

# 7.03 Final Exam

**Name:** \_\_\_\_\_

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**Section time:** \_\_\_\_\_

**There are 15 pages including this cover page**

**Please write your name on each page.**

<b>Question 1</b>	<b>24 points</b>
<b>Question 2</b>	<b>28 points</b>
<b>Question 3</b>	<b>28 points</b>
<b>Question 4</b>	<b>25 points</b>
<b>Question 5</b>	<b>28 points</b>
<b>Question 6</b>	<b>18 points</b>
<b>Question 7</b>	<b>25 points</b>
<b>Question 8</b>	<b>24 points</b>

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**1.** You are studying the regulation of a new enzyme in *E. coli*, which is expressed only when an inducer compound is present. You have available an amber mutant in the structural gene for the enzyme, designated  $\text{Enz}^-$ . You generate a collection of random Tn5 insertions in the *E. coli* chromosome and identify two insertions (called Tn5-1 and Tn5-2) that give constitutive expression of the enzyme. You carry out separate P1 transduction experiments with each insertion mutant. In the first experiment you grow P1 phage on a Tn5-1 strain and use the resulting lysate to infect an  $\text{Enz}^-$  mutant. All of the kanamycin resistant transductants express the enzyme constitutively. In the second experiment you grow P1 phage on a Tn5-2 strain and use the resulting lysate to infect an  $\text{Enz}^-$  mutant. In this case, none of the kanamycin resistant transductants express the enzyme.

**(a 8 pts.)** What can you conclude about each of the Tn5-1 and Tn5-2 mutations? Be as complete and specific as you can.

**(b 6 pts.)** You obtain an  $F'$  factor that contains the gene for the enzyme and surrounding region of the chromosome. When this  $F'$  is mated into the Tn5-1 strain the resulting merodiploid expresses the enzyme constitutively, but when this  $F'$  is mated into the Tn5-2 strain the resulting merodiploid exhibits normal regulation of the enzyme. What additional information do these experiments contribute to your understanding of the nature of either the Tn5-1 or Tn5-2 mutations.

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**(c 10 pts.)** Diagram two different regulatory pathways that would explain the behavior of the Tn5-1 and Tn5-2 mutations. For your answer you will need to represent the wild type functions affected by the transposon mutations in the pathways (e.g. you may want to represent the gene affected by Tn5-1 as “Gene 1”). Also remember to include the inducer in both pathways.

**2.** Flies have a daily activity cycle showing peak activity in the morning and at night. To find genes that control this circadian rhythm, you seek mutant flies that are still active at a time when normal flies are inactive. To make your screen easier, you decide to look for recessive mutations on the X chromosome.

**(a 8 pts.)** Depict an F1 screen that will allow you to find mutations on the X chromosome that recessively affect circadian rhythm.

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Your first screen design proves highly challenging because of variability in circadian behavior from fly to fly. You therefore realize you need a screen design that allows you to assess the circadian behavior of a population of flies carrying a mutation. You mutagenize a male that carries a mutation in the X-linked white gene ( $w^-$ , which recessively causes white eyes). You cross to a female that is heterozygous for a mutation, DTSa, which confers dominant temperature-sensitive lethality, and a balancer FM7a (DTSa/FM7a). FM7a confers a dominant “Bar” (eye shape) phenotype and recessive yellow body color (not recessive lethality).

  $w^-/Y$  male X DTSa/FM7a female

(b 6 pts.) You raise the F1 at the non-permissive temperature (non-permissive for DTSa). Give the **genotype and phenotype** a viable F1 female carrying a hypothetical X-linked circadian mutation “m1”.

(c 8 pts.) You cross individual F1 females to FM7a/Y males (one F1 female per cross in a vial). What will the **genotypes and phenotypes** of the F2 males and F2 females be? Depict the case for the cross involving the F1 female that carried m1.

(d 6 pts.) If m1 confers a recessive defect in circadian behavior, which F2 flies in the vial will show abnormal behavior? If m1 confers a dominant defect, which flies will be affected?

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**3.** Americans have a wild type strain of yeast called **strain 1**. You take **strain 1** and by mutagenesis collect a large number of mutations in that strain. These individual mutations are crossed to produce the quadruple mutant *ade1 trp1 his1 lys1*, which you call **strain 2**. You cross the original wild type **strain 1** that has no growth requirements by the quadruple mutant **strain 2** and dissect tetrads. Below are the tetrad types with the numbers of each type listed below.

**Strain 1 (American Wild Type) X Strain 2 (American *ade1 trp1 his1 lys1*)**

Growth on media lacking the indicated amino acid

	His	Trp	Lys	Ade		His	Trp	Lys	Ade
Spore 1	+	+	+	+		+	+	+	+
2	+	+	+	+		-	-	-	+
3	-	-	-	-		+	+	+	-
4	-	-	-	-		-	-	-	-
	6					1			

	His	Trp	Lys	Ade		His	Trp	Lys	Ade
Spore 1	+	+	+	+		+	-	-	+
2	+	-	-	+		-	-	-	+
3	-	+	+	-		+	+	+	-
4	-	-	-	-		-	+	+	-
	2					1			

**(a 8 pts.)** Based on these data, draw a genetic map showing the relative order and map distances in cM for the four genes in the cross using the American strain. Indicate any ambiguities.

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The Europeans have their own wild type strain of yeast they call **strain 3**. Like the Americans they make lots of mutations and by the same procedures make a quadruple mutant *ade1 trp1 his1 lys1*, which they call **strain 4**. You cross the original wild type **strain 3** that has no requirements by the quadruple mutant **strain 4** and dissect tetrads. Below are the tetrad types with the numbers of each type below each.

**Strain 3 (European Wild Type) X Strain 4 (European *ade1 trp1 his1 lys1*)**

Growth on media lacking the indicated amino acid

	His	Trp	Lys	Ade		His	Trp	Lys	Ade
Spore 1	+	+	+	+		+	+	+	+
2	+	+	+	+		-	-	-	+
3	-	-	-	-		+	+	+	-
4	-	-	-	-		-	-	-	-
	6					1			

	His	Trp	Lys	Ade		His	Trp	Lys	Ade
Spore 1	+	+	+	+		-	+	-	+
2	-	+	-	+		-	-	-	+
3	+	-	+	-		+	+	+	-
4	-	-	-	-		+	-	+	-
	2					1			

**(b 8 pts.)** Based on these data, draw a genetic map showing the relative order and map distances in cM for the four genes in the cross using the European strain. Indicate any ambiguities.

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(c 6 pts.) Diagram a genetic event that could account for the differences between the American and European strains.

(d 6 pts.) Does this finding allow you to generate a more precise genetic map from the two crosses? Explain.

**4.** Wild-type *C. elegans* animals with 2 X chromosomes (XX) are hermaphroditic and with one X chromosome (XO) are male. You are interested in the genetic regulation of the sexual fate.

(a 6 pts.) Loss-of-function of the *her-1* gene (denoted: *her-1(lf)*) recessively causes XO animals to be hermaphroditic. Furthermore, you find that the *her-1* gene is normally “On” (actively transcribed) in wild-type XO animals and “Off” (mRNA not present) in wild-type XX animals. Which sexual fate does *her-1* normally promote (male or hermaphrodite)?

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(b 9 pts.) You are interested in studying regulation of the *her-1* gene by seeking mutants that affect its male-specific expression. You identify two mutations (denoted *m1* and *m2*) that cause *her-1* to be “on” instead of “off” in XX animals. *m1/m1* and *m2/m2* XX animals are also males instead of hermaphrodites. *m1* is recessive and *m2* is dominant.

First, you perform experiments with *m1* and find that:

*m1* and *her-1(lf)* are unlinked.

*m1/m1; her-1(lf)/her-1(lf)* XX and XO animals are hermaphroditic (this notation indicates animals are homozygous for both mutations)

(i) Does *m1* cause an uninducible or constitutively active *her-1*-expression phenotype?

(ii) Is *m1* best described as a cis-regulatory mutation of *her-1* or a mutation in a trans-acting factor? Explain briefly.

(iii) Draw a pathway for regulation of the male sexual fate. Start your pathway with “XO” to indicate the fact that the counting of X’s must be the first step, and end your pathway with maleness. Take into consideration that *m1* is either a cis-regulatory mutation in *her-1* or a mutation in a different gene (for example, *geneM1*).



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Next you wish to characterize *m2*. (reminder, *m2* is dominant, see above).

*m2* and *her-1(lf)* are closely linked.

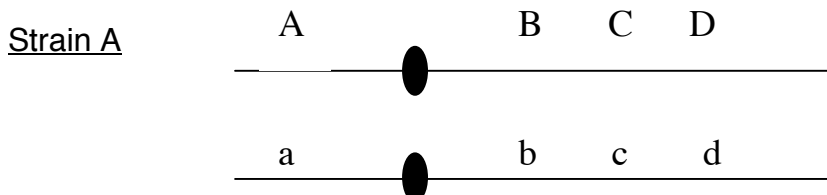
You make the following observations:

Genotype	XX animals	X0 animals
<i>m2 her-1(lf) / m2 her-1(lf)</i>	hermaphroditic	hermaphroditic
<i>m2 her-1(lf) / + +</i>	hermaphroditic	male
<i>m2 + / + her-1(lf)</i>	male	male

(c 4 pts.) Is *m2* best described as a candidate cis-regulatory mutation of *her-1* or a mutation in a trans-acting factor of *her-1*? Explain briefly.

(d 6 pts.) Diagram a model for the gene regulation of *her-1* that explains what normally happens in XX animals and XO animals. Propose the most plausible explanation for the affects of *m2*.

**5.** (a 6 pts.) You have a yeast diploid, **strain A**, with the genotype indicated below. Assume that a mitotic crossover occurs between markers B and C. Draw the two chromosome configurations in cells resulting from this event that will be homozygous for at least one allele. The black object is the centromere.



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**(b 8 pts.)** Each of the diploids resulting from the mitotic crossover undergoes meiosis. What will be the genotypes of the spores in the tetrads assuming that no meiotic recombination occurs?

Meiosis from Diploid 1	Meiosis from Diploid 2
Spore 1	Spore1
Spore 2	Spore2
Spore3	Spore3
Spore4	Spore 4

**(c 6 pts.)** Another **strain A** diploid undergoes a mitotic non-disjunction event for the chromosome containing ABCD. Draw the chromosome configuration of the two cells resulting from that event.

**(d 8 pts.)** Each of the cells resulting from the mitotic crossover undergoes meiosis. What will be the genotypes of the spores in the tetrads assuming that no meiotic recombination occurs? Indicate any ambiguities.

Meiosis from Diploid 1	Meiosis from Diploid 2
Spore 1	Spore1
Spore 2	Spore2
Spore3	Spore3
Spore4	Spore 4

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**6.** Consider three different inherited diseases, each present at a frequency of  $10^{-4}$  in a population that undergoes random mating. Disease 1 is due to an autosomal recessive allele, Disease 2 is due to an autosomal dominant allele, and Disease 3 is due to an X-linked recessive allele. Assume that the fitness of individuals affected by each disease = 0.

**(a 9 pts.)** Assuming that each disease has reached a steady state balance between new mutations and selection against affected individuals, what fraction of the of the affected individuals should have new mutations for

Disease 1:

Disease 2:

Disease 3 (considering affected males only):

**(b 9 pts.)** The prevalence of first cousin marriages in the population at large is  $10^{-3}$ . What fraction of the affected individuals will have parents who are first cousins for

Disease 1:

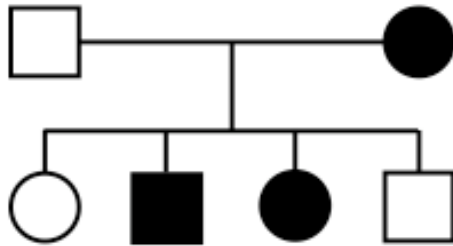
Disease 2:

Disease 3 (considering affected males only):

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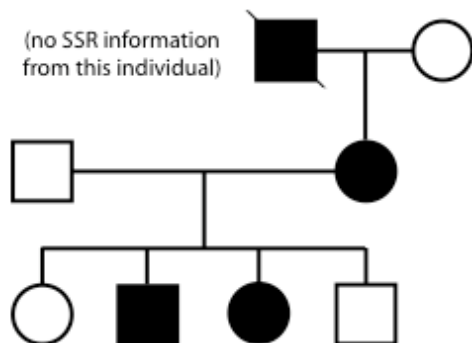
**7.** You identify a family with an autosomal dominant disease that you wish to map. It is useful to calculate the theoretical maximum LOD score that a family of a given size and structure might contribute.

**(a 5 pts.)** For the pedigree below, set up the equation, for  $\theta = 0$ , for the theoretically maximum LOD score that could be obtained using an SSR that is genetically inseparable from (shows no recombination with) the disease locus. (There is no need to calculate a final LOD score). Assume throughout this question that DNA samples are available for all **living** individuals. Also assume complete penetrance and no new mutations.



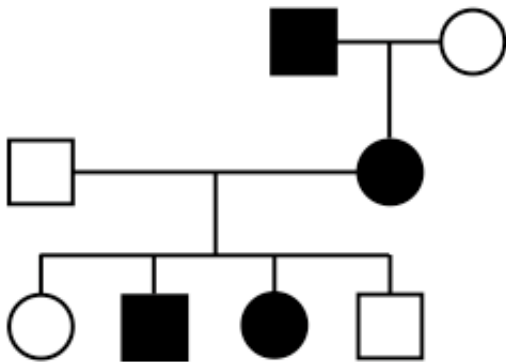
The rest of this question involves the same pedigree with each successive part revealing more information about the family. For each part, provide the equation for the maximum LOD score for  $\theta = 0$  as for part **a**).

**(b 5 pts.)**

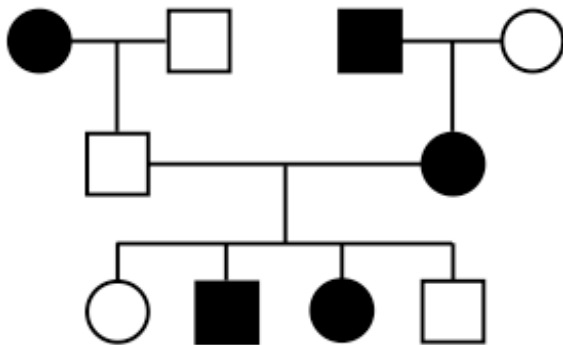


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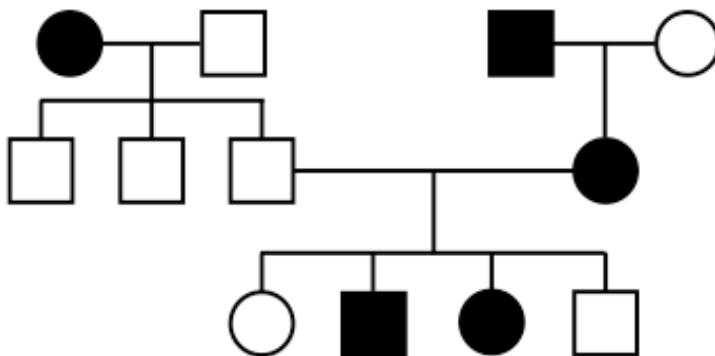
**(c 5 pts.)**



**(d 8 pts.)**



**(e 5 pts.)**



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**8.** While having a picnic at a local pond you make a curious observation about some resident snails. The snail shells come in one of two coiling patterns: right-handed (dextral) and left-handed (sinistral). You take the snails back to the lab for genetic analysis. First you establish true-breeding dextral and sinistral strains, which you use for 2 crosses.

Dextral



Sinistral



**(a 8 pts.)**

**cross 1**

Sinistral female X Dextral male  
F1: 56/56 are sinistral

**cross 2**

Sinistral male X Dextral female  
F1: 47/47 are dextral

Propose a genetic explanation for these observations (note: there is no evidence for imprinting in snails).

**(b 8 pts.)**

using F1s from cross 1

F1 sinistral female X F1 sinistral male  
F2: 51/51 are dextral

using F1s from cross 2

F1 dextral female X F1 dextral male  
F2: 52/52 are dextral

(i) Specify the genotypes and their ratios of the F2 progeny if left/right coiling is specified by a single locus.

(ii) If left/right coiling is specified by a single locus, which allele (the one that confers left or the one that confers right-handedness) is dominant? Explain how this can be concluded.

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You set up multiple crosses using single F2 Dextral female snails crossed to stock (true breeding) Sinistral male snails and find the results of the crosses fall into two categories. You set up a total of 20 crosses using one female and one male for each cross (Note: you use the dextral F2 females that were derived from original cross 1, but the same results would be obtained with F2 females derived from original cross 2):

F2 Dextral females X stock sinistral males

Class 1: 15 crosses yield 100% dextral progeny

Class 2: 5 crosses yield 100% sinistral progeny

(c 8 pts.) (i) Indicate the genotypes of the F2 animals you anticipate to have been used in Class 1 and Class 2 crosses.

(ii) Are these data consistent with a single locus with two alleles explaining sinistral versus dextral coiling or multiple loci? Explain your conclusion (briefly).