Problem set 4
(Discussion on May 26)

Problem 1

Applications of CRISPR/Cas. We have discussed the CRISPR/Cas system in class, which allows researchers to cut double-stranded DNA in defined locations and constitutes a powerful new tool for gene editing. There are many (potential) applications of the CRISPR/Cas system.

a) Find an interesting (potential) application of the CRISPR/Cas technique. There are many useful resources online. As a starting point, you can e.g. use the fairly extensively referenced Wikipedia article (`https://en.wikipedia.org/wiki/CRISPR_gene_editing`) or this *wired* article (`https://www.wired.com/story/wired-guide-to-crispr/`).

b) Give a brief summary of "your" application of CRISPR/Cas. This should be short, keywords or 2-3 paragraphs of text are sufficient. You can include 1-2 graphs (which can be taken from references). In describing your application, you should address the following points (addressing these points is generally a good way to outline and present scientific projects):
PROBLEM: What problem is being addressed? What are the authors trying to achieve?
SIGNIFICANCE: Why is the work important? Why should anyone care?
APPROACH: How is the problem being addressed? What did the authors do?

c) We will present several applications in class!

Problem 2

Electrostatics for folded RNAs and proteins. Electrostatics typically play a much more important role for folded RNA molecules than for folded proteins. Here, we will derive simple estimates of the electrostatic energies involved. Let us consider a hypothetical folded RNA of 100 nucleotides and a equally hypothetical folded protein consisting of 100 amino acids. Let us further assume that they both have approximately spherical and close-packed shapes and that they consist of exactly equal amounts of all canonical nucleotides or amino acids, respectively.

a) Estimate the sizes (i.e. radii) of the spherically-folded RNA and protein. You can assume that they both have a density of 1.35 g/ml. The molecular weight of an amino acid is on average 110 Da, that of a nucleotide 330 Da.

b) What is the total charge of the hypothetical protein and RNA, if we assume that all nucleotides and amino acids are in their standard charge state at physiological conditions?

c) Assume that the charges calculated in part b) are uniformly distributed over the spheres with radii computed in part a). What is the electrostatic energy of the two uniformly charged spheres in vacuum? In water?.

Problem 3

Debye-Hückel: Charged sphere in ionic solution. In class, we discussed the interaction of an infinite charged plane with an ionic solution. While an infinite plane can be a good model for a cell membrane, the more important and useful result is the solution for a charged sphere in solution. In this problem, you will derive the electrostatic potential for a charged sphere (with radius R and total charge Q) in ionic solution in the Poisson-Boltzmann limit. For simplicity, you can assume that there is a simple monovalent salt (i.e. one species of charge $+1$ and one ionic species of charge -1) with a bulk concentration of c_∞. In addition, you can assume that the sphere is only weakly charged, such that the exponential function of the Boltzmann factor can be simplified according to $\exp(\pm x) \approx 1 \pm x$.

a) Derive a differential equation for the electrostatic potential ϕ as a function of the radial distance from the sphere. You can essentially follow the derivation used in class. However, for the spherical problem, it is best to use a spherical coordinate system. Hint: The relevant differential operator in spherical coordinates reads

$$\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial\phi}{\partial r}\right) \tag{1}$$

b) Show that the solutions are of the form $\phi(r) = \frac{C_1}{r}\exp(-r/\lambda_D)$ where C_1 is a constant and λ_D is the Debye length $\lambda_D = \sqrt{(\epsilon\epsilon_0 k_B T)/(2e^2 c_\infty)}$. Hint: You can use an *Ansatz* of the form $\phi(r) = \frac{C_1}{r}\exp(-r/\lambda_D) + \frac{C_2}{r}\exp(r/\lambda_D)$. Show that this solves the differential equation. What happens to the C_2 term? As an extra exercise: What is the constant C_1 in terms of the parameters of the problem?

c) What is the value of the Debye length λ_D for 100 mM monovalent salt (an approximately physiological salt concentration)? For 1.0 M salt?