MCB137L/237L: Physical Biology of the Cell
Spring 2025
Homework 3
(Due 2/11/25 at 2:00pm)

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1 Bacteria Taking Over the Earth

Assume that a single *E. coli* cell has all the nutrients it could possibly desire and that it (and all of its descendants) can grow without limit.

(a) How many bacterial cells would it take to make a giant colony that has the same mass as a human?

(b) How long would it take for a single cell to grow into a giant human-sized bacterial colony?

(c) How many bacteria cells would it take to make a giant colony that as the same mass as the Earth?

(d) How long would it take for a single cell to grow into a giant Earth-sized bacterial colony?

(e) How does the number you calculated in part (c) compare to the actual number of bacteria on Earth?

(f) In reality, the number of bacteria on Earth stays fairly constant from day to day and from year to year, rather than increasing exponentially. Briefly explain why this is the case.

2 Growth Curves and the Logistic Equation

Much of our understanding of the natural world is couched in the language of the subject now known as "dynamical systems." In a nutshell, the idea is to write down equations that tell us how some variable(s) of interest change in time. Often, this ends up being written in the form of coupled differential equations. Perhaps the most important and simplest of such

dynamical systems is the law of exponential growth (or decay), relevant to thinking about the early stages of growth of a culture of cells, for example. In this problem, you are going to revisit the discussion I give there by solving for the dynamics of a population of bacterial cells both analytically and numerically.

In class, we discussed the exponential growth equation. This equation has been the basis for the study of microbiology for years (read, for example, F. Neidhardt, *Bacterial Growth: Constant Obsession with dN/dt*, J of Bacteriology 181:7405 (1999) provided on the course website). If the number of cells is given by N and the growth rate is r, then this equation takes the form

$$\frac{dN}{dt} = rN. \tag{1}$$

We solved this equation in a variety of ways, both numerically and analytically, and found a solution given by

$$N(t) = N_0 e^{rt}, \tag{2}$$

where N_0 is the number of cells at $t = 0$.

(a) Of course, the solution shown above cannot be correct forever. For fast-growing *E. coli* estimate how long it would take for a single cell to produce enough progeny to cover the whole surface of the Earth.

A more realistic scenario is to account for the fact that, sooner or later, bacteria will run out of resources and halt their growth. For example, a liquid bacterial culture will saturate at a density of about 10^9 cells/ml. To account for these limited resources, we introduce a growth rate that depends on the number of cells, r_{new}

$$r_{new} = r\left(1 - \frac{N}{K}\right), \tag{3}$$

where K represents the maximum population size. Note that when N is very small compared to K, $r_{new} = r$ and growth is exponential. However, as N approaches K the growth rate will decrease. Thus, we get the so-called logistic equation

$$\frac{dN}{dt} = r_{new}N = rN\left(1 - \frac{N}{K}\right). \tag{4}$$

(b) What is the number of cells at which there is no growth and the population reaches steady state? Justify how you impose steady state on the logistic equation in order to figure out this number.

In class, we wrote pseudocode and then Python code to solve Equation 1 numerically using the so-called Euler method.

(c) Based on your pseudocode for exponential growth, write pseudocode to now solve the logistic equation. Make sure to comment your code appropriately at every step!

(d) Write Python code for your pseudocode. For reasonable choices of r and K, plot number of cells as a function of time for both exponential and logistic growth. Note that we don't want your raw code, just the plots generated by this code.

(e) Feel free to look at section "Computational Exploration: Growth Curves and the Logistic Equation" on page 103 of PBoC2.

3 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 1. A naturalist guide in the Okarito Lagoon in New Zealand's South Island once claimed that over the course of their ten-day, ten-thousand kilometer trip, these amazing 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.

One of the most powerful tools for estimation is dimensional analysis. Here, we will use this type of analysis to estimate the drag force experienced by flying godwits as they migrate. This sort of analysis makes it possible to quickly answer questions such as whether the drag force increases linearly or quadratically with the length of the birds. In dimensional analysis, we amass the various physical parameters that we imagine will dictate the drag force with their attendant units on the right hand side of the equation. In this case, we will consider the density of air (ρ), the speed of the birds (v) and the size of the birds (L, representing the size of the cross-section of the bird). On the left hand side, we have the drag force, resulting in

$$F_{drag} = \mathrm{C}\rho^{\alpha} v^{\beta} L^{\gamma}, \tag{5}$$

where C is a dimensionless constant that we will not consider further. Note that in the equation we have proposed a set of exponents α, β and γ for each variable. The idea of dimensional analysis is to find the exponents that balance the units on each side of the equation as a means to uncover the scaling of the drag force with the various physical parameters we proposed.

(a) Using dimensional-analysis arguments, work out how the drag force experienced by the 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 Equation 5.

(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.

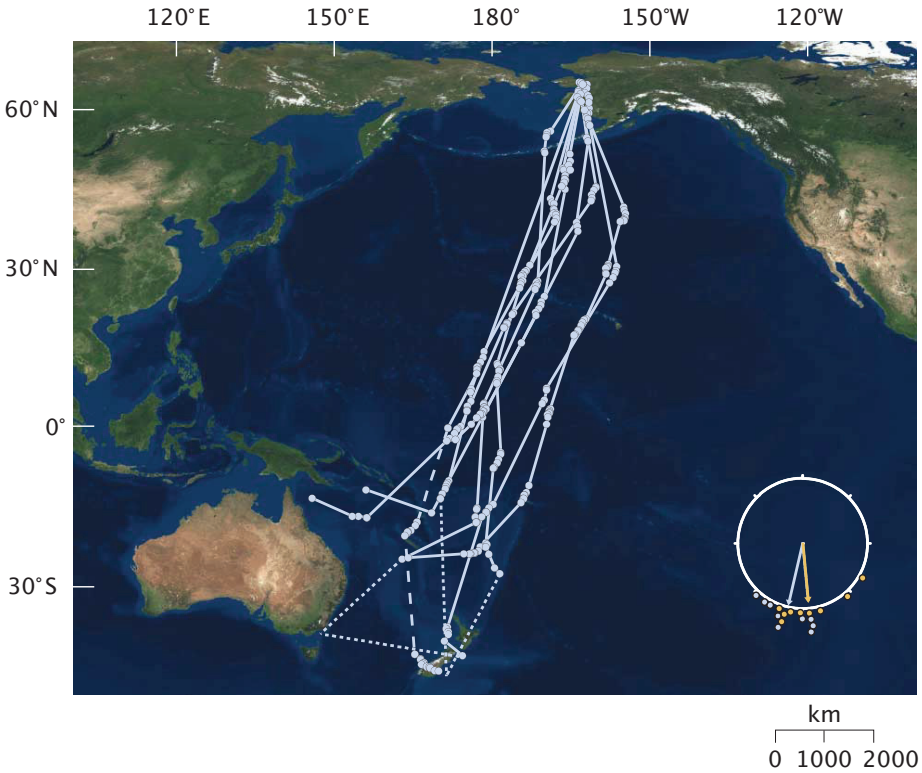

Figure 1: Map showing the migration pattern of the bar-tailed godwit. Adapted from Gill *et al.*, Extreme endurance flights by landbirds crossing the Pacific Ocean: ecological corridor rather than barrier?, Proc Biol Sci. 2009 Feb 7; 276(1656): 447-457.

(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. What fraction of the bird's body mass would be loss during such a migration based on these estimates?

4 Post-Translational Modifications and "nature's escape from genetic imprisonment"

In a very interesting article ("Post-translational modification: nature's escape from genetic imprisonment and the basis for dynamic information encoding"), Prof. Jeremy Gunawardena discusses how we should think about post-translational modifications as a way of expanding the natural repertoire of the 20-letter amino acid alphabet. Similarly, Prof. Christopher Walsh wrote a whole book entitled "Posttranslational Modifications of Proteins: Expanding Nature's Inventory," again making the point that by adding chemical groups to proteins we can significantly change their properties.

(a) Provide at least one mechanistic idea about how adding a chemical group to a protein can alter its structure or function. Your answer should be offered in less than a paragraph, but should be concrete in its assertions about how these modifications change the protein. Why does Gunawardena refer to this process of post-translational modification as "escape from genetic imprisonment"?

(b) As a toy model of the combinatorial complexity offered by post-translational modifications, let's imagine that a protein has N residues that are able to be phosphorylated (NOTE: please comment on which residues these are—the answer is different for bacteria and eukaryotes). How many distinct states of the protein are there as a result of these different phosphorylated states? Make an approximate estimate of the mass associated with a phosphate group and what fraction of the total mass this group represents. Similarly, give some indication of the charge associated with a phosphate group. What ideas do you have about how we can go about measuring these different states of phosphorylation?

(c) In this part of the problem, we make a very crude estimate of the number of sites on a protein that are subject to phosphorylation. To do so, imagine that the protein is a sphere with N residues. How does the radius of that sphere depend upon the number of residues in the protein? Given that estimate, what is the number of residues that are on the surface? Given that number, what fraction of those are phosphorylatable? Remember, these are crude estimates. Work out these results for a concrete case of a typical protein with roughly 400 amino acids.

(d) Let's close out these estimates by thinking about a bacterial cell. If all 3×10^6 proteins in such a cell can be phosphorylated with the number of different phosphorylation states that you estimated above, how many distinct cells could we make with all of these different states of phosphorylation.

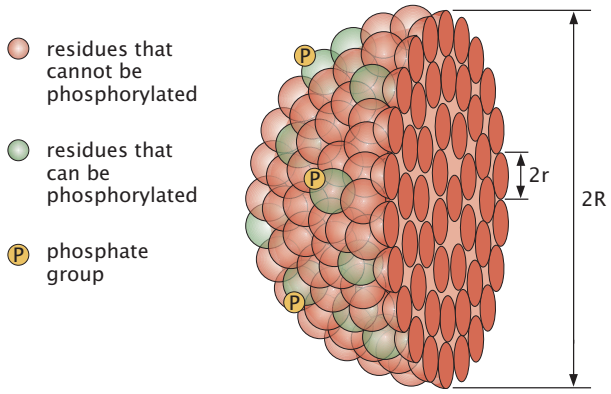

Figure 2: Schematic of a protein showing the surface residues that are available for phosphorylation.

5 Proteomic data on bacteria in different growth conditions

Read the paper by Schmidt and Heinemann and co-workers in which they use mass spectrometry to take the census of *E. coli* under a variety of different growth conditions. The outcome of this work was a census of the number of copies of roughly half of the proteins in this important bacterium.

(a) Using the data in the spreadsheet available with this homework, examine the numbers for the subunits of ATP-synthase. Write a short paragraph describing what ATP synthase is and what it does. Then, make an estimate of the number of ATPs it takes to make a new cell. In light of the number of ATP synthases counted by Heinemann and his group, are there enough to make all the ATPs needed to build a cell?

(b) Comment on the units on the y-axis of figure 2b of the Schmidt *et al.* paper. Specifically, justify those units in terms of what you know about the total number of proteins and the mass per protein. Do you think that the measurements pass the street fighters sanity check? Explain your conclusions.