

## Index

Page numbers in italics refer to figures. Page numbers in bold denotes entries in tables.

- absorbing boundary conditions 148, 184, 198, 208, 213, 406
- accommodation 449
- acetylcholine 118, 119, 205
  - binding 120, 192
  - charges 34, 34
- acetylcholine receptor 34, 132, 133, 133, 192, 234, 241, 362, 374
- channel structural parameters and conductances **371**
- ligand association rate **204**
- acetylcholinesterase 34, 205–206, 206
  - ligand association rate **204**
- acid-base catalysis 268–270
  - $\beta$ -galactosidase 270–271, 271
  - general-acid catalysts 269, 270, 271
  - general-base catalysts 269, 269
- acidic phosphate groups in nucleic acids 53, 302
- action potentials 434
  - axon geometry and conduction 455–457, 456
- channel diversity 457–458
- current–voltage curves and thresholds 447–450, 448
- definition 434–439, 435, 437, 438
- dendritic integration 466–468, 467
- Hodgkin–Huxley equations 442–446, 444, 447
- myelin 453, 453–455
- oscillations 461–466
- propagation 450–453, 452
- repetitive activity and the A-current 458–461, 459, 460
- voltage clamp 439, 439–441, 440
- activation energies 169–170, 264, 274
- activation of ion channels 442
- active transport across membranes 351–352, 386
- activity coefficient for ions 279, 279–283, 353
  - definition 280
  - infinite dilution 281, 281
- A-current 458–461, 459, 460, 468
- additivity 128, 129
- adenine–thymine base pairs, hydrogen bonding 52
- ADP 130
- alanine (ala) 8, 38, 81, 85, 119
- helix continuation parameter **81**
- alcohols 48
- alkaline phosphatase 211
- allosteric enzymes 130–132, 257–258
- allosteric interactions 111
  - allosteric transition 112
  - binding and response 115–116
  - binding site interactions 121, 121–122
- energy balance in one-site model 116–117, 117
- G-protein coupled receptors 117–121, 120
- hemoglobin 126, 126–127
- ligand-gated channels 132–133, 133
- macroscopic and microscopic additivity 128–130
- Monod–Wyman–Changeux (MWC) model 123–126
  - energetics 127, 127–128, 128
  - enzymes 257
- one binding site and one allosteric interaction 112–115, 113
- phosphofructokinase 130–132, 131, 132
- subunit–subunit interactions 134, 134–136
- Szabo–Karplus (SK) model 137–140, 139
- $\alpha$ -helices 49, 73, 85
  - capping 81
  - mathematical analysis 74
  - proteins 49, 49, 50
  - stability 73
- amino acids
  - helix continuation parameters **81**
  - side chains 268
- Anisidoris* snail 459, 461
- arginine 17, 18, 119, 283
- arginine (arg), helix continuation parameter **81**
- Arrhenius equation 169
- Arrhenius plot 170
- asparagine (asn), helix continuation parameter **81**
- aspartate 8, 42, 119, 206, 272
- aspartic acid (asp), helix continuation parameter **81**
- ATP 130
- axial resistivity 401
- axons
  - geometry and conduction 455–457, 456
  - reflections 457
  - speed and size 452
  - supernormal 449
  - varicosities 456, 456, 457
- bacteriorhodopsin 208
- barnacle muscle fibers 462, 464
- barnase 86, 189, 189, 190, 192
- $\beta$ -sheets in proteins 49, 68–71, 70, 189
- binding energy in enzymes 258–259
- binomial distribution 154, 156, 243, 309, 320
- binomial expansion 124, 138, 155, 471
- Bohr effect 127, 140
- Boltzmann constant 4
- Boltzmann distribution 2, 4, 5, 17, 56, 161, 182, 260, 277, 288, 307, 313, 362, 378
  - activation energies 169
  - reaction coordinate 179
- Boltzmann equation 17, 22, 293, 443, 462
- Boltzmann weight 2, 32, 57, 74, 96
- bond vibrations 3
  - frequency 44
  - kinetic energy 3
  - normal modes 46, 102, 103
- Born energy 28
- Briggs–Haldane mechanism 254
- Brønsted equation 174, 270
- Brønsted slopes 268–270
- Brownian motion 142, 283, 336
- buffers 269, 269
- burst analysis 232, 232
- n-butane 56–58, 57
- cable equation 403, 403–406, 454
- cable length constant ( $\lambda$ ) 405
- cable theory 400
  - analysis of neurons 418, 418–422, 420, 421
- branches and equivalent cylinder representation 412–413, 413
  - steady-state 413–415, 415
  - time constants 415–418

- cable parameters **406**
- compartmental models **428**, 428–431, 450, 467
- current steps in a finite cable **411–412**
- current through membranes and cytoplasm **401**, 401–403
- steady-state in a finite cable **406–407**, 408
- synaptic integration in dendrites
  - analytical models **422–423**, 423
  - compartmental models **430–433**, 431, 432
  - impulse responses **423–425**, 424
  - realistic synaptic inputs **425–428**, 427
- calcium chloride, activity coefficient **281**, 281
- calcium ion channels **207**, 208, 392, 458, 462
- calmodulin, ligand association rate **204**
- capacitance
  - circuit **329**
  - ionic layers **290**
- carbamylcholine **118**, 119
- carbon–carbon bonds **44**
  - force constant **261**
- carbonic anhydrase **177**, 273–275, 274, 355
- carboxypeptidase **268**
- catalytic efficiency of enzymes **253**
- cation–π interactions **33**, 33–35, 47
- central-limit theorem **65**, 156
- channel noise **186**, 321, 323, 327–328, 328
- channel structure **367**
  - Eisenman selectivity sequences **374–376**, 375, 398
  - energy barriers and channel properties **371–374**, 372
  - gramicidin A **370**, 378–380, 384, 393
  - KcsA channel **71**, 394, 394–399, 396
  - Ohmic channels **370**, 370–371, 372, 376, 384
  - rate theory for multibarrier channels **380**, 380–384, 383
  - single-file channels **371**, 390, 390–394, 397
  - single-ion channels **384–390**
  - structural parameters and conductances **371**
- characteristic equation of a matrix **223**, 242, 475
- characteristic ratio **62**, 63
  - charge-dipole interactions **31**, 31–32
- choline **291**, 441
- chymotrypsin **248**, 250, 256, 258, 259, 272
  - hydrolysis rates **250**
  - ligand association rate **204**
- chymotrypsin inhibitor-2 **190**, 191, 192
- circuit noise **329**, 329–331
  - mean-square voltage **329**
- classical configuration integral **3**, 46, 301
- closed-time distribution **185**, 232, 233, 236, 237, 240, 241
- coils, random **72**, 73, 106, 107, 163–164
  - frictional coefficients **163**
  - molecular behavior **68**
  - statistics **60**, 60–62
  - stretching **67–68**
- collision frequency **198**, 200
- compartmental models **428**, 428–430
  - synaptic integration in dendrites **430–433**, 431, 432, 450, 467
- concerted binding **91–93**
- configurational entropy **71**, 72, 107
- configurational free energy **94**, 106–107, 107, 129
- configurational partition functions **58–60**
- conservation of total number of moles **227**, 228
  - loss of **237–240**, 240
- constant-field equation **353**, 360
  - extended form **361**
- cooperative units **11**, 16, 79, 123, 303
- cooperativity within systems
  - allosteric transitions **123**, 130
  - helix-coil transitions **53**, 78, 79, 79
  - hydrogen bonds **41**, 43
  - molecular associations **91**
    - concerted binding **91–93**
    - nearest-neighbor interactions **94**
    - sequential binding **93–94**
  - protein folding **72**, 86–87
  - thermal transitions **11–12**
  - voltage-induced transitions **19–21**, 20
- correlation function **322–328**, 331–338
- Coulomb's law **25**
  - contribution to potential energy **280**
- Coulomb potential **25–27**, 31, 276, 277, 279–282, 298, 300, 302, 375
- Coulombic interactions **32**, 34, 177, 206, 398
- counterions *see* ions and counterions
- cratic contribution **100**
- creatine kinase **334**, 335, 335
- critical assessment of protein structure prediction (CASP) **52**
- cysteine (cys), helix continuation parameter **81**
- cytoplasm **401**, 401–403
  - resistance **401**, 429
  - viscosity **335**, 406
- de Broglie wavelength, thermal **99**, 179
- Debye length **277–278**, 287, 289
- Debye–Hückel limiting law **281**, 282
  - dilute solutions **282**
  - exact at infinite dilution **283**
  - ionic atmospheres **281**, 282
- Debye–Hückel screening **297–305**
- degeneracy **57**, 75, 84, 138
- delta function **144**, 423, 479
- denaturants of proteins **11**, 13, 48, 187–192
- dendrites **419**
  - action potentials **466–468**, 467
  - synaptic integration
    - analytical models **422–423**, 423
    - compartmental models **430–433**, 431, 432
    - impulse responses **423–425**, 424
    - realistic synaptic inputs **425–428**, 427
- desensitization **133**
- detailed balance **116**
  - kinetics of multi-state systems **228**
  - loss of **237–240**, 240
  - rate processes **170–182**
- dielectric constant **25**, 30, 31, 35, 36, 38, 41, 47, 51, 272, 276, 287, 363, 368, 376, 402, 406
- diffusion **142**
  - diffusion equation **66**
    - from microscopic theory **159–160**
  - diffusion-limited associations **197–200**, 198
  - diffusion-limited dissociations **200–201**
  - friction **160–162**, 336

- diffusion (cont.)
  - Gaussian distribution 156–159, 157
  - lateral diffusion in membranes 164–165
  - macromolecules, diffusion constants 163–164, 164
  - deviation from Stokes-Einstein relation 163
  - macroscopic diffusion and Fick's laws 142–143
  - solving the diffusion equation 143–144
    - diffusion across an interface 146–148, 147, 148
    - diffusion with boundary conditions 148–150, 149
    - one-dimensional diffusion from a point 144–146, 145
    - three-dimensional diffusion from a point 146
  - steady-state 150–151
    - long pipe 151
    - porous membrane 153–154
    - small hole 152, 152–153
  - Stoke's law 162, 162–163
- dimensionality, reduction in 107–108, 108, 212–214
- dipicrylamine 369, 369
- dipole-dipole interactions 32, 49, 398
- dipole moment 26, 31, 31, 32, 35, 49, 395, 396
- dipoles
  - induced dipoles 32–33
  - interactions with charges 31, 31–32
- dispersion force (London force) 35, 39, 43, 52
- lipid bilayers 54
- DNA 52–53, 62
  - binding 94, 112, 214
  - electrostatic repulsion 298, 298
  - flexibility parameters 63
  - formation of circular form from linear form 67
  - melting 302–305, 305
  - random coil behavior 68
- Donnan potentials 341–343, 342, 344, 346
- effective segment length of macromolecules 62–63
- eigenvalues 46, 223, 474–476
  - multisubunit kinetics 244
- eigenvectors 223, 224, 474–476
  - three-state model 225
- Einstein's equation for diffusion and friction 161, 267, 347
- Eisenman theory of selectivity 374–376, 375, 376, 398
- elastase 248, 250
- electrogenic membrane pumps 354, 355
- electroneutrality 288, 342, 343, 346
- electrophoresis 294–297, 295
  - mobility of ions 295
  - sheer force 295
  - velocity of ions 294
- electrostatic self-energy 27–29
- electrostatic stress 267
- elementary weight 57
  - partition function 58
- enthalpy 6, 37, 41
  - Coulomb's law 26
  - hydration 28, 28
  - ions in water 27
  - thermal denaturation of proteins 9–12, 10, 72, 87
- entropy 6
  - of electrostatic interactions 26
  - ions in water 27
  - protein denaturation 71–73
    - unfolding entropy 72
  - rotational entropy 263–264
  - translational entropy 260, 260–263, 263
- enzyme catalysis 248
  - acid-base catalysis 268–270
  - $\beta$ -galactosidase 270–271, 271
  - allosteric enzymes 257–258
  - friction in an enzyme-substrate complex 267–268
- hydrolysis rates 250
- Kramers rate theory 259–260
- Michaelis-Menten kinetics 251–254
- pre-steady-state kinetics 256–257
- proton transfer in carbonic anhydrase 273–275, 274
- proximity and translational entropy 260, 260–263, 263
- rotational entropy 263–264
- serine proteases 272–273
- steady-state approximations 254–256
- transition state complementarity 264–267, 266
- utilization of binding energy 258–259
- equipartition of energy 23, 104, 313–317, 329
- equivalent cylinder representation 412–413, 413
  - steady-state 413–415, 415
  - time constants 415–418
- Euler's formula 479
- excluded volume effect 43, 63, 64, 70, 72, 281
  - theta solvents 65
- exponential relaxations 167–169, 169
- extended constant-field equation 361
- eye, light detection 311–313, 312, 313
- Eyring theory 179–180
- Fick's laws 142–143
  - first law 142
  - second law 143
- fluctuations 307
  - channel noise 327, 328
  - circuit noise 329, 329–331
  - deviations from the mean 307–308
  - energy fluctuations in macromolecules 315–317
  - equipartition of energy 313–315
  - fluorescence correlation spectroscopy 164, 332, 332
  - friction and the fluctuation-dissipation theorem 336, 338
- Poisson distribution 309, 309–311, 310
- protein ionization 317–319
- single-channel current 320–322, 321
- statistics of light detection by the eye 311–313, 312, 313
- two-state systems 319–320
  - correlation function 322–324
- Wiener-Khintchine theorem 324–327, 331
- fluorescence correlation spectroscopy 164, 332, 332, 335
- fluorescence recovery after photobleaching (FRAP) 164, 165
- fluorescent proteins 334, 335
- flux 198, 200, 347
  - Ussing flux ratio 351–352, 390
    - definition 352
- folding of proteins 46, 82–86
  - cooperativity 86–87
  - good-folding amino acid sequences 84

- hydrophobic interactions 47, 48  
 native state 46, 71, 82, 85, 85  
     jigsaw puzzle picture 86  
     molten-globule 82  
     oil droplet picture 86  
     time taken 72  
 Fourier analysis 477, 477–480, 478  
 Fourier integral 324, 423  
 Fourier transform 144, 149,  
     150, 324, 325, 408,  
     410, 423  
     additive noise 324, 325  
     fluctuations 324, 326  
     inverse 327  
     Lorentzian 328  
 free energy  
     change in 5  
         electrostatic 15  
         pressure-induced transitions 12  
     protein ionization 284  
     thermal denaturation of  
         proteins 6  
 configurational free energy 94,  
     106–107, 107  
 global states of proteins 2, 3, 4  
 interactions 21  
 linear analysis 192  
 linear relations 172–175,  
     173, 175  
 Marcus relation 177–178, 178  
 molar free energy 5  
     standard state 95  
 rotational free energy 101–102, 263  
 translational free energy 98–101,  
     260–263  
     change in 101  
     translation contribution to  $\Delta G^\circ$   
         99, 100  
 vibrational free energy 102–104  
     change in 104  
     vibrational contribution 102  
 freely jointed chains 60, 60  
 freely rotating chains 61  
 friction 160–162  
     electrophoretic mobility 294  
 enzyme–substrate complexes  
     267–268  
 fluctuation–dissipation theorem  
     336, 338  
 frictional coefficients 163  
     Stoke's law 162, 162–163  
 fructose-1,6-diphosphate 130  
 fructose-6-phosphate 130, 131  
 fura-2 196, 197
- GABA 183, 236, 374  
 $\beta$ -galactosidase 270, 271  
 gas constant 4  
 gating current 18, 18–19  
 gating particle 442  
 gauche conformation of *n*-butane 56,  
     57, 57  
 Gaussian distribution  
     polymers 65  
         random walks 156–159, 157  
 Gaussian integrals 481–482  
 geometric series 471  
 Gibbs–Helmholtz equation 10  
 global states of proteins 1, 4  
     allosteric transitions 112, 113, 117,  
         121, 174  
     compliance 21–23, 22  
     definition 2–4  
     equilibrium between two global  
         states 4–5  
     free energy 2, 3, 4  
     partition function 3  
     transitions 12–14  
     transitions induced by  
         denaturants 13  
     transitions induced by temperature  
         5–7, 6  
     transitions induced by voltage 14,  
         14–17  
         cooperativity 19–21, 20  
         steepness factor 16, 16  
         transition voltage 16, 16  
 glutamate 85, 206, 270–271, 271, 283,  
     292, 355  
 glutamic acid (glu), helix  
     continuation parameter 81  
 glutamine 17, 18, 85  
 glutamine (gln), helix continuation  
     parameter 81  
 glycine (gly) 38, 81, 85, 394  
     helix continuation parameter 81  
 glycine receptors 374  
 Goldman–Hodgkin–Katz current  
     equation 348, 357–360,  
         359, 361, 362, 363, 364,  
         372, 434  
 Goldman–Hodgkin–Katz voltage  
     equation 349, 350, 352–354,  
         354, 357, 360, 387  
 good-folding amino acid sequences 84  
 Gouy–Chapman equation 287  
 Gouy–Chapman theory 285–288, 294,  
     296–297, 302  
     Stern's improvements 288–291  
 G–protein coupled receptors  
     117–121, 120, 122  
 gramicidin A 374, 378–380, 393  
     channel structural parameters and  
         conductances 371  
 green fluorescent protein (GFP) 70, 71  
 guanine–cytosine basepairs,  
     hydrogen bonding 52  
 harmonic oscillators 21, 44, 100,  
     103, 104  
 harmonic potentials 22, 44–46  
 heat capacity 37, 41, 315, 316  
 helix–coil transition/theory 53, 60,  
     73–74, 74, 87, 94, 303  
 helical propensities 80–82  
 mathematical analysis 74–78  
     mean number of helical  
         residues 76  
         results 78, 78–79  
 Helmholtz–Smoluchowski  
     equation 296  
 hemoglobin 70, 70, 137–140, 164,  
     267, 319  
     allosteric interactions 126, 126–127  
     iron–heme binding sites 140  
     linear free energy relation 174, 174  
     oxygen binding 92  
     pH sensitivity 140  
 Hill coefficient 92, 93, 94, 125–126  
     sequential binding 93  
 Hill equation 92, 92, 126, 126, 135, 136  
 Hill plot 92  
 hippocampal neuron 406, 430, 431  
 histidine (his) 249–251, 266, 272,  
     272–275  
     helix continuation parameter 81  
 Hodgkin–Huxley equations 442–446,  
     444, 447  
 Hodgkin–Keynes model 390, 392  
 horseradish peroxidase 206–207  
     ligand association rate 204  
 H–P (hydrophobic–polar amino acids)  
     lattice model 83  
     modeling 83, 83  
     oil droplet picture 86  
     sequences 84  
         good-folding 84  
 hydration force 39  
 hydrogen bonds 39–43  
     energies 42  
 enzyme–substrate 41, 42  
     energies 42  
 force constant 261

- hydrogen bonds (cont.)  
 nucleic acids 52  
     adenine-thymine base pairs 52  
     double-helix formation 52  
     guanine-cytosine base pairs 52  
 proteins 48, 49, 83  
      $\alpha$ -helices 49, 49, 50  
      $\beta$ -sheets 49  
 stretching force constant 45  
 strong bonds 272–273  
     histidine-aspartate 272  
     pK of histidine 272, 273  
     water 41, 82  
 hydrophobic forces 36–39, 38, 48, 54,  
     85, 105–106  
     protein folding 47, 72, 83–86, 190  
 hydrophobic matching 53
- ideal polymer chains 64  
 central-limit theorem 65
- ideal solutions  
 deviation from 279  
 infinite dilution 281
- inactivation of ion channels 442
- insulin 103, 104
- image forces 29, 29–31, 30, 38, 283, 363,  
     368–371, 377, 377, 379, 395
- internal motions in proteins 267
- inverse Fourier transform 480
- ion hydration energy 28, 28  
 ion size 376
- ion hydration shell 281
- ion permeation 339, 368 *see also*  
 channel structure  
 Donnan potentials 341–343, 342  
 forces within ion channels 376,  
     376–378, 377
- Nernst potentials 339–341, 340
- permeation without channels  
 367–369, 369
- ionic atmosphere 279, 282  
 Debye-Hückel limiting law 281
- ionic double layer 287
- ions and counterions 276–277  
 activity coefficient 279,  
     279–283, 353  
 contribution of screening to  
     potential energy 280
- counterion condensation 300–302  
 Debye-Hückel screening 297–305
- DNA melting 302–305, 305
- electrophoretic mobility  
 294–297, 295  
 velocity 294
- ionization of proteins 283–285  
 membrane surface charge 285–288,  
     361–362  
     Stern's improvements of  
         Gouy-Chapman theory  
         288–291  
 Poisson-Boltzmann equation and  
     Debye length 277–278  
 surface charge and channel  
     conductance 291–293  
 surface charge and voltage gating  
     293–294, 294
- isoleucine (ile), helix continuation  
 parameter 8, 9, **81**
- jigsaw puzzle picture for protein  
 folding 86
- Johnson noise 331
- K system of enzymes 257, 258
- KcsA channel 71, 71, 394, 394–399, 396
- kinetics of associations 194  
 bimolecular associations 194–195  
 binding to DNA 214  
 binding to membrane receptors  
     208–211, 209  
 diffusion-limited associations  
     197–200, 198  
 diffusion-limited dissociations  
     200–201  
 protein-ligand association rates  
     203–205, **204**  
 acetylcholinesterase  
     205–206, 206  
 evolution of speed 205  
 horseradish peroxidase 206–207
- proton transfer 207–208  
 rates **207**
- reduction in dimensionality  
 212–214
- site binding 201–203, 202  
 small perturbations 195–196, 197
- kinetics of multi-state models 216  
 general solution to multi-state  
     systems 221–225
- general treatment of single-channel  
 kinetics 234–236, 236
- initial conditions 219–220, 220
- loss of stationarity, conservation  
 and detailed balance  
     237–240
- multisubunit kinetics 242–244, 243
- random walks and stretched  
 kinetics 244–246, 246
- relation between single-channel  
 and macroscopic kinetics  
     236–237
- separation of time scales 220–221  
 single-channel kinetics 232, 232
- single-channel correlations  
     240–242, 241
- stationarity, conservation and  
 detailed balance 226–228
- three-state model 216–219  
 matrix notation 225  
 single-channel kinetics  
     229–232, 231
- Kirchoff's law 404
- Koshland-Nemethy-Filmer (KNF)  
 model 134, 134–136
- Kramers' theory 180–183  
 enzymes 259–260, 267–268
- ion channels 445
- $\beta$ -lactamase, ligand association  
 rate **204**
- Langevin equation 336, 397
- Laplacian differential operator 143,  
     146, 285, 485
- Lennard-Jones potential 43, 44,  
     51, 95
- leucine 38, 85, 86
- leucine (leu), helix continuation  
 parameter **81**
- Levinthal's paradox 73
- ligand-gated channels 132–133, 133
- ligands 202, 203  
 frequency of binding to receptors  
     211
- protein-ligand association rates  
     203–205, **204**  
 acetylcholinesterase  
     205–206, 206  
 evolution of speed 205  
 horseradish peroxidase 206–207
- reduction in dimensionality  
 212–214
- light detection by the eye 311–313,  
     312, 313
- like-dissolves-like rule 36
- Linderström-Lang model of protein  
 ionization 283
- linear transformations of matrices  
 472–473
- linkage 122
- lipid bilayers 14, 23, 30, 39, 53–54, 54,  
     108, 164–165, 357, 363,  
     367–369

- dispersion force (London force) 36, 54  
 hydration forces 39  
 melting 54  
 lobster axon 406  
 lock-and-key stereospecific interactions 43  
 London force *see* dispersion force  
 loop formation 66–67  
 Lorentzian 328  
 lysine 18, 85, 250, 283  
 lysine (lys), helix continuation parameter 81  
 lysozyme 70, 71, 156, 264  
     diffusion constant 156, 164  
     unfolding by thermal denaturation 7–9, 8, 12  
     melting curves 8, 9  
 macromolecules, conformations of 56  
     backbone rotations in proteins 68–71, 69  
 n-butane 56–58  
     *trans* and *gauche* conformations 56, 57, 57  
 configurational partition functions and polymer chains 58–60  
 effective segment length 62–63  
 energy fluctuations 315–317  
 entropy of protein denaturation 71–73  
 flexibility parameters for chain molecules 63  
 helix continuation parameters for amino acids 81  
 helix-coil theory 78, 78–79  
     helical propensities 80–82  
 helix-coil transition 73–74, 74  
     mathematical analysis 74–78  
 loop formation 66–67  
 nonideal polymer chains and theta solvents 63–65  
 probability distributions 65–66  
 protein folding 82–86  
     cooperativity within 86–87  
 random coil behavior of molecules 68  
     statistics of random coils 60–62  
     stretching of random coils 67–68  
 macroscopic additivity 128–130  
 Marcus theory 177–178, 178  
     enzyme catalysis 273–275, 274  
 Markov processes 160, 184  
 matrix algebra
- determinants 473–474  
 eigenvalues, eigenvectors and diagonalization 46, 77, 225, 474–476  
 linear transformations 472–473  
 positive semidefinite 45  
 Maxwell time constant 402, 403  
 mean capture time 213  
 mean number of helical residues 76  
 mean-square displacement 23, 145, 155, 160, 314  
 mean-square end-to-end length 61  
 membrane capacitance 402, 405, 428, 429, 452, 456  
 membrane conductance 21, 348, 370, 400, 429, 440  
 membrane potentials 339, 343  
     cells 343–344  
         muscle, skeletal 345–346  
         neurons 345, 345, 350–351  
 divalent ions 360–361  
 Goldman-Hodgkin-Katz current equation 357–360, 359, 360–363, 364  
 Goldman-Hodgkin-Katz voltage equation 350, 352–354, 354, 360  
 membrane pumps 354–355  
 membrane transporters 355, 358  
 permeability to sodium and potassium ions 347, 347–349  
 rate theory 362–365, 363  
 surface charge 361–362  
 Ussing flux ratio and active transport 351–352  
 membrane time constant 405  
 membranes  
     binding 108–109, 109  
     current flow 401, 401–403  
     lateral diffusion 164–165  
     protein associations 107–108, 108  
     proteins 53–54, 54  
         hydrophobic matching 53  
     pumps 354–355  
     receptor binding 208–211, 209  
     resistance 401  
     surface charge 285–288, 361–362  
         Stern's improvements of Gouy-Chapman theory 288–291  
     transmembrane voltage 14, 14  
     transporters 355, 358  
 methionine (met), helix continuation parameter 81
- Michaelis-Menten equation 91, 252, 253  
 enzyme catalysis 251  
 microscopic additivity 128–130  
 microstates of proteins 2, 3  
     entropy 3  
     partition function 2, 3  
     thermal denaturation 6, 6  
 minimum potential energy conformation of polypeptides 70, 71  
 mitochondria 355  
 molecular associations 89  
     association equilibrium in solution 89–91, 90  
     binding to membranes 108–109, 109  
     configurational free energy 94, 106–107, 107  
     contact formation 95–96  
     cooperativity 91  
         concerted binding 91–93  
         nearest-neighbor interactions 94  
         sequential binding 93–94  
     protein association in membranes 107–108, 108  
     rotational free energy 101–102  
     solvation effects 105–106  
     statistical mechanics of association 96–98  
 thermodynamics of associations 94–95  
 translational free energy 98–101  
     change in 101  
     translation contribution to  $\Delta\dot{G}$  99, 100  
 vibrational free energy 102–104  
     change in 104  
     vibrational contribution 102  
 molecular crowding 165  
 molecular forces 25  
     bond flexing and harmonic potentials 44–46  
     cation- $\pi$  interactions 33, 33–35, 47  
     charge-dipole interactions 31–32  
     Coulomb potential 25–27  
     dispersive forces 35–36  
     electrostatic self-energy 27–29  
     hydration forces 39  
     hydrogen bonds 39–43  
     hydrophobic forces 36–39, 38  
     image energy 29–31  
     induced dipoles 32–33  
     protein force fields 50–52

- molecular forces (cont.)
  - stabilizing forces in nucleic acids 52–53
  - stabilizing forces in proteins 46–50
    - steric repulsions 43
  - molten-globule native state 82
  - Monod-Wyman-Changeux (MWC) model 123–126, 126, 284
    - energetics 127, 127–128, 128
    - enzymes 257
    - hemoglobin 126, 139–140
    - phosphofructokinase 130–132
      - ligand-gatol channels 133
  - Morris-Lecar model 462, 464
  - muscle, membrane potentials 345–346
  - myelin 453, 453–455
  - native states of proteins 46, 71, 82, 85, 85
    - jigsaw puzzle picture 86
    - molten-globule 82
    - oil droplet picture 86
  - Neher-Steinbach model 234
  - Nernst equation 340, 356
  - Nernst potentials 339–341, 340, 344, 344, 356, 357, 364
  - Nernst–Planck equation 162
  - NEURON computer program 430, 467
  - neurons *see also* axons; dendrites
    - cable analysis 418, 418–422, 420, 421
    - compartmental model 428, 428
    - membrane potentials 345, 345, 350–351
  - neurotransmitters 34, 89, 118, 184, 205, 235, 351, 355, 393, 423, 457
  - neutrophils 355
  - Newton's equation of motion 51, 397
  - nodes of Ranvier 453
  - nonideal behavior of ionic solutions 279, 280, 300, 353–354
  - nonideal polymer chains 63–65
  - normal modes of vibration 46, 102, 103
  - nucleic acids
    - acidic phosphate groups 53
    - stabilizing forces 52–53
      - hydrogen bonds 52
  - nullclines 464, 465
  - Nyquist's theorem 331
  - Ohmic channels 370, 370–371, 372, 372, 376, 384
  - smallest channels 371
  - Ohm's law 359, 403, 404
  - oil droplet picture for protein folding 86
  - open-time distribution 184, 185, 229, 231, 234, 235, 236, 238, 240, 323
  - orotidine monophosphate decarboxylase 266
  - ouabain 355
  - Overton theory 367
  - oxycarbenium intermediate 264
  - pancreatic trypsin inhibitor 267
  - Parseval's theorem 326
  - partition coefficient
    - ion permeation 368
    - inorganic ions 368
  - partition function 58
    - association mechanics 96
    - N residue chain 76
    - polymers and monomers 59
    - protein global states 3
    - protein microstates 2, 3
      - thermodynamic stability 3
      - sum over elementary weights 58
    - translational partition function 99
  - passive voltage changes 400
  - pathway counting 240–242, 241, 387–388
  - Pauli exclusion principle 43
  - permeability ratio 350, 352–353, 360, 362, 387, 387–388, 389, 436
  - persistence length 53, 63, 298
  - phenylalanine 34, 38, 42, 42, 119, 205
  - phenylalanine (phe), helix continuation parameter **81**
  - phosphofructokinase 130–132, 131, 132
  - photoreceptor cells 312, 313
  - pi-electrons, interactions with cations 33, 33–35, 34, 47
  - Poisson distribution 309, 309–311, 310
    - definition 309
    - fluctuations in molecule number 311, 333
    - photon absorption 312
    - RMS deviations 311
  - Poisson equation 26, 277, 296, 402
  - Poisson–Boltzmann equation 277–278, 283, 292, 293
    - linearized form 279, 282, 283
    - membranes 285, 286
    - uniformly charged cylinder 297
  - polar and spherical coordinates 484, 484–485
  - polarizability of molecules 33, 35
  - poly-l-alanine, flexibility parameters **63**
  - polyelectrolyte solutions
    - counterion condensation 300–302
    - Debye–Hückel screening 297–305
  - polyethylene 59, 62
    - flexibility parameters **63**
  - polymer chains
    - configurational partition functions 58–60
    - nonideal 63–65
  - polypeptide backbone of proteins 68, 69
    - minimum potential energy conformation 70, 71
    - rotations 69
  - poly proline 70, 70, 72
  - positive semidefinite matrices 45
  - potassium ion channels 136, 291, 292, 292, 294, 437, 439, 439–441, 440, 463
  - power spectrum 326, 328, 328
  - proline 81, 250, 265
  - proline (pro), helix continuation parameter **81**
  - proline racemase 265, 265
  - protein engineering 192
  - proteins
    - allosteric proteins 115
    - $\alpha$ -helices 49, 49, 50
    - associations in membranes 107–108, 108
    - backbone rotations 68–71, 69
    - $\beta$ -sheets 49
    - conformational states 1
    - denaturation by other variables 12–14
    - denaturants 13
  - denaturation by temperature 5–7, 6
    - cooperativity 11–12
    - entropy 71–73
    - lysozyme unfolding 7–9
    - melting curves 8, 8, 9
    - number of global transitions 11
    - rate 188
    - steepness and enthalpy 9–11, 10
    - thermal unfolding 106
    - transition temperature ( $T^*$ ) 6
  - energy fluctuations 317
  - fluorescence 334, 335
  - folding 46, 82–86

- cooperativity 86–87
- good-folding amino acid sequences 84
- hydrophobic interactions 47, 48
- jigsaw puzzle picture 86
- native state 46, 71, 82, 85, 85
- oil droplet picture 86
- time taken 72
- force fields 50–52
- global states 1, 4
  - compliance 21–23, 22
  - definition 2–4
  - equilibrium between two global states 4–5
  - free energy 2, 3, 4
  - microstates 2, 3, 6
  - partition function 2, 3
  - transitions induced by temperature 5–7
  - transitions induced by voltage 14, 14–17, 16, 16, 19–21, 20
- global transitions 1–2
- ionization 283–285
  - fluctuations 317–319
- membrane proteins 53–54, 54
  - hydrophobic matching 53
- predicting structure 51
  - critical assessment of protein structure prediction (CASP) 52
- protein-ligand association rates 203–205, 204
  - acetylcholinesterase 205–206
  - evolution of speed 205
  - horseradish peroxidase 206–207
- random coil behavior 68
- stabilizing forces 46–50
  - electrostatic contributions 47
  - hydrogen bonds 48, 49
- voltage-gated channels 17–18, 18
  - gating current 18, 18–19
  - S4 amino acid segment 17, 18
- proton transfer 207–208
  - rates 207
- quantum effects on bonds 3, 314
- quantum mechanics 40, 99–101, 179, 264
- Rall branching rules 412, 417, 418
- Rall model for neurons 418, 418, 420, 421, 421, 422
- Ramachandran plots 69, 70
- random walks 154–156
- binding to membrane receptors 210, 210
- Gaussian distribution 156–159, 157
- kinetics of multi-states 244–246, 246
- rate processes 167
  - activation energies 169–170
  - diffusion over a barrier 180–183
  - exponential relaxations 167–169, 169
- Eyring theory 179–180
- ion movements within ion channels 377
- linear free energy relations 172–175, 173, 174, 175
- Marcus free energy relation 177–178, 178
- membrane potentials 362–365, 363
- multibarrier channels 380, 380–384, 383
- reaction coordinate and detailed balance 170–182, 171, 172
- reaction coordinate for global transitions 186–193, 187
- single-channel kinetics 183, 183–186, 185
- voltage-dependent rate constants 175–176, 176, 177
- reaction coordinate 170–182, 171, 172, 173, 204, 249, 258–262, 260, 267–268, 274
  - global transitions 186–193, 187
- rectification 373, 374
- red blood cells 355
- reflecting boundary conditions 150, 213, 407, 411
- refractive index 35
- relaxed (R) state 112, 113, 117
  - hemoglobin 126
- repetitive activity 458–461, 459, 460
- resting potential of cells 343
- retina 312
- rhodopsin 312
- ribonuclease A 107
- root-mean-square (rms) end-to-end distance 64
- root-mean-square (rms) length 58
- root-mean-square (rms) velocity of a molecule 156, 336
- rotational entropy 263–264
- rotational free energy 101–102
- rotational isomer model 61, 62
- rubber and elastic molecules 13, 68
- S4 amino acid segment in voltage-gated channels 17, 18
- saddle points 186, 187
- Saffman-Delbrück equation 165
- saltatory conduction 454
- selectivity filters 374, 395, 398
- self-energy (Born eqcag) 27–31, 30, 177, 280, 283
- sequential binding 93–94
- serine (ser) 12, 81, 248, 272, 272
  - helix continuation parameter 81
- serine proteases 248–251, 249, 260, 272–273
  - hydroxyl group 272
- serotonin 393
- sheer force 295
- simple elastic spring 68
- single-channel current and conductance 132, 183, 232, 320–322, 321, 370, 378, 390, 443
- single-file channels 371, 390, 390–394
- single-ion channels 384–390, 385, 387
- sink of diffusion 151
- sodium chloride 276, 278
  - activity coefficient 281, 281
  - osmolarity of solutions 279
- sodium ion channels 293, 436, 437, 439, 439–441, 440
  - activation 442
- solvation effects on molecular associations 105–106
- solvents 47, 64, 368
- source of diffusion 151
- space constant ( $\lambda$ ) 405
- spectral density 326
- S-peptide 107
- spherical and polar coordinates 484, 484–485
- squid giant axon 406, 439, 439, 440, 443, 444, 446
  - firing 458, 459
  - frequency response 458
  - speed and size 452
- stability 226
- stabilizing forces in proteins 46–50
- stacking interaction 52
  - double-helix formation 52
- standard state, molar free energy 95
- state counting 234–236, 236
- stationarity 226, 228
  - loss of 237–240, 240

- statistics
  - light detection by the eye 311–313, 312, 313
  - random coils 60, 60–62
  - steady-state diffusion 151
    - long pipe 151
    - porous membrane 153–154
    - small hole 152, 152–153
  - steepness factor 16, 16
  - steric repulsions 43
  - Stern layer 289, 289, 290
  - Stern’s improvements of Gouy–Chapman theory 288–291
  - Stirling’s approximation 157
  - Stoke’s law 162, 162–163, 165, 295, 297
  - Stokes–Einstein relation 163, 199, 203, 335
  - stretched kinetics 244–246, 246
  - supernormal axons 449
  - superoxide dismutase 206
    - ligand association rate 204
  - surface potential 287, 290, 292, 293, 294, 361–362
  - synapses 184, 468
    - intergration in dendrites
    - analytical models 422–423, 423
    - compartmental models 430–433, 431, 432
    - impulse responses 423–425, 424
    - realistic synaptic inputs 425–428, 427
    - synaptic current 186
  - Szabo–Karplus (SK) model 123, 126, 137–140, 139
  - Tanford  $\beta_T$  value 188
  - Taylor series 470, 470
  - tense ( $T$ ) state 112, 113, 117
    - hemoglobin 126
  - thermal de Broglie wavelength 99, 179
  - thermodynamics in molecular associations 94–95
- theta solvents 65
- threonine (thr) 7–9, 12, 81, 119, 266, 394
  - helix continuation parameter 81
- threonine–valine–glycine–tyrosine–glycine (TVGYG) sequence 394, 395, 398
- threshold stimulus 436
- trans* conformation of *n*-butane 56, 57, 57
- transition states 169
  - complimentarity 264–267, 266
- transition temperature ( $T^*$ ) 6
  - DNA melting 302–305
  - melting curves 8
  - steepness and enthalpy 9–12, 10
- transition voltage 16, 16
- translational entropy 260, 260–263, 263
- translational free energy 98–101
  - change in 101
  - translation contribution to  $\Delta G^\circ$  99, 100
- translational partition function 99
- transmembrane voltage 14, 14, 339
- transmission coefficient 180
- transverse resistivity 402
- triose phosphate isomerase 204
- trypsin 248, 250
  - hydrolysis rates 250
- tryptophan 34, 47, 205, 250
- tryptophan (trp), helix continuation parameter 81
- tubulin 334, 335, 335
- turnover number of enzymes 252
- tyrosine 34, 41, 42, 119, 205, 266, 267, 394
  - tyrosine (tyr), helix continuation parameter 81
- tyrosyl-tRNA synthase 41, 42, 265, 266
- unfolding of proteins 6, 12, 106
  - denaturants 13
  - entropy 72
- lysosome 7–9
  - melting curves 8, 8, 9
  - rate 188
- Ussing flux ratio 351–352, 390
  - definition 352
- V system of enzymes 257, 258
- valine (val) 8, 38, 81, 394
  - helix continuation parameter 81
- van’t Hoff enthalpy 10
- van’t Hoff equation 10
- varicosities on axons 456, 456, 457
- vibrational energy of bonds 3
  - frequency of vibration 44
  - kinetic energy 3
  - normal modes 46, 102, 103
- vibrational free energy 102–104, 129
- voltage clamp 439, 439–441, 440
- voltage-dependent rate constants 175–176, 176, 177
- voltage-gated channels 17–18, 18, 293–294, 294, 439–450, 457–458
  - dendritic 466–468
  - gating current 18, 18–19
  - S4 amino acid segment 17, 18
- water
  - dielectric constant 26
  - temperature dependence 27
  - enthalpy of solvated ions 27
  - entropy of solvated ions 27
  - hydration energy 28, 28
    - ion size 376
  - hydration forces 39
  - hydrogen bonds 41, 82
  - hydrophobic force 37, 37, 38
- wave equation 451
- Wiener–Khintchine theorem 324, 331
- zeta-potential 296