Name: _____

7.03 Exam I -- 2015

Name: _____
(write your name on every page of this exam)

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

Please write your name on each page.

Only writing on the FRONT of every page will be graded.
(You may use the backs, but only as scratch paper.)

Question 1	32 pts
Question 2	34 pts
Question 3	34 pts

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Question 1 – You have isolated two different yeast mutants, *arg1*$^-$ and *arg2*$^-$, that cannot synthesize the amino acid argenine. They require argenine to be added to the medium for growth (i.e. they are arg$^-$).

a) (6 points) You mate the *arg1*$^-$ and *arg2*$^-$ mutants and the resulting diploids are Arg$^+$. What does this tell you about these mutations and their interaction?

These are recessive mutants that complement.

+2 for recessive

+4 for complement

(+2 for complement but concluding mutations in the same gene)

(b) (6 points) You next sporulate the diploids from part **(a)**. Among a total of 150 tetrads, the following tetrad types are seen.

Type:	4 *arg*$^-$	3 *arg*$^-$: 1 Arg$^+$	2 *arg*$^-$: 2 Arg$^+$
Number:	96	45	9

You want an *arg1*$^-$: *arg2*$^-$ double mutant haploid. What is the easiest way to identify such a mutant without further analysis/experimentation?

Find an NPD (2 WT, 2 mutant) tetrad. The two mutant spores in this tetrad are arg1-:arg2- double mutants.

+3 for NPD tetrad

+3 for saying the mutants spores in the NPD are double mutants

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c) (6 points) You choose a single tetrad for further analysis. The four spores from a single tetrad show the following properties: Spore 1 = MAT**a**Arg$^+$, Spore 2 = MAT**a** *arg*$^-$, Spore 3 = Mat**α** *arg*$^-$ and Spore 4 = Mat**α** *arg*$^-$. You perform two of the possible matings that can occur between these haploids and find that the diploid produced by mating Spore 2 and Spore 3 is *arg* $^-$ while the diploid produced by mating Spore 2 and Spore 4 is Arg$^+$. What type of tetrad is this? Which spore is the double mutant? Explain your reasoning.

The spore is a tetratype (3:1 mutant:wt ratio, with 1 double mutant, 2 single mutants and 1 wt cell). Spore 3 is the double mutant. Mating spores #2 and #4 gives rise to Arg+ diploids, so they must be arg- haploids that complement (single mutants). Mating spores #2 and #3 yields Arg- diploids (they fail to complement). Spore #1 is wt and spores #2 and #4 are singles. Thus, spore #3 must be a double.

+2 for tetratype identification

+4 for identifying spore 3 = double

d) (8 points) Given the number of tetrads of each type, what is the distance between the Arg1 and Arg2 mutations?

T+6NPD/2E = 45 + 6(9)/2(150) = 99/300 = 33cM

-1 if equation correct but calculation error

-2 if minor equation error

-4 if incorrectly plug in tetratype number

e) (6 points) You have isolated a mutation that you call argX$^-$ that activates a parallel pathway for argenine biosynthesis. An argX$^-$ mutation on its own is Arg$^+$, and when argX$^-$ is combined with a arg1$^-$ mutation, the double mutant is Arg$^+$. Describe a cross that you would perform – and the interpretation of the outcome – to determine whether argX$^-$ is dominant or recessive.

Cross the argX- arg1- haploid to an arg1- haploid. If the diploid is Arg+, then argX- is dominant (arg1- alleles must be present to differentiate between dominant or recessive).

+4 for the correct cross
+2 for correct interpretation of the outcome
+1 for any haploid cross (except for crosses to WT)
0 points for any diploid cross

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Question 2 - Consider three recessive *Drosophilia* traits specified by the hypothetical X-linked genes La, Cy, and Mo.

(a) (8 points) A female fly with all three traits is mated to a wild-type male. What fraction of the female progeny will have all three traits? What fraction of the male progeny will have all three traits?

0% of females (all het recessive)

100% of males (all haploid recessive alleles)

+4 for male fraction
+4 for female fraction

(b) (8 points) The genes are, in order, **La-Cy-Mo**. A female fly heterozygous at all three loci (but not necessarily with all of the recessive alleles on the same chromosome) is test crossed to a male that is homozygous recessive at all three loci. All eight possible phenotypic classes are found among the progeny.The rarest classes are la^- cy^- Mo+ and La+ Cy+ mo^- (a plus indicates the wild type phenotype for a given trait). The female fly was produced by crossing flies from two different true-breeding lines (homozygous at all loci). What were the phenotypes of the two parental lines?

Double crossovers must be needed to produce rarest classes, so the female fly must be:

female la- Cy+ Mo+ over La+ cy- mo-

This female was produced by crossing true breeding la- Cy+ Mo+ homozygotes with La+ cy- mo- homozygotes.

+7 for writing a genotype instead of a phenotype
+6 for writing the wrong generation, but with the correct genotypes
+4 only one parental phenotype correct
+2 both parental phenotypes wrong, but began working out mother's genotype correctly

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(c) (10 points) As measured by two-factor crosses, the distance between La and Cy is 20 cM and the distance between Cy and Mo is 10 cM. Out of 1000 progeny flies from part (b) how many would you expect to have the phenotype la^- cy^- Mo+?

0.2 x 0.1 = a double recombination rate of 0.02
0.02 x 1000 = 20 double recombinants, half of which will be each double recombinant allele.

So, 10 flies should be la- cy- Mo+

Partial credit:
+1 for identifying it will be the double crossover offspring
+1 for concluding it's rare
+2 for noting that the number of double crossovers w/ our desired phenotype = ½ the number of double recombinants

-3 for calculating the correct number of double recombinants but did not divide by 2 to get the correct phenotype

(d) (8 points) The distance between La and Mo can be calculated to be 30 cM by adding the two genetic distances given in part (c). If the distance between La and Mo was measured directly in a two-factor cross what would be the measured distance in cM?

30cM minus the contribution of double crossovers. We know from part **(c)** that there is a double recombination rate of 0.02, indicating two crossover events.

2*0.02x100= 4 cM.

So, the total will be 30cM – 4cM = 26cM.

+2 for correct equation
+2 if say <30 cM
+2 for an explanation of why <30
+1 for mentioning double crossover accounting

-2 for 28 cM (not taking into account double recombination = two crossover events
0 points for using tetrad formula

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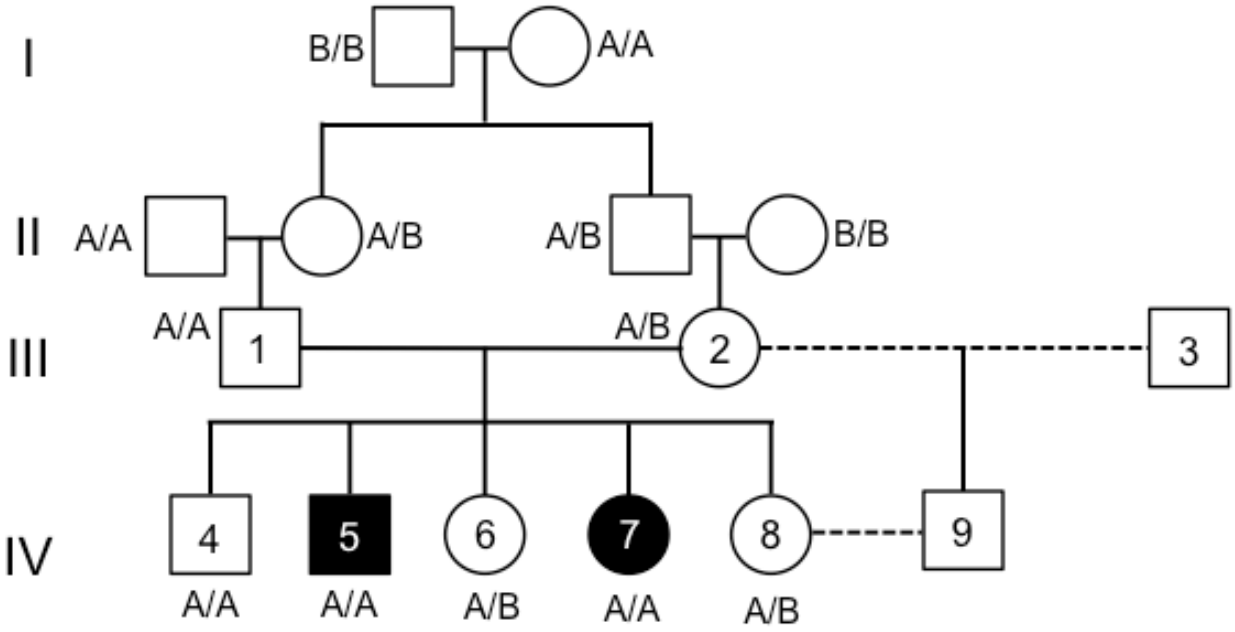
Question 3

Examine the following pedigree for questions 3a-c:



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

Autosomal recessive

+3 for autosomal
+3 for recessive

(b) (8 points) Given that person #3 is not a carrier, what is the probability that both persons #8 and #9 are carriers?

2/3 (for #8) x ½ (for #9) = **1/3**

+3 for P(8 is a carrier) = 2/3
+3 for P(9 is a carrier) = 1/3
+2 for multiplying to find the probability that both are carriers

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(c) (8 points) If persons #8 and #9 have 5 unaffected children, what is the probability that their next child will be affected (hint – use Bayes theorem)?

(XIY) = (YIX)(X)/(YIX)(X) + (YI[1-X])(1-X)

(XIY) = $(3/4)^5(1/3)/(3/4)^5(1/3) + 1(2/3) = (3/4)^5/(3/4)^5 + 2 = 0.24/2.24 = 0.11$

.11 x .25 = **0.0275**

+1 for writing out Bayes theorem correctly
+3 for putting numbers into the theorem
+2 for solving Bayes correctly
+2 for solving for the probability of the child not being affected
(no extra penalty for carrying a wrong answer from b)

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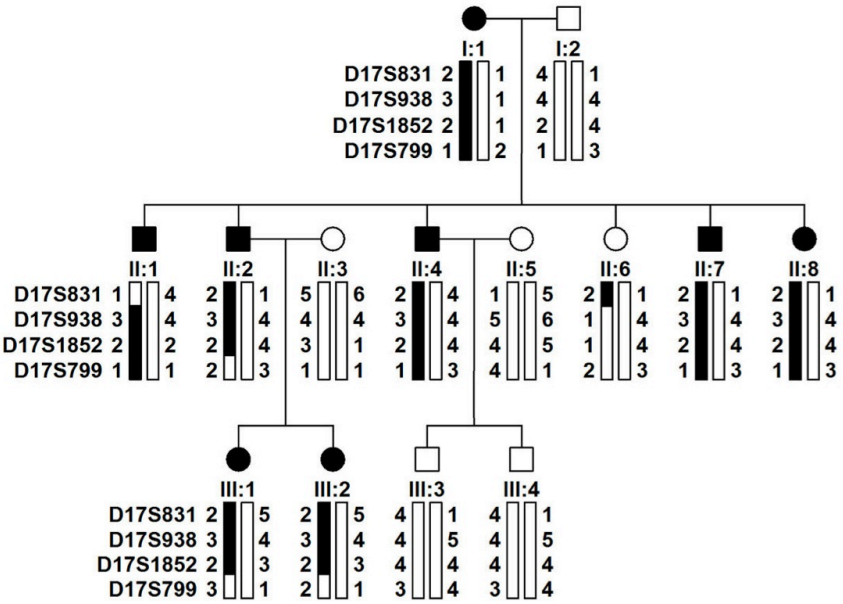
Examine the following pedigree for questions 3d-e:



The pedigree above is a Chinese family exhibiting an inherited loss of photoreceptor cells in the eye known as cone dystrophy in which four microsatellite markers have been genotyped for each family member.

The authors report the highest calculated LOD score in this pedigree for any marker to be 2.71 at q=0. For markers D17S381 and D17S799 the LOD score $=-\infty$ at q=0.

(d) (6 points) Of the two remaining markers (D17S938 and D17S1852), which of them would have a LOD score at q=0, of 2.71, or would they both have a LOD score q=0 of 2.71? Explain your answer briefly.

Both lack recombination events with the disease phenotype so they should both have the highest linkage value of 2.71 at theta=0

+3 for correct answer
+3 for explanation

(e) (6 points) Where, relative to the four markers in the pedigree, could the mutation causing cone dystrophy in this family be located? Be as specific as possible.

The mutation could exist at any locus between D17S831 and D17S799
+3 for stating some location between D17S831 and D17S799
+3 for not specifying a specific location