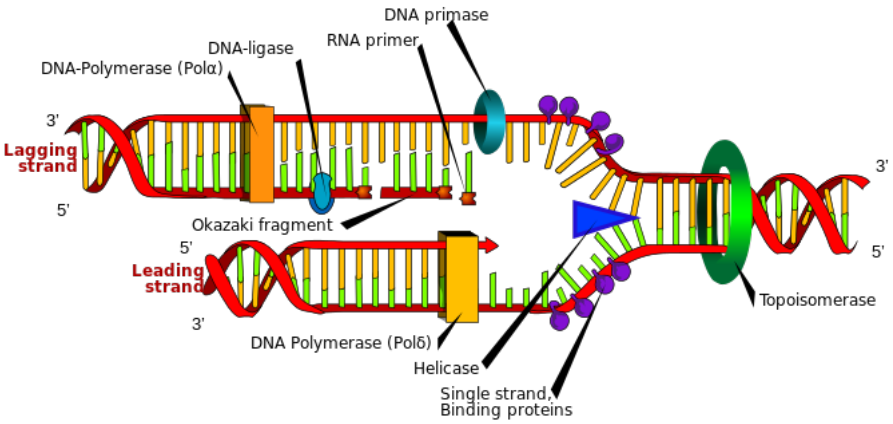
Solutions to problem set 3

Problem 1

Challenges with DNA replication.

a) Since the DNA strands are antiparallel, unzipping of the DNA by a helicase from one end means that you have one 5' end and one 3' end. Since polymerases can only ever synthesize DNA in the 5' to 3' direction, the strand of the parent DNA with the 3' end makes for a "easy" template, since the polymerase can directly synthesize the complementary strand 5' to 3'; this strand is called the *leading strand*. The strand of the parent DNA with the 5' is more problematic; this strand is called the *lagging strand*. To directly synthesize the complementary strand, you would have to synthesize DNA in the 3' to 5' direction, which is impossible.

b) The solution that nature uses is to synthesize the completementary strand to the lagging strand DNA in shorter segments, called *Okazaki fragments*. For the synthesis of the *Okazaki fragments*, the polymerase moves in the opposite direction of the advancing helicase and is "lagging" behind the leading strand synthesis, since it has to wait for the helicase to advance some distance before it can make a new fragment, hence the name lagging strand. The entire process is coordinated in a the so-called replisome, which involves several other proteins in addition to a helicase and the two polymerases. A schematic of a replication fork with some of the protein involved and the leading and lagging strands is shown below (Source: `https://en.wikipedia.org/wiki/DNA_replication`).



c) In class we learned that the *E. coli* genome is $4.2 \cdot 10^6$ bp (see Lecture 1; the exact number depends on the strain, but does not matter for the general argument here) and that it doubles, under good growth conditions, in 20 min or less. Two replisomes copying at 800 bp/s will take $4.2 \cdot 10^6$ / (800 s $\cdot$ 2) $\approx$ 2600 s $\approx$ 43 min to copy the entire genome - roughly twice as long as the doubling time!

d) The solution that *E. coli* uses is to actually start the next round of replication before the entire genome has been copied. In other words, more than two replisomes (and more than two copies of the genome) are active at a given time. A nice explanation with some images is given here: `http://sandwalk.blogspot.de/2008/05/dna-replication-in-e-coli-solution.html`.

Problem 2

Debye-Hückel: Charged sphere in ionic solution.

a) Choose a spherical coordinate system. Due to symmetry, the angles do not matter and we can consider the problem as an effective 1D problem in the radial coordinate. Following steps identical to the ones carried out in class for the infinite plane, we have that the bulk concentration far from the sphere is $c_+ = c_- = c_\infty$. At finite distance r, the concentrations for the positive and negative species are given by (for generality, we include the valency z, which is simply equal to one in our case):

$$c_+ = c_\infty \exp(-ze\phi(r)/k_B T) \tag{1}$$

$$c_- = c_\infty \exp(+ze\phi(r)/k_B T) \tag{2}$$

Taking into account the mobile charges, the Poisson equation then reads (where $\rho(r)$)is the charge density):

$$\nabla^2\phi(r) = -\frac{\rho(r)}{\epsilon\epsilon_0} = \frac{zec_\infty}{\epsilon\epsilon_0}\left(\exp(ze\phi(r)/k_B T) - \exp(-ze\phi(r)/k_B T)\right) \tag{3}$$

This is the Poisson-Boltzmann equation for a simply 1:1 ionic solution. Now we linearize the exponential, an approximation known as the Debye-Hückel limit:

$$\nabla^2\phi(r) = \frac{2z^2e^2c_\infty}{\epsilon\epsilon_0 k_B T}\phi(r) = \frac{1}{\lambda_D^2}\phi(r) \tag{4}$$

In the last step, we have introduced the Debye length λ_D. We now need to write the Laplace operator for the radial coordinate to get the differential equation for $\phi(r)$:

$$\nabla^2\phi(r) = \frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial\phi(r)}{\partial r}\right) = \frac{1}{\lambda_D^2}\phi(r) \tag{5}$$

b) To show that the *Ansatz* $\phi(r) = \frac{C_1}{r}\exp(-r/\lambda_D) + \frac{C_2}{r}\exp(r/\lambda_D)$ solves the differential equation 5, we can simply plug it in and show that, after applying the chain and product rules, it satisfies the equation. Far away from the sphere the potential is zero, by convention, and therefore the exponentially growing part of the solution has to be zero, i.e. the constant C_2 has to be zero, leaving the C_1 term as the relevant solution.

The key observation here is that for an ionic solution, the potential of a sphere does not simply fall as $\propto 1/r$ (as it would in vacuum or air), but that there is an additional exponential cut-off with a characteristic length scale given by λ_D.

c) Debye length λ_D for 100 mM monovalent salt $\approx$ 9.6 Å; Debye length at 1.0 M salt $\approx$ 3.0 Å. See the separate matlab code for the calculation. There are even online calculators (see e.g. `http://www.surfchem.info/calculate/Debye/`). This means that in ionic solutions, electrostatic interactions are strongly reduced over rather short distances.