Exams

Fall 1997

7.03 Exam 1

Name: _____

Section: _____ TA: _____

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

There are six pages including this cover page

Please write your name on each page.

Please...

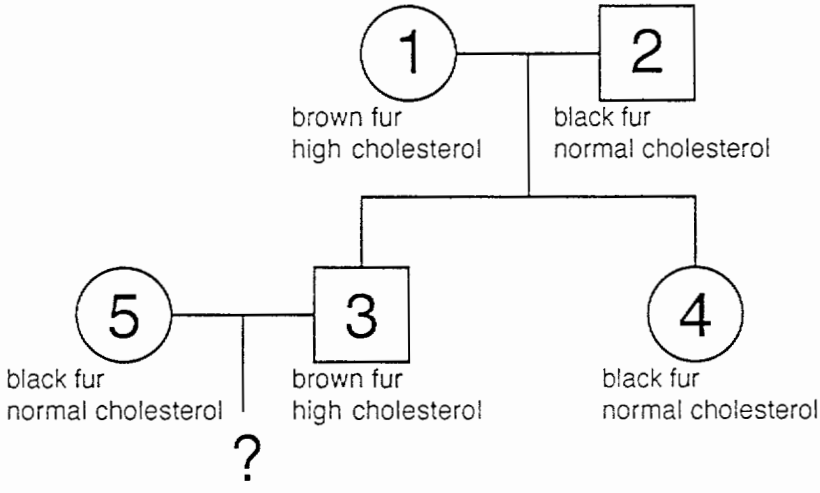
- Look over the entire exam so you don't spend too much time on hard questions leaving the easy questions unanswered.
- Check your answers to make sure that they make sense.
- To help us give partial credit, show your work and any assumptions that you make.

Question 1 30 points
Question 2 40 points
Question 3 30 points

Name: SOLUTION SET

1. Consider the hypothetical mouse traits for high blood cholesterol and black fur. The trait for high cholesterol is specified by a dominant allele designated **H C**, whereas the wild-type allele for normal cholesterol levels is designated **hc**. Black fur is specified by a recessive allele designated **bl**, whereas the wild-type allele which gives brown fur is designated **BL**. The genes for both of these traits are 30 cM apart on the same autosome. Assume that both traits are completely penetrant.

A brown female with high cholesterol (indicated as 1 below) is mated to a black male with normal cholesterol (indicated as 2). The progeny from this cross include a brown male with high cholesterol (indicated as 3) and a black female with normal cholesterol (indicated as 4). The crosses in this problem are represented in the following pedigree:



(a 12 pts.) Give the genotypes of each of the mice.

(Example: Mouse 5 genotype: $\frac{bl \quad hc}{bl \quad hc}$)

Mouse 1 genotype: $\frac{BL \quad HC}{bl \quad hc}$ or $\frac{BL \quad hc}{bl \quad HC}$

Mouse 2 genotype: $\frac{bl \quad hc}{bl \quad hc}$

Mouse 3 genotype: $\frac{BL \quad HC}{bl \quad hc}$

Mouse 4 genotype: $\frac{bl \quad hc}{bl \quad hc}$

Name: SOLUTION SET

(**b** 8 pts.) Mouse 3 is mated to a black female with normal cholesterol (indicated as 5). If four mice are produced from this cross, what is the probability that all four will have brown fur?

Mouse #3 $\frac{BL}{bl}$ × $\frac{bl}{bl}$ Mouse #5

↓

$\frac{Bl}{bl}$ or $\frac{bl}{bl}$

p(? has brown fur) = $\frac{1}{2}$

For a litter of four, $(\frac{1}{2})^4 = \frac{1}{16}$

(**c** 10 pts.) Given that a progeny mouse from the cross described in part **b** has black fur, what is the probability that it will also have high cholesterol?

#3 $\frac{BL\ HC}{bl\ hc}$ × $\frac{bl\ hc}{bl\ hc}$

↓

$\frac{BL\ HC}{bl\ hc}$, $\frac{bl\ hc}{bl\ hc}$ — parental class (70% total) — 35%

$\frac{BL\ hc}{bl\ hc}$, $\frac{bl\ HC}{bl\ hc}$ — recomb. class (30%) — 15%

.35+.15 = .5 black mice

so, for all mice with black fur that have high cholesterol,

$\frac{.15}{.35+.15} = .30$ or 30%

2. Mutations in the white gene on the X chromosome of *Drosophila* give white eyes instead of the normal red. You have isolated both a dominant white-eyed mutation (designated **w-1**) and a recessive white-eyed mutation (designated **w-2**).

(**a** 6 pts.) A white-eyed male from the **w-1** line is crossed to a wild-type female. What color eyes will the female progeny from this cross have? What color eyes will the male progeny have?

$X^{w\text{-}1^D} Y \otimes X^{w\text{-}1^+} X^{w\text{-}1^+}$

♀ white $\{ X^{w\text{-}1^+} X^{w\text{-}1^D}, X^{w\text{-}1^+} X^{w\text{-}1^D} \}$ ♂ red $\{ X^{w\text{-}1^+} Y, X^{w\text{-}1^+} Y \}$

(**b** 6 pts.) One of the female progeny from the cross in part **a** is mated to a white-eyed male from the **w-2** line. What fraction of the white-eyed progeny from this cross will be female?

$X^{w\text{-}1^+ w\text{-}2^+} X^{w\text{-}1^D w\text{-}2^+} \otimes X^{w\text{-}1^+ w\text{-}2^R} Y$

↓

♀ red ⇐ $X^{w\text{-}1^+ w\text{-}2^+} X^{w\text{-}1^+ w\text{-}2^R}$ $X^{w\text{-}1^+ w\text{-}2^+} Y$ ⇒ red ♂

♀ white ⇐ $X^{w\text{-}1^D w\text{-}2^+} X^{w\text{-}1^+ w\text{-}2^R}$ $X^{w\text{-}1^D w\text{-}2^+} Y$ ⇒ white ♂

∴ 2 white progeny ⇒ ½ of white-eye progeny are ♀'s

Name: Solutions

(**c** 8 pts.) A white-eyed female from the cross described in part **b** is crossed to a wild-type male. Among 500 male progeny produced by this cross there are 5 that have red eyes. What is the distance between **w-1** and **w-2** in cM?

white-eyed ♀ of (b) $\Rightarrow \frac{X^{w\text{-}1^D\ w\text{-}2^+}}{X^{w\text{-}1^+\ w\text{-}2^R}} \Rightarrow \frac{1^D\ 2^+}{1^+\ 2^R}$

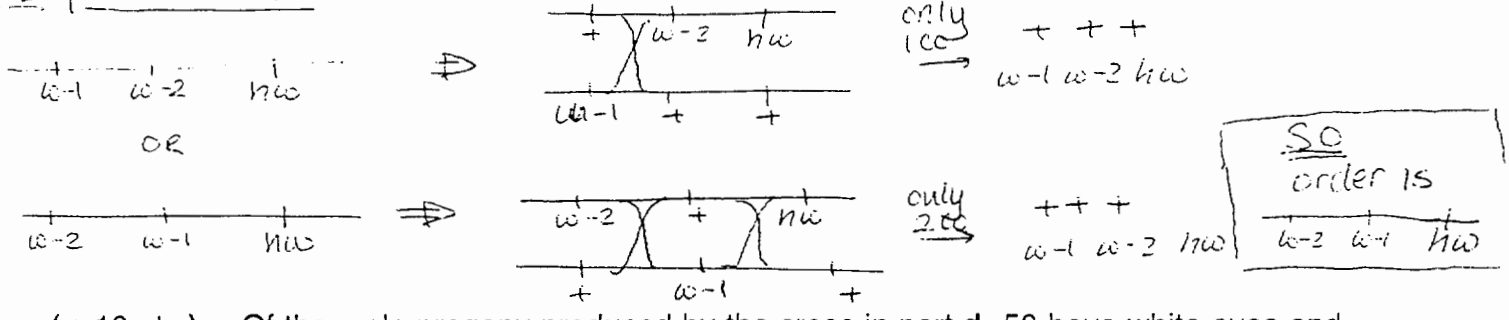
gametes
$1^D\ 2^R$ (recomb)
$1^D\ 2^+$
$1^+\ 2^R$
(Recomb) $1^+\ 2^+$ ⇒ red eyes
5.

$\therefore cM = \frac{2 \times 5}{500} \times 100 = 2\ cM$

(**d** 10 pts.) The gene for hairy-wings (**hw**) is also on the X chromosome and is linked to the white gene. A female fly from a line that is true-breeding for both hairy wings and the **w-2** allele is crossed to a male fly that has normal wings and the **w-1** allele. An F_1 female from this cross is mated to a wild-type male and a large number of male progeny from this cross are examined. Three of the male progeny have red eyes and all of these red-eyed males have hairy wings. Draw a genetic map showing the most likely order of **hw**, **w-1**, and **w-2**.

0 of red eyed wt wings. $X^{+++}Y$ ← rarest — double crossover

2 possible order



(**e** 10 pts.) Of the male progeny produced by the cross in part **d**, 50 have white eyes and hairy wings. Each of these male flies is mated to a wild-type female. 35 of these crosses produce female progeny with red eyes, and 15 of the crosses produce female progeny with white eyes. Give the distance between the genes for white-eyes and hairy-wings in cM.

recombinant → 15
parental → 35

$\frac{15}{50} \times 100 = 30\ cM.$

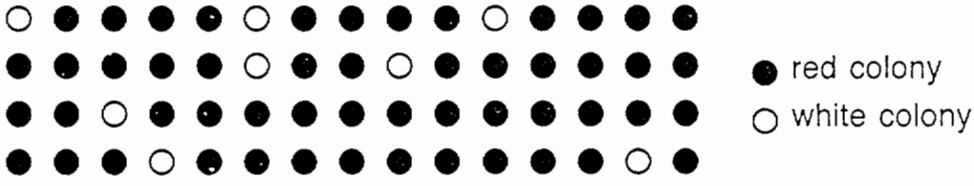
Name: SOLUTION SET

3. Mutations in several of the genes of the adenine biosynthetic pathway cause yeast cells to accumulate a red pigment, and therefore to form red colonies. You have isolated two new mutants that give red colonies designated **ade-1** and **ade-2**.

(a 6 pts.) You cross an **ade-1** strain to an **ade-2** strain and the resulting diploid forms white colonies. What can you now conclude about the nature of the **ade-1** and **ade-2** mutations?

ade-1 and ade-2 are recessive.
ade1- and ade2 complement each other - they are in different genes.

(b 8 pts.) The diploid from part **a** is sporulated and 15 tetrads are dissected. The plate with the colonies that grow up after tetrad dissection looks like this:



How many tetrads are there of each type?

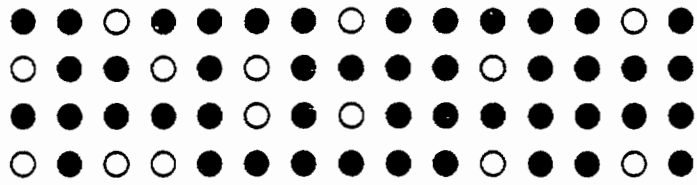
PD = 8 T = 6 NPD = 1

What is the distance between the **ade-1** and **ade-2** mutations in cM?

$$cM = \frac{T + 6NPD}{2\mathcal{L}} = \frac{6+6}{30}(100) - \frac{12}{30}(100) = 40\ cM$$

Name: SOLUTION SET

(c 8 pts.) You isolate a third mutant that forms red colonies designated **ade-3**. You cross **ade-1** to **ade-3** and dissect 15 tetrads. The tetrad dissection plate looks like this:



● red colony
○ white colony

How many tetrads are there of each type?

PD = 8 T = 0 NPD = 7

What can you say about the **ade-1** and **ade-3** mutations?

ade1 & ade3 are unlinked from each other.

ade1 & ade3 are on different chromosomes.

Part d omitted

7.03 Exam 2

Name: Solutions

Section: _____ TA: _____

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

There are six pages including this cover page

Please write your name on each page.

Please...

- Show your work and any assumptions that you make.
- Check your answers to make sure that they make sense.

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

Name: _____

1. You have made a mutation in the cI gene of phage λ by inserting four extra base pairs in this gene at a restriction enzyme site. This mutation is designated **cI-1** and gives clear plaques rather than the normal turbid plaques. You have another mutant λ strain called **s** which forms small plaques. You cross an **s** mutant with a **cI-1** mutant and examine 100 of the resulting plaques. The following types are found:

Plaque type	Number
large turbid	14
large clear	33
small turbid	37
small clear	16

(**a** 5 pts.) What is the distance between **cI-1** and **s** in map units?

$$\frac{14+16}{100} \times 100 = \boxed{30 \text{ m.u.}}$$

(**b** 5 pts.) You have isolated a deletion that removes 10% of the phage λ DNA but does not affect any of the normal functions of the phage (i.e. otherwise wild-type phage with the deletion make large turbid plaques). You cross a wild-type phage carrying the deletion to a double mutant phage carrying both the **cI-1** and **s** mutations. The following plaque types result from this cross:

Plaque type	Number
large turbid	88
large clear	4
small turbid	6
small clear	92

What is the measured distance between **cI-1** and **s** in map units? What does this result indicate about the position of the deletion on the genetic map with respect to **cI-1** and **s**?

$$\frac{4+6}{190} \times 100 = \boxed{5.3 \text{ m.u.}}$$

the deletion is between cI-1 and s

Name: _____

(**c** 10 pts.) Given the effect of the deletion on the distance between **cI-1** and **s**, what is the total genetic length of the phage in map units?

30 m.u. - 5.3 mu. = 24.7 m.u.

24.7 m.u. = 10% (total genetic length)

total genetic length = 247 m.u.

(**d** 5 pts.) Recall that the **cI-1** mutation was produced by an insertion of four base-pairs into the coding sequence of the cI gene. By treating **cI-1** mutant phage with proflavine you isolate a revertant that now makes turbid plaques. When this revertant is crossed to wild type, mostly phage with turbid plaques are produced but a few phage with clear plaques are seen. What kind of reversion mutation could explain this result? Be as specific as you can.

the revertant mutation is intragenic

and involves some sort of frameshift

e.g. a -1 deletion
or +2 addition

(**e** 10 pts.) You cross the revertant isolated in part **d** to an **s** mutant. Out of 1000 phage produced from this cross, 20 have clear plaques. Of these clear plaques, 15 are large and 5 are small. What is the distance between **cI-1** and the reversion mutation and what is their relative order with respect to **s**?

clear plaques are the result of a crossover between the original mutation and the reversion mutation, so the 20 phage that produce clear plaques are representative of the recombinant classes

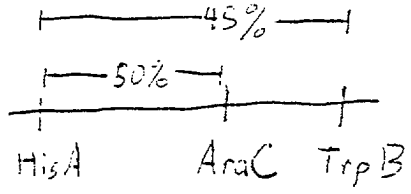
$\frac{20}{1000} \times 100 =$ 2 m.u.

Name: _____

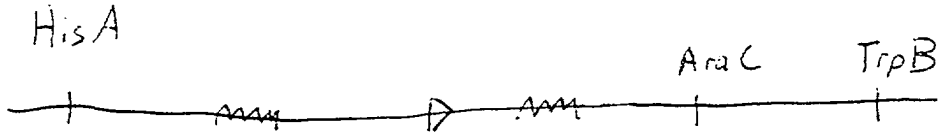
2. Consider a portion of the *E. coli* chromosome that carries the genetic markers hisA, trpB, and araC. Phage P1 is grown on a wild type host and the resulting phage are then used to infect a hisA$^-$ trpB$^-$ araC$^-$ recipient strain. His$^+$ transductants are selected and then tested for the presence of the other markers. The phenotypes of 100 His$^+$ transductants are given below.

Phenotype	Number
Trp$^+$ Ara$^+$	45
Trp$^-$ Ara$^+$	5
Trp$^-$ Ara$^-$	50

(**a** 10 pts.) Draw a map giving the relative order and the cotransductional distances between the markers hisA, trpB, and araC



(**b** 5 pts.) You have isolated an Hfr derivative of wild type *E. coli* that transfers the hisA marker early and trpB and araC markers late. Draw a diagram of the Hfr showing where F is inserted and its orientation.



(**c** 5 pts.) In a cotransduction mapping experiment, phage P1 is grown on the Hfr strain described in part **b**. These phage are then used to infect a trpB$^-$ araC$^-$ recipient strain. Would you expect the cotransduction frequency of Trp$^+$ and Ara$^+$ to be greater than or less than 50%? Why?

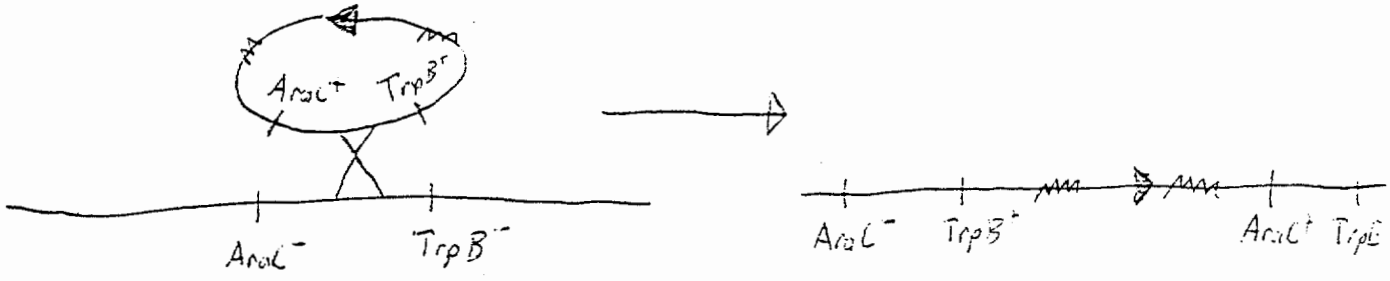
Greater than 50%. You know from part a) that AraC and TrpB are close together. You also know that the F plasmid did not integrate between AraC and TrpB.

Name: _____

(**d** 5 pts.) How would you select for an F' derived from the Hfr strain described in part **b**? (Be sure to give the genotypes of any strains that you would use).

mate to F^- Ara^- Trp^- Str^R and select for strains that are Ara^+, Trp^+, Str^R after a short mating.

(**e** 10 pts.) An F' carrying the trpB+ and araC+ markers is isolated from Hfr strain described in part **b**. You introduce this F' into a trpB− araC− strain and then isolate an Hfr that can transfer hisA+ efficiently. This Hfr transfers trpB+ early but transfers araC+ late. Draw a diagram of the recombination event that produced this Hfr.



Question 3

Part a omitted

Name: _____

(b 22 pts.) Are the lacZ product (ß-gal) and the lacY product (permease) constitutive (C) inducible (I) or uninducible (Un) in the following seven strains?

	ß-gal	permease
lac $O^+ Z^- Y^-$ / F' lac $O^c Z^+ Y^+$	C	C
lac $O^+ Z^+ Y^+$ / F' lac $O^c Z^- Y^-$	I	I
lac $I^+ Z^- Y^-$ / F' lac $I^s Z^+ Y^+$	Un	Un
lac $I^+ Z^+ Y^+$ / F' lac $I^s Z^- Y^-$	Un	Un
lac $I^{-d} Z^- Y^-$ / F' lac $I^s Z^+ Y^+$	C	C
lac $I^+ O^c Z^- Y^+$ / F' lac $I^s O^+ Z^+ Y^-$	Un	C
lac $I^{-d} O^c Z^- Y^+$ / F' lac $I^s O^+ Z^+ Y^-$	C	C

7.03 Exam 3

Name: Solutions

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.

Please...

- Show your work and any assumptions that you make.
- Check your answers to make sure that they make sense.

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

Question 1 omitted

2. The *HIS4* gene in yeast is regulated by the positive regulator *GCN4* and the negative regulator *GCD1*. The phenotypes of null mutants in these regulators on *HIS4* induction are:

gcn4$^-$	uninducible
gcd1$^-$	constitutive
gcn4$^-$ *gcd1*$^-$	uninducible

(a 8 pts.) Draw the epistasis pathway for *HIS4* regulation by these regulators.

gcd1 ⊣ gcn4 ⟶ His 4

Name: Solutions

Another positive regulator of *HIS4* is *GCN2*. The phenotypes of mutants are:

gcn2⁻	uninducible
gcn2⁻ gcd1⁻	constitutive

(b 7 pts.) Redraw the epistasis pathway adding *GCN2*.

gcn2 ⊣ gcD1 ⊣ gcn4 ⟶ his4

Gain of function mutations can be isolated in either *GCN2* (*GCN2^c*) or in *GCN4* (*GCN4^c*). Either mutation results in constitutive expression of *HIS4*.

(c 10 pts.) Give the phenotypes of the following double mutants and provide a one sentence explanation for your answer:

GCN2^c gcn4⁻ uninducible : gcn4 is epistatic to gcn2

gcn2⁻ GCN4^c constitutive : gcn4 is epistatic to gcn2

Finally, gain of function mutations in *GCD1* (*GCD1^un*) are found resulting in uninducibility of *HIS4*.

(d 10 pts.) Give the phenotypes of the following double mutants and provide a one sentence explanation for your answer.

GCD1^un GCN2^c uninducible : Gcd1 is epistatic, so it always represses gcn4

GCD1^un GCN4^c : constitutive : gcn4 is epistatic, so it always activates his4

Name: Solutions

3. (a 5 pts.) Consider an isolated island population. If the population is in Hardy-Weinberg equilibrium and 16% of the islanders exhibit a recessive blood antigen, what is the frequency of the allele for the antigen?

$q^2 = .16$

$q = .4$

(b 10 pts.) The blood antigen is originally nonexistent in the mainland population, but after extensive migration of islanders to the mainland half of the mainland population is finally composed of islanders. How many times more prevalent will the blood antigen be If there is no interbreeding between the original mainland population and the newly arrived islander population than if there is random interbreeding between the two populations?

No interbreeding

$f(aa) = .16 \cdot (.5)$ — double population

$= .08$

interbreeding:

$\frac{.4 + 0}{2} = q = .2$

$q^2 = .04 = f(aa)$

2 times

(c 5 pts.) You hypothesize that the relatively high frequency of the blood antigen in the island population is the result of a balanced polymorphism. If the selective advantage of the heterozygote is 10%, what selective disadvantage for the homozygotes with the blood antigen would be needed to explain the allele frequency in the island population?

$q = h/s$

$.4 = .1/s$

$s = .25$

(d 10 pts.) Consider a population in which first cousin matings occur at a frequency of 0.008 and second cousin matings occur at a frequency of 0.032 (assume that the remainder of matings are between unrelated individuals). Given that half of the individuals with a recessive trait have parents that are either first or second cousins, calculate the allele frequency for the trait.

f_1(1st cousin marriages) $= \frac{1}{16}$

f_2(2nd cousin marriages) $= 1/64$

$q^2 = f_1 q(.008) + f_2 q(.032)$

$q^2 = \frac{1}{16} q(.008) + \frac{1}{64} q(.032)$

$q = \frac{1}{16}(.008) + \frac{1}{64}(.032)$

$q = 1 \times 10^{-3}$

7.03 Final Exam

Name: Solutions

Section: _____ **TA:** _____

There are thirteen pages including this cover page

Please write your name on each page.

Question 1	25 points
Question 2	25 points
Question 3	25 points
Question 4	25 points
Question 5	25 points
Question 6	25 points
Question 7	25 points
Question 8	25 points

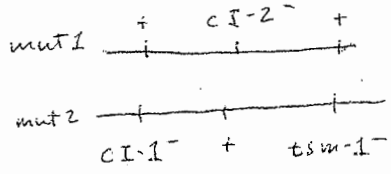
Note: Question #1 was purposely omitted.

Name: _____

2. You have isolated two mutations in the cI gene of phage λ; both mutants produce phage with clear plaques rather than turbid plaques. You have also isolated a mutation tsm-1, which produces temperature-sensitive phage that cannot form plaques at high temperature. Mapping experiments generate the map below (cI-1 and cI-2 are 0.5 mu apart and tsm-1 and cI-2 are 4 mu apart).

(a 20 pts.) You cross a cI-2 mutant to a cI-1 tsm-1 double mutant and examine 1000 plaques. In the table below give the number of plaques of each type that you would expect to find.

	Number
temperature-sensitive clear	~498
temperature-sensitive turbid	~2
temperature-resistant clear	~500
temperature-resistant turbid	~0



Phenotype	Genotype	#	
temp-sens clear	$cI\text{-}1^- cI\text{-}2^+ tsm\text{-}1^-$	$(\frac{99.5}{100})(\frac{96}{100})(1000)(\frac{1}{2}) = 477.6$	~498
	$cI\text{-}1^+ cI\text{-}2^- tsm\text{-}1^-$	$(\frac{99.5}{100})(\frac{4}{100})(1000)(\frac{1}{2}) = 19.9$	
	$cI\text{-}1^- cI\text{-}2^- tsm\text{-}1^-$	$(\frac{0.5}{100})(\frac{4}{100})(1000)(\frac{1}{2}) = 0.1$	
temp-sens turbid	$cI\text{-}1^+ cI\text{-}2^+ tsm\text{-}1^-$	$(\frac{0.5}{100})(\frac{96}{100})(1000)(\frac{1}{2}) = 2.4$	~2
temp-res clear	$cI\text{-}1^- cI\text{-}2^+ tsm\text{-}1^+$	$(\frac{99.5}{100})(\frac{4}{100})(1000)(\frac{1}{2}) = 19.9$	~500
	$cI\text{-}1^+ cI\text{-}2^- tsm\text{-}1^+$	$(\frac{95.5}{100})(\frac{96}{100})(1000)(\frac{1}{2}) = 477.6$	
	$cI\text{-}1^- cI\text{-}2^- tsm\text{-}1^+$	$(\frac{0.5}{100})(\frac{96}{100})(1000)(\frac{1}{2}) = 2.4$	
temp-res turbid	$cI\text{-}1^+ cI\text{-}2^+ tsm\text{-}1^+$	$(\frac{0.5}{100})(\frac{4}{100})(1000)(\frac{1}{2}) = 0.1$	~0

Name: _____

3. A recessive X-linked trait is present in the population at an allele frequency of 0.6. A man with the trait marries a woman who does not express the trait.

(a 5 pts.) What is the probability that their son will express the trait?

$p = 0.4$
$q = 0.6$

$X^-Y + X^+X^?$

$p(\text{son affected}) = p(\text{Mom is carrier}) \times p(\text{Mom passes allele})$

$= 2pq \times \frac{1}{2}$

$= pq = (0.4)(0.6) = \boxed{0.24}$

(b 5 pts.) What is the probability that their daughter will express the trait?

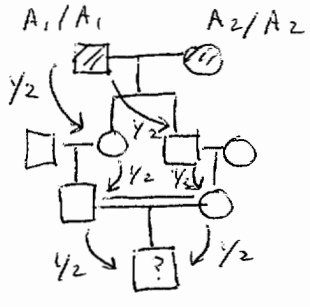
$p(\text{daughter affected}) = \boxed{0.24}$

Suppose that there are two different autosomal genes that are 40 cM apart and that recessive alleles in either gene will cause albinism. An albino man marries an albino woman but their children all appear normal.

(c 5 pts.) Give an explanation for this finding.

Nonallelic heterogeneity - that is, there are more than 1 gene involved that could cause albinism.

(d 10 pts.) If two of the grandchildren of the albino couple have a child together, what is the probability that this child will be albino?



$p(A_1/A_1) = (\frac{1}{2})^6 = \frac{1}{64}$

$p(A_2/A_2) = \frac{1}{64}$

$F = 2 \times \frac{1}{64} = \frac{1}{32}$

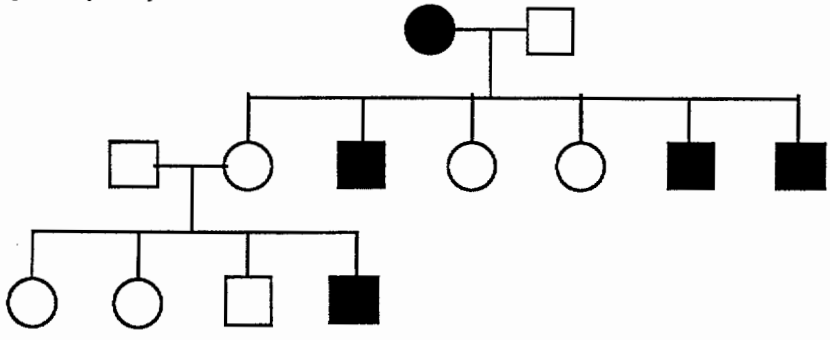
$p(\text{great-grandchild affected}) = F \times q = \frac{1}{32} \times 0.6 = \boxed{0.019}$

Name: _____

4. For each of the following pedigrees, propose the most likely mode of inheritance. Assume a rare trait with complete penetrance.

Part (a) was purposely omitted.

(b 6 pts.)



X-linked Recessive.

Note: Questions #5 + #6 were purposely omitted.

Name: _____

7. Bacterial cells can grown on soda by inducing a sodase. Mutants in four different genes are isolated which alter induction as shown:

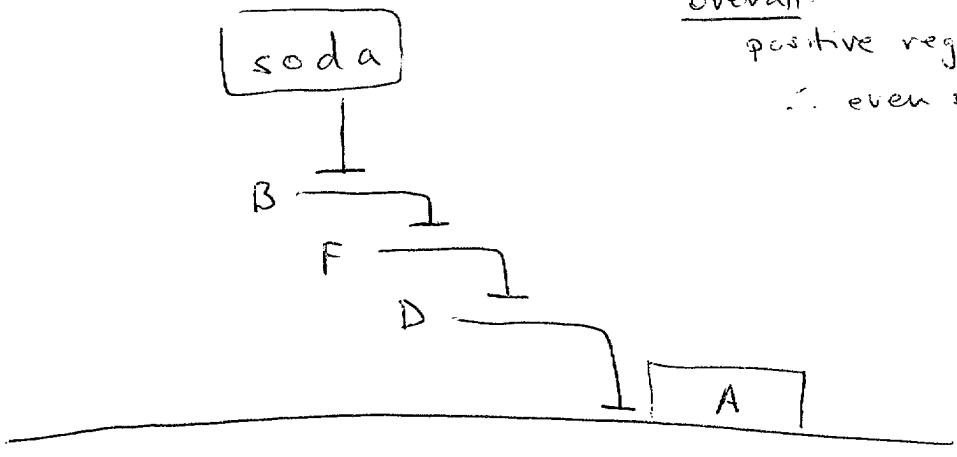
Strain	Induction of sodase	
	– soda	+ soda
wild type	–	+
sodA⁻	–	–
sodB⁻	+	+
sodD⁻	+	+
sodF⁻	–	–
A⁻B⁻	–	–
A⁻D⁻	–	–
B⁻F⁻	–	–
D⁻F⁻	+	+

(a 5 pts.) Which gene is most likely to be the structural gene for sodase?

A epistatic to B
A " " D
F " " B
D " " F

} A gene (b/c it's epistatic to all others)

(b 10 pts.) Draw a regulatory pathway showing the action of the other three genes on sodase expression.



overall:
positive regulation
∴ even # repressors

Name: _____

You find an unusual allele of sodB, called sodB*, which behaves as shown:

Strain	Induction of sodase	
	- soda	+ soda
sodB*	–	–

(c 5 pts.) Provide a brief explanation for the behavior of this mutation.

sod B^* is a super repressor (similar to $lacI^s$) that prevents soda from binding to it. There could be a molecular defect in the soda binding pocket. Therefore, sod B always represses.

(d 5 pts.) What would be the phenotype of a B^*D^- double mutant and why?

B^*D^- double mutant would be constitutive b/c D is epistatic to B.