39.314 INTRODUCTORY CYTOGENETICS
FINAL EXAMINATION

December 18 , 2004
Time: 1:30 p.m. to 3:30 p.m.
Location: Brown Gym, Seats 385-396

This examination consists of questions totaling 100 points, and is worth 35% of the final grade.

Ways to write a readable and concise answer:
i. Just answer the question. Save time by specifically addressing what is asked. Don't give irrelevant background if it doesn't contribute to the question that was asked.
ii. Avoid stream of consciousness. Plan your answer by organizing your key points, and then write a concise, coherent answer. Make your point once, clearly, rather than repeating the same thing several times with no new information.
iii. Point form, diagrams, tables, bar graphs, figures are welcome. Often they get the point across more clearly than a long paragraph.
iv. Your writing must be readable. If I can't read it, I can't give you any credit.

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1) (10 points) RAPD markers for two loci, A and B are tested for genetic linkage by crossing two parents and selfing the F1s. One of the original parents was homozygous for the presence of a band (+) for both markers , while the other parent was homozygous for the absence of a band (-), for both markers. Rewrite the table, indicating, for the four phenotypic classes, the expected ratios of progeny in a segregating F2 population. Assume that "tightly-linked", means that no recombination is detected between A and B loci, and that A and B are linked in coupling.

Marker A	Marker B	Unlinked + + x - - --- --- --- --- + + - -	tightly-linked, in coupling + + x - - ---- ----
+	+		
+	-		
-	+		
-	-		

2) (15 points) Traditionally, transformation of novel genes into plants and animals has employed various methods for delivering DNA into cells (eg. transfection, microinjection, *Agrobacterium* infection), but these methods all ultimately depend upon the DNA repair mechanisms of the target cell to insert the DNA into chromosomes at a random location.

Recently, artificial chromosomes have been developed for plants, although they are not yet available or mamalian cells.

a) What are the three critical features needed to create an artificial chromosome?

b) List two advantages that would be provided by transformation with artificial chromosomes, compared to random insertion of genes.

3) (15 points)
Given the following definitions:

N: Genome size
f_{mr}: fraction of the genome that is middle repetitive
X : $KC_0t_{½\ (pure)}$, Complexity
l_{mr}: average length of a middle repetitive sequence

write a phrase that describes what the following equations tell you?

a) $a = f_{mr}N$

b) $b = X/l_{mr}$

c) $c = a/X$

4) (10 points) ESTs are cDNA clones for which partial sequence is available, usually from a single sequencing reaction. This question distinguishes between what ESTs can tell you, and what they can't. Complete the sentence for ANY 5 of the following:

a) Map position: An EST, by itself doesn't tell you the map position of a gene, but it can be used to find the position by _____.
b) Amino acid sequence: An EST tells you some of the amino acid sequence of a protein, if you can determine _____.
c) Locations of introns: An EST can tell you the location of some of the introns if you also know _____.
d) Gene function: An EST can't tell you the function of gene from the sequence alone, but that sequence can be used to infer function if _____.
e) Gene copy number: If a gene exists as a multigene family, a large EST population can tell you a minimal estimate of copy number but _____.
f) Gene expression: ESTs can tell you whether or not a gene is expressed in a given tissue or developmental stage, but if you want to know _____ the ESTs must be used in gene array experiments.

5) (20 points) Fill in the blanks.

_____i_____ can generate both deletions and duplications in a single event. Double-stranded breaks in a chromosome can also generate deletions, because one of the resultant chromosomal fragments will be lacking a _____ii_____ and therefore cannot segregate reliably. Introduction of alien chromosomes through crosses with _____iii_____ can also cause deletions in some or all of a chromosome. Once duplications and deletions exist, their

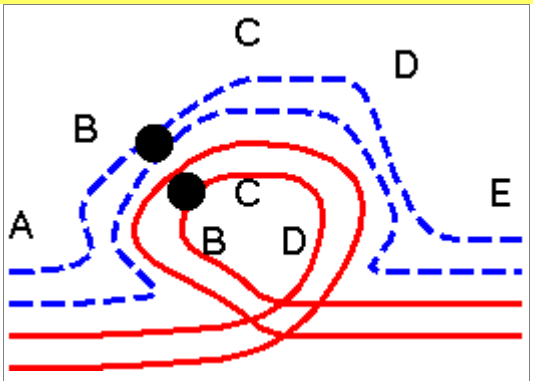
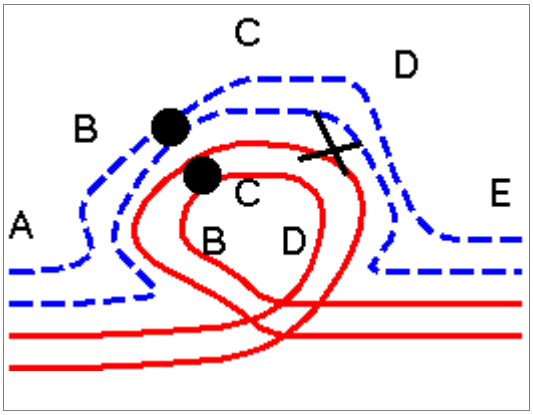
effects on chromosome pairing in heterozygotes can result in new duplications and deletions occurring in subsequent generations as a result of _____iv_____ cycles. Ring chromosomes also can cause deletions and duplications. There is no fundamental reason why ring chromosomes shouldn't be able to replicate and segretate normally. However, if v_____ occurs, there will almost certainly be a duplication and deletion.

Another mechanism for chromosomal evolution is transposition. The first transposon discovered was the Ds element, which is flanked by _____vi_____ . Normally, a Ds element will stay at a fixed chromosomal location. However, if a Ds-bearing maize line is crossed with a maize line containing the Ac element, _____vii_____ . This is possible because the Ac element carries a gene for _____viii_____ which is lacking in Ds. In the presence of Ac, Ds mobilization caused _____ix_____ of the colorless phenotype to colored. The earlier the excision of Ds occurs during kernel development, the _____x_____ the colored sectors will be.

6) (15 points)

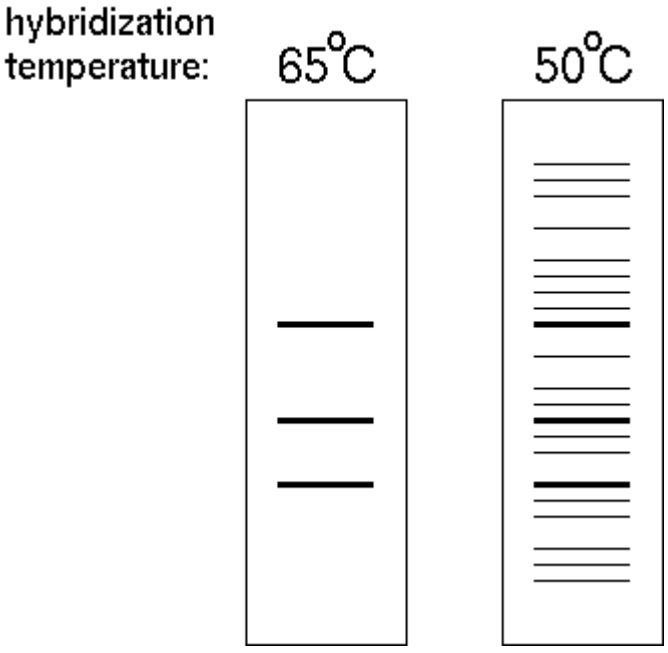
a) What kind of inversion is shown in the table below?

b) For each of the three cases shown in the table, list how many normal, inverted, and recombinant chromosomes would be found.

Inversions	
No crossover:	
Single crossover within inversion:	

7) (10 points) Suppose you wanted to clone sequences that had arisen after the divergence of humans from chimps. Outline a step by step procedure using Hydroxyapatite (HAP) columns to isolate sequences that appear in the human genome, but not in the chimp genome. (You could answer this question either with a list of steps or a flow chart.)

8) (5 points)
A southern blot of mouse genomic DNA was hybridized with a mouse cDNA clone at 65°C, showing three bands. The blot was washed and re-hybridized with the same probe, but this time at 50°C with dozens of bands now visualized. It is well-known that at high temperatures, close-to perfect match is required for two sequences to hybridize. The lower the temperature, the more mismatches are tolerated.



What do these results tell you about the evolution of this sequence in the rodent genome?