BE/APh161: Physical Biology of the Cell
Homework 2
Due Date: Wednesday, January 21, 2026

"Whatever you can do or dream you do, begin it. Boldness has genius, power and magic in it." - William Hutchison Murray in his 1951 book The Scottish Himalayan Expedition

This second problem set follows the same spirit of the first problem set by asking you to continue your skills as an order-of-magnitude thinker. As before, when doing street fighting estimates, the goal is to do simple arithmetic of the kind that all numbers take the values 1, few (f) or 10. few $\times$ few = 10, etc. Please do not provide estimates with multiple "significant" digits that are meaningless. Be thoughtful about what you know and what you don't know. You may use the Bionumbers website (http://bionumbers.hms.harvard.edu/) to find key numbers (examples are masses of amino acids (BNID 104877) and nucleotides (BNID 103828), the speed of the ribosome (BNID 100059), etc.), but please provide a citation to the Bionumber of interest as shown above. However, for many of these problems the essence of things is to do simple estimates, not to look quantities up. In particular, if in doubt, use the square root rule

$$x_{guess} = \sqrt{x_{low} x_{high}}, \tag{1}$$

which instructs us to take a lower and upper bound guess and then to take their geometric mean (which is the same as averaging their exponents). Also, as last time, though we are going to lean into AI in imaginative ways, this is another assignment where I want you to do the opposite of use the devices of the modern world - just use your brain and your own sense of things, no AI.

1. Photons and your eyes: Seeing the North Star.

Polaris has been known to generations of northern hemisphere navigators as a tool for finding latitude by simple geometrical measurements with a sextant. In this problem you are asked to estimate the amount of light reaching our eyes from that famed star. The luminosity of Polaris is roughly 2000 times that of the Sun. Use that the solar irradiance at Earth is about 1000 W/m^2 and that Polaris is at a distance of 430 light years from Earth. For photon-counting estimates, you will need to adopt a typical visible photon energy

(for example, corresponding to a wavelength of order 500–600 nm) and state what you chose.

(a) What is the power output of Polaris?

(b) How many photons cross the pupil of your eye each second coming from this famous star and what is the corresponding mean spacing between photons along the line of propagation (that is, use the mean inter-arrival time and multiply by the speed of light)? For the pupil size, adopt and justify a diameter.

(c) What is the mean rate of arrival of photons to a single cone cell in the eye? State and justify the assumptions you need about how the star's image is distributed on the retina and the effective collecting area associated with a cone. Comment on what your answer implies about how vision works when photon arrivals are sparse. Your eye is not measuring a continuous intensity, it is counting rare events against noise and integrating over time.

(Problem adapted from R. W. Rodieck's 1998 book *The First Steps in Seeing*)

2. Kelvin, Darwin and the Age of the Earth.

One of the great scientific debates of the 19th century was the age of the Earth and the Sun. In that time there was no knowledge of nuclear reactions, and the estimates based on known physics were very troubling for people like Darwin who assumed that life had existed on Earth for times much longer than these estimates would suggest. These estimates, most famously done by Lord Kelvin, also seemed to contradict estimates based on geological evidence, which suggested that the age of the Earth was more than a few hundred million years. This debate with Lord Kelvin really perturbed Darwin as shown in Figure 1.

(a) Assume that the Sun gets its power from burning something like coal. How long until the Sun burns out? Burning any ordinary chemical fuel will give the same order-of-magnitude estimate because chemical energies per unit mass are all of the same rough scale. Use your understanding of food to come up with your estimate of the energy density of fuel in units of J/kg. You will need the Sun's mass $M_\odot \approx 2 \times 10^{30}$ kg and its luminosity $L_\odot \approx 4 \times 10^{26}$ W.

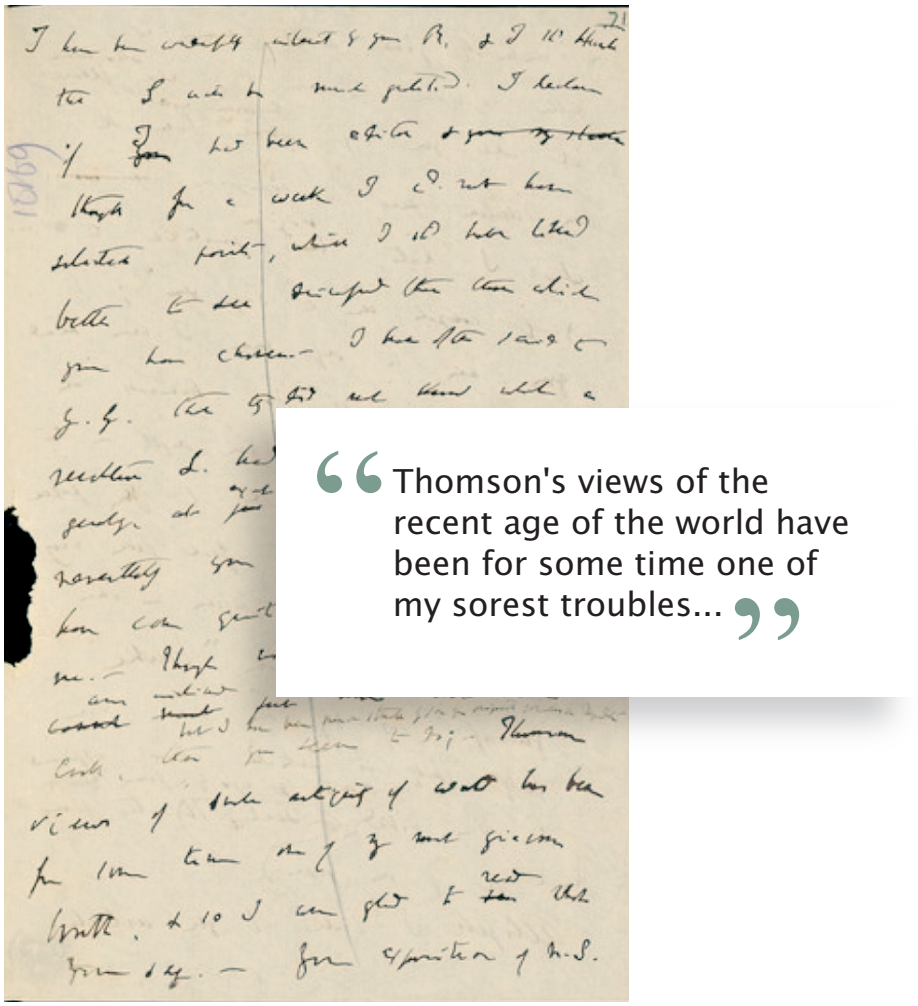

Figure 1: Letter from Charles Darwin to Alfred Russel Wallace in which he acknowledges the troubling implications of Lord Kelvin's estimates on the age of the Earth. Though the handwriting is nearly illegible to my eyes, the phrase “Thomson's views of...” can be found clearly about two-thirds of the way down. The transcription of the letter is given in the main text of this vignette. This letter, numbered DCP-LETT-6706, is housed in the Darwin Correspondence Project and dated 14 April 1869.

(b) Assume that the Sun gets its energy from gravity, the release of gravitational potential energy as it contracts or assembles into a star. The key insight is that this energy can be written simply as

$$E_{\rm grav} = -\frac{3}{5}\frac{GM_{\rm star}^2}{R_{\rm star}}. \tag{2}$$

I love this calculation and if you want extra credit, you can derive it. Otherwise, feel free to use it as an off-the-shelf result. In light of this total energy, how long until the Sun burns out? (This is the Kelvin estimate.) State clearly what you assume for the Sun's radius $R_\odot$ and whether you take the available radiated energy to be $|E_{\rm grav}|$ or some fraction of it.

(c) Provide intuition in a paragraph or less as to why either Darwin or Kelvin could have an opinion about what constitutes a long time or short time. What kinds of evidence, timescales, or physical processes were most salient to each of them?

3. RNA Polymerase and Rate of Transcription.

One of the ways in which we are trying to cultivate a "feeling for the organism" is by exploring the processes of the central dogma. Specifically, I want you to have a sense of the number of copies of the key molecular players in the central dogma as well as the rates at which they operate. Further, I argue that it is critical you have a sense of *how* we know these numbers.

(a) If RNA polymerase subunits β and β' together constitute approximately 0.5% of the total mass of protein in an *E. coli* cell, how many RNA polymerase molecules are there per cell, assuming each β and β' subunit within the cell is found in a complete RNA polymerase molecule? The subunits have a mass of 150 kDa each. State clearly what you use for the total protein mass per cell, for example, based on your estimate from Homework 1. (Adapted from problem 4.1 of Schleif, 1993.)

(b) Rifampin is an antibiotic used to treat *Mycobacterium* infections such as tuberculosis. It inhibits the initiation of transcription, but not the elongation of RNA transcripts. The time evolution of an *E. coli* ribosomal RNA (rRNA) operon after addition of rifampin is shown in Figures 2(A)–(C). An operon is

a collection of genes transcribed as a single unit. Use the figure to estimate the rate of transcript elongation and report your answer in nucleotides per second. Use the beginning of the "Christmas-tree" morphology on the left of Figure 2(A) as the starting point for transcription.

(c) Using the calculated elongation rate estimate the frequency of initiation off of the rRNA operon. Make clear how you estimated the typical spacing between adjacent RNA polymerases along the operon and report your answer in initiations per second. These genes are amongst the most transcribed in *E. coli*.

4. Composition of a cell.

Here we are going to do a rough atomic census of living material by thinking about the principal ingredients of a cell. To get a sense of the chemical makeup of the dry mass of a cell, we are going to focus only on proteins and nucleic acids. Each subpart requires assumptions on your part about cells and their molecular contents. State your assumptions explicitly (with units), give a one-sentence justification (either from memory, intuition, or a cited source such as Bionumbers / Cell Biology by the Numbers), and then carry them through consistently.

(a) Provide a simple and clean estimate for the volume and mass of a typical bacterium such as *E. coli*.

(b) Assume that 1/3 of the mass of a bacterium is dry mass and for simplicity, we ascribe all of that dry mass either to proteins or nucleic acids. We will take our elemental composition of a "typical" amino acid to be $N_1C_5O_2H_8$ and a "typical" nucleotide to be $P_1N_5O_7C_{10}H_{14}$. Given that roughly half the dry mass of the cell is protein, work out the total protein mass in the cell, then estimate the number of protein molecules by adopting and defending a typical protein size (mass or length). From that, infer the number of amino acids per cell.

(c) As an alternative approach to estimating the total number of proteins in *E. coli*, assume that the bacterium is tightly packed with proteins (think of golf balls in a bathtub). How does this compare to the estimate from part (b)? If your two answers differ by more than an order of magnitude, identify

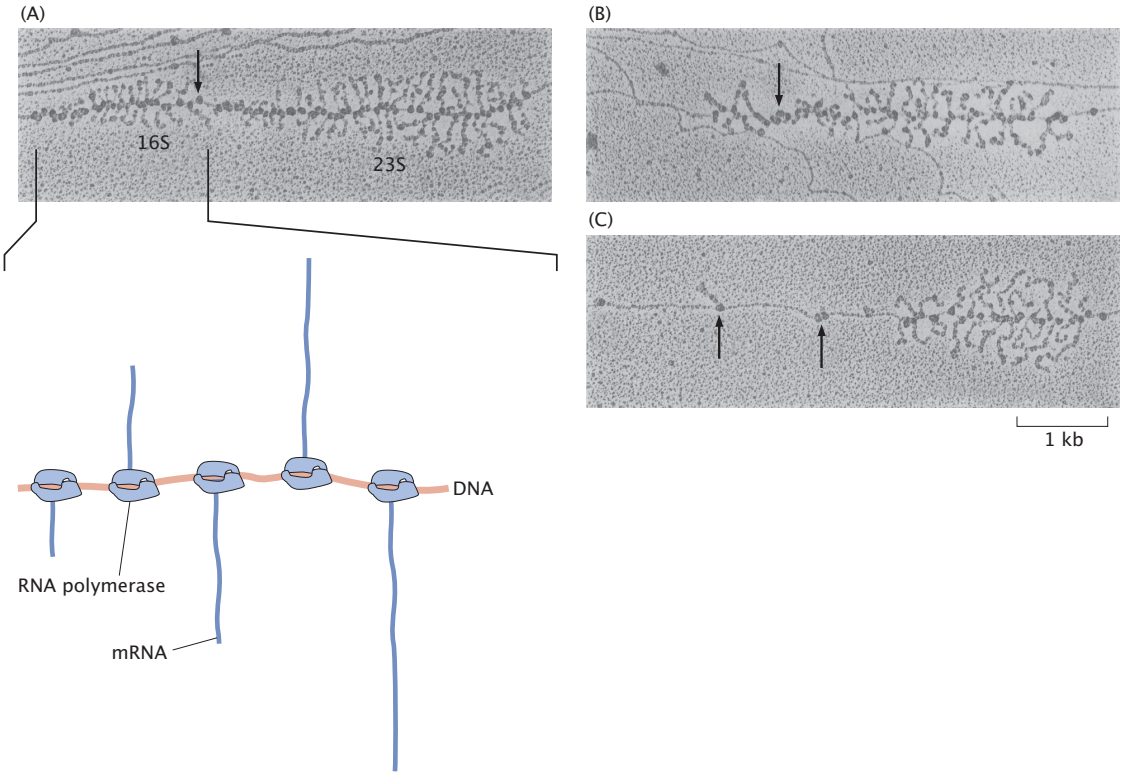

Figure 2: Effect of rifampin on transcription initiation. Electron micrographs of *E. coli* rRNA operons: (A) before adding rifampin, (B) 40 s after addition of rifampin, and (C) 70 s after exposure. No new transcripts have been initiated, but those already initiated are carrying on elongation. In parts (A) and (B) the arrow signifies the site where RNaseIII cleaves the nascent RNA molecule producing 16S and 23S ribosomal subunits. RNA polymerase molecules that have not been affected by the antibiotic are marked by the arrows in part (C). (Adapted from L. S. Gotta et al., *J. Bacteriol.* **173**(20), 6647–6649 (1991).)

which assumption is responsible.

(d) Work out the number of nucleotides in the genome of our bacterium of interest. State clearly whether you estimated this from assumptions about genes or whether you looked up a genome size (and cite your source if you did).

(e) Finally, figure out how many ribosomes are needed, translating at roughly 15 aa per second, to translate all of those proteins required to make a new cell within one division time. State and justify the division time you use. How many nucleotides are present in the ribosomal RNA making up all of these ribosomes?

(f) Given all of these numbers from the rest of this problem, you are now able to work out the overall composition of a cell. Provide an approximate formula for the stoichiometry of a bacterium.

5. A feeling for the complete blood count (CBC) test.

Typical results for a complete blood count (CBC) are shown in Table 1. Assume that an adult has roughly 5 L of blood in his or her body. Choose either the male or female reference values (state which) and use street-fighting arithmetic. Based on these values estimate:

(a) The number of red blood cells. How does this compare to your estimate for the total number of cells in a human body and what does it tell you about how abundant red blood cells are?

(b) The percentage in volume they represent in blood. Do this in two ways: first using the hematocrit value, and second by combining the RBC count with the mean corpuscular volume (MCV). Comment on whether the two agree at the order-of-magnitude level.

(c) Their mean spacing. State the simple geometric model you are using to convert number density into a spacing.

(d) The total amount of hemoglobin in the blood.

Test	**Value**
Red blood cell count (RBC)	Men: $\approx(4.3\text{–}5.7) \times 10^6$ cells/μL
	Women: $\approx(3.8\text{–}5.1) \times 10^6$ cells/μL
Hematocrit (HCT)	Men: $\approx(39\text{–}49)\%$
	Women: $\approx(35\text{–}45)\%$
Hemoglobin (HGB)	Men: $\approx(13.5\text{–}17.5)$ g/dL
	Women: $\approx(12.0\text{–}16.0)$ g/dL
Mean corpuscular hemoglobin (MCH)	$\approx(26\text{–}34)$ pg/cell
MCH concentration (MCHC)	$\approx(31\text{–}37)\%$
Mean corpuscular volume (MCV)	$\approx(80\text{–}100)$ fL
White blood cell count (WBC)	$\approx(4.5\text{–}11) \times 10^3$ cells/μL
Differential (% of WBC):	
Neutrophils	$\approx(57\text{–}67)$
Lymphocytes	$\approx(23\text{–}33)$
Monocytes	$\approx(3\text{–}7)$
Eosinophils	$\approx(1\text{–}3)$
Basophils	$\approx(0\text{–}1)$
Platelets	$\approx(150\text{–}450) \times 10^3$ cell/μL

Table 1: Typical values from a CBC. (Adapted from R. W. Maxwell, Maxwell Quick Medical Reference, Tulsa, Maxwell Publishing Company, 2002.)

(e) The number of hemoglobin molecules per red blood cell. State clearly how you convert from grams of hemoglobin to molecules.

(f) The number of white blood cells in the blood. As an optional extension, use the differential to estimate the counts of neutrophils and lymphocytes.

(g) The number of platelets in the blood. Then, based on your answers, rank RBC, WBC, and platelets by abundance in blood and comment briefly on whether the most abundant "cell" in blood is also the most abundant cell type in the human body.

6. Migration of the bar-tailed godwit

Animal migrations are one of the greatest of interdisciplinary subjects, bringing together diverse topics ranging from animal behavior to the physics of

navigation to the metabolism required for sustained long-distance travel. The bar-tailed godwit is a small bird that each year travels between Alaska and New Zealand on the same kind of incredible nonstop voyage taken by happy tourists in modern long-distance jetliners as shown in Figure 3. During a visit to New Zealand's South Island, one of us had the chance to see these amazing birds in Okarito Lagoon with a naturalist guide who claimed that over the course of their ten-day, ten-thousand kilometer trip, these migratory birds lose 1/3 of their body mass. In this problem, we make a series of simple divide-and-conquer estimates to see whether this claim might be true. State and justify the numerical values you adopt for ρ, v, and L.

(a) Using dimensional-analysis arguments, work out how the drag force experienced by flying godwits depends upon the density of air (ρ), the speed of the birds (v) and the size of the birds (L). Specifically, work out the coefficients α, β and γ in the expression

$$F_{drag} = \mathrm{C}\rho^{\alpha} v^{\beta} L^{\gamma}, \tag{3}$$

where C is a dimensionless constant that we will not consider further.

(b) Work out the power expended by the bar-tailed godwit to overcome the drag force. Then, work out the total energy expended during the ten-day migration in overcoming this drag force. State and justify how you convert from the 10,000 km and 10 day information to an estimate of the flight speed.

(c) Given that burning fat yields 9 kcal/g, work out the number of grams of fat that would need to be burned to sustain the ten day flight of the bar-tailed godwit. Make clear what you assume about conversion efficiency between metabolic energy and mechanical work (for example, treat it as 100% for a lower bound, or adopt a plausible efficiency and state it). What fraction of the bird's body mass would be lost during such a migration based on these estimates, and how does it compare to the claimed 1/3 loss?

7. Real Estate for the Factories of ATP Synthesis

We are captivated by the tension between those things about living organisms that are universal and those things that are baroque and specific to a given organism. One of the nearly universal features of living organisms

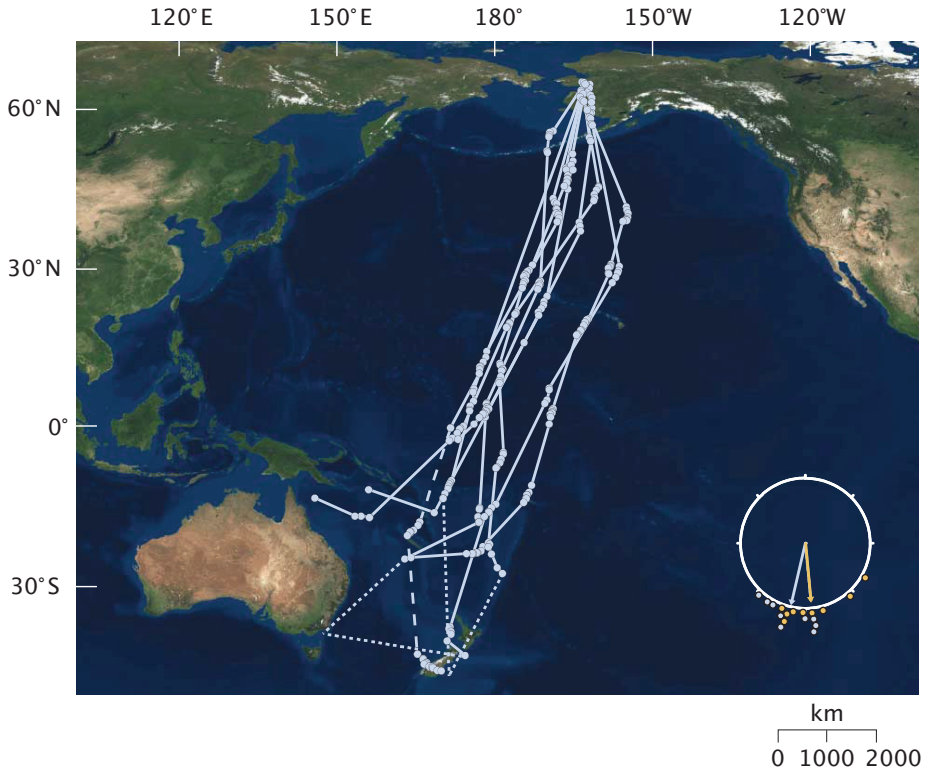

Figure 3: Map showing the migration pattern of the bar-tailed godwit. Adapted from Gill *et al.*, "Extreme endurance flights by landbirds crossing the Pacific Ocean: ecological corridor rather than barrier?", *Proc. Biol. Sci.* 276(1656), 447–457 (2009).

on our planet is their use of ATP hydrolysis as an energy source for a huge variety of processes. A key empirical observation is that many cells operate with a roughly constant ATP demand per unit volume. Where does all of this ATP come from? Cells have tiny molecular machines known as ATP synthase in the membrane which use an ion gradient to drive the rotation of these machines to produce ATP. However, ATP is consumed throughout the volume of cells, but is produced on membranes. This leads to the possibility that as cells get bigger, there may be a point at which the surface area is insufficient to keep up with the demands of the cytoplasmic volume. Indeed, this problem explores the hypothesis that for cells above a certain size, ATP synthesis at the plasma membrane (such as in bacteria) no longer suffices and that a new specialized energy factory (i.e. the mitochondria) is required.

In what follows, keep careful track of two different quantities: a volumetric ATP demand density q with units of ATP/(μm^3 s) and a surface ATP production flux j with units of ATP/(μm^2 s).

(a) By considering the cost of protein synthesis for a dividing bacterium with a fast division time of 1000 s, justify the assertion that the volumetric ATP demand density is of order

$$q \approx 10^6 \frac{\text{ATP}}{\mu m^3 \ s}. \tag{4}$$

State and justify the numerical values you adopt and comment briefly on whether protein synthesis is plausibly a dominant contribution to the ATP budget at the level of order-of-magnitude accuracy.

(b) As shown in Figure 4, estimate the surface ATP production flux j supplied by ATP synthase on a membrane, in units of ATP/(μm^2 s). Your result will depend upon an areal density of ATP synthase (number per μm^2) multiplied by an ATP production rate per synthase (ATP/s). State your assumptions explicitly.

(c) Now consider a spherical cell of radius R whose cytoplasm demands ATP at volumetric rate density q and whose surface can supply ATP at flux j. The total ATP demand is $q(4\pi R^3/3)$ and the total ATP supply is $j(4\pi R^2)$. Use these to compute the maximum radius $R_{\max}$ such that surface ATP production can keep up with volume demand. Express your final result both as

a formula in terms of j and q and as a numerical estimate using your values from parts (a) and (b). Comment on how eukaryotes evade this surface-area limitation.

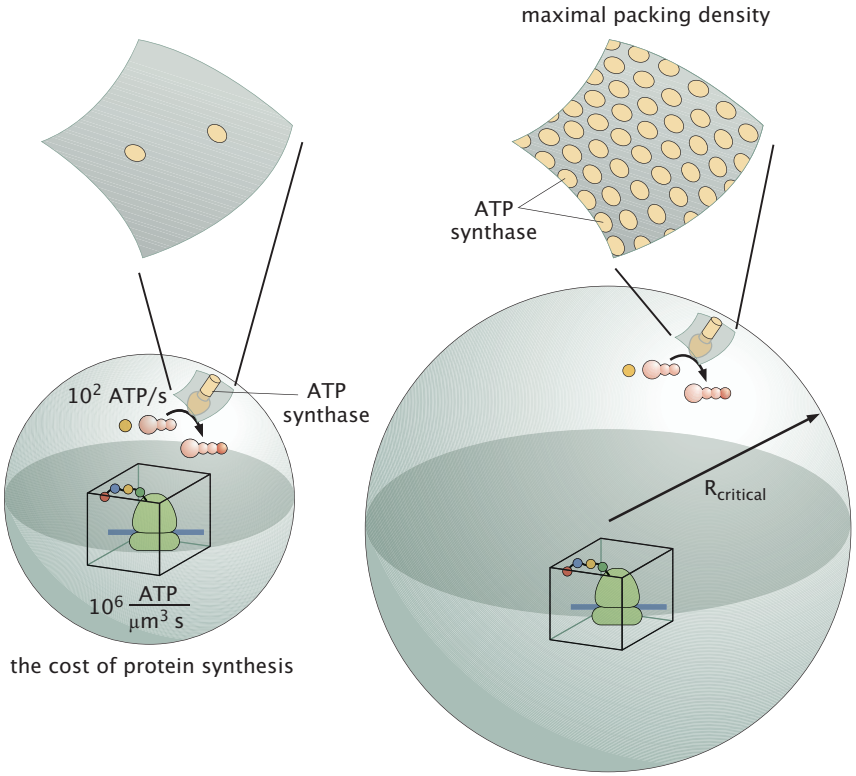

Figure 4: Surface coverage of bacterial cells with ATP synthase. For small cells, the demands of the cytoplasmic power consumption can be met by ATP synthases on the plasma membrane. However, for larger cells, there is not enough surface area to keep up with the demands of the power needs of the cellular interior.