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## Problem Set 6

The answer key will be posted by **Tuesday July 28**. Try to solve the problem sets always first without the answer key. Remember, your goal is to be able to solve biochemical problems in the exams. If you can not solve one of the problems try to solve it together with one of your classmates or ask your GSI during discussion section. Don't just wait for the answer key. The answer key should only confirm that you solved the problem correctly!

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Exercises and Problem Sets are for extra practice and exam preparation, and should not be turned in.

### Recommended problems from the book:

- Chapter 8: 1, 2, 3, 6, 8, 9, 11, 12, (15)
- Chapter 24: 1, 3, 4, 5, 7, 8, 9, (14)
- Chapter 25: 2, 3, 4,

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### 1. A double-stranded DNA molecule contains 20% adenine. Determine the number of cytosine bases if the DNA molecule is:

- (a) 1000bp long
- (b) 1cm long

### 2. DNA Sequences

Write the DNA base sequences that complement each of the following DNA strands.

a) 5' AATCGCCCATTCAGTTC 3'

b) 5' CGATTGGCTTA 3'

### 3. Writhe and Twist

Starting with a closed circular DNA of 5250 base pairs with  $\sigma = -0.004$  (assume 10.5 bp/turn for B-DNA).

- (a) Calculate the writhe (W) of this DNA.
- (b) Calculate the twist (T) and linking number (L) for this DNA.
- (c) Calculate the circumference of the circular DNA when  $W = 0$ .
- (d) Now, if 13 base pairs have melted out, as in the initiation of the replication bubble in *E. coli*, calculate the twist (T), linking number (L), and writhe (W) for the resulting circular DNA.

(e) Calculate T, L, and W after half the closed circular DNA has been replicated.

#### 4. Eucaryotic Chromosomes

In eukaryotic chromosomes, 150 bp of DNA are wrapped 1.8 times around the nucleosome core proteins, and there are 100 bp of DNA between each nucleosome.

- (a) Calculate the diameter of a nucleosome core particle.
- (b) Calculate the superhelical density of eukaryotic DNA.

#### 5. DNA packing

A human mitochondrion (about  $1.5\mu\text{m}$  in size) contains 16569 base pairs of DNA.

- (a) Calculate the packing ratio for DNA in the mitochondria.
- (b) Does this suggest that mitochondria have nucleosomes (briefly explain your answer)?

#### 6. DNA Replication

The following are some examples of problems that can occur during DNA replication. Identify the defective enzyme or enzymes that would cause each problem.

- (a) Mismatched base pairs are found in the newly synthesized DNA.
- (b) RNA bases are found in the newly synthesized DNA.
- (c) Replication on the leading strand is not initiated.
- (d) Replication forks are not formed.

#### 7. DNA Replication II

In the fruit fly *Drosophila melanogaster*, DNA replication at a single replication fork occurs at a rate of about 2600 nucleotide pairs per minute. The DNA molecule occurring in one of the largest chromosomes of this species has been estimated to contain  $6 \times 10^7$  nucleotide pairs.

- (a) If replication of this molecule was initiated at a single origin in the middle of the chromosome, estimate the time, in days, required for complete replication of the chromosome.
- (b) Estimates based on living cells indicate that this chromosome replicates in about four minutes. Assuming that the origins are spaced equally along the DNA, how many of them would be required to completely replicate this chromosome in four minutes?

## Exam Questions from 2008

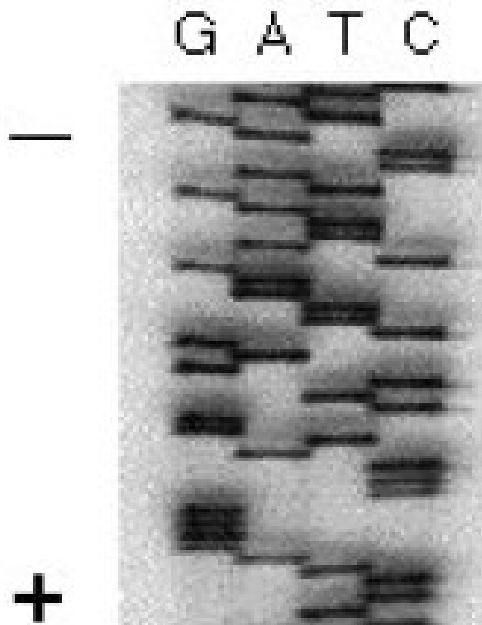
8. *Pelagibacter ubique*

*Pelagibacter ubique* has the smallest genome yet found in a free-living organism. The contour length of the relaxed circular chromosome is  $445\mu\text{m}$ . In your analysis you find the chromosome has a superhelical density of  $-0.33$ . What is its Lk? What is the Twist and the Writhe? Describe in one sentence its topological properties.

## 9. Sanger sequencing

Below you see an autoradiogram of an electrophoresis gel from Sanger sequencing.

- (a) Write down the sequence of this DNA from 5' to 3' (cluster the letters into threes please):



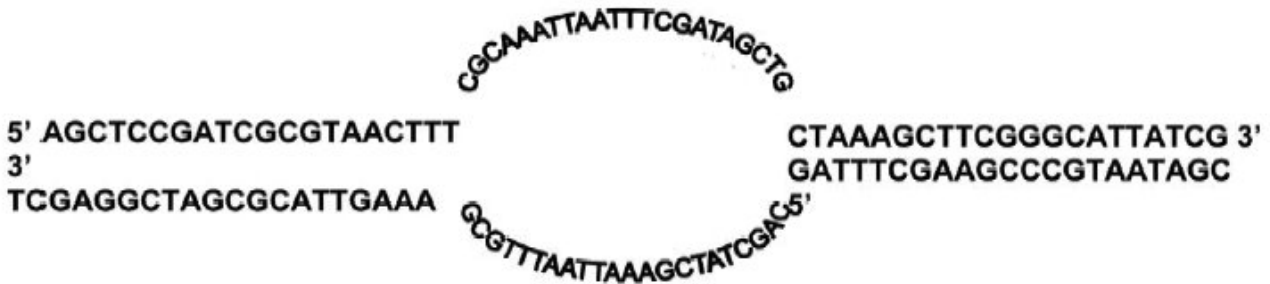
- (b) Find the ORF and indicate its location on your sequence.  
 (c) Translate this cDNA sequence into the Protein sequence corresponding to the ORF. Translate as much as you can.  
 (d) A new student rotating through a lab attempts to sequence this strand of DNA again using the Sanger method with the proper radioactively labeled primer:





### 10. Replication Bubble

Below is a depiction of a replication bubble.



- Place the following primer on the diagram above: 5'– GCUAUCG –3' and represent the direction of replication by an arrow.
- Is the primer made out of DNA or RNA?
- If the replication fork moves to the right, will the primer be used to create the leading strand of replication or the lagging strand? Explain your answer.
- If you answered lagging strand, explain why this leads to discontinuous replication. If you answered leading strand, explain how this leads to continuous replication.

### 11. *Saccharomyces cerevisiae*

The size of the *Saccharomyces cerevisiae* (yeast, the one you use to bake cakes!) genome is about  $1.5 \times 10^7$  base pairs. Yeast, which uses 400 replication origins to replicate its 17 chromosomes, takes 30 minutes to complete S phase (replicate its genome). Assume all replicons are the same size, initiate replication at the same time during the cell cycle and are replicated at the same rate.

- How many base pairs will be replicated every minute per replicon?
- How fast does a yeast replication fork move (give your answer in micrometer)?
- Telomeres are special and necessary for the proper replication of eukaryotic chromosomes. Telomeres are not required for the replication of bacterial chromosomes. What important role do telomeres serve and what replaces the function of the telomere in bacteria?