Problem set 3
(Hand in by May 18)

Problem 1

Challenges with DNA replication. In class, we have discussed some aspects of DNA replication. Here we will explore some problems that cells face when replicating their genetic material.

a) The basic view of DNA replication (famously alluded to by Watson and Crick in the last sentence of their paper on DNA structure) is that in replication, the DNA double helix is "unzipped" and that each strand forms the template for creating a new complementary strand, thus creating two exact copies of the DNA. The unzipping proceeds from one end of the double-stranded DNA and is carried out by so-called helicases that work in coordination with the two DNA polymerases that copy each strand in a complex called the replisome. What fundamental problem occurs due to the fact that DNA polymerases can only synthesize new strands from the 5' to the 3' end?

b) Can you think of possible solutions to the problem in the previous part?

c) In prokaryotes, replication of the circular genome starts from a DNA region called *origin of replication*. Two replisomes start from the *origin of replication* in opposite directions and each runs half around the circular genome, where they meet and stop replicating (called *termination*). The speed of replisomes in E. coli has been measured to be roughly 800 bp/s. What problem do you see, given what you have learned in class about the size of E. coli's genome and its doubling time?

d) Can you think of solutions to E. coli's problem?

Problem 2

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 credit 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?