

Contents

1	Mechanics	1
1.1	Distances and Sizes	1
1.2	Forces and Translational Equilibrium	3
1.3	Rotational Equilibrium	4
1.4	Vector Product	5
1.5	Force in the Achilles Tendon	6
1.6	Forces on the Hip	7
1.7	The Use of a Cane	9
1.8	Work	10
1.9	Stress and Strain	12
1.10	Shear	13
1.11	Hydrostatics	13
1.12	Buoyancy	14
1.13	Compressibility	15
1.14	Viscosity	15
1.15	Viscous Flow in a Tube	15
1.16	Pressure-Volume Work	18
1.17	The Human Circulatory System	19
1.18	Turbulent Flow and the Reynolds Number	21
	Symbols Used	23
	Problems	24
	References	29
2	Exponential Growth and Decay	31
2.1	Exponential Growth	31
2.2	Exponential Decay	33
2.3	Semilog Paper	34
2.4	Variable Rates	35
2.5	Clearance	36
2.6	Multiple Decay Paths	37
2.7	Decay Plus Input at a Constant Rate	38
2.8	Decay with Multiple Half-Lives and Fitting Exponentials	38
2.9	The Logistic Equation	39
2.10	Log-log Plots, Power Laws, and Scaling	39
2.10.1	Log-log Plots and Power Laws	39
2.10.2	Food Consumption, Basal Metabolic Rate, and Scaling	40

Symbols Used	42
Problems	42
References	47
3 Systems of Many Particles	49
3.1 Gas Molecules in a Box	50
3.2 Microstates and Macrostates	51
3.3 The Energy of a System: The First Law of Thermodynamics	53
3.4 Ensembles and the Basic Postulates	54
3.5 Thermal Equilibrium	56
3.6 Entropy	58
3.7 The Boltzmann Factor	58
3.8 The Nernst Equation	59
3.9 The Pressure Variation in the Atmosphere	60
3.10 Equipartition of Energy and Brownian Motion	60
3.11 Heat Capacity	61
3.12 Equilibrium When Particles Can Be Exchanged: The Chemical Potential	61
3.13 Concentration Dependence of the Chemical Potential	62
3.14 Systems That Can Exchange Volume	63
3.15 Extensive Variables and Generalized Forces	64
3.16 The General Thermodynamic Relationship	64
3.17 The Gibbs Free Energy	65
3.17.1 Gibbs Free Energy	65
3.17.2 An Example: Chemical Reactions	66
3.18 The Chemical Potential of a Solution	67
3.19 Transformation of Randomness to Order	69
Symbols Used	70
Problems	71
References	79
4 Transport in an Infinite Medium	81
4.1 Flux, Fluence, and Continuity	81
4.1.1 Definitions	81
4.1.2 The Continuity Equation in One Dimension	82
4.1.3 The Continuity Equation in Three Dimensions	82
4.1.4 The Integral Form of the Continuity Equation	83
4.1.5 The Differential Form of the Continuity Equation	84
4.1.6 The Continuity Equation with a Chemical Reaction	85
4.2 Drift or Solvent Drag	85
4.3 Brownian Motion	85
4.4 Motion in a Gas: Mean Free Path and Collision Time	86
4.5 Motion in a Liquid	87
4.6 Diffusion: Fick's First Law	87
4.7 The Einstein Relationship Between Diffusion and Viscosity	89
4.8 Fick's Second Law of Diffusion	91
4.9 Time-Independent Solutions	92
4.10 Example: Steady-State Diffusion to a Spherical Cell and End Effects	94
4.10.1 Diffusion Through a Collection of Pores, Corrected	95
4.10.2 Diffusion from a Sphere, Corrected	95
4.10.3 How Many Pores Are Needed?	96
4.10.4 Other Applications of the Model	96
4.11 Example: A Spherical Cell Producing a Substance	96
4.12 Drift and Diffusion in One Dimension	98
4.13 A General Solution for the Particle Concentration as a Function of Time	99
4.14 Diffusion as a Random Walk	100
Symbols Used	102
Problems	102

References	108
5 Transport Through Neutral Membranes	111
5.1 Membranes	111
5.2 Osmotic Pressure in an Ideal Gas	112
5.3 Osmotic Pressure in a Liquid	114
5.4 Some Clinical Examples	115
5.4.1 Edema Due to Heart Failure	116
5.4.2 Nephrotic Syndrome, Liver Disease, and Ascites	116
5.4.3 Edema of Inflammatory Reaction	116
5.4.4 Headaches in Renal Dialysis	116
5.4.5 Osmotic Diuresis	116
5.4.6 Osmotic Fragility of Red Cells	117
5.5 Volume Transport Through a Membrane	117
5.6 Solute Transport Through a Membrane	119
5.7 Example: The Artificial Kidney	120
5.8 Countercurrent Transport	121
5.9 A Continuum Model for Volume and Solute Transport in a Pore	122
5.9.1 Volume Transport	123
5.9.2 Solute Transport	124
5.9.3 Summary	127
5.9.4 Reflection Coefficient	127
5.9.5 The Effect of Pore Walls on Diffusion	128
5.9.6 Net Force on the Membrane	128
Symbols Used	129
Problems	129
References	133
6 Impulses in Nerve and Muscle Cells	135
6.1 Physiology of Nerve and Muscle Cells	135
6.2 Coulomb's Law, Superposition, and the Electric Field	137
6.3 Gauss's Law	138
6.4 Potential Difference	141
6.5 Conductors	142
6.6 Capacitance	143
6.7 Dielectrics	143
6.8 Current and Ohm's Law	145
6.9 The Application of Ohm's Law to Simple Circuits	146
6.10 Charge Distribution in the Resting Nerve Cell	148
6.11 The Cable Model for an Axon	149
6.12 Electrotonus or Passive Spread	153
6.13 The Hodgkin-Huxley Model for Membrane Current	154
6.13.1 Voltage Clamp Experiments	154
6.13.2 Potassium Conductance	156
6.13.3 Sodium Conductance	157
6.13.4 Leakage Current	158
6.14 Voltage Changes in a Space-Clamped Axon	158
6.15 Propagating Nerve Impulse	159
6.16 Myelinated Fibers and Saltatory Conduction	160
6.17 Membrane Capacitance	163
6.18 Rhythmic Electrical Activity	164
6.19 The Relationship Between Capacitance, Resistance, and Diffusion	165
6.19.1 Capacitance and Resistance	165
6.19.2 Capacitance and Diffusion	165
Symbols Used	167
Problems	168
References	175

7	The Exterior Potential and the Electrocardiogram	177
7.1	The Potential Outside a Long Cylindrical Axon	177
7.2	The Exterior Potential is Small	179
7.3	The Potential Far From the Axon	180
7.4	The Exterior Potential for an Arbitrary Pulse	181
7.5	Electrical Properties of the Heart	184
7.6	The Current-Dipole Vector of the Heart as a Function of Time	186
7.7	The Electrocardiographic Leads	186
7.8	Some Electrocardiograms	189
7.9	Refinements to the Model	189
7.9.1	The Axon Has a Finite Radius	190
7.9.2	Nonuniform Exterior Conductivity	191
7.9.3	Anisotropic Conductivity: The Bidomain Model	191
7.10	Electrical Stimulation	192
7.11	The Electroencephalogram	196
	Symbols Used	196
	Problems	197
	References	201
8	Biomagnetism	203
8.1	The Magnetic Force on a Moving Charge	203
8.2	The Magnetic Field of a Moving Charge or a Current	205
8.2.1	The Divergence of the Magnetic Field Is Zero	205
8.2.2	Ampere's Circuital Law	205
8.2.3	The Biot-Savart Law	206
8.2.4	The Displacement Current	207
8.3	The Magnetic Field Around an Axon	208
8.4	The Magnetocardiogram	209
8.5	The Magnetoencephalogram	211
8.6	Electromagnetic Induction	213
8.7	Magnetic Stimulation	214
8.8	Magnetic Materials and Biological Systems	214
8.8.1	Magnetic Materials	215
8.8.2	Measuring Magnetic Properties in People	216
8.8.3	Magnetic Orientation	217
8.9	Detection of Weak Magnetic Fields	218
	Symbols Used	219
	Problems	220
	References	224
9	Electricity and Magnetism at the Cellular Level	227
9.1	Donnan Equilibrium	227
9.2	Potential Change at an Interface: The Gouy-Chapman Model	229
9.3	Ions in Solution: The Debye-Hückel Model	231
9.4	Saturation of the Dielectric	233
9.5	Ion Movement in Solution: The Nernst-Planck Equation	234
9.6	Zero Total Current in a Constant-Field Membrane: The Goldman Equations	236
9.7	Membrane Channels	238
9.8	Noise	242
9.8.1	Shot Noise	242
9.8.2	Johnson Noise	242
9.9	Sensory Transducers	243
9.10	Possible Effects of Weak External Electric and Magnetic Fields	244
9.10.1	Introduction	244
9.10.2	Effects of Strong Fields	244
9.10.3	Fields in Homes are Weak	244
9.10.4	Epidemiological Studies	245

9.10.5	Laboratory Studies	245
9.10.6	Reviews and Panel Reports	245
9.10.7	Electric Fields in the Body	246
9.10.8	Electric Fields in a Spherical Cell	246
9.10.9	Electrical Interactions and Noise	247
9.10.10	Magnetic Interactions and Noise	247
	Symbols Used	248
	Problems	249
	References	253
10	Feedback and Control	255
10.1	Steady-State Relationships Among Variables	256
10.2	Determining the Operating Point	257
10.3	Regulation of a Variable and Open-Loop Gain	257
10.4	Approach to Equilibrium without Feedback	259
10.5	Approach to Equilibrium in a Feedback Loop with One Time Constant	259
10.6	A Feedback Loop with Two Time Constants	262
10.7	Models Using Nonlinear Differential Equations	263
10.7.1	Describing a Nonlinear System	264
10.7.2	An Example of Phase Resetting: The Radial Isochron Clock	265
10.7.3	Stopping an Oscillator	268
10.8	Difference Equations and Chaotic Behavior	268
10.8.1	The Logistic Map: Period Doubling and Deterministic Chaos	269
10.8.2	The Bifurcation Diagram	270
10.8.3	Quasiperiodicity	271
10.9	A Feedback Loop with a Time Constant and a Fixed Delay	272
10.10	Negative Feedback Loops: A Summary	273
10.11	Additional Examples	274
10.11.1	Cheyne–Stokes Respiration	274
10.11.2	Hot Tubs and Heat Stroke	274
10.11.3	Pupil Size	274
10.11.4	Oscillating White-Blood-Cell Counts	275
10.11.5	Waves in Excitable Media	275
10.11.6	Period Doubling and Chaos in Heart Cells	276
	Symbols Used	277
	Problems	277
	References	283
11	The Method of Least Squares and Signal Analysis	285
11.1	The Method of Least Squares and Polynomial Regression	285
11.1.1	The Simplest Example	285
11.1.2	A Linear Fit	286
11.1.3	A Polynomial Fit	287
11.1.4	Variable Weighting	288
11.2	Nonlinear Least Squares	288
11.3	The Presence of Many Frequencies in a Periodic Function	289
11.4	Fourier Series for Discrete Data	290
11.4.1	Introducing the Fourier Series	290
11.4.2	Equally Spaced Data Points Simplify the Equations	290
11.4.3	The Standard Form for the Discrete Fourier Transform	291
11.4.4	Complex Exponential Notation	291
11.4.5	Example: The Square Wave	292
11.4.6	Example: When the Sampling Time Is Not a Multiple of the Period of the Signal	292
11.4.7	Example: Spontaneous Births	293
11.4.8	Example: Photosynthesis in Plants	294
11.4.9	Pitfalls of Discrete Sampling: Aliasing	294
11.4.10	Fast Fourier Transform	295

11.5	Fourier Series for a Periodic Function	295
11.6	The Power Spectrum	296
11.7	Correlation Functions	298
11.7.1	Cross-Correlation of a Pulse	298
11.7.2	Cross-Correlation of a Nonpulse Signal	299
11.7.3	Cross-Correlation Example	299
11.7.4	Autocorrelation	299
11.7.5	Autocorrelation Examples	299
11.8	The Autocorrelation Function and the Power Spectrum	300
11.9	Nonperiodic Signals and Fourier Integrals	301
11.9.1	Introduce Negative Frequencies and Make the Coefficients Half as Large	301
11.9.2	Make the Period Infinite	302
11.9.3	Complex Notation	303
11.9.4	Example: The Exponential Pulse	303
11.10	The Delta Function	304
11.11	The Energy Spectrum of a Pulse and Parseval's Theorem	304
11.11.1	Parseval's Theorem	305
11.11.2	Example: The Exponential Pulse	305
11.12	The Autocorrelation of a Pulse and Its Relation to the Energy Spectrum	305
11.13	Noise	306
11.14	Correlation Functions and Noisy Signals	308
11.14.1	Detecting Signals in Noise	308
11.14.2	Signal Averaging	308
11.14.3	Power Spectral Density	309
11.14.4	Units	309
11.15	Frequency Response of a Linear System	310
11.15.1	Example of Calculating the Frequency Response	311
11.15.2	The Decibel	311
11.15.3	Example: Impulse Response	312
11.16	The Frequency Spectrum of Noise	312
11.16.1	Johnson Noise	312
11.16.2	Shot Noise	315
11.16.3	$1/f$ Noise	315
11.17	Testing Data for Chaotic Behavior	316
11.17.1	Embedding	316
11.17.2	Surrogate Data	316
11.18	Stochastic Resonance	317
11.18.1	Threshold Detection	317
11.18.2	Feynman's Ratchet	318
	Symbols Used	319
	Problems	319
	References	323

12 Images 325

12.1	The Convolution Integral and its Fourier Transform	325
12.1.1	One Dimension	325
12.1.2	Two Dimensions	326
12.2	The Relationship Between the Object and the Image	327
12.2.1	Point-Spread Function	327
12.2.2	Optical-, Modulation-, and Phase-Transfer Functions	328
12.2.3	Line- and Edge-Spread Functions	329
12.3	Spatial Frequencies in an Image	329
12.3.1	Summary	331
12.4	Two-Dimensional Image Reconstruction from Projections by Fourier Transform	331
12.5	Reconstruction from Projections by Filtered Back Projection	332
12.6	An Example of Filtered Back Projection	335
	Symbols Used	337

Problems	337
References	340
13 Sound and Ultrasound	343
13.1 The Wave Equation	343
13.1.1 Plane Waves in an Elastic Rod	343
13.1.2 Plane Waves in a Fluid	344
13.2 Properties of the Wave Equation	345
13.3 Acoustic Impedance	346
13.3.1 Relationships Between Pressure, Displacement and Velocity in a Plane Wave	346
13.3.2 Reflection and Transmission of Sound at a Boundary	346
13.4 Comparing Intensities: Decibels	347
13.4.1 The Decibel	347
13.4.2 Hearing Response	347
13.5 The Ear and Hearing	348
13.6 Attenuation	349
13.7 Medical Uses of Ultrasound	350
13.7.1 Ultrasound Transducers	350
13.7.2 Pulse Echo Techniques	352
13.8 The Doppler Effect	353
Symbols Used	354
Problems	354
References	357
14 Atoms and Light	359
14.1 The Nature of Light: Waves versus Photons	359
14.2 Atomic Energy Levels and Atomic Spectra	361
14.3 Molecular Energy Levels	362
14.4 Scattering and Absorption of Radiation; Cross Section	364
14.5 The Diffusion Approximation to Photon Transport	367
14.5.1 General Theory	367
14.5.2 Continuous Measurements	368
14.5.3 Pulsed Measurements	368
14.5.4 Refinements to the Model	369
14.6 Biological Applications of Infrared Scattering	369
14.6.1 Near Infrared (NIR)	369
14.6.2 Optical Coherence Tomography (OCT)	370
14.6.3 Raman Spectroscopy	371
14.6.4 Far Infrared or Terahertz Radiation	372
14.7 Thermal Radiation	372
14.8 Infrared Radiation from the Body	375
14.8.1 Atherosclerotic Coronary Heart Disease	376
14.9 Blue and Ultraviolet Radiation	377
14.9.1 Treatment of Neonatal Jaundice	377
14.9.2 The Ultraviolet Spectrum	377
14.9.3 Response of the Skin to Ultraviolet Light	378
14.9.4 Ultraviolet Light Causes Skin Cancer	380
14.9.5 Protection from Ultraviolet Light	380
14.9.6 Ultraviolet Light Damages the Eye	381
14.9.7 Ultraviolet Light Synthesizes Vitamin D	381
14.9.8 Ultraviolet Light Therapy	381
14.10 Heating Tissue with Light	381
14.11 Radiometry and Photometry	383
14.11.1 Radiometric Definitions	383
14.11.2 Photometric Definitions	387
14.11.3 Actinometric Definitions	388
14.12 The Eye	388

16.3.2	Scintillation Detectors	442
16.3.3	Gas Detectors	444
16.3.4	Semiconductor Detectors	445
16.3.5	Thermoluminescent Dosimeters	445
16.3.6	Chemical Dosimetry	445
16.3.7	Digital Detectors	446
16.4	The Diagnostic Radiograph	446
16.4.1	X-ray Tube and Filter	446
16.4.2	Collimation	447
16.4.3	Attenuation in the Patient: Contrast Material	447
16.4.4	Antiscatter Grid	450
16.4.5	Film-Screen Combination	450
16.4.6	Computed and Direct Radiography	450
16.5	Image Quality	450
16.6	Angiography and Digital Subtraction Angiography	453
16.7	Mammography	453
16.8	Fluoroscopy	454
16.9	Computed Tomography	454
16.10	Biological Effects of Radiation	457
16.10.1	Cell-Culture Experiments	458
16.10.2	Chromosome Damage	458
16.10.3	The Linear-quadratic Model	460
16.10.4	The Bystander Effect	460
16.10.5	Tissue Irradiation	461
16.10.6	A Model for Tumor Eradication	463
16.11	Radiation Therapy	463
16.11.1	Classical Radiation Therapy	464
16.11.2	Modern X-ray Therapy	465
16.11.3	Charged Particles and Neutrons	465
16.12	Dose Measurement	467
16.13	The Risk of Radiation	468
16.13.1	Equivalent and Effective Dose	468
16.13.2	Comparison with Natural Background	469
16.13.3	Calculating Risk	470
16.13.4	Radon	472
	Symbols Used	473
	Problems	474
	References	477
17	Nuclear Physics and Nuclear Medicine	481
17.1	Nuclear Systematics	482
17.2	Nuclear Decay: Decay Rate and Half-Life	484
17.3	Gamma Decay and Internal Conversion	484
17.4	Beta Decay and Electron Capture	485
17.5	Calculating the Absorbed Dose from Radioactive Nuclei within the Body	488
17.6	Activity and Cumulated Activity	489
17.6.1	The General Distribution Problem: Residence Time	490
17.6.2	Immediate Uptake with No Biological Excretion	490
17.6.3	Immediate Uptake with Exponential Biological Excretion	490
17.6.4	Immediate Uptake Moving through Two Compartments	491
17.6.5	More Complicated Situations	491
17.6.6	Activity per Unit Mass	492
17.7	Mean Energy Emitted per Unit of Cumulated Activity	492
17.8	Calculation of the Absorbed Fraction	493
17.8.1	Nonpenetrating Radiation	493
17.8.2	Infinite Source in an Infinite Medium	493
17.8.3	Point Source of Monoenergetic Photons in Empty Space	494

17.8.4	Point Source of Monoenergetic Photons in an Infinite Isotropic Absorber	494
17.8.5	More Complicated Cases—the MIRD Tables	494
17.9	Radiopharmaceuticals and Tracers	495
17.9.1	Physical Properties	495
17.9.2	Biological Properties	497
17.10	Sample Dose Calculation	498
17.11	Auger Electrons	500
17.12	Detectors; The Gamma Camera	500
17.13	Single-Photon Emission Computed Tomography	501
17.14	Positron Emission Tomography	502
17.15	Brachytherapy and Internal Radiotherapy	503
17.16	Radon	505
	Symbols Used	506
	Problems	507
	References	512
18	Magnetic Resonance Imaging	515
18.1	Magnetic Moments in an External Magnetic Field	515
18.2	The Source of the Magnetic Moment	516
18.3	The Magnetization	517
18.4	Behavior of the Magnetization Vector	518
18.5	A Rotating Coordinate System	519
18.5.1	Transforming to the Rotating Coordinate System	519
18.5.2	An Additional Oscillating Field	520
18.5.3	Nutation	521
18.5.4	π and $\pi/2$ Pulses	521
18.6	Relaxation Times	522
18.7	Detecting the Magnetic Resonance Signal	524
18.8	Some Useful Pulse Sequences	525
18.8.1	Free-Induction-Decay (FID) Sequence	525
18.8.2	Inversion-Recovery (IR) Sequence	525
18.8.3	Spin-Echo (SE) Sequence	526
18.8.4	Carr-Purcell (CP) Sequence	526
18.8.5	Carr-Purcell-Meiboom-Gill (CPMG) Sequence	527
18.9	Imaging	527
18.9.1	Slice Selection	528
18.9.2	Readout in the x Direction	529
18.9.3	Projection Reconstruction	530
18.9.4	Phase Encoding	530
18.9.5	Other Pulse Sequences	531
18.9.6	Image Contrast and the Pulse Parameters	533
18.9.7	Safety	534
18.10	Chemical Shift	534
18.11	Flow Effects	535
18.12	Functional MRI	536
18.13	Diffusion and Diffusion Tensor MRI	536
	Symbols Used	537
	Problems	538
	References	542
A	Plane and Solid Angles	543
A.1	Plane Angles	543
A.2	Solid Angles	543
B	Vectors; Displacement, Velocity, and Acceleration	545
B.1	Vectors and Vector Addition	545
B.2	Components of Vectors	546

17.8.4	Point Source of Monoenergetic Photons in an Infinite Isotropic Absorber	494
17.8.5	More Complicated Cases—the MIRD Tables	494
17.9	Radiopharmaceuticals and Tracers	495
17.9.1	Physical Properties	495
17.9.2	Biological Properties	497
17.10	Sample Dose Calculation	498
17.11	Auger Electrons	500
17.12	Detectors; The Gamma Camera	500
17.13	Single-Photon Emission Computed Tomography	501
17.14	Positron Emission Tomography	502
17.15	Brachytherapy and Internal Radiotherapy	503
17.16	Radon	505
	Symbols Used	506
	Problems	507
	References	512
18	Magnetic Resonance Imaging	515
18.1	Magnetic Moments in an External Magnetic Field	515
18.2	The Source of the Magnetic Moment	516
18.3	The Magnetization	517
18.4	Behavior of the Magnetization Vector	518
18.5	A Rotating Coordinate System	519
18.5.1	Transforming to the Rotating Coordinate System	519
18.5.2	An Additional Oscillating Field	520
18.5.3	Nutation	521
18.5.4	π and $\pi/2$ Pulses	521
18.6	Relaxation Times	522
18.7	Detecting the Magnetic Resonance Signal	524
18.8	Some Useful Pulse Sequences	525
18.8.1	Free-Induction-Decay (FID) Sequence	525
18.8.2	Inversion-Recovery (IR) Sequence	525
18.8.3	Spin-Echo (SE) Sequence	526
18.8.4	Carr-Purcell (CP) Sequence	526
18.8.5	Carr-Purcell-Meiboom-Gill (CPMG) Sequence	527
18.9	Imaging	527
18.9.1	Slice Selection	528
18.9.2	Readout in the x Direction	529
18.9.3	Projection Reconstruction	530
18.9.4	Phase Encoding	530
18.9.5	Other Pulse Sequences	531
18.9.6	Image Contrast and the Pulse Parameters	533
18.9.7	Safety	534
18.10	Chemical Shift	534
18.11	Flow Effects	535
18.12	Functional MRI	536
18.13	Diffusion and Diffusion Tensor MRI	536
	Symbols Used	537
	Problems	538
	References	542
A	Plane and Solid Angles	543
A.1	Plane Angles	543
A.2	Solid Angles	543
B	Vectors; Displacement, Velocity, and Acceleration	545
B.1	Vectors and Vector Addition	545
B.2	Components of Vectors	546

B.3 Position, Velocity, and Acceleration	546
C Properties of Exponents and Logarithms	549
D Taylor's Series	551
E Some Integrals of Sines and Cosines	555
F Linear Differential Equations with Constant Coefficients	557
F.1 First-order Equation	558
F.2 Second-order Equation	558
G The Mean and Standard Deviation	561
H The Binomial Probability Distribution	563
I The Gaussian Probability Distribution	567
J The Poisson Distribution	571
K Integrals Involving e^{-ax^2}	575
L Spherical and Cylindrical Coordinates	577
M Joint Probability Distributions	579
M.1 Discrete Variables	579
M.2 Continuous Variables	580
N Partial Derivatives	581
O Some Fundamental Constants and Conversion Factors	583
Index	585