Contents

Part I Introduction

1	Biotechnology - History, Processes, and Products 3
i.1	Definition 4
1.2	Development of Biotechnology 4
1.2.1	Unconscious Use of Biotechnology: Processes in the Manufacture of Foodstuffs 4
1.2.2	Biotechnological Processes without Absolute Prohibition of Foreign Infections 8
1.2.3	Biotechnological Manufacture of Products with the Exclusion of Foreign Microbes 8
1.2.4	Application of Important Results of Basic Research to Biotechnology
1.3	General Observations of Biotechnological Processes 9
1.4	Importance of Biotechnology 12
1.5	Literature 14

Part II Fundamentals of Biotechnology

2

	Genetic Procedures for Strain
	Improvement 17
2.1	Introduction 18
2.2	Bacteria (Schizomycetes) 18
2.2.1	Definition of Terms 18
2.2.2	Classification 21
2.2.3	Bacteria of Biotechnological
	Importance 22
2.2.4	General Remarks on Cultivation,
	Maintenance, and Storage 22
2.3	Fungi (Mycophyta) 27
2.3.1	Definition of Terms 27
2.3.2	Classification 32
2.3.3	Biotechnologically Important
	Fungi 42
2.3.4	General Remarks on Cultivation,
	Maintenance, and Storage 42
2.4	Strain Improvement 46
2.4.1	Selection 46
2.4.2	Selection with Subsequent
	Mutation 46
2.4.3	Selection and Mutation with
	Subsequent Recombination 48
2.4.4	Gene Manipulation 50

Literature 59

2.5

Microorganisms - Biology and

3	The Metabolism of Micro-	4	Secondary Metabolism 107
	organisms 67		
	9	4.1	Introduction 108
3.1 3.2	Introduction 68 Basic Metabolism 68	4.2	Occurrence of Secondary Metabolites in Microorganisms 108
3.2.1	Function of the Enzymes 69	4.3	Variations in the Secondary
3.2.2	Coenzymes and Prosthetic Groups		Metabolism 111
	70	4.4	Special Chemical Groups and Basic
3.2.3	Hydrogen Transfer Reactions 71		Intermediates in the Secondary
3.2.4	Mechanisms of ATP Regeneration		Metabolism 112
• • • • • • • • • • • • • • • • • • • •	71	4.4.1	Covalently Bound Chlorine or
3.2.5	Uptake of Substrates into the Cell		Bromine 112
•	73	4.4.2	Unusual Nitrogen Compounds 113
3.2.6	Degradation of Carbon and Energy	4.4.3	Unusual Compounds Containing
	Sources 74		Phosphorus 113
3.2.7	Synthesis of the Low-Molecular-	4.4.4	Unusual Organometallic Com-
	Weight Constituents of the Cell 78		pounds 114
3.2.8	Synthesis of Macromolecular	4.4.5	Boron-Containing Metabolites 114
	Constituents of the Cell 80	4.4.6	Unusual Amino Acids 114
3.2.9	Regulation 81	4.4.7	Unusual Ring Systems 114
3.2.10	Substrates of Microorganisms and	4.5	Function of Secondary
	Degradation Pathways 84		Metabolites 117
3.3	Assignment of the Most Important	4.5.1	Secondary Metabolism as Derailed
	Secretion Products to the Metabolic		Primary Metabolism 117
	Types of Microorganisms 92	4.5.2	Secondary Metabolites as
3.4	Metabolic Types 92		"Biochemical Appendices" 117
3.4.1	Basic Properties of Fermentative	4.5.3	Secondary Metabolites as Waste
	Organisms 93		Products, Shavings from an
3.4.2	Basic Properties of Organotrophic		Imperfectly Functioning Intermediate
	Aerobically Respiring Micro-	4.5.4	Metabolism 117
	organisms 96	4.5.4	Secondary Metabolites as Products
3.4.3	Basic Properties of Lithotrophic	455	of Detoxification Mechanisms 118
	Aerobically Respiring Bacteria 98	4.5.5	Secondary Metabolites as Results of
3.4.4	Basic Properties of "Anaerobically	456	an Inhibited Growth 118
	Respiring" Bacteria 100	4.5.6	The Secondary Metabolism as a Playing Field of Biochemical
3.4.5	Basic Properties of Phototrophic		Evolution 118
	Organisms 102	4.6	Biogenesis and Biosynthesis of
3.5	The Impulse to Research 103	4.0	Secondary Metabolites 120
3.6	Literature 104	4.6.1	Polyketides 123
3.6.1	Cited Literature 104	4.6.1	Amino Acids as Structural Units of
3.6.2	Further Reading 104	7.0.2	Secondary Metabolites 126
		4.6.3	Sugars as Structural Units of
		7.0.5	Secondary Metabolites 129

4.6.4	Mevalonic Acid as a Structural Unit	6.3	Selection of the Reactor 186
	of Secondary Metabolites 129	6.3.1	Characteristics Predetermined by the
4.7	Biological Effects of Secondary		Nature of the Organism Used 186
	Metabolites Outside the Producing	6.3.2	Characteristics Predetermined by the
	Cell 130		Properties of the Medium 187
4.8	Literature 130	6.3.3	Characteristics Predetermined
			by the Parameters of the Biochemical
			Process 189
_	TO	6.3.4	Characteristics Predetermined by the
5	Plant and Animal Cell		Site 189
	Culture 133	6.4	Submerged Reactors and their
			Characterization 189
5.1	Introduction 134	6.4.1	Power Input by Mechanically Moved
5.2	Plant Cell Cultures 134		Internal Devices 190
5.2.1	General 134	6.4.2	Power Input by Liquid Circulation
5.2.2	Work with Plant Cell Cultures 134		with an External Pump 203
5.2.3	Biotechnological Application 139	6.4.3	Power Input by Compressed Gas
5.2.4	Agricultural Use of Plant Cell		208
	Culture Technique 139	6.5	Surface Reactors and their
5.2.5	Use of Plant Cell Cultures in		Characterization 211
	Industry 142	6.5.1	Solid Nutrient Substrates 211
5.2.6	Summary 149	6.5.2	Fluidized Bed Reactors 212
5.2.7	Literature: Plant Cell Cultures 149	6.5.3	Agitated Solid Bed Reactors 212
5.3	Animal Cell Cultures 153	6.5.4	Tray Reactors 212
5.3.1	General 153	6.5.5	Packed-bed Reactors 212
5.3.2	Experimental Work with Animal Cell	6.5.6	Film Reactors 213
	Cultures 154	6.5.7	Immersing Surface Reactors 214
5.3.3	Technological Uses of Animal Cell	6.5.8	Immobilized Cells 214
	Cultures 161	6.6	Comparison of Reactors 215
5.3.4	Prospects 172	6.7	Reactors in Industry 216
5.3.5	Literature: Animal Cell Cultures 173	6.7.1 6.7.2	Present State of the Art 216
		6.8	Trends of Further Development 216 Practical Advice on the Choice of
		0.0	Reactors 216
6	Bioreactors 179	6.9	Literature 217
•	Biological 175	6.10	Explanation of the Symbols 222
6.1	Introduction 180	0.10	Explanation of the Symbols 222
6.2	Basic Concepts 181		
6.2.1	Batch Operation 181		
6.2.2	"Extended Culture" Operation 181	7	Biological Regulation and
6.2.3	Continuous Operation 181		Process Control 225
6.2.4	Production of Heat During Cell		
•	Growth 183	7.1	Introduction 226
6.2.5	Stirring Power 183	7.2	Characteristics of the Biological
626	Ovygen Transfer 184		Control Cycle 234

X	Contents

7.2.1	Structure 234	8.5	Purification 303
7.2.2	Gene Expression 236	8.5.1	Crystallization 304
7.2.3	Regulation of Enzyme Activity 236	8.5.2	Chromatography 304
7.2.4	Relevant Process Parameters 242	8.6	Drying 312
7.3	Measurement Technique 242	8.6.1	Contact Dryers 313
7.3.1	Principles 242	8.6.2	Convection Dryers 314
7.3.2	Exemplary Measurement Tech-	8.6.3	Freeze-dryers 314
	nique 245	8.7	Evaluation of Separation Processes
7.4	Regulation Technique 258	0.0	316
7.5	Process Computers 262	8.8	Literature 317
7.5.1	Tasks of Process Computers 264		
7.5.2	Requirements for Process		
	Computers 271		
7.5.3	Hardware 271		
7.5.4	Software 275	n	
7.5.5	Process Computers in	Pari	t III
7.6	Biotechnology 276 Literature 277	Proc	cesses and Products
8	Product Recovery in Bio- technology 279	9	Biotechnological Processes for the Manufacture of Foodstuffs
			and Fodders 325
8.1	Introduction 280		
8.2	Separation 280	9.1	Introduction 326
8.2.1	Flocculation and Flotation 280	9.2	Foodstuffs and Fodders of Plant
8.2.2	Filtration 281		Origin 326
8.2.3	Centrifugation 285	9.2.1	Silage 326
8.3	Disintegration 288	9.2.2	Fermented Vegetables 329
8.3.1	Disintegration of Animal and Plant	9.2.3	Asian Fermentation Products 333
	Tissue 288	9.2.4	Raising Agents for Baked Products
8.3.2	Disintegration of Microorganisms		337
	289	9.2.5	Fermentation of Semiluxury
8.4	Enrichment 292		Consumer Goods 342
8.4.1	Concentration by Thermal	9.2.6	Cultivation of Edible Fungi 343
	Processes 292	9.3	Foodstuffs and Fodders of Animal
8.4.2	Extraction 293		Origin 346
8.4.3	Membrane Filtration 295	9.3.1	Milk and Dairy Products 346
8.4.4	Freeze-concentration 299	9.3.2	Meat and Sausage Products 371
8.4.5	Ion-exchange Processes and	9.4	Starter and Ripening Cultures 373
	Adsorption with Adsorber Resins	9.4.1	Definition 373
	299	9.4.2	Manufacture 373
8.4.6	Precipitation Reactions 302	9.5	Literature 376

10	Fermentation Processes - Ethanol, Wine, Beer 381	11.3 11.3.1 11.3.2	Products 440 Organic Acids 440 Amino Acids 449
10.1	Ethanol 382	11.3.3	Polysaccharides 449
10.1.1	General Observations 382	11.3.4	Vitamins and Provitamins 456
10.1.2	Importance of Alcohol 382	11.3.5	Alcohols and Solvents 459
10.1.3	Raw Material 382	11.3.6	Miscellaneous Products 464
10.1.4	Auxiliary Materials 383	11.4	Literature 468
10.1.5	Fermenting Organisms (Yeasts) 383		
10.1.6	Preparation of the Fermentation Substrate 384		
10.1.7	Formation of Ethanol 389	12	Enzymes 473
10.1.8	Recovery of Ethanol (Distillation)		-
10.1.0	395		
10.1.9	Utilization of Slops (Stillage) 397	12.1	Basic Concepts 474
	Potable Alcohol 398	12.2	Production of Enzymes 476
	Literature 401	12.2.1	-
10.2	Wine 404	12.2.2	Selection of Suitable Strains and
10.2.1	General Observations 404		Mutants of Microorganisms 467
10.2.2	Harvesting of the Grapes and	12.2.3	Nutrient Media 477
	Pressing 407	12.2.4	Fermentation 478
10.2.3	Fermentation 411	12.3	Isolation of Enzymes 480
10.2.4	Wine Finishing 417	12.3.1	Disintegration of Biological
10.2.5	Improvement Processes 419		Material 480
10.2.6	Literature 424	12.3.2	Precipitation Processes 481
10.3	Beer 425	12.3.3	Separation of Solids 483
10.3.1	Definition of the Term 425	12.3.4	Purification 486
10.3.2	Raw Materials 425	12.3.5	
	Preparation of the Malt 427	12.3.6	_
10.3.4	Preparation of the Beer 429	12.3.7	Drying 491
10.3.5	Literature 435	12.3.8	Storage and Transport 491
		12.4	Immobilization of Enzymes 492
		12.5 12.5.1	Industrial Enzymes 493 Proteases 493
11	Primary Metabolites 437	12.5.1	α-Amylases 499
**	1 Illiary Metabolites 437	12.5.2	Glucoamylase 500
11.1	Introduction 438	12.5.4	Pullulanase 501
11.2	Technical Processes 438	12.5.5	Glucose Isomerase 501
11.2.1	Surface Processes on Solid	12.5.6	Pectinases 504
	Substrates 438	12.5.7	Cellulases 504
11.2.2	Surface Processes on Liquid	12.5.8	β-Galactosidase 504
	Substrates 438	12.5.9	Other Enzymes 504
11.2.3	Submerged Processes, Anaerobic	12.6	Therapeutic Use of Enzymes 506
	438	12.7	Enzymatic Analysis 507
11.2.4	Submerged Processes, Aerobic 439	12.8	Literature 509

583

13	Antibiotics and Other	14.7.5	1,2-Dehydrogenation 583
	Secondary Metabolites 515	14.7.6	Ester Saponification and Oxidation
	•		of Hydroxy Groups 584
13.1	Introduction 516	14.7.7	Reduction of Keto Groups 584
13.2	β-Lactams 528	14.7.8	Sterol Side-Chain Degradation 585
13.2.1	Penicillins 528	14.7.9	Other Types of Reactions in
13.2.2	Cephalosporins and		Microbiological Transformations of
	7-Methoxycephalosporins 530		Steroids 586
13.2.3	New Basic β-Lactam Skeletons 533	14.8	Prostaglandins 586
13.3	Aminoglycosides 537	14.8.1	Imitation of the Biogenesis of
13.4	Tetracyclines 541		Prostaglandins 587
13.5	Macrolide Antibiotics 543	14.8.2	Chemical Synthesis with Supporting
13.6	Anthracycline Antibiotics 546		Microbiological Reaction Steps 587
13.7	Ansamycins 548	14.8.3	Microbial Transformations of Native
13.8	Literature 552		or Artificial Prostaglandins 590
		14.9	Miscellaneous Products 590
1.4	Distance for a strong FC2	14.10	Literature 594
14	Biotransformations 563		
14.1	Introduction 564	1.5	Dead satisfied of Milanchial
14.2	Methods 564	15	Production of Microbial
14.2.1	General 564		Biomass 601
14.2.2	Transformation Techniques 565		
14.3	Amino Acids 566	15.1	Definition and Review 602
14.3.1	Resolution of Racemates by	15.2	Raw Materials 604
	Enantioselective Hydrolysis 568	15.2.1	Basic Chemical Substances and
14.3.2	Formation of L-Amino Acids from		Intermediates 604
	Synthetic Precursors 571	15.2.2	Complex Organic Compounds 606
14.3.3	Degradative Biotransformations	15.2.3	Sources of Nitrogen 607
	572	15.2.4	
14.4	Vitamins 574	15.2.5	Energy Demand 608
14.5	Carotenoids and Related	15.3	Microorganisms 608
	Compounds 577	15.3.1	Methane-assimilating
14.6	Antibiotics 578		Microorganisms 608
14.6.1	Microbiological Transformations	15.3.2	Methanol-assimilating
	580		Microorganisms 610
14.6.2	Modified Biosynthesis of	15.3.3	Ethanol- and Acetate-assimilating
	Antibiotics 580		Microorganisms 610
14.6.3	Mutasynthesis 581	15.3.4	•
14.7	Steroids 581		Microorganisms 610
14.7.1	11-\alpha-Hydroxylation 582	15.3.5	Carbon-dioxide-assimilating
14.7.2	11-β-Hydroxylation 582		Microorganisms 610
14.7.3	16-α-Hydroxylation 583	15.4	Processes and Apparatus 611
1474	Hydroxylation of Other Positions	15.4.1	Preparation of the Raw Material

611

15.4.2	Fermentation 612	16.10	Biology of the Formation of
15.4.3	Processing 613		Methane 638
15.5	Process Examples 613	16.10.1	Hydrolytic and Acid-forming
15.5.1	Biomass from Methane 615		(Fermentative) Bacteria 639
15.5.2	Biomass from Methanol 615	16.10.2	Bacteria Forming Acetic Acid and
15.5.3	Biomass from Ethanol 616		Hydrogen (Acetogenic Bacteria)
15.5.4	Biomass from Normal Paraffins		639
	616	16.10.3	Methane-forming (Methanogenic)
15.5.5	Biomass from Carbohydrate-		Bacteria 641
	containing Raw Materials 616	16.11	Technical Processes 643
15.5.6	Biomass from Carbon Dioxide 617	16.11.1	Sludge Digestion 643
15.5.7	Biomass Products and Economic	16.11.2	Degradation of Wastewater Highly
	Aspects 618		Loaded with Organic Matter 645
15.6	Economic Aspects 620	16.12	Process Conditions 648
15.6.1	Variables Resulting from the	16.12.1	Composition of the Wastewater 649
	Process 620	16.12.2	Temperature 650
15.6.2	Product-specific Variables 621		pH 651
15.7	Literature 622		Biological Purification of Waste Air
			and Degradation of Solid Wastes
			653
16	Environmental Biotechnology	16.13	Processes for the Biological
10	•		Purification of Waste Air 653
	623	16.14	Processes for the Biological
	Purification of Wastewater by		Degradation of Solid Wastes 653
	Aerobic Processes 624	16.15	Literature 657
16.1	Historical Development 624		
16.2	Wastewater 624		
16.2.1	Communal Sewage 625		
16.2.2	Industrial Effluents 626	17	Microbial Leaching 661
16.2.3	Properties of the Substrate		8
	"Wastewater" 627		
16.3	Aims and Limitations of the Aerobic	17.1	Introduction 662
	Biological Processing of Wastewater	17.2	Microorganisms 662
	Purification 627	17.2.1	Thiobacilli 662
16.4	Trickling Filter Process 628	17.2.2	Thermophilic Microorganisms 663
16.5	Activated Sludge Process 631	17.3	Reaction Mechanisms 663
16.6	Lagoon Process 635	17.3.1	Direct Bacterial Leaching 663
16.7	Sewage Treatment Processes as	17.3.2	Indirect Bacterial Leaching 664
	Special Forms of Biotechnology	17.4	Modification of the Bacterial
	636		Activity 665
16.8	Column Wastewater Reactors 636	1 7.4.1	Nutrients 665
10.0		17.4.2	pH and Eh 666
	Purification of Effluents by	17.4.3	Temperature 666
	Anaerobic Processes 638	17.4.4	Chemistry and Mineralogy of the
16.9	General 638		Leaching Material 666

17.4.5	Grain Size and Concentration of the Substrate 667	Appendix
17.4.6	Surface-active Agents and Organic	
	Extractants 667	
17.4.7	Heavy Metals 667	
17.4.8	Light 668	
17.5	Microbial Leaching Processes 668	Appendix I
17.5.1	Laboratory Investigations 668	Journals, Periodicals, Reviews 700
17.5.2	Technical Leaching Processes 672	,
17.6	Technical Applications 675	
17.6.1	Leaching of Copper Ores 675	Appendix II
17.6.2		Biotechnological Abbreviations,
17.7	Future Aspects 678	-
17.8	Literature 680	Formulas, and Symbols 704
		A II.1 Fermentation Térms 704
10	Essentia Assesta of Formanta	A II.2 Biotechnological Formulas 706
18	Economic Aspects of Fermenta-	A II.3 Biochemical Compounds and
	tion Processes 685	Abbreviations 706
	- 4	A II.4 Genetic Engineering Terms 707
18.1	Introduction 686	A II.5 Selection of Antibiotics
18.2	Main Factors of Profitability 687	(Names and Formulas) 708
18.2.1	Energy 688	A II.6 Technical Terms at the Fermenter
	Fermentation Substrates 689	715
18.2.3		A II.7 Basic Physical Magnitudes 716
18.2.4		
18.2.5	Capital Costs 691	
18.3	Examples of Products 691 Manufacturing Costs for	Appendix III
18.3.1	Penicillin G 691	Laws, Guidelines, and Instructions
18.3.2	Manufacturing Costs for Penicillin	717
16.3.2	Amidase 693	/1/
18.3.3	Manufacturing Costs of Citric Acid	
10.5.5	694	Annondiv IV
18.3.4		Appendix IV
10.5.4	Alcohol 694	Basic Information for Working in
18.3.5	Manufacturing Costs of Bioprotein	Biotechnology 719
10.5.5	from Methanol 695	
18.4	Economic Data for Various	A IV.1 Selection of Culture Collections
10.7	Manufacturers and Product	719
	Capacities of Bioproducts 695	A IV.2 Substrates for Fermentations 719
	capacities of Erobrogado ove	A IV.3 Basic Operations of Fermentation
		and Recovery Techniques 724
		A IV.4 Flow Sheets of Typical
		Biotechnological Processes 735
		A IV.5 Types of Reactors 742

Biotechnological Apparatus 743

A V.2 Some Manufacturers of Important Products 746

Appendix VI **Products from Biotechnological** Processes 750

Subject Index