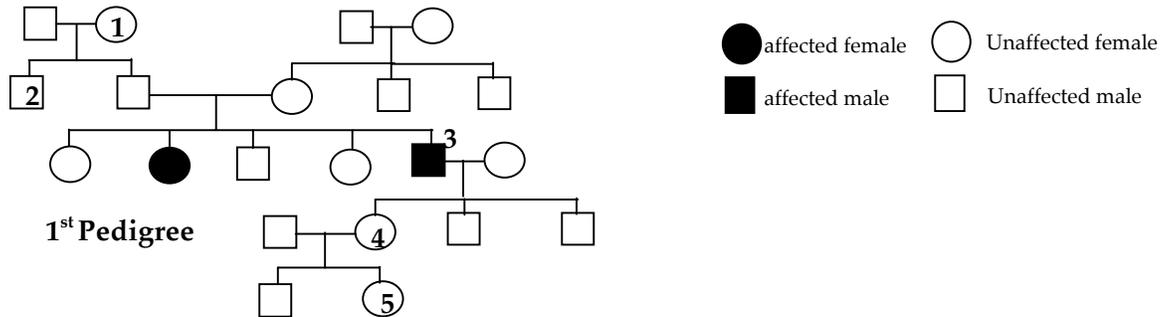


7.016 Problem Set 3

Question 1

The following human pedigree shows the inheritance pattern of a specific disease within a family. Assume that the individuals marrying into the family for all generations (except the parental generation) do not have the allele associated with the disease phenotype and that no other mutation arises spontaneously. Also assume complete penetrance.



a) Circle the **most likely** mode of inheritance for this disease. Choose from: autosomal dominant, autosomal recessive, X-linked dominant, X-linked recessive.

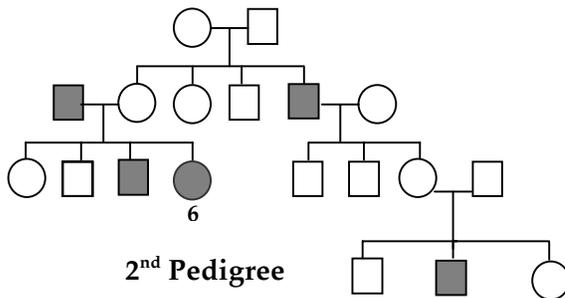
b) Write **all possible** genotypes of the following individuals in the pedigree. Use the uppercase "A" or "X^A" for the allele associated with the dominant phenotype and lowercase "a" or "X^a" for the allele associated with the recessive phenotype.

Genotype(s) of Individual 2:

Genotype(s) of Individual 4:

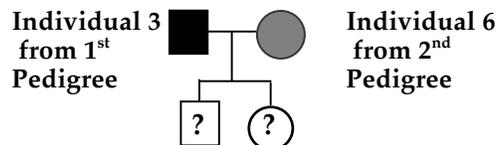
c) What is the probability that Individual 5 will be a carrier?

d) The following human pedigree shows a family affected by a **different disease**. Assume that the individuals marrying into the family do not carry any allele associated with the affected phenotype and that no other mutation spontaneously occurs. Also assume complete penetrance



Note: Use the notation such as "R or X^R" for the allele associated with the dominant phenotype and "r or X^r" for the allele associated with the recessive phenotype.

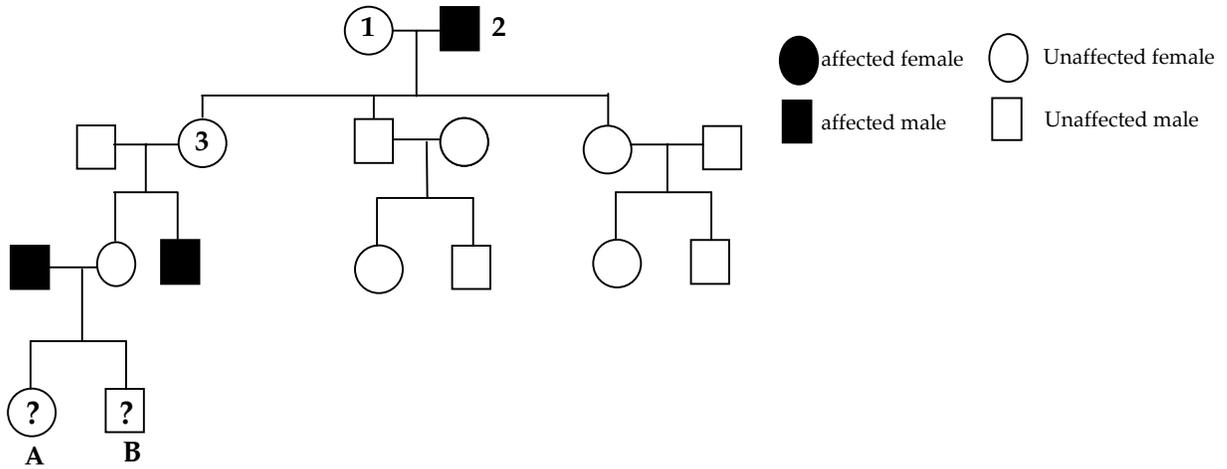
Individual 3 from the 1st pedigree has a second marriage with Individual 6 from the 2nd pedigree. They have a son and a daughter as shown below.



- i. What would be the **genotype** of their **son** for the two genes?
- ii. What would be the **genotype** of their **daughter** for the two genes?

Question 2

You are analyzing the following human pedigree. Assume that the individuals marrying into the family (except the parental generation) do not carry any allele associated with the disease phenotype and that no other mutation spontaneously occurs. Also assume complete penetrance. Use the letter "R or X^R" for the allele associated with the dominant phenotype, "r or X^r" for the allele associated with the recessive phenotype.



a) Circle the **most likely** mode of inheritance of this disease? Choose from: autosomal dominant, autosomal recessive, X-linked dominant, X-linked recessive.

b) List **all possible** genotypes of the following individuals in the pedigree.

Genotype(s) of **Individual 1**:

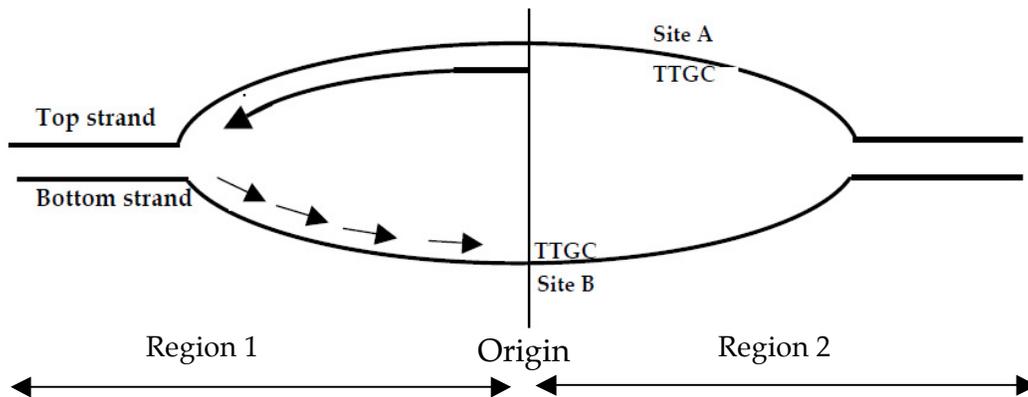
Genotype(s) of **Individual 3**:

c) What is the probability of **Individual A** being affected?

d) What is the probability of **Individual B** being affected?

Question 3

Shown below is the schematic of a replicating DNA in a **bacterial cell**.



a) On the diagram, label the 5' and the 3' ends of the parental DNA strands.

b) Identify the strand(s) (choose from *Top*, *bottom*, *both* or *neither*)...

i. Which serves as a template for the synthesis of a **continuous** strand in **Region 2**.

Question 3 continued

- ii. Which will not replicate if the cells have a **non-functional helicase** in Regions 1 & 2. **Explain** why you selected this option.

Region 1:

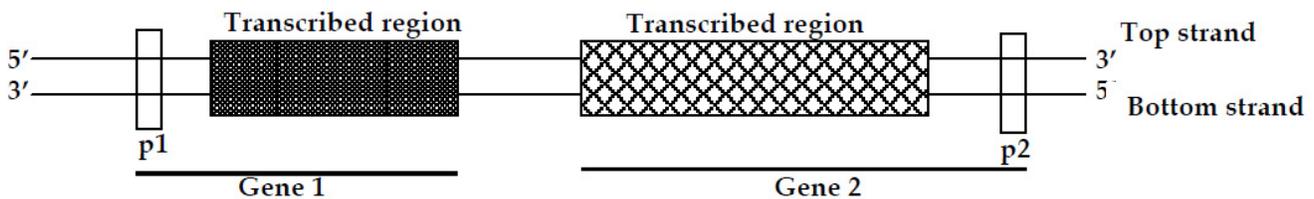
Region 2:

- c) To which site (**A or B or both**) can primer 5'AACG3' bind during replication?

d) Each replication cycle, during each cell division in eukaryotes, results in the shortening of chromosomal ends. This process is slowed down by the action of telomerase enzyme that adds telomere repeats (5'TTAGGG3') to the chromosomal ends. **Explain** how the telomerase activity may regulate the number of mitotic divisions a cell can have during its lifetime.

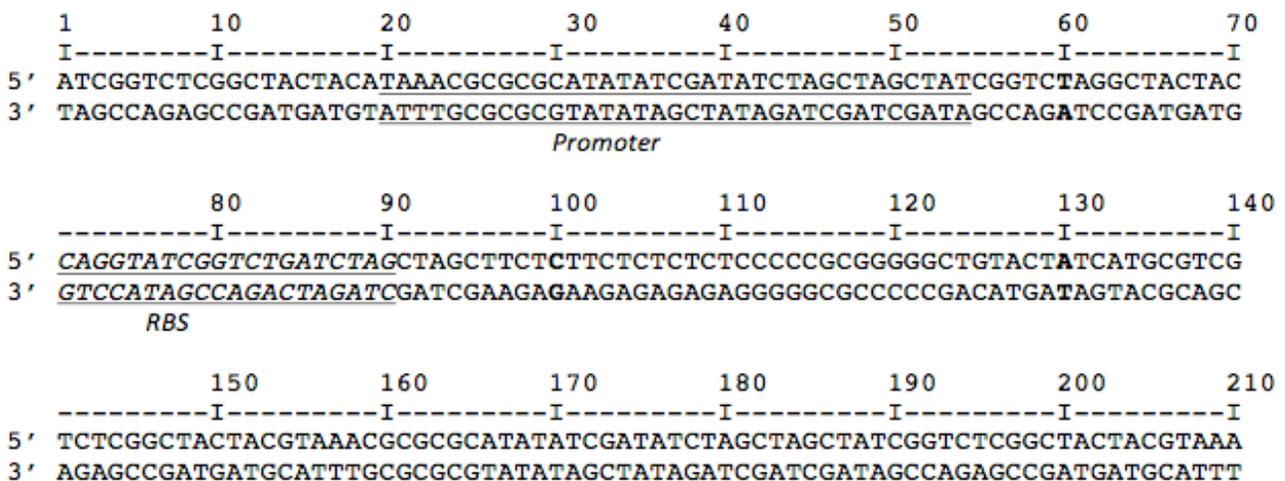
Question 4

The following schematic shows the chromosomal location of Gene 1 and Gene 2. The corresponding promoters for Gene 1 (p1) and Gene 2 (p2) are shown.



- a) On the schematic, use arrows to show the direction of transcription of **Gene 1** and **Gene 2**.

b) The following is the partial DNA sequence of Gene 1. *Note: The underlined sequence (from position 20-54) represents the promoter for Gene 1 and the underlined and italicized sequence (from position 71-90) represents its ribosomal binding (RBS) site. Transcription begins at and includes the bold T (Top)/A (bottom) base pair at position 60.*



- i. Which strand (*Top/ bottom*) is the template strand for transcription of Gene 1?

Question 4 continued

ii. What are the first 6 nucleotides of the mRNA transcribed from Gene 1?

5' _____ 3'

iii. What are the first 4 amino acids encoded by Gene 1? *Note: A codon chart is provided on the last page of this problem set.*

N _____ C

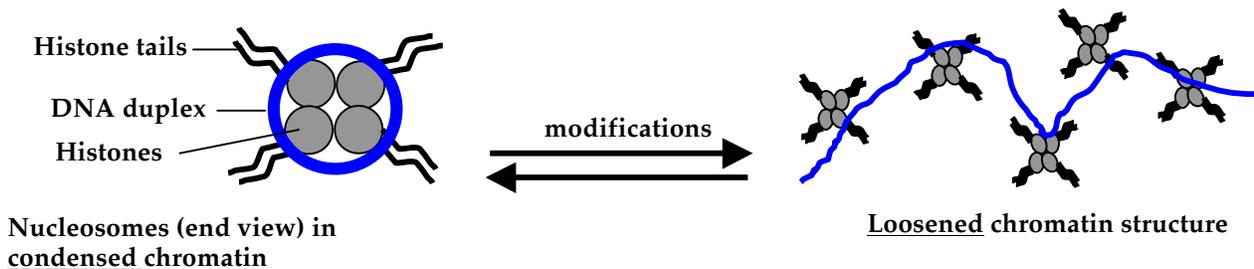
c) You have found mutant alleles of Gene 1 that have insertion of the following three base pairs immediately **after** the C/G base pair at positions, 70, 100 and 150. Complete the table below for each of the following mutations.

5' CGA 3'
3' GCT 5'

	Positions of insertions of the above sequence		
	After 70 th base pair	After 100 th base pair	After 150 th base pair
Effect on the length of protein (<i>longer than/ shorter than/ same as the protein produced by the wild-type allele of Gene 1</i>). Explain.			
If the protein is produced, will it be functional? Explain.			

d) Chromatin is a dynamic structure comprised of DNA and histone proteins. Chemical modifications of histones affect state of chromatin condensation and gene transcription. More than a fifth of histone's amino acids are lysine and arginine. **Explain** why this is crucial to the packing of DNA.

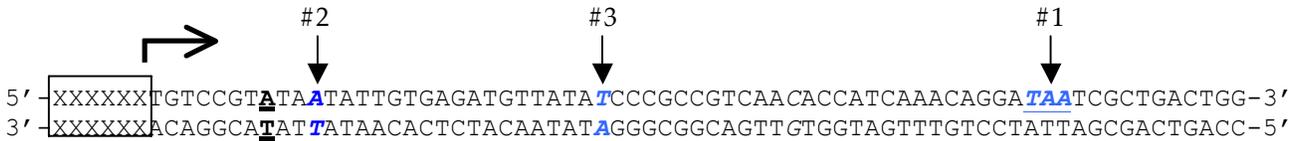
e) The schematic below represents the chromatin in a *condensed* or *loosened* state.



- Which of the above states (*condensed/ loosened*) represents a replicating DNA molecule?
- Which of the above states (*condensed/ loosened*) represents the DNA that is being transcribed?
- Which state (*condensed / loosened*) of chromatin would you expect to see in a cell that has been treated with DNA methylase that adds methyl groups to the cytosine bases in the promoter region of a gene? **Explain** why you selected this option.

Question 5

You are looking at the sequence of a eukaryotic gene that encodes a small peptide. Part of the promoter specific for this gene is indicated by the boxed sequence and the direction of transcription is shown by an arrow. Transcription starts at and includes the bold and underlined A/T (top strand/bottom strand) base pair.



- Give the mRNA sequence of the first 15 bases transcribed from this gene and label its 5' and 3' ends.
- Give the first five amino acids of the peptide that would be translated from the mRNA for this gene and label its N and C ends?
- Give the base sequence and label the 5' and the 3' ends of the anti-codon on the tRNA that inserts the 2nd amino acid into the nascent polypeptide.
- Would a 3rd base substitution within the codon for the second amino acid in the above mRNA transcript always change the resulting protein sequence? **Explain** your answer.
- Do the italicized and underlined nucleotides **TAA** (shown in blue and indicated as #1) correspond to a stop codon for the peptide that is encoded by this gene? Briefly **explain** your answer.
- For each of the following mutations, indicate how the change in the DNA alters the resulting peptide as it compares to the normal functioning peptide. Your choices are: longer than, shorter than, of the same size but different sequence, or no change compared to the normal functioning peptide. For each, **explain** your answer.
 - You add an extra G/C (*top strand/bottom strand*) base pair after the A/T base pair that is shown in blue, italicized and labeled as #2.
 - The T/A base pair, which is shown in blue, italicized and labeled as #3, is changed to a G/C base pair.

Question 6

You are studying transcription in a plant whose leaves fluoresce blue in response to touch. You have the information that the TATA binding factor in this plant specifically binds to the 5'-TATAAT-3' sequence and recruits other components of the transcription apparatus to form a transcription initiation complex. Once RNA polymerase has bound to this region, it begins transcribing **from** the 25th nucleotide **downstream** of 5'-TATAAT-3' sequence.

a) You decide to examine the following **segments of chromosomal DNA** from this plant. For each of the sequences below **box** the template strand of the DNA.

Chromosomal DNA segment I

5' -CCGATATAATGAGATGTCGTCTGGGCCTTCGGGTCTCGTTTTCGGTTCC-3'
3' -GGCTATATTACTCTACAGCAGACCCGGAAGCCAGAGCAAACGCCAAGG-5'

Chromosomal DNA segment II

5' -GGCTTTAATGCTCTACAGCAGACCCGGAAGCCAGATTATACGGATCG-3'
3' -CCGAAATTACGAGATGTCGTCTGGGCCTTCGGGTCTAATATGGCCTAGC-5'

b) Following is an mRNA transcript that encodes a small peptide. The start codon is shown in blue and the intron is shown in yellow and underlined.

5' -GACUAAGAUCAUUUGGGCAACACAGUGCACUUUCCAGUUUGGCGAACCCUGA-3'

10 20 30 40 50

You create the following mutants. **Circle** the mutant from the choices below, which will generate a premature stop codon.

- The 6th base in the **above transcript** was changed from **A** to **U**.
- The 16th base in the **above transcript** was changed from **G** to **A**.
- The 12th base in the **above transcript** was changed from **U** to **C**.

c) The fidelity of transcription is far less compared to replication. **Explain** why is this so. Also **explain** why the cell can tolerate the errors in transcription much better than the errors in replication.

Codon Chart (You can detach this page)

	U	C	A	G
U	UUU Phe (F)	UCU Ser (S)	UAU Tyr (Y)	UGU Cys (C)
	UUC "	UCC "	UAC "	UGC "
	UUA Leu (L)	UCA "	UAA Stop	UGA Stop
	UUG "	UCG "	UAG Stop	UGG Trp (W)
C	CUU Leu (L)	CCU Pro (P)	CAU His (H)	CGU Arg (R)
	CUC "	CCC "	CAC "	CGC "
	CUA "	CCA "	CAA Gln (Q)	CGA "
	CUG "	CCG "	CAG "	CGG "
A	AUU Ile (I)	ACU Thr (T)	AAU Asn (N)	AGU Ser (S)
	AUC "	ACC "	AAC "	AGC "
	AUA "	ACA "	AAA Lys (K)	AGA Arg (R)
	AUG Met (M)	ACG "	AAG "	AGG "
G	GUU Val (V)	GCU Ala (A)	GAU Asp (D)	GGU Gly (G)
	GUC "	GCC "	GAC "	GGC "
	GUA "	GCA "	GAA Glu (E)	GGA "
	GUG "	GCG "	GAG "	GGG "

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