Chapter 1: Genetics Problems

Genetics Problems

If you were a geneticist, you would study genes. This statement is particularly true today in an era in which, in some organisms, the entire genome has been sequenced and nearly every gene has been identified.

Today, once a gene has been identified, the protein (or RNA) that it encodes can be inferred. Yet even when the gene and the resulting protein are known, the <u>function</u> of that gene may remain a mystery.

If you were Gregor Mendel, you would have studied mutant plants. In 1866, Gregor Mendel was performing what many see as the first genetic experiments, and he did not even know genes existed! Mendel postulated the existence of "particles" (genes) whose function he could draw conclusions about. If his mutant had yellow seeds instead of green seeds, then a "particle," i.e., a gene, controlled seed color, and this gene was altered in his yellow mutant.

Modern day geneticists use a wide array of tools and techniques. They study genes by searching vast databases of genetic information, but they also study genes much as Mendel did, by beginning with a mutant that is clearly distinguishable from what is standard or normal. In this chapter, we have given you different genetics problems that will allow you to practice and build on the concepts introduced by Gregor Mendel. The very first question is meant to be diagnostic. Work through the problem on your own and then look at our approach to solving it. If any of the underlined terms are unfamiliar, please consult your book's chapter on Mendelian Genetics.

(1) PROBLEMS INVOLVING ONLY ONE GENE

In general, the problems in each section begin with the most straightforward and become more complex as you proceed. They are grouped hierarchically; that is, Problems 1.1.x all deal with one gene, two alleles, simple dominance, while Problems 1.2.x all deal with more complex problems.

Diagnostic Question:

You are given two blue beetles and two black beetles.

a) Cross 1: You <u>mate</u> (or <u>cross</u>) blue beetle #1 to black beetle #1 and obtain 220 black beetles in the <u> F_1 generation</u>.

- What is the <u>dominant phenotype</u>?
- What is the <u>recessive phenotype</u>?
- What are the <u>genotypes</u> of the two parents and the offspring? Be sure to indicate which allele is associated with the dominant phenotype.

b) Cross 2: You mate blue beetle #2 to black beetle #2 and obtain 55 blue beetles and 65 black beetles. What are the genotypes of the two parents and the offspring?

c) Cross 3: You mate two black offspring produced in Cross 2. What are the possible genotypes and phenotypes of the offspring? What are the expected proportions of these genotypes and phenotypes?

Answer to Diagnostic Question:

a) Cross 1: You mate blue beetle #1 to black beetle #1 and obtain 220 black beetles.

What is the dominant phenotype? Because there are a large number of offspring, all of which are black, you can assume that black is the dominant phenotype.

What is the recessive phenotype? *Blue.*

What are the genotypes of the two parents and the offspring? Be sure to indicate which allele is associated with the dominant phenotype.

Because black is the dominant phenotype and there are a large number of offspring, all of which are black, you can assume that the black parent is <u>homozygous</u> for the <u>allele</u> associated with the dominant <u>phenotype</u>. By convention you would use uppercase letters for the <u>allele</u> associated with the dominant phenotype. In this instance we have assigned the genotype BB to black beetle #1. The genotype of blue beetle #1 must be bb; otherwise, it would not have the blue phenotype.

b) Cross 2: You mate blue beetle #2 to black beetle #2 and obtain 55 blue beetles and 65 black beetles. What are the genotypes of the two parents and the offspring? *Some of the offspring have the recessive blue phenotype and must therefore have the genotype bb. Thus, the genotype of blue beetle #2 must be* **bb** *and the genotype of black beetle #2 must be* **Bb**. *Also, based on (a), you know that blue has the genotype bb.*

c) Cross 3: You mate two black offspring produced in Cross 2. What are the possible genotypes and phenotypes of the offspring? What are the expected proportions of these genotypes and phenotypes?

The black offspring from \hat{C} ross 2 must have the genotype Bb, so Cross 3 is Bb \times Bb.

	В	b
В	BB	Bb
D	black	black
b	Bb	bb
υ	black	blue

The <u>genotypic ratio</u> is 1 (BB) : 2 (Bb) : 1(bb). The <u>phenotypic ratio</u> is 3 black beetles to 1 blue beetle.

(1.1) One gene; two alleles; simple dominance

In this section, we deal with models that consider only a single trait or characteristic (phenotype), for example, green seeds or yellow seeds. The trait of interest is determined by a single gene that has two alleles.

Problems:

(1.1.1) Consider some hypothetical flowers in which color is controlled by one gene and green color is dominant to blue color. **G** is the symbol for the allele associated with the dominant phenotype, green flowers, and **g** is the symbol for the allele associated with the recessive phenotype, blue flowers.

Give the expected ratios of offspring from the following crosses:

a) GG X GG

b) $gg \times gg$

c) Gg X gg

d) Gg \times Gg

e) Green × Green (note that there may be several possibilities here; give them all)

f) Blue \times Blue (note that there may be several possibilities here; give them all)

(1.1.2) For each of the following sets of data, give a genetic model that explains all the data. A genetic model contains the following:

- the number of genes and alleles involved, e.g., "tooth shape is controlled by one gene with two alleles."
- a statement of which phenotype is dominant and which is recessive.
- symbols denoting each allele such that uppercase letters are associated with the dominant phenotype and lowercase letters are associated with the recessive phenotype.
- the genotypes of all the individuals involved.
- a) Cross 1: Red-eyed mouse × white-eyed mouse

gives F₁: all red-eyed

Cross 2: Red-eyed $F_1 \times \text{red-eyed } F_1$

gives F ₂ :	36 red-eyed
0 -	13 white-eyed

b) Cross 1: Long-eared mouse × short-eared mouse

gives F ₁ :	12 long-eared
0	10 short-eared

Cross 2: Long-eared $F_1 \times \text{long-eared } F_1$

gives F₂: 34 long-eared 14 short-eared

(1.1.3) Achondroplasia is a form of dwarfism controlled by one gene with two alleles. Two achondroplastic dwarfs marry and have a dwarf child and later have a second child who is of normal size.

Based on this:

a) Is achondroplasia a recessive or a dominant phenotype?

b) What are the genotypes of the two parents?

(1.1.4) Assuming that the following traits involve only one gene with two alleles, give <u>all</u> models that are consistent with the data. For each model, indicate the genotypes of the individuals involved (indicate any ambiguities), which phenotype is dominant, and which phenotype is recessive.

a) Red fly \times red fly gives one blue fly progeny.

b) Brown cow \times white cow gives one brown cow progeny.

(V1) Virtual Genetics Lab I The Virtual Genetics Lab II (VGLII) is a computer simulation of Genetics in a hypothetical insect that allows us to perform virtual genetic experiments. It has a variety of features that we will introduce gradually. In this first problem, you will use VGLII to generate appropriate offspring from a simulated cross of two individuals that you select. This simple use of VGLII is designed as practice with the genetic models we have discussed and as a warm-up for later VGLII problems.

1) Go to the web page for this problem: http://intro.bio.umb.edu/MOOC/jsVGL/JsVGL_V1.html	Virtual Genetics Lab
2) Click the "Load" button to load this problem.	Instructions:
	Click "Load" to load the problem des Note that this is a simplified version Load Cross Two

3) You will see a cage containing some creatures in the "Cages with Organisms for crossing" panel:

-Cá	age 1 ——				
Г	Organisms Collected From the Wild				
	Wing-	Organisms	Counts -		
	Red	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	11 0 ⁷ 08 Q		
	Yellow 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0				

These creatures have a random assortment of genotypes. They represent a population of flies that might have been collected in the wild. They are not necessarily pure-breeding, nor is it clear if any are the offspring of any others.

4) Click on the tab marked Genetic Model" in the left panel and you should see this:

Instructions	Genetic M	odel	About jsVGL		
XX/XY sex determination Gene(s) on Autosome(s): -Gene 0:Wing Color Two Allele Simple Dominance					
	Red is recessiveYellow is dominant				
Genotype	Phenotype]			
Red/Red	Red				
Red/Yellow Yellow					
Yellow/Yellow					

This gives the details of the genetic model for the inheritance of Wing color in this particular problem. Each time you click "Load" on this page, you will get this same genetic model, although the offspring of a particular cross may be different. In later VGLII problems, the genetic model will be selected randomly.

The model can be written in the usual form:

	<u>Phenotype</u> Yellow wings (dominant) Red wing (recessive)	Associated allele Y y
or:	<u>Phenotype</u> yellow wing yellow wing red wing	<u>Genotype</u> YY Yy yy

You should do this as a matter of course for *every* VGLII problem that you solve: every time you try out a new genetic model to explain your data, write out the model explicitly as shown above. This will help you to understand more clearly the different types of genetic models; it will make careless mistakes less likely.

In the cage, the insects are sorted by phenotype and sex. The left-hand column contains individual male and female symbols that represent individual insects that you can select for crossing. The next column shows a count of each phenotype and sex. In this case, there are:

11 males with red wings 8 females with red wings

5 males with yellow wings

8 females with yellow wings

Problems Involving One Gene

You can find the genotype of any insect by putting the cursor over it and leaving it there for a few seconds. A box will pop up giving the details of that insect's genotype. For example, if the box shows:

A:{Yellow-Wing}/{Red-Wing} XY

This means that the genotype is:

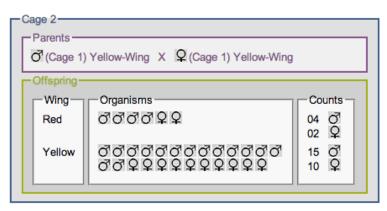
Yellow-wing – the first allele is yellow-wing (Y)

Red-wing – the second allele is red-wing (y)

therefore, this individual has genotype Yy. For the time being, you can ignore the "A:" and "XX" or "XY".

5) You can select an individual for crossing by clicking on it. Select one male and one female insect of either phenotype from any cage. Find their genotypes as described above. Predict the ratio of yellow-wing:red-wing offspring using a Punnett square.

6) Cross the two parents you selected in part (5) by clicking the "Cross Two" button. A new cage should appear containing the offspring of your cross. For example, the cage below was created by crossing a Yy (yellow-wing) male with a Yy (yellow-wing) female; our model would predict 75% Y_ (YY or Yy) (yellow-wing) and 25% yy (red-wing) offspring:



The cage in the figure shows:

25 (15 male + 10 female) yellow wings

6 (4 male + 2 female) with red wings

This is roughly equal to a 3:1 phenotype ratio. It is not perfectly 3:1 because the offspring are generated by random combination of the parent's alleles, as they are in nature. Because of this, small numbers of offspring will only approximate the expected ratios. If you clicked "Cross Two" several times for this same pair of parents and added the results together, you would get closer to a 3:1 ratio.

a) You can now select any male and any female insect, find their genotypes, predict their offspring, and test your predictions. Do this for as many crosses as it takes to convince yourself that you understand how this works.

b) As you do this for many crosses, you will see that, although the offspring ratios are not exactly what the Punnett square would predict, it is possible to make some statements about the expected offspring. These statements would use phrases like "none," "all," "roughly equal," and "more than" to describe the expected ratios in these small samples of offspring. For each of the crosses described below, give a phrase that uses one or more of the phrases listed above that accurately describes the expected genotype and phenotype ratios of the offspring.

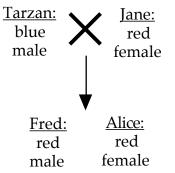
- i) YY \times YY
- ii) YY \times Yy
- iii) YY \times yy
- iv) $Yy \times Yy$
- v) Yy \times yy
- vi) yy \times yy
- c) Try a new VGLII problem.
 - o go to http://intro.bio.umb.edu/MOOC/jsVGL/JsVGL_WarmUp1.html
 - Click "New Practice Problem" if you want to be able to look at the answer as you work. This problem will look like the one above.
 - You will get a cage with a randomly chosen character. There will be two randomly chosen traits of that character. One is dominant; the other is recessive.
 - Define appropriate symbols for this genetic model.
 - As you did in part (a), choose a random pair of parents, get their genotypes, predict the expected offspring, cross them, and check your prediction. Keep crossing until you are sure you understand. To try another problem, follow the steps in part (c).

Don't worry about all the submission instructions; they refer to another use of this page.

(1.1.5) What is the simplest explanation that accounts for the following results? Give the genotype of each mouse.

- A brown mouse was crossed with a white mouse, producing 10 brown and 13 white F₁ mice.
- Two white F₁ mice were crossed, giving all white progeny.
- Five pairs of brown F_1 mice were crossed, giving a total of 56 brown and 20 white progeny.

(1.1.6) You are studying coat color in tribbles, a sexually reproducing, diploid species of hypothetical mammals. Tribbles can be either red or blue, and you have other evidence which shows that coat color is determined by a single gene with two alleles (B and b). You cross two tribbles, Tarzan and Jane, and they produce two tribble pups, Fred and Alice:

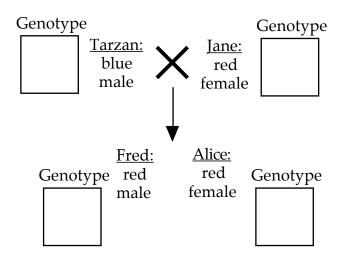


a) Give a plausible one autosomal gene, two-allele model to explain these data:

i) Based on your model, give the color phenotype of each of the following genotypes:

<u>Genotype</u>	<u>Phenotype (color)</u>
BB	
Bb	
bb	

ii) Based on your model, give the genotypes of each of the individuals in the following pedigree. Indicate any ambiguities.

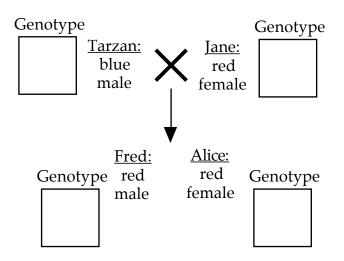


b) Give a <u>different</u> one autosomal gene, two-allele model for the inheritance of coat color in tribbles that is consistent with the pedigree at the beginning of this problem. To be considered "different," your answer to part b(i) must be different from your answer to part a(i). Parts a(ii) and b(ii) may also be different, but differences in part a(ii) <u>alone</u> do not constitute a "different" model.

i) Based on your model, give the color phenotype of each of the following genotypes:

<u>Genotype</u>	<u>Phenotype (color)</u>
BB	
Bb	
bb	

ii) Based on your model, give the genotypes of each of the individuals in the pedigree. Indicate any ambiguities.



c) You decide to use the rapid reproductive rate of tribbles to distinguish between the two models. You decide to cross two of the tribbles you have and collect many offspring from this cross. You design your cross carefully so that the results of the cross will allow you to determine which is the correct model, (a) or (b).

i) Which two tribbles will you cross? Circle your choices.

Tarzan	Jane	Fred	Alice
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ii) What will be the results of the cross of part c(i) if your model from part (a) is true? Give the expected ratio of coat colors.

iii) What will be the results of the cross of part c(i) if your model from part (b) is true? Give the expected ratio of coat colors.

(1.1.7) Recently, some scientists proposed a genetic model to explain the inheritance of left- and right-handedness in humans. Their model is as follows:

Handedness	is	controlled	bv	one	gene	with	two allel	es:
1 Iunacanceoo	10	controlled	$\sim y$	one	Serie		the uner	CU .

Thanded he by one gene what two uncles.			
Allele	Contribution to phenotype		
R	right-handed (dominant)		
r	undetermined handedness (recessive)		
Therefore:			
<u>Genotype</u>	Phenotype		
RR, Rr	right-handed		
rr	undetermined: half of these children develop into left-handed individuals and half develop into right-handed individuals.		

a) Based on this model, two Rr parents (right-handed) have a 1/8 chance of having a left-handed child. Explain why this is so.

b) Based on this model, can a left-handed mother and a right-handed father have a left-handed child? Justify your answer.

c) Based on this model, can two left-handed parents have a right-handed child? Justify your answer.

d) One problem with this model is that it is consistent with virtually any combination of left-handed or right-handed parents and offspring. What data, if any, could you imagine finding that would not be consistent with this model?

(V2) Virtual Genetics Lab II Here, you will use VGLII in a more advanced mode, and you will have to figure out how the trait is inherited without looking at the answer. This will provide you with more practice with this material. There are many successful ways to approach problems like these; we will begin by looking at a problem that we have already worked through for you.

Launch VGLII using this link:

http://intro.bio.umb.edu/MOOC/jsVGL/JsVGL_V2.html

Be sure that you see a set of two cages. We will go through them in the order that we generated them.

Cage 1 looks lie this:

-Cage 1			
C Organisms C	Collected From the Wild		
Antenna	Organisms	Counts	
Long	ୢୄୖ୶୶୶୶୶ୢୣୖ ଡ଼ୣଡ଼	06 0 ⁷ 05 Q	
Pointy	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	07 0 ⁷ 07 Q	

Some flies had long antennae and others had pointy antennae. Our task is to determine whether long or pointy is the dominant phenotype.

Given only the two phenotypes (long and pointy) and the constraints given for this problem (only one gene; no sex linkage), there are two possible models for the inheritance of this trait. It is good practice to do this at the start of each problem that you work on.

Model A (long dominant)		Model B: (pointy dominant)		
<u>Phenotype</u> long (domin pointy (rece		<u>Phenotype</u> pointy (dom long (recessi		
	or:		or:	
<u>Genotype</u> LL Ll ll	<u>Phenotype</u> long long pointy	<u>Genotype</u> PP Pp pp	<u>Phenotype</u> pointy pointy long	

The next step is to cross two individuals and look at the resulting offspring to see which model fits. In this problem, we have already done one cross for you: we crossed the two circled insects in Cage 1 and got Cage 2:

Cage 2 Parents Or (Cage 1)	Long-Antenna X 🝳 (Cage 1) Long-Antenna	
Offspring —	Organisms	Counts
Antenna –	ರೆರೆರೆರೆರೆರೆರೆರೆರೆರೆರೆರೆರೆರೆರೆರೆರೆ	19 O ¹
Long	ರೆರೆ ೪ ೪ ೪ ೪ ೪ ೪ ೪ ೪ ೪ ೪ ೪ ೪	13 Q

There are several important things to notice about Cage 2:

• The top line in the Cage window says "(Cage 1) Long-Antenna X (Cage 1) Long-Antenna" This translates as "the parents are a male from Cage (1) with long antennae and a female from Cage (1) with long antennae." You can click on the male and female symbols to select those particular parents. This is true for all cages except Cage 1 (which has no parents).

 The results in Cage 2 can be summarized as: Parents: long × long
 ↓
 Offspring: 32 with long antennae

You will need to use this type of analysis when you are working through other VGLII problems as well.

Which model(s) are consistent with the results of the cross that is shown in Cage 2? Starting with Model A, the long parents can be either LL or Ll. LL \times LL, Ll \times LL, and LL \times Ll produce only long offspring, so the parents could have any of these genotypes. However, if the parents were both Ll, they would be expected to produce a 3:1 ratio of long to pointy offspring. Since we don't see any pointy offspring with a relatively large number of offspring, it is very unlikely that the parents are Ll \times Ll. In general, when using VGLII, the numbers will not come out to exact "Mendelian ratios" because of the small number of offspring. It is therefore useful to think of these ratios in more descriptive terms, as shown below:

<u>Mendelian Ratio (A:B)</u>	Descriptive Phrase
1:0	all A; no B
0:1	all B; no A
1:1	roughly equal amounts of A and B
3:1	more Á than B
1:3	more B than A

In the case of Cage 2, we would describe the results as "all long," which is what we would expect from a cross of $L_X L_$.

Problems Involving One Gene

Next, try Model B. In this case, the long parents must both be pp. Since pp X pp gives all pointy offspring, this model is also consistent with this model.

Since this cross result is consistent with both Model A and Model B, you cannot tell which is correct without doing more crosses. You should do some more crosses to see what happens.

The most conclusive pieces of evidence are cross results that are consistent only with one alternative model or the other. It will be useful to keep these in mind when solving VGLII problems in the future.

a) Which cages give results that are consistent only with Model A? Why?

b) Which cages give results that are consistent with both Model A and Model B? Why?

c) What other types of results are consistent only with Model A or consistent only with Model B? Why?

d) Make some other predictions based on this model and test them by making crosses.

e) You should now solve a problem on your own. To do this, you:

- Go to http://intro.bio.umb.edu/MOOC/jsVGL/JsVGL_WarmUp1.html
- Click "New Graded Problem".

You will then have a problem to work through like the one above. One trait will be dominant and the other recessive; your task is to keep crossing until you are convinced which is which. At this level, there is no way to see the model or genotypes; you must decide for yourself when you have enough data to be confident in your choice of model.

You can check your work by clicking the "Save" button and looking at the "Grade Info" box.

Hints:

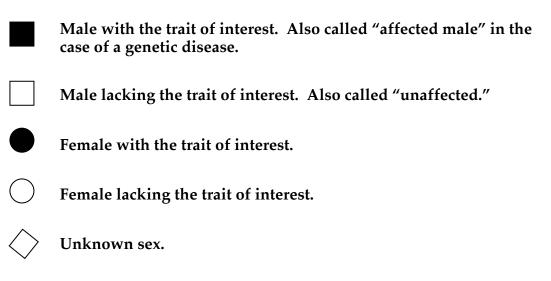
- 1. Start by writing out the two possible genetic models.
- 2. Think about what kinds of results would be conclusive (as described above) and keep your eyes open for these.
- 3. Consider the results of each cross carefully before doing another cross.
- 4. Once you have a strong suspicion that a particular model is correct, design crosses to test this model as we did above.

You should do several problems this way until you are confident that you understand how to solve them reliably. As you gain more experience, you can use VGLII in a manner that more closely approximates the way a geneticist would work in a research lab where the "correct answer" is not known. One possible progression is given below:

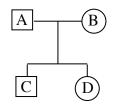
- You may want to start by working problems where you can check your work by looking at the model and genotypes as we have shown. For these problems, click "New Practice Problem", these involve one gene; one trait is dominant to the other.
- As a next step, try to work a practice problem until you are confident that you have found the correct genetic model. Then, and only then, you can check your work by showing the model in the Genetic Model tab.
- You can then move on to working "graded" problems. Here, the genetic models are the same as in practice mode, but you cannot see the model or genotypes. Here, you can work until you are confident in your choice of model and then have a friend check your work. There are several ways to do this:
 - You explain the results of each cage to your friend.
 - Your friend picks any two individuals and you predict the expected offspring. You then do the cross to see if your prediction is correct.

(1.2) Pedigrees involving one gene, I

Another way to present genetic data is a pedigree. Pedigrees are useful diagrams for presenting data from many crosses, where each cross generates only a small number of offspring. Pedigrees are a standard tool for evaluating inheritance patterns in humans. Pedigrees use the following symbols to represent the sex and the phenotype of individuals:



Relationships between individuals are indicated by lines; as shown, A and B are the parents of C and D.



Genetic traits or diseases can be inherited in several different ways. The first two we will consider are:

• <u>Autosomal Dominant</u>: the disease allele gives the *dominant* phenotype.

Allele Contribution to phenotype

D disease (dominant)

d normal (recessive)

Genotype	Phenotype	Symbols
DD	affected	■ or ●
Dd	affected	■ or ●
dd	normal	\Box or \bigcirc

• <u>Autosomal Recessive</u>: the disease allele has the *recessive* phenotype. Allele Contribution to phenotype

ł	Allele Contribution to prienotype		
	N normal (dominant)		
	n disease (recessive)		
	Genotype Phenotype Symbols		
	NN	normal	\Box or \bigcirc
	Nn	normal	\Box or \bigcirc
	nn	affected	\blacksquare or \blacksquare

Problems:

(1.2.1)

a) Consider cystic fibrosis, an autosomal recessive genetic disease.

i) Define appropriate allele symbols for cystic fibrosis.

ii) Draw a pedigree for a family in which two unaffected parents have a son with cystic fibrosis and an unaffected daughter.

iii) What is the genotype of the unaffected daughter? Indicate any ambiguity or multiple possibilities.

iv) What is the chance that the next child in this family will have cystic fibrosis?

b) Consider Marfan syndrome, an autosomal dominant genetic disease.i) Define appropriate symbols for Marfan syndrome.

ii) Draw a pedigree for a family in which both parents have Marfan syndrome and they have an unaffected son and an unaffected daughter.

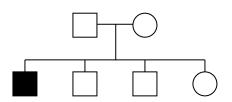
iii) What is the genotype of the unaffected son? Indicate any ambiguity or multiple possibilities.

iv) What is the chance that the next child in this family will have Marfan syndrome?

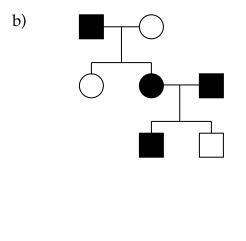
(1.2.2) For each of the following pedigrees:

- Determine whether the disease is inherited in a dominant or recessive manner.
- Define appropriate allele symbols.
- Give the genotypes of all individuals in the pedigree; be sure to indicate any ambiguities or multiple possibilities. Refer back to page 21 for an explanation of the pedigree symbols.

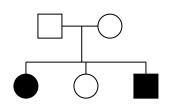
a)



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c)



(1.2.3) Although you can solve any pedigree problem by trying all the possible genetic models, this can be rather time-consuming. An alternative method involves looking at pedigrees for particular arrangements of parents and offspring that can rule out one or another mode of inheritance. This can be a more rapid way to eliminate possible modes of inheritance.

For example, one diseased parent and one normal parent having one diseased offspring is consistent with <u>both</u> autosomal dominant and autosomal recessive inheritance. Other arrangements are consistent only with one or the other.

a) For each of the following statements, mark if they are true for autosomal recessive and/or autosomal dominant diseases:

 i) Diseased parents can have diseased offspring. True for autosomal recessive diseases? True for autosomal dominant diseases? 	Yes Yes	No No
ii) Normal parents can have normal offspring.True for autosomal recessive diseases?True for autosomal dominant diseases?	Yes Yes	No No

iii) Even if both parents are normal, they can have diseased offspring.

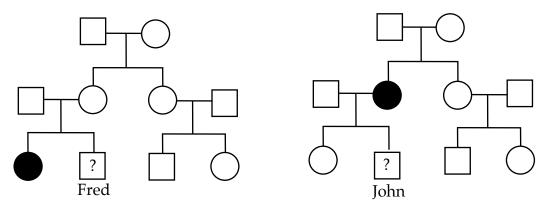
1 , , ,	1	0	
 True for autosomal recessive diseases? 		Yes	No
 True for autosomal dominant diseases? 		Yes	No

iv) Even if both parents are diseased, they can have normal offspring.

- True for autosomal recessive diseases? Yes No
- True for autosomal dominant diseases? Yes No

b) Can any of these statements be used to rule out one or the other mode of inheritance? Can you apply any of these to problem 1.2.2? How?

(1.2.4) Shown below are two pedigrees for a <u>rare autosomal recessive</u> genetic disease. Fewer than 1 in 1,000 people are carriers for this disease.



Fred and John are as yet unborn children of parents who are concerned that they may be affected with the genetic disease. Based on the above pedigrees, which individual, Fred or John, has a greater risk of being affected by the disease? Why?

(1.2.5) Read the attached information and consider the pedigree for the family described, then answer the following questions.

a) Who appears to have Marfan syndrome?

b) What are the chances that the offspring of the affected individuals will have Marfan syndrome?

Marfan Syndrome Description:

- Inherited as an autosomal dominant trait.
- Defect of connective tissue formation.
- Some common features of the syndrome (not all are present in all cases):
 - Tall stature
 - Long, thin limbs (relative to height)
 - Prominent shoulder blades
 - Spinal curvature (scoliosis)
 - Protruding or caved-in breastbone
 - o Flat feet
 - Dislocated eye lens (may require glasses)
 - Detached retina
 - Long fingers and thumbs
 - General joint and cartilage trouble
- Cause of heart valve abnormalities and weakening of the aortal wall. During heavy exercise, the weakened aortal wall can burst, leading to almost instantaneous death.
- No genetic or biochemical test for this syndrome at the time these data were collected.

Information on Family Members

• Anne:

Anne is 16 years old and is a junior in high school. She has read some information in the popular press on Marfan syndrome, and she and her parents are concerned that Anne might have this syndrome. Her general physician has referred her to the Genetics Counseling Clinic. Anne is 5' 11" and wears contact lenses to correct for myopia (nearsightedness). She plays on her school's varsity volleyball and basketball teams. NCAA scouts are already interested in her playing ability, and there is a chance she will be offered college scholarships in both sports. Her armspan/height ratio is 1.08:1. (In one group of 27 adults, this ratio was 1.006 with standard deviation = 0.03.)

Siblings:

• David:

Age 25, married to Jessica, age 25, one daughter named Kristi, age 3 months. David wears glasses, is 6' 3", has long fingers and toes, played basketball and ran track in high school, and had some knee problems that developed during his high school athletic career. Jessica is 5' 8", wears no glasses, and has no health complaints other than occasional migraine headaches. She and David had one miscarried pregnancy in the first trimester before the birth of Kristi.

• Cheryl:

Age 14, 5' 9", no glasses, has a slight case of scoliosis. She was born with club feet, which responded well to corrective treatment.

Parents:

• Mary:

Age 47, 5'7'', wears glasses, and has hay fever. Has been diagnosed with carpal tunnel syndrome and mild diabetes. Had two miscarriages in addition to her three children.

• Peter:

Age 49, 6' 1", wears glasses, concave chest, high blood pressure, partial lens dislocation in left eye, and long fingers and toes. Has complained about chronic tennis elbow.

Aunts and Uncles:

Mary's Siblings:

• Dorothy:

Age 46, wears glasses, 5' 3", no major health problems. Had an ovarian fibroid tumor removed at age 40. Married and has four children.

• Ellen:

Age 50, 5′ 5″, high cholesterol, has been diagnosed with irritable bowel syndrome. Unmarried, no children.

• Eric:

Age 51, 6' 1", wears reading glasses, has recurrent back problems from a car accident, suffers from exercise-induced asthma. Is married and has two children from his first marriage and three from his second.

Peter's Siblings:

• Frank:

Age 55, 6' 4", wears glasses, slight hearing loss in one ear. Was treated for alcoholism, is a heavy smoker, and has developed a chronic cough. Divorced, the father of two children.

• Alice:

Age 56, 5' 7", wears glasses, arthritis in left shoulder. Married, has one daughter and a son who was born with cerebral palsy.

• John:

Deceased, heart attack at age 46, 6' 2", had dislocated lens in right eye. He and his wife had three children. Their youngest daughter is slightly mentally retarded.

• Larry:

Age 58, 6'3'', no glasses, high blood pressure. Divorced twice, lives alone now. Had two children by his first marriage and one by his second. Is a heavy drinker.

Grandparents:

Anne's Maternal Grandparents:

• Evelyn:

Died at age 76 of stroke, 5' 4", arthritis in hands and feet, wore reading glasses. Was said to have had as many as five miscarriages.

• William:

Age 81, no glasses, 5' 10", no major health problems. Has a slight limp due to bad right knee, occasional rashes, and hemorrhoids.

Anne's Paternal Grandparents:

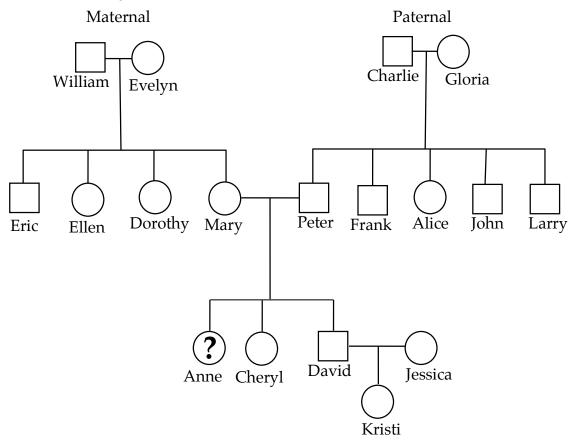
• Gloria:

Age 86, 5' 8", high blood pressure, some knee and ankle problems. Is concerned about her constipation. Wears glasses for distance and reading.

• Charlie:

Died at age 44 of a heart attack, severe vision problems, described as long and lanky. Contracted polio at age 26. He was wheelchair dependent following polio treatment.

Anne's Family Tree:



Pedigrees Involving One Gene, I

(1.3) One gene; more complex models, I

In this section, we will deal with more complex single-gene models. The models are more complex because i) they do not follow simple dominance or ii) there are more than two alleles for the gene.

a) Two alternatives to simple dominance are incomplete dominance and codominance. To evaluate these more complex models, let's first review simple dominance. So far, we have evaluated a single gene trait with two alleles in the following way. We could have homozygous organisms with the genotypes:

<u>Genotype</u>	<u>Phenotype</u>
AĂ	red
aa	blue

If the heterozygote (genotype Aa) is red, then red is the dominant phenotype and blue is the recessive phenotype.

In *incomplete dominance*, the heterozygote has an *intermediate* phenotype, a phenotype different from either of the homozygotes. For example, we could have homozygous organisms with the genotypes:

<u>Genotype</u>	<u>Phenotype</u>
TT	Tall
T'T'	short
TT′	medium height, this is <u>intermediate</u> between tall and short

In *codominance*, the heterozygote has a *mixture of both* homozygote phenotypes. For example:

<u>Genotype</u>	<u>Phenotype</u>
TŤ	red
T'T'	blue
TT′	a mixture of both red and blue

In both cases, the heterozygote can be distinguished from either of the homozygotes. Lowercase letters were not used as allele symbols because the lowercase letters symbolize alleles associated with a recessive phenotype. b) The complexity of genetic models increases when you have more than two alleles of a gene because the number of possible genotypes increases. If a gene has three alleles, then six possible genotypes exist. A classic example of a gene in which there are three alleles is the blood-type gene in humans. The three blood types are A, B, and O, so it might make sense to use A, B, and O as the allele symbols. This creates a problem because the genotypes and the phenotypes are then easily confused. For that reason, we will use symbols like these when dealing with more than two alleles of the same gene: I^A , I^B , or i.

Blood type in humans is a good example problem for this because it shows both simple dominance and codominance.

Example problem

With respect to blood type in humans, all possible genotypes are given below.GenotypePhenotype

<u>Jenotype</u>	Phenotyp
I ^A I ^A	type A
$I^{B}I^{B}$	type B
ii	type O
I ^A i	type A
I ^B i	type B
$I^A I^B$	type AB

a) Given this information, circle all the true statements.

Type A blood is dominant to type B blood.

Type A blood is dominant to type O blood.

Type O blood is recessive to blood types A and B.

Type A and type B blood types are codominant.

Type B blood is codominant to type A blood and dominant to type O blood.

Type B blood is incompletely dominant to type A blood but dominant to type O blood.

b) A dad with type B blood and a mom with type A blood have a child with type O blood. Give the genotypes of the two parents.

Answers to example problem

a) Given this information, circle all the true statements.

Type A blood is dominant to type B blood.

Type A blood is dominant to type O blood.

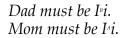
Type O blood is recessive to blood types A and B.

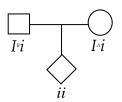
Type A and type B blood types are codominant.

Type B blood is codominant to type A blood and dominant to type O blood.

Type B blood is incompletely dominant to type A blood but dominant to type O blood.

b) A dad with type B blood and a mom with type A blood have a child with type O blood. Give the genotypes of the two parents.





Problems:

(1.3.1) Suppose that the height of a hypothetical plant is controlled by one gene with two incompletely dominant alleles.

a) What phenotypes would be expected in the offspring from a cross of a tall plant and a short plant?

b) What phenotypes would be expected in the offspring from a cross of two medium plants?

(1.3.2) Suppose that the hair length of a hypothetical mammal is controlled by one gene with two codominant alleles.

a) What phenotypes would be expected in the offspring of the cross of a long-haired critter and a short-haired critter?

b) What phenotypes would be expected in the offspring of a cross of two critters with mixed long and short hair?

(1.3.3) Suppose that color in a hypothetical flower is controlled by one gene with three alleles. Assume that blue color is dominant to all, and red color is dominant to green, but recessive to blue. Using the alleles C^{B} , C^{R} , and c, construct a table of all six possible genotypes and the corresponding phenotypes.

(1.3.4) Consider the flower color in a hypothetical plant. Make a genetic model that fits the following data and give the genotypes of the different groups of individuals.

Cross 1: Blue-flowered plant \times white-flowered plant

gives F₁: all pale-blue-flowered

Cross 2: Pale-blue $F_1 \times$ pale-blue F_1

gives F₂: 27 blue 49 pale-blue 24 white (1.3.5) You are studying eye color in an imaginary fly. You know that red, white, and green eye colors are seen and that eye color is controlled by a single gene.

Cross 1:

 $\overline{You cross}$ two green-eyed flies and get some green-eyed and some white-eyed offspring.

a) Given only cross 1, generate the simplest genetic model that fits the data. i) Define your allele symbols clearly.

ii) What are the genotypes of the two parents of cross 1?

iii) What is/are the genotype(s) of the green-eyed offspring?

Cross 2:

 \overline{red} -eyed imes white-eyed gives half red-eyed and half green-eyed offspring

b) Now give a genetic model that fits <u>all the data from both crosses</u>: <u>Note:</u> your answers to parts (a) and (b) need not be the same.

i) Define your allele symbols clearly.

ii) What are the genotypes of the two parents of <u>cross 2</u>?

(1.3.6) You're the director of Beth Israel Hospital's maternity ward, and you have four mixed-up babies, with blood types of O, A, B, and AB. The four sets of desperate parents are threatening to sue you if you don't get their babies back. You know the blood types (phenotypes) of the parents are:

i) AB and O

ii) A and O

iii) A and AB

iv) O and O

You also know that each set of parents has only one child (no sets of twins, that is). Match each baby with its parents.

(1.3.7) You solved the baby mystery with flying colors and received a commendation from the hospital director for brilliance. Two days later, however, you are faced with an even more complicated situation: a male (George, type B blood) and a female (Sallie, type A blood) claim that a newborn (Fred, type B blood) is their son.

a) Given this information, is it possible that George and Sallie are Fred's parents? (explain briefly)

b) You learn that George's father has type A blood and his mother has type B blood. Given this information, is it possible that George and Sallie are Fred's parents? (explain briefly)

c) On further investigation, you find that George's sister has type O blood. Given this information, is it possible that George and Sallie are Fred's parents? (explain briefly)

d) Finally, you discover that both of Sallie's parents are type AB. Given this information, is it possible that George and Sallie are Fred's parents? (explain briefly)

(1.3.8) A woman with blood type O has a child with blood type O. She claims that her friend, Bob, is the child's father.

a) Bob's blood type is A. Can he be excluded as the father on this evidence alone?

b) Does the fact that Bob's mother has type A blood and his father has type AB blood exclude him from being the parent?

c) Does the additional information that Bob's mother's parents are both AB permit him to be excluded?

(1.3.9) You are working in the maternity ward of a major Boston hospital. There are three babies in your care:

<u>Baby</u>	Blood type
Cathy	А
Steve	В
Rodger	0

One of the doctors has lost all the information matching the babies with their parents. Your job is to match the babies with their parents. So far, you have blood-type data on only two couples:

- Couple #1: **Tom** (type AB) and **Ann** (type A)
- Couple #2: **Peter** (type B) and **Sally** (type B)

The other couple has not yet given you blood samples. With the data you have, you try to match the babies and parents.

a) Given the information on the previous page, can you <u>rule out</u> any of the couples as the parents of any of the babies? Explain your reasoning.

b) You learn that Ann's parents have blood types AB and AB. Based on the information you have <u>so far</u>, can you exclude any of the couples as the parents of any of the babies? Explain your reasoning.

c) You learn that Peter's parents have blood types B and O and that Sally's parents have blood types AB and AB. Based on the information you have <u>so far</u>, can you exclude any of the couples as the parents of any of the babies? Explain your reasoning.

(V3) Virtual Genetics Lab III In this section, you will work VGLII problems that include a larger set of possible models. All involve one gene with two or three alleles and a maximum of three different phenotypes. The problems involve the following four models:

- *Two alleles with simple dominance* this will yield two different phenotypes. You have worked with problems of this type before; we have included them in this set to make you stretch your knowledge of genetics a little.
- *Two alleles with incomplete dominance* this will yield three different phenotypes: homozygote 1, homozygote 2, and the heterozygote. Because VGLII chooses traits randomly, the heterozygote's phenotype may not be intermediate between the two homozygotes (for example, six legs may be the heterozygote of four legs and two legs).
- *Three alleles with "hierarchical" dominance* this will yield three different phenotypes. In this case, A¹ is dominant to A² and A³, A² is dominant to A³ and recessive to A¹, and A³ is recessive to all. It is not clear that situations such as these occur in nature, but we have included them to help you explore more advanced genetic models.
- *Three alleles with "circular" dominance* this will yield three different phenotypes. In this case, B^A is dominant to B^B, B^B is dominant to B^C, and B^C is dominant to B^A. It is not clear that situations such as these occur in nature, but we have included them to help you explore more advanced genetic models.

We have generated a VGLII problem with each of these types of inheritance so that you can explore the differences between these models. To run them, double-click on the VGL icon in the "Genetics" folder. Then choose "Open Work…" from the File menu and select one of the following files from the "**APAIB/VGL Files**" in *111 Materials*:

- *Two alleles with incomplete dominance* **Problem3_ID.wr2** In this case:
 - \circ W^Y W^Y = yellow wing color
 - \circ W^B W^B = black wing color
 - \circ W^B W^Y = brown wing color
- *Three alleles with "hierarchical" dominance* **Problem3_HD.wr2** In this case:
 - \circ W^L W^L = black wing color
 - \circ W^R W^R = brown wing color
 - \circ W^G W^G = green wing color
 - \circ W^L W^R = black wing color
 - \circ W^L W^G = black wing color
 - \circ W^R W^G = brown wing color
- *Three alleles with "circular" dominance* **Problem3_CD.wr2** In this case:
 - \circ B^L B^L = black body color
 - \circ B^R B^R = brown body color
 - \circ **B**^P **B**^P = purple body color
 - \circ B^L B^R = black body color
 - $\circ \quad B^{L} B^{P} = brown body color$
 - $\circ \quad B^{R} B^{P} = purple \text{ body color}$

Be sure to click "Show model and all genotypes" and click "Continue."

Spend some time working with each model to be sure that you understand the differences between them.

Now that you are familiar with these models, you should try a few problems where you have to determine the model yourself.

As a reminder, since VGLII selects characters and traits randomly, the particular traits do not necessarily indicate the dominance relationships. That is, although you might expect otherwise, having no antennae may be dominant to having antennae. Similarly, having four legs may not be the heterozygote of two legs and six legs.

You should solve several VGLII problems at this level; keep at it until you are sure that you understand the differences between simple, incomplete, hierarchical, and circular dominance and how to tell them apart.

- Double-click the VGLII icon in the "Genetics" folder.
- Choose "New Problem" from the "File" menu.
- Select "VGL/Level07.pr2" to start; it allows practice mode. Try not to look at the "answer" at first.
- Solve the problem.
- Have a friend check your work. Your friend picks any two insects and you predict the expected offspring. You then do the cross to see if your prediction is correct. You can also move up to Level 8, which has the same genetic models but does not allow you to look at the answer.

Chapter 1: Genetics Problems

(1.3.10) You are studying a strange (and hypothetical) population of alien plants; these plants are diploid. You find plants in two colors: purple and blue. You do some crosses to find out how color is inherited.

<u>Cross 1</u>			Cross 2				
<u>P:</u> <u>F</u> :	purple 247 20	X ↓ 7 purple 62 blue	blue	<u>P:</u> <u>F:</u> :	purple	× ↓ 460 purpl	blue e

a) <u>Based on this information only</u>, give a genetic model of color inheritance in these plants. Define appropriate allele symbols and give their contribution to phenotype:

You find some red plants and do some more crosses:

<u>Cross 3</u>	Cross 4	<u>Cross 5</u>	
purple × purple	purple \times purple	blue 🗙 red	
↓ 3:1 purple:blue	∛ 3:1 purple:red	all blue	

b) Based on all the information provided in this question, give a genetic model of color inheritance in these plants. Define appropriate allele symbols and give their contribution to phenotype:

c) Using the symbols you defined in part (b), give the genotypes of the following parents. If more than one genotype is possible, <u>give all possibilities</u>.

• Cross 1	purple parent	
• Cross 2	purple parent	
• Cross 3	purple parent	
• Cross 4	purple parent	
• Cross 5	blue parent	

One Gene; More Complex Models, I

(1.3.11) A zoologist friend of yours has just discovered a new creature whose most striking characteristic is its vivid coat colors. She has promptly named the creature *Marge tribblicus*, commonly known as the tribble. Tribbles come in coat colors of pink, green, red, or white. Your friend is interested in understanding the inheritance of tribble coat colors and asks you for your help. She gives you pure-breeding green, red, and white tribbles. You set up the following crosses with them:

<u>Cross 1:</u> produced:	P:	one green tribble \times one red tribble F_1 : 10 green tribbles
<u>Cross 2:</u> produced:	P:	one green tribble \times one white tribble F_1 : 10 green tribbles

After these results you plan cross 3 where you cross the green F_1 tribbles from cross 1 with the green F_1 tribbles from cross 2:

Cross 3:	P: green F_1 tribble from cross 1 \times green F_1 tribble from cross 2
produced:	F_1 : 31 green tribbles and 10 pink tribbles

a) What is the simplest explanation for the results from these three crosses? Give the genotypes of each class of progeny.

b) Predict the results of a cross of the pink F_1 tribble from cross 3 and a pure-breeding green tribble.

(1.4) One gene; sex linkage

In this section you will explore problems that follow simple dominance and have two alleles for the gene of interest. What is unique about these problems is that the gene of interest is carried on one of the sex chromosomes. All diploid organisms have two copies of each chromosome, the exception being the sex chromosomes. In mammals, females have two copies of the X chromosome but males have only one copy of the X chromosome and one copy of the Y chromosome. Different organisms have alternative sex determination systems. In birds, males have two of the same sex chromosomes and females have two different sex chromosomes. Male birds have the genotype, with respect to the sex chromosomes, of ZZ. Female birds have the genotype, with respect to the sex chromosomes, of ZW.

The inheritance pattern of a single gene trait carried on a sex chromosome differs from the autosomal inheritance patterns that we have seen so far. For example, in the following fly cross:

Female with short wings ll	× ↓	Male with long wings LL
50%	Ll	Females with long wings
50%	Ll	Males with long wings
Because all offspring get one chro		me from each parent, they all get an L allele from

dad and they all show the dominant phenotype.

But in a cross where the gene of interest is on the X chromosome, we see a different outcome. Note the standard allele symbols designating X chromosome linkage.

Female with short wings $X^{l} X^{l}$	× ↓	Male with long wings $X^L Y$
50% 50%	$\begin{array}{c} X^L X^l \\ X^l Y \end{array}$	Females with long wings Males with short wings

All offspring get one sex chromosome, X^1 , from mom. They also must get a sex chromosome from dad, but it can be either X^L or Y. A fly that gets the X^L from dad is female and shows the dominant phenotype. A fly that gets Y from dad is male and shows the recessive phenotype because he has only one allele for the wing length trait, the X^1 allele.

With traits carried on the X chromosome (X-linked traits), males will tend to show recessive traits more frequently than females. In general, you should suspect sex linkage if you see a result where particular phenotypes are not equally distributed between the different sexes. For example, this result:

- <u>#</u> <u>Phenotype</u>
- 25 red male
- 22 green male
- 26 red female
- 24 green female

does not suggest sex linkage because there are roughly equal numbers of red and green males and females. This does not mean that sex linkage is not involved, just that this result, on its own, does not provide evidence for sex linkage. On the other hand, this result:

- <u>#</u> <u>Phenotype</u>
- 25 red male
- 27 green female

strongly suggests sex linkage. Although there are both red and green offspring and both males and females, you see that there are no green males and no red females – the phenotypes are not distributed equally by sex.

Problems

(1.4.1) Consider the following X-linked trait in a hypothetical mammal with XX/XY sexdetermination where red eyes are dominant to white eyes.

a) Predict the expected offspring from the following crosses:

i) White-eyed female \times red-eyed male.

ii) Red-eyed female \times white-eyed male (there are two possibilities here; give both).

Consider the following Z-linked trait in a hypothetical bird with ZZ/ZW sex determination where red eyes are dominant to white eyes.

b) Predict the expected offspring from the following crosses:

i) White-eyed female \times red-eyed male (there are two possibilities here; give both).

ii) Red-eyed female \times white-eyed male.

(1.4.2) There are now four possible modes of inheritance to consider when solving human pedigrees:

- Autosomal recessive (AR)
- Sex-linked recessive (SLR)
- Autosomal dominant (AD)
- Sex-linked dominant (SLD)

In most of the problems in this book, we will not consider sex-linked dominance. This is because sex-linked dominant diseases are very rare, but, more important, it is very difficult to tell a sex-linked dominant pedigree from an autosomal dominant one (see later).

As we have said before, when working pedigrees, it is often useful to have certain diagnostic configurations that can be used to rule out one or more modes of inheritance. For each of the three types of inheritance listed below, give a combination of parents (either diseased or normal) that give offspring (either diseased or normal) that are <u>inconsistent</u> with that mode of inheritance.

a) A combination that is inconsistent with autosomal recessive.

b) A combination that is inconsistent with sex-linked recessive.

c) A combination that is inconsistent with autosomal dominant.

(V4) Virtual Genetics Lab IV In these two problems, you will work with XX/XY and then ZZ/ZW sex linkage.

a) In this VGLII problem, eye color is controlled by a gene located on the X chromosome. In these insects, females are XX and males are XY, and short wing is dominant to knobbed wing.

- go to http://intro.bio.umb.edu/MOOC/jsVGL/JsVGL_V4a.html
- Click on the "Genetic Model" button.

Select two insects, get their genotypes, predict the expected offspring, and check your prediction. Keep doing this until you are sure you understand the differences between this and autosomal inherited characters.

b) In this VGLII problem, body color is controlled by a gene located on the Z chromosome. In these insects, females are ZW, males are ZZ, and black eye is dominant to yellow eye.

- go to http://intro.bio.umb.edu/MOOC/jsVGL/JsVGL_V4b.html
- Click on the "Genetic Model" button.

Select two insects, get their genotypes, predict the expected offspring, and check your prediction. Keep doing this until you are sure you understand the differences between this and autosomal inherited characters.

(1.5) Pedigrees involving one gene, II

In analyzing pedigrees, the objective is to produce a genetic model that fits the data given. Assume the trait is associated with one gene with two alleles, one disease allele and one normal allele. A complete model includes the following two components. 1) The mode of inheritance: autosomal recessive, sex-linked recessive, or autosomal dominant.

* Note that there are two ways that questions regarding the mode of inheritance can be phrased:

Which modes of inheritance are consistent with this pedigree? Of the three modes of inheritance, which can explain this pedigree? There can be more than one answer to this question.

What is the most likely mode of inheritance? If more than one mode is consistent with the pedigree, then it is sometimes possible to decide which of the consistent modes is more likely. To evaluate which mode of inheritance is more likely, determine the number of unrelated carriers that are required for each mode. If you can assume that unrelated carriers are rare, the mode that requires the fewest unrelated carriers is the more likely.

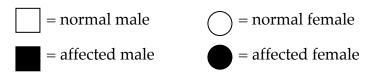
2) The genotypes of all individuals in the pedigree.

If the trait is rare, individuals who marry into the family are unlikely to be carriers. We also assume that rare events like nondisjunction and mutation do not occur.

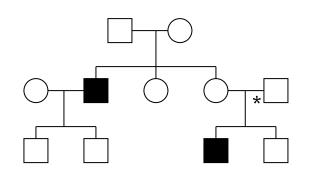
(1.5.1) For each of the following pedigrees:

- What is the most likely mode of inheritance for this trait?
- Give the genotypes of all individuals in this pedigree.
- Suppose the couple indicated with an asterisk have another son. What is the chance that he will be affected?

Key to Symbols:

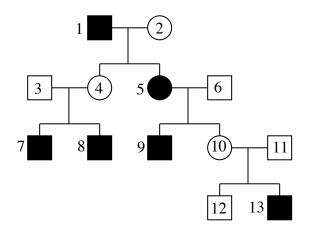






a)

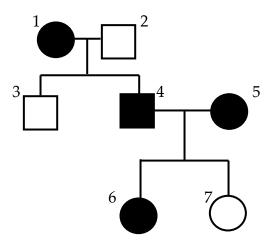
(1.5.2) Consider the following pedigree for a <u>rare</u> genetic trait:



a) What is the most likely mode of inheritance for this trait?

b) Based on your answer to part (a), define appropriate symbols and give the genotypes of all the members of this family.

(1.5.3) Consider the following pedigree for a rare human genetic trait.



- a) What is the most likely mode of inheritance of this trait?
- b) Based on your model of part (a), define appropriate allele symbols.
- c) Using your symbols from part (b), give the genotypes of all members of the family.

d) If 4 and 5 have another daughter, what is the chance that this daughter will be affected? Justify your answer.

(1.5.4) Hemophilia is a genetic disease that causes affected individuals to have difficulty forming blood clots. It is inherited as an X-linked recessive trait. Apparently, certain ancient cultures were aware of this. For example, the Talmud instructs Jews to perform circumcision (surgical removal of the foreskin) on all males **except** those whose mother's brother is a "bleeder" (hemophiliac).

a) Does this exemption make sense in genetic terms? Why or why not? Explain, using a pedigree.

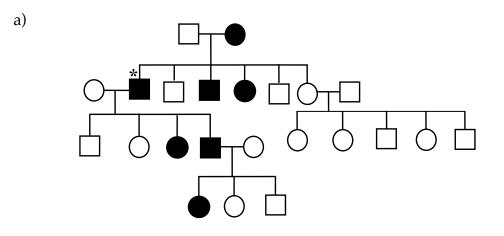
b) There is no similar exemption for a son whose father's brother is a bleeder. Is this an oversight, or does it make sense in genetic terms? Why or why not? Explain, using a pedigree.

c) Should an exemption be made for the son of a mother whose father is a bleeder? Explain.

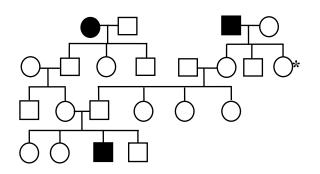
(1.5.5) For the following human pedigrees, determine:

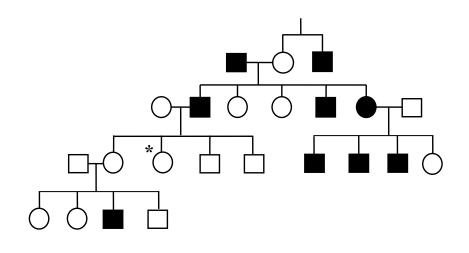
i) The most likely mode of inheritance.

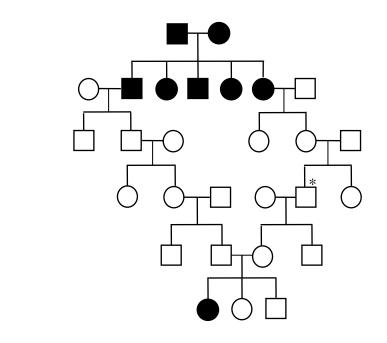
ii) The probable genotype of the individual marked with an asterisk (*). Assume that the disease allele is rare. "Rare" means that individuals who marry into the family are very unlikely to have the defective allele. Explain your reasoning and include any ambiguities. Be sure to define your genotype symbols clearly.



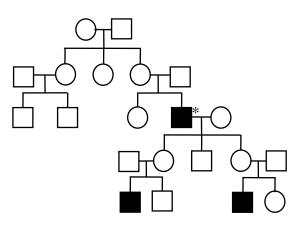
b)



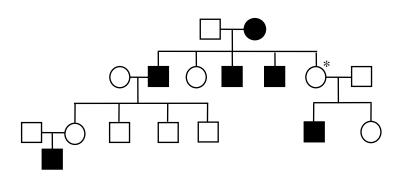




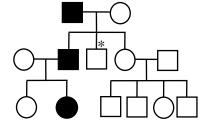
d)



f)



g)



(1.6) One gene; more complex models, II

(V5) Virtual Genetics Lab V In this section, you will work VGLII problems that include an even larger set of possible models. All involve one gene with two alleles and only simple dominance. They may involve autosomal or sex linkage. If they are sex-linked traits, they can be either XX/XY or ZZ/ZW. Your task is to find out:

1) Is this trait XX/XY sex linked, ZZ/ZW sex linked, or autosomal?

2) Which trait is dominant and which is recessive?

You should solve several VGLII problems at this level; keep at it until you are sure that you understand the differences between autosomal and sex-linked traits and how to tell them apart.

- Double-click the VGLII icon in the "Genetics" folder.
- Choose "New Problem" from the "File" menu.
- Select "**OneGene/OneGen06p.pr2**" to start; it allows practice mode. Try not to look at the "answer" at first.
- Solve the problem.
- Have a friend check your work. Your friend picks any two insects and you predict the expected offspring. You then do the cross to see if your prediction is correct. You can also move up to **OneGene/OneGene06.pr2**, which has the same genetic models but does not allow you to look at the answer.

(V6) Virtual Genetics Lab VI These are the most challenging VGLII problems. There are 12 possible genetic models. All the problems in VGLII involve genetic models with one gene that has two or three alleles. Based on this, there are several features that can vary:

- <u>The number of alleles;</u> this can be either:
 - <u>Two alleles</u> (Models 1, 2, 3, 4, 5, and 6). Given this, there are two possible **interactions between the alleles**:
 - <u>Simple Dominance</u> (Models 1, 3, and 5). The heterozygote has the same phenotype as the dominant homozygote.
 - <u>Incomplete Dominance</u> (Models 2, 4, and 6). The heterozygote has a different phenotype than either homozygote. In nature, this is usually intermediate; in VGL it need not be.
 - <u>Three alleles</u> (Models 7, 8, 9, 10, 11, and 12). Given this, there are two possible **interactions between alleles**:
 - <u>Hierarchical Dominance</u> (Models 7, 9, and 11). A is dominant to all; A' is dominant to A'' and recessive to A; A'' is recessive to all (A > A' > A'').
 - <u>Circular Dominance</u> (Models 8, 10, and 12). B is dominant to B'; B' is dominant to B''; B'' is dominant to B.
- <u>Whether the trait is sex linked or not;</u> this can be either:
 - <u>Not sex linked</u> (Models 1, 2, 7, and 8). The gene for the character is carried on an autosome so it is inherited identically in both sexes.
 - <u>Sex linked</u>. The gene for the trait is located on a sex chromosome so it is inherited differently in different sexes. **This can be either**:
 - <u>XX/XY</u> (Models 3, 4, 9, and 10). Females are XX; males are XY. Here, Y carries no genes except those needed to make the organism male.
 - <u>ZZ/ZW</u> (Models 5, 6, 11, and 12). Females are ZW; males are ZZ. Here, W carries no genes except those needed to make the organism female.

This leads to six possible genetic models.

- <u>Model 1</u>: 2 alleles; Simple Dominance; Autosomal.
- <u>Model 2</u>: 2 alleles; Incomplete Dominance; Autosomal.
- <u>Model 3</u>: 2 alleles; Simple Dominance; XX/XY Sex linked.
- <u>Model 4</u>: 2 alleles; Incomplete Dominance; XX/XY Sex linked.
- <u>Model 5</u>: 2 alleles; Simple Dominance; ZZ/ZW Sex linked.
- <u>Model 6</u>: 2 alleles; Incomplete Dominance; ZZ/ZW Sex linked.
- <u>Model 7</u>: 3 alleles; Hierarchical Dominance; Autosomal.
- <u>Model 8</u>: 3 alleles; Circular Dominance; Autosomal.
- <u>Model 9</u>: 3 alleles; Hierarchical Dominance; XX/XY Sex linked.
- <u>Model 10</u>: 3 alleles; Circular Dominance; XX/XY Sex linked.
- <u>Model 11</u>: 3 alleles; Hierarchical Dominance; ZZ/ZW Sex linked.
- <u>Model 12</u>: 3 alleles; Circular Dominance; ZZ/ZW Sex linked.

Your task is to find the genetic model that best fits your data.

Chapter 1: Genetics Problems

You should know that, since VGLII selects traits randomly, the particular traits do not necessarily indicate the dominance relationships. That is, although you might expect otherwise, having no antennae may be dominant to having antennae. Similarly, having four legs may not be the heterozygote of two legs and six legs.

You should solve several VGLII problems at this level; keep at it until you are sure that you understand the differences between the models and how to tell them apart.

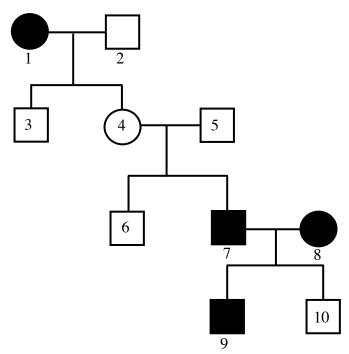
- Double-click the VGLII icon in the "Genetics" folder.
- Choose "New Problem" from the "File" menu.
- Select "VGL/Level09.pr2" to start; it allows practice mode. Try not to look at the "answer" at first.
- Solve the problem.
- Have a friend check your work. Your friend picks any two insects and you predict the expected offspring. You then do the cross to see whether your prediction is correct. You can also move up to Level 10, which has the same genetic models but does not allow you to look at the answer.

(3) CHALLENGE PROBLEMS

All different types of problems can be found in this section. The first part of the challenge is to establish what type of question you are dealing with. Ask yourself: Is the problem concerned with one gene or more than one gene? Does the inheritance pattern fit simple dominance or is it more complicated? Does the question involve linked genes? Once you decide where to begin, these problems may provide additional surprises.

Problems

(3.1) You are studying a human disease to see whether it is inherited or not. You construct the following pedigree and find that it is not consistent with any of the usual modes of inheritance.



a) Which part of the pedigree is inconsistent with <u>autosomal dominant</u> inheritance? Redraw that portion in the space below and explain why it is <u>inconsistent</u> with <u>autosomal dominant</u> inheritance. If more than one part of the pedigree is appropriate, you need draw only one part. You may explain in words or by using genotypes as you prefer.

b) Which part of the pedigree is inconsistent with <u>autosomal recessive</u> inheritance? Redraw that portion in the space below and explain why it is <u>inconsistent</u> with <u>autosomal recessive</u> inheritance. If more than one part of the pedigree is appropriate, you need draw only one part. You may explain in words or by using genotypes as you prefer.

c) Which part of the pedigree is inconsistent with <u>sex-linked recessive</u> inheritance? Redraw that portion in the space below and explain why it is <u>inconsistent</u> with <u>sex-linked recessive</u> inheritance. If more than one part of the pedigree is appropriate, you need draw only one part. You may explain in words or by using genotypes as you prefer.

d) If you changed **<u>one</u>** of the <u>unaffected</u> individuals to <u>affected</u>, the pedigree would be consistent with <u>autosomal recessive</u> inheritance. Which individual would you change? If more than one is possible, give only one.

(3.2) You are helping Sigourney Weaver study those nasty sci-fi aliens. You have found that the aliens are diploids, their genes behave like those of earth animals, and the two different sexes have different sex chromosomes, but you are unsure whether XX is female and XY is male or ZZ is male and ZW is female.

You discover that they have three blood types, which you label type α , type β , and type γ . While wearing a protective suit, you perform the following crosses and observe the results:

- Cross 1: male $\alpha \times$ female β 25% male α progeny: 25% male β 25% female γ 25% female β Cross 2: male $\beta \times$ female γ progeny: 50% male α 50% female β Cross 3: male $\gamma \times$ female β 50% male α progeny: 50% female γ Cross 4: male $\beta \times$ female β 50% male β progeny: 50% female β Cross 5: male $\gamma \times$ female γ progeny: 50% male γ 50% female γ Cross 6: male $\alpha \times$ female γ
 - progeny: 25% male α 25% male γ 25% female γ 25% female β

a) Based on these data, construct a simple, plausible model for the inheritance of blood type in these organisms. Be sure to indicate:

- the number of genes and alleles involved
- the genotypes that correspond to each blood type
- whether any of the blood type genes are located on sex chromosomes, and
- which sex determination system is being used; i.e., are females XX or ZW?

b) No females with blood type α were described above. Based on your model, is it possible to find a female with blood type α ? Explain your reasoning.