Bio393: Genetic Analysis **Name:**_____
Midterm

Question 1 (6 points):
White-nose syndrome is devastating insect-eating bat populations across the United States. It is caused by the fungus, *Pseudogymnoascus destructans*, and spreads during hibernation. In effort to control this pathogen, you grow it in the lab and want to identify compounds to kill it. Standard anti-fungal compounds work well, but some strains of the fungus survive treatments. Propose a hypothesis to explain how a mutation in a gene could cause drug resistance.

Question 2 (8 points):
You would like to identify a loss-of-function mutation in every one of the approximately 20,000 genes in *C. elegans.* You perform an EMS-mutagenesis experiment and isolate 2,000 mutant strains. After whole-genome sequencing, you find that 2,000 genes are devoid of predicted loss-of-function mutations and approximately 500 of the 2,000 genes are not mutated at all.

Provide explanations for (1) why you fail to recover loss-of-function mutations in every one of the 20,000 genes and (2) why you fail to recover any mutations in 500 genes.

Question 3 (6 points):
Blood type in humans is a codominant trait. A man with blood type A whose mother was blood type O has children with a woman with blood type B whose father was blood type O. What blood type(s) could the children inherit? Remember that two copies of the null allele result in blood type O.

(a) O only
(b) A, B, and O
(c) AB, A, B, and O
(d) AB only

Question 4 (6 points):
Using linkage mapping, you determined the genetic distance between A and B is 150 cM. What is the minimum number of intermediate markers between A and B that you would need to make this estimate possible? Please explain your reasoning.

Question 5 (8 points):
Remember that Alfred Sturtevant kept careful track of horse coat colors on his farm when he was growing up. He observed that a black mare crossed to a chestnut stallion produced all bay offspring. Mating these bay offspring gave rise to offspring of four different coat colors: black, bay, chestnut, and liver. Crossing liver offspring back to the black mare gave all black offspring. Crossing liver offspring back to the chestnut stallion gave all chestnut offspring. Explain how coat color is being inherited in horses and what the genotypes of each color are.

Question 6 (6 points):
You have three true-breeding strains of gerbils – all of which express the recessive white fur trait. You cross line1 to line2 and get gerbils with brown fur. Then, you cross line1 to line3 and get gerbils with white fur. Last, you cross line2 to line3 and get gerbils with brown fur. What is your interpretation of these results?

(a) The genes mutated in line1 and line2 are different
(b) The genes mutated in line1 and line3 are different
(c) The genes mutated in line2 and line3 are different
(d) Both (a) and (b) are true
(e) Both (a) and (c) are true

Question 7 (4 points each):
With respect to a typical genetic screen, please answer the following questions:

(a) What types of mutations are **most** common and why?

(b) What type of phenotype is **least** common and why?

(c) What phenotype is **most** often observed and why?

Question 8 (4 points each):
Over the past summer, you mentored a high school student in the lab. He worked hard but did not take any notes or keep a lab notebook. You had him look for suppressors of a mutant phenotype caused by a point mutation resulting in a null phenotype (not necessarily a stop codon mutation).

(a) How can you differentiate revertants (or back suppressors) from extragenic suppressors?

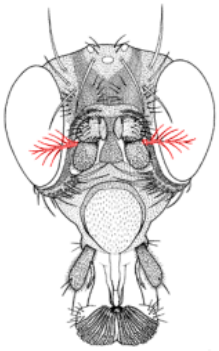
(b) Is it possible that he isolated an intragenic suppressor? Explain why or why not.

(c) What could you do to determine if the suppressor was a revertant or an intragenic suppressor?

(d) One of the suppressor mutations also suppresses mutant alleles of different genes. How might that suppressor act?

Question 9:

Drosophila "hear" sounds by feeling air vibrations with their arista or polarized hair structures between their eyes (red in image below). You are interested in the sensory programs underlying the recognition of air vibrations by the arista. Because few mutants affecting arista development exist, you design a genetic screen to identify them. Your focus is on chromosome 3, specifically on temperature-sensitive alleles. Using these alleles, you can sensitize arista development for future genetic studies. You have wild-type flies, a balancer stock Ser/TM6 [Antp], and two incubators (one at 22ºC and one at 29ºC). TM6 is marked with an *Antennapedia* allele [Antp] that causes a dominant transformation of antennae into legs, so you can easily see the presence of the balancer. Ser causes a dominant serrated wing phenotype.



(a, 20 points) Design a genetic screen to identify mutations that cause a temperature-sensitive recessive arista mutant phenotype. Be sure to specify bulk or single-pair crosses along with the rearing temperature for the flies.

You identify six temperature-sensitive alleles. To determine how many genes could be mutated, you set up complementation crosses.
(b, 6 points) Draw out a cross for *aristaless-1* and *aristaless-2* below.

You grow the cross progeny from the complementation test at the restrictive temperature and score for arista. The data are below.

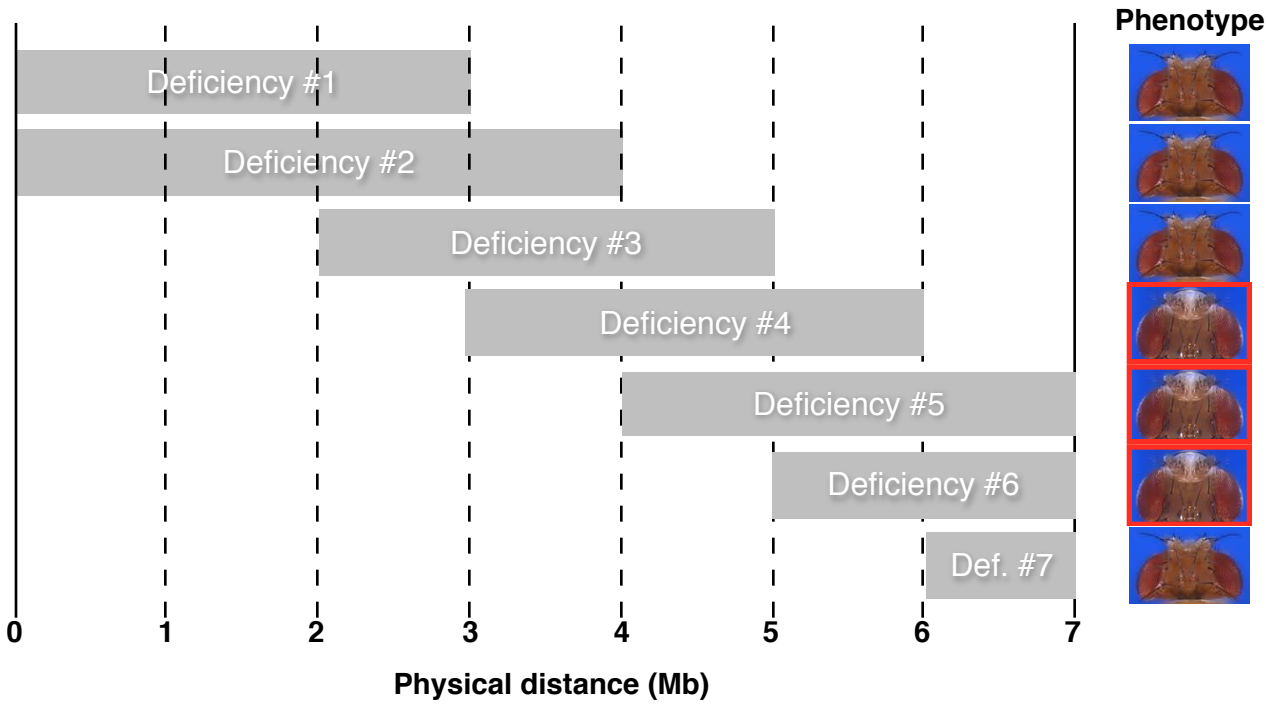
 Wild-type

 Aristaless mutant

	Wild-type	***aristaless-1***	***aristaless-2***	***aristaless-3***	***aristaless-4***	***aristaless-5***	***aristaless-6***
Wild-type							
aristaless-1							
aristaless-2							
aristaless-3							
aristaless-4							
aristaless-5							
aristaless-6							

(c, 6 points) Write out the complementation groups and any ambiguities.

You choose to map the location of the *aristaless-6* mutation using a collection of deficiencies that lack large parts of chromosome 3. Some but not all of these deficiencies remove or delete many genes including the gene mutated in *aristaless-6*. You cross *aristaless-6* mutant flies to each of the deficiencies and look at the aristaless phenotype in the heterozygous flies. The extents of the deficiencies and the aristaless phenotype data from the heterozygotes are below.



(d, 8 points) Where is the approximate physical location of the gene mutated in *aristaless-6* and how did you come to that conclusion?

(e, 4 points) In each deficiency heterozygote with the aristaless phenotype, the phenotype is more severe than the homozygous mutants. What is the nature of the *aristaless-6* mutation?

(f, 8 points) The *Drosophila* community has a very large resource of promoters that drive expression of your favorite gene in any tissue within the fly. Luckily for you, four promoters that express genes in tissues of interest exist: eye, leg, arista, and the whole body. You clone the gene mutated in the *aristaless-6* mutants and are interested in where in the fly the normal gene is required for function. Please describe the four transgenic strains you would like to produce and the predicted experimental outcome for each if the gene is required in the arista.