BE/APh161: Physical Biology of the Cell
Homework 6
Due Date: Wednesday, March 3, 2021

"One of the principal objects of theoretical research in any department of knowledge is to find the point of view from which the subject appears in its greatest simplicity." - Josiah Willard Gibbs

1. Elasticity, Hydrodynamics and Indicial Notation.

This problem aims to give you practice in thinking about indicial notation and gives you a chance to think further about the ideas concerning elasticity and hydrodynamics that we will spend several weeks on in class. A key notational convenience that will be afforded us is the use of the summation convention. The basic injunction is: *sum over all repeated indices.* You can learn about this in detail in the middle of the vignette on "Stress and Strain." So as to gain familiarity with this convention, work out the following examples.

(a) Write out $a_i b_i$ as a full sum and give its standard interpretation in vector analysis by writing it in vectorial form.

(b) The electric current density $\mathbf{j}$ is related to the applied electric field $\mathbf{E}$ through the relation $\mathbf{j} = \boldsymbol{\sigma}\mathbf{E}$. The tensor $\boldsymbol{\sigma}$ is known as the conductivity tensor. Write this relation in indicial notation and then do the sums. How many equations is this? Write them all out.

(c) The vector cross product can be written as $a_i = \epsilon_{ijk} b_j c_k$, where the Levi-Cevita symbol is defined as $\epsilon_{123} = \epsilon_{231} = \epsilon_{312} = 1$, $\epsilon_{132} = \epsilon_{213} = \epsilon_{321} = -1$ and 0 otherwise. Another way of stating this that the Levi-Cevita symbol is 1 for even permutations of ϵ_{123}, -1 for odd permutations and zero for all other cases. Using these conventions, show that the expression written in summation convention notation yields the correct components of the vector cross product.

(d) Write out $\partial(\rho v_i)/\partial x_i$ by following the edict of the summation convention.

(e) Rewrite ∇p in indicial notation. The gradient in pressure will be important to us when considering the Navier-Stokes equations.

(f) Write out $\mathbf{a} \cdot (\mathbf{b} \times \mathbf{c})$ in indicial notation.

(g) When we balance forces in continuum mechanics, we will be interested in the divergence of the stress tensor. Write out $\partial \sigma_{ij}/\partial x_j$ using the summation convention. How many equations is this? Write them all out.

(h) Write out

$$\frac{\partial E_1}{\partial x_1} + \frac{\partial E_2}{\partial x_2} + \frac{\partial E_3}{\partial x_3}, \tag{1}$$

in indicial form and in vectorial form using ∇.

(i) Consider the matrix equation $\mathbf{a} = \mathbf{M}\mathbf{b}$, where $\mathbf{a}$ and $\mathbf{b}$ are column vectors with three components and $\mathbf{M}$ is a 3×3 matrix. Write out the rules for matrix multiplication for this problem in indicial notation.

(j) $\frac{\partial v_i}{\partial x_i}$ (write this in direct vectorial notation also).

(k) Given a matrix $\mathbf{M}$, what is M_{ii}? What is another way of writing this? Consider the matrices $\mathbf{A}$ and $\mathbf{B}$. Write the ij^{th} element of the matrix $\mathbf{AB}$ in terms of the matrix elements of $\mathbf{A}$ and $\mathbf{B}$ individually. Use indicial notation.

(l) In the Navier-Stokes equations one encounters terms like $\mathbf{v} \cdot \nabla \mathbf{v}$. Rewrite this in indicial notation, using the summation convention.

(m) In linear elasticity, the stress tensor is of the form $\sigma_{ij} = C_{ijkl}\epsilon_{kl}$. Write out the components of σ_{11} and σ_{12} of the stress tensor by exploiting the summation convention.

(n) The equilibrium equations for elasticity are written as

$$\frac{\partial \sigma_{ij}}{\partial x_j} + b_i = 0. \tag{2}$$

b_i is the i^{th} component of the "body force" (e.g. gravity). This is three equations corresponding to $i = 1, 2, 3$. Write all three equations by using the summation convention.

(o) For the particular case of an isotropic, linear elastic solid, the elastic modulus tensor is of the form

$$C_{ijkl} = \lambda\delta_{ij}\delta_{kl} + \mu(\delta_{il}\delta_{jk} + \delta_{ik}\delta_{jl}). \tag{3}$$

In this case, find an expression for the stress $\sigma_{ij} = C_{ijkl}\epsilon_{kl}$ and the stored energy density of the solid, $W(\{\epsilon_{ij}\}) = \frac{1}{2}C_{ijkl}\epsilon_{ij}\epsilon_{kl}$. Write your expression for the stress in both indicial and vector notation. Also, use this form for the elastic modulus tensor to obtain the equilibrium equations (the so-called Navier equations) by plugging your result for σ_{ij} into

$$\frac{\partial\sigma_{ij}}{\partial x_j} = 0. \tag{4}$$

Note that we are looking at the particular case in which the body force has been set to zero.

(p) The Navier-Stokes equations are of the form

$$\rho(\frac{\partial v_i}{\partial t} + v_k\frac{\partial v_i}{\partial x_k}) = \mu\frac{\partial^2 v_i}{\partial x_k\partial x_k} - \frac{\partial p}{\partial x_i}. \tag{5}$$

Write all three equations by exploiting what you know about the summation convention. Also, write these equations in direct (vectorial) form.

2. Equation of Motion for Mean Cytoskeletal Filament Length

In class we discussed the rate equation protocol shown in Figure 1. Our application of the protocol in class was to the problem of a constitutive promoter and provided a dynamical equation for the average number of mRNAs per cell as a function of time. In this problem, you are going to imitate that analysis, but this time thinking about the average length of a cytoskeletal filament as a function of time. Imagine a situation in which we have a closed box in which a single cytoskeletal filament has been nucleated (using a nucleating factor, for example) and which is bathed in a reservoir of monomers, with the initial number of monomers being given by N_{tot}. Our goal is to compute $L(t)$, where L is the length of the filament as a function of time. The rate at which monomers attach is $k_{on}n_{free}$, where n_{free} is the number of free

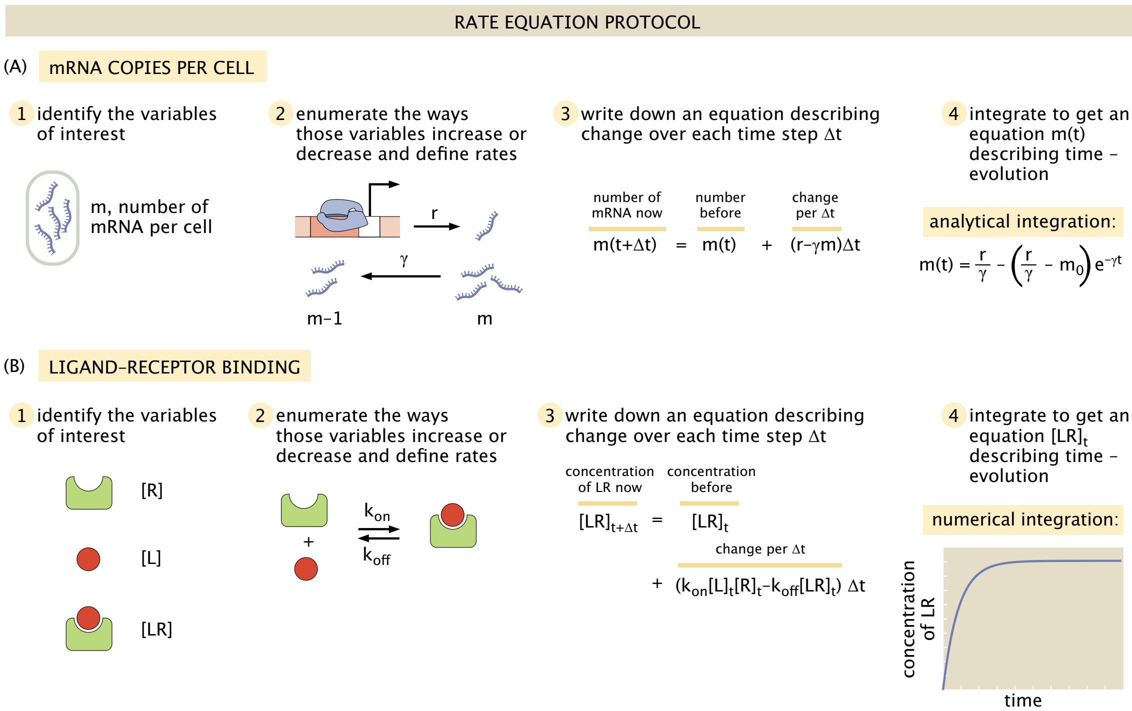


Figure 1: The rate equation protocol. To write dynamical equations for the time evolution of quantities of biological interest, there is a progression of steps.

monomers and the rate at which monomers detach from the tip of the growing filament is k_{off}. Write a dynamical growth equation for the dynamics of $L(t)$ and find the solution. What is the steady-state length of the filament? Make a plot of the length as a function of time - you can attempt to figure out reasonable choices of the parameters by looking at book.bionumbers.org or by looking at PBoC, but give an explanation of your choices. Also, compare and contrast the analysis here with that done in class for the constitutive promoter.

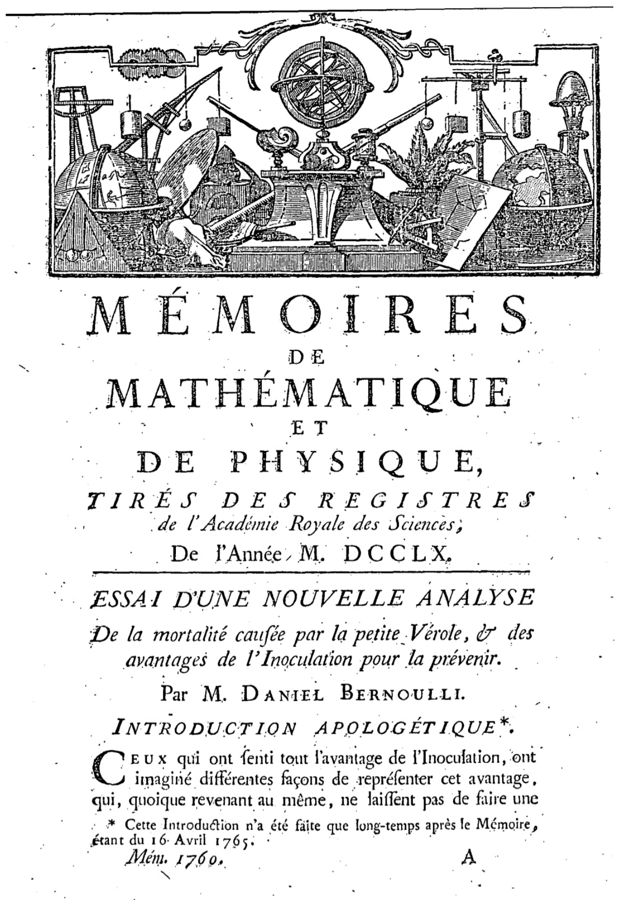
3. Physical Biology of Viruses.

The vignette from the section of the course on “rate equations for pandemics” will help you on this problem.

Since their discovery over 100 years ago, viruses have always occupied a central place in biology. One of the debates that has swirled around their existence is the simple question of whether or not they are "alive". During the Max Delbrück era, he was interested in finding the "hydrogen atom" of life and found bacterial viruses (the so-called bacteriophages - literally, bacteria eaters) would serve perfectly in that capacity. Several years ago when I was teaching this course, the big news was Zika virus and before that a very scary Ebola outbreak. This year, we are faced with the coronavirus, COVID-19. My own switch from condensed matter physics to biology was partly elicited by an amazing paper from the group of Carlos Bustamante at UC Berkeley who had figured out a way to measure the build up of pressure as DNA is packed into the bacteriophage capsid. In this problem, we take a random walk through the physical biology of viruses, honoring them as one of the most sophisticated, interesting and scary parts of the biological world.

(A) A simple model of viral spread through a population is the so-called SIR model, where S refers to susceptible, I refers to infected and R refers to recovered-removed. There is a long tradition running all the way back to the Greeks of trying to understand the population dynamics of disease spread. In 1760, the great Daniel Bernoulli mused on the topic of small pox and vaccinations as shown in Figure 2. If the rate of infection is given by r, and the rate of recovery is given by α, write three coupled differential equations for the dynamics of S, I and R. Choose reasonable values of those parameters based on looking at the current story of Coronavirus. Consider a closed and isolated city such as Wuhan, China (that is, make the clearly overly optimistic assumption that no one leaves or enters the city) and solve for the three variables as a function of time and plot them together on a common plot such as that shown in Figure 3. Explain the phase portrait in detail that is shown in Figure 4. Specifically, find an analytic expression for the parameter ρ which is the critical population size such that $dI/dt > 0$.

(B) How are viruses transmitted? Three key routes are through the respiratory tract, the digestive tract and the reproductive tract. In all three cases, our bodies are set up with a number of different tricks to resist infection including mucus and ciliary transport in our respiratory and digestive tracts and harsh conditions in our digestive tract such as low pH. The current coronavirus epidemic is passed through the respiratory tract and in this part of the problem, we appeal to Figure 5 for a look at the distribution of droplet



MÉMOIRES

DE

MATHÉMATIQUE

ET

DE PHYSIQUE,

TIRÉS DES REGISTRES

de l'Académie Royale des Sciences;

De l'Année M. DCCLX.

ESSAI D'UNE NOUVELLE ANALYSE

De la mortalité causée par la petite Vérole, & des avantages de l'Inoculation pour la prévenir.

Par M. Daniel Bernoulli.

*Introduction apologétique**.

Ceux qui ont senti tout l'avantage de l'Inoculation, ont imaginé différentes façons de représenter cet avantage, qui, quoique revenant au même, ne laissent pas de faire une

* Cette Introduction n'a été faite que long-temps après le Mémoire, étant du 16 Avril 1765.

Mém. 1760. A

Figure 2: Paper from Daniel Bernoulli, 1760 in which he considered a dynamic model of small pox.

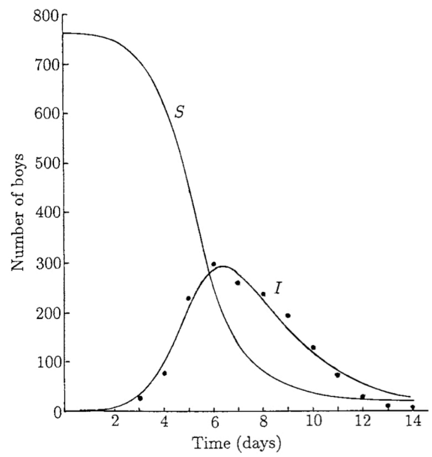


Figure 3: Influenza data from a boarding school for boys reported in *The Lancet* in 1978.

sizes. The claim is that a strong sneeze or cough can contain more than 10,000 such droplets. How much volume is that? Does that make sense? Estimate how many influenza or coronavirus particles will be carried in a typical droplet. I have not done all of these estimates carefully enough for my own satisfaction so this part of the problem is an adventure for all of us. A very interesting source of information on this is the work of Prof. Lydia Bourouiba from MIT who does visualization experiments on humans coughing. https://www.nature.com/articles/d41586-019-00065-5 - an excellent brief interview with Bourouiba on the physics of sneezing and coughing.

4. A feeling for the numbers: stress in biology.

One of the fundamental facts of life is changes in osmotic stress. To put it bluntly, sometimes the bacteria in our guts are all of a sudden exposed to pure water in a toilet bowl, resulting in a substantial hypoosmotic stress coming from a concentration change as much as $\Delta c = 1$ M. One simple equation of state for the osmotic pressure that results is the so-called van't Hoff equation which says that the osmotic pressure is given by the ideal solution form

$$\Pi = \Delta c k_B T, \tag{6}$$

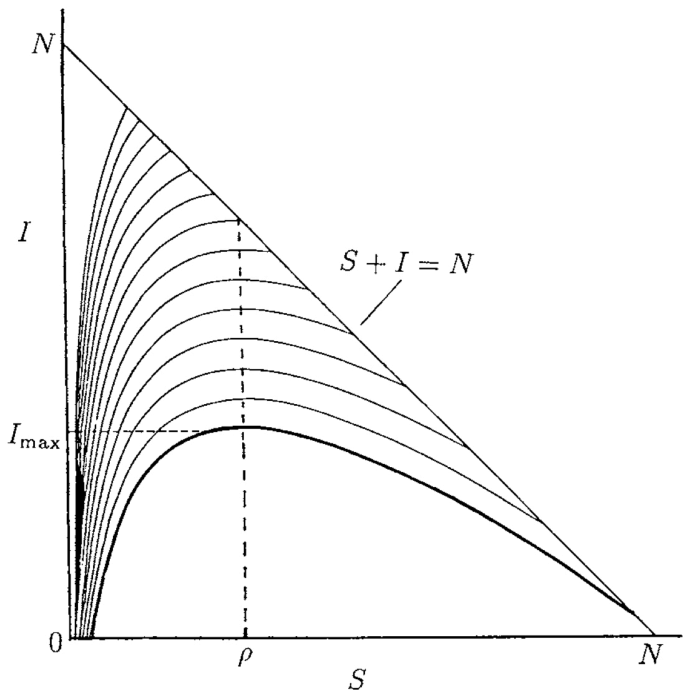


Figure 4: Phase portrait in the SIR model. The total population size is N. The number of susceptible individuals plus the number of infected individuals at $t = 0$ is equal to the population size. Thus, all subsequent evolution of the population must exist within the triangle since $S(t) + I(t) + R(t) = N$. ρ is the critical population size for the occurrence of an epidemic.

carrying droplet-nuclei which remained airborne after sneezing was found to decrease geometrically with time; only 4 % remained airborne after 30 min. and 2 % after 40 min.

In the present investigation, the droplet-nuclei produced in speaking, in coughing and in sneezing have been measured by a new technique, namely, by direct micrometry after their recovery from the air on to oiled slides. The sizes of the smaller respiratory droplets have been calculated from the sizes of these droplet-nuclei. The sizes of the larger respiratory droplets have been estimated from measurements made of stain-marks found on slides exposed directly to mouth-spray. By appropriate combination of these two sets of findings, the formulation of a comprehensive size distribution for the respiratory droplets has been attempted. The duration of aerial infection by droplet-nuclei has been observed by examination of the air at intervals after droplet-spray production, for the presence both of bacteria-carrying droplet-nuclei and of all microscopically visible droplet-nuclei.

THE MEASUREMENT OF DROPLETS AND DROPLET-NUCLEI

The following expiratory activities were tested: (1) *sneezes*, induced by snuff or by tickling the nasal mucosa with a throat swab; (2) *coughs with the mouth initially closed*, voluntarily performed with the lips, or with the tongue and the upper teeth, approximated at the start of expiration; (3) *coughs with the mouth open*, voluntarily performed with the mouth kept well open and the tongue depressed; (4) *speaking loudly one hundred words*, by counting from 'one' to 'a hundred'.

A. *The measurement of stain-marks on slides exposed directly to mouth-spray*

In order that even the smallest droplet-marks might be readily visible, some dye was introduced into the mouth just prior to each test. A little congo red, eosin or fluorescein powder was applied with a throat swab to the surfaces of the mouth and fauces; the heaviest application was made to the tip of the tongue, to the front teeth and to the lips, for droplet-spray originates largely from the secretions of the anterior mouth. Following solution of the dye, droplet-spray was produced by sneezing, by coughing or by speaking; it was directed at a celluloid-surfaced slide held 3 in. in front of the mouth in tests of speaking, and 6 in. in front of the mouth in tests of coughing and sneezing. The slide was examined under the microscope, and the diameters of the first few hundred droplet-marks encountered were measured with aid of a micrometer eyepiece. In the case of each type of expiratory activity, a number of tests, from 10 to 22, were carried out, involving the measurement of 3000 droplets.

In order to ascertain the relationship between the diameters of the droplets while in their original spherical state, and the diameters of the stain-marks which the droplets leave on evaporation after impinging and flattening upon a slide, the experiments of Strausz (1926) were repeated. With the low power of a microscope and a micrometer eyepiece, large drops of saliva (1–3 mm. in diameter) were measured, first while they hung from fine glass capillaries and then again after they had fallen, flattened and evaporated on a slide. When a glass slide was used, it was found, as it had been by Strausz, that the

Table 1. *The size distribution of the larger droplets*

Showing for each type of expiratory activity the diameters of 3000 droplets calculated as half the measured diameters of the stain-marks found on celluloid slides exposed a few inches in front of the mouth.

Diameter in μ	Sneezes	Coughs with mouth 'closed'	Coughs with mouth open	Speaking loudly
0–5	0	0	0	0
5–10	36	24	8	20
10–15	94	119	39	84
15–20	267	337	127	200
20–25	312	346	189	224
25–50	807	767	577	597
50–75	593	468	593	531
75–100	260	285	341	352
100–125	144	160	231	260
125–150	105	125	202	214
150–200	115	115	253	179
200–250	82	96	165	99
250–500	118	113	213	197
500–1000	59	40	52	41
1000–2000	8	5	10	2

diameters of the original droplets were about one-third those of the stain-marks. When a celluloid-surfaced slide was used, the diameters of the original droplets were about half those of the stain-marks. Celluloid slides were used throughout the present investigation, so the original droplet diameters have been calculated as half the measured diameters of the stain-marks. The size distribution so found for the droplets expelled in the different expiratory activities, is shown in Table 1. It will be noted that few droplets were found of less than 10 μ in diameter and none of less than 5 μ. It is presumed that droplets smaller than this possessed such a small mass, or evaporated rapidly to such a small mass, that they were carried past the slide in the deflected air stream.

Figure 5: Distribution of droplet sizes after a sneeze.

where Δc is the concentration jump across the relevant cell membrane. Work out the stress in Pa units for an osmotic stress experiment.

5. The Art of Estimation Revisited

One of the main objectives of this course was to make sure you leave with a sense of how to do order of magnitude thinking and to obtain simple estimates for biological (and other) phenomena, yielding what Barbara McClintock referred to as a feeling for the organism.

Figure 6: Ground finch in the Galapagos.

In this problem, the goal is actually to make yourself do quick drills to get reinforce the habit of just making guesses about quantities. I like the Spanish proverb: "Habits are like cobwebs, then cables." We need to get into the estimation habit. Do not look up any facts - you can look at the included pictures and just make a quick statement based upon less than 60 seconds of staring. When appropriate, try to use the square root rule that we discussed in class. For each case, give a brief, but thorough description of how you came by your estimates. Don't just quote a single number. Give us some context about how you got your result. These problems are chosen from a wide variety of different biological contexts and give us the chance to

Figure 7: Starling flock in Rome.

practice our skills at many scales and in many contexts.

(a) What is the thickness of the beak of a ground finch? (in mm) Make an estimate of the beak-to-beak variation in beak size between adult ground finches. Use Figure 6 to help in making a rapid estimate. The biological significance of this estimate is that measurements have shown that a difference in beak thickness of less than 0.1 mm can mean the difference between life and death for finches faced with a drought where cracking harder and less desirable seeds becomes necessary.

(b) How many starlings are in the flocks seen in Rome? How many kilograms of poop do these birds drop on Rome each day? Figures 7 and 8 can aid you in your thinking.

(c) When a bacterium is infected by a bacteriophage (a bacterial virus), what is the typical burst size of the viruses (i.e. how many viruses emerge from the cell after it lyses?) Begin by looking at Figure 9 and quickly telling us how big a bacterium is, how big a bacteriophage is. Then for figuring out

Figure 8: Consequences of starling flock in Rome.

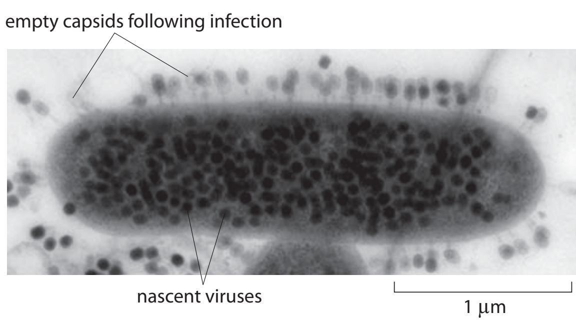


Figure 9: Burst size of an infected bacterium.

the burst size, use Figure 9, but don't count. Do quick estimating by picking a lower and upper bound.

(d) How many atoms are in a "typical" amino acid? Figure 10 shows the *side chains* of the amino acids and should help you quickly make an estimate. Similarly, give an estimate of the typical mass of amino acids in Dalton units (remember, a Dalton is the mass of one hydrogen atom). How many atoms are in a typical base. Figure 11 shows various representations of bases and DNA. Similarly, give an estimate of the typical mass of nucleotides in Dalton units.

(e) Use Figure 12 to estimate the speed of the ocean currents experienced by Rizal Shahputra. Using your estimate from the first part of the problem,

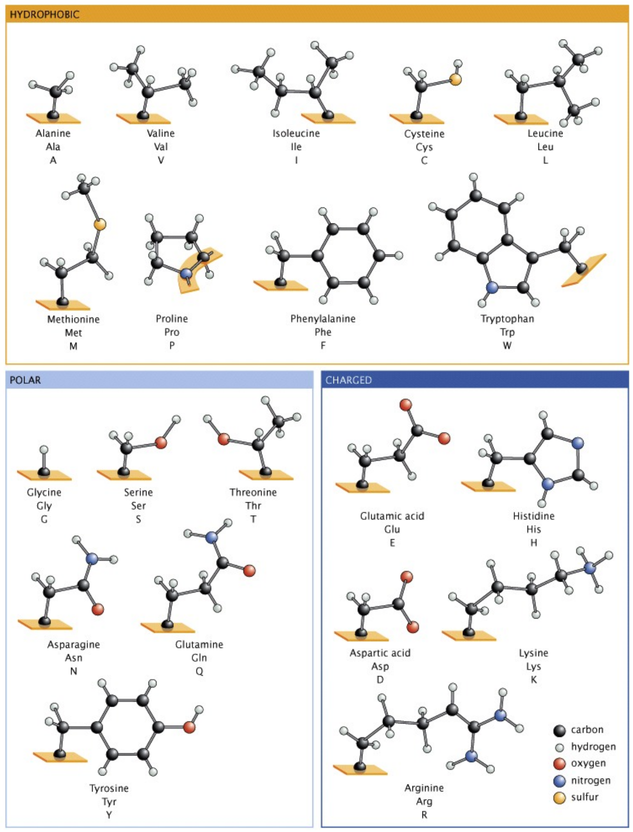


Figure 10: Amino acid side chains.

give an estimate of the time spent in the ocean by the tortoise shown in Figure 13 in its journey drifting from Aldabra (see Figure 14) to Tanzania! The reason I am asking you to do this problem is that the subject of biogeography of oceanic islands is one of the great evolutionary subjects. How do islands such as Hawaii, the Galapagos and Principe get colonized?

(f) In this part of the problem, you are going to do an integral by eyeballing. Figure 15 shows the spectrum of radiation reaching the earth. By approximating the curve as a rectangle work out a simple statement for the flux of radiation on the earth from the sun in units of W/m^2. Then, using the blue region, figure out the flux 10 m below the surface of the ocean.

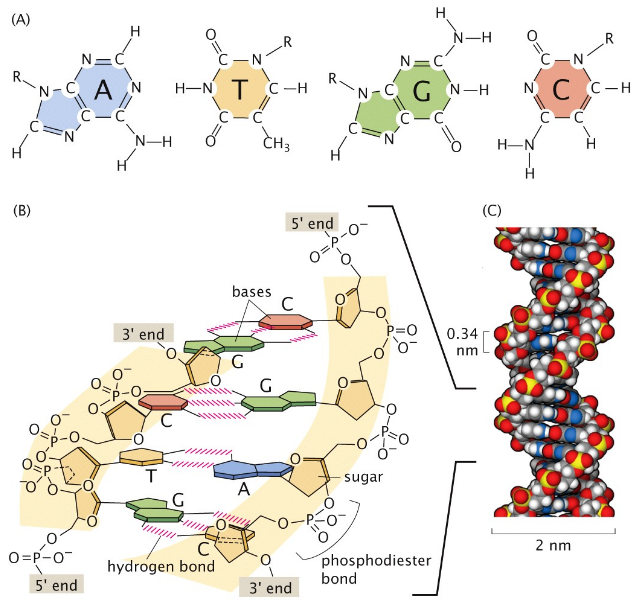


Figure 11: Structure of DNA.

(g) Every time an electron microscope is used to take an image it corresponds to roughly a 1μm $\times$ 1μm area. The electron microscope is used to explore the structure of the nanometer scale world of cells, for example. Biology is a subject characterized by great naturalist voyages in which figures such as Humboldt, Darwin, Wallace, Huxley and Hooker traveled around the world to try and collect data on biological diversity. The point of this problem is to get a sense of the *microscopic* diversity explored. Make an estimate of the total area looked at in biological samples using electron microscopes in the history of science. How does this correspond to the area of the Earth? What do you conclude about the extent to which we have "explored" the microbial diversity on the planet?

Tsunami man survives week at sea

An Indonesian man has been found floating on tree branches in the Indian Ocean, eight days after a devastating tsunami struck the region.

Rizal waved to a passing cargo ship

Rizal Shahputra, 23, said he was initially swept out to sea with other survivors and family members, but that one by one they drowned.

He was rescued on Monday by a passing container vessel.

He was taken to Malaysia where officials said he was in good condition - he survived eating floating coconuts.

Rizal said he was cleaning a mosque in Banda Aceh on the northern tip of Sumatra on 26 December when the tsunami struck. Children ran in to warn him, but he was swept out to sea, along with several other people.

"At first, there were some friends with me," Rizal told reporters. "After a few days, they were gone... I saw bodies left and right."

He drank rainwater, and ate coconuts, which he reportedly cracked open with a doorknob.

Rizal said at least one ship sailed by without noticing him before the MV Durban Bridge spotted him, 160km (100 miles) from Banda Aceh.

Figure 12: Article about tsunami survivor after Boxer Day earthquake in Indonesia in 2004.

Figure 1. The Aldabra tortoise at Kimbiji, shortly after its discovery in December 2004. Photograph: C. Muir.

Figure 13: Tortoise found in Tanzania after traveling across the ocean. Notice the barnacles that have attached to the tortoise.

Figure 14: Map showing the position of the Aldabra Atoll in the Indian Ocean.

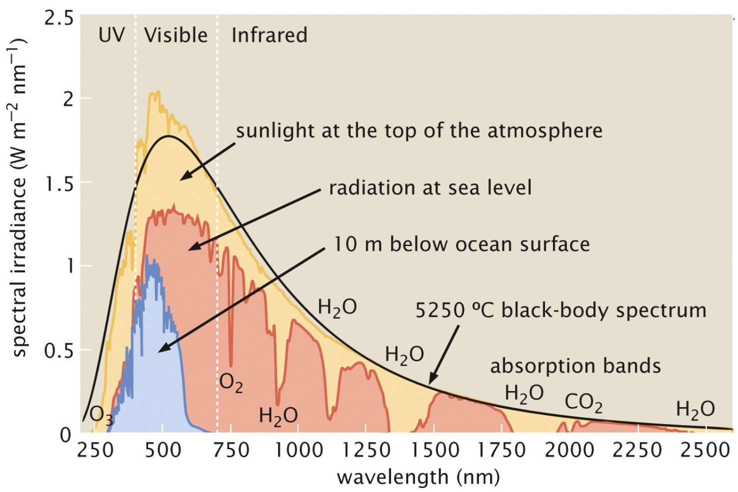


Figure 15: Spectrum of solar radiation reaching the Earth.