Name:_____ Section :_____

7.014 Problem Set 3

Answers to this problem set are to be turned in. Problem sets will not be accepted late. Solutions will be posted on the web.

Question 1

After acing the 7.014 Quiz 1, you take a well-deserved break and go "looking for Baker House." Somewhere in the tunnels you stumble on a device you have never seen before, and start playing with its dials. It turns out to be a time- and reality-transporting device. It lands you in the office of the editor of the journal *Nature* in February of 1953. This is a reality much like our own, except that in this reality no one has yet seen Rosalind Franklin's data.

The editor is happy to see you, since he believes the knowledge you acquired in 7.014 will help him with the decision he must make. In front of him are four papers proposing various models for the structure of DNA.

For each model below, indicate whether the editor should accept or reject the paper (i.e. whether the model is plausible or not) and explain your advice. If your advice is based on data the editor has not yet seen, explain what the data is and how it will affect the plausibility of the model. If your advice is based on data the editor is familiar with, explain how that data is either consistent or inconsistent with the model.

i. Model A: DNA is a double-stranded helix with sugar-phosphate backbones in the center, and bases sticking out into solution. In this model, the strands are running anti-parallel to each other.

ii. Model B: DNA is a four-stranded helix with bases looking inwards. The model claims to be based on the current crystallographic data.

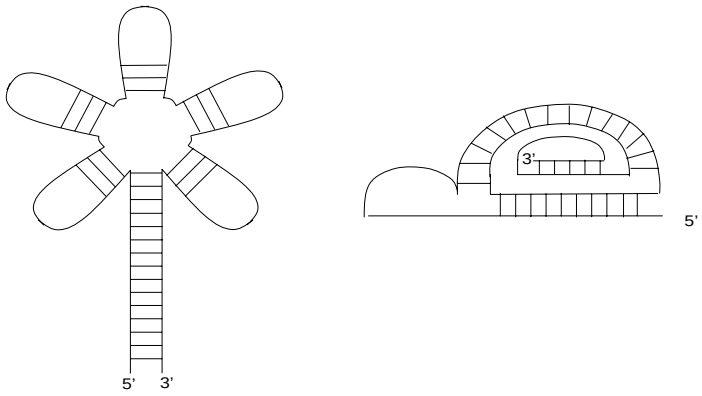
iii. Model C: DNA is a double-stranded helix with sugar-phosphate backbones on the outside, and bases in the middle, where purines (A and G) pair with purines and pyrimidines (T and C) pair with pyrimidines. The strands are running anti-parallel to each other.

iv. Model D: DNA is a double-stranded helix with sugar-phosphate backbones on the outside, and bases in the middle. In this model, the strands are running parallel to each other.

Question 2

After a 7.014 nucleic acids lecture, a budding young artist named Moe Nay wanted to explore the shapes a single-stranded DNA molecule can take. He sketched the two shapes below. His TA was impressed with Moe's imagination and artistic ability, but she informed Moe that only one of his sketches was feasible. In the sketches, the lines indicate complementary base pairing.

a) Which of the sketches below is possible? Circle the <u>correct</u> one.



b) What is wrong with the other drawing?

c) What is the minimal number of primers that would be needed to create a complementary DNA strand to the DNA strand in the correct drawing? Why?

d) On the drawing above, indicate the position(s) of the primer(s) needed to create an entire complementary strand. Label 5′ and 3′ of the primer(s).

e) Would the new double stranded molecule assume the shape similar to one in the drawing? Why or why not?

Question 3

a) In the Meselson and Stahl experiment, what part of the DNA gets labeled with ^{15}N?

b) Would any other macromolecule get labeled in that experiment? If yes, what is it?

c) In the Meselson and Stahl experiment, where on the CsCl gradient would the following DNA be found (low, middle, high):
   i. Double stranded DNA where both strands are labeled
   ii. Double stranded DNA where one strand is labeled
   iii. Double stranded DNA where neither strand is labled

Semi-conservative replication was only one of the models of DNA replication proposed after the discovery of DNA structure. One of the other models was called conservative replication. In that model, new copies of both DNA strands would be made, but after replication was complete, the two "old" strands would stay together in a double helix, and the two "new" strands would form another double helix.

In Meselson and Stahl experiment, a culture is grown on media with ^{15}N, and switched to light N at time=0.

d) If the mechanism is semi-conservative, what would you expect to see on the CsCl gradient after allowing the specified number of rounds of replication:

# rounds replication after switching to light N	Number of Bands	Location of bands (low, middle, high)
None		
One		
Two		
Three		

e) If the mechanism is conservative, what would you expect to see on the CsCl gradient after allowing the specified number of rounds of replication:

# rounds replication after switching to light N	Number of Bands	Location of bands (low, middle, high)
None		
One		
Two		
Three		

f) Treating the DNA samples with heat can break the hydrogen bonds that hold paired strands together. When the DNA is cooled, strands will re-pair <u>but not necessarily with their original partner</u>. If replication is conservative and you briefly treated the DNA samples with heat, how would that change your results from a Meselson-Stahl experiment?

g) If you discovered a new species of bacteria, would you repeat the Meselson and Stahl experiment on it, or assume the mechanism of replication is semi-conservative? Why?

Question 4

a) What (if any) editing function (5′→3′ exo; 3′→5′ exo; or mismatch repair) could repair the following mistakes made by a DNA polymerase?

i. adds an extra nucleotide

ii. puts in a wrong nucleotide

iii. slides backwards 3 nucleotides on the template strand, creating a repeat

b) In the table below a number of mutant DNA polymerases are listed. For each polymerase, indicate which property of replication (rate of binding, frequency of mutation, or rate of replication) will definitely be affected, and how (decrease or increase).

Mutant DNA Pol	Rate of DNA Binding	Frequency of Mutation	Rate of Replication
Does not distinguish between DNA and RNA strands			
Frequently falls off of the DNA			
Frequently misreads template DNA			
Low specificity for correct nucleotides			
Does not distinguish between dNTPs and dNDPs			
Poor catalyst of the nucleotide addition reaction			
Missing binding site for processivity factor			

c) If a DNA polymerase contains a mutation that allows it to strongly bind RNA strands, can the polymerase now function as an RNA polymerase? Why or why not?