7.03 Problem Set 1

Due Wednesday, February 15, 2015 by 3 PM

1. You have isolated 6 mutant yeast strains that are uracil auxotrophs (ura$^-$). You wish to begin characterizing these mutants and decide to begin by crossing each mutant strain to the wild type strain and achieve the following results:

Cross	**Resulting diploid**
Mut 1 x WT	WT
Mut 2 x WT	WT
Mut 3 x WT	WT
Mut 4 x WT	WT
Mut 5 x WT	ura$^-$
Mut 6 x WT	WT
Mut 7 x WT	WT

a) What do these results tell you about each of the mutations in these strains?

b) You decide to do a complementation test. What further information will this provide you?

c) You obtain the following results from your complementation test:

	Mut 1	Mut 2	Mut 3	Mut 4	Mut 5	Mut 6	Mut 7
Mut 1	ura$^-$	ura$^-$	WT	WT	ura$^-$	ura$^-$	WT
Mut 2		ura$^-$	WT	WT	ura$^-$	ura$^-$	WT
Mut 3			ura$^-$	WT	ura$^-$	WT	ura$^-$
Mut 4				ura$^-$	ura$^-$	WT	WT
Mut 5					ura$^-$	ura$^-$	ura$^-$
Mut 6						ura$^-$	WT
Mut 7							ura$^-$

Sort these strains into complementation groups. Explain any ambiguities.

d) When doing some background reading, you discover that mutations in previously characterized genes (Ura1, Ura2, and Ura3) also give a ura$^-$ phenotype. You decide to see if your strains are mutant in any of these genes. After testing Mut 1, you find it fails to compliment Ura2, but does compliment Ura1 and Ura3. Fill in the following table in a way that is consistent with this observation.

	ura1$^-$	**ura2$^-$**	**Mut1**	**Mut1 x ura1$^-$**	**Mut1 x ura2$^-$**
Ploidy	Haploid				
Genotype	ura1$^-$	ura2$^-$			
Phenotype	ura$^-$	ura$^-$	ura$^-$		

2. A myotonic goat, also known as a fainting goat, is a goat whose muscles will freeze when it is startled, causing it to tip over. (An internet search for "fainting goat" will turn up many videos of this phenomenon.) This phenotype is caused by a recessive allele in a single gene.

You own a fainting goat with white hair. This hair color is the result of a single gene, and the allele for white hair is recessive. However, you want to breed gray fainting goats. You acquire a goat that is true-breeding for the dominant gray hair color allele (and homozygous for the dominant, non-fainting allele) and mate it with your white fainting goat.

a) What genotypes are present in the F1 generation? What phenotypes are present?

b) You decide to cross the resulting F1 goats. What phenotypes are present in the F2 generation, and in what proportions?

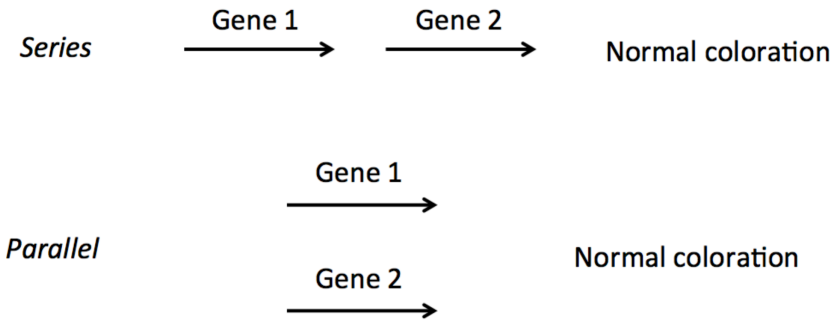
c) In your F2, you have generated some of your desired goats: gray and fainting. However, what you really want is a line of true-breeding (homozygous at all alleles) gray and fainting goats. What proportion of the F2 goats **that are gray and fainting** will be true-breeding for both of those phenotypes?

d) Design a cross that can determine whether a gray, fainting goat is true-breeding.

e) You decide to also breed your goats to have spots, which are caused by a single dominant allele. After some hard work, you have two goats that you know are heterozygous at all three alleles. If you cross them, what fraction of the resulting offspring will have all three **dominant** phenotypes?

3. You are studying the genetics of body color in the fruit fly, *Drosophila melanogaster*. You have discovered a strange new phenotype in which the flies have polka dots on their bodies. Based on your previous research on fly color, you hypothesize that two genes have an effect on this phenotype.

However, there are two ways that a pair of genes in a biochemical pathway can act: in series or in parallel. If the genes work in series, both genes are necessary for the fly to have wild-type coloration; therefore, **only one** gene would need to have its function disrupted in order for the fly to have the mutant phenotype. If the genes work in parallel, either one of the genes is necessary for the fly to have wild-type coloration; therefore, **both** genes need to have their function disrupted in order for the fly to have the mutant phenotype.



Another factor is the nature of each gene's mutant allele. The mutant allele in each gene can be either dominant or recessive. (Although mutations that disrupt gene function, known as loss-of-function mutations, are usually recessive, it is still possible for them to be dominant, so we need to consider that possibility.) This leads to six possible models for the pathway to work:

1. The genes work in series and both mutant alleles are dominant.
2. The genes work in series, and one mutant allele is dominant and one mutant allele is recessive.
3. The genes work in series and both mutant alleles are recessive.
4. The genes work in parallel and both mutant alleles are dominant.
5. The genes work in parallel, and one mutant allele is dominant and one mutant allele is recessive.
6. The genes work in parallel and both mutant alleles are recessive.

a) You have a true-breeding, polka-dotted fly and cross it with a wild-type fly. The resulting F1 generation all have normal body color, without any polka dots. Which of the six models listed above are still possible, given this experimental result? Explain your reasoning.

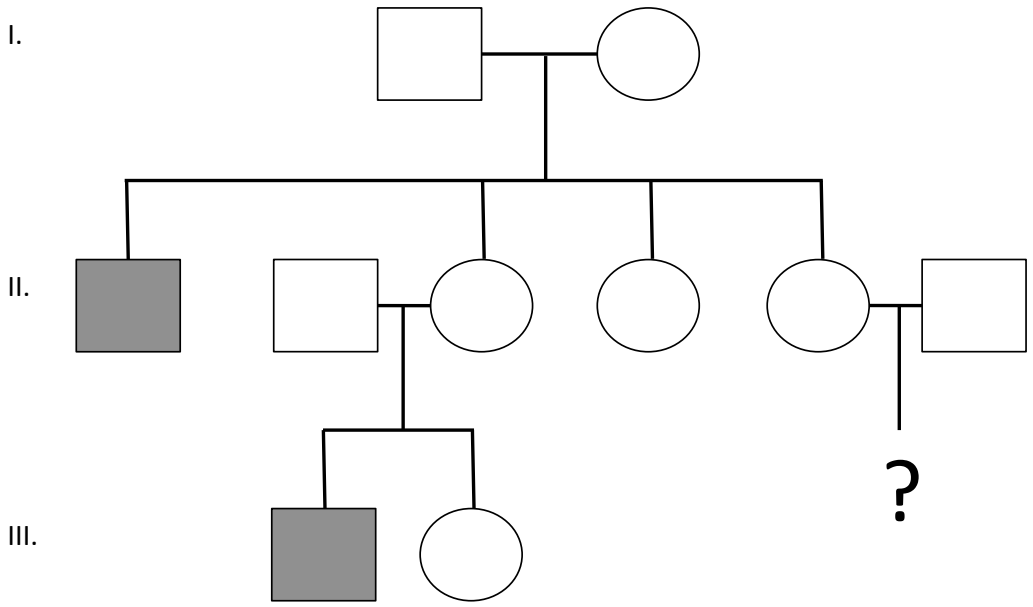
b) You cross the F1 flies to generate the F2 generation. What proportion of wild-type to polka-dotted flies would be expected for each of the models that were **not** rejected in part a?

c) You take 30 flies from F2 and see that 6 of them have polka dots. Using the χ^2 test, which of the remaining models can be rejected? Use the table of χ^2 values below for your calculations.

p value:	.995	.975	0.9	0.5	0.1	0.05	0.025	0.01	0.005
df = 1	.000	.000	.016	.46	2.7	3.8	5.0	6.6	7.9
df = 2	.01	.05	.21	1.4	4.6	6.0	7.4	9.2	10.6
df = 3	.07	.22	.58	2.4	6.3	7.8	9.3	11.3	12.8

d) When you bring your results to your adviser, she points out that you haven't considered the possibility that you original, true-breeding polka-dotted fly simply had a recessive allele at a single gene that caused the polka dots. Use the χ^2 test with your observation that 6 out of 30 of the F2 flies had polka dots to test this hypothesis. Can you reject this possibility with the χ^2 test? If not, how many flies would you need, assuming that you will observe polka dotted flies in the exact ratio predicted by the two-gene model that you didn't reject in part c, in order to reject this one-gene hypothesis? (Don't worry about an exact number; anything within 20 of the exact number is fine.)

4. You are a genetic counselor who has just been hired by a family with the following pedigree, where filled symbols indicate diseased individuals.



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

b) On the pedigree, assign genotypes to all individuals in the pedigree. If there are any ambiguities, list all possible genotypes and the probability of each.

c) The family wants to know what the probability is that the child indicated by ? will be affected by this disease. In your answer, state all possible genotypes for each parent. State probability of each genotype and disease phenotype for both male and female offspring. Assume no new mutations arise and that the disease allele is rare.

d) The first child is a male with the disease. Does this change the probability that a second child will also be disease free? If so, state the new probability for both male and female children.