MCB C142 / IB C163 MIDTERM I  
Fall 2008

NAME (Please print): ____ KEY ________________________________  
STUDENT ID #:______________________________

***IMPORTANT REMINDERS***

Print your name and ID# on every page of the exam.  
You will lose 0.5 point/page if you forget to do this.

Check that you have 13 pages total, including this cover page. The last five pages are work space only (no problems), that you may remove from the exam to use. Work space pages will not be graded, but must be turned in, whether you use them or not.

Only the front of each page will be graded. If you use the back of a page or a work space page, you must transcribe your answer to the space provided on the front of the page.

This is a closed book, closed note exam. No calculators allowed.

Look through the entire exam before starting. You do not have to start with Question 1. 
Read each question entirely before beginning. 
Write legibly. Show your calculations.

Written regrade requests must be presented to your GSI within 7 days after exams are returned. To be eligible for a regrade, your answers must be in pen. Answers in pencil, erasable ink, or corrected with white-out will not be accepted for regrades.

(Do not write below this line)

PROBLEM 1  a_____ b_____ c_____ d_____  ____ / 25
PROBLEM 2  a_____ b_____ c_____ d_____ e_____ f______  ____ / 35
PROBLEM 3  a_____ b_____ c_____ d_____  ____ / 35
PROBLEM 4  a_____ b_____ c_____ d_____  ____ / 25
PROBLEM 5  a_____ b_____ c_____ d_____  ____ / 30

TOTAL  ____ / 150
Question 1 (25 points)

The pedigree below is for a very rare disease. A pair of identical twins is indicated with a horizontal line that joins both symbols together and with two lines that join together at a vertex.

(a) What mode of inheritance most likely describes the genetic basis of the disease depicted in the above pedigree? Include whether dominant/recessive and autosomal/sex-linked and explain your answer. (6 pts)

Autosomal dominant. Dominant because it appears every generation – affected children have affected parents. Autosomal because affected parents pass the disease to approximately half their progeny, with sons and daughters equally affected.

(b) If there are any individuals in the above pedigree who must carry the disease allele, but do not express the trait, circle them on the pedigree. If not, circle NONE here. (6 pts)

(c) What mode of inheritance most likely describes the genetic basis of the disease depicted in the above pedigree? Include whether dominant/recessive and autosomal/sex-linked and explain your answer. (6 pts)

X-linked recessive. Recessive because it skips generations and because unaffected parents have affected children. X-linked because females I-1, II-3, and II-5 are carriers who pass the disease on to half their sons and none of their daughters.

(d) If there are any individuals in the pedigree who must carry the disease allele, but do not express the trait, circle them on the pedigree. If not, circle NONE here. (7 pts)
Question 2 (35 points)
You are investigating the linkage relationship between three Drosophila recessive traits, each determined by a single gene: waxy wings (w), purple eye (p), and short antenna (s). A triply heterozygous, phenotypically wildtype F1 female was testcrossed to the appropriate male, and phenotypes of the 1000 progeny were scored.

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>purple eye, short antenna</td>
<td>95</td>
</tr>
<tr>
<td>wildtype</td>
<td>110</td>
</tr>
<tr>
<td>waxy wings</td>
<td>105</td>
</tr>
<tr>
<td>purple eye</td>
<td>296</td>
</tr>
<tr>
<td>waxy wings, purple eye, short antenna</td>
<td>90</td>
</tr>
<tr>
<td>waxy wings, short antenna</td>
<td>304</td>
</tr>
</tbody>
</table>

(a) Indicate the genotype of the male that was crossed with the F1 female to give rise to the progeny shown above. Show allele order on each chromosome. (1 pt)

\[ p \ w \ s / p \ w \ s \quad OR \quad s \ w \ p / s \ w \ p \]

(b) Indicate the genotype of the F1 female. Show allele order on each chromosome. (4 pts)

\[ p \ w^+ \ s^+ / p^+ \ w \ s \quad OR \quad s^+ \ w^+ \ p / s \ w \ p^+ \]

(c) Draw the linkage map. Indicate the gene order and show genetic distance in map units. Show your calculations. (10 pts)

We are expecting 8 classes, but get only 6. The missing class of recombinants (those recombinant for w) tells us what gene is in the middle.

\[
\text{distance between } p \text{ and } w: (110+90+0+0)/1000 \times 100 = 20 \text{ mu}
\]
\[
\text{distance between } w \text{ and } s: (95+105+0+0)/1000 \times 100 = 20 \text{ mu}
\]

\[
\text{Map: } s--------------------------w--------------------------p \\ 20 \text{ mu} \quad 20 \text{ mu}
\]
**Question 2, continued**

(d) Carefully redraw your linkage map here. (2 pts)

Map:  
```
 s----------------------------------w----------------------------------p
  20 mu  20 mu
```

(e) Calculate the interference in the region, if any, and comment on its meaning. (5 pts)

Flies recombinant for w relative to the other two markers represent the double crossover class and these phenotypic classes are completely missing, meaning that no double crossovers occurred in the interval and that interference is complete (full, \(=1\)). (Saying this is enough for full credit; if you calculated the coefficient of coincidence, etc. that’s fine too!)

(f) If interference were the opposite of that calculated above in (e), indicate the phenotypic classes of progeny and numbers expected in the table below, assuming 1000 progeny. Use space to the right and below to explain your reasoning and show your calculations. (8 pts)

<table>
<thead>
<tr>
<th>Phenotypic class</th>
<th># expected</th>
</tr>
</thead>
<tbody>
<tr>
<td>purple eye</td>
<td>320</td>
</tr>
<tr>
<td>short antenna, waxy wings</td>
<td>320</td>
</tr>
<tr>
<td>wildtype</td>
<td>80</td>
</tr>
<tr>
<td>short antenna, waxy wings, purple eye</td>
<td>80</td>
</tr>
<tr>
<td>short antenna, purple eye</td>
<td>80</td>
</tr>
<tr>
<td>waxy wings</td>
<td>80</td>
</tr>
<tr>
<td>waxy wings, purple eye</td>
<td>20</td>
</tr>
<tr>
<td>short antenna</td>
<td>20</td>
</tr>
</tbody>
</table>

If there is no interference, then we will observe the expected number of DCO phenotypic classes (those recombinant for w relative to the other 2), which is just 0.2 x 0.2 or 0.04, 4% of the total progeny or 40 individuals. We split these between the two DCO phenotypic classes (20 each).

To figure the number of individuals in the phenotypic classes recombinant for p relative to the other two:

\[
20 = \left(\frac{x + 20 + 20}{1000} \times 100\right)
\]

\[
x = 160 \text{ (split between the 2 classes)}
\]

To figure the number of individuals in the phenotypic classes recombinant for s relative to the other two:

\[
20 = \left(\frac{x + 20 + 20}{1000} \times 100\right)
\]

\[
x = 160 \text{ (split between the 2 classes)}
\]

(this is the same as above)

The parentals make up the difference, split between the two classes (320 each). 
\[
(1000 – 160 – 160 – 40 = 640)
\]
Question 3 (35 pts)
You cross a wild-type Neurospora strain to a strain requiring uracil and glutamine for growth. You score the resulting tetrad types, noting the genotype and the order of spore pairs within the ascus. (Note: there are eight spores in each ascus; we do not show the mitotic division).

<table>
<thead>
<tr>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
<th>VI</th>
<th>VII</th>
</tr>
</thead>
<tbody>
<tr>
<td>URA⁺ GLU⁺</td>
<td>URA⁺ GLU⁺</td>
<td>URA⁺ GLU⁺</td>
<td>URA⁺ GLU⁺</td>
<td>URA⁺ GLU⁺</td>
<td>URA⁺ gl⁻</td>
<td>URA⁺ gl⁻</td>
</tr>
<tr>
<td>ura⁻ gl⁻</td>
<td>ura⁻ GLU⁺</td>
<td>ura⁻ GLU⁺</td>
<td>ura⁻ GLU⁺</td>
<td>ura⁻ GLU⁺</td>
<td>ura⁻ GLU⁺</td>
<td>ura⁻ GLU⁺</td>
</tr>
<tr>
<td>41</td>
<td>16</td>
<td>32</td>
<td>2</td>
<td>6</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

a) Is there a linkage relation between these two genes? What criteria did you use to determine your answer? (5 pts)

Yes, the genes are linked. The # PDs (43) greatly exceed the #NPDs (3).

b) Draw the best genetic map to explain the observed results. Indicate all relevant genetic distances, both between genes and between each gene and its centromere. Calculate recombination frequency (RF) and the corrected map distance (MD). Show your calculations. (15 pts)

RF between ura and glu = [1/2 (54) + 3)]/100 *100 =30 map units.
Corrected map dist. accounting for DCOs = [1/2 (54) + 3(3)]/100 * 100 = 36 map units.
Dist. between ura and centromere = 1/2 (32+2+6+4)/100 * 100 = 21 map units
Dist. between glu and centromere = 1/2 (16+2+6+2)/100 * 100 = 13 map units

<table>
<thead>
<tr>
<th>ura</th>
<th>glu</th>
</tr>
</thead>
<tbody>
<tr>
<td>21 m.u.</td>
<td>13 m.u.</td>
</tr>
</tbody>
</table>

(30-36 m.u. between genes)
Question 3, continued
(c) Is there a discrepancy between RF and corrected MD above? If so, account for the difference by explaining why one equation is more accurate than the other. (5 pts)

Yes, there is a discrepancy. RF takes into account only 4-strand DCOs, whereas MD accounts for all DCOs.

You obtain a Neurospora yeast strain from another laboratory that can grow on minimal media (URA$^+$ GLU$^+$). You cross this strain to the strain from your laboratory that requires uracil and glutamine for growth (ura$^-$ glu$^-$). You sporulate the resulting diploid and collect 50 tetrads. You observe that many tetrads contain some shrunken, inviable spores. All the tetrads containing 4 viable spores are PD tetrads. The chromosomes of both strains are of normal size and do not appear to be missing bands; however, in the diploid, the centromere position appears different between two homologs of one particular chromosome.

(d) What is the most likely reason for the discrepancy in tetrad types observed when the two different URA$^+$ GLU$^+$ haploid strains (the one from your lab and the one from the other lab) are used to construct the diploid? Explain. Your answer should clearly explain the differences observed in spore viability and in distribution of tetrad types in the two different crosses. (10 pts)

The URA$^+$ GLU$^+$ haploid strain from the other laboratory probably contains a large pericentric inversion that includes both the URA and GLU genes. When SCOs occur in the inversion loop in the inversion heterozygote, the spores bearing the recombinant chromosomes are inviable, because the recombinant products contain duplications and deletions. Tetrads containing inviable spores cannot be scored. (The only type of DCO that gives 4 viable spores is a two-strand DCO, and this tetrad would be scored as a PD.)
Question 4 (25 pts)
Karen is a carrier of a recessive mutation in keratinosin, an X-linked gene. Loss of keratinosin function causes keratinosis. The symptoms included poor teeth, skin thickening, and defective sweat gland formation, especially on the hands and feet. A centromeric gene encoding an enzyme with several allelic isoforms (A, B, and C) is very closely linked to the keratinosin gene. Karen carries the A and B isoforms, and the A form is linked to the mutated keratinosin allele. Karen has no symptoms of keratinosis. Karen’s partner Bob carries the C isoform of the linked enzyme and is not affected by the disease. (Note: For this problem, Klinefelter males can carry 2 or more X chromosomes, in addition to a Y chromosome)

(a) Karen and Bob’s first child is a normal male that does not have keratinosis. What form(s) of the linked enzyme does this child carry? (5 pts)

B. (The child inherited the non-mutant bearing chromosome from mom, thus carries the B form of the linked enzyme.)

(b) Karen and Bob’s second child is an XXY Klinefelter male that has keratinosis. The child only has the A form of the linked enzyme. In which parent and when (Meiosis I or II) did the non-disjunction event occur? (5 pts)

Non-disjunction of the X occurred in Mom during Meiosis II. (The child carries two mutant-bearing X chromosomes, both linked to the A form of the enzyme.)

(c) Karen and Bob’s third child is an unaffected Klinefelter male carrying one copy each of the A, B, and C enzyme isoforms. Indicate the number and type of sex chromosomes in this child. In which parent and when (Meiosis I or II) did non-disjunction occur? (5 pts)

Non-disjunction of the sex chromosomes in both Mom and Dad happened during Meiosis I to generate the gametes that united to make this XXXY Klinefelter male.

(In order to carry all three enzyme isoforms, this child must have 3 X chromosomes, thus be an XXXY Klinefelter male. He got the A and B forms from mom and the C form (and a Y chromosome) from dad.)

(d) Karen and Bob’s fourth child is a daughter carrying the A and C isoforms of the linked enzyme. The daughter is mildly affected. The skin on her feet and legs lack sweat glands, but her teeth show no signs of deterioration. Provide the most likely explanation for why this child shows some mild symptoms of keratinosis. (10 pts)

The fourth child shows mild symptoms due to X-inactivation. Many or all cells giving rise to the teeth were clonally derived from precursor cells that inactivated the maternally-inherited disease-carrying X chromosome, thus the teeth are unaffected. On the other hand, many or all cells giving rise to skin tissue of the lower extremities were derived from precursor cells that inactivated the paternally-inherited X chromosome, thus these cells have the disease phenotype.
**Question 5 (30 pts)**
You are a mouse breeder who is interested in adding new coat color phenotypes to your collection. You mate a purebreeding mouse strain with chestnut-colored fur with a purebreeding strain with wheat-colored fur and all the progeny have wheat-colored fur. When you cross F1 individuals and examine the progeny, you get 90 wheat and 70 chestnut mice.

(a) How is wheat and chestnut coat color determined in mice? (10 pts)

*There are two genes controlling coat color. The genes show complementary gene action, so that the mouse must carry dominant alleles of both genes in the coat color pathway to generate wheat colored fur. If they carry only recessive alleles at one or both loci, they have chestnut fur.*

(b) What is the genotype of the purebreeding chestnut strain? (5 pts)

`aa bb` (where A = gene 1 and B = gene 2 required in the pathway for wheat fur color)

(c) What is the genotype of the purebreeding wheat-colored strain? (5 pts)

`AA BB` (where A = gene 1 and B = gene 2 required in the pathway for wheat fur color)

(d) Now you cross the F1 mice to your purebreeding chestnut strain. What phenotypes do you expect among the progeny and in what proportions? (10 pts)

*This is essentially a testcross:*

`F1 individual Aa Bb   x   homozygous recessive aa bb`

*The F1 makes four types of gametes: AB, Ab, aB and ab. Only the first gamete listed will generate a wheat-colored mouse when fertilized by a gamete carrying recessive alleles (ab) from the testcross parent (purebreeding chestnut mouse). The others will not carry a dominant allele at both loci, thus will have chestnut fur. The phenotypic ratio will be 3 chestnut:1 wheat.*