawa, Katsunori Yoshikawa, Yoshihiro Toya, Tomokazu Shirai, and Fumio Matsuda</i>
7.1	General Introduction 213
7.2	Transcriptome Analysis of Microbial Status in Bioprocesses 214
7.2.1	Introduction 214
7.2.2	Microbial Response to Stress Environments and Identification of Genes Conferring Stress Tolerance in Bioprocesses 215
7.2.3	Transcriptome Analysis of the Ethanol-Stress-Tolerant Strain Obtained by Evolution Engineering 217
7.3	Analysis of Metabolic State Based on Simulation in a Genome-Scale Model 219
7.3.1	Introduction 219
7.3.2	Reconstruction of GSMs and Simulation by FBA 219
7.3.3	Using Prediction of Metabolic State for Design of Metabolic Modification 221
7.4	¹³ C-Based Metabolic Flux Analysis of Microbial Processes 223
7.4.1	Introduction 223
7.4.2	Principles of ¹³ C-MFA 223
7.4.3	Examples of ¹³ C-MFA in Microbial Processes 225
7.5	Comprehensive Phenotypic Analysis of Genes Associated with Stress Tolerance 227
7.5.1	Introduction 227
7.5.2	Development of a High-Throughput Culture System 228
7.5.3	Calculation of Specific Growth Rate 228
7.5.4	Results of Comprehensive Analysis of Yeast Cells Under Conditions of High Osmotic Pressure and High Ethanol Concentration 228
7.5.5	Identification of Genes Conferring Desirable Phenotypes Based on Integration with the Microarray Analysis Method 230
7.6	Multi-Omics Analysis and Data Integration 230
7.7	Future Aspects for Developing the Field 231
	Acknowledgments 233
	References 233
8	Control of Microbial Processes 237
	<i>Kazuyuki Shimizu, Hiroshi Shimizu, and Toshiomi Yoshida</i>
8.1	Introduction 237
8.2	Monitoring 238
8.2.1	Online Measurements 238
8.2.2	Filtering, Online Estimation, and Software Sensors 239
8.2.3	Algorithm of Extended Kalman Filter and Its Application to Online Estimation of Specific Rates 239
8.3	Bioprocess Control 242
8.3.1	Control of Fed-Batch Culture 242

8.3.2	Online Optimization of Continuous Cultures	244
8.3.3	Cascade Control for Mixed Cultures	246
8.3.4	Supervision and Fault Detection	249
8.4	Recent Trends in Monitoring and Control Technologies	250
8.4.1	Sensor Technologies and Analytical Methods	251
8.4.2	Control Technologies	252
8.5	Concluding Remarks	253
	Abbreviations	254
	References	254

Part III Plant Cell Culture and Engineering 259

9	Contained Molecular Farming Using Plant Cell and Tissue Cultures	261
	<i>Stefan Schillberg, Nicole Raven, Rainer Fischer, Richard M. Twyman, and Andreas Schiermeyer</i>	
9.1	Molecular Farming – Whole Plants and Cell/Tissue Cultures	261
9.2	Plant Cell and Tissue Culture Platforms	263
9.2.1	Cell Suspension Cultures	263
9.2.2	Tissue Cultures	264
9.2.3	Light-Dependent Expression Platforms	264
9.3	Comparison of Whole Plants and <i>In Vitro</i> Culture Platforms	265
9.4	Technical Advances on the Road to Commercialization	267
9.4.1	Improving the Quantity of Recombinant Proteins Produced in Cell Suspension Cultures	267
9.4.2	Improving the Quality and Consistency of Recombinant Proteins Produced in Cell Suspension Cultures	269
9.5	Regulatory and Industry Barriers on the Road to Commercialization	271
9.6	Outlook	273
	Acknowledgments	275
	References	275
10	Bioprocess Engineering of Plant Cell Suspension Cultures	283
	<i>Gregory R. Andrews and Susan C. Roberts</i>	
10.1	Introduction	283
10.2	Culture Development and Maintenance	286
10.3	Choice of Culture System	288
10.4	Engineering Considerations	291
10.4.1	Cell Growth and Morphology	291
10.4.2	Gas Requirements	292
10.4.3	Aggregation	292
10.4.4	Medium Rheology	293
10.4.5	Shear Sensitivity	293
10.5	Bioprocess Parameters	294

10.5.1	Medium Composition and Optimization	294
10.5.2	Temperature and pH	294
10.5.3	Agitation	295
10.5.4	Aeration	295
10.6	Operational Modes	296
10.7	Bioreactors for Plant Cell Suspensions	297
10.7.1	Conventional Bioreactors	297
10.7.1.1	Stirred-Tank Reactors	297
10.7.1.2	Pneumatic Bioreactors	300
10.7.2	Disposable Bioreactors	301
10.8	Downstream Processing	303
10.8.1	Specialized Metabolite Extraction and Purification	303
10.8.2	Recombinant Protein Extraction and Purification	304
10.9	Yield Improvement Strategies	306
10.9.1	Specialized Metabolites and Recombinant Proteins	306
10.9.1.1	Cell Immobilization	306
10.9.1.2	<i>In Situ</i> Product Removal	306
10.9.2	Specialized Metabolite Specific Strategies	307
10.9.2.1	Elicitation	307
10.9.2.2	Metabolic Engineering	308
10.9.3	Recombinant-Protein-Specific Strategies	309
10.9.3.1	Expression Systems	309
10.9.3.2	Minimizing Post-Translational Loss of Recombinant Proteins	309
10.10	Case Studies	310
10.10.1	Protalix and the ProCellEx™ Platform	310
10.10.1.1	Background	311
10.10.1.2	The ProCellEx® Platform	311
10.10.1.3	Future Outlook	312
10.10.2	Phyton Biotech, Paclitaxel, and Plant Cell Fermentation (PCF™)	314
10.10.2.1	Background	314
10.10.2.2	Why Plant Cell Culture?	314
10.10.2.3	Plant Cell Fermentation (PCF™)	315
10.10.2.4	PCF™ Compared to Other Production Platforms	315
10.11	Conclusion	315
	References	316
11	The Role of Bacteria in Phytoremediation	327
	<i>Zhaoyu Kong and Bernard R. Glick</i>	
11.1	The Problem	327
11.1.1	Metals and Organics in the Environment	328
11.1.2	Traditional Clean-up Procedures	328
11.2	Defining Phytoremediation and Its Components	329
11.3	Role of Bacteria in Phytoremediation	330
11.3.1	Biodegradative Bacteria	330

11.3.2	Plant-Growth-Promoting Bacteria	333
11.3.2.1	Role of IAA	333
11.3.2.2	Role of Ethylene	335
11.3.2.3	Role of Nitrogen Fixation	336
11.3.2.4	Role of Siderophores	339
11.3.3	Interaction with Mycorrhizae	340
11.4	Examples of Phytoremediation in Action	342
11.5	Summary and Perspectives	343
	References	344

Part IV Animal Cell Cultures 355

12	Cell Line Development for Biomanufacturing Processes	357
	<i>Mugdha Gadgil and Wei-Shou Hu</i>	
12.1	Introduction	357
12.2	Host Cell	359
12.2.1	Host Cell Engineering	359
12.3	Vector Components	360
12.3.1	Promoter/Enhancer	360
12.3.2	Intron	362
12.3.3	Poly-Adenylation Signal	362
12.3.4	Selection Marker	363
12.3.5	Secretion Leader Sequence	364
12.3.6	Components for Plasmid Cloning in <i>E. coli</i>	364
12.4	Transfection	365
12.4.1	Method of Transfection	365
12.4.2	Plasmid Conformation	366
12.5	Integration of Foreign DNA into Host Chromosome	366
12.5.1	Site-Specific Integration	367
12.5.2	Use of cis-Acting DNA Elements	367
12.6	Amplification	369
12.7	Single-Cell Cloning	370
12.7.1	Culture Medium for Single-Cell Cloning	371
12.7.2	Automated High-Throughput Screening for High-Producer Clones	372
12.8	Selecting the Production Clone	373
12.8.1	Screening Platform	373
12.8.2	Adaptation	374
12.8.3	Process and Product Attributes	374
12.8.4	Scale-Down Model	375
12.9	Clone Stability	376
12.10	Conclusion	376
	Acknowledgments	377
	References	377

13	Medium Design, Culture Management, and the PAT Initiative	383
	<i>Ziomara P. Gerdtzen</i>	
13.1	Historical Perspective on Culture Medium	383
13.2	Cell Growth Environment	384
13.2.1	Natural Cellular Environment	384
13.2.1.1	The Role of Medium	384
13.2.1.2	Medium Design	384
13.3	Media Types	386
13.4	Medium Components	387
13.4.1	Growth-Associated, Unconsumed, and Catalytic Components	388
13.4.1.1	Growth-Associated Components	388
13.4.1.2	Unconsumed Components	388
13.4.1.3	Catalytic Macromolecular Components	388
13.4.2	Water in Media Preparation	388
13.4.3	Sugars and Amino Acids	390
13.4.3.1	Sugars as the Main Carbon Source	390
13.4.3.2	Amino Acids	390
13.4.4	Vitamins, Nucleosides, Fatty Acids, and Lipids	392
13.4.4.1	Vitamins' Role	392
13.4.4.2	Fatty Acids and Lipids	393
13.4.5	Bulk Ions and Trace Elements	395
13.4.6	Non-Nutritional Medium Components	396
13.4.6.1	Phenol Red	396
13.4.6.2	Sodium Bicarbonate Buffer	396
13.4.6.3	Alternative Buffers	397
13.4.6.4	Antioxidants	398
13.4.6.5	Mechanical-Damage-Protective Agents	398
13.4.6.6	Antibiotics	399
13.5	High Molecular Weight and Complex Supplements	400
13.5.1	Serum	400
13.5.1.1	Functions of Serum in Cell Culture Medium	400
13.5.1.2	Disadvantages of Serum in Cell Culture Medium	401
13.5.2	Insulin and Insulin-Like Growth Factors	402
13.5.3	Transferrin	402
13.5.4	Serum Albumin and Other Carrier Proteins	403
13.5.5	Cell Adhesion Molecules	404
13.5.6	Protein Hydrolysates	405
13.5.7	Lipid Supplements	406
13.6	Medium for Industrial Production	407
13.6.1	Medium Design and the PAT Initiative	409
13.7	Conclusions	411
	References	412
	Further Reading/Resources	416

14	Advanced Bioprocess Engineering: Fed-Batch and Perfusion Processes 417
	<i>Sarika Mehra, Vikas Chandrawanshi, and Kamal Prashad</i>
14.1	Primary Modes of Bioreactor Operation 417
14.2	Fed-Batch Mode of Operation 419
14.2.1	Design of Feed Composition 419
14.2.2	Feeding Strategies for Fed-Batch Culture 422
14.2.2.1	Culture Working Volume as Control 423
14.2.2.2	Concentration of Indicator Metabolite as Control 423
14.2.2.3	Nutrient Consumption Rate as Control 426
14.2.2.4	Predicted Growth Rate as Control 427
14.2.2.5	Culture pH as Control 427
14.2.2.6	Oxygen Uptake Rate as Control 428
14.2.3	Mode and Frequency of Feeding 429
14.2.4	Challenges in Fed-Batch Culture and Future Directions 430
14.3	Perfusion Mode of Bioreactor Operation 435
14.3.1	Types of Perfusion Devices 435
14.3.1.1	Gravity Settlers 435
14.3.1.2	Filtration 438
14.3.1.3	Centrifuges 441
14.3.1.4	Hydrocyclones 443
14.3.1.5	Acoustic Settlers 444
14.3.2	Feeding Strategies for Perfusion Cultures 445
14.3.2.1	Cell-Density-Based Feeding 445
14.3.2.2	Metabolite-Based Feeding 445
14.3.3	Challenges in Perfusion Culture and Future Directions 446
14.4	Use of Disposables in Cell Culture Bioprocesses 447
14.5	Analytical Methods to Monitor Key Metabolites and Parameters 450
14.5.1	Enzymatic Assays 450
14.5.2	Spectroscopy-Based Methods 452
14.5.3	Chromatography-Based Methods 452
14.5.4	Microscopy-Based Methods 452
14.5.5	Electrochemical Methods 453
14.6	Concluding Remarks 453
	Nomenclature 455
	References 456
	Further Reading/Resources 468

Part V Environmental Bioengineering 469

- 15 Treatment of Industrial and Municipal Wastewater: An Overview about Basic and Advanced Concepts 471**
Jyoti K. Kumar, Parag R. Gogate, and Aniruddha B. Pandit
- 15.1 Types of Wastewater 471
- 15.2 Biological Treatment 471
- 15.3 Wastewater Regulations 473
- 15.4 Biological Treatment Processes 473
- 15.5 Aerobic Techniques 475
- 15.5.1 Mathematical Modeling 475
- 15.5.2 Types of Aerobic Treatment 476
- 15.5.2.1 Activated Sludge Process (ASP) 476
- 15.5.2.2 Trickling Filters 481
- 15.5.2.3 Rotating Biological Contactors (RBCs) 483
- 15.5.2.4 Submerged Biological Contactors (SBCs) 484
- 15.5.2.5 Powdered Activated Carbon Treatment (PACT) Systems 484
- 15.5.2.6 Membrane Bioreactors 484
- 15.5.2.7 Biological Aerated Filters (BAFs) 485
- 15.5.2.8 Hybrid Processes-Integrated Fixed Film Activated Sludge System 486
- 15.5.2.9 Use of Ultrasound to Improve the Sludge Characteristics 487
- 15.6 Anaerobic Techniques 488
- 15.6.1 Types of Anaerobic Treatment Systems 489
- 15.6.1.1 Upflow Anaerobic Sludge Blanket (UASB) 489
- 15.6.1.2 Anaerobic Baffled Reactors (ABR) 490
- 15.6.1.3 Anaerobic Fluidized Bed Reactors 491
- 15.6.1.4 Expanded Granule Sludge Blanket (EGSB) Reactor 492
- 15.6.1.5 Anaerobic Membrane Reactors 492
- 15.6.2 Improvements for Sludge Management 494
- 15.7 Aerobic–Anaerobic Processes 495
- 15.8 Modified Biological Processes 496
- 15.8.1 Cavitation 496
- 15.8.2 Fenton Chemistry 500
- 15.8.3 Ozonation 501
- 15.8.4 Photocatalysis 503
- 15.8.5 Overview of Literature Dealing with Combined Processes 505
- 15.8.6 A Typical Case Study of Biodegradability Enhancement of Distillery Wastewater Using Hydrodynamic Cavitation 507

15.8.7	Short Case Study of Intensification of Biological Oxidation Using Acoustic Cavitation/Fenton Chemistry	509
15.8.8	Summary of Pretreatment Approaches	511
15.9	Overall Conclusions	511
	List of Acronyms/Abbreviations	512
	List of Variables and Coefficients	513
	References	514
16	Treatment of Solid Waste	521
	<i>Michael Nelles, Gert Morscheck, Astrid Lemke, and Ayman El Naas</i>	
16.1	Biological Treatment of Source Segregated Bio-Waste	522
16.1.1	Composting	522
16.1.1.1	Composting Process	522
16.1.1.2	Composting Technologies	525
16.1.1.3	Compost Use and Quality	531
16.1.1.4	Status of Composting in Europe and Germany	532
16.1.2	Anaerobic Digestion	532
16.1.2.1	Process of Anaerobic Digestion	532
16.1.2.2	AD Technologies	534
16.1.2.3	Digestate Use and Quality	538
16.1.2.4	Status of Anaerobic Digestion in Europe and Germany	538
16.2	Mechanical–Biological Treatment of Mixed Municipal Solid Waste	538
16.2.1	MBT Technologies	539
16.2.1.1	MBT – Mechanical–Biological Treatment	539
16.2.1.2	MBS – Mechanical–Biological Stabilization	540
16.2.1.3	MPS – Mechanical–Physical Stabilization	541
16.2.1.4	Status for Germany and Europe	541
16.3	Biological Treatment of Agricultural Waste	542
16.4	Conclusion	542
	References	542
17	Energy Recovery from Organic Waste	545
	<i>Yutaka Nakashimada and Naomichi Nishio</i>	
17.1	Advantage of Methane Fermentation for Energy Recovery from Organic Matter	545
17.2	Basic Knowledge of Methane Fermentation of Organic Wastes	546
17.3	Conventional Methane Fermentation Process	549
17.4	Advanced Methane Fermentation Processes	551
17.4.1	Methane Fermentation of Organic Wastes with High Salinity	551
17.4.2	Methane Fermentation of Nitrogen-Rich Organic Wastes with High Ammonia	552
17.5	Hydrogen Production from Organic Wastes	555
17.5.1	Hydrogen Production Combining Methane Fermentation	555
17.5.2	Hydrogen Production by Various Anaerobic Bacteria	556

17.5.3	Feasible Substrates for Hydrogen Production	558
17.5.4	Bioreactor for High-Rate Hydrogen Production	559
17.6	Upgrading of Biogas from Organic Wastes Based on Biological Syngas Platform	561
17.6.1	Bioduel Production from Syngas by Acetogens	562
17.6.2	Development of Genetic Engineering Tools of Acetogens	563
17.7	Conclusions	564
	References	565
18	Microbial Removal and Recovery of Metals from Wastewater	573
	<i>Michihiko Ike, Mitsuo Yamashita, and Masashi Kuroda</i>	
18.1	Microbial Reactions Available for Metal Removal/Recovery	574
18.1.1	Bioprecipitation/Biomineralization	575
18.1.2	Biovolatilization	577
18.1.3	Biosorption	578
18.1.4	Bioleaching	581
18.2	Selenium Recovery by <i>Pseudomonas stutzeri</i> NT-I	583
18.2.1	<i>Pseudomonas stutzeri</i> NT-I as a Versatile Tool for Selenium Recovery	583
18.2.2	Selenium Recovery by Bioprecipitation	585
18.2.3	Selenium Recovery by Biovolatilization	586
18.3	Future Prospects	587
18.3.1	Toward Environmental Conservation and Solutions to Resource Depletion	587
18.3.2	Development of Removal and Recovery Strategies for Other Elements	589
18.3.3	Potential for Practical Application	589
18.4	Conclusions	590
	References	590
19	Sustainable Use of Phosphorus Through Bio-Based Recycling	597
	<i>Hisao Ohtake</i>	
19.1	Introduction	597
19.2	Microbiological Basis	598
19.2.1	P _i Acquisition in Bacteria	598
19.2.2	Bacterial polyP Accumulation	599
19.3	Bio-Based P Recycling	600
19.3.1	Biological P Removal	600
19.3.2	P _i Release from polyP-Rich Sludge	601
19.3.3	P _i Recovery from Aqueous Solution	602
19.4	Other Options for P Recycling	604
19.4.1	Land Application of Biosolids	604
19.4.2	Animal Manure Management	605
19.4.3	Biosolubilization of Immobilized P _i	606

19.4.4	Industrial P Recycling	606
19.5	Conclusions	607
	References	609

	Index	613
--	--------------	------------

List of Contributors

Gregory R. Andrews

Worcester Polytechnic
Institute Goddard Hall
Department of Chemical
Engineering
100 Institute Road
Worcester
MA 01609
USA

Uwe T. Bornscheuer

University of Greifswald
Institute of Biochemistry
Felix-Hausdorff-Str. 4
17487 Greifswald
Germany

Klaus Buchholz

University of Braunschweig
Institute for Technical
Chemistry
Hans-Sommer-Strasse 10
38106 Braunschweig
Germany

Vikas Chandrawanshi

Indian Institute of
Technology Bombay
Department of Chemical
Engineering
Powai
Mumbai 400076
India

Ayman El Naas

University of Rostock
Faculty of Agricultural
and Environmental
Sciences
Department of Waste
Management and
Material Flow
Justus-von-Liebig-Weg 6
18059 Rostock
Germany

Rainer Fischer

Fraunhofer Institute for
Molecular Biology and
Applied Ecology IME
Forckenbeckstrasse 6
52074 Aachen
Germany

and

RWTH Aachen University
Institute for Molecular
Biotechnology
Worringerweg 1
52074 Aachen
Germany

Chikara Furusawa

Osaka University
Graduate School of
Information Science and
Technology
Department of Bioinformatic
Engineering
1-5 Yamadaoka
Suita
Osaka 565-0871
Japan

and

RIKEN
Quantitative Biology
Center
6-2-3 Furuedai
Suita
Osaka 565-0874
Japan

Mugdha Gadgil

CSIR-National Chemical
Laboratory
Chemical Engineering
and Process Development
Division
Dr Homi Bhabha Road
Pune
Maharashtra 411008
India

Ziomara P. Gerdtsen

University of Chile
Centre for Biotechnology
and Bioengineering (CeBiB)
Department of Chemical
Engineering and
Biotechnology
Beauchef 850
Santiago 8370448
Chile

Bernard R. Glick

University of Waterloo
Department of Biology
200 University Avenue
West Waterloo
ON N2L 3G1
Canada

Parag R. Gogate

Institute of Chemical
Technology (Deemed
University)
Chemical Engineering
Department
N. P. Road Matunga (East)
Mumbai
Maharashtra 400019
India

Takashi Hirasawa

Osaka University
Graduate School of
Information Science and
Technology
Department of Bioinformatic
Engineering
1-5 Yamadaoka
Suita
Osaka 565-0871
Japan

and

Tokyo Institute of Technology
Department of Bioengineering
4259 Nagatsuta-cho
Midori-ku
Yokohama 226-8501
Japan

Takeshi Honda

National Institute of
Advanced Industrial
Science and Technology
Advanced Manufacture
Research Institute
807-1 Shuku
Tosu
Saga 841-0052
Japan

and

Yamaguchi University
Graduate School of Medicine
Department of Pharmacology
1-1-1 Minamikogushi
Ube
Yamaguchi 755-8505
Japan

Wei-Shou Hu

University of Minnesota
Department of Chemical
Engineering and
Materials Science
421 Washington Ave SE
Minneapolis
MN 55455
USA

Michihiko Ike

Osaka University
Graduate School of
Engineering
Division of Sustainable
Energy and Environmental
Engineering
2-1 Yamadaoka
Suita
Osaka 565-0871
Japan

Zhaoyu Kong

Nanchang University
School of Life Science
999 Xuefu Avenue
Nanchang 330031
China

Jyoti K. Kumar

Institute of Chemical Technology
(Deemed University)
Chemical Engineering
Department
N. P. Road Matunga (East)
Mumbai
Maharashtra 400019
India

Masashi Kuroda

Osaka University
Graduate School of
Engineering
Division of Sustainable
Energy and Environmental
Engineering
2-1 Yamadaoka
Suita
Osaka 565-0871
Japan

Astrid Lemke

University of Rostock
Faculty of Agricultural
and Environmental
Sciences
Department of Waste
Management and
Material Flow
Justus-von-Liebig-Weg 6
18059 Rostock
Germany

Fumio Matsuda

Osaka University
Graduate School of
Information Science and
Technology
Department of Bioinformatic
Engineering
1-5 Yamadaoka
Suita
Osaka 565-0871
Japan

Sarika Mehra

Indian Institute of
Bombay
Department of Chemical
Engineering
Powai
Mumbai 400076
India

Masaya Miyazaki

National Institute of
Advanced Industrial
Science and Technology
Advanced Manufacture
Research Institute
807-1 Shuku
Tosu
Saga 841-0052
Japan

and

Kyushu University
Interdisciplinary
Graduate School of
Engineering Science
Department of Molecular
and Material Sciences
6-1 Kasuga-koen
Kasuga
Fukuoka 816-8580
Japan

Gert Morscheck

University of Rostock
Faculty of Agricultural
and Environmental Sciences
Department of Waste
Management and
Material Flow
Justus-von-Liebig-Weg 6
18059 Rostock
Germany

Yutaka Nakashimada

Hiroshima University
Graduate School of
Advanced Sciences of
Matter
Department of Molecular
Biotechnology
1-3-1 Kagamiyama
Higashi-Hiroshima 7398530
Japan

Michael Nelles

University of Rostock
Faculty of Agricultural
and Environmental Sciences
Department of Waste
Management and
Material Flow
Justus-von-Liebig-Weg 6
18059 Rostock
Germany

Naomichi Nishio

Hiroshima University
Graduate School of
Advanced Sciences of
Matter
Department of Molecular
Biotechnology
1-3-1 Kagamiyama
Higashi-Hiroshima
7398530
Japan

Hisao Ohtake

Waseda University
Phosphorus Atlas
Research Institute
2-2 Wakamatsu
Shinjuku
Tokyo 162-0056
Japan

Maria Elena Ortiz-Soto

Julius-Maximilians-Universität
Würzburg
Institut für Organische
Chemie
Am Hubland
97074 Würzburg
Germany

Aniruddha B. Pandit

Institute of Chemical
Technology (Deemed
University)
Chemical Engineering
Department
N. P. Road Matunga (East)
Mumbai
Maharashtra 400019
India

Kamal Prashad

Indian Institute of
Technology Bombay
Department of Chemical
Engineering
Powai
Mumbai 400076
India

Nicole Raven

Fraunhofer Institute for
Molecular Biology and
Applied Ecology IME
Forckenbeckstrasse 6
52074 Aachen
Germany

Susan C. Roberts

Worcester Polytechnic
Institute Goddard Hall
Department of Chemical
Engineering
100 Institute Road
Worcester MA 01609
USA

Andreas Schiermeyer

Fraunhofer Institute for
Molecular Biology and
Applied Ecology IME
Forckenbeckstrasse 6
52074 Aachen
Germany

Stefan Schillberg

Fraunhofer Institute for
Molecular Biology and
Applied Ecology IME
Forckenbeckstrasse 6
52074 Aachen
Germany

and

Justus-Liebig University
Giessen
Phytopathology Department
Institute for Phytopathology
and Applied Zoology
Heinrich-Buff-Ring 26-32
35392 Giessen
Germany

Jürgen Seibel

Julius-Maximilians-Universität
Würzburg
Institut für Organische
Chemie
Am Hubland
97074 Würzburg
Germany

Hiroshi Shimizu

Osaka University
Graduate School of
Information Science and
Technology
Department of Bioinformatic
Engineering
1-5 Yamadaoka
Suita
Osaka 565-0871
Japan

Kazuyuki Shimizu

Kyushu Institute of
Technology
680-4, Kawazu Iizuka
Fukuoka 820-8502
Japan

and

Keio University
Institute of Advanced
Bioscience
246_2 Mizukami
Kakuganji
Tsuruoka
Yamagata 997-0017
Japan

Tomokazu Shirai

RIKEN
Center for Sustainable
Resource Science
1-7-22 Suehiro
Tsurumi
Yokohama
Kanagawa 230-0045
Japan

Yoshihiro Toya

Osaka University
Graduate School of
Information Science and
Technology
Department of Bioinformatic
Engineering
1-5 Yamadaoka
Suita
Osaka 565-0871
Japan

Richard M. Twyman

TRM Ltd.
PO Box 463
York YO11 9FJ
UK

John M. Woodley

Technical University of
Denmark (DTU)
Department of Chemical
and Biochemical Engineering
Soltofts Plads
2800 Lyngby
Denmark

Hiroshi Yamaguchi

National Institute of
Advanced Industrial
Science and Technology
Advanced Manufacture
Research Institute
807-1 Shuku
Tosu
Saga 841-0052
Japan

and

Tokai University
Liberal Arts Education
Center
Kawayo
Minamiaso
Kumamoto 869-1404
Japan

Mitsuo Yamashita

Shibaura Institute of
Technology
Faculty of Engineering
Department of Applied
Chemistry
3-7-5 Toyosu Koto-ku
Tokoyo 135-8548
Japan

Toshiomi Yoshida

Osaka University
International Center for
Biotechnology
2-1 Yamadaoka
Suita
Osaka 565-0871
Japan

Katsunori Yoshikawa

Osaka University
Graduate School of
Information Science and
Technology
Department of Bioinformatic
Engineering
1-5 Yamadaoka
Suita
Osaka 565-0871
Japan

1 Introduction

Toshiomi Yoshida

1.1 Introduction

The European Federation of Biotechnology proposed a definition of biotechnology as “The integration of natural science and organisms, cells, parts thereof and molecular analogs for products and services.” The Concise Oxford English Dictionary states “biotechnology is the exploitation of biological processes for industrial and other purposes especially the genetic manipulation of microorganisms for the production of antibiotics, hormone, and so on” [1].

Biochemical engineering has developed as a branch of chemical engineering, and deals with the design and construction of unit processes that involve biological molecules or organisms. Biochemical engineering is often taught as a supplementary option to students of chemical engineering or biological engineering courses because of the overlap in the curriculum and similarities in problem-solving techniques used in both professions. Its contribution is widely found in the food, feed, pharmaceutical, and biotechnological industries, and in water treatment plants.

Biological engineering or bioengineering is the application of the concepts, principles, and methods of biology to solve real-world problems using engineering methodologies and also its traditional sensitivity to the cost advantage and practicality. In this context, while traditional engineering applies physical and mathematical sciences to analyze, design, and manufacture inanimate tools, structures, and processes, biological engineering primarily utilizes knowledge of molecular biology to study, investigate, and develop applications of living organisms. In summary, biological engineers principally focus on applying engineering principles and the knowledge of molecular biology to study and enhance biological systems for varied applications.

Referring to the above review and brief discussion, it is proposed to have a section titled “Applied Bioengineering” be included in the Wiley Biotechnology Series. This section will deal with recent progress in all subjects closely related to “engineering and technologies” in the field of biotechnology; widening the coverage beyond conventional biochemical engineering and bioprocess engineering

to include other biology-based engineering disciplines. The topics involved were selected specifically from the perspective of practical applications.

The volume “Applied Bioengineering” comprises five topics: enzyme technology, microbial process engineering, plant cell culture, animal cell culture, and environmental bioengineering. Each topic is figured in several chapters, though with more chapters pertaining to environmental bioengineering. This field has seen an increase in active research as mentioned below because of growing awareness and concern about conservation, remediation, and improvement of the environment.

The later part of this chapter provides a brief overview on the developments in bioengineering, referring to recent highly cited research.

1.2

Enzyme Technology

Recently, several attempts have been made to screen organic-solvent-tolerant enzymes from various microorganisms [2]. The ligninolytic oxidoreductases are being improved utilizing protein engineering by the application of different “omics” technologies. Enzymatic delignification will soon come into practical use in pulp mills [3]. Enzyme stabilization has been attempted using various approaches such as protein engineering, chemical modification, and immobilization [4].

Microbial glucose oxidase has garnered considerable interest because of its wide applications in chemical, pharmaceutical, food, beverage, clinical chemistry, biotechnology, and other industries. Novel applications of glucose oxidase in biosensors have further increased its demand [5]. Numerous oxidative biotransformation studies have demonstrated that enzymes have diverse characteristics and wide range of potential, and established applications [6]. Multienzymatic cascade reactions used in the asymmetric synthesis of chiral alcohols, amines, and amino acids, as well as for C–C bond formation, have been extensively studied [7].

1.3

Microbial Process Engineering

1.3.1

Bioreactor Development

Stirred-tank bioreactors are used in a large variety of bioprocesses because of their high rates of mass and heat transfer and excellent mixing. Theoretical predictions of the volumetric mass transfer coefficient have been recently proposed, and different criteria for bioreactor scale-up have been reported [8].