

LAB 10 – Principles of Genetic Inheritance

Objectives

1. Examine the nature of probability.
2. Solve various types of genetics problems.

Overview

In this laboratory you will learn about the basic principles of genetic inheritance, or what is commonly referred to as “**genetics**”. A true appreciation of the nature of genetic inheritance will require solving of a variety of genetics problems, and to do so you will need to understand several related concepts, some which should be familiar and others which may be new to you. Thus you will begin this lab by examining the concepts of **genes**, **gamete** production by **meiosis**, and **probability**. You will then use these concepts to work through a series of genetics problems addressing various aspects of genetic inheritance in plants and animals.

Part 1: KEY GENETIC CONCEPTS

We all know that when living organisms reproduce, their offspring are much like their parents. Chickens don't give birth to lizards and apple trees don't give rise to pine trees. So what is the biological basis for this obvious reality? You probably already know this has to do with genes, genes one inherits from one's parents. However the process of passing on genes from one generation to the next is more complex than it may appear.

The simplest form of genetic inheritance involves **asexual** reproduction. This is the case when a single parent organism passes its genes to offspring which are basically clones of the parent (i.e., genetically, and for the most part, physically identical). Although this mode of reproduction is quite convenient (imagine if you could simply have children identical to yourself, no partner necessary!), it has one extremely significant shortcoming: **NO genetic diversity!** For some species asexual reproduction works quite well, however for most plants and animals (including humans) this just won't cut it, genetic diversity is too important.

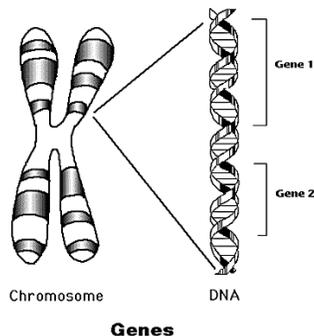
So how is genetic diversity produced? The answer is **sexual reproduction**: the production of **gametes** (sperm and eggs) by **meiosis** followed by the fusion of sperm and egg (fertilization) to form a new, genetically unique individual. Although a lot more work, sexual reproduction “shuffles” the genes of each parent producing a unique combination of parental genes in each and every offspring. This is the sort of genetic inheritance we will focus on, genetic inheritance based on sexual reproduction.

Through sexual reproduction, each offspring inherits a *complete* set of genes from each parent, however the study of genetic inheritance is generally limited to one or two genes at a time. Thus when you begin to work with genetics problems you will focus initially on a single gene at a time, and then learn how to follow the inheritance of more than one gene. To focus on large numbers of genes would be rather complicated and is not necessary for our purposes.

Before you begin to examine genetic inheritance via genetics problems, you will need to understand some important concepts that are central to the process: the nature of **chromosomes**, **genes** and genetic **alleles**; the process of **gamete production** by **meiosis**; and the concept of **probability**. Once these concepts and their associated terminology are clear, you will then be ready to immerse yourself into the world of genetic inheritance.

Chromosomes, Genes and Alleles

As you learned previously, **chromosomes** are extremely long pieces of DNA in the nuclei of cells that contain up to a thousand or more genes each. Each species of organism has a characteristic number of chromosome types: distinct chromosomes each having a unique set of genes and a unique length. For example, the fruit fly *Drosophila* has only 4 types of chromosomes – 3 **autosomes** (non-sex chromosomes) and the X and Y **sex chromosomes**. Human beings (*Homo sapiens*) on the other hand have 23 types of chromosomes – 22 autosomes and the sex chromosomes (X and Y) as illustrated in the human male **karyotype** shown below (notice the X and Y sex chromosomes):



Notice one more thing about this human karyotype: there are two of each autosome as well as two sex chromosomes. This is because human beings are **diploid**, which means having **two** of each chromosome type. Most plants and animals are in fact diploid, and as we investigate the process of genetic inheritance we will only concern ourselves with diploid species. However you should be aware that not all organisms are diploid. Some are normally **haploid** (one of each chromosome) such as the fungi, and some may have more than two of each chromosome (e.g., four of each = **tetraploid**, eight of each = **octoploid**) as seen in a fair number of plant species as well as a few animal species.

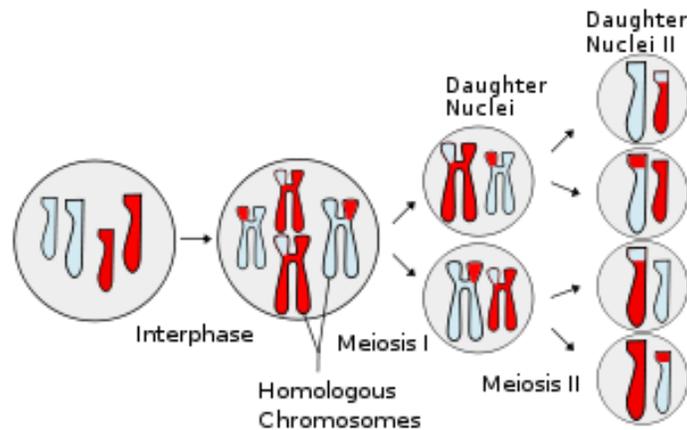
As shown in the diagram to the left, **genes** are discrete sections of chromosomal DNA responsible for producing a specific protein or RNA molecule. The process of **gene expression**, the production of protein or RNA from a gene, will be addressed in next week's lab.

The functional protein or RNA molecule produced from a particular gene is its **gene product**. It is important to realize that the DNA sequence of a gene, and hence its gene product, can vary within a species. In other words, a particular gene in a species such as *Homo sapiens* can have different versions, what are referred to in genetics as **alleles**. The gene products produced from an organism's genetic alleles account for its physical and behavioral characteristics, what we collectively call an organism's **traits**. Specific traits an individual exhibits, whether physical or behavioral, are referred to as the individual's **phenotype**. The specific genetic alleles an individual has for a particular gene is the individual's **genotype**. As you shall soon see, an individual's phenotype is largely determined by its genotype.

Since diploid organisms have two alleles for each gene, an individual can have two copies of the *same* allele for a gene or two different alleles. If the alleles are the same, the individual is said to be **homozygous** for that gene. If the alleles are different, the individual is said to be **heterozygous** for that gene. When an individual is heterozygous for a gene, one allele may override or “mask” the other allele by determining the phenotype regardless of the other allele. In this situation, the allele that determines the phenotype is said to be **dominant** while the other allele is said to be **recessive**. The terms dominant and recessive are *relative* terms just like the terms *big* and *small*. Something is only big or small in relation to something else, and in the same way an allele for a gene is only dominant or recessive in relation to another allele for the same gene.

Meiosis and the Production of Gametes

Sexual reproduction in diploid plant and animal species requires the production of haploid **gametes** by the process of **meiosis** which is illustrated below.



Since meiosis was covered in the previous lab, we won't review the process in much detail other than to remind you of several key points that pertain to genetic inheritance:

- 1) Diploid organisms have **two** of each chromosome type, one haploid set of chromosomes inherited from the mother (**maternal** chromosomes) and another haploid set inherited from the father (**paternal** chromosomes), and thus **two alleles** for each gene, one maternal allele and one paternal allele.
- 2) The haploid gametes produced by meiosis (egg or sperm) contain **one** of each chromosome type (e.g., **one** of each autosome and **one** sex chromosome), and thus contain only **one allele** for each gene.
- 3) It is completely random which chromosome of a given type, maternal or paternal, ends up in a gamete produced by meiosis. Thus it is completely random which allele for a particular gene (maternal or paternal) ends up in a gamete.
- 4) Since an individual has only two alleles for each gene, there is a 50% chance that either allele (maternal or paternal) will end up in a given gamete.

These points are central to the study of genetics as it pertains to sexual reproduction. Diploid parent organisms produce large numbers of haploid gametes, any of which may fuse at the moment of fertilization to produce a diploid **zygote**, a genetically unique new individual. It is the combination of alleles inherited from each parent that determine the genotype and phenotype of each new offspring.

Given the variety of possible genotypes and phenotypes for the offspring of any two parents, genetics must also address the **probability** of each possibility. So before you begin working with genetic crosses it is important that you understand basic concepts of probability...

Probability

To understand genetic inheritance, you need to have a basic understanding of **probability**. Probability refers to the *likelihood* that something will happen as opposed to what actually happens. For example, we all know that a single coin flip has a 50% chance of being “heads” or “tails”, thus the probability of heads is 50% or 0.5 or $\frac{1}{2}$ as is the probability of tails. However we also know that we cannot know what the outcome of a single coin flip will be. All we can do is predict the likelihood or **probability** of each possible outcome, in this case heads or tails.

When analyzing the inheritance of genes you will also be dealing with probabilities. When two organisms mate and produce offspring we cannot know what genetic alleles will be inherited by a given individual (genotype) or its physical characteristics (phenotype). We can only predict the *likelihood* of various characteristics based on the probability of inheriting particular genetic alleles from each parent. The next two exercises will help illustrate the nature of probability and help prepare you to solve genetics problems.

Exercise 1A – Probability and sample size

In this exercise you will perform several sets of coin flips. This will be done to compare the predicted outcomes based on probability to the actual outcomes, and how this relates to sample size (i.e., the number of repetitions):

1. On your worksheet, determine the expected numbers of heads and tails for sample sizes of 10 and 50 coin flips (the probability of heads is 50% or 0.50, as is the probability of tails).
2. Perform 5 sets of 10 coin flips, recording the numbers of heads and tails for each set on your worksheet and calculating the corresponding percentages.
3. Combine the results for all 5 sets of coin flips on your worksheet to get a total number of heads and tails out of 50 coin flips and calculate the corresponding percentages.
4. Add your group’s numbers of heads and tails for 50 coin flips to the table on the white board. Once all groups have done the same, record the total numbers of heads and tails for the **entire class** on your worksheet and calculate the corresponding percentages.
5. On your worksheet, compare the actual results to expected results for each set of 10 coin flips as well as the combined set of 50 coin flips and answer the corresponding questions.

When flipping a coin there are only two possible outcomes, each with the same probability. Sometimes, however, you must deal with more than two possible outcomes, each with a different probability. This is the case, for example, when you roll a pair of dice, for which there are eleven possible outcomes in terms of the total sum: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12.



The probabilities of each possible sum of the dice are not the same. If you have ever played a board game (or craps!) you know for example that a roll totaling 7 is much more likely than a roll totaling 2. So why are the probabilities different? It has to do with how many different combinations add up to a given sum. For example, to roll a pair of dice and get a sum of 2, both dice must show a “1”. There is no other way to roll a total of 2 with a pair of dice. There are *six* different ways, however, to roll a 7:

<u>Red die</u>	<u>Black die</u>	<u>total</u>
1	6	7
6	1	7
2	5	7
5	2	7
3	4	7
4	3	7

So how do you determine the probabilities of each possible sum of the dice? As shown in the matrix below, there are 6 x 6 = 36 different combinations yielding 11 possible sums:

	black 1	black 2	black 3	black 4	black 5	black 6
red 1	2	3	4	5	6	7
red 2	3	4	5	6	7	8
red 3	4	5	6	7	8	9
red 4	5	6	7	8	9	10
red 5	6	7	8	9	10	11
red 6	7	8	9	10	11	12

Each die has six possible outcomes (1 through 6), each of which are equally likely and each of which can be paired with any roll on the other die. Looking carefully at the matrix, you can see there is one combination out of 36 that yields a sum of 2 (probability = 1/36 or 0.028 or 2.8%), two combinations that yield a sum of 3 (2/36 or 0.056 or 5.6%), three combinations that yield a sum of 4 (3/36 or 0.083 or 8.3%), and so on.

If you think about it, the rolling of a pair of dice is actually *two* events that happen to occur simultaneously. Whether you roll the red die or black first, or both at the same time, is irrelevant. The probability of rolling a sum of 2 (“snake eyes”) for example is still 1/36, regardless of the timing. This leads to an important rule regarding probability commonly referred to as the “product rule”:

*The probability of a specific combination of two or more outcomes is the **product** of the probabilities of each individual outcome.*

In our “snake eyes” example, the probability of rolling 1 on the red die is $1/6$ and the probability of rolling 1 on the black die is $1/6$, thus the probability of rolling 1 on both the red die **AND** the black die is $1/6 \times 1/6$ which equals $1/36$. Another example would be the probability of flipping two coins and having both turn up “heads”, or in other words the probability of coin 1 **AND** coin 2 both yielding “heads”. Using the rule above the probability would be $1/2 \times 1/2$ which is $1/4$.

Another important rule commonly called the “sum rule” or “addition rule” addresses probability when there are *multiple* ways to arrive at a particular outcome:

*The probability of an outcome that can occur in multiple ways is the **sum** of the probabilities of each individual outcome.*

For example, we have already determined that the probability of rolling a sum of 3 with a pair of dice is $2/36$ since there are 2 different ways to obtain a sum of 3: red 1 plus black 2 ($1/36$) **OR** red 2 plus black 1 ($1/36$). Each outcome yields a roll of 3 and by adding both probabilities you arrive at an *overall* probability of $2/36$.

Another example would be the flipping of a coin. The probability of flipping heads **OR** tails on a given toss is clearly 100%: 50% heads + 50% tails = 100%. What about the probability of flipping two coins and getting heads for one and tails for the other? There are actually two ways this can occur:

heads from coin 1 *and* tails from coin 2 ($50\% \times 50\% = 25\%$)

OR

tails from coin 1 *and* heads from coin 2 ($50\% \times 50\% = 25\%$)

In this case the overall probability of getting one heads and one tails from two coin flips is $25\% + 25\%$ which equals 50%.

You are now ready for the next set of exercises in probability, and keep in mind that the probability of X **AND** Y occurring means you *multiply*, and the probability of X **OR** Y occurring means you *add*.

Exercise 1B – Multiple outcomes with variable probabilities

In this exercise you will perform multiple rolls of a pair of dice. This will demonstrate the nature of probability when there are more than two possible outcomes, each with different probabilities:

1. On your worksheet, determine the probability of each possible sum for a pair of dice, and the expected occurrences of each sum in 72 rolls of the dice.
2. Roll a pair of dice 72 times, recording the results on your worksheet as you do so, and answer the corresponding questions on your worksheet.

Part 2: SOLVING GENETICS PROBLEMS

Important Tools for Solving Genetics Problems

Before you begin to solve genetics problems it is important that you are familiar with the types of symbols used to represent genetic alleles as well as two important tools you will use to solve genetic problems. Let's first address the symbols for genetic alleles:

Symbolizing Alleles

Genetic alleles are generally represented by a single letter, with the dominant allele being upper case and the recessive allele being lower case:

dominant allele – **A**

recessive allele – **a**

When working with more than one gene in a genetic problem, the alleles of each gene will be represented using a different letter:

Gene 1

dominant allele – **A**

recessive allele – **a**

Gene 2

dominant allele – **B**

recessive allele – **b**

When writing the genotype for an individual it is best to keep the alleles for a particular gene next to each other and to list a dominant allele before a recessive allele:

Aa Bb

If an allele is unknown, represent it as a line or underscore:

A_ bb

When there are more than two alleles for a gene, different superscripts on a single letter are commonly used to distinguish alleles:

alleles – **C^x, C^y, C^z**

genotype – **C^xC^y**

When a gene is located on the X chromosome ("X-linked gene"), alleles are represented by superscripts on a capital X. In males a "Y" without a superscript is used to symbolize the Y chromosome which would not have an allele for the X-linked gene:

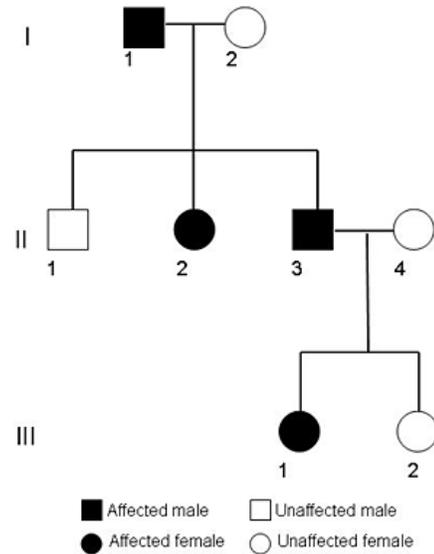
female genotype for an X-linked gene – **X^AX^a**

male genotype for an X-linked gene – **X^AY**

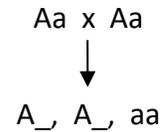
Pedigrees

For some problems it will be helpful to diagram a pedigree of all family members relevant to the problem as shown here for three generations of a hypothetical family.

As you can see, males are represented by squares and females by circles. Individuals exhibiting the phenotype of concern have a filled-in symbol. Pedigrees are useful in that they allow you to represent all familial relationships visually so that you can fill in and deduce as many genotypes as possible. In addition, they also allow you to deduce the mode of inheritance of the condition in question (i.e., dominant vs recessive condition, sex-linked vs autosomal gene).



On many occasions you may find it simpler to diagram your pedigree without shapes and colors, and simply represent individuals in the pedigree by their genotypes (or as much of the genotype as you know) as shown to the right.



Punnett squares

Another extremely useful tool is the **Punnett square**, which is basically a grid or matrix showing all possible combinations of gametes from each parent to produce offspring. A Punnett square is useful if you know the genotypes of the parents being crossed. Once you determine all possible haploid gametes for each parent you simply fill out the Punnett square as shown below:

cross: Aa (female) x Aa (male)

gametes: A & a (female); A & a (male)

	A	a
A	AA	Aa
a	Aa	aa

By placing the different gametes for each parent along either side of a Punnett square, it becomes easy to fill in all possible combinations of egg and sperm. All that's left is to determine the probabilities of each genotype and/or phenotype. This gets a bit more complicated when dealing with two genes, however the principle is the same as shown in the next example:

cross: Aa Bb x Aa bb

gametes: AB, Ab, aB & ab; Ab & ab

	AB	Ab	aB	ab
Ab	AA Bb	AA bb	Aa Bb	Aa bb
ab	Aa Bb	Aa bb	aa Bb	aa bb

Notice that the Punnett square doesn't have to be a square at all, it simply needs to accommodate all parental gametes and their possible combinations, nothing more.

Types of Genetics Problems

Solving genetics problems involves using the known characteristics of some individuals to deduce unknown characteristics of other individuals. The characteristics given will relate to phenotype (physical description), genotype (genetic alleles), or both. In general, the genetics problems you will be asked to solve are of two basic types:

- 1) Characteristics of the parents are given and you must determine the probabilities of each possible type of offspring.
- 2) Characteristics of the offspring are given and you must deduce characteristics of the parents.

Regardless of which type of problem you are solving, you will need to use the principles we have addressed in Part 1 (genes, alleles, meiosis, gametes, probability), the tools reviewed in the previous section, and basic logic and common sense. The approach to solving each type of problem, however, is slightly different.

Solving Type 1 problems

In Type 1 problems, you will be given characteristics of the parents being crossed and asked to figure out the probabilities of all possible genotypes and/or phenotypes in the offspring. Solving such problems will require 4 basic steps:

- 1) **Determine the genotypes of both parents and write out the cross.**
 - genotypes may be given in the problem or you may have to deduce them
- 2) **Determine the genotypes of *all* possible gametes produced by each parent, and write them on opposing sides of a Punnett square.**
 - gametes are *haploid* and thus have one allele for each gene of interest
- 3) **Fill in all offspring genotypes in the Punnett square.**
 - all possible combinations of different eggs and sperm must be accounted for
- 4) **Determine the probabilities of each possible genotype/phenotype in the offspring.**

To illustrate these steps let's solve the sample problem below:

*In pea plants, purple flower color is determined by a dominant allele **P** and white flower color is determined by a recessive allele **p**. If two heterozygous pea plants with purple flowers are crossed, what are the probabilities of each possible genotype and phenotype in the offspring?*

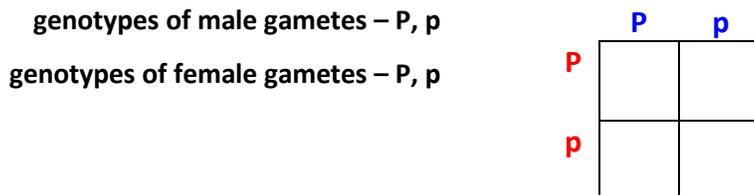
Step 1: Write out the genotypes of each parent in the cross.

Due to the phrase "two heterozygous pea plants with purple flowers are crossed" we know that the genotypes of the parents being crossed must be:

$$Pp \times Pp$$

Step 2: Determine the genotypes of all different gametes produced by each parent, and arrange them on either side of a Punnett square.

Due to meiosis, each parent will produce haploid gametes containing either the **P** allele or the **p** allele, each in equal proportions (50% of each):



Step 3: Determine all possible genotypes in the offspring.

Simply fill in the **Punnett square** with the genotypes of all possible unions of gametes:

	P (1/2)	p (1/2)
P (1/2)	PP (1/4)	Pp (1/4)
p (1/2)	Pp (1/4)	pp (1/4)

NOTE: The probabilities of each gamete and each resulting offspring genotype are shown in parentheses, though this normally would not be necessary.

Step 4: Summarize the probabilities of each possible genotype/phenotype in the offspring.

The Punnett square above reveals that there are only 4 different combinations of sperm and egg yielding 3 possible genotypes and 2 possible phenotypes. Probabilities are determined by following the **product rule** (e.g., **P and P** in a gamete = $\frac{1}{2} \times \frac{1}{2} = \frac{1}{4}$) and the **sum rule** (e.g., **Pp or Pp** = $\frac{1}{4} + \frac{1}{4} = \frac{1}{2}$):

<u>Genotypes</u>	<u>Phenotypes</u>
$\frac{1}{4}$ PP	$\frac{3}{4}$ purple flowers ($\frac{1}{4} + \frac{1}{4} + \frac{1}{4}$)
$\frac{1}{2}$ Pp ($\frac{1}{4} + \frac{1}{4}$)	$\frac{1}{4}$ white flowers
$\frac{1}{4}$ pp	

Once you complete step 4 you will have your answer. Whether you represent the probabilities as fractions, decimals or percentages is up to you. All that matters is that the value for each probability, regardless of how it is presented, is correct. Now you are ready for the next exercise in which you will solve similar problems on your own...

Exercise 2A – Type 1 genetics problems

For the following two problems, tall plant height is determined by a dominant allele (**T**) and short plant height is determined by a recessive allele (**t**). Determine the probabilities for all possible **genotypes and phenotypes** of the offspring resulting from each cross.

1. homozygous dominant (**TT**) x heterozygous (**Tt**)
2. heterozygous (**Tt**) x homozygous recessive (**tt**)

Solving Type 2 problems

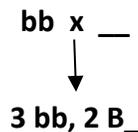
In Type 2 problems you will be given the characteristics of offspring and must figure out the characteristics of one or both parents. To solve such problems simply follow these two steps:

- 1) **Diagram a pedigree containing all individuals in the problem, and indicate the genotypes of as many individuals as possible using the information provided.**
- 2) **Use the pedigree to deduce the information the problem asks for.**

Let's do a sample problem of this type:

*In cats, black fur color is determined by a dominant allele **B** and white fur color is determined by a recessive allele **b**. A white cat gives birth to 3 white kittens and 2 black kittens. What is the genotype and phenotype of the father?*

Step 1: Diagram a pedigree showing the genotypes.



The phenotypes given for the mother cat and her kittens indicate the genotypes above (for this problem a full pedigree is not necessary, a simple diagram such as this will suffice).

Step 2: Deduce missing genotypes in pedigree to arrive at the answer.

Since some of the kittens are white (**bb**), both parents must carry the white allele (**b**). Since some of the kittens are black (**B_**), at least one parent must have a black allele (**B**) which in this case can only be the father. Thus the father cat must be **black** with the genotype **Bb**, which is the answer to the problem. Though not asked in the problem, you can also deduce that the black kittens all have the genotype **Bb** since all kittens receive a white allele (**b**) from the mother. Keep in mind, **it is always a good idea to confirm your answer with a Punnett square based on the parental genotypes you have deduced.**

$$\begin{array}{c}
 \text{bb} \times \text{Bb} \\
 \downarrow \\
 3 \text{ bb}, 2 \text{ Bb}
 \end{array}$$

Exercise 2B – Type 2 genetic problems

Albinism in human beings (lack of skin pigment) is due to a recessive allele. Use **A** to represent the dominant “normal” allele and **a** to represent the recessive albinism allele in solving the two problems below:

1. An albino child is born to two parents with normal skin pigmentation. What are the genotypes of the parents?
2. An albino woman has 8 children with the same man, 5 of which are albino. What can you conclude about the father?

Incomplete Dominance, Codominance, and Multi-Allelic Inheritance

The problems you have solved so far are relatively straightforward as far as genetics problems go. In each case the problem involved only one gene, two alleles, and the alleles were either dominant or recessive. The next few problems you will solve involve some new issues that are frequently encountered in genetics.

The first issue is **incomplete dominance**, which occurs when a heterozygous genotype results in a phenotype that is intermediate between the two homozygous phenotypes. For example, two different alleles for a single gene result in three different colors of carnation flowers. The **R** allele results in red pigment production (red) and the **r** allele results in a *lack* of pigment production (white). The three possible genotypes and phenotypes are shown below:

<u>Genotype</u>	<u>Phenotype</u>
RR	red carnations
Rr	pink carnations
rr	white carnations

This clearly is not complete dominance, otherwise the heterozygotes (**Rr**) would have red flowers. The white allele is still considered recessive since it results in the *lack* of pigment. However there is less red pigment with one red allele (**Rr**) than with two red alleles (**RR**). Thus in this case we would say that the red allele is *incompletely* dominant over the white allele.

The nice thing about incomplete dominance is that the phenotype reveals the genotype, something you will appreciate when you solve problems such as those in the next exercise...

Exercise 2C – Incomplete dominance

*In snapdragons, red flowers are produced by homozygous **RR** plants and white flowers are produced by homozygous **rr** plants. Heterozygous plants (**Rr**) produce pink flowers. Solve the following problems on your worksheet, being sure to show all your work:*

1. Indicate the probabilities of each genotype and phenotype resulting from the a cross between two pink snapdragons.
2. A cross between two snapdragons produced 15 offspring with red flowers and 17 offspring with pink flowers. What are the genotypes and phenotypes of the parents?

Some traits involve a gene that has more than two alleles. One such example is human ABO blood type which is determined by a single gene with three different alleles. The “A” and “B” alleles each result in a different glycoprotein on the surface of red blood cells. When present in the same individual, both alleles are expressed equally resulting in the AB blood type. This is an example of **codominance**. The “O” allele produces no glycoprotein and thus is recessive to both the “A” and “B” alleles. Based on these relationships the three alleles are symbolized I^A , I^B , and i , with the various ABO genotypes and phenotypes summarized below:

<u>Genotype</u>	<u>Blood Type</u>
$I^A I^A$	A
$I^A i$	A
$I^B I^B$	B
$I^B i$	B
$I^A I^B$	AB
ii	O

Refer to the information above as you solve genetic problems involving human ABO blood type in the next exercise...

Exercise 2D – Multi-allelic inheritance and codominance

Solve the following problems on your worksheet, being sure to show all your work:

1. Indicate the probabilities of each genotype and phenotype in the children of a woman with blood type O and a man with blood type AB.
2. A woman with blood type A and a man with blood type B have 3 children, one each with blood types A, B and O. What are the genotypes of the parents?

Sex Linkage

All of the genetic problems you have solved up to this point involve genes on an **autosome**, i.e., any chromosome that is *not* a sex chromosome. For genes on autosomes, inheritance patterns are generally no different for males and females. This is not the case, however, for genes on the X and Y sex chromosomes. Females have two X chromosomes and thus two alleles for each gene on the X chromosome. Males have only one X chromosome along with a single Y chromosome. With very few exceptions, genes on the X chromosome are *not* found on the Y chromosome and vice versa. Thus males will have only one allele for each gene on the X chromosome.

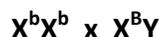
As a result of this disparity, the inheritance patterns for genes on the sex chromosomes are different for males versus females. This phenomenon is called **sex linkage**, which refers to genetic inheritance that differs depending on the sex of the individual. Genes on the X chromosome, referred to as **X-linked**, and genes on the Y chromosome, referred to as **Y-linked**, exhibit sex linkage or **sex-linked inheritance**. Because there are so few genes on the Y chromosome, we will limit our focus to X-linked genes.

The approach to solving genetic problems involving X-linked genes is basically the same as for autosomal genes. The alleles for X-linked genes are symbolized using an “X” with a superscript representing the allele (e.g., X^A). In place of a second allele in males the symbol “Y” is used, with no superscript, to represent the Y chromosome. Let’s now look at a sample problem:

In humans, a genetic allele responsible for color-blindness is recessive and X-linked. If a color-blind woman and a man with normal color vision plan to have children, what sort of color vision would you predict in their children?

Step 1: Write out the genotypes of each parent in the cross.

Using X^B and X^b to represent the dominant normal and recessive color-blindness alleles, respectively, the only possible genotypes for “a color-blind woman and a man with normal color vision” are:



Step 2: Determine the genotypes of all different gametes produced by each parent.

By meiosis, the woman produces eggs all with the genotype X^b . The man produces sperm containing his X chromosome (X^B) or his Y chromosome:

genotype of female gametes – X^b
genotypes of male gametes – X^B or Y

Step 3: Determine all possible genotypes in the offspring.

Simply draw a **Punnett square** accounting for all parental gametes and fill in all possible genotypes for the children:

	X^B	Y
X^b	X^BX^b	X^bY

Step 4: Summarize the probabilities of each possible genotype/phenotype in the offspring.

Whenever the results of a cross differ for males and females, you should indicate the probabilities for male and female genotypes/phenotypes separately. The answer to this problem therefore is best expressed as follows:

100% of their girls will have normal color vision (though all will be carriers)

100% of their boys will be color-blind

Hopefully it is clear that the method of solving an X-linked genetic problem is really not much different than solving any other problem. Some general features of X-linked genes you may have realized by solving this problem and should keep in mind are:

- sons always receive their X chromosome from their mother (dad contributes Y)
- daughters always receive their father's X chromosome
- females are diploid for X-linked genes and can be **carriers** of recessive alleles
- males are **hemizygous** for X-linked genes (have only one allele) and thus show the phenotype of the single allele inherited from the mother

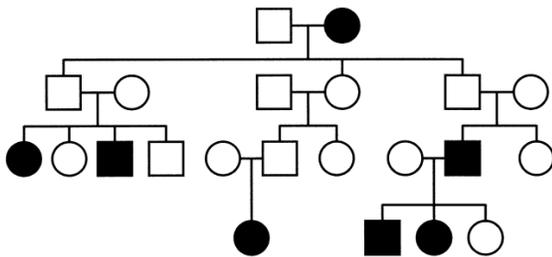
Exercise 2E – X-linked inheritance

Hemophilia, like color-blindness, is an X-linked recessive condition. Solve the following problems on your worksheet, being sure to show all your work:

1. A normal woman whose father is a hemophiliac marries a normal man. What are the odds that hemophilia will afflict any given male child? any given female child?
2. A couple has three children, a normal boy and a boy and girl each with hemophilia. What can you say about the parents?

Interpreting Pedigrees

As mentioned earlier, pedigrees can be a very useful tool to visualize phenotypes in a family lineage (see page 8 of this lab). Once a pedigree has been produced one can deduce the likely mode of inheritance of the genetic condition (i.e., dominant vs recessive, autosomal vs X-linked) and as a result determine the genotypes of various individuals in the pedigree. To illustrate this let's consider some examples:

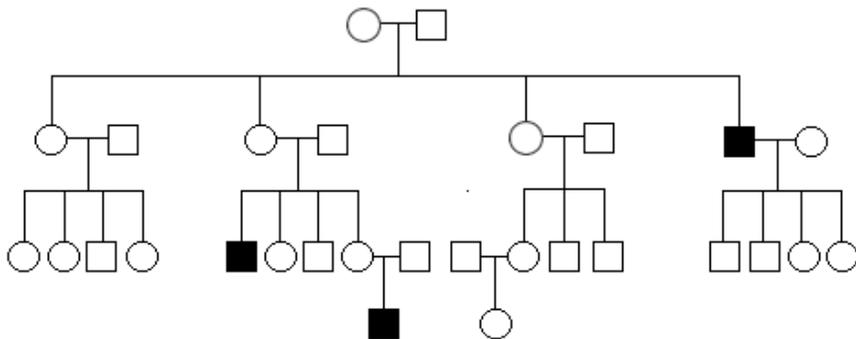


This pedigree reveals an **autosomal recessive** mode of inheritance, i.e., the gene responsible for the genetic condition is recessive and located on an autosome (non-sex chromosome). The condition is clearly recessive since unaffected couples have affected children. This would not be possible with a dominant allele. You will also notice that the condition “skips a generation” which also is only possible with a recessive

allele. It also appears to be autosomal since males and females are affected equally (recall that males are far more likely to be affected by an X-linked recessive condition). You should also examine affected females such as the one at the top of the pedigree. If a condition is actually X-linked then all sons of affected females would have the condition. If this is not the case, as in this pedigree, the gene must be on an autosome.

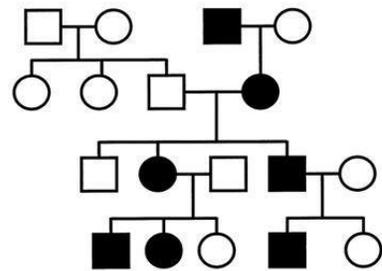
Once the mode of inheritance has been determined, genotypes can then be deduced for everyone in the pedigree. For example, all affected individuals above must be homozygous recessive (aa) and if two unaffected parents have affected children, they both must be heterozygous (Aa). For some unaffected individuals the second allele cannot be deduced based on the pedigree and thus is unknown (A?).

Here is an example of a pedigree revealing a genetic condition to be **X-linked recessive**. This condition is recessive for the same reasons as the previous pedigree. It is most likely X-linked since only males are affected. However this cannot be said with 100%

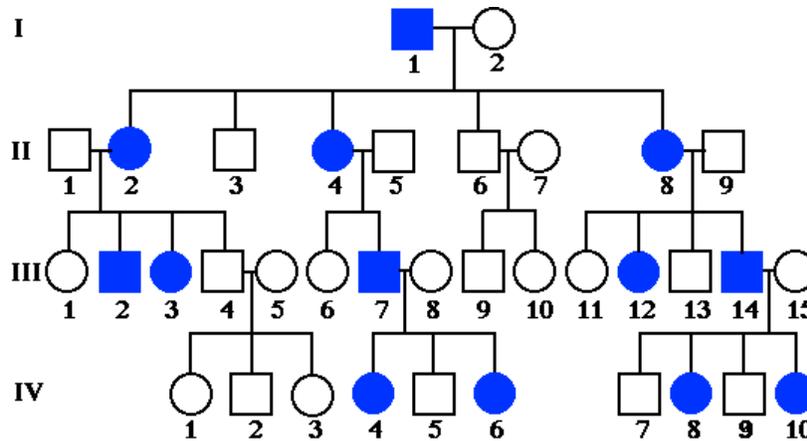


certainly since there is a slight chance the gene responsible for this condition is autosomal and by random chance only males are affected in this family.

The next example shows an **autosomal dominant** condition. Notice that, consistent with a condition caused by a dominant allele, there are affected individuals who show up every generation. Also, there are no unaffected couples having affected children as you would see with a recessive condition. This condition cannot be X-linked since, if it was, all fathers would pass the condition to their daughters since all daughters receive their fathers X chromosome. If you look carefully you will see one affected father having an unaffected daughter making it certain that the locus of this mutant allele is an autosome.



The last example on the next page shows an **X-linked dominant** condition. It has all the characteristics of a dominant condition as indicated for the previous pedigree. You can tell if the condition is X-linked by looking at the offspring of an affected man and an unaffected woman (there are 3 such couples in this pedigree). Remember that fathers give their X chromosome to all daughters and their Y chromosome to all sons. Thus if the condition is X-linked and dominant, all daughters of these men should be affected and all of their sons should be unaffected. All 7 daughters of these men have the condition, whereas none of their 5 sons are affected. The odds of this occurring for an autosomal dominant condition would be 2^{-12} or 1 in 4096 since there would be a 50% chance for each daughter to inherit the condition and a 50% chance for each son to be unaffected. Therefore it is almost certain that this genetic condition is dominant and X-linked.



In the next exercise for this lab you will practice diagramming and interpreting pedigrees.

Exercise 2F – Interpreting pedigrees

Solve the following problems on your worksheet, being sure to show all your work:

1. Examine the pedigree on your worksheet and determine the mode of inheritance (dominant or recessive, autosomal or X-linked). Based on the mode of inheritance, determine the genotypes of each individual in the pedigree representing any unknown alleles with a question mark (?).
2. A hypothetical mutation in a single gene results in a “zombie” phenotype. A normal man and woman have 3 children – a zombie girl, a normal girl and a normal boy. The man has a normal sister and mother but his father is a zombie. The woman has a normal brother and both her parents are normal. Diagram a pedigree of this family and determine the mode of inheritance for the zombie condition. Once you have done so, determine the genotypes of all family members and indicate any unknown alleles with a question mark (?).

The Inheritance of Multiple Genes

When following the inheritance of more than one gene, the approach is similar to single gene inheritance. The trick is to correctly determine all different parental gametes and keep track of the alleles for each gene. To illustrate how this is done, let’s do a sample problem:

*In pea plants, flower color is determined by a dominant purple allele **P** and a recessive white allele **p**, and plant height is determined by a dominant tall allele **T** and a recessive short allele **t**. A tall pea plant with purple flowers that is heterozygous for both genes is crossed with a short plant with purple flowers that is heterozygous for flower color. What are the probabilities of each possible phenotype in the offspring?*

Step 1: Write out the genotypes of each parent in the cross.

Tt Pp (tall purple plant) x tt Pp (short purple plant)

These are the only genotypes consistent with the information given in the problem.

Step 2: Determine the genotypes of all different gametes produced by each parent.

By meiosis, each parent will produce haploid gametes containing one allele for each gene. The different gametes produced by each parent are:

TP, Tp, tP, tp (tall purple plant)

tP, tp (short purple plant)

Step 3: Determine all possible genotypes in the offspring.

Draw a **Punnett square** showing the gametes for each parent and fill in the genotypes of all possible offspring:

	TP	Tp	tP	tp
tP	Tt PP	Tt Pp	tt PP	tt Pp
tp	Tt Pp	Tt pp	tt Pp	tt pp

Step 4: Summarize the probabilities of each possible phenotype in the offspring.

Based on the Punnett square, 3 out of 8 genotypes give a “tall purple” phenotype, 3 of 8 “short purple”, 1 of 8 “tall white”, and 1 of 8 “short white”. Thus the probabilities of all possible phenotypes in the offspring are:

- 3/8 – tall with purple flowers**
- 3/8 – short with purple flowers**
- 1/8 – tall with white flowers**
- 1/8 – short white flowers**

Problems such as this can get rather complicated, however if you keep track of all alleles properly at each step, you can easily solve any such problem.

Exercise 2G – Genetics problems involving two genes

Solve the following problems on your worksheet, being sure to show all your work:

1. Indicate the probabilities of all phenotypes in the offspring of two tall pea plants with purple flowers, both of which are heterozygous for both genes.
2. A normal woman with an albino father and no family history of hemophilia plans to have children with a hemophiliac man with normal skin pigmentation whose mother is albino. Determine the probabilities of all possible phenotypes in their children.

Before you leave, please make sure your table is clean, organized, and contains the supplies listed below so that the next lab will be ready to begin. Thank you!

Supply List: Set of 10 pennies in container; Pair of dice (2 colors)

LABORATORY 10 – WORKSHEET

Name _____

Section _____

Exercise 1A – Probability and sample size

Probability of heads = _____

Probability of tails = _____

Fill in the table to the right with your **predictions** of heads and tails in 10 and 50 coin flips **based on the probabilities above**:

	10 coin flips	50 coin flips
heads		
tails		

Record the numbers of heads & tails and the percentages for your **actual** coin flips:

set >	1	%	2	%	3	%	4	%	5	%	all	%
heads		%		%		%		%		%		%
tails		%		%		%		%		%		%
TOTAL	10	100%	10	100%	10	100%	10	100%	10	100%	50	100%

Use the table on the right to record the **results for the entire class** (which should be compiled on the whiteboard):

	class	percent
heads		%
tails		%
TOTAL		100%

- Compare the results for sample sizes of 10, 50 and the whole class and comment on which sample size comes closest to the **probability** of heads and tails you determined above.

Exercise 1B – Multiple outcomes with variable probabilities

Refer to the matrix on page 5 of the lab description to fill in the probabilities for each sum of the dice ($n/36$), the predicted number of occurrences for each sum in 72 rolls of the dice, and your actual results:

sum >	2	3	4	5	6	7	8	9	10	11	12	total
probability (n/36)												1
expected out of 72												72
actual numbers												72

- How well did your actual rolls of the dice correlate with the expected numbers based on probability?

- How could you improve this exercise to see if the probabilities you determined are truly accurate?

NOTE: As you solve the following sets of genetics problems, be sure to SHOW YOUR WORK!

Exercise 2A – Type 1 genetics problems

1. homozygous dominant (**TT**) x heterozygous (**Tt**)

2. heterozygous (**Tt**) x homozygous recessive (**tt**)

Exercise 2B – Type 2 genetics problems

1. An albino child is born to two parents with normal skin pigmentation. What are the genotypes of the parents?

2. An albino woman has 8 children with the same man, 5 of which are albino. What is the father's genotype?

Exercise 2C – Incomplete dominance:

1. Indicate the probabilities of each genotype and phenotype resulting from the a cross between two pink snapdragons.

2. A cross between two snapdragons produced 15 offspring with red flowers and 17 offspring with pink flowers. What are the genotypes and phenotypes of the parents?

Exercise 2D – Multi-allelic inheritance and codominance

1. Indicate the probabilities of each genotype and phenotype in the children of a woman with blood type O and a man with blood type AB.

2. A woman with blood type A and a man with blood type B have 3 children, one each with blood types A, B and O. What are the genotypes of the parents?

Exercise 2E – X-linked Inheritance

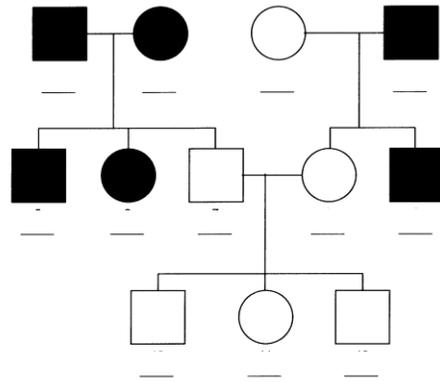
1. A normal woman whose father is a hemophiliac marries a normal man. What are the odds that hemophilia will afflict any given male child? any given female child?

2. A couple has three children, a normal boy and a boy and girl each with hemophilia. What can you say about the parents?

Exercise 2F – Interpreting pedigrees

1. Examine the pedigree shown and determine the mode of inheritance:

- a) dominant or recessive (circle one)
- b) autosomal or X-linked (circle one)



Based on the mode of inheritance, fill in the genotypes of each individual in the pedigree representing any unknown alleles with a question mark (?).

2. A hypothetical mutation in a single gene results in a “zombie” phenotype. A normal man and woman have 3 children – a zombie girl, a normal girl and a normal boy. The man has a normal sister and mother but his father is a zombie. The woman has a normal brother and both her parents are normal. Diagram a pedigree of this family and determine the mode of inheritance for the zombie condition. Once you have done so, determine the genotypes of all family members and indicate any unknown alleles with a question mark (?).

Exercise 2G – Genetics problems involving two genes

1. Indicate the probabilities of all phenotypes in the offspring of two tall pea plants with purple flowers, both of which are heterozygous for both genes.

2. A normal woman with an albino father and no family history of hemophilia plans to have children with a hemophiliac man with normal skin pigmentation whose mother is albino. Determine the probabilities of all possible phenotypes in their children.

Supplemental Problems

To ensure you understand the key aspects of genetic inheritance you will need to practice solving genetic problems much like the ones you've solved in this laboratory. What follows are sets of genetic problems grouped by category. Your instructor will indicate which of the following additional genetic problems you should solve on your own in order to complete this laboratory. Be sure to do these problems on a separate sheet of paper and to **show your work**.

SINGLE GENE PROBLEMS

The following four problems all relate to albinism, where "n" represents the gene for albinism and "N" represents the gene for normal pigmentation.

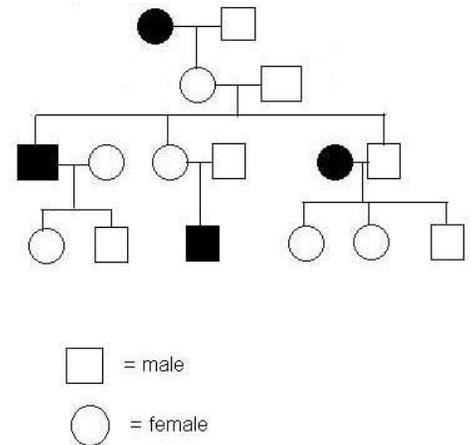
1. What would be the expected genotypes and phenotypes of the children and their relative frequencies from the following crosses (assume there are many children)?

a) NN x nn	b) Nn x nn
c) Nn x Nn	d) nn x nn
2. A normally pigmented man marries an albino woman. If their first child is albino, what are the genotypes of the child and each parent? If the parents have more children, what other genotypes are possible?
3. An albino man marries a normally pigmented woman. They have 13 children, all of whom are normally pigmented. What are the likely genotypes of the children and parents?
4. A normally pigmented man whose father is albino marries an albino woman, both of whose parents are normally pigmented. They have three children, two normally pigmented and one albino. Indicate the genotypes for all three generations of this family (*this best done by drawing a pedigree of the family*).

In Drosophila, a type of fruit fly, the long-wing allele (L) is dominant over the vestigial-wing allele (l):

5. In a cross between a heterozygous long-winged male and a vestigial-winged female, what phenotypes and genotypes would be expected and in what proportions?
6. In a cross between two heterozygous long-winged flies, what phenotypes and genotypes would be expected and in what proportions?
7. If a heterozygous long-winged fly is mated with a homozygous long-winged fly, what percentage of the offspring would be expected to be homozygous long-winged? Would there be any vestigial-winged flies?
8. A long-winged fly mated with a fly having vestigial wings produces 35 long-winged and 33 vestigial-winged offspring. What are the genotypes of the parents and the offspring?
9. Mating a long-winged fly with a vestigial-winged fly produced 256 offspring, all of which were long-winged. What are the genotypes of the parents? Mating two of the F₁ offspring would produce what types of offspring in the F₂ generation?
10. In flies, gray body color is dominant over black body color. What would be the phenotypic and genotypic ratios of the progeny from a cross between a homozygous gray fly and a homozygous black fly? What would be the result of mating two of the F₁ offspring? Which of these F₂ offspring would always breed true when mated with siblings of the same phenotype?

11. The pedigree on the right shows the occurrence of cystic fibrosis, an autosomal recessive condition, in 4 generations of this family (individuals with cystic fibrosis are represented by black symbols). Determine the genotypes as best you can for each family member. (use **F** for the normal allele and **f** for the recessive mutant allele)



PROBLEMS INVOLVING TWO GENES

12. In guinea pigs, a rough coat is dominant over a smooth coat, and black hair is dominant over white hair. A rough-coated, black guinea pig whose mother is smooth and white is mated with a smooth, white guinea pig. What types of offspring would they produce and in what proportions?
13. A rough, black guinea pig bred with a rough, white one yielded the following offspring: 28 rough black, 31 rough white, 11 smooth black, and 9 smooth white. What are the genotypes of the parents?
14. Two rough, black guinea pigs produce two offspring, one rough white and the other smooth black. If these same parents were to have additional offspring, what proportion of phenotypes would you expect?
15. Mating a red-eyed fly with curved wings and a brown-eyed fly with straight wings yields F_1 offspring that are all red-eyed with straight wings. What proportion of phenotypes would you expect in the F_2 generation after crossing two of the F_1 flies?
16. In *Drosophila*, red eye color is dominant over brown eye color and pigmented ocelli (simple eyes located on the back of the head as opposed to the more prominent compound eyes) are dominant over white ocelli. A brown-eyed fly with pigmented ocelli is mated with a fly having red eyes and white ocelli, and some of their offspring have brown eyes and white ocelli. What are the genotypes of the parents?
17. In *Drosophila*, gray body color is dominant over ebony, and straight wings are dominant over curved. A gray-bodied female with curved wings is mated with a gray-bodied male with straight wings, yielding some ebony, curved-wing offspring. What other types of offspring could be produced and in what proportions?
18. A purple-flowered Jimson weed plant with smooth leaves is crossed with a white-flowered, spiny-leaved plant yielding 320 purple, spiny and 312 purple, smooth offspring. If these two types of offspring are bred together, what proportion of phenotypes would you expect in the offspring (assume spiny is dominant over smooth)?

For the next 3 problems, assume that brown eyes (B**) are dominant over blue eyes (**b**), and right-handedness (**R**) is dominant over left-handedness (**r**). (In reality, modifying factors complicate the inheritance of these traits)**

19. A right-handed, blue-eyed man whose father is left-handed marries a left-handed, brown-eyed woman from a family in which all the members have been brown-eyed for several generations. What types of children would be expected from this marriage regarding these phenotypes?

20. A brown-eyed, right-handed man marries a blue-eyed, right-handed woman. Their first child is blue-eyed and left-handed. If other children are born to this couple, what proportion of phenotypes could they expect in terms of eye color and handedness?
21. A right-handed, blue-eyed man marries a right-handed, brown-eyed woman. They have two children, one left-handed and brown-eyed and the other right-handed and blue-eyed. By a later marriage with another woman who is also right-handed and brown-eyed, the man has nine children, all of whom are right-handed and brown-eyed. What are the genotypes of this man and his two wives?

X-LINKED PROBLEMS

For these problems keep in mind that color-blindness and hemophilia are both X-linked recessive conditions.

22. Can a human male be homozygous for an X-linked character? From which parent does a male receive his X-linked genes? To which sex among his offspring does he transmit his X-linked genes? To which sex does a male transmit genes located on his Y chromosome?
23. Color-blindness is an X-linked recessive phenotype. A girl of normal vision whose father is color-blind marries a color-blind man. What sort of children might they have in terms of color vision.
24. A color-blind boy's parents and grandparents all have normal vision. What are the genotypes of his mother maternal grandmother?
25. Yellow body color in *Drosophila* is an X-linked characteristic that is recessive to gray body color (*Drosophila* females are XX and males XY as in humans). A gray female mated with an unknown male and produced some yellow and some gray offspring of both sexes. What is the *genotype* of the original female? What is the *phenotype* of the male with which she mated?
26. An albino, non-hemophiliac man marries a normally pigmented, non-hemophiliac woman whose father has hemophilia and whose mother is albino. What kinds of children might they have and in what proportions? (*recall that albinism is due to an autosomal recessive allele*)
27. Two normal-visioned parents have a color-blind son. What are the genotypes of the parents? What are the chances of their next child being a color-blind daughter?
28. In humans, migraine is due to an autosomal dominant allele. A normal-visioned woman who has never suffered from migraine headaches takes her daughter to a doctor for an examination. In the examination the doctor discovers that the girl is color-blind and suffers from migraine headaches. What does the doctor automatically know about the girl's father?
29. In humans, aniridia (a type of blindness) is due to an autosomal dominant allele, and optic atrophy (another type of blindness) is due to a recessive X-linked allele. A man blind from optic atrophy marries a woman blind from aniridia. Assuming that the woman is homozygous for both genes, would any of their children be expected to be blind? If so, what type of blindness would they have?
30. A non-hemophiliac man who is blind from aniridia (see previous problem) and whose mother is not blind marries a non-hemophiliac woman who is not blind and whose father has hemophilia. If they have four sons, what phenotypes would these boys likely have?
31. If the couple in the previous problem were to have 4 daughters, what would their phenotypes likely be?
32. A color-blind woman marries a normal-visioned man and they have two color-blind sons and two daughters one of which is color-blind. One son marries a normal-visioned woman and they have three

color-blind daughters and two normal-visioned sons. The second son marries a normal-visioned woman and they have two normal-visioned sons and two color-blind daughters. Diagram a pedigree of this family. What is the mode of inheritance of color blindness in this family? Based on the mode of inheritance, determine the genotypes of all family members and indicate any unknown alleles with a question mark (?).

MULTIPLE ALLELE PROBLEMS

In rabbits, four alleles for a single gene affecting coat color have the following relationships:

$$C > c^{ch} > c^h > c$$

Thus there are four possible phenotypes which are associated with the following genotypes:

full color – $C_ (C \text{ with any other allele})$

chinchilla – $c^{ch}c^{ch}$ or $c^{ch}c^h$ or $c^{ch}c$

Himalayan – c^hc^h or c^hc

albino – cc

33. Would it be possible for a cross between two chinchilla rabbits to result in both Himalayan and albino offspring? (be sure to qualify your answer)
34. A litter of rabbits contains four full-colored rabbits, two chinchillas and one albino. What must have been the genotypes of the parents?
35. For the following crosses indicate the phenotypes of the parents and the expected proportions of all possible offspring:

a) $Cc \times Cc^{ch}$

b) $c^{ch}c \times c^{ch}c$

c) $Cc^h \times Cc^h$

d) $c^hc \times cc$

e) $c^hc \times c^hc$

In mice, three alleles for a single gene affecting coat color have the following relationships:

$$A^Y > A > a$$

There are four possible phenotypes which are associated with the following genotypes:

yellow coat – A^YA or A^Ya

lethal (mice die in utero) – A^YA^Y

agouti (gray) – AA or Aa

black – aa

36. For the following crosses indicate the phenotypes of the parents and the expected proportions of all possible offspring:
- a) $A^Ya \times Aa$
- b) $A^Ya \times A^Ya$
- c) $AA \times Aa$
- d) $A^YA \times A^Ya$
- e) $A^YA \times A^YA$