Index

a

accelerating phase 48
acoustic wave separation 270
active transport 13
acute respiratory failure (ARF) 246
adsorption 159
adsorption equilibrium 159
adsorption isotherms 160
aerated stirred tank 114
aerobic fermentation 7, 195
affinity chromatography (AFC) 167, 174–175, 233, 235, 271
agitation 210
airlift reactors 119
alternating tangential flow (ATF) 268, 269
anchorage-dependent tissue cells 203
angiotensin-I converting enzyme (ACE) 43
animal cell culture 203
antibodies 175
antifoam agents 190
antigen recognition 175
area per transfer unit (ATU) 251
arithmetic mean 61
Arrhenius equation 29
arteries 241
artificial intelligence (AI) 221–222, 268, 277
artificial kidney 255
artificial lung 242
artificial neural network (ANN) 222
axial flow impeller 108

b

batch culture, growth phases in 47–49
batch fermentors 51–52, 197
batch operation 7–8
batch reactor 30, 94–96, 100, 113, 121
batchwise heat sterilization 150–151
β-galactosidase 42
bile 262
bioartificial liver devices 262
biochemical reactors 94
biochemical variables 212
biopharmaceutical production process 267
  CHO-based monoclonal antibody production 267–270
  downstream processing 270–273
  innovations 277–278
  quality control 275–277
  virus clearance 273–275
bioprocess control 213
bioprocesses 27, 127, 139, 207
bioprocess instrumentation, process variables 208–213
bioprocess plants 3
bioreactions 27
bioreactor cultivation 268–270
bioreactors 27, 71
  airlift reactors 119–121
  bubble columns 115–119
  bubbling gas–liquid reactors 102–106
  definition 93
  fundamental concepts 94–102

bioreactors (*contd.*)
gas dispersion in stirred tanks 114–115
mechanically stirred tanks 106–114
microreactors 122–123
packed-bed reactors 121
types 93
biosensors 212
blood dialyzers 129
blood oxygenator 242, 245–247, 253
break point 165, 166
Briggs–Haldane approach 36
bubble caps 76
bubble column 77, 115–119
bubble column fermentor 183
bubble point 156
bubble size distribution 117
bubbling gas–liquid reactors 118
bubbling-type fermentors 190
buffer layer 20

c

carbon dioxide desorption 193–195
carboxymethyl cellulose (CMC) 17, 251
cell disruption 145
cell growth 45–47
factors affecting 49–50
cell kinetics 45
batch culture, growth phases in 47–49
batch fermentors 51–52
cell growth 45–47
cell growth, factors affecting 49–50
continuous stirred-tank fermentor 52, 53
cell line development 268
cell yields, of several microorganisms 47
centrifugation 142
chemical engineering 3, 4, 13
chemical equilibrium 6, 7
chemical method 103
chemical reaction, rates of 27
chemical variables 211
chemostat 52, 202
CHO-based monoclonal antibody production 267
bioreactor cultivation and continuous processing 268–270
cell line development and genetic engineering 268
chromatography 159, 167, 271, 272, 274, 277
scale-up 234
separation by 167–175, 231–235
cleaning-in-place (CIP) 271
clearance 255, 258
closed-loop system with feedback 214
clotting 240
column diameter 233
competitive inhibition 38–40
complements 240
consistency index 17, 186
constant pattern of adsorption zone 165
continuous ambulatory peritoneal dialysis (CAPD) 257
continuous heat sterilization 151–154
continuous ion exchange chromatography (cIEX) 272
continuous operation 7–8
continuous processing 268–270
continuous stirred-tank fermentor (CSTF) 52, 53, 201–202
continuous stirred-tank reactor (CSTR) 94, 95
conventional filtration 139
CO_2/O_2 212
coronary arteries 242
corrosion-resistant materials 75
critical quality attributes (CQAs) 267
cross-flow filtration (CFF) 141, 230–231
C_A/r_p versus C_A plot 36–37

d

dead-end filtration 228
Deborah number 193
decelerating phase 48
declining phase 48
deep shaft reactor 119
dialysance 259
dialysis 127–129
differentiation method 30

diffusion coefficient 14
diffusivity 14
dilution rate 95
dimensional analysis 5
dimensional equations 5
dimensionless equations 5
dimensionless numbers 5
dimensions 4
direct-binding method 177
disk-stack centrifuge 143
dissolved oxygen (DO) 105, 125, 193, 207, 211, 223
  control 219–220
  stat 221
doubling time 46
downflow fixed-bed adsorber 163
downstream processing (DSP) 139, 225, 270
  polishing process and final purification 272–273
  protein A chromatography 271–272
driving forces 13
dynamic method 105

e

Eadie–Hofstee plot 37–38
elasticity 17
elastic modulus 17
electrolytes 189
elementary reaction 28
elution curve 171
emulsions 191
encapsulation 263
energy balance 9–11
engineering 3–5
  branch of 4
  calculations 4
enhancement 80
enhancement factor 80, 81, 89, 103, 105, 190, 248, 249, 252
enzyme-linked immunosorbent assay methods (ELISA) 176–178
enzyme reactors 202–203
equilibria 6
equilibrium 6, 28
  model 168
erythrocytes 239
expert system 222
exponential growth phase 48
extensive properties 6
external loop (EL) airlift reactor 120–121
extracorporeal membrane oxygenation (ECMO) 247

f

fed-batch culture 268
fed-batch fermentors 198–199
fermentation broths 17, 190
fermentation media 46
fermentor 183
fibrinogen 240
Fick's law 14
film coefficient estimation 62
  forced flow of fluids across tube bank 64
  forced flow of fluids through tubes 62–64
  jacketed or coiled vessels, liquids in 64–65
film coefficients 57–60
  correlations for 81
    packed beds, single-phase mass transfer 83
    single-phase mass transfer inside or outside tubes 81–82
  of heat and mass transfer 22–24
  mass transfer 71–75
filtration 139
filtration flux 140
first-order reactions, rate equations for 30–33
fixed-bed adsorber 163
fixed-bed separation 235
flat membranes 135
flat plates 263
flooding 84, 115
flow behavior index 17
fluid flow 15–17
foaming 210

forced flow of fluids
  across tube bank 64
  through tubes 62–64
fouling factor 66, 67
fouling resistance 66
Fourier's law 14
Freundlich-type empirical isotherm 160
Fuzzy control 222

g

gas absorption calculations 74
gas and liquid velocities, mass transfer 84
gas flow rate 211
gas–gas heat exchanger 66
gas holdup 102, 116
gas–liquid mass transfer 189
gas-side mass transfer coefficient 77
gas-sparged liquids 110
gas-sparged stirred tanks 111–112
gas volume per volume of liquid per minute (VVM) 196
gel chromatography 167, 172–173
genetic engineering 268
gene transfection 268
glass fermentors 183
glomerular filtration rate (GFR) 254–255
gravity settler 143
growth curve 47

h

Hagen–Poiseuille equation 19
half-life 32
Hatta number 81
Hatta theory 80
heart–lung machine 242
heat conduction 13–14
heat exchanger 57
heat/thermal conductivity 14
heat transfer 57, 186–187
  condensing vapors and boiling liquids 65
  film coefficient estimation 62–64
  jacketed or coiled vessels, liquids in 65
  mean temperature difference 60–62
  overall coefficient estimation 66–68
  overall coefficients and film coefficients 57–60
heat transmission 57
height equivalent to the theoretical plate (HETP) 170
hemodialyzers 256–258
hemofiltration (HF) 257
hemoglobin 243
hemolysis 240
Henderson–Hasselbalch equation 245
Henry's constant 75
Henry's law constant 6
heparin 240
hepatic lobules 262
hepatocytes 262
high-throughput clone screening 268
hollow fiber 81, 263
hollow-fiber (capillary)-type membrane oxygenators 246
hollow-fiber membranes 135
host cell proteins (HCPs) 271, 272
HTUs 85–87
human kidney 253
human liver 261
hydrolysis 43

i

immobilized enzymes 100
immunological assays 175
inclusion bodies 145
industrial fermentors 184
inhibitor constant 39
integration method 30
intensive properties 6
interfacial area 102, 117
internal loop (IL) airlift reactor 119
International System of Units (SI) 4
intracorporeal oxygenators 247
irreversible first-order reaction 30
irreversible second-order reaction 33
isocratic elution 167

j

jacketed or coiled vessels, liquids in 64–65
J-factor 83–84
joule (J) 5

k

kinetic energy (KE) 9
Kozeny–Carman equation 141

l

lag phase 47
laminar blood flow 247
laminar film 20
laminar flow 15, 17–20
laminar sublayer 20
Langmuir-type isotherm 160
leukocytes 240
light transmission technique 103
Lineweaver–Burk plot 36
  of hydrolysis reaction 41
liquid boiling 65
liquid chromatography 231
liquid column chromatography 159, 167, 169
liquid flow rate 211
liquid–liquid heat exchanger 66
liquid–liquid mass transfer 74
liquid mixing 113
liquid phase mass transfer with chemical reactions 79–81

m

macrophages 240
mass transfer
  correlations for film coefficients 81–84
  equipment, types of 75–77
  liquid phase mass transfer with chemical reactions 79–81
  overall coefficients and film coefficients 71–74
  packed column performance 84–91
  penetration model 78
  stagnant film model 78
  surface renewal model 79
mass transfer coefficient 103
mass transport 13
material (mass) balance 8
mean temperature difference 60–62
membrane-based nanofiltration 274
membrane filters 154
membrane modules 135
membrane separation processes 78
membrane-type oxygenators 253
metabolic engineering 268
Michaelis constant 39
Michaelis–Menten approach 34–37
microfiltration (MF) 127, 132, 133, 141
microreactors 122–123
mixing time 113
mobile phase, velocity of 232
molecular diffusion 14
molecular viscosity 15
momentum transfer 15
monoclonal antibodies 273
Monod equation 49, 51, 199, 201, 221
multi-attribute methods (MAM) 276, 277
multicolumn countercurrent solvent gradient purification (MCSGP) 272
multistage adsorption 162

n

nanofiltration (NF) 128
Newtonian fluid 16, 19
noncompetitive inhibition 40
non-Newtonian fluids 16
non-Newtonian liquids 185, 192, 193
number of transfer units (NTU) 86, 87, 251, 259
Nusselt number 62

o

On–off (two-positioned) controller 215–216
overall coefficient estimation 66–68
overall coefficients 57–60
  mass transfer 71–74

oxidation-reduction potential (ORP) 211
oxygenation 242
oxygen transfer rate (OTR) 211, 247–252, 270
oxyhemoglobin dissociation curve 243

p

packed bed 263
  single-phase mass transfer 83
packed bed reactor 121
packed column 75–76, 84
  gas and liquid velocities 84
  rates and effective interfacial areas 87–91
  volumetric coefficients and HTUs 85–87
packed-(fixed-) bed column 77
packed particles, radius of 232
passive transport 13
penetration model 78
periodic countercurrent chromatography (PCC) 272
peritoneal dialysis 257
permeation 127
pH 211
pH and temperature control 218
photographic method 103
photosynthetic microalga 53
pH stat control 220
physical equilibria 7
physical transfer processes
  film coefficients of heat and mass transfer 22–24
  fluid flow and momentum transfer 15–17
  heat conduction and molecular diffusion 13–14
  laminar versus turbulent flow 17–20
  turbulent flow, transfer phenomena in 20–22
physical variables 209
plasma 239
plate column 76
plate filter 140
plug flow reactor (PFR) 94, 96, 97
polishing process 272–273
potential energy (PE) 9
power consumption 210
Prandtl number 62, 83
pressure 210
process analytical technology (PAT) 270, 277
product consistency 276
product quality system (PQS) 275
proportional-integral-derivative (PID) control 216–218
protein A affinity chromatography 271–272

q

Quality by Design (QbD) 267, 275
  framework 267, 268
quality control (QC) 275–276
  product consistency and safety 276
  tests in 276–277

r

rate model 171
rate of chemical or physical process 7
rates 6
rates of adsorption 161
rates of chemical reaction 27–28
  elementary reaction and equilibrium 28
  first- and second-order reactions, rate equations for 30–34
  temperature dependence of reaction rate constant 29
rates of enzyme reactions 33–34
  evaluation 36–38
  inhibition and regulation 38–44
  kinetics 34–37
reaction kinetics
  rates of chemical reaction 27–34
  rates of enzyme reactions 33–44
real-time release testing (RTRT) 277
residence time distribution (RTD) modeling 270

respiratory quotient (RQ) 220
reverse osmosis (RO) 128, 133–134
Reynolds number 5, 17, 20, 62, 83, 108–110, 113, 114, 143, 152, 154, 171, 185, 242, 260, 261
rotary drum filter 140
Rushton turbine 107, 110, 113–115

s

sample volume injected 233
sandwich method 178
sanitation 237
scaling-up fermentors 195–196
second-order reactions, rate equations for 30–33
sedimenter 143
semi-batch reactor 94
serum 240
set-point control 214
shear rate 15
shear stress 15
single-phase mass transfer
  inside or outside tubes 81–82
  in packed beds 83
single-stage adsorption 162
sinusoids 262
SI system 4
solutes, diffusivities of 232
specific growth rate 46, 270
spiral membranes 135
spleen 241
spray column 77
stage model 170
stagnant film model 78
stationary phase 48
steady-state mass balance method 104
sterilization 149
sterilizing filtration 154–157
stirred tank fermentor 183
stirred-tank reactors 114
stirred tanks 107
stirrer power requirements 185
Stokes 16
streamline flow 15
subcutaneous arteriovenous shunt 256
substrate analogs 38
substrates 34
sulfite oxidation method 104, 189
surface diffusion 162
surface renewal model 79
surfactants 190
suspension 263

t

tangential flow filtration (TFF) 270, 273
temperature 209
temperature dependence of reaction rate constant 29
thermal cell death, kinetics of 149–150
Thiele modulus 99
tissue engineering 263
transport phenomena 13
trypsin 41
tubing sensor method 212
tubular centrifuge 142
tubular membranes 135
turbidity 210
turbidostat 52, 202
turbulent blood flow 248
turbulent core 20
turbulent flow 17–20
  transfer phenomena in 20–22

u

ultrafiltration (UF) 127, 129–132, 139, 142, 173
ultrasonication 145
ungassed liquids 108
uniformly mixed batch reactor 95
units 4
unsteady-state mass balance method 104

v

van't Hoff equation 133
vapor condensation 65
veins 241

viral safety assurance, in biopharmaceuticals 274
virus clearance 273
  regulatory and validation requirements 275
  viral inactivation and 273–274
viscoelastic fluids 17
viscosity 210
viscous flow 15
volatile matters 212
volume–surface mean bubble diameter 103
volumetric coefficients 85–87

y

yield stress 16