Physical Biology of the Cell Erratum

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Biological Structures: Rulers at Many Different Scales

Page 34, second to last paragraph, after eqn. 2.5. The paragraph should read: "Here we use the fact that $1 L = 10^{15} \mu m^3$. This result could have been obtained even more easily by noting yet another simple rule of thumb, namely, that one molecule per *E. coli* cell corresponds roughly to a concentration of 2 nM."

Page 43, sentence before eqn. 2.8. The sentence should read: "The packing fraction (defined as the ratio of the volume taken up by the genome to the volume of the nucleus) associated with the yeast genomic DNA can be estimated by evaluating the ratio".

Figure 2.32, page 67. The caption should read: "Illustration of a complex network of cells formed by neurons. GFP fluorescence is used to label a collection of neurons from the brain of a rat. Particular neurons were targeted using lentiviruses. (Adapted from M. Brecht et al., *J. Neurosci.* 24:9223, 2004.)"

Brecht at al. reference, page 73. The correct reference is "Brecht, M, Fee, MS, Garaschuk, O, et al. (2004) Novel approaches to monitor and manipulate single neurons in vivo, J. Neurosci., 24(2), 9223."

$4 CHAPTER \ 2. \ BIOLOGICAL \ STRUCTURES: RULERS \ AT MANY \ DIFFERENT \ SCALES$

When: Stopwatches at Many Scales

Figure 3.1, page 76. The correct figure is shown below.

Figure 3.6, page 86. The caption should be replaced by "Universal phylogenetic tree. This diagram shows the similarity among ribosomal RNA sequence for representative organisms from all major branches of life on Earth. The ribosome is made up of different subunits which migrate at different rates during centrifugation."

Third sentence, page 114. The size of the *X. laevis* genome should read "3100 Mbp".



Figure 3.1: Gallery of biological time scales. Logarithmic scale showing the range of times scales associated with various biological processes. The time scale is in seconds.

Who: Bless the Little Beasties

Figure 4.7, page 129. The caption should read: "Electron micrograph of the T4 (large) and ϕ 29 (small) bacteriophage. (Adapted from S. Grimes et al., *Adv. Virus Res*/ 58:255, 2002.)"

Experiments on Phage and Their Bacterial Hosts Demonstrated That Natural Selection Is Operative in Microscopic Organisms, page 130. The third sentence in the third paragraph should read: "If the resistance was induced, they reasoned that if they diluted some original culture into several different cultures and infected them with phage, roughly the same number of resistant colonies should be found per culture."

Mechanical and Chemical Equilibrium in the Living Cell

Estimate: The Energy Budget Required to Build a Cell, page 179, last paragraph. The sentences "Comparing the total amount of biosynthetic energy required by adding up all of the components in Table 5.2, about 10^{10} ATP equivalents are required or about 6×10^8 molecules of glucose. Thus, it requires about one-third as much glucose just to pay for labor as it does to provide the actual building materials for constructing a new cell." should read as follows: "Comparing the total amount of biosynthetic energy required by adding up all of the components in Table 5.2, about 10^{10} ATP equivalents are required or about 3×10^8 molecules of glucose. Thus, it requires about one-fifth as much glucose just to pay for labor as it does to provide the actual building materials for constructing a new cell."

Problem 5.5, page 212. A new sentence in a new line should be added to the bottom end of this problem saying "(This problem was adapted from Ralph Baierlein, Thermal Physics, Cambridge University Press, 1999.)"

$10 CHAPTER \ 5. \ MECHANICAL \ AND \ CHEMICAL \ EQUILIBRIUM \ IN \ THE \ LIVING \ CELL$

Entropy Rules!

6.1.1 A First Look at Ligand-Receptor Binding, page 219. The last sentence on the page should read: "The neat feature of this situation is that although there are many realizations of each class of state, the Boltzmann factor is the same for each realization of these classes of state as shown in Figure 6.4." Math Behind the Models, page 229. The fist sentence should read: "The Boltzmann formula is the foundation of statistical mechanics. It relates the probability of a microstate to its energy, $p_i = e^{-\beta \varepsilon_i}/Z$." Last equation, page 231. The identity should read

$$\left(\frac{N+n-1}{N}\right)^{-m} = e^{-m\ln[(N+n-1)/N]}.$$

Two-State Systems: From Ion Channels to Cooperative Binding

Line 16, page 262. The equation for the change in the outer radius should read as follows

$$\Delta R_{out} \approx (R/R_{out})\Delta R$$

Equation 7.29, page 271. The equation should read as follows

$$Z = \underbrace{1}_{\text{unoccupied}} + \underbrace{e^{-\beta(\varepsilon-\mu)} + e^{-\beta(\varepsilon-\mu)}}_{\text{single occupancy}} + \underbrace{e^{-\beta(2\varepsilon+J-2\mu)}}_{\text{both sites occupied}}.$$
 (7.29)

Problem 7.5, page 279. The equation in part (c) should read

$$\left(\frac{[O_2]}{K_{O_2}}\right)^{n_{O_2}} \left(\frac{K_{CO}}{[CO]}\right)^{n_{CO}} = 1.$$

14CHAPTER 7. TWO-STATE SYSTEMS: FROM ION CHANNELS TO COOPERATIVE BINDING

Random Walks and the Structure of the Macromolecules of the Cell

Page 285. The title of the first section on this page should read: "The Probability of a Given Macromolecular State Depends Upon Its Microscopic Degeneracy"

Figure 8.3, page 285. The correct figure is shown below.

Sentence after eqn. 8.15, page 287. The sentence should read: "Note that the derived approximate formula is a probability for values of R which come in multiples of 2a, since R is either always an even or odd multiple of 2a, depending on whether N is even or odd."

Eqn. 8.26, page 290. The equation should read

$$\langle \mathbf{R}^2 \rangle = \left\langle \int_0^L \mathrm{dst}(s) \cdot \int_0^L \mathrm{dut}(u) \right\rangle.$$
 (8.26)

Sentence before "Estimate", page 294. The sentence should read: "Tethering scenarios posit that chromosomes have particular physical locations because they are held there by tethering molecules. Possible tethering scenarios are shown in Figure 8.9."

Eqn. 8.38, page 300. The equation should read

$$P(x) = \sqrt{\frac{1}{2\pi N a^2}} e^{-(x-x_0)^2/2Na^2}.$$
(8.38)

Equation 8.46, page 302. The equation should read as follows

$$\sum_{n=1}^{\infty} \frac{\mathrm{d}A_n(N)}{\mathrm{d}N} \sin\left(\frac{n\pi}{L}x\right) = -\frac{a^2}{2} \sum_{n=1}^{\infty} A_n(N) \left(\frac{n\pi}{L}\right)^2 \sin\left(\frac{n\pi}{L}x\right).$$
(8.46)



Figure 8.3: Random walk configurations. The schematic shows all of the allowed conformations of a polymer made up of three segments $(2^3 = 8 \text{ conformations})$ and their corresponding degeneracies.

Equation 8.47, page 302. The equation should read as follows

$$\frac{\mathrm{d}A_m(N)}{\mathrm{d}N} = -\frac{a^2}{2} \left(\frac{m\pi}{L}\right)^2 A_m(N). \tag{8.47}$$

Second to last sentence, page 304. The sentence should read: "Fourier coefficients are computed using eqn 8.54, and we find $a_0 = 1$, $a_n = 0$ for any other value of n, $b_n = 0$ for n even, and $b_n = 2/(\pi n)$ for n odd."

Sentence after eqn. 8.59, page 307. The sentence should read: "Since we are interested in cyclization we can assume that the distance δ is much smaller than the polymer size, $N^{1/2}a$."

Figure 8.28. The reference in the caption should read: "Adapted from P. D. Thomas and K. A. Dill, *Proc. Natl Acad. Sci.* 93:11628, 1996"

Electrostatics for Salty Solutions

Equation 9.18, page 336. The equation should read as follows

$$\frac{\partial E_x(x,y,z)}{\partial x} + \frac{\partial E_y(x,y,z)}{\partial y} + \frac{\partial E_z(x,y,z)}{\partial z} = \frac{\rho(x,y,z)}{D\epsilon_0}.$$
 (9.18)

Eqn. 9.39, page 341. The equation should read as follows

$$U = k_B l_B \frac{8R^3}{r^4}.$$
 (9.39)

Figure 9.16, page 347. The correct figure is shown below.



Figure 9.16: Charged membrane in a salty solution. The presence of the charged membrane sets up a nonuniform distribution of positive and negative ions in the vicinity of the membrane. The density of counterions is increased in the vicinity of the membrane, while the density of like-charged ions is decreased. The graphs show the number density and electric potential as a function of the distance from the membrane.

Beam Theory: Architecture for Cells and Skeletons

Equation 10.9, page 363. The equation should read

$$E_{bend} = \frac{K_{eff}}{2} \int_0^L \left| \frac{\mathrm{d}\mathbf{t}}{\mathrm{d}s} \right| \mathrm{d}s, \qquad (10.9)$$

because \mathbf{t} is a vector.

Line 2 after equation 10.29, page 371. The sentence should read: "This follows because $\Delta S_{loop} = S_{loop} - S_{total} = k_B \ln(W_{loop}/W_{total})$, and W_{loop}/W_{total} is nothing more than $p_0,...$ "

Figure 10.16, page 376. The label of the x-axis should read " $L^{-1/2}$ (nm^{-1/2})". Sentence after equation 10.45, page 379. The first equation should read as follows: " $p(d_s) = -dG_{charge}/dV$ ".

Equation 10.46, page 379. The equation should read as follows

$$f(d_s) = -\frac{\mathrm{d}\nu(d_s)}{\mathrm{d}d_s} = \frac{1}{\sqrt{3}}p(d_s)d_s.$$
 (10.46)

Sentence after equation 10.51, page 382. The equation should read: "Hence, the total volume taken up by the 10^7 histones is $\sim 2.3 \times 10^9$ nm³ which should be..."

Sentence before equation 10.53, page 383. The sentence should read as follows: "In light of eqn 10.8, the energy stored in each turn of the DNA by virtue of its deformation is given by".

Equation 10.54, page 383. The equation should read as follows:

$$G_{DNA-histone} = 4\pi R_{DNA}\gamma_{ad}, \qquad (10.54)$$

Line 15, page 384. The sentence should read "... to its target site as a two-step process: first the DNA...".

Figure 10.32, page 394. The correct figure is shown below.



Figure 10.32: Schematic of the buckling process. (A) A beam of length L is loaded at the ends with compressive forces. At sufficiently large forces, the beam undergoes buckling. (B) Geometric parameters used to characterize the buckling process.

Equation 10.66, page 395. The equation should read as follows

$$E_{tot} = \underbrace{\frac{\xi_p k_B T}{2} \frac{L}{R^2}}_{\text{elastic energy}} - \underbrace{F(L-x)}_{\text{loading device}}, \qquad (10.66)$$

Equation 10.86, page 402. The equation should read

$$E_{tot} = \frac{Lk_BT}{2} \sum_{w} \left((\xi_p w^2 + f) |t_x(w)|^2 + |t_y(w)|^2 \right).$$
(10.86)

Problem 10.1(d), page 403. The tangent-tangent correlation function should read $\langle \mathbf{t}(s) \cdot \mathbf{t}(0) \rangle = e^{-\theta(s)^2/2}$ because \mathbf{t} is a vector.

Biological Membranes: From the Golgi Apparatus to Membrane Fusion

Line 43, page 425. "cristae junctions" should be replaced with "crista junctions".

Sentence after equation 11.14, page 427. The sentence should read "Therefore, to determine the area stretch modulus K_a we need to plot the right-hand side of eqn 11.11 against the right-hand side of eqn 11.14 and the resulting slope if K_a .

Third line after equation 11.29, page 438. "crista" should be replaced with "cristae".

Figure 11.42, page 445. The correct figure is shown below.

Figure 11.44, page 449. The label of the y-axis of the plot should read G_{MscL} .

22CHAPTER 11. BIOLOGICAL MEMBRANES: FROM THE GOLGI APPARATUS TO MEMBRANE



Figure 11.42: Deformation energy due to an ion channel. Schematic showing how to take a one-dimensional elastic problem for an ion channel and to turn it into a two-dimensional membrane deformation problem for a cylindrical (approximately) membrane protein such as MscL. (A) Geometry of the onedimensional problem. (B) Wrapping the one-dimensional solution to create a deformed annulus. (C) The final deformed configuration showing the annulus of deformed material.

The Mathematics of Water

Equation 12.14, page 463. The equation should read

$$\Delta m \mathbf{a} = \delta \mathbf{F}^p + \delta \mathbf{F}^\nu, \tag{12.14}$$

Problem 12.4(a), page 478. The statement should read: "Show that the drag coefficient for a sphere of radius R rotating at angular velocity ω is given by $K\eta R^3$, where K is a numerical factor. For rotational motion the drag coefficient relates the angular velocity to the frictional torque. Use the approach that led to the Stokes formula in the chapter. The idea is to say that the size of the viscous stresses is $\nu/R = \omega$, the area over which they act is R^2 . Combine these two to get the force, and then the torque."

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Random Walks: A Statistical View of Biological Dynamics

Line after equation 13.21, page 495. The sentence should read: "we can write eqn 13.20 as".

Line 10, page 497. The sentence should read "The width of the Gaussian is $\sqrt{2Dt}$ and hence, it increases as the square-root of the time."

Last paragraph, page 508. The first five sentences from "The condition in eqn 13.76..." to "...we have a situation almost as good as a fully adsorbing surface?" should be replaced with: "These results raise an interesting biological question. What we learn is that decorating a cell surface with too many receptors adds nothing further to the ability of that surface to take on board further ligands. To state this issue more precisely, we ask: how many receptors do we need before we have a situation almost as good as a fully adsorbing surface?" Equation 13.82, page 509. The equation should read as follows

$$1 \ \mu M = 6 \times 10^{23} \times 10^{-6} \ L^{-1} = 600 / \mu m^3.$$
 (13.82)

Problem 13.7, page 512. The equation should read as follows

$$I = \frac{4\pi Dac_{\infty}}{1 + \frac{\pi a}{Ns}}$$

26 CHAPTER 13. RANDOM WALKS: A STATISTICAL VIEW OF BIOLOGICAL DYNAMICS

Life in Crowded and Disordered Environments

Equation 14.3, page 521. The equation should read

$$p_{bound} = \frac{1}{1 + \frac{\Omega - L - C}{L} e^{\beta \Delta \varepsilon_L}}.$$
(14.3)

Equation 14.34, page 533. The equation should read

$$S_{rw} = \frac{3}{2}k_B,$$
 (14.34)

28CHAPTER 14. LIFE IN CROWDED AND DISORDERED ENVIRONMENTS

Rate Equations and Dynamics in the Cell: Cytoskeleton Under Construction

Line 9, page 573. The sentence should read "Starting with a solution of monomers, if the concentration is above c^* , then the filaments will grow, but below c^* they will shrink."

Equation 15.87, page 575. The equation should read as follows

$$t = \frac{1 \ \mu \text{m}^2}{2 \left(\underbrace{\frac{4}{1000} \ \mu \text{m}}_{a}\right)^2 1 \ s^{-1}} \approx 9 \text{ hours.}$$
(15.87)

Last sentence of first paragraph, page 580. The sentence should read as follows: "The plus end has a faster growth rate than the minus end, and also a faster shrinkage rate."

Figure 15.31, page 581. The correct figure is shown below.



Figure 15.31: Growth rate for the case where the rates for each end of the filament are different. Above the critical concentration (c^*) , both ends grow and below the critical concentration, both ends shrink.

Dynamics of Molecular Motors

Figure 16.13, page 601. The caption should read "Examples of rotary motors. (A) The bacterial flagellum is like a tiny propeller driven by the gradient of hydrogen ions across the bacterial inner membrane..."

Figure 16.14, page 602. The caption should read "... In a few cases, multiple helical forms can be seen attached to the same bacterium resulting in frayed bundles..."

Line 9, page 603. The sentence should read "... the host cytoskeleton to drive their motility."

Line 12, page 604. The sentence should read "... the DNA template contributes to pulling the viral genome into the host cell."

Figure 16.32, page 617. The caption should read "... This can occur either while the motor remains stationary with respect to the filament (with rate constant k_B) or while the motor takes a single step backwards (with rate constant k_A)..."

First paragraph, page 630. The first sentence of the paragraph should read "As discussed in the previous chapter, the dissociation constant is equal to the monomer concentration m^* at which the average filament length is not changing in time."

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Biological Electricity and the Hodgkin-Huxley Model

Second sentence, second paragraph, page 660. The sentence should read "As we saw in Chapter 16, skeletal muscle myosin heads cannot actually bind to acting until Ca²⁺ ions have bound to troponin, displacing it from its position masking the myosin binding sites (this was shown in Figure 16.38 on p. 625)". Line 25, page 662. The equation in that line should read $C_{area} = C/A_{patch} \approx 0.4 \ \mu F/cm^2$.

Line 33, page 662. The equation should read $C_{area} = 1 \ \mu F/cm^2$. Equation 17.8, page 662. The equation should read

$$\Delta Q \approx \Delta V_{mem} C_{area} \times 2\pi r l = 10^{10} e/\mathrm{cm} \times l. \tag{17.8}$$

34CHAPTER 17. BIOLOGICAL ELECTRICITY AND THE HODGKIN-HUXLEY MODEL

Sequences, Specificity and Evolution

Equation 18.10, page 696. The equation should read

$$p(x) = \kappa \lambda e^{-\lambda x - \kappa e^{-\lambda x}}.$$
(18.10)

Figure 18.13, page 707. In the caption, after the sentence "JH2 has four new mutations, but the first mutation has reverted." the following sentence should be added: "The antibiotic susceptibility testing of the individual isolates shows that bacteria in the patient developed resistance to the three classes of antibiotics that had been used during treatment, rifampin, vancomycin, and beta-lactams (including imipenem and oxacillin). Interestingly the later isolates were also resistant to daptomycin, although this class of antibiotic had not been used to treat the patient."

Section 18.3.4, page 708. The fist paragraph should read: "One of the key ideas stemming in part from the molecular analyses of evolution is the formulation of a *universal* tree of life. The idea behind a bioinformatic investigation of the tree of life was to find a deeply conserved but slowly varying set of genes that are common to all life forms and to measure their sequence excursions over evolutionary time scales. To that end, the RNA structural content of the ribosome has served as a superb gold standard, because all living organisms have ribosomes with roughly similar structures, and it is widely accepted that the last common universal ancestor of all life on Earth must have used ribosomes that were comparable to the modern forms. By analyzing the ribosomal RNA genes from a broad variety of organisms, it is possible to classify them on the basis of their sequence similarity. Examples of these different sequences are shown in Figure 18.15."

Figure 18.19, page 714. The correct figure is shown below High Specificity Costs Energy, page 716. Eqns. 18.25 and 18.26 need to



Figure 18.19: Plot of the error rate as a function of the difference in free energy of binding. When the tRNA binds to the mRNA there is a favorable free energy of binding. If the anticodon on the tRNA is not the correct partner of the codon on the mRNA, there is a less favorable binding free energy. The plot shows how the error rate depends upon the free-energy difference between the binding of the correct and incorrect tRNA.

be replaced by

$$R + T_{corr} \underset{k_{-}^{(1)}}{\overset{k_{+}^{(1)}}{\underset{k_{-}^{(2)}}{\overset{k_{+}^{(2)}}{\underset{k_{-}^{(2)}}{\overset{k_{-}^{(2)}}{\underset{k_{-}^{(2)}}{\underset{k_{-}^{(2)}}{\overset{k_{-}^{(2)}}{\underset{k_{-$$

and

$$R + T_{err} \xrightarrow{p_{+}^{(1)}}_{p_{-}^{(1)}} RT_{err} \xrightarrow{p_{+}^{(2)}}_{p_{-}^{(2)}} \qquad RT_{err}^{*} \rightarrow \text{elongation} \qquad (18.26)$$

$$\downarrow p_{d}$$

$$R + T_{err}.$$

Eqns. 18.27 through 18.29 are then changed to

Finally, eqn. 18.30 needs to be replaced by

$$f = \frac{k_{-}^{(1)}k_{-}^{(2)} + k_{-}^{(1)}k_d + k_{+}^{(2)}k_d}{p_{-}^{(1)}p_{-}^{(2)} + p_{-}^{(1)}p_d + p_{+}^{(2)}p_d}.$$
(18.30)

Page 720, Further Reading. The reference to Dobzhansky should read: "Dobzhansky, T (1973) Nothing in biology makes sense except in the light of evolution, *American Biology Teacher* **35**, 125. A fascinating article that examines evolution from a variety of different angles."

Biological Networks: The Organization of Regulation and Signaling in Space and Time

Fig. 19.6. The caption should read: "Examples of repressor molecules interacting with DNA. From top to bottom the relevant repressors are: TetR (pdb 1QPI), IdeR (pdb 1U8R), FadR (pdb 1HW2), and PurR (pdb 1PNR). The point of the figure is to give an impression of the relative sizes of repressors and their target regions on DNA and to illustrate how these transcription factors deform the DNA double helix in the vicinity of their binding site. These drawings are renditions of actual structures from X-ray crystallography. (Courtesy of D. Goodsell.)"

Eqns. 19.7 and 19.8, pages 733 and 734. The equations should read

fold change =
$$\frac{p_{bound}(A \neq 0)}{p_{bound}(A = 0)} = \frac{1 + (N_{NS}/P)e^{\beta\Delta\varepsilon_{pd}}}{1 + (N_{NS}/PF_{reg}(A))e^{\beta\Delta\varepsilon_{pd}}}$$
 (19.7)

and

fold change
$$\approx F_{reg}(A)$$
. (19.8)

Fig. 19.12, page 734. The correct figure is shown below



Figure 19.12: Fold change due to activators. Fold change in gene expression as a function of the number of activators for different activatorRNA polymerase interaction energies using P = 500, $\Delta \varepsilon_{pd} = -5.3 k_B T$ and $\Delta \varepsilon_{ad} = -13.12 k_B T$ based on *in vitro* measurements.

Fig. 19.26, page 749. The correct figure is shown below.



Figure 19.26: Regulatory architecture for a genetic switch. There are two promoters which are under the transcriptional control of the gene product of the partner promoter.

First paragraph of page 751. The end of the paragraph should read: "Therefore there is the possibility that the two curves x and f(f(x)) intersect at more than one point, leading to multiple steady states. The detailed stability analysis is performed in the appendix at the end of the chapter."

Figure 19.28, page 752. The y-axis of the plots should be labeled "u" and their x-axis should be labeled "v".

First sentence after eqn. 19.45, page 754. The sentence should read: "For simplicity, we have chosen the rate constants for protein and mRNA degradation $(K_p \text{ and } K_m)$, as well as the rate constants associated with mRNA transcription (γ) , translation (T), repressor binding (K_b) , and the leakiness of the repressor $(gamma_0)$, to be the same for all three species." Note: This error is also present in the 2nd printing of the book.

Eqns. 19.52, page 755. The equation should read

$$X = -\frac{\alpha n m^{n-1}}{\left(1 + m^n\right)^2}.$$
(19.52)



Fig. 19.31, page 758. The correct figure is shown below.

Figure 19.31: Solution to the dimensionless repressilator equations. (A) Stability diagram showing the parameter regions for which the steady state solutions are stable. (B) Time evolution of protein concentrations for three choices of parameters. In the top figure $\alpha = 5.0$ and $\beta = 1.0$. In the middle figure, $\alpha = 5.0$ and $\beta = 5.0$. In the bottom figure, $\alpha = 3.0$ and $\beta = 1.0$. In all three cases we use a Hill coefficient n = 2 and $\alpha_0 = 0$. The initial conditions in all three cases are $m_1 = 0.2$, $m_2 = 0.1$, $m_3 = 0.3$, $p_1 = 0.1$, $p_2 = 0.4$ and $p_3 = 0.5$. (C) Relation between mRNA concentration and protein concentration as well as an expanded view of concentrations for all three proteins.

Second sentence after eqn. 19.89, page 771. The sentence should read: "The essence of the analysis is to examine the sign of the parameter λ ."