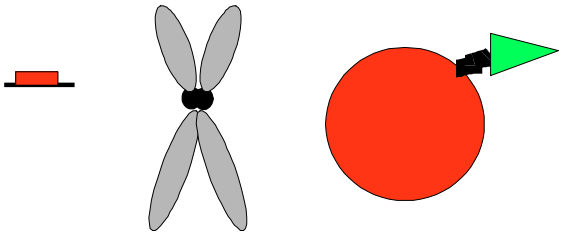
Biol 213 GENETICS (Fall 2000): Problem Sets 7

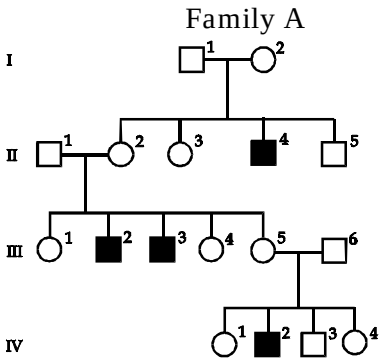
Extensions to Mendelian Analysis

PS7.1. Suppose that phenylketonuria (PKU) happens to be relatively common in two primitive tribes. The Moxies live close to starvation, surviving almost exclusively on the nut of the gum-gum tree. The Wazoos are hunters and thrive on the inexhaustible herds of wild okapi. From pedigrees you have taken, you observe the PKU appears to be a dominant trait amongst the Wazoos but a recessive trait amongst the Moxies. How can that be? If you have more than one hypothesis, what would you look for to distinguish them?

PS7.2. Draw a picture that can help you see the relationship between the *I* gene, the I^A and I^B alleles, and the proteins they encode. Use and combine the icons shown to the right (feel free to use as many copies as you like and to modify them as necessary).

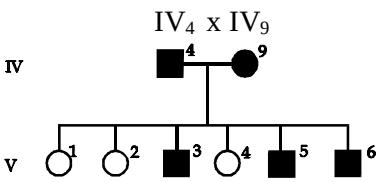


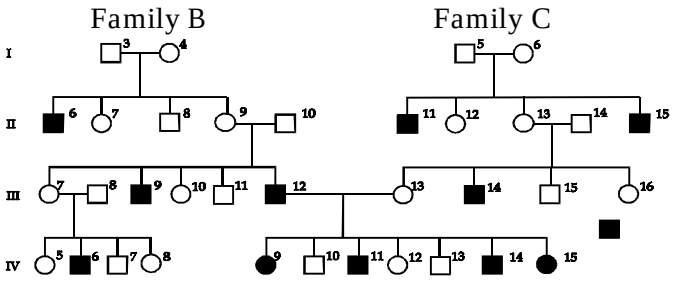
PS7.3. Retinitis pigmentosum (RP) is a rare inherited condition that eventually results in the loss of night vision. The pedigrees to the right (taken from Wirth *et al* (1988) Genomics 2:263) describe three families with a history of RP.



a. Explain from the pedigrees of Families A, B, and C how RP is inherited. Be sure you can account for all individuals.

b. Individual IV_2 from Family A and individual IV_9 from Family C marry and produce the family shown below. NOW how can you account for the pattern of inheritance of RP?





PS7.4. Booker, Problem 4.28. (note that the answer is in the back of the book)

PS7.5. Thalassemia is a type of human anemia common in Mediterranean populations. The disease occurs in two forms: major and minor. Individuals affected by thalassemia major are homozygous for a mutant gene and invariably die in childhood. Individuals affected by thalassemia minor are heterozygous for that gene.

a. A male and female both have thalassemia minor. What is the probability that a child of theirs will also have thalassemia minor?

b. Non-identical twin babies are deposited on your doorstep. Fortunately, you're a geneticist and know what to do in such situations. The first baby you examine turns out to have thalassemia major. What's the probability that the second will also turn out to have thalassemia major?

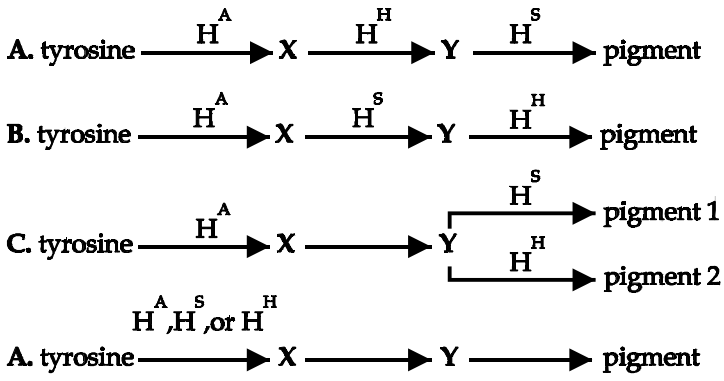
PS7.6. The color of rabbit fur is controlled by different alleles at the *H* locus. Pure bred chinchilla rabbits have silver hair and a genotype of H^sH^s. Pure bred himalayan rabbits are white except for their extremities (nose, feet, etc.), which are pigmented, and their genotype is H^hH^h. Albino rabbits are always homozygous H^aH^a. A rabbit cage contains a white female rabbit with dark extremities, an albino male, and a silver male. You don't know whether the rabbits are pure bred. The female has twelve offspring from the same litter: three like her, six silver, and three albino. Presume simple dominant / recessive relationships between the three alleles.

a. Which male rabbit was the father of the litter?

b. What are the genotypes of the parents?

c. What can you say about the dominance relationships amongst the three alleles?

d. Which of the metabolic pathways below is / are consistent with the information given:



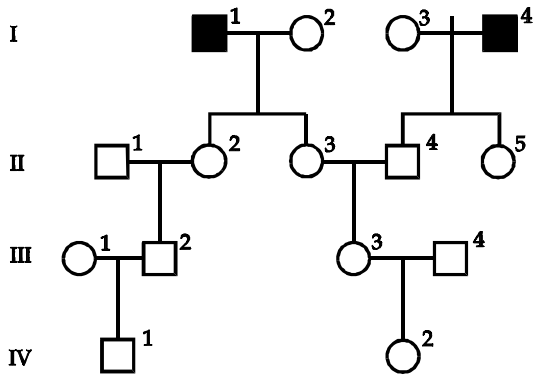
PS7.7. Two separate breeds of true-breeding albino mice mate and produce F_1 progeny, all normal. When the F_1 progeny mate with each other, the following F_2 offspring are observed: 125 normal mice, 88 albino mice, and 11 severely albino mice. (See also Chapter 4, Solved Problem 1 and Problems 18 and 22)

a. Suggest genotypes for the parents and progeny, based on a hypothesis to explain the observed phenotypes, and assess the validity of the hypothesis using a χ^2 test.

b. A phenotypically normal male is crossed with a severely albino female, both mice chosen at random from mice of the appropriate phenotype. What is the probability that an offspring of theirs will be severely albino?

c. An albino male is crossed with a severely albino female, both mice chosen at random from mice of the appropriate phenotype. Now what is the probability that an offspring of theirs will be severely albino?

PS7.8. Renal rickets is a rare kidney condition that is inherited as an autosomal recessive trait. Examine the pedigree to the right of a family with a history of the disease.



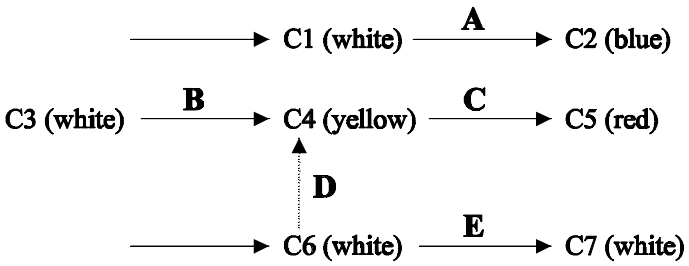
a. List the genotypes of all individuals to the extent possible.

b. If individuals IV_1 and IV_2 marry, what is the probability that their first child has renal rickets?

c. Suppose their first child was indeed affected. What is the probability that their second child is also affected?

PS7.9. The skin of the bright orange South American toad secretes a lethal neurotoxin. Assume that the toxin is produced by an enzyme encoded by a gene that has two alleles: *T* (dominant, wild-type enzyme) and *t* (recessive, no enzyme produced). The neurotoxin is secreted by means of a protein **S** produced by the wild-type gene *S*. The recessive allele *s* does not produce protein **S**. A toad that cannot manufacture the toxin and is also *Ss* is mated with a toad that cannot secrete the toxin and is heterozygous at *T*. What fraction of the progeny will be poisonous to the touch, that is, able both to manufacture and to secrete the toxin?

***PS7.10.** Suppose that purple flower color is produced by the combination of two biochemical pathways shown to the right, one producing red pigment and the other producing blue pigment. Letters above each segment of the pathways represent the enzyme catalyzing the reaction.



Only the blue and red end products normally accumulate; the intermediate compounds (e.g. yellow compound C_3) are generally at too low a concentration to make a difference. A third pathway is normally irrelevant. The intermediate C6 is normally at so low a concentration that it does not contribute to the production of C4 (yellow). Only if its concentration builds up does the reaction catalyzed by **D** become important.

This situation is different in certain mutants. Mutants defective in one or more of the enzymes shown give rise to flowers that are red, blue, yellow, green (blue + yellow), or white. Presume that the wild-type allele of genes encoding an enzyme is dominant in all cases. From the ratios of phenotypes of F_2 progenies shown below, deduce what must be the genotypes of their true-breeding parents.

a. 9 purple : 3 green : 4 blue

b. 9 purple : 3 red : 3 blue : 1 white

c. 13 purple : 3 blue

d. 9 purple : 3 red : 3 green : 1 yellow

***PS7.11. Match each of the alleles described below with one of the following relationships of the associated phenotype to the wild-type phenotype:

A. The mutant phenotype is probably dominant over wild-type
B. The mutant phenotype is probably recessive to wild-type

a. Protein CD4 on the surface of human cells is the major attachment point of HIV, required for the virus' entry into cells. A mutant allele, *F43-S49*, is missing a considerable portion of the gene that encodes CD4. Consider the mutant phenotype of resistance to HIV infection.

b. Amyotrophic lateral sclerosis (also known as Lou Gehrig disease) causes progressive neurodegeneration. The cause of the disease is a defect in an enzyme, superoxide dismutase, that reduces the toxic effects of O_2. 10% of cases of the disease are inherited. One family with a history of the disease carries an allele encoding superoxide dismutase with a mutation in the active site. Consider the mutant phenotype of progressive degeneration.

c. The antibiotic streptomycin binds to ribosomes and causes them to misread mRNA. The resulting defective protein made by ribosomes affected by streptomycin gums up the cell and kills it. The ribosomal protein that binds streptomycin is encoded by the gene *rpsL*. A mutant allele, *rpsL50*, exists that encodes a protein that does not bind streptomycin, and so ribosomes carrying this protein are immune to the effects of streptomycin. Consider the mutant phenotype of resistance to streptomycin.

***PS7.12. A tribe of basketball players intermarry with a tribe of horse jockeys to produce very tall offspring. The F_2 offspring of this hybrid generation exhibit a range of heights, from very small to very tall, with gradations in between.

a. How might you account for these observations?

b. Reinterpret your answer to **a** in light of the facts that:

(1) Height is controlled by multiple growth hormones, all protein.

(2) The hormones are encoded by separate genes on separate chromosomes.

(3) 1 to 2% of the F_2 progeny are very small and somewhat less than half are very tall.

PS7.13. Duchenne muscular dystrophy is an *X*-linked recessive disease. *X* chromosomes carrying the recessive allele are denoted X^M. Sickle cell anemia is an autosomal disease carried on chromosome 11. Affected chromosomes are denoted C^S. An asymptomatic female is heterozygous for both diseases. The normal chromosomes are denoted simply *X* and *C*.

a. List the genotypes (with respect to these two loci) of all the possible gametes that she can produce.

b. List the genotypes if during first meiotic division, nondisjunction occurs, affecting the *X* chromosomes of one of her oocytes.

***PS7.14.** A couple wants to know what the probability is that their anticipated child will be affected by a rare recessive disease. A person in the general population has a probability of one in a thousand of carrying the recessive allele. What is that probability, knowing only that::

a. It's *X*-linked, and the male is affected.

b. It's *X*-linked, and the female's father is affected

c. It's *X*-linked, and the male's father is affected

d. It's autosomal, and the female's uncle and the male's sister are affected

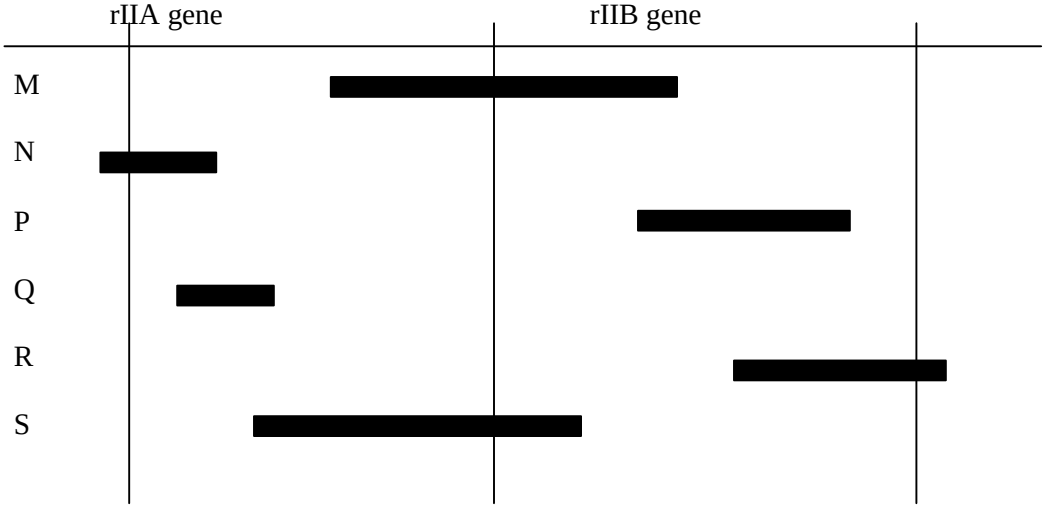
e. It's autosomal, and the couple already has a child, which is affected

f. It's autosomal, both members of the

g. couple are affected, but their only child is not.

Extensions to Recombination, Linkage, and Mapping

***7.15** Using the tester strains shown below, you are trying to map the mutation in a new T4 rII- mutant.



a. You separately coinfect the new T4 rII- mutant with each tester strain in *E. coli* B at a high MOI and obtain a billion progeny phage from each cross. You take a million progeny phage from each cross and plate them with *E. coli* K at a low MOI. The next day, you count the plates. What do you conclude based on this data?

Cross	# Plaques on *E. coli* K
new mutant x M	32
new mutant x N	48
new mutant x P	205
new mutant x Q	19
new mutant x R	215
new mutant x S	0

b. You carry out complementation tests with the new mutant and testers P and Q. The new mutant and tester P complement each other, but the new mutant and tester Q do not complement each other. Is this data consistent with your recombination mapping results? Would it have been helpful to have this data before you carried out the recombination tests? If so, why?

*****7.16** You have two pure breeding lines of maize, one tall with yellow kernels, the other short with purple kernels. You cross the two lines and find that all of the F1 progeny are tall with purple kernels. You then self the F1 plants and obtain the following F2 progeny:

122 tall, purple 59 short, purple
57 tall, yellow 2 short, yellow

a. What is the dominant form of each trait?
b. What are the genotypes of the parents and the F1 progeny?
c. Before you obtained the F2 data above, what would you have predicted?
d. What assumptions is your answer to c. based on?
e. Test whether your prediction adequately explains the data.
f. What is your explanation now?

*****7.17** You take one of the F1 plants from above and cross it to a tester plant. You obtain the following progeny:

98 tall, yellow 102 short, purple
24 tall, purple 26 short, yellow

a. Why do a testcross?
b. What can we determine from this data?

*****7.18** A mouse has the genotype: $\frac{\text{ABDeF}}{\text{a b d e f}}$

Draw the minimum number of recombination events required to generate the following gametes:

a. AbDEf **b.** abDef **c.** abDeF **d.** ABDeF

e. What proportion of the gametes will be AbDeF if the map distance between A-B, B-D, D-E, and E-F are each 10 m.u.?

*****7.19** Virgin wildtype female *Drosophila melanogaster* were mated with brown-eyed, vestigial-winged, four-jointed-leg males. The F1 progeny were all wildtype. Virgin F1 females were mated with brown-eyed, vestigial-winged four-jointed-leg males in a 3-point testcross. The following testcross progeny were obtained:

18 wildtype
20 brown-eyed, vestigial winged, four-jointed leg
6 vestigial-winged, four-jointed leg
5 brown-eyed
4 brown-eyed, four-jointed leg
4 vestigial-winged
1 brown-eyed, vestigial-winged
0 four-jointed leg

a. What is the dominant form of each trait?
b. What are the genotypes of the parents and the F1 progeny?
c. Before you obtained the testcross data above, what would you have predicted?
What is the key assumption behind your prediction?
d. What are the double recombinant phenotypic classes?
e. What is the order of the genes?
f. What are the map distances between the genes?

For More Practice on Linkage & Mapping:
Brooker Chapter 5, Conceptual Questions 2, 3, 4, 8, 12, 13 (part A only), 16

For More Practice on T4 Complementation and Recombination:
Brooker Chapter 6, Conceptual Questions 15, 16, 18; Experimental Question 4

7.20 The year is 2009 and you are a practicing MD. Trouble walks into your office. She's thirtyish, air-blown blond hair, lots of rocks. She's a mess.

"Doctor!" she sobs. "You must help me!"

"What's up sis?" you snap.

"It's my brother Milford. He's got Purple Tongue Syndrome!"

Yeah, yeah,... you heard it all before. The rare X-linked recessive condition that causes progressive tongue bloat until the distended organ hangs hideously, oxygen-starved from the victim's mouth. "So what's it to you? You want some tongue depressors?"

"No,... you see, my husband Austin Finkelwart..."

"You don't mean the fabulously wealthy 80 year old Austin Finkelwart, president of Finkelwart Enterprises?" you snort.

"If you must know, yes. He married me because he thought I had PTS. He wants an heir to his fortune that can't answer him back. Of course I knew all about the disease from Milford, and so I responded to his ad wearing a purple balloon, and now..." she burst out sobbing again.

You take a closer gander at her... just as you thought. "So the old geezer knocked you up, and you're afraid the kid's not going to know enough to come out with a balloon."

She nods, dabbing her eyes.

"Well," you continue. "You may still be in luck." You do a quick calculation.

a. *What is the probability that your patient's child will have PTS, presuming that her and Milford's parents are not affected?*

"Thank you doctor," she says after hearing your results. "But there's more. I had an amniocentesis performed, and..."

You slam your hand to your forehead. "Look lady, I can't help you unless you tell me everything from the start. Is the kid a boy or a girl?"

"A boy," she sniffles.

b. *<u>Now</u> what is the probability that the child will have PTS?*

"But that's not the problem, doctor. The amniocentesis said that the child has an abnormally low level of glucose-6-phosphate dehydrogenase, another X-linked trait."

"OK, so he's got GP6D deficiency. It maps -- what is it? -- about 2 map units away from PTS. What do you think I went to medical school for? Anyway, so what?"

"But I know the trouble GP6D deficiency has caused Milford,... Poor Milford bears this affliction also."

"Oh he does, does he?" you mutter, but your mind is ablaze. Then the truth slams home like a ton of bricks.

c. *Draw a pedigree, including your patient, her child, her parents, and Milford, and give <u>the most probable genotypes</u> for each.*

d. *Which of Milford's parents carries the gene for G6PD deficiency?*

e. *What is the probability that that parent carries G6PD deficiency and PTS on the same chromosome?*

f. *What is the probability that your patient carries G6PD and PTS on the same chromosome?*

g. *What is the probability that the child has PTS?*