Exams

Fall 1993

Name:_____

Recitation day_____, time_____,

7.03 Hour Exam 1

October 1, 1993

Write your name on all **five** pages.

Indicate your recitation section on this page

Write all answers on this handout only

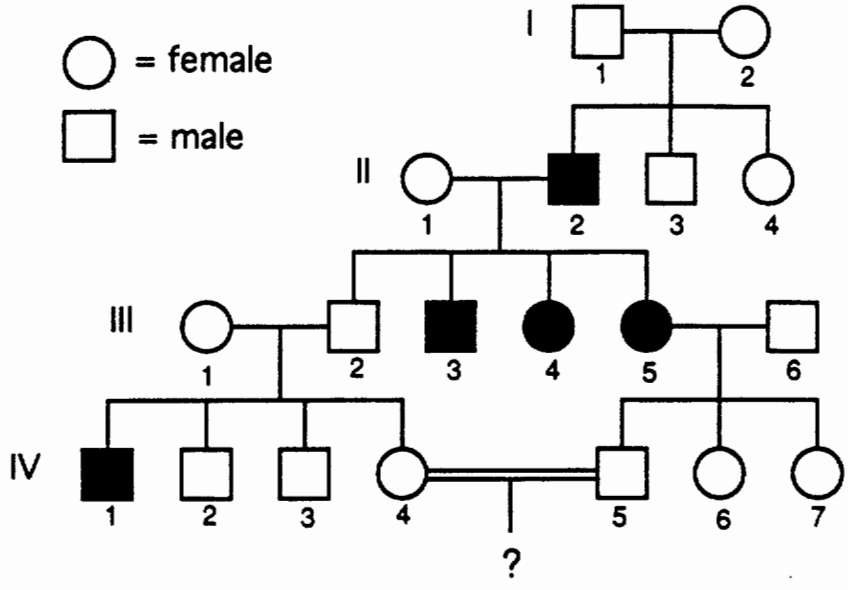
Exam begins at **11:05** and ends at **11:55**

Time will be announced when 5 and 1 minutes remain.

Problem 1	30 points
Problem 2	30 points
Problem 3	40 points
Total	100 points

Name:_____

1 In the following human pedigree individuals exhibiting a common inherited allergy to milk are shown by solid figures and unaffected individuals are shown by open figures.



(a 5pts.) Assuming complete penetrance, what is the probable mode of inheritance of the milk allergy?

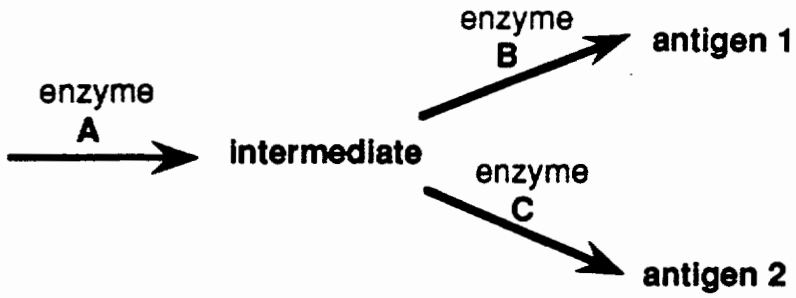
(b 10pts.) Give the genotypes of the following individuals using **+** to indicate the normal allele and **m** to indicate the allele specifying the milk allergy. In ambiguous cases indicate all possible genotypes.

	Genotype		Genotype
II-1		**III-2**	
II-2		**III-5**	
II-3			

(c 15pts.) If cousins **IV-4** and **IV-5** have a child together what is the probability that the child will have the milk allergy?

Name:_____

2 Consider two different antigen molecules produced on the blood cells of wild type mice according to the biosynthetic pathway below.



Mice homozygous for recessive alleles that block the production of enzyme A (genotype a/a) do not make either antigen 1 or antigen 2. Mice homozygous for recessive defects in enzyme B (genotype b/b) do not make antigen 1. Mice homozygous for recessive defects in enzyme C (genotype c/c) do not make antigen 2.

(a 8pts.) Two different true breeding strains of mice have been isolated that do not make either antigen 1 or antigen 2. When an individual from one strain is crossed with an individual from the other strain all of the F1 mice produce <u>both</u> antigens. Write out the genotypes for both strains. (Use A, B, and C to designate the wild type and a, b, and c to designate the defective alleles of the three enzymes).

(b 12pts.) Two of the F1 mice are crossed to one another. The possible phenotypes for the F2 progeny are shown below. What proportion of the F2 will be represented by each phenotype on average?

	<u>Fraction of F2</u>		<u>Fraction of F2</u>
antigen 1^+, antigen 2^+		antigen 1^+, antigen 2^-	
antigen 1^-, antigen 2^-		antigen 1^-, antigen 2^+	

Name:_____

(**2c** 10pts.) Among the F2 there will be mice of several different genotypes that are phenotypically antigen 1^- and antigen 2^-. Suppose you wanted to test whether a given F2 mouse that does not express either antigen is defective in production of enzyme A. What genotype would you choose for a mouse used for such a test cross of the F2 mouse? Describe the possible outcomes of this cross and how you would interpret them.

3 (**a** 5pts.) Suppose that in an isolated population there exists a very rare inherited anemia which is autosomal recessive. Given the frequency of the allele for the anemia as **q**, calculate the probability that a child will be born with the anemia assuming random mating. Express your answer as a function of **q**.

(**b** 5pts.) What is the probability as a function of **q** that a given individual in the population is a heterozygote? Use the approximation that is valid for small **q**.

Name:_____

(c 10pts.) In this population marriages between a niece and her biological uncle occur quite often. Given the niece in such a marriage is heterozygous for the allele for the anemia, what is the probability that her child will have the anemia? This is the joint probability that her husband (and uncle) is also heterozygous and that the child of two heterozygotes is homozygous.

(d 10pts.) Given that uncle-niece marriages occur at a frequency of **0.008**, use the answers derived above to calculate the frequency within the population with which children with the anemia are produced by uncle-niece marriages. Express your answer as a function of **q**.

(e 10pts.) If half of the children with the anemia come from uncle-niece marriages and half come from marriages with no obvious inbreeding, what is **q**? If helpful, you may use the approximation that the frequency of random marriages is about one.

EXAM #1 SOLUTIONS

Problem 1:

a) The mode of inheritance must be **autosomal recessive**. X-linked recessive is not a possibility, since male IV,5 is not affected.

b) II,1: m/+ III,2: m/+

II,2: m/m III,5: m/m

II,3: m/+ or +/+

c) The probability that the child has the milk allergy is the joint probability that both parents are heterozygous multiplied by the probability that the child will receive two copies of the mutant gene-one from each parent.

p(mother heterozygous)=2/3 (mother is either +/+ or m/+)

p(father heterozygous)=1

p(child will inherit both mutant copies)=1/4

total probability= 2/3(1)(1/4)=**1/6**

Problem 2:

a) One strain must be of genotype **aaBBCC**, while the other must be **AAbbcc**. This is the only way the F1 could produce both antigens(AaBbCc).

b) antigen 1+,antigen 2+ must have the genotype A-B-C-. The proportion will be 3/4*3/4*3/4 = **27/64** from the cross AaBbCcxAaBbCc.

antigen 1+,antigen 2- must have the genotype A-B-cc. The proportion will be 3/4*3/4*1/4 = **9/64**

antigen 1-,antigen 2+ must have the genotype A-bbC-. The proportion will be 3/4*1/4*3/4 = **9/64**.

antigen 1-,antigen 2- will comprise the rest of the population, or 1-(27/64+9/64+9/64) = **19/64**.

c) The possible genotypes that would give antigen 1-,antigen 2- phenotypes are:

A-bbcc

aaB-C-

aabbC-

aaB-cc

aabbcc In order to distinguish the genotypes that are deficient for enzyme A, the proper testcross would be to an **aaBBCC** mouse. Any mouse that is aa will produce all antigen 1-,antigen 2- offspring when crossed to the above testcross mouse. Any mouse that has at least one good copy of enzyme A will produce antigen 1+,antigen2+ offspring Many students chose AAbbcc as the genotype for their testcross. This will not allow you to distinguish the aabbcc mice from A-bbcc mice. Using this testcross, one would conclude the

aabbcc mouse was not deficient in enzyme A, since it produces all antigen 1-,antigen2- offspring! Other students chose a mouse that was heterozygous for A (Aa) for their testcross. This would not allow you to draw a distinct conclusion between aa and Aa mice. In theory, if the mouse to be tested was aa, 1/2 of the progeny from the testcross would be antigen 1-,antigen 2- . If the mouse to be tested was Aa, 1/4 of the progeny would be antigen 1-, antigen2-. Given that mice do not have large litters, it may be very difficult to distinguish between these two possibilities. Finally, some students outlined a series of crosses for their answer. The hallmark of a testcross is that it is only one cross that will allow you to determine the genotype in question!

Problem 3

a Random mating means the population is in Hardy-Weinberg equilibrium. Thus the frequency of children born with the disease is simply $\mathbf{q^2}$.

b With a population in H-W equilibrium the frequency of heterozygotes is simply 2pq. Since q is small p is about 1, so the frequency of heterozygotes is **2q**.

c Since we are told that the niece is a heterozygote we do not use p or q at all in this part of the problem. If the niece is a heterozygote the chance that the uncle's sibling has the disease allele is 1/2. If the uncle's sibling is a heterozygote the chance the uncle has the disease allele is 1/2. If both the uncle and the niece are heterozygous for the disease allele the chance that they will have an affected child is 1/4. Thus p(affected child) = (1/2)(1/2)(1/4) = **1/16**.

d The chance that any woman is a heterozygote is 2q (see part b). The chance that this woman marries her uncle is .008. The chance that this uncle/niece couple have an affected child is 1/16 (see above). Thus the frequency within the population with which children with the anemia are produced by uncle-niece marriages is: (2q)(.008)(1/16) = **q/1000**.

e If half the affected children come from uncle-niece marriages and half come from marriages with no inbreeding we simply set the answer to part d equal to the answer in part a. $q^2 = q/1000$. Solving for q we get **q = 1/1000**.

Name:_____

Recitation day_____, time_____,

7.03 Hour Exam 2

October 20, 1993

Write your name on all **four** pages.

Indicate your recitation section on this page

Write all answers on this handout only

Exam begins at **11:05** and ends at **11:55**

Time will be announced when 5 and 1 minutes remain.

Problem 1	30 points
Problem 2	40 points
Problem 3	30 points
Total	100 points

Name:_____

1 The two hypothetical autosomal human genes **xey** and **stm** are 10 map units apart. Dominant alleles of **xye** are completely penetrant and cause crossed eyes. Dominant alleles of **stm** are completely penetrant and cause small thumbs. A cross-eyed, small thumbed woman marries a normal man and they have four children. Two of the children are cross-eyed and two of the children have small thumbs.

(a 10 pts) Would you expect either of the woman's parents to be cross-eyed and have small thumbs?

(b 10 pts) The woman is pregnant with a fifth child. What is the probability that this child will be cross-eyed and have small thumbs? (Hint — don't use Bayes Theorem for this problem.)

(c 10 pts) Oocytes, are the diploid cells that by meiosis, give rise to the gamete egg cells in a woman. What fraction of the oocytes in the woman in this question, will have a crossover event occur between the **xey** and **stm** genes during meiosis?

Name:_____

2 Consider two different yeast genes that we will call RED1 and RED2. Recessive mutations in either gene cause the yeast colonies to turn red rather than the normal white color. A haploid **red1⁻** mutant is crossed to a haploid **red2⁻** mutant. The resulting white diploid is sporulated and tetrads are dissected. There are three types of tetrads with respect to colony color:

Type I	Type II	TypeIII
2 red: 2 white	3 red: 1 white	4 red

(a 5 pts) Classify each of the types as either PD, NPD or T tetrads.

Type I = Type II = Type III =

(b 10 pts) Of 100 tetrads dissected 6 are of type I, 34 are of type II, and 60 are of type III. What is the measured genetic map distance between **RED1** and **RED2**?

(c 10 pts) The **TRP1** gene is completely linked to its centromere. When a **trp1⁻** mutant is crossed to a **red1⁻** mutant and 100 tetrads are dissected, no T type tetrads are found. How many T type tetrads would you expect to find if a **trp1⁻** mutant is crossed to a **red2⁻** mutant and 100 tetrads are dissected?

(d 15 pts) A mutation in a new red gene, **RED3**, is discovered. When a **red1⁻** mutant is crossed to a **red3⁻** mutant, tetrads of the three types described above are seen. For this cross, of 100 tetrads dissected 15 are of type I, 67 are of type II, and 18 are of type III. If a **red3⁻** mutant were crossed to a **trp1⁻** mutant, how many tetrads out of 100 would you expect to have 2 red, Trp^+ spores and 2 white, Trp^- spores?

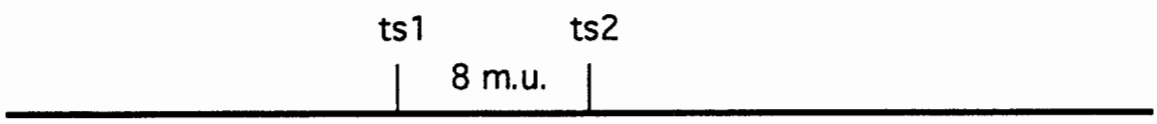
Name:_____

3 Consider a phage for which there are two temperature sensitive mutations, **ts1**$^-$ and **ts2**$^-$. Phage with either of these mutations will form plaques at 30° but not at 40° (you should assume that the double mutant **ts1**$^-$, **ts2**$^-$ will also form plaques at 30° but not at 40°). To perform a recombination test between these mutations **ts1**$^-$, **ts2**$^+$ and **ts1**$^+$, **ts2**$^-$ phage are infected into host bacteria so that each bacterial cell gets multiple copies of both phage. The infected cells are grown at 30° to allow growth of the mutant phage and to allow recombination between phage.

(a 10 pts) Given that the distance between **ts1** and **ts2** is 8 m.u., what fraction of the phage from this cross will be wild type? In other words, what fraction of the phage will make plaques when plated at 40°?

(b 10 pts) A new mutation that causes mottled plaques is isolated. The allele that causes the mottled phenotype is designated **mot**$^-$ whereas the wild type allele is designated **mot**$^+$. A **ts1**$^-$, **mot**$^-$ phage is crossed to a wild type (**ts1**$^+$, **mot**$^+$) phage. The phage resulting from this cross are plated at 40° and 4% make mottled plaques. What is the distance between **ts1** and **mot** in map units?

(c 10 pts.) A **ts1**$^-$, **ts2**$^+$, **mot**$^+$ phage is crossed to a **ts1**$^+$, **ts2**$^-$, **mot**$^-$ phage. From this cross, phage that can grow at 40° are isolated and it is found that 96% of these phage have mottled plaques. On the map below show the position of the **mot** locus. Be sure to indicate the distance to either **ts1** or **ts2** in map units.



Answers to 7.03 Exam #2

1 a) No. You would expect that most offspring come from non-recombinant gametes. Since the children are small thumbed, normal eyed or normal thumbed, cross eyed these are most likely the non-recombinant genotypes. Therefore the mother's genotype is xye +/+ smt, so one grandparent was only cross eyed and the other only small thumbed.

1 b) 5%. From the definition of map units we know there is a 10% chance of being a recombinant gamete for xye and stm. Remeber that half of those recombinants will be wt and half will be stm **and** xye. So there is only a 5% chance the child will be double mutant.

1 c) 20%. From the definition of map units we know that 10% of the gametes are recombinant. There must be crossovers in 20% of the oocytes to yield 10% recombinant gametes.

20/100 oocytes with a cross over --> 40/400 recombinant chromosomes-->
-->10% recombinant gametes.

2 a) Type 1 = NPD Type 2 = TT Type 3 = PD

2 b) **35 m.u.** Just apply the tetrad formula for linked genes.
35 m.u. = 100[34 + 6(6)/2(100)]

2 c) 34 TT expected. The fact that the trp1- and red1- cross yielded no tetratypes means that the two genes are unlinked, and both are completely linked to their respective centromeres. For the trp1-, red2- cross we know the markers are unlinked (because red1 is linked to red 2 and red1 and trp1 are unlinked). Any crossover event that gives a tetratype tetrad for markers red1 and red2 (the situation in problem 2b) will lead to a tetratype tetrad between markers red2 and trp1. So the answer is you'd expect the same number of tetratypes as in 2b, **34** tetratypes.

2 d) expect 17 or 16.6. The data in the problem suggests the two marker s are unlinked. So you expect a 1:4:1 ratio of PD:TT:NPD. Thus 1/6 of the tetrads should be of PD (2 red, trp+ 2 white trp-). 1/6(100)=16.6 or 17.

3 a) 4%. 8 m.u.= 100(# recombinant phage)/total
The number of recombinant phage is 8%. Remember only half of the recombinants are wt the other half are ts1-,ts2-. So the fraction of wt will be .08(1/2)=.04

3b) 4 m.u. Of the phage growing at 40°C (ts1+) 4% of them are recombinant (mot-). mu = # recombinant phage out of the total. We are missing half the recombinant phage because they are ts1-,mot+ and can not grow at 40°C. However we are also missing half the total because one of the parentals ts1-,mot- also can not grow at 40°C. So map units is simply .04(100).

3c)
The rare class is ts1+, ts2+, mot+, they represent only 4% of the plaques growing on the plate. This must be the result of a double crossover event. Therefore ts1 is between mot and ts2.

Name:_____

Recitation day_____, time_____, TA_____

7.03 Hour Exam 3

November 10, 1993

Write your name on all **six** pages.

Indicate your recitation section on this page.

Do **all** work on this handout only.

Exam begins at **11:05** and ends at **11:55.**

Time will be announced when 5 and 1 minutes remain.

Problem 1	35 points
Problem 2	35 points
Problem 3	30 points
Total	100 points

Name:_____

1 Some mutations of the **Lac** operon are defined as follows:

I^s : An allele of the repressor that is unable to bind inducer molecule but will still bind to operator DNA.

I^{-d} : A dominant repressor mutation that does not bind the operator and prevents wild-type repressor from binding operator.

O^c : An operator mutation that will not bind repressor.

P^- : A promoter mutation that will not bind RNA polymerase.

Z^- : An allele of the lacZ gene that does not make active ß-galactosidase enzyme.

Y^- : An allele of the lac permease gene that does not make active permease.

The levels of ß-galactosidase activity in a wild type strain with or without inducer are shown below

	+IPTG	-IPTG
$I^+ P^+ O^+ Z^+$	high	low

Fill in this table indicating either high or low levels of ß-galactosidase for each of the following strains with or without inducer.

	+IPTG	-IPTG
(a 5pts) $I^s P^+ O^c Z^-/F'I^+ P^+ O^+ Z^+$		
(b 5pts) $I^s P^+ O^+ Z^-/F'I^+ P^+ O^c Z^+$		
(c 5pts) $I^+ P^+ O^+ Z^-/F'I^+ P^- O^c Z^+$		

Name:_____

Starting with a strain that is **$I^+ P^+ O^+ Z^- Y^+ / F' I^+ P^+ O^+ Z^+ Y^-$** you isolate two different mutants that <u>constitutively</u> express ß-galactosidase activity. For each mutant you assay both ß-galactosidase activity and permease activity with or without inducer.

	ß-galactosidase activity	
	<u>+IPTG</u>	<u>-IPTG</u>
Mutant 1	high	high
Mutant 2	high	high

	Permease activity	
	<u>+IPTG</u>	<u>-IPTG</u>
Mutant 1	high	low
Mutant 2	high	high

Assuming that each mutant alters only one element of the **lac** operon, figure out the genotypes of Mutant 1 and Mutant 2. If more than one genotype is possible give all of the possibilities. You need only consider the types of mutant alleles given at the begining of this problem. Undesignated elements in your written genotypes will be assumed to be wild type.

(d 10pts) Mutant 1 = **/F'**

(e 10pts) Mutant 2 = **/F'**

Name:_____

2 You have two true-breeding varieties of elongated pumpkins (strain#1 and strain#2). Wild-type pumpkins are round. When crossed to wild type, strain#1 and strain#2 produce round pumpkins.

(**a** 10pts) You cross strain#1 with strain#2 and find that all F1 pumpkins are elongated, and after self-fertilization you find that all F2 pumpkins are elongated.

i. What are the genotypes and phenotypes of the parents, the F1 and F2 generation.

ii. Is the phenotype of strain#1 and strain#2 dominant or recessive to the phenotype of the wild-type strain?

iii. Circle the concept(s) that characterize(s) the observed relationship between strain#1 and strain#2 best:

complementation epistasis redundancy

suppression enhancement

Name:_____

(**b** 25pts) You discover a new true-breeding variety of round pumpkin (strain#3) and make the following observations:
-When **strain#3** is crossed to **wild type**, the F1 progeny pumpkins are round, and after self-fertilization, 3/16 of the F2 pumpkins are elongated and all other pumpkins are round.
-When **strain#3** is crossed to **strain#1**, the F1 pumpkins are elongated, and after self-fertilization, 1/4 of the F2 pumpkins are round and 3/4 are elongated.

i. Give the genotypes and phenotypes of the parents, the F1 and F2 generation of the cross between strain#3 and wild type.

ii. Give the genotypes and phenotypes of the parents, the F1 and F2 generation of the cross between strain#3 and strain#1.

iii. Is the phenotype of strain#3 dominant or recessive to that of strain#1?

iv. Circle the concept(s) that characterize(s) the observed relationship between strain#1 and strain#3 best:

complementation epistasis redundancy

suppression enhancement

Name:_____

3 Consider three genes in *E. coli* **A**, **B**, and **C** whose order and exact spacing are not known. Transducing phage P1 is grown on an **A⁺ B⁺ C⁺** host and this phage lysate is used to infect an **A⁻ B⁻ C⁻** recipient. **A⁺** transductants are selected and the frequencies of cotransduction of the other markers are shown below:

A⁺ B⁺ C⁺	80%
A⁺ B⁺ C⁻	4%
A⁺ B⁻ C⁺	15%
A⁺ B⁻ C⁻	0.6%

(a 10pts) Of the genetic intervals **A–B** and **A–C** which is larger? Give cotransduction frequencies for B and C.

(b 15pts) An **F'** factor that carries the wild-type copies of all three genes **A⁺**, **B⁺**, and **C⁺** is mated into an **F⁻ A⁻ B⁻ C⁻** recipient. From this strain an Hfr is isolated that transfers **A⁺** and **B⁺** early and **C⁺** very late. Draw the structure of the **F'** (not the Hfr) showing the order of the **A**, **B**, and **C** genes and the orientation of the origin of transfer.

(c 5pts) In cloning of the **A** gene a new gene **D** is discovered 10 kilobases away. The transducing phage P1 packages random 50 kilobase segments of the chromosomal DNA per phage. Which frequency is greater: The frequency that **A** and **D** are packaged into the same phage or the cotransduction frequency of **A** and **D** under **A⁺** selection? Explain briefly.

Solutions to Exam 3

mean = 64

Problem 1

a) Since the super repressor (I^s), a trans-acting factor, is present there will be no lacZ expressed under any conditions. O^c has no effect since it is cis-acting (on Z^-). Thus the answer is **low low**

b) Now O^c is in cis with Z^+ so this gene is expressed constitutively: **high high**

c) Since there is no promoter (P^-), a cis acting element, to drive any transcription. Thus no lacZ is expressed under any conditions: **low low**

d) The only way to express Z constitutively and have Y under normal regulation is to alter a cis-acting element: **$I^+P^+O^+Z^-Y^+/F'$ $I^+P^+O^cZ^+Y^-$**

e) The only way to have constitutive expression of both Z and Y with only one change is to have I^{-d} present. It can be on either the chromosome or the F' since I is trans-acting: **$I^{-d}P^+O^+Z^-Y^+/F'$ $I^+P^+O^+Z^+Y^-$ or $I^+P^+O^+Z^-Y^+/F'$ $I^{-d}P^+O^+Z^+Y^-$**

A few students changed the same element on both the F' and the chromosome. This would work if they both had O^c or I^-. Getting two mutations at once is very unlikely.

Problem 2a)

i (6pts) The cross of each elongated mutant to the round wild-type yields all round pumpkins. This tells you that both strains carry recessive mutations. When these two strains are crossed to each other the F1 are all elongated. Since both mutations are recessive and the F1 has the mutant phenotype these two mutations must be in the same gene!!! This is in fact a complementation test. The two mutations fail to complement each other and thus are in the same gene. Note that there is only one gene involved here. Always go for the simplest model that fits all the data because we really are not trying to trick you!

Pumpkin	Genotype	Phenotype
Wild type	**AA**	**round**
Strain 1	**a1a1**	**elongated**
Strain 2	**a2a2**	**elongated**
F1 (1x2)	**a1a2**	**elongated**
F2	**a1a2, a1a1, a2a2**	**elongated**

ii (2pts) Both strains are **recessive** to wild-type. (See above)

iii (2pts) **Complementation** (See above)

Problem 2b)

i.(10 pts.) The fact that 3/16 of the progeny in the F2 generation are elongated tells us that there are two mutant genes segregating independently. Therefore, strain 3 must contain two mutations in two genes. Since it is a true-breeding strain, it must be homozygous for these two mutations. If we designate the two genes as A and B, then the parental, F1, and F2 crosses are as follows:

Pumpkin	Genotype	Phenotype
wild type	**AABB**	**round**
strain 3	**aabb**	**round**
F1 (3xWT)	**AaBb**	**round**
F2	**9 A_B_**	**round**
	3 aaB_	**elongated**
	3 A_bb	**round**
	1 aabb	**round**

Therefore, strain 3 contains a mutation (designated as "a") that causes elongated pumpkins. However, strain 3 also contains a mutation that either suppresses, or is epistatic to, the "a" mutation and causes round pumpkins. This mutation (designated as "b") only suppresses, or is epistatic, when it is homozygous. That is the reason we see 3/16 of the progeny in the F2 are elongated, since they are homozygous for aa, but are not homozygous for bb.

ii. (10 pts) Since in the F2 generation we see a 3:1 ratio, there must be only one gene segregating that is different between strain 3 and strain 1. We know from above that strain 3 carries a mutation that causes elongated pumkins. We also know that strain 1 carries a mutation for elongated pumpkins, but does not carry a suppressor or epistatic mutation. Therefore, we can conclude that strain 3 and strain 1 carry mutations in the same gene which contribute to the elongated pumpkin phenotype. They differ in the suppressor, or epistatic gene:

Pumpkin	Genotype	Phenotype
strain 1	**aaBB**	**elongated**
strain 3	**aabb**	**round**
F1 (1x3)	**aaBb**	**elongated**
F2	**1 aaBB**	**elongated**
	2 aaBb	**elongated**
	1 aabb	**round**

Some students tried to explain the 3:1 ratio as actually a 12:4 ratio resulting from a dominant mutation. This model is inconsistent with the fact that strain 1, when crossed to wild type, gives all round pumpkins. Therefore, the mutation in strain 1 must be recessive (see part a,ii.).

iii. (3pts.) When strain 3 is crossed to strain 1 all the resulting progeny are elongated. The phenotype of strain 3 is therefor **recessive** to that of strain 1.

iv. (2pts.) As stated above, the results show that strain 3 contains a mutation that **suppresses,** or is **epistatic** to, the mutation that causes elongated pumpkins. In addition, these results tell us that strain 1 and strain 3 carry mutations in the same gene. Therefore, the mutations do not **complement** each other. Credit was given for any of the correct answers, but no credit was given if an incorrect answer was circled.

Problem 3:

a) Cotransduction frequencies for A-B: 80% + 4% = **84%**
Cotransduction frequencies for A-C: 80% + 15% = **95%**

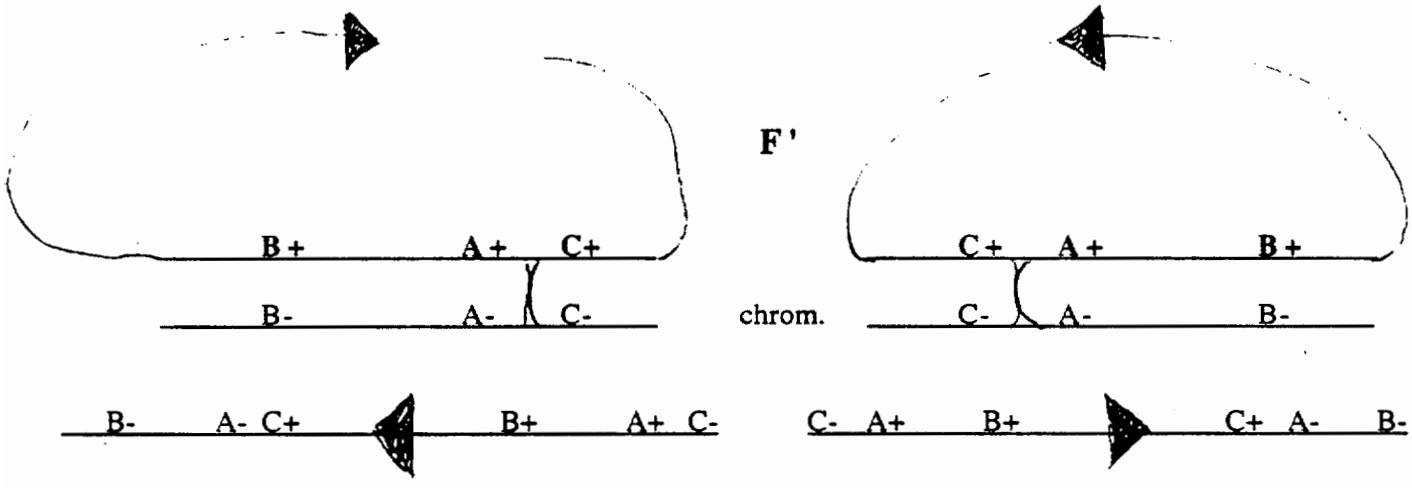
The closer two markers are to each other the higher the co-transduction frequency. **Thus the A-B interval is the larger of the two.**

b) Many students misread this question. The question did not ask for the F' derived from the Hfr strain. It asked for the F' that integrated to become an Hfr strain. The order of the genes was determined from the information in part a).
The map derived from the data in part a was as follows:

A crossover outside both B and C	A+B+C+	80%
A crossover outside B and in interval 2	A+B+C-	4%
A crossover outside C and in interval 1	A+B-C+	15%
A crossover in interval 1 and interval 2	A+B-C-	0.6%

Note that other combinations are not possible since they result in A- (we selected A+).

The crossover event to generate an Hfr that transfers A+ and B+ early and C+ late:



c) Two answers were accepted:

The frequency that A and D are both packaged into the same phage, given that A is packaged, is greater than the co-transduction frequency of these two markers since this requires both co-packaging and an appropriate recombination event.

The frequency that A and D are packaged into the same phage is actually quite low if you do not assume that a phage has either marker. Since you select for A+ transductants you might expect that since D is only 10kb away it will be co-transduced at a reasonable frequency. With this explanation it is possible to imagine that the co-transduction frequency of A and D might be greater than the frequency with which they are packaged into the same phage.
No points were awarded if there was no explanation to justify the answer.

Note - Exam #4 omitted

Name_____

T.A._____

7.03 FINAL EXAM

December 14, 1993

WRITE YOUR NAME ON ALL 14 PAGES.
INDICATE YOUR RECITATION SECTION ON THIS PAGE.
WRITE ALL ANSWERS ON THIS HANDOUT ONLY.

The exam begins at **1:30pm** and ends at **4:30pm.**
Time will be announced when **15** minutes and **3** minutes remain.

Advice: if you get stuck on one question, go on to the next one!
Three pages of scratch paper are at the end.

Problem 1	30	points
Problem 2	25	points
Problem 3	20	points
Problem 4	15	points
Problem 5	12	points
Problem 6	12	points
Problem 7	12	points
Problem 8	34	points
Problem 9	40	points
Total	200	points

Name_____

1 Consider an autosomal allele in rabbits that causes extreme nearsightedness when homozygous and that causes partial nearsightedness when heterozygous. Two populations of rabbits are tested for nearsightedness and the frequencies within these populations of rabbits with vision problems are given below.

	Extremely nearsighted	Partially nearsighted
Population A	0.18	0.24
Population B	0.09	0.42

(a 5pts) Is population A in Hardy-Weinberg equilibrium? Yes (No)
Circle the correct answer.

Is population B in Hardy-Weinberg equilibrium? (Yes) No
Circle the correct answer.

(b 5pts) Rabbits from the two populations are mixed in equal numbers. After one generation of random mating within this new population what will the frequencies of extremely nearsighted and partially nearsighted rabbits be?

$q_A = 0.18 + \frac{1}{2} \cdot 0.24 = 0.3$

$q_B = \sqrt{0.09} = 0.3$

$q_{new} = \frac{0.3+0.3}{2} = 0.3$

$P(\text{extremely nearsighted}) = 0.3^2 = 0.09$

$P(\text{partially nearsighted}) = 2 \times 0.7 \times 0.3 = 0.42$

Extremely nearsighted	Partially nearsighted
0.09	0.42

Question 1 continued

A population of rabbits is in Hardy-Weinberg equilibrium for the nearsightedness allele until a road is built through their territory putting the nearsighted rabbits in grave danger. We will consider two possible modes of selection now imposed on the rabbit population.

Mode 1: Extremely nearsighted rabbits are always killed by cars before they reproduce. Partially nearsighted and normal rabbits are essentially never hit by cars.

Mode 2: Both extremely nearsighted and partially nearsighted rabbits have a 20% chance of being killed by a car before they reproduce. Rabbits with normal eyesight are essentially never hit by cars.

(c 10pts) If the frequency of the nearsightedness allele is 0.1, which mode of selection will drive down the allele frequency faster in the first few generations after the road is built?

mode 1 : loss = sq^2 for $s=1$, $q=.1$ $\Rightarrow$ 0.01

mode 2 : loss = $sq^2 + \frac{1}{2}s(2pq)$ for $s=.2$, $q=.1$ $\Rightarrow$ 0.02

mode 2

(d 10pts) If the frequency of the nearsightedness allele is 0.5, which mode of selection will drive down the allele frequency faster in the first few generations after the road is built?

mode 1 loss = sq^2 for $s=1$, $q=.5$ $\Rightarrow$ 0.25

mode 2 loss = $sq^2 + \frac{1}{2}s(2pq)$ for $s=.2$, $q=.5$ $\Rightarrow$ 0.1

mode 1

Name_____

2 Consider two temperature sensitive mutations in yeast, **tsm1** and **tsm2**. When a **tsm1** strain is crossed to a **tsm2** strain the diploids are <u>not</u> temperature sensitive. When these diploids are sporulated, tetrads of three types are found. In the table below ts^- means temperature sensitive and ts^+ means wild type growth.

Type I	Type II	Type III
ts^+	ts^+	ts^-
ts^+	ts^-	ts^-
ts^-	ts^-	ts^-
ts^-	ts^-	ts^-
NPD	T	PD

(a 7pts) From 50 tetrads; 2 are type I, 12 are type II and 36 are type III. What is the distance in map units between **tsm1** and **tsm2**?

$$100 \times \frac{6 \times 2 + 12}{2 \times 50} = 24 \text{ mu}$$

(b 8pts) If the strains from this cross were not ordered into tetrads, the map distance between the two mutations could still be calculated. Using the standard definition of map units and the fraction of the 200 strains from the cross that are ts^+, calculate the distance between **tsm1** and **tsm2**.

for every ts^+, we assume another hidden recombinant in the ts^-'s

$$\frac{2 \cdot (2 \cdot 2 + 1 \cdot 12)}{4 \cdot 50} \times 100 = 16 \text{mu}$$

(c 5pts) Say you need a strain that has both **tsm1** and **tsm2** mutations. Without any further testing, which of the strains from the tetrad analysis would you pick?

take the ts- spores from NPD tetrads

(d 5pts) Four strains from one of the type II tetrads have the following properties:

Strain 1: Mating type α, ts^+
Strain 2: Mating type α, ts^-
Strain 3: Mating type a, ts^-
Strain 4: Mating type a, ts^-

Strain 2 is crossed to strain 3 and the resulting diploid is ts^+. Which of these four strains has both the **tsm1** and **tsm2** mutations?

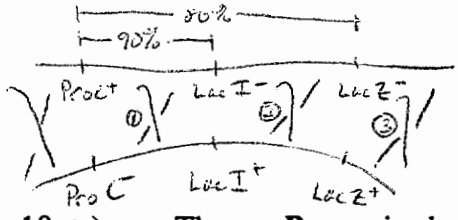
Strain 4

Name_____

3 (a 10pts) The **proC** gene lies very close to the **lac** operon on the *E. coli* chromosome. **proC** shows 90% cotransduction with a **lacI⁻** nonsense mutation and 80% cotransduction with a **lacZ⁻** nonsense mutation. In a transduction experiment, phage are grown on a **proC⁺, lacI⁻, lacZ⁻** host. The resulting transducing phage are used to infect a **proC⁻, lacI⁺, lacZ⁺** recipient and **proC⁺** transductants are selected. Three phenotypic classes are found among the **proC⁺** transductants: regulated expression of β-galactosidase, constitutive expression of β-galactosidase, and no β-galactosidase expression. Give below the expected frequencies of each of the three phenotypic classes (assume no quadruple crossovers).

If 2nd clo ot:

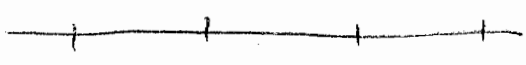
Regulated expression	Constitutive expression	No expression
① 10%	② 10%	③ 80%



(b 10pts) The **proB** gene is also closely linked to the **lac** operon. In a transduction experiment, phage are grown on a **proB⁺, lacI⁻, lacZ⁻** host and are used to infect a **proB⁻, lacI⁺, lacZ⁺** recipient. Of the **proB⁺** transductants, most show either regulated expression or no expression of β-galactosidase. Transductants that show constitutive β-galactosidase expression are extremely rare. Draw a map of the **lac** region showing the relative order of the **proC, proB, lacI** and **lacZ** genes (don't worry about distances).

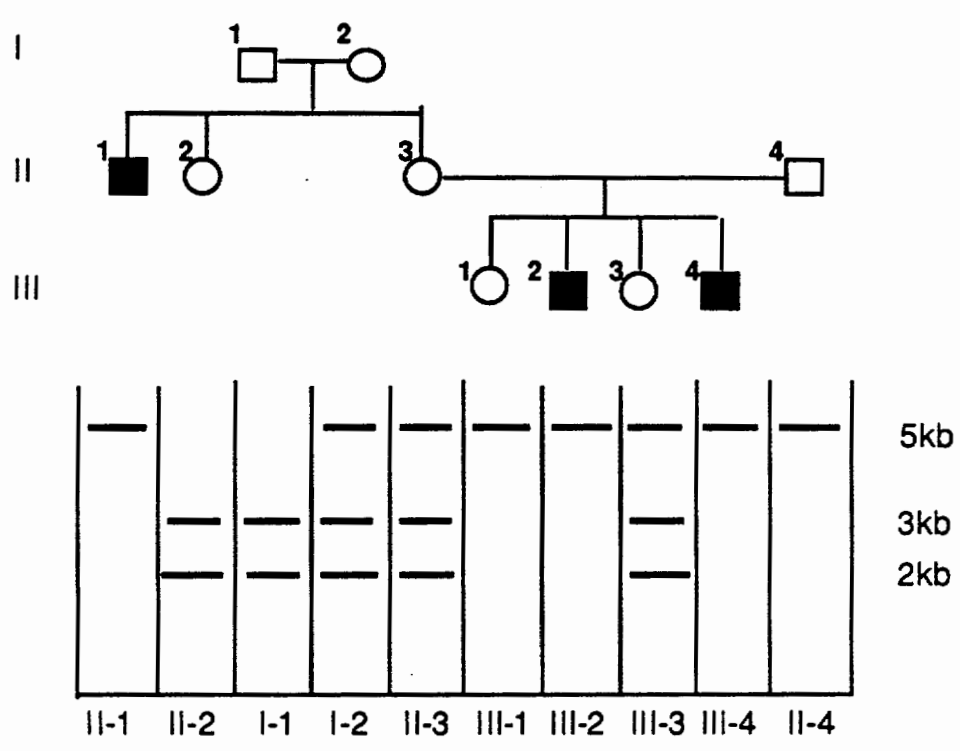
Const. is rarest

order: Pro C Lac I Lac Z Pro B



Name_____

4 Below is the pedigree of a family in which a rare, fully penetrant neurological disorder is inherited. A particular DNA probe is used to analyze a restriction enzyme fragment digest from each of the members of the family. Restriction fragments from each individual are found to hybridize with the probe as shown below.
(circle female, square male, filled afflicted.)



(a 2pts) What is the mode of inheritance of this disorder?

X-linked

(b 3pts) What is the size of the DNA fragment that is linked to the mutation responsible for the disorder?

5 kb

(c 5pts) Identify all unaffected members of the family who probably are carriers..

I-2
II-3
III-1

(d 5pts) Could any other unaffected member(s) have inherited the mutation? Explain briefly!

Yes, if there was a crossover between the marker fragment and the disease allele.

Question #5 omitted

6 (12pts) You have two true breeding brown-eyed stocks of Drosophila. When individuals from either stock are crossed with red-eyed wild-type flies you have a 3:1 ratio of brown to red-eyed phenotypes in the F2 generation. When individual flies of the two brown-eyed stocks are crossed with each other, all of the F1 flies are brown-eyed.

For each question below, circle the T preceding each statement that is true and the F preceding each statement that is false. More than one statement may be true.

(T)	F	1. The mode of inheritance is most likely recessive.
(T)	F	2. The mode of inheritance is most likely autosomal.
T	(F)	3. The mode of inheritance could include two genes.
(T)	F	4. The F2 progeny from the cross between the brown-eyed stocks could be all brown- eyed.
T	(F)	5. The F2 progeny from the cross between the brown-eyed stocks could display a 1:1 ratio of brown eyed to wild-type phenotypes.
T	(F)	6. The F2 progeny from the cross between the brown-eyed stocks could display a 15:1 ratio of phenotypes.

Name_____

Question #7 omitted

8 You have a strain of Drosophila homozygous for an autosomal recessive mutation (*purple* (*pr*)) that causes a recessive brown eye color. In your *pr* strain you find a male fly which has the wild-type eye color red. You assume that this is a suppressor mutation which you call *sup-1*. You cross the red-eyed, *sup-1* male with females from the *pr* strain and find that all female progeny are red-eyed and all male progeny have brown eyes.

(a 3pts) Is the suppression caused by the *sup-1* mutation recessive or dominant?

(b 3pts) Is *sup-1* autosomal or sex-linked?

(c 8pts) Determine the phenotypic ratio of brown and red-eyed females and males in the next (F2) generation. (Be sure to specify ratios among males and females!)

	brown	red
females	1	1
males	1	1

You are given a second red eyed stock that is homozygous for *pr*. Assuming that this is a new suppressor mutation, you call this mutation *sup-2*. You cross females from this strain to the *sup1* red-eyed male from (a). In the F1 progeny all females have red eyes and all males have brown eyes.

(d 8pts) Determine the phenotypic ratio of brown- and red-eyed females and males in the next generation (F2).

	brown	red
females	3	5
males	3	5