

Index

a

- accelerated growth phase 189
- acetate 371
- acetone–butanol–ethanol (ABE) fermentation 575
- acetyl-CoA 556
- acrylic acid 415
- Actinobacillus succinogenes* 507, 509, 510
- adsorption, of SA 536
- aeration 195
- affinity chromatography 149
- agitation 195
- air-lift
 - bioreactors (ALRs) 227
 - fermenter 12
 - reactors 9–11, 86
- alkaline-type anion exchange resin (NERCB04) 536
- amino acids 362
- glutamate 172, 173, 351, 352
- L-lysine 361
- amino sugars 373
- Anaerobiospirillum succiniciproducens* 510, 511, 513
- anti-cancer drugs
 - biosynthetic pathways 251, 261, 262
 - chemical synthesis 240
 - CPT quinoline alkaloids 258
 - elicitation 241
 - gene discovery 242
 - in microbial hosts 262
 - podophyllotoxin lignans 256
 - microbial system 241
 - plant in vitro cell and tissue culture 240
 - precursor feeding 241
 - taxane diterpenoids 250

Aspergillus

- *A. flavus* 530
- *A. niger* 530
- *A. terreus* 455
- arabinose 371
- automatic cell factory manipulation system (ACFM) 14

b

- Bacillus subtilis* 171, 475
- benzaldehyde 283
- β-Carotene 318
- bio-based chemicals 161
- bio-based plastics 393
- bio-based polyamide PA5.10 403
- biofuels 161
- BIOHOCH reactor 11
- bioinformatic techniques 249
- bioisoprene
 - challenges 489
 - enzymes 477
 - formation 475
 - scale up fermentation 487
 - metabolic pathways 477
 - novel substrates 494
- biological oxygen demand (BOD) 34
- biomass
 - deconstruction methods 563
 - lignocellulose 548, 563
 - – consolidated bioprocessing 167
 - – pretreatment and enzymatic hydrolysis 166
 - starch
 - – consolidated bioprocessing 164
 - – pretreatment and enzymatic hydrolysis 163
- bioreactor 13
 - air-lift bioreactors 227

- bioreactor (*contd.*)
 - anaerobic 86
 - bubble columns and air-lift reactors 86
 - cell immobilization 224
 - fluidized-bed bioreactors 226
 - fixed bed and fluidized bed 144
 - hollow fiber and membrane reactors 145
 - membrane 227
 - packed-bed bioreactor 226
 - process strategies and control 145
 - scale-down 56
 - single use 144
 - stirred tank 83
 - stirred-tank reactor 225
- bioreactor design
 - solid-state fermentation
 - - column/fixed bed fermenters 198
 - - criteria 198
 - - drum bioreactors 199
 - - shallow-tray fermenter 198
- bioreactor modeling
 - compartment models
 - - micro-macromixer model 90
 - - Monte Carlo simulation method 90
 - - two-phase multi-compartment model 89
 - - two-region mixing model 89
 - computational fluid dynamics models
 - - hybrid multizonal 91, 92
 - - unstructured continuum approach (Euler–Euler) 92
 - large-scale industrial fermentations
 - - bio-based product overview 83
 - - global status 81
 - - global trends 82
 - mathematical modeling 88
 - trial-and-error approach 87
- biosensors, L-lysine 377
- biosynthesis
 - L-lysine 363
 - putrescine 396
- biosynthetic pathway
 - anticancer drugs 251, 261, 262
 - camptothecin 260
 - paclitaxel 251
 - podophyllotoxin 257
 - terpenoid indole alkaloid (TIA) 245
- biotechnological production of flavors 275
- bioconversion processes 277
- *de novo* synthesis 276
- traditional fermentations 275
- bubble columns 86
- butanedioic acid, *see* succinic acid (SA)
- butanol fermentation
 - *Clostridium acetobutylicum* 578
- c**
- ¹³C-MFA 350, 351
- Corynebacterium glutamicum*
 - flexible feedstock 369
 - L-lysine biosynthesis in 364
- CadA protein 456
- cadaverine, diaminopentane (DAP) 399
- cambial meristematic cells (CMCs) 246, 251
- paclitaxel 252
- camptothecin (CPT) 258
- biosynthetic pathway 260
- chemical structures 259
- Candida boidinii* 522
- carbon flux 322, 323, 328
- carotenoids 317
- biosynthesis 319
- metabolic engineering 321
- microbial production 319
- cell culture technology
 - bioreactor
 - - fixed bed and fluidized bed 144
 - - for suspended cells 142
 - - hollow fiber and membrane reactors 145
 - - process strategies and control 145
 - - requirements 140
 - - single use 144
 - downstream process
 - - biopharmaceutical production 146, 147
 - - challenges 150
 - - harvesting and clarification 147, 148
 - - impurities 148, 149
 - - medium design 139
 - - physiology and kinetics 132
 - - population dynamics 134
 - - resolved modeling and data treatment 136
 - - resolved online monitoring and process control 138
 - - separation methods and analytics 135
 - - systematic investigation 134
 - products and tissue engineering application 129
 - regulatory and safety issues 150
 - sources 131
 - cell immobilization 207
 - applications 206, 218
 - - mammalian and insect cell 221
 - - microorganism 219
 - - plant cell culture 221
 - bioreactor 224
 - - air-lift bioreactors 227

- – fluidized-bed bioreactors 226
 - – membrane 227
 - – packed-bed bioreactor 226
 - – stirred-tank reactor 225
 - challenges and recommendations 228
 - support materials 207
 - techniques 207
 - with calcium alginate gel 211
 - cell recycle batch fermentation 175
 - cell surface engineering 165
 - cell-culture bioreactors 28
 - cellobiohydrolases (CBHs) 174
 - cellulose 371
 - isobutanol production from 586
 - cephalosporin C
 - continuous sterilization system 39
 - fermentation flow diagram 37
 - media and energy consumption for 38
 - operating temperature 36
 - production flow diagram 36
 - seed train and main fermentation for 38
 - chemically defined medium (CDM) 526
 - Clasen process 548
 - Clostridium acetobutylicum*
 - genetics tools 577
 - metabolic engineering 578
 - n-butanol biosynthesis 576
 - Clostridium thermocellum* 169
 - CMCs, *see* cambial meristematic cells (CMCs)
 - CoA-independent *dha* operon pathway 422
 - CoA-independent *pdu* operon pathway 425
 - compartment models
 - micro-macromixer model 90
 - Monte Carlo simulation method 90
 - two-phase multi-compartment model 89
 - two-region mixing model 89
 - computational fluid dynamics (CFD) 28, 62
 - gas stirred tanks
 - bubble size 105
 - gas fractions 104, 105
 - glucose uptake 110
 - oxygen uptake 111
 - hybrid multizonal 91
 - industrial practice 93
 - mesh partitioning 123
 - single phase
 - flow of water 93
 - mass balance 93
 - multi-impeller fermenter 97
 - stirred tank flow 96
 - turbulence modeling 95
 - structured segregated approach (Euler–Lagrange) 118
 - cell responses to, large bioreactors 118
 - dynamic tools and methods 114
 - mathematical models capturing 114, 115
 - metabolically structured model 117
 - two phase flow 100
 - Euler–Euler model 100
 - interaction forces 102
 - turbulence modeling 103
 - computational methods 555
 - computer-aided modeling approaches 310
 - confined impeller stirred tank (CIST) 63
 - consolidated bioprocessing (CBP) 482
 - biorefinery concept 163
 - lignocellulose 167
 - starch utilization 164
 - continuously stirred tank reactor (CSTR) 9
 - Corbion Purac 529
 - Corynebacterium efficiens* 352
 - Corynebacterium glutamicum* 171, 339, 352, 512, 514, 518
 - biosynthesis 345
 - electron microphotograph 343
 - future perspectives 354
 - peptidoglycan 344
 - CRISPR/Cas 9, 557
 - crystallization 535
- d**
- dedifferentiation-derived calluses (DDCs) 246, 251
 - paclitaxel 252
 - degradation pathways
 - 3-hydroxypropionic acid 415
 - de novo* synthesis, flavors 276
 - Deltaldh-pCRA717* strain 512
 - desaccelerated growth phase 189
 - diamine metabolism in bacteria 395
 - diaminobutane (DAB) 395
 - diaminopentane (DAP) 399
 - dicarboxylic acids 374
 - dissolved oxygen tension (DOT) 63
 - distillation technology
 - ethanol 547
 - docetaxel 250
 - downstream processes (DSP)
 - centrifugation 148
 - challenges 150
 - harvest and clarification 149
 - harvesting and clarification 147, 148
 - impurities 148, 149
 - drum bioreactors 199

- e**
- economically feasible process 174
 - electrodialysis
 - of succinic acid 534
 - engineering and design aspects
 - plant design
 - – automation and process control 21
 - – biosafety and containment constraints 21
 - – dedicated single product vs. multiproduct facility 20
 - – design constraints and guidelines 21
 - – GMP vs. non-GMP operation 21
 - – mixing and mass transfer 27
 - – oxygenation 32
 - – scale and mode of operation 20
 - – seed lines 24
 - – temperature control and heat transfer 31
 - – vessel geometry 26
 - process development 18
- Entrophospora infrequens* 259
- environmental heterogeneity
 - cell responses to 62
 - physiological effects of
 - – further observations 72
 - – negative effects 68
 - – positive effects 71
- Escherichia coli* 170, 322, 515, 519, 520, 525
 - biological processes 62
 - 3-hydroxypropionic acid 431, 434
 - isobutanol tolerance 588
- ethanol
 - biomass deconstruction methods 563
 - distillation technology 547
 - evolutionary strain improvement 557
 - genetic manipulation 556
 - genome-Wide Evolution 557
 - fermentation 530
 - humanity's relationship with 547
 - membrane engineering 555
 - metabolic burdens during 562
 - metabolic pathway engineering 550, 553
 - production 547
 - reverse engineering of improved strains 561
 - screening of expression libraries 559
- etoposide 256
- eugenol, vanillin flavors 278
- Euler–Euler (E–E) model 100
- Euler–Lagrange (E–L) model
 - cell responses, large bioreactors 118
 - dynamic tools and methods 114
- mathematical models capturing 114, 115
- metabolically structured model 117
- extracapillary space (ECS) 227
- f**
- farnesyl pyrophosphate (FPP) 322
- fatty acid biosynthesis 343
- fermentation
 - ABE 575
 - historic overview 4
 - vitamin C 311–314, 316
- ferulic acid, vanillin flavors 280
- flavor and fragrance 271, 272
- flavors
 - benzaldehyde 283
 - biotechnological production 275
 - green note compounds 291
 - lactones 285
 - molecule 273
 - Nootkatone 293
 - 2-phenylethanol 281
 - production 274
 - raspberry ketone 289
 - Regulation (EC) 273
 - vanillin 277
- fluidized bed bioreactors (FBRs) 226
- flux scanning based on enforced objective flux (FSEOF) 319
- Fourier transform ion cyclotron resonance mass spectrometry (FTICR-MS) 261
- g**
- gas chromatography (GC) 261
- gas stirred tanks
 - bubble size 105
 - gas fractions 104, 105
 - glucose uptake 110
 - oxygen uptake 111
- genetic manipulation
 - ethanol 556
- genome stream-lined *Corynebacterium glutamicum* strains 375
- geraniol-10-hydroxylase (G10H) 259
- geranylgeranyl pyrophosphate (GGPP) 322
- global transcription machinery engineering (gTME) 560
- glutamic acid fermentation 339, 352
 - anaplerotic reactions 348
 - biosynthesis 345
 - cell surface structure 343
 - discovery 340
 - future perspectives 354
 - industrial production process 353

- metabolic engineering 350
- 2-oxoglutarate dehydrogenase 346, 347
- gluconic acid production 61
- Gluconobacter oxydans* 311
- glycerol 374, 510, 527
- glyoxylate shunt 521, 532
- GMP production 23
- green note compounds, flavors 291

- h***
- harvested cell culture fluid (HCCF) 147
- high-performance liquid chromatography (HPLC) 261
- high-throughput sequencing technologies 315
- hollow fiber and membrane reactors 145
- hybrid multizonal models 91
- hydroxymethylglutaryl-CoA (HMG-CoA) 481
- 3-hydroxypropionic acid 413
 - CO₂ fixation 413
 - CoA-independent dha operon pathway 422
 - CoA-independent pdu operon pathway 425
 - degradation pathways 415
 - *Escherichia coli* 431, 434
 - from glucose 417, 419, 437
 - from glycerol 421, 423, 437, 438, 440
 - hybrid process 444
 - industrial applications 412
 - *Klebsiella pneumoniae* 426, 434
 - limitations 440
 - production 414, 416
 - redirecting flux 426

- i***
- immobilization 141, *see also* cell immobilization
 - insect cells 223
 - mammalian 223
 - microorganisms 220
 - plant cell 222
- industrial-scale fermentation
 - basic operating modes 8
 - cephalosporin C production 36
 - contemporary
 - airlift reactor 9
 - bioreactor design 8, 9
 - CSTR 9, 11
 - cultivation of hairy plant roots 13
 - large-scale design and operating criteria 11
 - -- simple batch culture 7
 - cost analysis 42
 - economic aspects of, market perspective 14
 - economic drivers for 15
 - engineering and design aspects
 - plant design 20
 - -- process development 18
 - influence of process-and facility-related aspects, on cost structure 47–48
 - investment 43
 - monoclonal antibody production 39
 - non-sterile fermentations 42
 - operational cost, cost of manufacture 46
 - organisms used 5
 - return on invested capital 48
- interconnected stirred tank reactors (STR-STR) 64
- ion exchange chromatography 149
- irinotecan
 - chemical structures 259
- isobutanol production 583
 - biochemistry 583
 - cellulose 586
 - CO\$_2\$ 586
 - *Escherichia coli* 588
 - keto-acid pathway 581, 588
 - sugar 584
 - waste protein 587
- isoeugenol, vanillin flavors 278
- isopentenyl pyrophosphate (IPP) 319
- isoprene 475
 - biosynthetic process 482, 497
 - chassis strains 485
 - derivatives 497
 - future prospects 491
 - historical development of 476
 - hosts for 495
 - microbial production 477
 - MVA/MEP pathways 480
 - production 476
 - substrate 481
 - value-added 497
- itaconic acid
 - *Aspergillus terreus* 455
 - chemical structure of 454
 - economy 453
 - history 453
 - metabolic engineering for 462
 - metabolism of 461
 - outlook 467
 - physiological effects 461
 - production conditions 459
 - *Ustilago maydis* 459

- k**
- keto-acid pathway 581, 588
 - Ketogulonigenium vulgare* 312, 313
 - KJ134 strain 524
 - Klebsiella pneumoniae*
 - 3-hydroxypropionic acid 426, 434
- I**
- lactic acid 373
 - lactic acid bacteria (LAB) 173
 - lactones 285
 - lag phase 189
 - large-scale fermentation
 - contemporary
 - - airlift reactor 9
 - - bioreactor design 8
 - - CSTR 9, 11
 - - cultivation of hairy plant roots 13
 - - simple batch culture 7
 - economic aspects of, market perspective 14
 - economic drivers for 15
 - industrial
 - - bio-based product overview 83
 - - global status 81
 - - global trends 82
 - organisms 5
 - large-scale reactors 10
 - L-ascorbic acid (L-AA) 310
 - biosynthesis reconstruction 316
 - fermentation process 311–314, 316
 - production 311
 - levoglucosan 373
 - L-gulono-1,4-lactone oxidase (GUL oxidase) 316
 - lignin, vanillin flavors 281
 - lignocellulose
 - ethanol production process 162
 - hydrolysis of cellulose 167
 - pretreatment and enzymatic hydrolysis 166
 - production of chemicals
 - - native cellulase-producing microbes 168
 - - recombinant cellulose-utilizing microbes 169
 - lignocellulosic biomass 371, 548, 563
 - L-lysine
 - amino acids 361
 - biosynthesis 363, 364
 - *Corynebacterium glutamicum* 369
 - economic importance 362
 - industrial processes 368
 - production 362
 - riboswitches 379
 - strain development 363, 378
 - transcriptional regulators 377
 - logarithmic or exponential growth phase 189
 - lycopene 318, 319, 321–323
- m**
- malonyl-CoA 413, 415, 417, 420, 421
 - Mannheimia succiniciproducens* 526, 531
 - mass spectrometry (MS) 261
 - MEP pathway 492, 494
 - isoprene 480
 - metabolic engineering
 - carotenoids 321
 - *Corynebacterium glutamicum* 350
 - ethanol 550, 555
 - glutamic acid fermentation 350
 - itaconic acid 462
 - putrescine 398
 - resveratrol 326
 - metabolic flux analysis (MFA) 350
 - metabolically structured model 117
 - micro-macromixer model 90
 - microbial hosts for anticancer drugs 262
 - microbial production, isoprene 477
 - microbial vitamin production facility 23
 - Micrococcus glutamicus* 339
 - microorganism growth rate
 - biomass measurement 192
 - definition 189
 - growth phases 189
 - molasses 370
 - monosodium glutamate (MSG) 339, 340
 - Monte Carlo simulation method 90
 - multi-compartment scale-down systems 64
 - multi-Scalar Analysis of Library Enrichments (SCALES) method 560
 - MVA pathway 493, 494
 - isoprene 480
 - mycolic acid 344
- n**
- NADPH
 - L-lysine 366
 - n-butanol
 - biosynthesis 576, 580
 - with driving forces 582
 - non-native producers 580
 - production 574
 - negative effects
 - nematicide 417
 - negative growth phase 189
 - Nippon Zeon 476
 - non-oxidative cyclic (NOG) pathway 491
 - Nootkatone, flavors 293

- Nothobranchiusfurzeri* 326
 nuclear magnetic resonance (NMR) 261
 nutraceuticals 309
 – carotenoids 317
 – future perspectives 328
 – resveratrol 323
 – vitamin C 310
- o**
 one-compartment scale-down systems
 (OCSDS) 63
 operational expenditure (OPEX) 46
 Oral sun protectants 318
 organic acids 369
 2-oxoglutarate dehydrogenase complex
 (ODHC) 346–349
 – enzymatic activity 347
 oxygenation 32
- p**
 packed-bed bioreactors (PBR) 226
 paclitaxel 250
 – biosynthetic pathway 251
Pantoea agglomerans 322
 pantothenate kinase (PANK) gene 519
 penicillin 343, 344, 347, 348
 pentose phosphate pathway (PPP) 176
 PEP carboxykinase (PEPCK) genes 516,
 517
 PEP carboxylation 507
 petroleum-isoprene 477
 2-phenylethanol 281
 phosphoenolpyruvate carboxylase (PPC)
 348
 physiological effects of 68
 – on animal cells 70
Pichia pastoris 32
 plant cell immobilization 222
 plant design
 – mixing and mass transfer 27
 – oxygenation 32
 – seed lines 24
 – temperature control and heat transfer 31
 – vessel geometry 25
 plant design, fermentation
 – automation and process control 21
 – biosafety and containment constraints 21
 – dedicated single product vs. multiproduct
 facility 20
 – design constraints and guidelines 21
 – GMP vs. non-GMP operation 20–21
 – scale and mode of operation 20
 plug-flow reactor connected to a stirred tank
 reactor (STR-PFR) 65
 podophyllotoxin (PTOX) 256
 – biosynthetic pathway 257
 – chemical structures 256
 poly(butylene succinate) (PBS) 505
 polyphenols 323
 precipitation
 – of succinic acid 533
 putrescine, diaminobutane (DAB) 395
 – biosynthesis and pathway regulation 396
 – metabolic engineering 398
 – metabolism 396
 pyrimidines 415
 pyrroloquinoline quinone (PQQ) 315
 pyruvate carboxylase (pycA) 521
 pyruvate dehydrogenase (PDH) 559
 pyruvate formate lyase (PFL) 552
- r**
 raspberry ketone 289
 reactive extraction
 – of succinic acid 535
 recombinant glycoproteins 130
 resveratrol 323
 – biosynthesis 324
 – metabolic engineering 326
 resveratrol O-methyltransferase (ROMT)
 324
 riboswitches 379
 Rushton impeller 28, 29
- s**
Saccharomyces cerevisiae 174, 530, 533
 – shuttle vectors 556
 scale-down process
 – analytical techniques
 – differential gene expression and protein
 accumulation 67
 – mathematical modeling 68
 – metabolic studies 66
 – physical measurements 67
 – bioreactor 56
 – characteristic time 59, 60
 – – design and cell engineering 72
 – – mathematical models 58
 – – oxygen consumption time 60
 – – regime analysis 59, 62
 – – environmental heterogeneity
 – – cell responses to 62
 – – physiological effects of 68
 – – heterogeneity, large scale 56
 – – multi-compartment system 64
 – one-compartment scale-down system 63
 – physical conditions 55
 – simulators 63

- scale-up process, solid-state fermentation
 - aeration and agitation 196
 - heat removal and moisture balance 197
 - laboratory process 196
 - large scale inoculum development 196
 - medium sterilization 196
 - pH control 197
 - shallow-tray fermenter 198
 - shuttle vectors 556
 - simultaneous saccharification and fermentation (SSF) 167
 - single-use bioreactors 144
 - solid-state fermentation (SSF) 187–189
 - applications 201
 - bioreactor design
 - column /fixed bed fermenters 198
 - criteria 198
 - drum bioreactors 199
 - shallow-tray fermenter 198
 - challenges 202
 - definition 187
 - factors affecting 192
 - aeration and agitation 195
 - inoculum type 194
 - moisture 193
 - pH 194
 - temperature 193
 - water activity 193
 - food industry 187
 - fundamental aspect
 - microorganism growth rate 189
 - selection of microorganism 188
 - product recovery 197
 - scale-up process
 - aeration and agitation 196
 - heat removal and moisture balance 197
 - laboratory process 196
 - large scale inoculum development 196
 - medium sterilization 196
 - pH control 197
 - schematic representation 188
 - SSF, *see* simultaneous saccharification and fermentation (SSF); solid-state fermentation (SSF)
 - standard design parameters 26
 - starch 370
 - consolidated bioprocessing 164
 - ethanol production process 162
 - pretreatment and enzymatic hydrolysis 163
 - stationary growth phase 189
 - stirred tank bioreactor (STR) 225
 - fermentations 84
 - fundamental aspect 84, 85
 - Rushton Turbine impellers 84
 - size 83
 - study 84
 - silage juice 373
 - succinic acid (SA) 505, 545
 - *Actinobacillus succinogenes* 507, 509, 510
 - adsorption 536
 - advantage and disadvantage 508
 - *Anaerobiospirillum succiniciproducens* 510, 511, 513
 - *Corynebacterium glutamicum* 512, 514, 518
 - dual phase fermentation 507
 - electrodialysis 534
 - *Escherichia coli* 515, 519, 520, 525
 - *Mannheimia succiniciproducens* 526, 531
 - *Saccharomyces cerevisiae* 530, 532, 533
 - microbial production of 505
 - precipitation-based recovery 533, 534
 - producers and fermentation strategies 506
 - reactive extraction 535
 - recovery of 534, 535
 - thermal polycondensation 505
 - sucrose 370
 - sugar
 - isobutanol production from 584
 - Sumerian barley 548
 - suspension cell cultures 246, 251
 - Swarm influences 103
- t**
- taxane diterpenoids 250, 262
 - teniposide 256
 - terpenes/terpenoids, flavors 293
 - terpenoid indole alkaloids (TIA) 243, 245
 - pathway 247, 249, 250
 - topotecan, chemical structures 259
 - tricarboxylic acid (TCA) cycle 505
 - Trichosporon cutaneum* 11
 - two-compartment scale-down systems (TCSDS) 64
- u**
- Ustilago maydis* 459
- v**
- vacuum distillation 535
 - vanillin flavors 277
 - eugenol 278
 - ferulic acid 280

– isoeugenol 278
– lignin 281
vinblastine 243, 244
vinca alkaloids 243
vincristine 243, 244
vindesine 243
vinorelbine 243
vitamin C 310
– biosynthesis reconstruction 316
– fermentation process 311–314, 316
– production 311

W

waste protein
– isobutanol production from 587
water activity 193

X

xylitol dehydrogenase (XDH) 175
xylose reductase (XR) 175
xylose 371
xylulokinase activity 555

