

Name: _____

7.03 Exam I

Name: Answer Key

Recitation Section (circle one) – Mo1:00 Mo2:00 Mo3:00 Tu10:00 Tu11:00 Tu12:00

Exam starts at 11:05 and ends at 11:55

Please write your name on each page.

Please...

- Look over the entire exam so you don't spend too much time on hard questions leaving easy questions unanswered
 - Check answers to make sure they make sense
- To help us give partial credit, show your work and state any assumptions that you make

Question 1	34 points
Question 2	32 points
Question 3	34 points

1. You have identified two yeast mutants that are unable to grow on culture plates in the absence of methionine. You call them $met1^-$ and $met2^-$.

a) (6 points) Mating either of these haploid strains to wild type strains yields diploids that can grow in the absence of methionine. Additionally, diploids generated by crossing $met1^-$ and $met2^-$ haploids can also grow in the absence of methionine. What do these data tell you about the $met1^-$ and $met2^-$ mutations?

- (+3) 1) $met1^-$ and $met2^-$ are recessive to wild type
- (+3) 2) $met1^-$ and $met2^-$ complement, \therefore they are most likely mutations in different genes

b) (6 points) Sporulation of diploids generated from the $met1^-$ and $met2^-$ haploid cross produces tetrads of the following variety:

tetrad variety 1

4 met^-

tetrad variety 2

3 met^- , 1 Met^+

Out of 40 tetrads, 37 are variety 1 and 3 are variety 2. Classify each variety as either parental ditype (P), tetatype (T), or nonparental ditype (NPD). If the genes are linked, provide the genetic distance between them.

$$\begin{aligned} \text{Variety 1} &= P \quad (+2) \\ \text{Variety 2} &= T \quad (+2) \end{aligned}$$

$PD >> NPD \therefore$ linked

no NPD \therefore tightly linked, no DCO

$$\text{Distance} = 100 \times \frac{T}{2\Sigma} = 100 \times \frac{3}{2(40)} = 3.75 \text{ cM}$$

*2

c) (6 points) You isolate a third mutant, $met3^-$, that cannot grow on culture plates in the absence of methionine. When $met3^-$ haploids are mated to $met1^-$ haploids, the resulting diploids are unable to grow in the absence of methionine. What does this result tell you about the relationship between the $met3^-$ and $met1^-$ mutations.

- 1) $met1^-$ and $met3^-$ do not complement,
 - a) if $met3^-$ is recessive to wild type they are likely mutations in the same gene
 - b) $met3^-$ could be dominant to wild type

+6 for either answer

d) (8 points) When the diploids generated by mating $met3^-$ haploids with $met1^-$ haploids are sporulated, tetrads of the following varieties are produced:

tetrad variety 1

4 met^-

tetrad variety 2

3 met^- , 1 Met^+

tetrad variety 3

2 met^- , 2 Met^+

Out of 40 tetrads, 6 are variety 1, 26 are variety 2, and 8 are variety 3. Classify each variety as either parental ditype (P), tetatype (T), or nonparental ditype (NPD). What does this result tell you about the relationship between the $met3^-$ and $met1^-$ mutations? If the genes are linked, provide the genetic distance between them.

$PD \approx NPD \therefore$ unlinked (+2)

1 = PD
2 = T
3 = NPD] +4

As they are unlinked, they must be mutations in different genes. Therefore $met3^-$ is likely dominant. (+2)

e) (8 points) Based on the above data, what is the most likely relationship between the $met3^-$ and $met2^-$ mutations? If you mated $met3^-$ and $met2^-$ haploid strains, what would the phenotype of the resulting diploid be? If you sporulated this diploid and examined 80 tetrads, predict the number and variety of tetrads that would be observed.

As $met3^-$ is dominant, the resulting diploid will be unable to grow in the absence of methionine. (+4)

Since $met1$ and $met2$ are tightly linked and $met1$ and $met3$ are unlinked, $met2$ and $met3$ will be unlinked. PD : T : NPD

1 : 4 : 1

~ 14 : 53 : 13

2. You are investigating three autosomal recessive *Drosophila melanogaster* mutants. Flies that are homozygous for the pr^- mutation have purple eyes (wild type eyes are red). Flies that are homozygous for the cy^- mutation have curly wings (wild type wings are straight). Flies that are homozygous for the al^- mutation have antenna that are aristaless (as opposed to wild type antenna).

You have two true-breeding lines of flies that you mate together to generate F1 flies. All F1 flies have red eyes, straight wings and wild type antenna. You then mate F1 females with males that have purple eyes, curly wings and are aristaless. In the resulting F2 generation, you examine 1200 flies and document the following phenotypes:

<u>Phenotype</u>	<u>Number</u>
Red eyes, straight wings, normal antenna	27 flies
Purple eyes, curly wings, normal antenna	545 flies
Purple eyes, curly wings, aristaless	32 flies
Red eyes, straight wings, aristaless	530 flies
Red eyes, curly wings, aristaless	33 flies
Purple eyes, straight wings, normal antenna	29 flies
Red eyes, curly wings, normal antenna	4 flies

Most common =
 } parental

a) (6 points) Using the gene symbols pr^- (or Pr^+ for wild type), cy^- (or Cy^+ for wild type) and al^- (or Al^+ for wild type), show the genotype of both true-breeding parental strains used to generate the F1 flies. The order of the genes does not need to be indicated here.

parental were: 1) purple eyes, curly wings, normal antennae

pr^-/pr^- cy^-/cy^- al^+/al^+

2) Red eyes, straight wings, aristaless

pr^+/pr^+ cy^+/cy^+ , al^-/al^-

b) (6 points) What is the reciprocal class for purple eyed, curly winged, aristaless flies? How many flies are in this class?

$pr^- cy^- al^-$ purple, curly, aristaless

$pr^+ cy^+ al^+$ reciprocal = [red eyes, straight wings, normal antenna = 27 flies]

c) (6 points) What is the genetic distance between the pr and cy genes?

parents: 1) cy^- / pr^- Recomb: 1) $cy^- pr^+$ Red + curly = $33 + 4$
and 2) cy^+ / pr^+ 2) $cy^+ pr^-$ (Recomb, so single crossover)

$$\text{MAP Distance} = 100 \left[\frac{\# \text{ recomb}}{\text{Total}} \right] = 100 \left[\frac{33 + 4 + 29}{1200} \right] = 5.5 \text{ cM}$$

d) (6 points) What is the genetic distance between the cy and al genes?

parents: 1) $cy^- al^+$ Recomb: 1) $cy^- al^- \rightarrow$ curly + aristaless = $32 + 33$
2) $cy^+ al^-$ 2) $cy^+ al^+ \rightarrow$ straight / WT antenna = $27 + 29$

$\begin{array}{c} cy^- \quad al^+ \\ \times \quad \times \\ cy^+ \quad al^- \end{array}$ * 4 Double crossover
progeny retain parental cy^-/al^+ genotype, so
2 crossovers between them

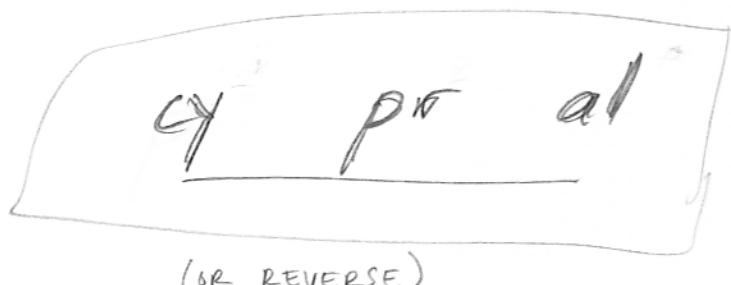
$$\left. \begin{array}{l} 3) \text{ Double crossover} = 2(4) \\ \text{MAP distance} = 100 \left[\frac{32 + 33 + 27 + 29 + 2(4)}{1200} \right] = \end{array} \right]$$

e) (8 points) Draw a genetic map showing the pr, cy and al loci in the correct order.

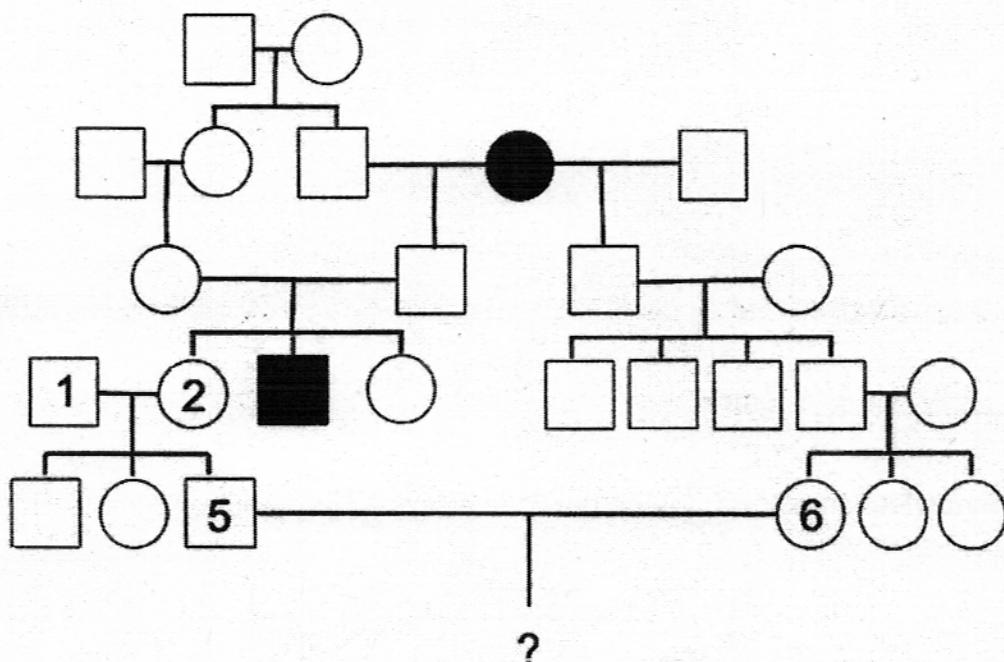
10.75 cM

pr is in the middle because double crossover progeny retain parental cy^-/al^+

Dbl Crossover: $\begin{array}{c} cy^- \quad pr^- \quad al^+ \\ \xrightarrow{\quad} \quad \times \quad \times \quad \backslash \\ cy^+ \quad pr^+ \quad al^- \end{array}$



3. Examine the following pedigree showing a very rare, completely penetrant disease.



a) (6 points) What is the most likely mode of inheritance for this disease?

Autosomal recessive (6 points. All or nothing.)

- Both males and females are affected
 - Disease skips generations
- } not required for credit; no credit given for stating these.

b) (6 points) What is the probability that the first child (?) of parents 5 and 6 will be affected?

$$\begin{aligned} P(\text{? is affected}) &= P(5 \text{ is a carrier}) \times P(6 \text{ is a carrier}) \times P(\text{? is affected} | \text{both parents are carriers}) \\ &= \frac{1}{3} \times \frac{1}{4} \times \frac{1}{4} \\ &= \frac{1}{48} \quad (6 \text{ points}) \end{aligned}$$

- 2 points for correct probability for each parent (4 points in total), ~~without including~~ P(? is affected | both parents are carriers).
- No credit awarded for simply having $P(\text{? is affected} | \text{both parents are carriers}) = \frac{1}{4}$.

c) (6 points) If this child (?) is affected, what is the probability that both parents are carriers.

100% (6 points. All or nothing.)

- Since child is affected and both parents are unaffected, both parents MUST be carriers. } not required for credit

Note: Bayes' theorem is NOT required to answer this question. No credit is awarded for stating the formula for Bayes' theorem, or if Bayes' theorem is used to calculate the wrong answer.

d) (8 points) If parents 5 and 6 have three unaffected daughters, what is the probability that the next child will be affected? (hint: use Bayes Theorem)

X: both parents are carriers

Y: 3 unaffected daughters.

Using Bayes' theorem,

$$\begin{aligned} P(X|Y) &= \frac{P(Y|X) \times P(X)}{P(Y)} \\ &= \frac{P(Y|X) \times P(X)}{P(Y|X) \times P(X) + P(Y|\bar{X}) \times P(\bar{X})} \\ &= \frac{\left(\frac{3}{4}\right)^3 \times \frac{1}{2}}{\left(\frac{3}{4}\right)^3 \times \frac{1}{2} + 1 \times \frac{1}{2}} \\ &= \frac{27}{731} \text{ (or } 0.0369\text{)} \end{aligned}$$

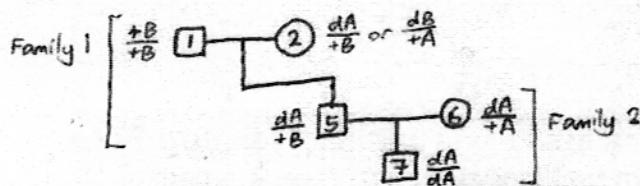
$\therefore P(\text{next child affected}) = P(X|Y) \times P(\text{child affected} | \text{both parents are carriers})$

$$\begin{aligned} &= \frac{27}{731} \times \frac{1}{4} \\ &= \frac{27}{2924} \text{ (or } 0.00923\text{)} \quad (\underline{8 \text{ points}}) \end{aligned}$$

- 6 points if $P(X|Y)$ is calculated correctly, but $P(\text{next child affected})$ was not calculated.
- If wrong $P(X)$ from part (b) was used, full credit is awarded, PROVIDE all other steps are correct.
- 3 points for correctly stating formula for Bayes' theorem AND correctly defining X and Y.
- 1 point if only formula for Bayes' theorem was stated, without defin X and Y, or if X and Y are defined wrongly.

e) (8 points) Parents 5 and 6 have an affected son – we'll call him #7 (designated as "?" in the pedigree). You suspect that marker M1 may be linked to the disease locus. Provide a LOD score for linkage between the disease locus and the marker, given the following M1 genotypes (there are two alleles, A and B).

Family Member	1	2	5	6	7
M1 - A	—	—	—	—	—
M1 - B	—	—	—		



Note for solution 1:

LOD score for individual 5 is not included because it works out to 0. Work it out to convince yourself.

Solution 1:

$$\begin{aligned} \text{LOD score} &= \log_{10} \left[\frac{P(7 = dA/dA | \text{completely linked})}{P(7 = dA/dA | \text{unlinked})} \right] \\ &= \log_{10} \left(\frac{\frac{1}{2} \times \frac{1}{2}}{\frac{1}{4} \times \frac{1}{2}} \right) \\ &= \log_{10} (2) \\ &= \underline{0.3 \quad (8 \text{ points})} \end{aligned}$$

Solution 2:

2 informative individuals – 5 and 7. ($0.3 + 0.3$)

But phase for family 1 unknown. (-0.3)

$$\therefore \text{LOD score} = (0.3 + 0.3) - 0.3 = \underline{0.3 \quad (8 \text{ points})}$$

- 2 points for correctly identifying each informative individual (4 points maximum)
- 2 points for correctly identifying family with unknown phase (2 points maximum).