

# Chapter 1

## Mendel

In the middle of the nineteenth century, an Austrian monk, Gregor Mendel, toiled for almost 10 years systematically breeding pea plants and recording his results. Like many of his contemporaries, Mendel was intrigued with heredity and wanted to uncover the laws behind it. In 1864, just five years after the publication of Charles Darwin's *Origin of Species*, Mendel presented his results to the local natural history society in Brunn<sup>1</sup> which published his paper in their proceedings one year later (Mendel, 1865).

To be honest, many historians surmise that Mendel's presentation and his paper were quite boring. They were crammed with numbers and percentages about green versus yellow peas, round versus wrinkled peas, axial versus terminal inflorescences, yellow versus green pods, red-brown versus white seed coats, etc. To make matters worse, many of these traits were cross-tabulated. Hence, his audience had to listen to numbers about round and yellow versus wrinkled and yellow versus round and green versus wrinkled and green pea plants.

Perhaps as a consequence of this, no one paid attention to Mendel, and the basic principles of genetics that he elucidated in his presentation and subsequent paper went unrecognized until shortly after the turn of the 20th century. Today, a *Mendelian trait* is a trait due to a single gene that follows classic Mendelian transmission. Likewise, a *Mendelian disorder* is one influenced by a single locus. In this chapter, we examine what Mendel accomplished and the terminology that has evolved to relate a single gene to an observed trait.

Figure 1.0.1: Gregor Mendel at age c. 40.



Image from [http://en.wikipedia.org/wiki/Gregor\\_Mendel](http://en.wikipedia.org/wiki/Gregor_Mendel)

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<sup>1</sup>During Mendel's time, Brunn was the capital of Moravia in the Austro-Hungarian empire. Today, it is called Brno and is in the Czech Republic. Mendel's monastery and pea garden are popular tourist destinations.

Table 1.1: Mendel's three laws.

Law	Explanation
Dominance	When two different hereditary factors are present, one will be dominant and the other will be recessive.
Segregation	Hereditary factors are discrete. Each organism has two discrete hereditary factors and passes one of these, at random, to an offspring.
Independent Assortment	The discrete hereditary factors for one trait (e.g., color of pea) are transmitted independently of the hereditary factors for another trait (e.g., shape of pea).

Mendel postulated three laws: (1) dominance, (2) segregation, and (3) independent assortment. Table 1.1 presents these laws and their definitions. First note the phrase “hereditary factor” in the table. This is the term that Mendel used in his original paper. The term *gene* was coined in 1909 by the Danish botanist Wilhelm Johannsen.

In the following sections, we will examine some of Mendel's actual data and try to deduce how Mendel may have arrived at them.

## 1.1 The law of dominance

Figure 1.1.1: Mendel's cross for round and wrinkled peas.

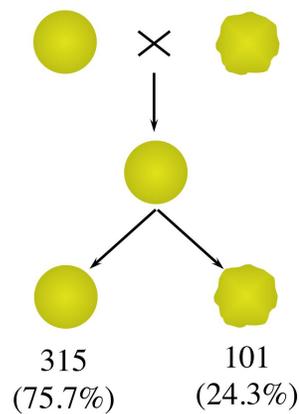


Figure 1.1.1 presents the results of one of Mendel's breeding experiments. Mendel began with two lines of yellow peas that always bred true. One line consistently gave round peas while the second always gave wrinkled peas. In a classic Mendelian cross, this is called the *parental* generation and two strains are abbreviated as P<sub>1</sub> and P<sub>2</sub>.

Mendel cross bred these two strains by fertilizing the round strain with pollen from the wrinkled strain and fertilizing the wrinkled strain with pollen from the round plants. This generates what is called the *first filial* generation or F<sub>1</sub>. The seeds from the next generation were all round. At this point, Mendel probably asked himself, “Whatever happened to the hereditary information about making a wrinkled pea?” Mendel did not stop at this point. He cross-fertilized

all the pea plants in this generation with pollen from other plants in the same generation. When their progeny matured, he noticed a very curious phenomenon—wrinkled peas reappeared! How could this happen when all the parents of these plants had round seeds? Obviously, the middle generation in Figure 1.1.1, despite being all round, still possessed some hereditary information for making a wrinkled pea. But somehow that information was not being expressed. Hence, Mendel surmised, some hereditary factors are dominant to other hereditary factors. In this case, a round shape is dominant to a wrinkled shape.

## 1.2 The law of segregation

Figure 1.1.1 gives the number and percentage of round and wrinkled peas in the third generation, technically called the *second filial* generation and abbreviated as  $F_2$ . There were just about three round seeds for every wrinkled seed. This ratio of 3 plants with the dominant hereditary factor to every one plant with the recessive factor kept coming up time and time again in Mendel's breeding program. There were 3.01 yellow seeds for every green seed; 3.15 colored flowers to every white flower; 2.95 inflated pods to every constricted pod. Mendel must have spent considerable time cogitating over a sound, logical reason why this 3:1 ratio should always appear.

To answer this question, let us return to Figure 1.1.1 and consider the middle generation in light of the law of dominance. Obviously, because they are themselves round, these plants must have the hereditary information to make a round pea. They must also have the hereditary information to make a wrinkled pea because one quarter of their progeny are wrinkled. Hence, these peas have two pieces of hereditary information. Mendel's stroke of genius lay in applying elementary probability theory to this generation—what would one expect if these two types of hereditary information were discrete and combined at random in the next generation?

The situation for this is depicted in Table 9.2 where  $R$  denotes the hereditary information for making a round pea and  $W$ , the information for a wrinkled pea. The probability that a plant in the middle generation transmits the  $R$  information is simply the probability of a heads on the flip of a coin or  $1/2$ . Thus, the probability of transmitting the  $W$  information is also  $1/2$ . Hence, the probability that the male parent transmits the  $R$  information and the female parent also transmits the  $R$  information is  $1/2 \times 1/2 = 1/4$ . All of the progeny that receive two  $R$ s will be round.

Similarly, the probability that the male transmits  $R$  while the female transmits  $W$  is also  $1/2 \times 1/2 = 1/4$  as is the probability that the male transmits  $W$  and the female,  $R$ . Thus,  $1/4 + 1/4 = 1/2$  of the offspring will have both the  $R$  and the  $W$  information. They, however, will all be round because  $R$  dominates  $W$ . At this point, Mendel's model predicts that  $3/4$  of all the offspring will be round.

The only other possibility in Table 1.2 is that both the male and female

Table 1.2: Expectation of round and wrinkled peas in the second filial generation.

Male Parent:		Female Parent:			
		Factor	Prob.	Factor	Prob.
Factor	Prob.	<i>R</i>	1/2	<i>W</i>	1/2
<i>R</i>	1/2	<i>RR</i>	1/4	<i>RW</i>	1/4
<i>W</i>	1/2	<i>WR</i>	1/4	<i>WW</i>	1/4

plant will transmit *W*. The probability of this is also  $1/2 \times 1/2 = 1/4$ . So the remaining  $1/4$  of the progeny will receive only the hereditary information on making a wrinkled pea and consequently will be wrinkled themselves. “Voila!” Mendel must have thought, “The hereditary factors are discrete. Every plant has two hereditary factors and passes only one, at random, to an offspring.” In such a breeding design, the “grandpeas” will always have a 3:1 ratio of dominant trait to recessive trait.

### 1.3 Law of independent assortment

A scientist who achieves success using one particular technique always uses that technique in the initial phase of solving the next problem. Mendel was probably no exception. His success in using the mathematics of probability to develop the law of segregation undoubtedly influenced his approach to his next problem, that of dealing with two different traits at once.

Figure 1.3.1: Mendel’s dihybrid cross: Pea shape (round v. wrinkled) and pea color (yellow v. green).

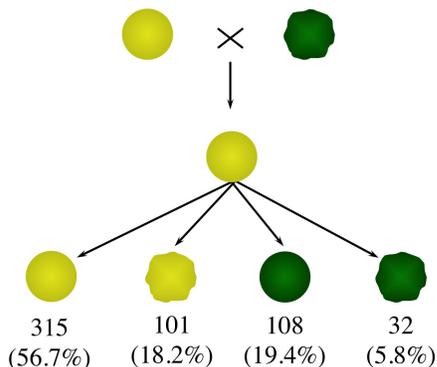


Figure 1.3.1 gives the results of his breeding round, yellow plants with wrinkled green plants and keeping track of both color and shape in the subsequent generations. The middle generation is all yellow and round. Hence, yellow is the dominant hereditary factor for color; and round, as we have seen, is the dominant for shape. The next generation is both confirmatory and troubling. First, there are a total of 423 round and 133 wrinkled peas, giving a ratio of 3.18 to 1, very close to the 3:1 ratio expected from the laws of dominance and segregation. Also confirming these predictions is the 2.97 to 1 ratio of yellow to green peas.

This generation, however, has combinations of traits not seen in either of the previous generations—wrinkled,

Table 1.3: Gametes and their probabilities from an  $F_1$  plant in a dihybrid cross of pea shape ( $R$  = round,  $W$  = wrinkled) and pea color ( $Y$  = yellow,  $G$  = green).

Shape:		Color:			
Factor	Prob.	Factor	Prob.	Factor	Prob.
		$Y$	$1/2$	$G$	$1/2$
$R$	$1/2$	$RY$	$1/4$	$RG$	$1/4$
$W$	$1/2$	$WY$	$1/4$	$WG$	$1/4$

yellow peas and round, green peas. What can explain this? Once again, the mathematics of probability gave a solution. Mendel's hypothesis was that the hereditary factors for pea color are independent of the hereditary factors for pea shape. The mathematical calculations for deriving the expected number of plants of each type in the third generation are more complicated than those for deriving the law of segregation, but they follow the same basic principles of probability theory.

Each plant in the  $F_1$  generation will have four discrete hereditary factors, the  $R$  and  $W$  factors that we have already discussed and the  $Y$  (for yellow) and  $G$  (for green) factors that determine color. The first step is to calculate the expected gametes from an  $F_1$  plant under Mendel's hypothesis of independent assortment. We have already seen that the probability that an  $F_1$  plant transmits, say, a round ( $R$ ) hereditary factor is  $1/2$ . By similar logic, the probability that a  $F_1$  plant transmits a yellow ( $Y$ ) hereditary factor for color is also  $1/2$ . If the hereditary factors for the two traits—shape and color—are independent, then the probability of transmitting a gamete with a round ( $R$ ) and a yellow ( $Y$ ) factor equals the product of these two probabilities or  $1/2 \times 1/2 = 1/4$ . Table 1.3 enumerates all possible gametes, along with their probabilities, from an  $F_1$  plant in this dihybrid cross. The four possible gametes are  $RY$ ,  $WY$ ,  $RG$ , and  $WG$  and the probability of each one equals  $1/4$ .

The next step is to tabulate the probable outcomes in the  $F_2$ . These can be computed by enumerating all possible gametes from the female as a function of all possible gametes from the male plant. With four possible gametes from the female and four from the male, there will be 16 different possible outcomes in the  $F_2$ . The probability of each is  $1/4 \times 1/4 = 1/16$ . Figure 1.3.2 shows these outcomes by genotype and, graphically, the observed traits. To construct the observed traits, recall that round ( $R$ ) is dominant to wrinkled ( $W$ ) and yellow ( $Y$ ) is dominant to green ( $G$ ).

We can see now why there are combinations of observed traits in the  $F_2$  that were not present in either of the original parental plants. Consider the second row and second column of the probable offspring in Figure 1.3.2. These offspring are yellow and wrinkled, a combination not seen in the original parents (see the two parental strains in Figure 1.3.1). These plants came about because both the male and female in the  $F_1$  generation transmitted the  $W$  hereditary factor they received from their green, wrinkled parent but the  $Y$  color factor that they

Figure 1.3.2: Enumeration of outcomes in the  $F_2$  from a dihybrid cross of pea shape ( $R$  = round,  $W$  = wrinkled) and pea color ( $Y$  = yellow,  $G$  = green).

Male gamete:	Female gamete:			
	$RY$	$WY$	$RG$	$WG$
$RY$	$RR, YY$ 	$RW, YY$ 	$RR, YG$ 	$RW, YG$ 
$WY$	$WR, YY$ 	$WW, YY$ 	$WR, YG$ 	$WW, YG$ 
$RG$	$RR, GY$ 	$RW, GY$ 	$RR, GG$ 	$RW, GG$ 
$WG$	$WR, GY$ 	$WW, GY$ 	$WR, GG$ 	$WW, GG$ 

received from their other parent—the yellow, round one.

The predicted outcomes in Figure 1.3.2 also closely agree with the observed outcomes from Figure 1.3.1. Nine-sixteenths of the offspring are expected to be round and yellow, three-sixteenths will be round and green, another three-sixteenths will be wrinkled and yellow, and the remaining one-sixteenths should be wrinkled and green. Indeed, this expected 9:3:3:1 ratio is very close that observed by Mendel. Were this to happen today, Mendel would have high-fived all the monkettes who helped him to plant and to count the peas (and probably to harvest and dine on them as well) and dashed off a paper to *Science* or *Nature*.<sup>2</sup> Instead, he patiently tabulated his results and embarked on the journey to Brunn.

## 1.4 Mendel's laws: Exceptions

The majority of seminal scientific discoveries never get things completely right. Instead, they turn science in a different direction and make us think about problems in a different way. It often takes years of effort to fill in the fine points and find the exceptions to the rule. Mendel's laws follow this pattern. None of the three laws is completely correct. We know now that some hereditary factors are codominant, not completely dominant, to others—one can cross red with white petunias and get pink offspring, not the red or white ones that Mendel would have predicted.

We also know that the law of segregation is not always true in its literal sense. In humans, the X and the Y chromosome are indeed discrete, but they not passed along entirely at random from a father—slightly more boys than girls are conceived.

<sup>2</sup>*Science* and *Nature* are the two most prestigious science journals in the world today.

Finally, we also know that not all hereditary factors assort independently. Those that are located close together on the same chromosome tend to be inherited as a unit, not as independent entities.

These exceptions, however, are individual trees within the forest. Mendel's great accomplishment was to orient science toward the correct forest. Hereditary factors do not "blend" as Darwin and others of his time thought; they are discrete and particulate, as Mendel postulated. As Mendel conjectured, we have two hereditary factors, one of which we received from our father and the other from our mother. We do not have 23 hereditary factors, one on each chromosome, as the early cell biologist Weissman theorized. And two different hereditary factors, provided that they are far enough away on the same chromosome or located on entirely different chromosomes, are transmitted independently of each other. Mendel's basic concepts provided a paradigm shift and sparked the nascent science of genetics at the turn of the century, an achievement that the humble monk was never recognized for during his life.

## 1.5 Terminology

Before we continue, some terminology is in order. In molecular biology, what Mendel called an "hereditary factor" is now known as a *gene*. The molecular biology definition of a gene is a section of DNA that contains the blueprint for a polypeptide chain. The term *locus* (plural = *loci*) is a synonym for a gene.

A gene may be either monomorphic or polymorphic. To grasp the meanings of these two terms, imagine that we obtained the nucleotide sequence of a gene on all of humanity. A *monomorphic gene* is one in which the sequence of As, Cs, Gs, and Ts is the same for all strands of DNA. A *polymorphic gene* is one in which there are several common "spelling variations" of the gene. Arbitrarily, "common" is defined as a nucleotide sequence with a prevalence of 1% or higher.

The spelling variations at a gene are called *alleles*. Unfortunately, many geneticists also use the term gene to refer to an allele, sowing untold confusion among beginning genetics' students, so let us examine a specific case to explain the technical difference between a gene and an allele.

The ABO gene (or ABO locus) is a stretch of DNA close to the bottom of human chromosome 9 that contains the blueprint for an protein that sits within the plasma membrane of red blood cells. Not all of us, however, have the identical sequence of the A, T, C and G nucleotides along this DNA sequence. There are spelling variations or alleles that exist in the human gene pool at the ABO locus. The three most common alleles are the A allele, the B allele, and the O allele.

Because we all inherit two number nine chromosomes—one from mom and the other from dad—we all have two copies of the ABO locus. By chance, the spelling variation at the ABO stretch of DNA on dad's chromosome may be the same as the spelling variation at this region on mom's chromosome. An organism like this is called a *homozygote* (*homo* for "same" and *zygote* for "fertilized egg"). The strict definition of a homozygote is an organism that

has the same two alleles at a gene. For the ABO locus, those who inherit two A alleles are homozygotes as are those who inherit two B alleles or two O alleles. A *heterozygote* is an organism with different alleles at a locus. For example, someone who inherits an A allele from mom but a B allele from dad is a heterozygote.

Wilhelm Johanssen (1909), the person who coined the term gene, also proposed an important distinction between the genotype and the phenotype. The *genotype* is defined as the two alleles that a person (or group of people) has at a locus. At the ABO locus, the genotypes are AA, AB, AO, BB, BO, and OO. (There is a tacit understanding that the heterozygotes AO and OA are the same genotype.) The word “genotype” may also be used as a vague designation of genetic predisposition without identifying either the genes or the alleles. As example is the statement “he has the genotype for obesity.”

A *phenotype* is defined as the observed characteristic or trait. Height, weight, extraversion, intelligence, interest in blood sports, memory, and shoe size are all phenotypes.

There is not always a simple, one-to-one correspondence between a genotype and a phenotype. For example, there are four phenotypes at the ABO blood group—A, B, AB, and O. These phenotypes come about when a drop of blood is exposed to a chemical that reacts to the molecule produced from the A enzyme and then to another chemical that reacts specifically to the enzyme produced from a B allele. (The O allele produces no viable enzyme, so there is no reaction).

If someone takes a drop of your blood, adds the A chemical to it, and observes a reaction, then it is clear that you must have at least one A allele—although, of course, you may actually have two A alleles. If the person takes another drop of your blood, adds the B chemical, and observes a reaction, and then you must have phenotype AB. In this case, your genotype must also be AB. If a reaction occurs to the A chemical but not to the B chemical, then you have phenotype A but could be genotype AA or genotype AO—the test cannot distinguish one of these genotypes from the other. Similarly, if your blood fails to react to the A chemical but reacts to the B chemical, then you are phenotype B, although it is uncertain whether your genotype is BB or BO. When there is no reaction to either the A or the B chemical, and then the phenotype is O and the genotype is OO.

Finally, there are several terms used to describe allele action in terms of the phenotype that is observed in a heterozygote. When the phenotype of a heterozygote is the same as the phenotype of one of the two homozygotes, then the allele in the homozygote is said to be *dominant* and the allele that is “not observed” is termed *recessive*. Because the heterozygote with the genotype AO has the same phenotype as the homozygote AA, then allele A is dominant and O is recessive. Similarly, allele B is dominant to O, or in different words, allele O is recessive to B.

When the phenotype of the heterozygote takes on a value somewhere between the two homozygotes, then allele action is said to be *partially dominant*, *incompletely dominant*, *additive*, or *codominant*. Because the genotype AB gives a different phenotype from both genotypes AA and BB, one would say that al-

leles A and B are codominant with respect to each other. (The term additive would equally apply, but this phrase is usually used when the phenotypes are numbers and not qualities.) Note carefully that allele action is a *relative* and not an absolute concept. For example, the allele action of A depends entirely on the other allele—it is dominant to O but codominant to B.

## 1.6 Application of Mendel's laws: The Punnett rectangle

In high school biology, you were all exposed to a Punnett square. Indeed, the Tables 1.3 and 1.2 as well as 1.3.2 are all examples of Punnett squares. This elementary technique was developed by Reginald Punnett who in 1905 arguably wrote the first textbook of genetics (Punnett, 1905).

High school has also taught us that a square is a specific case of a more general geometric form, the rectangle. We can now generalize and develop the concept of a Punnett rectangle to apply Mendel's concepts of heredity to calculating the genotypes and phenotypes of offspring from a given mating type. The advantages of a rectangle are that it can deal with more genetic situations than a square and it can do so with greater efficiency. The generic steps for constructing a Punnett rectangle are listed in Table 1.4. Let us examine these steps with a simple example.

### 1.6.1 A simple example

Consider the mating of woman who has genotype AO at the ABO blood group locus and a man who also has genotype AO. From Step 1 in Table 1.4, the mother's egg can contain either allele A (with a probability of  $1/2$ ) or allele O (also with a probability of  $1/2$ ). From Step 2, the father's sperm may contain either A or O, each with a probability of  $1/2$ . The row and column labels for this Punnett rectangle given in Table 1.5.

Step 3 requires entry of the offspring genotypes into the cells of the rectangle. The upper left cell represents the fertilization of mother's A egg by father's A sperm, so the genotypic entry is AA. The upper right cell represents the fertilization of mother A egg by father's O sperm, giving genotype AO. Following these rules, the genotypes for the lower left and lower right cells are, respectively, OA and OO.

We are now at Step 4 in Table 1.6—calculating the probabilities of the offspring's genotypes. To do this we multiply the row probability by the column probability. For the upper left cell, the row probability is  $1/2$  and the column probability is also  $1/2$ , so the cell probability is  $1/2 \times 1/2 = 1/4$ . It is obvious that each cell for this example will have a probability of  $1/4$ . The completed Punnett rectangle is given in Table 1.6.

In Steps 5 and 6, we must complete a table of genotypes and, if needed, phenotypes. To complete Step 5, we note that there are three unique genotypes in the cells of the Punnett rectangle—AA, AO, and OO (remember that genotype

Table 1.4: Steps in using a Punnett rectangle to compute the distribution of offspring genotypes and phenotypes from a parental mating.

Step	Operation
1	Write down the genotypes of the mother's gametes along with their associated probabilities. These will label the rows of the rectangle.
2	Write down the genotypes of the father's gametes along with their associated probabilities. These will label the columns of the rectangle. (Naturally, it is possible to switch the steps—mother's gametes forming the columns and father's gametes, the rows—without any loss of generality.)
3	The genotype for each cell within the rectangle is the genotype of the row gamete united with the genotype of the column gamete. Enter these for all cells in the rectangle.
4	The probability for each cell within the rectangle equals the probability of the row gamete multiplied by the probability of the column gamete. Enter these for all cells in the rectangle.
5	Make a table of the unique genotypes of the offspring and their probabilities. If a genotype occurs more than once within the cells of the Punnett rectangle, then add the cell probabilities together to get the probability of that genotype.
6	If needed, make a table of the unique phenotypes and their probabilities from the table of genotypes. If two or more genotypes in the genotypic table give the same phenotype, then add the probabilities of those genotypes together to get the probability of the phenotype.

Table 1.5: Steps 1 and 2 in constructing a Punnett rectangle.

Female Gamete:		Male Gamete:			
Allele	Prob.	Allele	Prob.	Allele	Prob.
A	1/2	A	1/2	O	1/2
O	1/2				

Table 1.6: Results of a Punnett rectangle after Step 4.

Female Gamete:		Male Gamete:			
		Allele	Prob.	Allele	Prob.
Allele	Prob.	A	1/2	O	1/2
A	1/2	AA	1/4	AO	1/4
O	1/2	OA	1/4	OO	1/4

Table 1.8: Expected genotypes and phenotypes and their frequencies from a mating of an AO women and an AO man.

Genotype	Frequency	Phenotype	Frequency
AA	1/4	A	3/4
AO	1/2	O	1/4
OO	1/4		

OA is the same as AO). Genotypes AA and OO occur only once, so the probability of each of these genotypes is  $1/4$ . Genotype AO, on the other hand, occurs twice, once in the upper right cell and again in the lower left. Consequently, the probability of the heterozygote AO is the sum of these two cell probabilities or  $1/4 + 1/4 = 1/2$ . Table 1.7 gives the genotypes and their frequencies for the offspring of this mating.

Step 6 requires calculation of the phenotypes from the genotypes. Because allele A is dominant in the ABO blood system, both genotypes AA and AO will have phenotype A. The probability of phenotype A will be the sum of the probabilities for these two genotypes or  $1/4 + 1/2 = 3/4$ . Genotype OO will have phenotype O. Because genotype OO occurs only once, the probability of phenotype O is simply  $1/4$ . The complete table of genotypic and phenotypic frequencies is given in Table 1.8.

Table 1.7: Expected offspring genotypes and their frequencies.

Genotype	Frequency
AA	1/4
AO	1/2
OO	1/4

### 1.6.2 A two-locus example

The logic of the Punnett rectangle may be applied to genotypes at more than one locus. The only requirement is that all the loci are unlinked, i.e., no two loci are located close together on the same chromosome. (Later on, we deal with the case of Punnett rectangles with linked loci.)

The Punnett rectangle for two loci will be illustrated by calculating tradi-

Table 1.9: Mothers's gametes and probabilities.

ABO Locus:		Rhesus Locus:				
		Allele	Prob.		Allele	Prob.
Allele	Prob.	+	1/2		-	1/2
O	1.0	O+	1/2		O-	1/2

tional blood types. Traditional blood-typing for transfusions uses phenotypes at two genetic loci. The first is the ABO locus and the second is the Rhesus locus. Although the genetics of the Rhesus locus are actually quite complicated, we will assume that there are only two alleles, a “plus” or + allele and a “minus” or - allele. The + allele is dominant to the - allele, so the two Rhesus phenotypes are + and -. The blood types used for transfusions and blood donations concatenate the ABO phenotype with the Rhesus phenotype, giving phenotypes such as A+, B-, AB+, etc. Our problem? What are the expected frequencies for the offspring of a father with genotype AO/+ (read “genotype AO at the ABO locus and genotype + at the Rhesus locus”) and a mother who is genotype OO/+?

The trick to the problem of two unlinked loci is to go through the Punnett rectangle steps three times. In the first pass, the Punnett rectangle is used to obtain the genotypes for the maternal gametes. The second pass calculates the paternal gametes, and the third and final pass uses the results from the first two passes to get the offspring genotypes.

The mother in this problem has genotype OO/+. Because the ABO and rhesus loci are unlinked, the probabilities for the ABO locus are independent of those for the rhesus locus. This permits us to use a Punnett rectangle to derive the maternal gametes. The rows of the rectangle are labeled by the contribution to the maternal egg from mother's ABO alleles and their probabilities. Here, mother can give only an O. Consequently there will be only one row to the rectangle, and it will be labeled O and have a probability of 1.0. The columns are labeled by the contribution of mother's rhesus alleles and their probabilities. In the present case, the columns will be labeled + and -, each with probability 1/2. The completed Punnett rectangle needed to get the maternal gametes and their probabilities is given below in Table 1.9.

From this table, we see that there are two possible maternal gametes, each with a probability of 1/2. The first has one of mother's O alleles at the ABO locus and the + allele at the Rhesus locus, giving gamete O+. The second gamete, O-, contains one of mothers O alleles but her - allele at Rhesus.

The second pass through the Punnett rectangle is used to calculate father's gametes. His contribution to the gamete from his alleles at the ABO locus may be either allele A, with probability 1/2, or O, also with probability 1/2. Thus, there will be two rows to father's Punnett rectangle, one labeled A and the other labeled O, each with probability 1/2. Like mother, father is a heterozygote at Rhesus. Hence the columns for his table will equal those for the maternal table. The Punnett rectangle for the paternal gametes is given below in Table 9.11.

Table 1.10: Father's gametes and probabilities.

ABO Locus:		Rhesus Locus:				
		Allele	Prob.		Allele	Prob.
Allele	Prob.	+	1/2		-	1/2
<b>A</b>	1/2	<b>A+</b>	1/4		<b>A-</b>	1/4
<b>O</b>	1/2	<b>O+</b>	1/4		<b>O-</b>	1/4

Father has four different paternal gametes, each with a probability of 1/4. The first possible gamete carries father's A allele at the ABO locus and father's + allele at the Rhesus locus (A+). Analogous interpretations apply to the remaining three gametes—A-, O+, and O-.

We may now construct the last Punnett rectangle to find the offspring genotypes and their frequencies. In this rectangle, the rows are labeled by the maternal gametes and their probabilities and the columns by the paternal gametes and their probabilities. This will give a rectangle with two rows and four columns. This rectangle (with rows and columns switched for efficiency) is given in Table 1.11.

Because the ordering of the alleles for a heterozygote is immaterial, genotypes AO, +- and AO, +- in Table 1.11 are identical. So are genotypes OO, +- and OO, -+. Hence, the table of expected genotypes can be written as the one in Table 1.12. The table also gives the phenotypes associated with the genotypes. Adding together those rows with identical phenotypes gives the following phenotypic frequencies: 3/8 or 37.5% of the offspring are expected to have blood type A+; 1/8 or 12.5% will have blood type A-; 3/8 or 37.5% will have blood type O+; and 1/8 or 12.5% will have blood type O-.

### 1.6.3 X-linked loci

In mammals, genetic females have two X chromosomes while genetic males have one X chromosome and one Y chromosome. The Y chromosome is much smaller than the X chromosome and contains many fewer loci than the X. Thus, many genes on the X chromosome—in fact, the overwhelming number of genes—do

Table 1.11: Expected offspring genotypes and their frequencies from an OO, +- woman and an AO, +- man.

Father:		Mother:				
		Gamete	Prob		Gamete	Prob
Gamete	Prob	O+	1/8		O-	1/4
<b>A+</b>	1/4	<b>AO, ++</b>	1/8		<b>AO, +-</b>	1/8
<b>A-</b>	1/4	<b>AO, -+</b>	1/8		<b>AO, --</b>	1/8
<b>O+</b>	1/4	<b>OO, ++</b>	1/8		<b>OO, +-</b>	1/8
<b>O-</b>	1/4	<b>OO, -+</b>	1/8		<b>OO, --</b>	1/8

Table 1.12: Expected offspring genotypes, phenotypes and frequencies from an OO, +- woman and an AO, +- man.

Genotype:	Phenotype:	Prob.
AO, ++	A+	1/8
AO, +-	A+	1/4
AO, --	A-	1/8
OO, ++	O+	1/8
OO, +-	O+	1/4
OO, --	O-	1/8

Table 1.13: Expected genotypes and phenotypes from a mating between a man with hemophilia and a female carrier.

Mother:		Father:			
		Gamete	Prob.	Gamete	Prob.
Gamete	Prob.	X-a	1/2	Y	1/2
X-A	1/2	XX, Aa Female, Carrier	1/4	XY, A Male, Normal	1/4
X-a	1/2	XX, aa Female, Hemophilia	1/4	XY, a Male, Hemophilia	1/4

not have counterparts on the Y.<sup>3</sup> Such loci are called *X-linked genes*.

For X-linked genes, females have two alleles, one on each X, whereas males have only one allele, the one on their single Y chromosome. The trick to dealing with this situation in a Punnett squares is to include the chromosome when writing a gamete. Hence, if a mother is genotype Aa for a locus on the X chromosome, we will write her gametes as X-A and X-a instead of just A and a. A father who is genotype A, for example, will have his gametes written as X-A and Y. Note that father's gamete containing the Y chromosome does *not* have an allele associated with it because the locus does not exist on the Y.

To illustrate this technique, consider the offspring from a mating between an Aa female and an a male where allele a causes hemophilia, a locus located on the X chromosome but not on the Y chromosome. Hemophilia is a recessive disorder, so in phenotypic terms, this mating is between a hemophiliac male and a normal, but carrier, female. The Punnett rectangle for the male and female gametes along with the genotypes and phenotypes of the offspring is given in Table 1.13.

## 1.7 Conclusions

This chapter introduced the principles of Mendelian genetics. But, as was stated in the text, these principles introduced a paradigm shift that was not entirely

<sup>3</sup>The few loci on the Y that are also on the X are called *pseudoautosomal loci*.

correct. Mendel's law of dominance did not apply universally to all hereditary factors. This is not a major problem because we can always amend his laws to allow for "partial dominance" or "codominance."

On the other hand, Mendel's law of independent assortment has been demonstrated to be incorrect in a significant number of cases. A major reason is that "hereditary factors," as Mendel called them, are not an enormous number of individual discrete particles within a cell. Instead, many of them appear to be linearly arranged on the physical molecules of inheritance, the chromosomes. The concept of the linear arrangement of hereditary factors is the topic of the next exposition of quantitative genetics—linkage.

## 1.8 References

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