

Table of Contents

Foreword to the Princeton Science Library Edition	ix
Preface to the Expanded Edition	xiii
Preface (1983)	xv
Introduction	3
Chapter 1. Diffusion: Microscopic Theory	5
One-dimensional random walk	6
Two- and three-dimensional random walks	11
The binomial distribution	12
The Gaussian distribution	14
Chapter 2. Diffusion: Macroscopic Theory	17
Fick's equations	17
Time-dependent solutions to Fick's equations	21
Steady-state solutions to Fick's equations	25
Chapter 3. Diffusion to Capture	37
Probability of capture	38
Mean time to capture	42
Chapter 4. Diffusion with Drift	48
Random walk with drift	48
Fick's equations for diffusion with drift	50
Viscous drag	51
Sedimentation rate	58
Electrophoresis	62
Chapter 5. Diffusion at Equilibrium	65
Derivation of the Boltzmann equation	68
The importance of kT	70
Mean-square velocity	71
Einstein-Smoluchowski relation	71

vi—Table of Contents

Equilibrium sedimentation	72
Density-gradient sedimentation	73
Isoelectric focusing	74
 Chapter 6. Movement of Self-propelled Objects	 75
Life at low Reynolds number	75
Flagellar propulsion	78
Motility of <i>Escherichia coli</i>	81
Rotational diffusion	81
Random changes in direction	85
Poisson statistics	86
Bacterial diffusion	93
 Chapter 7. Other Random Walks	 95
Countercurrent distribution	95
Partition chromatography	100
Sedimentation field-flow fractionation	102
Autocorrelation analysis	105
 Appendix A. Probabilities and Probability Distributions	 111
Probabilities	111
Probability distributions	113
The binomial distribution	118
The Gaussian distribution	121
The Poisson distribution	123
 Appendix B. Differential Equations	 125
Ordinary differential equations	125
Partial differential equations	129
Numerical solutions	131

Table of Contents—vii

Appendix C Addendum to Chapter 6	134
Strategies for chemotaxis	134
Movement of cells across artificial membranes	136
Movement of ions across cell membranes	139
 Appendix D Constants and Formulas	 143
Bibliography	145
Index	149

Introduction

Biology is wet and dynamic. Molecules, subcellular organelles, and cells, immersed in an aqueous environment, are in continuous riotous motion. Alive or not, everything is subject to thermal fluctuations. What is this microscopic world like? How does one describe the motile behavior of such particles? How much do they move on the average? Questions of this kind can be answered only with an intuition about statistics that very few biologists have. This book is intended to sharpen that intuition. It is meant to illuminate both the dynamics of living systems and the methods used for their study. It is not a rigorous treatment intended for the expert but rather an introduction for students who have little experience with statistical concepts.

The emphasis is on physics, not mathematics, using the kinds of calculations that one can do on the back of an envelope. Whenever practical, results are derived from first principles. No reference is made to the equations of thermodynamics. The focus is on individual particles, not moles of particles. The units are centimeters (cm), grams (g), and seconds (sec).

Topics range from the one-dimensional random walk to the motile behavior of bacteria. There are discussions of Boltzmann's law, the importance of kT , diffusion to multiple receptors, sedimentation, electrophoresis, and chromatography. One appendix provides an introduction to the theory of probability. Another is a primer on differential equations. A third lists some constants and formulas worth committing to memory. Appendix A

4—Introduction

should be consulted while reading Chapter 1 and Appendix B while reading Chapter 2. A detailed understanding of differential equations or the methods used for their solution is not required for an appreciation of the main theme of this book.

Index

- adsorber, diffusion to: disk-like, 27–28, 30–33; ellipsoidal, 29; planar, 18–19, 41–46; spherical, 26–27, 38–41, 47
- agarose, 64
- ampholytes, 74
- aperture, circular, diffusion through, 28, 34–36
- autocorrelation, 105–110
- axon, 139–141
- bacterium: chemotaxis of, 94, 134–138; diffusion of, 93–94, 134–138; inability to coast, 76–77; propulsion of, 78–81; Reynolds number of, 75–76
- barrier, reflecting, planar, 34–36, 43–45
- binomial: coefficient, 118; distribution, 13, 118–121
- Boltzmann: constant, 5, 142; distribution, equation, 66–70, 72, 102–104, 143
- Bose-Einstein statistics, 70
- Brownian movement, 5, 77, 134
- bubble, viscous drag on, 56
- buoyancy, 58–59, 73–74
- capacitance, electrical, 29
- capture: mean time to, 42–46; probability of, 38–42, 46–47
- cells: diffusion through pores between, 35; diffusion to receptors on, 30–33; movement across membranes, 136–138; sedimentation of, 56, 62
- centrifuge, 58–62, 72–74
- cesium chloride, 64, 73
- chemotaxis: bacterial, 94, 134–138; strategies for, 134–136
- chromatography: autocorrelation analysis of, 106–109; gas, high-pressure liquid, partition, 100–101
- coefficient, *see* diffusion coefficient; frictional drag coefficient; partition coefficient; viscosity coefficient
- compound events, 112–113
- convective flow, 15–16, 60, 63–64
- correlation time, 50, 109
- countercurrent distribution, 95–100
- density gradient, 15, 60–61, 73–74, 125–128, 131–133
- differential equations: numerical solutions to, 131–133; ordinary, 125–129; partial, 129–131. *See also* diffusion equation; heat equation; Laplace equation; Poisson equation
- diffusion: bacterial, 93–94; current, 27–36, 39, 41–42; in a Boltzmann distribution, 67–68, 103–104; in a pipe, 23–25, 130–133; from a point source, 22–23; through a circular aperture, 28, 34–36; to an adsorbing disk, 27–28, 30–33, 36; to an adsorbing ellipsoid, 29; to an adsorbing sphere, 26–27, 38–41, 47; with drift, 48–51, 94, 134–138
- diffusion coefficient: of disk, ellipsoid, 56–58; of small molecule in air, 16; of small molecule in water, 10, 16, 142; of sphere, 56, 83, 142; rotational, definition of, 81–83; translational, definition of, 10, 18–19
- diffusion equation: derivations,

150—Index

- diffusion equation (*cont.*)
 - 17–21, 50–51; including drift, 50–51; steady-state solutions of, 25–36, 38–39, 41–42; time-dependent solutions of, 21–25, 131–133
- diffusion resistance, 31–36
- disk: diffusion to, 27–28, 30–33, 36; viscous drag on, 56–58, 84–85
- distribution, *see* binomial distribution; Boltzmann distribution; Gaussian distribution; Poisson distribution; Poisson interval distribution
- DNA: diffusion of repressor along, 44–45; separation of, 64, 74
- drag, *see* viscous drag
- drift, random walk with, 48–50, 94, 137–138
- droplet, viscous drag on, 56
- effective mass: definition of, 58; of a sphere, 62
- Einstein-Smoluchowski relation, 49, 71–72
- electrical analogue: for diffusion current, 29, 31–34; for mean time to capture, 46
- electrical potential, across membrane, 139–141
- electrophoresis, 62–64, 74
- ellipsoid: diffusion to, 29; viscous drag on, 56–58, 84–85
- equilibrium: distribution, 65–70, 135–136; sedimentation, 72–74
- error function, 22–23
- escape, *see* capture
- Escherichia coli*, *see* chemotaxis; motility
- expectation value, *see* mean value
- Fermi-Dirac statistics, 70
- Fick's equation, *see* diffusion equation
- fish, Reynolds number of, 76
- flagellum, *see* propulsion
- flow, *see* viscous flow
- flux: of bacteria, 135–138; of diffusing particles, 17–21; of ions, 139–141
- frictional drag coefficient, rotational: definition of, 82; of disk, ellipsoid, sphere, 83–85
- frictional drag coefficient, translational: definition of, 49; of bubble, disk, droplet, ellipsoid, sphere, 56–58
- Gaussian distribution, 14–16, 22, 73, 121–123
- gel, 64
- Goldman equation, 140
- heat equation, 21
- ion: electrophoresis of, 62–64, 74; isoelectric focusing of, 74; movement across membrane of, 139–141
- isoelectric focusing, 74
- kinetic energy, 5, 71, 81
- kT , 5, 70–71, 81, 142
- Laplace equation, 35, 47, 131
- Laplacian, 21
- leaves, *see* stomata
- lysozyme, 5, 14, 58, 101
- mean value: definition of, 114–115; of velocity of molecules during chromatography, 99, 105, 107. *See also* binomial distribution; Gaussian distribution; Poisson distribution; Poisson interval distribution
- mean-square: angular displacement, 82, 143; displacement, 9–10, 142; velocity, 5, 71. *See*

- also* root-mean-square
- membrane: movement of bacteria
 - across, 136–138; movement of ions across, 139–141; potential, 139–141
- methylcellulose, 53
- micropipette, as a point source, 22–23
- motility, bacterial, 75–86, 91–94, 134–138
- mutually exclusive outcomes, 111

- Nernst potential, 141
- normal curve of error, 122–123
- normal distribution, *see* Gaussian distribution
- numerical methods for solving differential equations, 131–133. *See also* simulation

- ordinary differential equations, *see* differential equations

- partial differential equations, *see* differential equations
- partition: chromatography, 100–101; coefficient, 96
- pH gradient, 74
- pheromones, detection of, 34
- pipe: diffusion in, 23–25, 131–133; flow through thin rectangular, 53–54
- plating bacteria, 90
- point source, diffusion from, 22–23
- poise, units, 52
- Poisson: distribution, 88–89; 123–124; equation, 46, 131; interval distribution, 87–88
- polyacrylamide, 64, 100
- power, to push cell, 77
- pressure, driving flow, 53–54
- probability: classical or a priori, 111; conditional, 112; distributions, 113–118; of capture, 37–42, 46–47; machine, 117
- propulsion, flagellar, 78–79

- radioactive decay, 90–91
- random changes in direction, 85–86, 93–94
- random walk: biased, 50, 94, 97, 134–138; computer simulation of, 11–12, 68, 91–92, 104; in one dimension, 6–7, 48–50, 81–82; in two, three dimensions, 11–12, 81, 83–84, 91–92; rotational, 81–82; step length, 14; step rate, 14; with drift, 48–50
- receptors: bacterial, 134; diffusion to, 30–33
- resistance, diffusion, 31–36
- Reynolds number, 75–76
- ribosome, 59, 63
- root-mean-square: displacement, 9–10; velocity, 5, 60. *See also* mean-square
- rotational diffusion, 81–85
- runs, bacterial, 80–81, 86, 91–94, 134–136

- S*, units, 59
- scale height, 67, 103
- Schlieren optics, 61
- sedimentation: equilibrium, 65–68, 72–74, 102–103; field-flow fractionation, 102–105; rate, 58–62
- separation: by countercurrent distribution, 95–100; by density-gradient sedimentation, 73–74; by electrophoresis, 62–64; by isoelectric focusing, 74; by partition chromatography, 100–101, 106–109; by sedimentation field-flow fractionation, 102–105; by sedimentation rate, 58–62; criterion for, 97–

152—Index

- separation (*cont.*)
 - 98; of variables, 126–127
- simulation: of bacterial motion, 91–92; of diffusion in Boltzmann distribution, 68; of diffusion in field-flow fractionation, 104; of diffusion in finite pipe, 131–133; of elution profiles in field-flow fractionation, 105; of Poisson process, 91; of random walk, 11–12, 68, 91–92, 104; of successive trials, 117
- sodium dodecyl sulfate, 64
- source, diffusion from: planar, 18–19, 34–35, 41–42; point, 22–23; spherical, 38–39
- sphere: adsorbing, 26–27, 38–41, 47; diffusion coefficient of, 56, 83, 142; effective mass of, 62; probability of capture by, 38–41, 47; sedimentation rate of, 62; viscous drag on, 55–56, 83, 142; with disk-like adsorbers, 30–33
- standard deviation: definition of, 115; of velocity of molecules during chromatography, 99, 106–108. *See also* binomial distribution; Gaussian distribution; Poisson distribution; Poisson interval distribution
- statistical independence, 112
- stomata, diffusion through, 36
- stoke, units, 52
- Stokes' law, 55
- sucrose gradient, 15, 60–61, 64, 125–128, 131–133
- Svedberg equation, 59
- torque: on a flagellar filament, 78–79; on a particle in a viscous medium, 82; on a swimming cell, 78
- tumbles, bacterial, 80–81, 86, 91–94, 134–136
- variance, *see* standard deviation
- viscosity coefficient: definition of, 52; of air, water, glycerol, 52–53
- viscous drag: on a bubble, 56; on a disk, 56–58, 84–85; on a droplet, 56; on a flagellar filament, 78–79; on a sphere, 55–56, 83, 142; on a swimming cell, 78; on an ellipsoid, 56–58, 84–85
- viscous flow: around a sphere, 54–55; basic equation for, 54; through a thin rectangular channel, 53–54
- viscous shear, 51–53, 55, 75