BIRLA INSITUTE OF TECHNOLOGY AND SCIENCE, PILANI

Second Semester 2012-2013

2 May 2013 8:00 – 11:00 am	**BIO F243 Genetics** **Comprehensive Examination**	Open-book type 35 marks (35%)

1. (a) You have obtained an interesting flower for your garden from your neighbor. The neighbor has given you two pure lines of the plant, one with red flowers and one with yellow flowers. You decide to cross them and find that you obtain all orange flowers. The curious molecular geneticist in you decides to test two independent hypotheses: Hypothesis 1: Incomplete Dominance; Hypothesis 2: Recessive Epistasis. The first step in your test is to self the F1 orange plants, which you complete only to find that the results do not statistically distinguish the two hypotheses. a) What ratio of yellow, orange, and red would you expect in the F_2 population for each hypothesis and b) what crosses would you complete next to definitively test your two hypotheses? **[2]**

(b) Two pink-flowered four-o'clock plants (showing incomplete dominance) were crossed to each other. What is the probability of obtaining a group of six plants containing one pink, two whites, and three reds? **[1]**

(c) Solve question #24 printed on page 106 of the course textbook only for pedigree charts corresponding to (a) and (b), assuming complete penetrance of the trait. Justify your answer choices. **[2]**

(d) Why do you think autosomal aneuploidies are more lethal than X-chromosome aneuploidies in humans? **[1]**

2. (a) Two recessive disorders in mice, droopy ears and flaky tail, are caused by genes that are located 6 mu apart on chromosome 3. A true breeding mouse with normal ears (*De*) and a flaky tail (*ft*) was crossed to a true-breeding mouse with droopy ears (*de*) and a normal tail (*Ft*). The F_1 offspring were then crossed to mice with droopy ears and flaky tails. If this testcross produced 100 offspring, what is the expected outcome? **[2]**

(b) Let's suppose a new strain of P1 has been identified that packages larger pieces of the *E. coli* chromosome. This new P1 strain packages pieces of the *E. coli* chromosome that are 5 minutes long. If two genes are 0.7 minutes apart along the *E. coli* chromosome, calculate the co-transduction frequencies using a normal strain of P1 and using this new strain of P1 that packages large pieces. What would be the experimental advantage of using this new P1 strain? **[1½]**

(c) A researcher has several different strains of T4 phage with single mutations in the same gene. In these strains, the mutations render the phage temperature sensitive. In this case, this means that temperature-sensitive phages can propagate when the bacterium, say, *E. coli* is grown at 32°C but cannot propagate themselves when *E. coli* is grown at 37°C. Think about Benzer's strategy for intragenic mapping and propose an experimental strategy to map the temperature-sensitive mutations. You may use a flow diagram to answer this question. **[2½]**

3. (a) Within living cells, a myriad of different proteins play important functional roles by binding to DNA and RNA. Some proteins bind to DNA (or RNA) but not in a sequence-specific manner. Others are highly sequence-specific. **[2]**

(i) Give an example of each of the two categories of DNA-binding proteins.

(ii) With regard to the three-dimensional structure of DNA, where would you expect DNA-binding proteins to bind if they recognize a specific base sequence? What about DNA-binding proteins that do not recognize a base sequence?

(b) Arrange the following list of eukaryotic gene elements in the order they would appear in the genome and in the direction traveled by RNA polymerase along the gene. Assume the gene's single intron interrupts the open reading frame. Note that some of these names are abbreviated and thus do not distinguish between elements in DNA versus RNA. For example, "splice-donor site" is an abbreviation for "DNA sequences transcribed into the splice donor site" because splicing takes place on the gene's RNA transcript, not on the gene itself. Geneticists often use this kind of shorthand for simplicity, even though it is imprecise. **[1½]**

(i) splice-donor site;	(ii) 3′ UTR;	(iii) promoter;
(iv) stop codon;	(v) nucleotide to which methylated cap is added;	
(vi) initiation codon;	(vii) transcription terminator;	
(viii) splice-acceptor site;	(ix) poly-A addition site;	(x) 5′ UTR.

(c) Which of the element names in the list of ten given in the previous question is/are <u>not</u> abbreviated? (That is, which of these elements actually occur in the gene itself?) **[½]**

(d) Explain why each of the following statements in incorrect. Be as comprehensive as you can be in your explanations. **[1]**

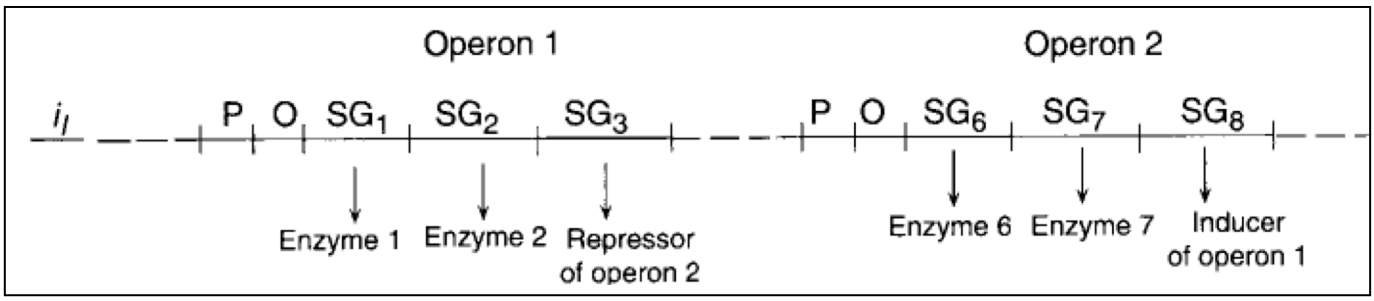
A. The sliding clamp is loaded once on each DNA strand, where it remains associated until replication is complete.

B. Primase requires a proofreading function that ensures there are no errors in the RNA primers used for DNA replication.

(e) Consider a segment of RNA with the sequence AGUCUAGGCACUGA. If you were told that this segment of RNA was in the middle of an mRNA that encoded a large protein, would you know which reading frame was used? How so? Also indicate the amino acids in this reading frame. **[1]**

(f) A point mutation changes a peptide sequence from Met-Asn-Trp-Ser-Gly to Met-Thr-Gly-Val. Write out the sequence of the portion of mRNA that corresponds to the original pentapeptide. **[1]**

4. (a) Consider the following inducible operons:



Suppose you supply the inducer of operon 1 for only a short time. Also assume the inducer and repressor have a short half-life. Starting with the first operon turned on and the second operon turned off, how would you describe the continuing action of these two operons after the original (exogenous) inducer has been used up? **[2]**

(b) Answer question #20 found on page 437 of the course textbook, with a brief explanation. **[1]**

(c) While transposons are found in both eukaryotes and prokaryotes, what is the major difference in the nature of transposons found in these domains? Why are transposons very tightly controlled in the genome? And how? **[2]**

5. (a) Explain the differences between chromosome painting and the older, more traditional method of staining chromosomes being prepared for karyotyping. Highlight the way in which each method identifies chromosomes by the unique sequences they contain. **[1]**

(b) Evidence suggests that the replication of DNA at the centromere occurs later than the replication of other chromosomal DNA. What is the simplest possible explanation for this observation? Why is there a delay in replicating regions similar in organization as that of the centromere? **[1]**

(c) Identical twins are excellent candidates for conducting research in human epigenetics. Why do you think this is the case? **[1]**

(d) What is the fundamental difference between the gene expression pattern of an imprinted gene and a gene that contributes to a Mendelian trait? At the molecular level, how do the mechanisms work? **[1]**

(e) How is a gene knockout different from transgenesis? Answer from the perspectives of both the methodology involved as well as the objectives served by these techniques. **[2]**

(f) Amplification of DNA sequences in *p53* mutants (in cancer) can be visualized using electron microscopy. Using a different technique, how could you detect amplification of a *specific sequence*? How could you detect gross rearrangements (> 10 Mb) of chromosomal DNA? **[1]**

6. (a) The events listed below are all necessary for homologous recombination to occur properly. Give the correct sequence (write the sequence of alphabets only). **[1]**

A. Holliday junction cut and ligated

B. strand invasion

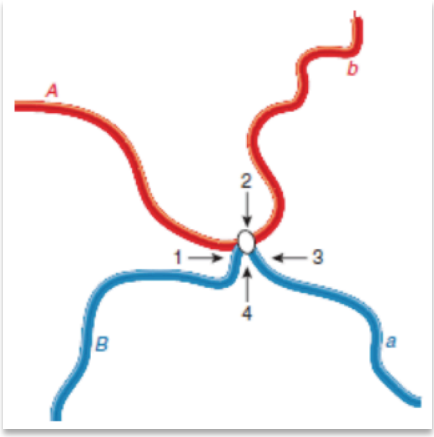
C. DNA synthesis

D. DNA ligation

E. double-strand break

F. nucleases create uneven strands

(b) A schematic drawing of an uncrossed Holliday junction is shown below. One chromatid carries a dominant allele labeled *A* and a recessive allele labeled *b*, and the other chromatid carries a recessive allele labeled *a* and a dominant allele labeled *B*. Where would the breakage of the crossed strands have to occur to get recombinant chromosomes? What would be the genotypes of the two recombinant chromosomes? **[½]**



(c) Let's suppose that you are a horticulturist who has recently identified an interesting plant with variegated leaves. How would you determine if this trait is nuclearly or cytoplasmically inherited? **[1]**

(d) In snails, an autosomal allele for a dextral snail shell (s^+) is dominant over the sinistral shell allele (s) and results from a genetic maternal effect. Suppose a snail *"Fancy"* is sinistral and is currently reproducing as a female (although it is hermaphrodite). Examine each of the following statements and state whether it is true or false, giving a brief justification. **[1½]**

(i) Fancy's mother must have been sinistral.

(ii) Fancy's genotype cannot be s^+s^+.

(iii) Some of the offspring produced by Fancy will be sinistral.