

7.03 Problem Set 1

Due before 5 PM on Wednesday, September 20

Hand in answers in recitation section or in the box outside of 68-120

1. Imagine a natural compound called Spindlestop, which shows promising anti-tumor activity. The primary source of Spindlestop is the bark of an endangered species of tree, but suppose that the yeast *S. cerevisiae* is found to produce Spindlestop in minute, yet detectable, quantities. To increase production, you isolate 30 yeast mutants with increased levels of Spindlestop. Mutants 1-15 are mating type a (MAT a) and mutants 16-30 are mating type α (MAT α).

The analysis begins by pairwise mating of each mutant to a wild-type strain and to the mutants of the opposite mating type. The amounts of Spindlestop produced by the resulting diploids are shown in the table below (“wt” indicates wild-type quantities, “+” indicates about 10X wild-type levels).

		MAT α Strains														
	Wild-type	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
Wild-type	wt	+	wt	wt	wt	wt	+	wt	+	+	wt	wt	wt	wt	wt	+
1	wt	+	wt	wt	wt	wt	+	wt	+	+	wt	wt	wt	+	wt	+
2	wt	+	wt	+	wt	wt	+	+	+	+	+	wt	wt	wt	+	+
3	wt	+	wt	+	wt	wt	+	+	+	+	+	wt	wt	+	+	+
4	wt	+	+	wt	+	+	+	wt	+	+	wt	+	+	wt	wt	+
5	wt	+	wt	+	wt	wt	+	+	+	+	+	wt	wt	wt	+	+
6	wt	+	wt	+	wt	wt	+	+	+	+	+	wt	wt	wt	+	+
7	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
8	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
9	wt	+	+	wt	+	+	+	wt	+	+	wt	+	+	wt	wt	+
10	wt	+	+	wt	+	+	+	wt	+	+	wt	+	+	wt	wt	+
11	wt	+	+	wt	+	+	+	wt	+	+	wt	+	+	wt	wt	+
12	wt	+	+	wt	+	+	+	wt	+	+	wt	+	+	wt	wt	+
13	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
14	wt	+	+	wt	+	+	+	wt	+	+	wt	+	+	wt	wt	+
15	wt	+	+	wt	+	+	+	wt	+	+	wt	+	+	wt	wt	+



MAT a Strains

- a) Which of the mutants are dominant and which are recessive?
- b) Based on the observed properties what can you conclude about the function of the gene affected by Mutant 1 with respect to Spindlestop production? What can you conclude about the gene altered by Mutant 7?
- c) What is anomalous about the behavior of Mutant 3? Provide a simple genetic explanation.

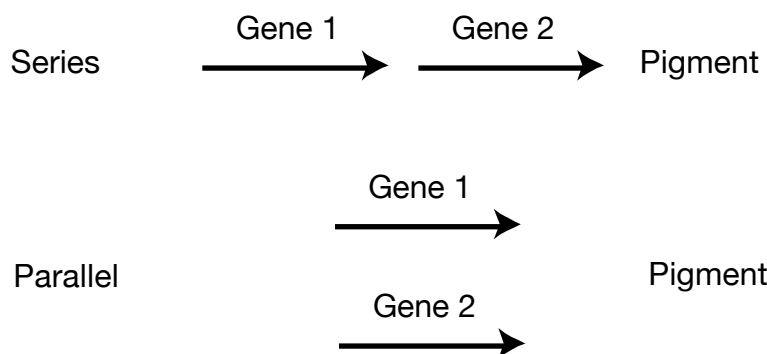
d) Organize the 30 mutations into complementation groups (genes). Please indicate any remaining ambiguities.

e) Based on these limited complementation data, what is the absolute minimum number of genes that must comprise the Spindlestop biosynthetic pathway? What is the maximum number of genes?

f) In an attempt to construct a yeast strain that produces even more Spindlestop than any of the existing mutants you decide to combine two of the recessive mutants to make a double mutant strain. Pick two of the mutants to combine and explain the reasoning for your choice.

2. Wild type mice are gray and in a large-scale breeding colony two white female mice arise from different parents. You would like to know whether the white phenotype is caused by two mutations in the same gene or in different genes. Using the concepts of dominance, recessivity, and complementation, describe a set of crosses and the interpretation of their outcomes that you would use to make this determination. Please be sure to indicate the circumstances that would prevent you from easily making this determination. (Assume you have available an unlimited number of true breeding wild-type gray mice.)

3. Genes that control coat color in mice can be thought of as steps in biochemical pathways whose products are pigmented compounds that give the fur its color. Albino mice have white fur because they lack the ability to make any pigment. Imagine mutations in two different genes that can, in certain combinations, block the production of pigment, yielding mutants with white fur. There are two different possible arrangements for two biochemical steps responsible for the formation of pigment: the two genes might act in *series* such that a loss of function of *either* gene would block the formation of pigment, or the two genes could act in *parallel* such that loss of function of *both* genes would be required to block the formation of pigment.



a) Say that you are given an albino mouse. When you cross this mouse to wild type all of the F1 progeny appear normal (i.e. like wild type). Consider the following three possibilities for the genetic basis of the albino trait: 1) recessive allele of a single gene, 2) recessive alleles of two genes acting in series 3) recessive alleles of two genes acting in parallel. For each of the three possibilities give the proportion of albino and normal looking mice among the F2 generation.

b) You cross the normal looking F1 mice among themselves producing 40 F2 mice; 15 are albino and 25 appear normal. Determine whether this data is consistent with each of the three possibilities outlined in part (a) and draw whatever conclusions you can about the inheritance of albinism. The table below gives chi square values for 1, 2 and 3 degrees of freedom. Use the convention that for $p < 0.05$ there is a statistically significant difference between the observed results and the results expected for a given model and therefore we can reject the model on the basis of the experimental data.

<i>p</i> 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

4. PKU is an autosomal recessive genetic disorder resulting from a loss of the enzyme phenylalanine hydroxylase, which converts phenylalanine to tyrosine. Without this enzyme, phenylalanine and its breakdown products accumulate to toxic levels resulting in mental retardation. Fortunately, individuals homozygous for the disease allele can be spared by a phenylalanine-free diet.

Say that Sarah has a brother with phenylketonuria (PKU), but she doesn't have the disease herself.

a) What is the probability that Sarah is a carrier for PKU?

Sarah's husband was detected to have PKU at birth but he has been treated with a phenylalanine-free diet. Sarah and her husband recently had their first child and are relieved that their child shows normal phenylalanine levels and thus is not homozygous for the disease allele.

b) Based on this new information use Bayes Theorem to compute an updated probability that Sarah is a carrier for PKU.