7.03 Exam 1

Name: KEY

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Exam starts at 12:05 and ends at 12:55

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 your answers to make sure that they make sense.
- To help us give partial credit, show your work and state any assumptions that you make.

Question 1	30 points
Question 2	38 points
Question 3	32 points

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1. (**a** 6 points) You have isolated two different true-breeding mutant strains of *Drosophila* with black bodies (designated **b1⁻** and **b2⁻**). When female flies from either the **b1⁻** or **b2⁻** strains are crossed to wild type males, the female progeny have wild-type brown bodies, whereas the male progeny have black bodies. What does this tell you about the **b1⁻** and **b2⁻** mutations? Be as complete as you can and explain your reasoning.

$♀ \frac{b1^-}{b1^-} \times ♂ \frac{+}{Y}$ ← If $b1^-$ is <u>X-linked</u>, the cross is as this diagram. This matches the observed.

↓

$♀ \frac{b1^-}{+} + ♂ \frac{b1^-}{Y}$

brown (wt) black (mutant)

Since the heterozygous female shows the wild type trait, $b1^-$ is <u>recessive</u> to the wild type allele with respect to body color.

$b2^-$ is the same as $b1^-$.

(**b** 10 points) Describe the cross(es) you would perform to determine whether or not **b1⁻** and **b2⁻** mutations are in the same gene. For your answer, describe exactly what outcomes you would look for and how they would be interpreted.

<u>Complementation test</u>

P $♀ \frac{b1^-}{b1^-} \times ♂ \frac{b2^-}{Y}$ (or $♀ \frac{b2^-}{b2^-} \times ♂ \frac{b1^-}{Y}$)

↓

$♂ \frac{b1^-}{Y}$ F1 $♀ \frac{b1^- \quad +}{+ \quad b2^-}$ if different genes, complement. ∴ wild type (brown)

OR

$♂ \frac{b1^-}{Y}$ F1 $♀ \frac{b1^-}{b2^-}$ if same gene, do not complement. ∴ mutant (black)

Only F1 females are used to determine complementation because males don't have one copy of each allele and thus give us no information about the interaction of the alleles.

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You cross a true breeding black bodied strain (**b1⁻**) to a true breeding black bodied white eyed strain (**b2⁻** and **w⁻**). F1 females are then crossed to wild type male flies. The following phenotypes are seen among 1000 *male* progeny:

Phenotype	Number
Black body, white eyes	455
Black body, normal eyes	445
Normal body, white eyes	86
Normal body, normal eyes	14

(**c** 4 points) What is the distance between the **b1⁻** and **b2⁻** mutations?

P ♀ $\frac{b1^- \; + \; +}{b1^- \; + \; +}$ x ♂ $\frac{+ \; b2^- \; w^-}{Y}$

↓

F1 ♀ $\frac{b1^- \; + \; +}{+ \; b2^- \; w^-}$ x $\frac{+ \; + \; +}{Y}$

↓

male progeny

P	b1⁻ + +	b,n		rare
	+ b2⁻ w⁻	b,w		
C	b1⁻ b2⁻ w⁻	b,w	14	same
	+ + +	n,n	14	
P	b1⁻ + w⁻	b,w		
	+ b2⁻ +	b,n		
C	b1⁻ b2⁻ +	b,n	86	same
	+ + w	n,w	86	

$100 \times \frac{14+14+86+86}{1000} = 20cM$

← crossover ♂s

← total ♂s

(**d** 10 points) Draw a map showing the relative positions of the **b1⁻**, **b2⁻** and **w⁻** mutations showing relevant distances in cM. Note that it is possible to estimate the **w – b** distance from the 3-factor cross data that is provided above.

Order Determination

double crossover of the correct order produces the rare category (abou

b1⁻ + +	+ w⁻ b2⁻	+ b1⁻ +
+ b2⁻ w⁻	b1⁻ + +	w⁻ + b2⁻
↓	↓	↓
b1⁻ b2⁻ +	+ + b2⁻	+ + +
+ + w⁻	b1⁻ w⁻ +	w⁻ b1⁻ b2⁻
NO	NO	YES

14cM 20cM

w⁻ b1⁻ b2⁻

$\boxed{w \rightarrow b1}$ $\frac{? \; + \; +}{? \; + \; +} = \frac{\text{crossover between b1 and b2 AND crossover between w and b1}}{\text{crossover between b1 and b2}}$

of all progeny that have a crossover between b1 and b2, producing normal body type, some portion will also undergo another crossover between b1 and producing normal body, normal eye progeny. Thus, all normal body progeny (86+14=100) is used as total progeny, and normal body, normal eye progeny (14) is used as crossover progeny. $100 \times \frac{14}{100} = 14$ cM.

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2. (**a** 6 points) You have isolated three yeast mutants that grow slowly and form small colonies. These mutants are designated *slo1*⁻, *slo2*⁻ and *slo3*⁻. When either a *slo1*⁻ or a *slo2*⁻ mutant is mated to wild type the resulting diploids form normal large colonies. Whereas when a *slo3*⁻ mutant is mated to wild type the resulting diploids form small colonies. What do these results tell you about the *slo1*⁻, *slo2*⁻ and *slo3*⁻ mutants?

slo1⁻ ⇒ Recessive

slo1⁻ x WT
↓
1⁻/+
LARGE

slo2⁻ ⇒ Recessive

slo2⁻ x WT
↓
2⁻/+
LARGE

slo3⁻ ⇒ Dominant

slo3⁻ x WT
↓
3⁻/+
SMALL

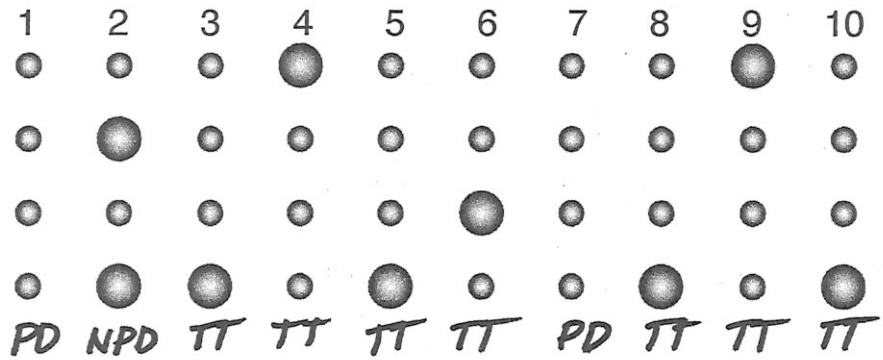
(**b** 4 points) A *slo1*⁻ mutant is mated to a *slo2*⁻ mutant. The resulting diploid grows normally. What does this tell you about the relationship between the *slo1*⁻ and *slo2*⁻ mutations?

COMPLEMENTATION TEST

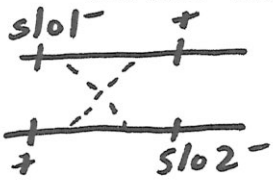
slo1⁻ x slo2⁻
⇓
1⁻/2⁻ (NORMAL, LARGE)

∴ → WT phenotype
- complementation
- different genes

(**c** 10 points) The diploid from part **b)** is sporulated and 10 tetrads from this cross are shown below. (The large colonies are the same size as wild type colonies).



What additional information does this data provide about the relationship between the *slo1*⁻ and *slo2*⁻ mutations? Be as specific as possible.



PD	TT	NPD
1⁻2+ Small	1⁻2+ small	1⁻2⁻ Small
1⁻2+ Small	1+2⁻ small	1⁻2⁻ Small
1+2⁻ Small	1⁻2⁻ Small	1+2+ Large
1+2⁻ Small	1+2+ Large	1+2+ Large
[4 SMALL]	[3 SMALL; 1 LARGE]	[2 SMALL; 2 LARGE]

Observed Ratio: 2PD : 7TT : 1NPD

~ 1PD : 4TT : 1NPD

∴ UNLINKED

OR

$cM = \frac{TT + 6NPD}{2t} \times 100 = 65\ cM$

∴ very loosely linked OR unlinked

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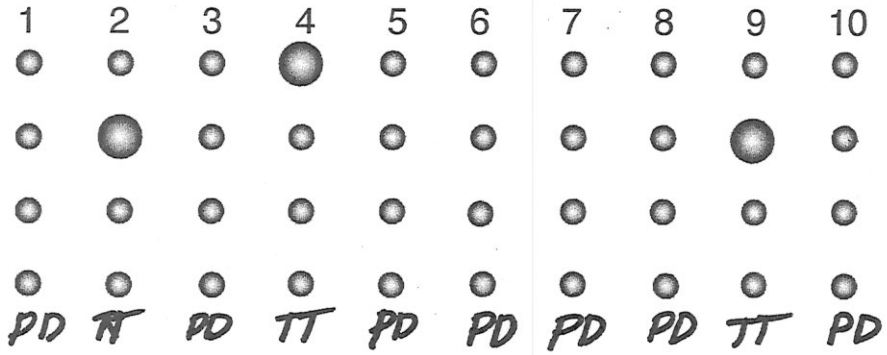
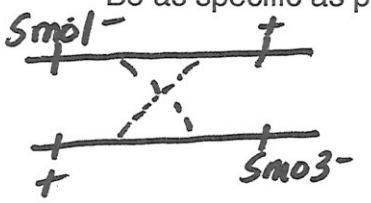
(d 4 points) Describe how you would isolate a *slo1*⁻ *slo2*⁻ double mutant colony from the tetrads shown in part **c**).

⇒ Take 2 small colonies from NPD tetrad (slo1⁻ slo2⁻)

(e 8 points) Next a *slo1*⁻ mutant is mated to a *slo3*⁻ mutant. The resulting diploid makes small colonies. This diploid is sporulated and 10 tetrads from this cross are shown below.



What do these results tell you about the relationship between the *slo1*⁻ and *slo3*⁻ mutations? Be as specific as possible.



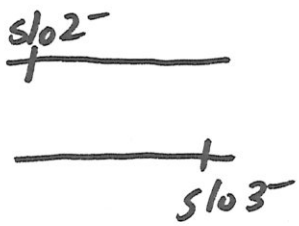
PD	TT	NPD
1⁻3⁺	1⁻3⁺	1⁻3⁻
1⁻3⁺	1⁺3⁻	1⁻3⁻
1⁺3⁻	1⁻3⁻	1⁺3⁺
1⁺3⁻	1⁺3⁺	1⁺3⁺
[4 SMALL]	[3 SMALL; 1 LARGE]	[2 SMALL; 2 LARGE]

Observed Ratio = 7 PD : 3 TT : 0 NPD

$$cM = \frac{TT + 6NPD}{2t} \times 100 = \frac{3 + 6(0)}{2(10)} \times 100 = 15\,cM \therefore \underline{\text{LINKED}}$$

(f 6 points) If you crossed a *slo2*⁻ mutant to a *slo3*⁻ mutant and dissected 12 tetrads, how many of these tetrads would you expect to have two large colonies and two small colonies? Explain your reasoning.

Since Smo1⁻ and slo3⁻ are tightly linked and slo1⁻ and slo2⁻ are unlinked, smo2⁻ and smo3⁻ will most likely be UNLINKED



⇒ 1 PD : 4 TT : 1 NPD

Look for NPD

$\frac{1}{6} \times 12$ tetrads = 2 NPDs

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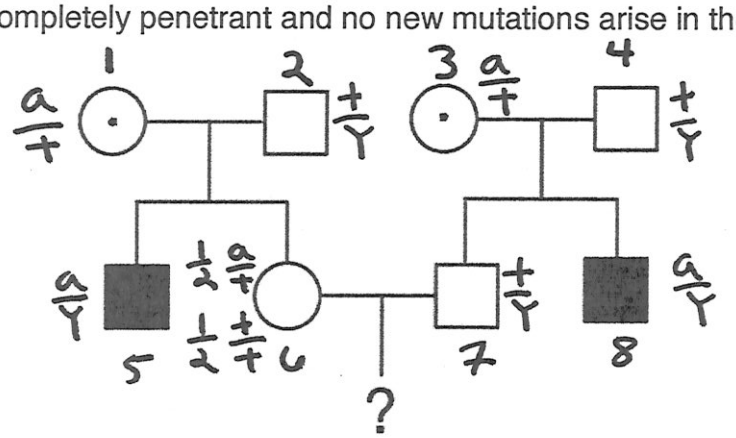
3. Consider the following pedigree showing inheritance of an X-linked recessive trait. (Assume the trait is completely penetrant and no new mutations arise in the individuals shown).



X-linked rec. trait = a

(**a** 8 pts.) What is the probability that a child indicated by **?** will be affected by the trait?

$p(? = ♂) \cdot p(6 = \frac{a}{+}) \cdot p(? \text{ is affected} \mid ? = ♂ \text{ AND } 6 = \frac{a}{+})$

$\frac{1}{2} \cdot \frac{1}{2} \cdot \frac{1}{2} = \boxed{\frac{1}{8}}$

(**b** 12 pts.) Say that the child indicated by **?** turns out to be a son who **does not have** the trait. Use Bayes Theorem to calculate the probability that a second child (either son or daughter) by the same couple would have the trait.

1st update $p(6 = \frac{a}{+} \mid ? = \text{unaff.})$, un = un affected by trait

$$p(6 = \tfrac{a}{+} \mid ? = un) = \frac{p(? = un \mid 6 = \frac{a}{+})\, p(6 = \frac{a}{+})}{p(? = un \mid 6 = \frac{a}{+})\, p(6 = \frac{a}{+}) + p(? = un \mid 6 = \frac{+}{+})\, p(6 =}$$

$p(6 = \frac{a}{+}) = \boxed{1/2}$

$p(? = un \mid 6 = \frac{a}{+}) = \left(\underbrace{\frac{1}{2} \cdot 1}_{♀} + \underbrace{\frac{1}{2} \cdot \frac{1}{2}}_{♂}\right) = \boxed{\frac{3}{4}}$

$p(6 = \frac{+}{+}) = \boxed{1/2}$

$p(? = un \mid 6 = \frac{+}{+}) = \boxed{1}$

$$\boxed{\therefore p(6 = \tfrac{a}{+} \mid ? = un) = \frac{3/4 \cdot \frac{1}{2}}{3/4 \cdot \frac{1}{2} + 1 \cdot \frac{1}{2}} = 3/}$$

2nd child $= p(♂) \cdot p(6 = \frac{a}{+} \mid ? = un) \cdot p(\text{getting trait}) = \frac{3}{7} \cdot \frac{1}{2} \cdot \frac{1}{2}$

$= \boxed{3/28}$

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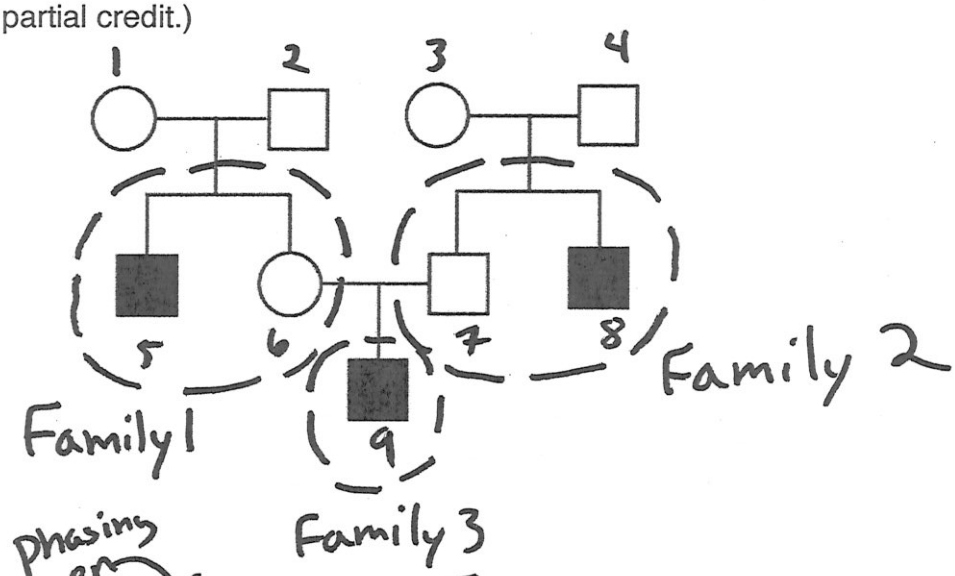
(c 12 pts.) Say that the child indicated by **?** turns out to be a son who **has** the trait as shown below. Calculate the maximum LOD score that could be obtained for a SSR marker that is completely linked to the gene for the trait. In other words, assume that you have an SSR marker that is completely linked to the gene for the trait and that is heterozygous in every female. Try to extract linkage information from as many of the individuals in the pedigree as possible, also pay close attention to whether phase information is available. (Show as much work as possible for partial credit.)

informative: 5, 6, 7, 8, 9

phase known: 9

phase unknown: 5, 6, 7, 8



$$LOD_{MAX}\ Fam1 = \log_{10}\left[\frac{\frac{1}{2}\left(\frac{1}{2}\right)^2}{\left(\frac{1}{4}\right)^2}\right] = \log_{10}(2) = 0.3$$

phasing pen

OR

$$LOD_{MAX}\ Fam1 = (2-1)\cdot 0.3 = 0.3$$

phasing penalty

LOD_{max} Fam2 is same as Fam1 = 0.3

$$LOD_{MAX}\ Fam3 = \log_{10}\left[\frac{\frac{1}{2}}{1/4}\right] = \log(2) = 0.3$$

$$LOD_{MAX} = LOD_{MAX}\ Fam1 + LOD_{MAX}\ Fam2 + LOD_{MAX}\ Fam3$$

$$LOD_{MAX} = 0.3 + 0.3 + 0.3 = \boxed{0.9}$$

Grading section

Question 1 30 points:_____

Question 2 38 points:_____

Question 3 32 points:_____

Total :_____