Exams

Fall 1996

7.03 Exam 1

Name: _____

Section: _____ TA: _____

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

There are five pages including this cover page

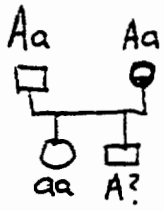
Please write your name on each page.

Remember ...

- Look over the entire exam so you don't get hung up on a hard question and leave easier questions unanswered
- Check your answers to make sure that they make sense
- If you can't answer a question, show your work for partial credit

Question 1	**25 points**
Question 2	**45 points**
Question 3	**30 points**

1. (a 5 pts.) Consider a hypothetical autosomal dominant trait for crossed-eyes. A man has crossed-eyes as do both of his parents but his sister has normal eyes. Assuming that the cross-eyed trait is completely penetrant, what is the probability that the man is homozygous for the cross-eyed trait?



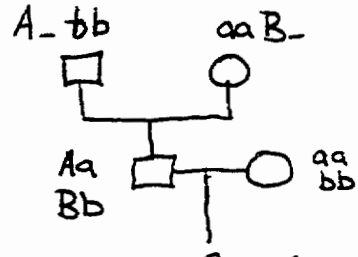
$$P(AA \mid \text{not } aa) = \frac{P(AA) \cdot P(\text{not } aa)}{P(\text{not } aa)} = \frac{1/4 \cdot 1}{3/4}$$

$$= \boxed{1/3}$$

(**b** 10 pts.) Consider a second hypothetical autosomal dominant trait for crooked-thumbs. A woman with crooked-thumbs and normal eyes marries the man from part (**a**) who has crossed-eyes and normal thumbs. They have a son who has crooked-thumbs and crossed-eyes. When the son grows up, he marries a woman with normal thumbs and normal eyes. What is the probability that their first child will have crossed-eyes and crooked thumbs if the loci for these two traits are unlinked?

A = gene for crossed eyes

B = gene for crooked thumbs

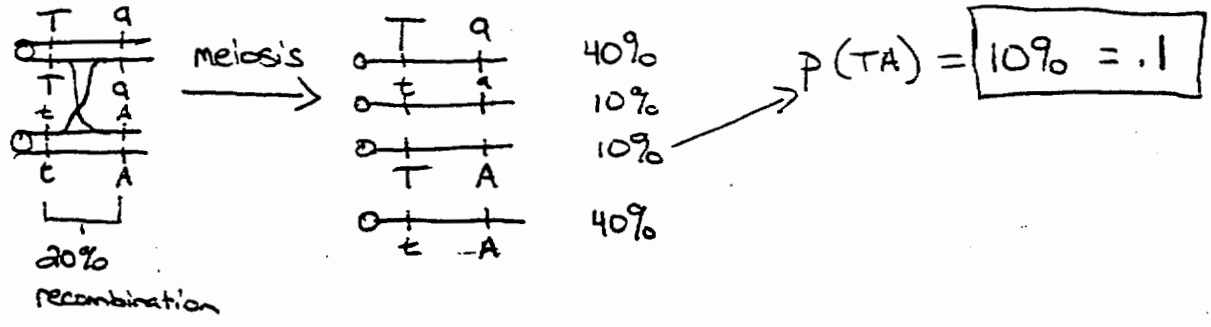


$$P(A\_B\_) = P(A) \cdot P(B)$$

$$= .5 \times .5 = \boxed{.25}$$

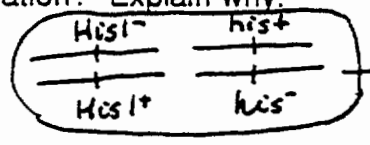
(**c** 10 pts.) What is the probability that the first child of the couple in part (**b**) will have crossed eyes and crooked thumbs if the loci for these two traits are 20 cM apart?

In meiosis in AaBb father above chromosome looks like this:

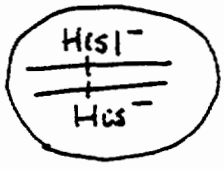


$$P(TA) = \boxed{10\% = .1}$$

2. (a 5 pts.) You have isolated a new His$^-$ yeast mutant (this strain will not grow unless histidine is provided in the medium). When you mate this mutant to wild-type the resulting diploid <u>can</u> grow without histidine. When you mate to a known His1$^-$ mutant the resulting diploid <u>can not</u> grow without histidine. Would you expect your new mutant to be linked to the His1$^-$ mutation? Explain why.

If 2 genes 

→ diploid is his$^+$

If 1 gene 

→ diploid is his$^-$ → if same gene, then **linked**

(b 5 pts.) In the analysis presented in part (a), what does the cross to wild type tell you and why was it important to do this control?

It tells you that his$^-$ is recessive.
If it were dominant, the complementation test would be invalid.

(c 10 pts.) You sporulate the diploid from part (a) that was formed by mating the new His$^-$ mutant to the His1$^-$ mutant. Given that these two His$^-$ mutations are 2 kbp (1000 base pairs) apart and that the average recombination frequency in yeast is 0.25 cM per kbp, how many tetratypes would you expect to find if 200 tetrads were analyzed?

$$2 \text{ kbp} \times .25 \frac{\text{cM}}{\text{kbp}} = .5 \text{ cM}$$

$$\text{Distance} = \frac{T + 6\,NPD}{2(\text{total})} \times 100 \quad \Rightarrow \quad 0.5 = \frac{T}{400} \times 100$$

$T = 2$

NPD = 0 due to small distance

(d 6 pts.) You cross a His1$^-$ mutant to a His2$^-$ mutant and analyze the resulting tetrads. Fill in the blanks below to give the number of His$^+$ and His$^-$ spores for each kind of tetrad.

Parental Ditype	Tetratype	Nonparental Ditype
0 His$^+$, 4 His$^-$	1 His$^+$, 3 His$^-$	2 His$^+$, 2 His$^-$
+ − + − − + − + } all His$^-$	+ − − + } His$^-$ − − + + His$^+$	− − − − } His$^-$ + + + + } His$^+$

(**e** 4 pts.) From the cross in part (**d**) you obtain 65 parental ditypes, 30 tetratypes, and 5 nonparental ditypes. How far apart are the His1 and His2 genes?

$$\text{Distance} = \frac{T + 6\,NPD}{2\,(\text{total})} = \frac{30 + 30}{200} = 30\,cM$$

Parts f+g omitted

3. (a 5 pts.) Consider three recessive *Drosophilia* traits specified by the hypothetical X-linked genes **Pb**, **Ni**, and **Ag**. 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 the all three traits?

$$♀ \frac{Pb\ Ni\ Ag}{Pb\ Ni\ Ag} \times ♂ \frac{+\ +\ +}{Y}$$

♀ progeny: $\frac{Pb\ Ni\ Ag}{+\ +\ +}$ ⇒ none will show traits (0%)

♂ progeny: $\frac{Pb\ Ni\ Ag}{Y}$ ⇒ all will show traits (100%)

(**b** 5 pts.) The genes are in order: **Pb – Ni – Ag**. A female fly heterozygous at all three loci 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 **Pb Ni +** and **+ + Ag** (a + indicates the wild type phenotype for a given trait). The female fly was produced by crossing flies from two different true-breeding lines. What were the phenotypes of the two lines?

Pb Ni + } rarest classes ⇒ result of double crossover, which switches the middle marker
+ + Ag }

∴ parental: $\frac{Pb\ +\ +}{+\ Ni\ Ag}$ (genotype of female fly)

produced by crossing a line with phenotype Pb ++, and a line with phenotype + Ni Ag.

(**c** 10 pts.) As measured by two-factor crosses, the distance between **Pb** and **Ni** is 20 cM and the distance between **Ni** and **Ag** is 10 cM. Out of 1000 progeny flies from part (**a**) how many would you expect to have the phenotype **Pb Ni +** ?

Pb Ni + is one of the 2 double crossover classes

$$p(Pb\ Ni\ +) = p(\text{crossover b/w Pb and Ni}) \times p(\text{crossover b/w Ni and Ag}) \times \frac{1}{2}$$

$$= 0.2 \times 0.1 \times \frac{1}{2} = 0.01$$

So out of a 1000 flies → $1000 \times 0.01 = \boxed{10}$ Pb Ni + fly.

(**d** 10 pts.) The distance between **Pb** and **Ag** can be calculated to be 30 cM by adding the two genetic distances given in part (**b**). If the distance between **Pb** and **Ag** was measured directly in a two-factor cross what would be the measured distance in cM?

In a two-factor cross we do not take double crossovers into account, we only count single crossovers.

p(single crossover b/w Pb and Ni and no crossover b/w Ni and Ag) =
$= 0.2 - 0.2 \times 0.1 = 0.18$

p(s.c.o. b/w Ni and Ag and no c.o. b/w Pb and Ni) $= 0.1 - 0.2 \times 0.1 = 0.08$

p(s.c.o. b/w Pb and Ag) $= 0.18 + 0.08 = 0.26$

⇒ distance of 26 cM

7.03 Exam 2

Name: Key

Section: _____ TA: _____

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

There are seven pages including this cover page

Please write your name on each page.

Remember to show your work and state your assumptions for partial credit

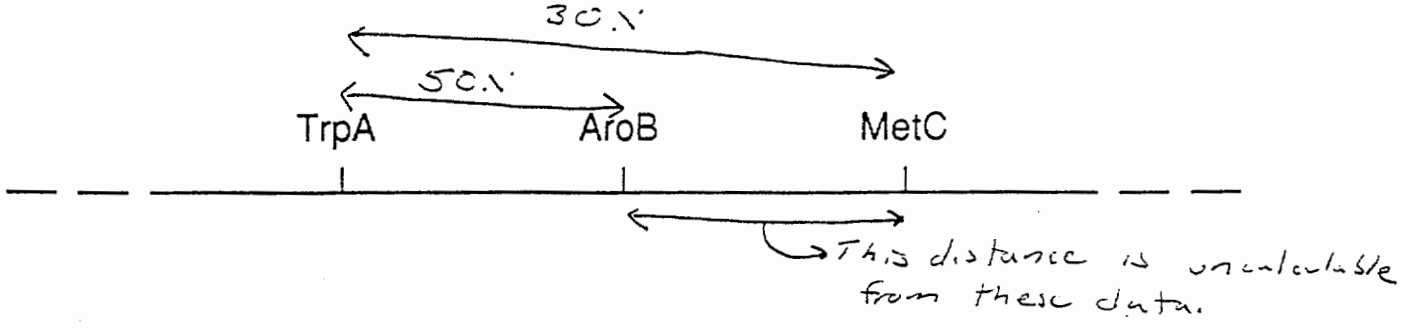
Question 1	35 points
Question 2	30 points
Question 3	35 points

Question 1 omitted

2. (a 10 pts.) Consider three *E. coli* markers that are closely linked in the order: TrpA, AroB and MetC. Phage P1 is grown on an F⁻ TrpA⁺ AroB⁻ MetC⁺ host. The resulting lysate is used to infect a TrpA⁻ AroB⁺ MetC⁻ recipient and TrpA⁺ transductants are selected. 100 transductants are analyzed and have the genotypes given below.

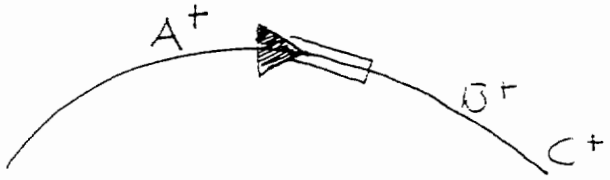
Genotype	Number	
TrpA⁺ AroB⁻ MetC⁺	30	← this is all C cotransduced
TrpA⁺ AroB⁺ MetC⁻	50	
TrpA⁺ AroB⁻ MetC⁻	20	← these 2 are all B transduced

On the map below indicate the distances between TrpA and AroB and between TrpA and MetC as cotransduction frequencies.



Name: _____

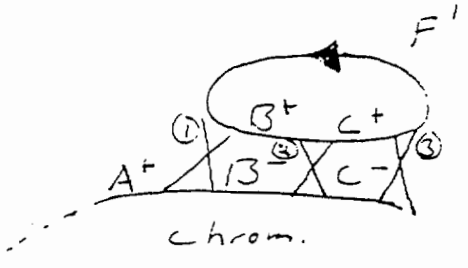
(**b** 5 pts.) Starting with a strain of genotype F+ TrpA+ AroB+ MetC+ you isolate an Hfr that can transfer TrpA+ efficiently and AroB+ and MetC+ very inefficiently. Draw a map showing the structure of the Hfr that includes the site of integration relative to the neighboring markers and the orientation of the origin of transfer.



(**c** 5 pts.) Phage P1 is grown on the Hfr strain isolated in part **b**. The resulting transducing phage are used to infect a TrpA− MetC− recipient and TrpA+ transductants are isolated. Given that the DNA length of F+ and phage P1 are both 10^5 base pairs, what fraction of these TrpA+ transductants will also be MetC+?

since the F+ is by itself 10^5 bp, there is no way 2 markers on either side of it can be co-transduced.. So Ø will be A+ and C+

(**d** 10 pts.) An F' is isolated from the Hfr in part **b** by selecting for early transfer of AroB+ and MetC+. The F' is transferred by conjugation into a AroB− and MetC− recipient and an Hfr is isolated by selection for a strain that can transfer TrpA+ efficiently. This Hfr transfers MetC+ early and AroB+ late. With as much detail as possible, draw out the structure of the Hfr.



① $A^+B^+C^+ \rightarrow B^-C^-$ B early so not it..

② $A^+B^-C^+ \rightarrow B^+C^-$ C early, B late ←

③ $A^+B^-C^- \rightarrow B^+C^+$ C late, so not it

Name: _____

3. The bacterium *X. aminus* induces expression of the enzyme arginase 100-fold when arginine is present. The enzyme arginase allows *X. aminus* to use arginine as a nitrogen source. Mutations in the linked genes **A** and **B** prevent utilization of arginine as a nitrogen source. A mutation in a third linked locus **R** results in constitutive expression of arginase. These results as well as the behavior of a merodiploid for genes **R**, **A**, and **B** are given below.

Genotype	Arginine	Arginase enzyme levels
wild-type	–	1
	+	100
R⁻A⁺B⁺	–	100
	+	100
R⁻A⁺B⁺/F' R⁺A⁻B⁻	–	1
	+	100

(a 5 pts.) Propose how the **R** gene regulates arginase expression.

R⁻ is a trans acting, recessive mutation that causes constitutive expression of ~~arginase~~ arginase => R is a repressor

When arginase levels are checked in **A⁻** or **B⁻** mutants the following is observed.

Genotype	Arginine	Arginase enzyme levels
R⁺A⁺B⁻	–	0
	+	0
R⁺A⁻B⁺	–	1
	+	1
R⁻A⁺B⁻	–	0
	+	0
R⁻A⁻B⁺	–	100
	+	100

Name: _____

(b 5 pts.) Give a model for the B gene product that are consistent with these data.

2 answers were accepted:

1. B is the permease gene
2. B is an activator of the permease gene that is repressed by R : R ⊣ B → permease

B could also be the promoter or the initiator, but these are not gene products.

(c 10 pts.) Give two distinct models for the A gene product that are consistent with these data.

1. A is a genetic activator that represses R
   A → R ⊣ permease
2. A could be the permease that allows arginine to enter the cell.

Theoretically, A could also be a mutation in the operator for B, that doesn't let the repressor leave the site (a gain of function mutation), but again, the operator is not a gene product.

(d 5 pts.) The **R⁻A⁻** mutant is found to be unable to use arginine as a nitrogen source. Which of your two models in part **c** for the function of the **A** gene does this finding support and why.

This favors the permease model. In R⁻A⁻ cells there is high levels of the arginase enzyme, but arginine cannot enter the cell, and so it will not be utilized.

(e 10 pts.) Starting with a merodiploid strain of genotype **R⁺A⁺B⁺/F' R⁺A⁺B⁺** you mutagenize and isolate a mutant that expresses high levels of arginase constitutively. After loss of the F' from your mutant strain expression of arginase is still constitutive. Propose two different explanations for the nature of the constitutive mutation.

4 answers were accepted, you only needed two:

1. a cis-dominant mutation in the operator: O^c
2. a dominant negative mutation in the repressor: R^{-d}
3. a gain of function mutation in the activator
4. a gain of function mutation in the promoter or initiator (i.e. the activator or RNA Pol always binds).

7.03 EXAM 3

November 20, 1996

NAME Answer key

SECTION _____

TA _____

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

There are eight pages including this cover page.

Please write your name on each page.

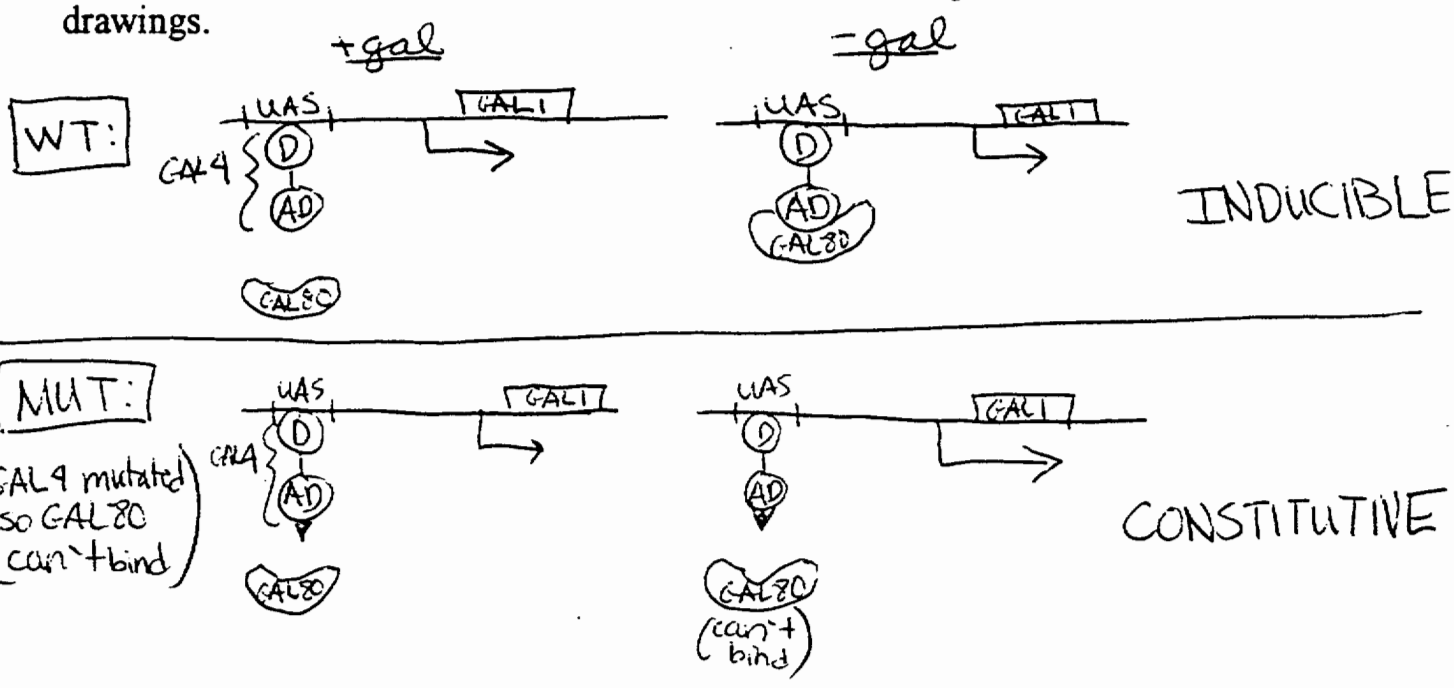
Remember to show your work and state your assumptions for partial credit.

Question 1	33 points
Question 2	17 points
Question 3	16 points
Question 4	34 points

Questions 1+2 omitted

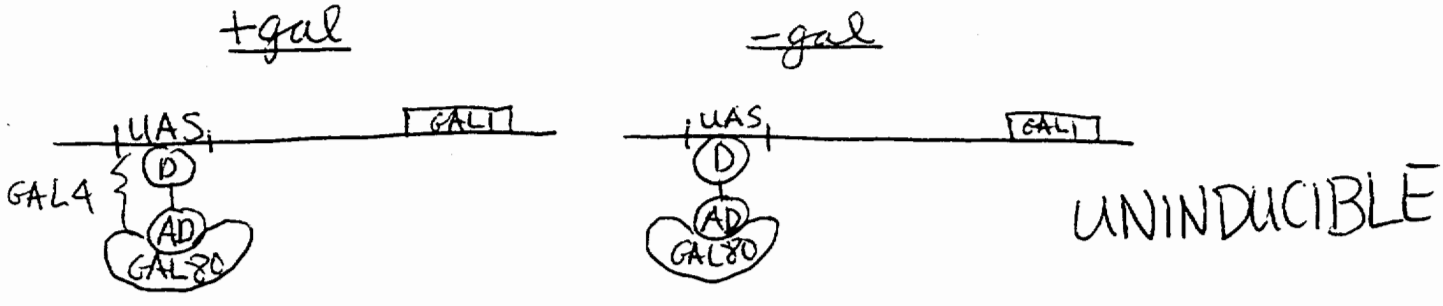
3. In the yeast GAL system, most mutants in GAL4 are uninducible and most mutants in gal80 are constitutive.

(a 6 points) Rare GAL4 constitutive mutants can be isolated in an otherwise wild type strain. What is the functional alteration in this mutant protein? Use drawings.



(b 10 points) Rare GAL80 uninducible mutants can also be isolated in an otherwise wild type strain. What is the functional alteration in this mutant protein? Use drawings.

GAL80 mutated so it is always bound to GAL4



EX: GAL80 is like a super-repressor
GAL80 can't bind gal anymore

Question 4 omitted

7.03 Final Exam

Name: Answer Key

Section: _____ TA: _____

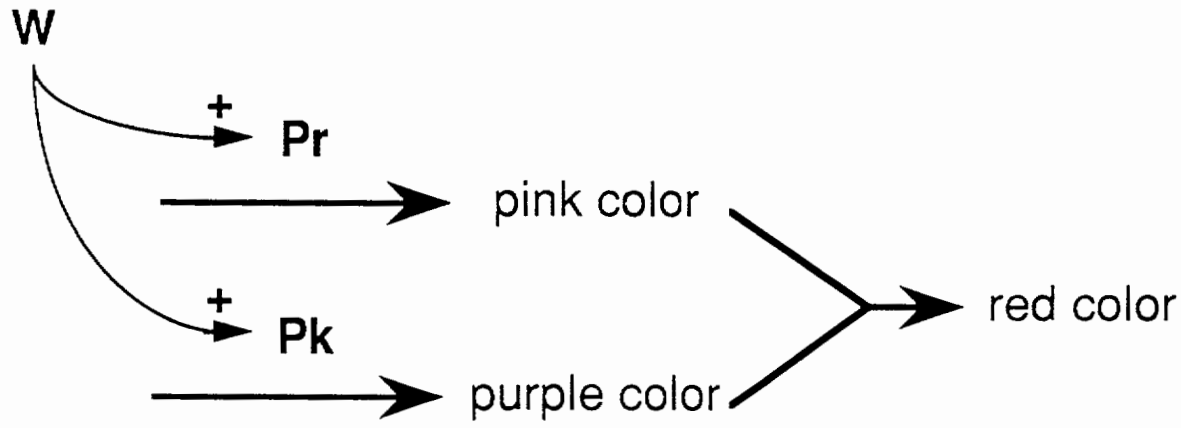
There are seventeen pages including this cover page

Please write your name on each page.

Question 1	25 points
Question 2	20 points
Question 3	25 points
Question 4	25 points
Question 5	30 points
Question 6	25 points
Question 7	24 points
Question 8	26 points

Name: _____

1. Consider a hypothetical type of fly whose eye color is specified by the following pathways:



The product of the **Pr** gene produces a pink pigment and the product of the **Pk** gene produces a purple pigment. In wild type flies the two pigments combine to produce dark red eyes. Homozygous **Pk⁻/Pk⁻** mutants have pink eyes and homozygous **Pr⁻/Pr⁻** mutants have purple eyes. The product of the **W** gene is a transcriptional activator that is necessary for expression of both **Pr** and **Pk** genes. In homozygous **W⁻/W⁻** strains neither pigment is produced giving white eyes. All three genes are autosomal; the **Pr** and **Pk** genes are 10 cM apart and the **W** gene is on a different chromosome.

(a 7 pts.) A true breeding purple-eyed strain is crossed to a true breeding white eyed strain. The F_1 progeny all have red eyes. The F_1 flies are mated among themselves to produce F_2 progeny. The following eye colors are observed among the F_2 flies: red, white, pink and purple. What are the genotypes of the two true breeding strains?

TRUE BREEDING PURPLE-EYED STRAIN

$$\frac{W^+}{W^+} \quad \frac{Pr^- \; Pk^+}{Pr^- \; Pk^+}$$

TRUE BREEDING WHITE EYED STRAIN

$$\frac{W^-}{W^-} \quad \frac{Pr^+ \; Pk^-}{Pr^+ \; Pk^-}$$

Name: _____

(**b** 7 pts.) Two different true-breeding strains with white eyes are crossed. The F_1 progeny from this cross all have red eyes. What are the genotypes of the two true breeding lines.

STRAIN 1

$$\frac{w^-}{w^-} \quad \frac{Pr^+ \; Pk^+}{Pr^+ \; Pk^+}$$

STRAIN 2

$$\frac{w^+}{w^+} \quad \frac{Pr^- \; Pk^-}{Pr^- \; Pk^-}$$

(**c** 11 pts.) F_1 flies from part (**b**) are then crossed to a **Pk⁻/Pk⁻ Pr⁻/Pr⁻ W⁻/W⁻** triple homozygous mutant strain. What fraction of the flies produced by this test-cross will have white eyes?

Strain A $\qquad$ Strain B

$$\frac{w^+}{w^-} \quad \frac{Pr^+ \; Pk^+}{Pr^- \; Pk^-} \times \frac{w^-}{w^-} \quad \frac{Pr^- \; Pk^-}{Pr^- \; Pk^-}$$

white eyes $= w^-/w^-$ or $\dfrac{Pr^- \; Pk^-}{Pr^- \; Pk^-}$

$= p(w^- \text{ from A}) + p(w^+ ; Pr^- Pk^- \text{ from A})$

$\times$ p(non-recomb

$= 1/2 + (1/4)(9/10)$

$= \frac{29}{40}$ or 72.5%

Questions 2+3 omitted

Name: _____

4. When *E. coli* cells are irradiated with a pulse of UV light, recA protein cleaves and thus inactivates the lexA repressor protein. LexA is the transcriptional repressor for uvrA, a gene involved in DNA repair, and other genes that arrest cell growth in response to DNA damage.

(**a** 5 pts.) You construct a fusion of the uvrA promoter and operator to lacZ (the gene that encodes ß-galactosidase) and introduce the fusion into a ΔlacZ lexA+ strain (strain 1). How would you expect ß-galactosidase expression to respond to a UV pulse in strain 1?

ß-gal expression will be induced by UV light

(**b** 5 pts.) You also introduce the fusion of the uvrA promoter to lacZ into a ΔlacZ strain that contains a mutant of the lexA gene that renders the lexA protein non-cleavable by recA (strain 2). How would you expect ß-galactosidase expression to respond to a UV pulse in strain 2?

ß-gal will be uninducible

Parts c+d omitted

Name: _____

5. Starting with a gal80$^-$ mutant (constitutive), a strain S1 is isolated that shows normal inducible expression of the GAL genes. When S1 is crossed to wild type, the following tetrads are observed:

4 Gal inducible	2 Gal inducible 2 constitutive	3 Gal inducible 1 constitutive
27	24	100

(a 7 pts.) What can you conclude from these data?

The 1 : 1 : 4 segregation in the cross indicates the suppressor mutation (sup 1) is unlinked to gal80. The sup1$^-$ mutation by itself has no effect on expression of the GAL genes (uninducible phenotype).

When S1 is crossed to a Δgal4 strain (Gal$^-$ phenotype), the following tetrads are observed:

2 Gal inducible 2 Gal$^-$
100

(b 8 pts.) What can you add to your conclusion from part **(a)**?

We only see one kind of tetrad; therefore sup 1 must be tightly linked to gal4. Most likely, sup 1$^-$ is a mutation in the gal4 gene.

Name: _____

Starting with the same gal80⁻ mutant strain, a different normally inducible strain is isolated, S2. When S2 is crossed to wild type, the following tetrads are observed:

4 Gal inducible	2 constitutive 2 Gal⁻	2 Gal inducible 1 Gal⁻ 1 constitutive
31	34	119

(**c** 7 pts.) What do you conclude from these data?

1:1:4 segregation => sup2 is unlinked to gal80.
By itself, sup2⁻ has a Gal⁻ phenotype.

Finally, when S1 and S2 are crossed, the following data are observed:

4 Gal inducible
100

(**d** 8 pts.) Now what can be added to your conclusion in part (**c**). Account for the differences when S1 in part (**a**) and S2 in part (**c**) are crossed to wild type.

We only see PD => most likely sup1 and sup2 are mutations in the same gene, in Gal4. They are different mutations, however. sup1⁻ has wt phenotype, while sup2⁻ is Gal⁻.

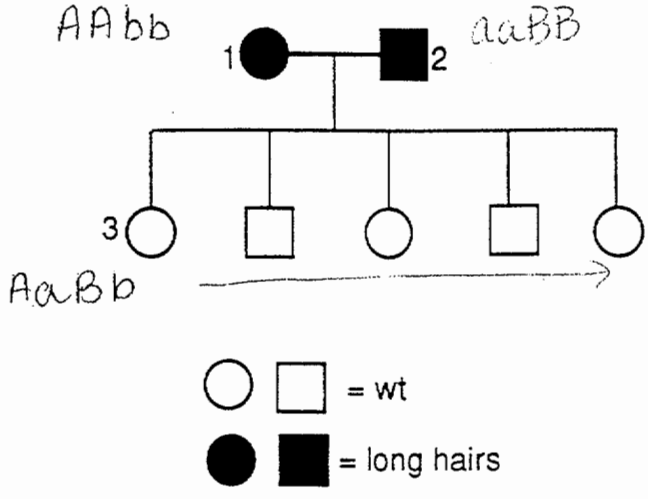
Question 6 omitted

Name: _____

7. In this question you have to explain the mode of inheritance in three pedigrees. Assume complete penetrance in all cases. Squares represent males and circles represent females.

Part a omitted

Two mice obtained from the wild with long hairs are mated, and you find the following.



(**b** 8 pts.) Explain the pedigree. Give genotypes of individuals 1, 2, and 3.

This is case of two seperate genes with recessive. mutations. The two mutations complement one another in this pedigree.

Part c omitted

Name: _____

8. (**a** 7 pts.) Consider two randomly mating human populations of <u>equal size</u> that reside on separate continents. An autosomal dominant trait is exhibited by 99% of the people in one population, and by 75% of the people in the other population. After frequent travel between the two continents becomes possible, the populations have the opportunity to mix. If mating between the two populations becomes random, what will the new frequency of the trait be for the mixed population?

Pop 1. $A/a + A/A = 99\%$

$\therefore a/a = 1\%$

$\therefore f(a) = .1$

Pop 2 $A/a + A/A = 75\%$

$\therefore a/a = 25\%$

$f(a) = .5$

mix, new $f(a) = \frac{.1+.5}{2} = .3$

$\therefore f(A) = .7$

$f(a/a) = .09$

$\therefore f(A/a) + f(A/A) = .91$

(**b** 7 pts.) A recessive inherited disease with a selective disadvantage of 0.1 occurs at a frequency of 10^{-4} in a randomly mating population. Say that the allele frequency for the disease was set by a balance between new mutations and selection against the homozygote. In any given generation, what fraction of the disease alleles within the population are new mutations? (You can use approximations that are accurate to within 10%).

$q = 10^{-2}$ $\quad q = \sqrt{\frac{u}{s}}$

$10^{-2} = \sqrt{\frac{u}{.1}}$ $\quad u = 10^{-5}$

new $q \rightarrow 10^{-5}$

total $q \rightarrow 10^{-2}$ $= 10^{-3}$