



CHAPTER OUTLINE

- 3.1 Mendel's Study of Pea Plants
- 3.2 Law of Segregation
- 3.3 Law of Independent Assortment
- 3.4 The Chromosome Theory of Inheritance
- 3.5 Studying Inheritance Patterns in Humans
- 3.6 Probability and Statistics

3

MENDELIAN INHERITANCE

An appreciation for the concept of heredity can be traced far back in human history. Hippocrates, a physician, was the first person to provide an explanation for hereditary traits (around 400 b.c.e.). Hippocrates' incorrect explanation was that "seeds" are produced by all parts of the body and then collected and transmitted to the offspring at the time of conception. Furthermore, these seeds were hypothesized to cause certain traits of the offspring to resemble those of the parents. This idea, known as pangenesis, was the first attempt to explain the transmission of hereditary traits from generation to generation.

The first systematic studies of genetic crosses were carried out by Joseph Kölreuter from 1761 to 1766. In crosses between different varieties of tobacco plants, the offspring were usually intermediate in appearance between the two parents. This observation led Kölreuter to conclude that both parents make equal genetic contributions to their offspring. Furthermore, it was consistent with the blending hypothesis of inheritance. According to this idea, the factors that dictate hereditary traits could blend together from generation to generation. The blended traits would then be passed to the next generation. Before the 1860s, the popular view, which combined the notions of pangenesis and blending inheritance, was that hereditary traits were rather malleable and could change and blend over the course of one or two generations.



The garden pea, studied by Mendel.

Zigzag Mountain Art/Alamy Stock Photo

However, the pioneering work of Gregor Mendel would prove instrumental in refuting this viewpoint.

In this chapter, we will first examine Mendel's crosses of pea plants. We begin our inquiry into genetics here because the inheritance patterns observed in pea plants are fundamentally related to inheritance patterns found in other eukaryotic species, such as corn, fruit flies, mice, and humans. Mendel's experiments revealed some simple laws that govern the process of inheritance. We will then explore the chromosome theory of inheritance that explains the relationship between the transmission of chromosomes during sexual reproduction and the pattern of transmission of traits observed by Mendel. In addition, we will consider how researchers were able to confirm the chromosome theory of inheritance by showing that certain genes are located on sex chromosomes.

In the last section of this chapter, we will examine some general concepts in probability and statistics. How are statistical methods useful? First, probability calculations allow us to predict the outcomes of simple genetic crosses, as well as the outcomes of more complicated crosses described in later chapters. In addition, we will explore the use of statistics to test the validity of genetic hypotheses that attempt to explain the inheritance patterns of traits.



3.1 MENDEL'S STUDY OF PEA PLANTS

Learning Outcomes:

1. Describe the characteristics of pea plants that make them a suitable organism to study genetically.
2. Outline the steps that Mendel followed to make crosses between different strains of pea plants.
3. Define the following terms: *strain*, *character*, and *trait* (or *variant*).

Starting in 1856, Gregor Mendel grew and crossed thousands of pea plants in a small 23- by 115-foot garden (**Figure 3.1**). The pea plants differed with regard to various traits. For example, some had purple flowers and others had white flowers. Mendel gathered a large amount of quantitative data concerning the outcomes of crosses between plants with different traits.

The culmination of Mendel's work, entitled *Experiments in Plant Hybridization*, was published in 1866. This paper was largely ignored by scientists at that time, possibly because of its title, which did not reveal its key observations. Another reason this work went unrecognized could be a lack of understanding of chromosomes and their transmission, a topic discussed in Chapter 2. Mendel reflected, "My scientific work has brought me a great deal of satisfaction and I am convinced that it will be appreciated before long by the whole world."

In 1900, the studies of Mendel were independently rediscovered by three biologists with an interest in plant genetics: Hugo de Vries, Carl Correns, and Erich von Tschermak. Within a few years, the influence of these studies was felt around the world. In this section, we will begin by considering the process of sexual reproduction in pea plants. We will then examine key features of pea plants that were advantageous from an experimental point of view. In Sections 3.2 and 3.3, we will explore how Mendel's experiments revealed fundamental laws that govern the transmission of traits from parent to offspring.

Sexual Reproduction in Pea Plants Occurs Via Pollination and Fertilization

Before we delve into Mendel's experiments, let's first consider how flowering plants reproduce. The reproductive features of the garden pea, *Pisum sativum*, are shown in **Figure 3.2**.

- The term **gamete** is used to describe haploid reproductive cells that fuse to form a zygote.
- Male gametes (**sperm cells**) are produced within **pollen grains** that form in the **anthers**.
- Female gametes (**egg cells**) are produced within **ovules** that form in the **ovaries**.
- For fertilization to occur, a pollen grain first lands on the **stigma**, an event called pollination. This event then stimulates the growth of a pollen tube (Figure 3.2c). The pollen tube enables sperm cells to enter the stigma and migrate toward an ovule. Fertilization takes place when a sperm



FIGURE 3.1 Gregor Johann Mendel (1822–1884).

National Library of Medicine

enters the micropyle, an opening in the ovule wall, and fuses with an egg cell, resulting in the formation of a zygote.

- Via cell division, a zygote first develops into a plant embryo within a pea seed. After the seed is planted, the seed germinates, and the embryo develops into a seedling and eventually a mature pea plant.

Pea Plants Can Reproduce by Cross-Fertilization or Self-Fertilization

Mendel's study of genetics grew out of an interest in ornamental flowers. Many plant breeders had previously conducted experiments aimed at obtaining flowers with new colors. When two distinct individuals with different characteristics are bred to each other, the experiment is called a **cross**, or a **hybridization**, and the offspring are referred to as **hybrids**. For example, a hybridization experiment could involve a cross between a purple-flowered plant and a white-flowered plant.

Certain properties of the garden pea were particularly advantageous for studying plant hybridization. First, the flowers of the garden pea are relatively large, making it easy to manipulate the anthers where the pollen is produced. In some

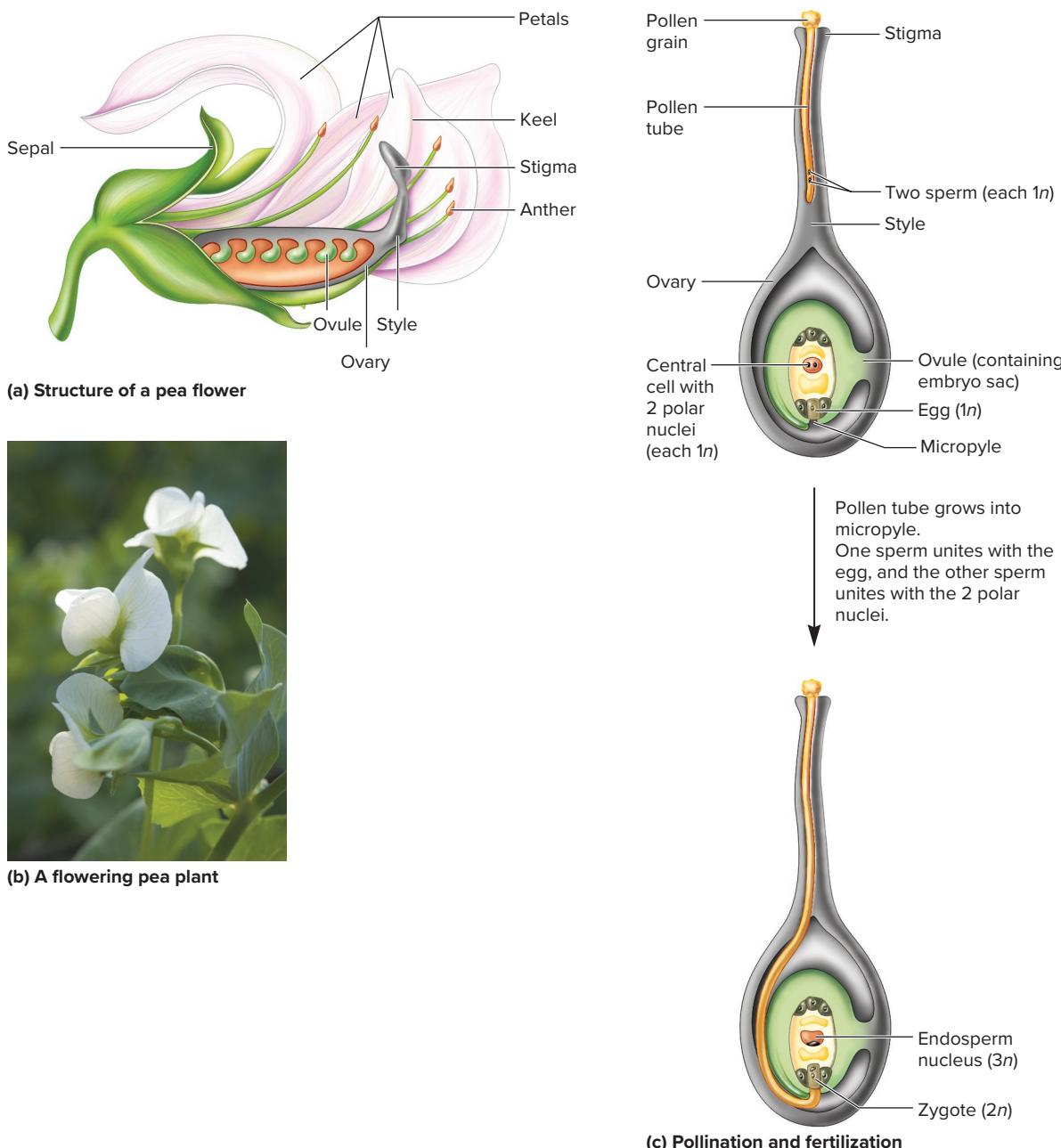


FIGURE 3.2 Flower structure and pollination in pea plants. (a) The pea flower produces both pollen and egg cells. The pollen grains are produced within the anthers, and the egg cells are produced within the ovules that are contained within the ovary. The keel is two modified petals that are fused and enclose the anthers and ovaries. In this drawing, some of the keel is not shown so that the internal reproductive structures of the flower can be seen. (b) Photograph of a flowering pea plant. (c) A pollen grain must first land on the stigma. After this occurs, the pollen grain sends out a long tube through which two sperm cells travel toward an ovule to reach an egg cell. The fusion between a sperm and an egg cell results in fertilization and creates a zygote. The second sperm fuses with a central cell containing two polar nuclei to create the endosperm. The endosperm, which is a major component of a pea seed, provides nutritive material for the developing embryo.

(b): np-e07/iStock/Getty Images

CONCEPT CHECK: Prior to fertilization, where are a pea plant's male gametes located?

experiments, Mendel wanted to make crosses between different plants. This process, known as **cross-fertilization**, requires that the pollen from one plant be placed on the stigma of another plant. The procedure is shown in **Figure 3.3**. Mendel was

able to pry open immature flowers and remove the anthers before pollen was produced. Therefore, these flowers could not make their own pollen. Instead, pollen was obtained from another plant by gently touching its mature anthers with a

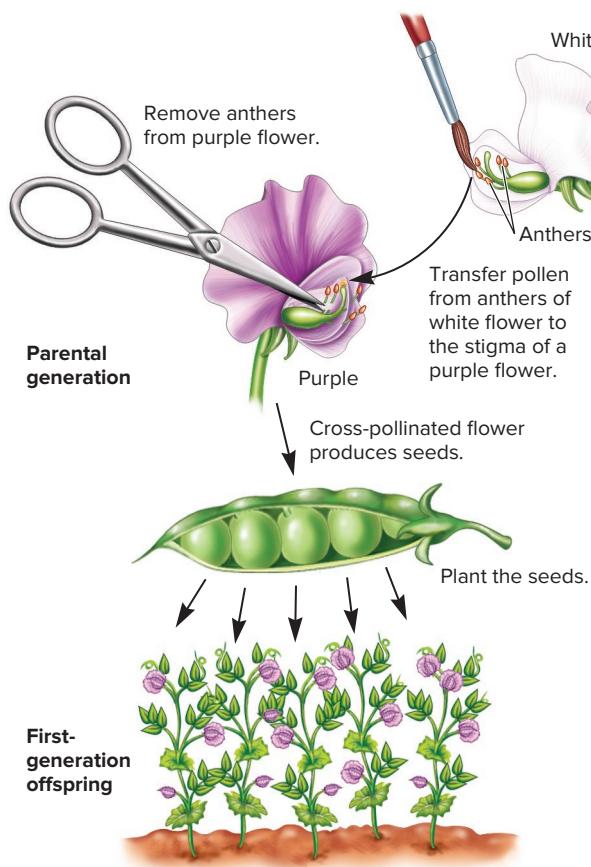


FIGURE 3.3 How Mendel cross-fertilized pea plants. This illustration depicts a cross between one plant with purple flowers and another with white flowers. The offspring from this cross are the result of pollination of the purple flower using pollen from a white flower.

CONCEPT CHECK: In this experiment, which plant, the white- or purple-flowered one, is providing the egg cells, and which is providing the sperm cells?

paintbrush. This pollen was applied to the stigma of the flower that already had its anthers removed. In this way, Mendel was able to cross-fertilize the pea plants, thereby obtaining hybrids.

In other experiments, Mendel allowed plants to reproduce by **self-fertilization**, which means that the pollen and eggs are derived from the same plant. In peas, two modified petals are fused to form a keel that encloses the reproductive structures of a flower. Because of this covering, pea plants naturally reproduce by self-fertilization. Usually, pollination occurs even before the flower opens. To achieve self-fertilization, Mendel simply let the pea plants reproduce naturally. In other words, the anthers were not removed.

Mendel Studied Seven Characteristics That Differed Among Strains of Pea Plants

A second experimental advantage of the garden pea is that it was available in different strains. Within agricultural species such as the garden pea, a **strain** is a genetically related group of individuals

that display one or more differences compared to another group of individuals. In this case, several garden pea strains varied in height and in the appearance of their flowers, seeds, and pods. For example, one strain had purple flowers and another strain had white flowers. These color differences were due to variation in a gene that controls flower color.

- The general characteristics of an organism are called **characters**. For example, flower color is a character of peas.
- The term **trait**, or **variant**, is typically used to describe the specific properties of a character. For example, purple flower color is a trait (or variant) of peas.
- Different strains of pea plants differed with regard to their traits (or variants).

Over the course of 2 years, Mendel tested the pea strains to determine if their traits bred true. Breeding true means that a trait does not vary in appearance from generation to generation. For example, if the seeds from a pea plant were yellow, the next generation would also produce yellow seeds. Likewise, if these offspring were allowed to self-fertilize, all of their offspring would also produce yellow seeds, and so on. A strain that continues to produce the same trait after several generations of self-fertilization is called a **true-breeding strain**.

Mendel focused on the analysis of characters that were clearly distinguishable between different true-breeding strains. **Figure 3.4** illustrates the seven characters that Mendel eventually chose to follow in breeding experiments. All seven were found in two variants. For example, one character was height, which was found in two variants: tall and short plants.

3.1 COMPREHENSION QUESTIONS

1. Which of the following were experimental advantages of using pea plants?
 - a. They came in several different varieties.
 - b. They were capable of self-fertilization.
 - c. They were easy to cross.
 - d. All of the above were advantages.
2. With regard to Mendel's experiments, the term *cross* refers to an experiment in which
 - a. the gametes come from different individuals.
 - b. the gametes come from a single flower of the same individual.
 - c. the gametes come from different flowers of the same individual.
 - d. Both a and c are true.
3. To avoid self-fertilization in his pea plants, Mendel had to
 - a. spray the plants with a chemical that damaged the pollen.
 - b. remove the anthers from immature flowers.
 - c. grow the plants in a greenhouse that did not contain pollinators (e.g., bees).
 - d. do all of the above.

CHARACTER	VARIANTS
Height	Tall Short
Flower color	Purple White
Flower position	Axial Terminal
CHARACTER	VARIANTS
Seed color	Yellow Green
Seed shape	Round Wrinkled
Pod color	Green Yellow
Pod shape	Smooth Constricted

FIGURE 3.4 An illustration of the seven characters that Mendel studied. Each character was found as two variants that were decisively different from each other.

CONCEPT CHECK: What do we mean when we say a strain is true-breeding?

3.2 LAW OF SEGREGATION

Learning Outcomes:

- Analyze Mendel's experiments involving single-factor crosses.
- State Mendel's law of segregation, and explain how it is related to gamete formation and fertilization.
- Predict the outcome of a single-factor cross or a self-fertilization experiment using a Punnett square.

In the previous section, we considered how cross-fertilization or self-fertilization experiments can be conducted on pea plants. In this section, we will examine how Mendel studied the inheritance of characters by crossing variants to each other. A cross in which an experimenter observes one character is called a **single-factor cross**. A cross between two parents with different variants for a given character produces single-character hybrids, also known as **monohybrids**. As you will learn, this type of experimental approach led Mendel to propose the law of segregation.

EXPERIMENT 3A

Mendel Followed the Outcome of a Single Character for Two Generations

Prior to conducting crosses in pea plants, Mendel did not have a hypothesis to explain the formation of hybrids. The goal of Mendel's experiments was to determine the quantitative relationships that govern the transmission of hereditary traits from parent to offspring. This rationale is called an **empirical approach**. Laws deduced from an empirical approach are known as empirical laws.

Mendel's experimental procedure is shown in **Figure 3.5**. This type of experiment began with true-breeding plants that differed in a single character. These are termed the **parental generation**, or **P generation**. Crossing true-breeding parents to each other, called a P cross, produces offspring that constitute the

F₁ generation, or first filial generation (from the Latin *filius*, which refers to a male offspring). As seen in the data, all plants of the F₁ generation showed the trait of one parent but not the other. This prompted Mendel to follow the transmission of this character for one additional generation. To do so, the plants of the F₁ generation were allowed to self-fertilize to produce a second generation called the **F₂ generation**, or second filial generation.

THE GOAL (DISCOVERY-BASED SCIENCE)

Mendel speculated that the inheritance pattern for a single character may follow quantitative natural laws. The goal of this experiment was to uncover such laws.

ACHIEVING THE GOAL

FIGURE 3.5 Mendel's analysis of single-factor crosses.

Starting material: Mendel began his experiments with true-breeding strains of pea plants that varied in only one of seven different characters (look back at Figure 3.4).

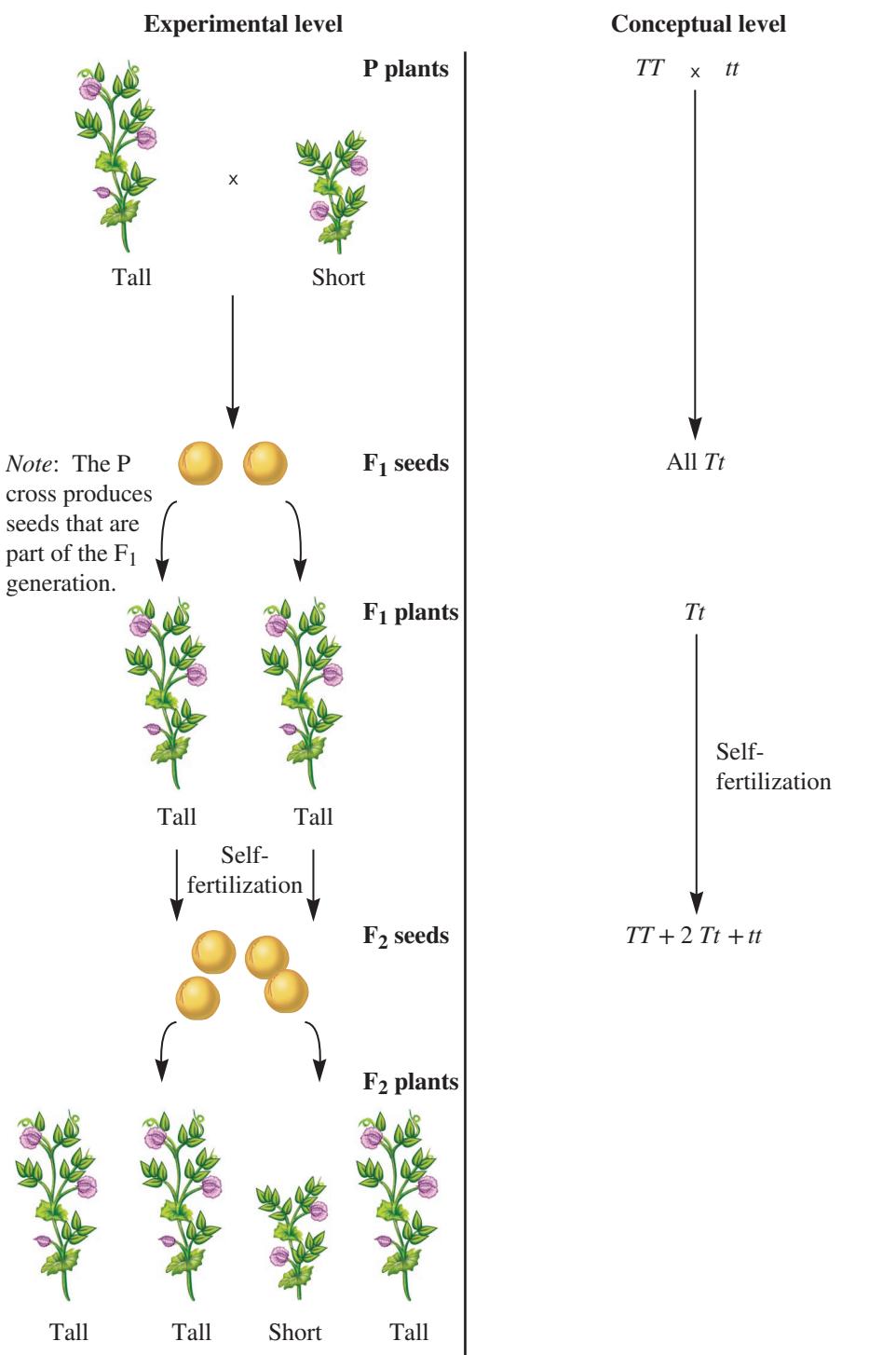
1. For each of seven characters, Mendel cross-fertilized two different true-breeding strains. Keep in mind that each cross involved two plants that differed in regard to only one of the seven characters studied. The illustration at the right shows one cross between a tall and short plant. This is called a P (parental) cross.

2. Collect the F₁ generation seeds. The following spring, plant the seeds and allow the plants to grow. These are the plants of the F₁ generation.

3. Allow the F₁ generation plants to self-fertilize. This produces seeds that are part of the F₂ generation.

4. Collect the F₂ generation seeds and plant them the following spring to obtain the F₂ generation plants.

5. Analyze the traits found in each generation.



THE DATA

P cross	F ₁ generation	F ₂ generation	Ratio of traits in F ₂ generation
Tall × short height	All tall	787 tall, 277 short	2.84:1
Purple × white flowers	All purple	705 purple, 224 white	3.15:1
Axial × terminal flowers	All axial	651 axial, 207 terminal	3.14:1
Yellow × green seeds	All yellow	6,022 yellow, 2,001 green	3.01:1
Round × wrinkled seeds	All round	5,474 round, 1,850 wrinkled	2.96:1
Green × yellow pods	All green	428 green, 152 yellow	2.82:1
Smooth × constricted pods	All smooth	882 smooth, 299 constricted	2.95:1
Total	All dominant	14,949 dominant, 5,010 recessive	2.98:1

Source: Mendel, Gregor, "Versuche über Pflanzenhybriden, Verhandlungen des naturforschenden Vereines in Brünn, Bd. IV für das Jahr 1865," *Abhandlungen*, 1866, 3–47.

INTERPRETING THE DATA

The data in the table are the results of producing an F₁ generation via cross-fertilization and an F₂ generation via self-fertilization of the F₁ plants. A quantitative analysis of these data allowed Mendel to propose three important ideas:

1. The data argued strongly against a blending mechanism of heredity. In all seven cases, the F₁ generation displayed traits that were distinctly like one of the two parents rather than traits that were intermediate in character. Mendel's first proposal was that one variant for a particular character is **dominant** to another variant. For example, the variant of green pods is dominant to that of yellow pods. The term **recessive** is used to describe a variant that is masked by the presence of a dominant trait but reappears in subsequent generations. Yellow pods and short height are examples of recessive variants. They can also be referred to as recessive traits.
2. When a true-breeding plant with a dominant trait was crossed to a true-breeding plant with a recessive trait, the dominant trait was always observed in the F₁ generation. In the F₂ generation, most offspring displayed the dominant trait, but some showed the recessive trait. How did Mendel explain this observation? Because the recessive trait appeared in the F₂ generation, a second proposal was made—the genetic determinants of traits are passed along as "unit factors" from generation to generation. The data were consistent with a **particulate theory of inheritance**, in which the factors that govern traits are inherited as discrete units that remain unchanged as they are passed from parent to offspring. Mendel referred to the genetic determinants as unit factors, but we now call them genes (from the Greek, *genesis*, meaning "birth," or, *genos*, meaning "origin").
3. When comparing the numbers of dominant and recessive traits in the F₂ generation, Mendel noticed a recurring pattern. Within experimental variation, a 3:1 ratio was observed between the dominant and the recessive trait. As described next, this quantitative approach allowed Mendel to make a third proposal—genes **segregate** from each other during the process that gives rise to gametes.

A 3:1 Phenotypic Ratio Is Consistent with the Law of Segregation

Mendel's research was aimed at understanding the laws that govern the inheritance of traits. At that time, scientists did not understand the molecular composition of the genetic material or its mode of transmission during gamete formation and fertilization. We now know that the genetic material is composed of deoxyribonucleic acid (DNA), a component of chromosomes. Each chromosome contains hundreds to thousands of shorter segments that function as genes—a term that was originally coined by Wilhelm Johannsen in 1909. A **gene** is defined as a unit of heredity that may influence the outcome of a trait in an organism. Each of the seven pea plant characters that Mendel studied is influenced by a different gene.

Most eukaryotic species, such as pea plants and humans, have their genetic material organized into pairs of chromosomes, as discussed in Chapter 2. For this reason, eukaryotes have two copies of most genes. These copies may be the same or they may differ. The term **allele** (from the Latin *alius* meaning "other")

refers to an alternative form of a particular gene. For example, the height gene in pea plants is found as a tall allele and a short allele. With this modern knowledge, the results shown in Figure 3.5 are consistent with the idea that each parent transmits only one copy of each gene (i.e., one allele) to each offspring. Using modern terminology, **Mendel's law of segregation** states the following:

The two copies of a gene segregate (or separate) from each other during the process that gives rise to gametes.

Therefore, only one copy of each gene is found in a gamete. At fertilization, two gametes combine randomly, potentially producing different allelic combinations.

Let's use Mendel's cross of tall and short pea plants to illustrate how alleles are passed from parents to offspring according to the law of segregation, and also to define some new genetic terms (**Figure 3.6**).

- The letters *T* and *t* are used to represent the alleles of the gene that determines plant height. By convention, the uppercase letter represents the dominant allele (*T* for tall

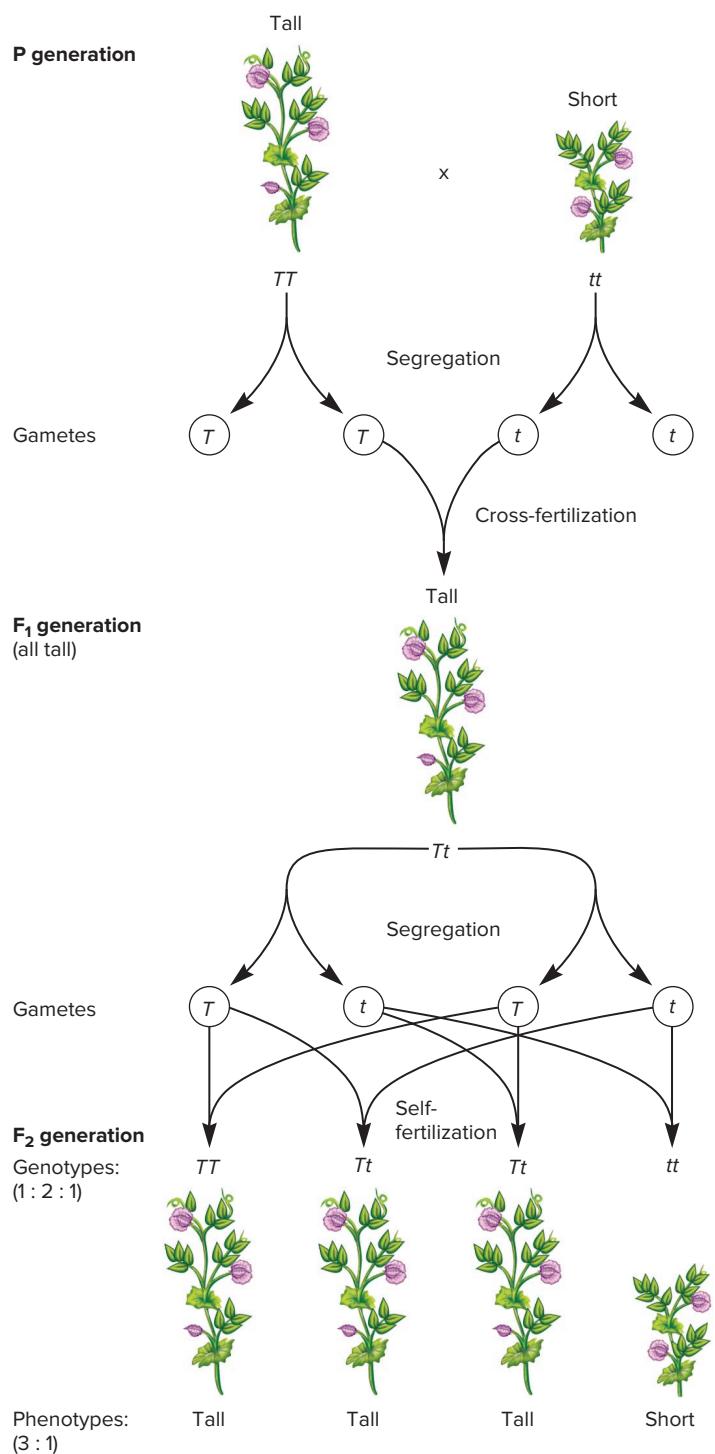


FIGURE 3.6 Mendel's law of segregation. This illustration shows a cross between a true-breeding tall plant and a true-breeding short plant and the subsequent segregation of the tall (T) and short (t) alleles in the F_1 and F_2 generations.

CONCEPT CHECK: With regard to the T and t alleles of pea plants, explain what segregation means.

height, in this case), and the recessive allele is represented by the same letter in lowercase (t , for short height).

- For the P cross, both parents are true-breeding plants (see Figure 3.6). Therefore, each one has identical copies of the height gene. When an individual has two identical copies of a gene, the individual is said to be **homozygous** with respect to that gene. (The prefix *homo-* means “like,” and the suffix *-zygo* means “pair.”) In the P cross, the tall plant is homozygous (TT) for the tall allele, and the short plant is homozygous (tt) for the short allele. These alleles segregate during the process that gives rise to gametes.
- In contrast, the F_1 generation is **heterozygous**, Tt , because every individual carries one copy of the tall allele and one copy of the short allele. A heterozygous individual carries different alleles of a gene. (The prefix *hetero-* means “different.”) The alleles in F_1 plants also segregate during the process that gives rise to gametes (see Figure 3.6). Their gametes can carry either a T allele or a t allele, but not both.
- The term **genotype** refers to the genetic composition of an individual. Following self-fertilization, TT , Tt , and tt are the possible genotypes of the F_2 generation. By randomly combining these alleles, the genotypes are produced in a $1\ TT : 2\ Tt : 1\ tt$ ratio.
- The term **phenotype** refers to observable traits of an organism. Because TT and Tt both produce tall phenotypes, a 3 tall:1 short ratio of phenotypes is observed in the F_2 generation.

A Punnett Square Can Be Used to Predict the Outcome of Crosses and Self-Fertilization Experiments

An approach to predict the outcome of simple genetic crosses and self-fertilization experiments is to use a **Punnett square**, a method originally proposed by Reginald Punnett. To construct a Punnett square, you must know the genotypes of the parents. With this information, the Punnett square enables you to predict the types of offspring the parents are expected to produce and in what proportions.

Step 1. Write down the genotypes of both parents. (In a self-fertilization experiment, a single parent provides the sperm and egg cells.) Let's consider an example in which a heterozygous tall plant is crossed to another heterozygous tall plant. The plant providing the sperm (via pollen) is viewed as the male parent and the plant providing the eggs is the female parent.

Male parent: Tt

Female parent: Tt

Step 2. Write down the possible gametes that each parent can make. Remember that the law of segregation tells us that a gamete carries only one copy of each gene.

Male gametes: T or t

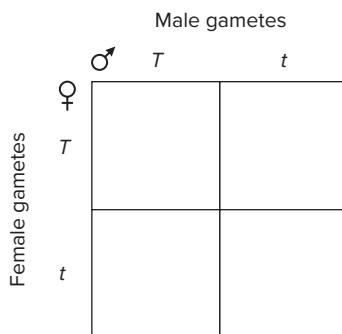
Female gametes: T or t

Step 3. Create an empty Punnett square. In the examples shown in this textbook, the number of columns equals the number of male gametes, and the number of rows equals

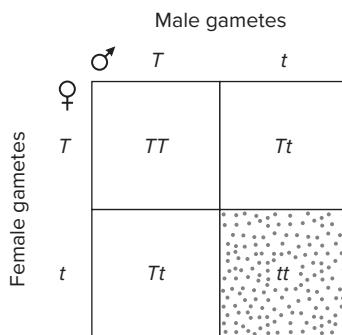


INTERACTIVE EXERCISE

the number of female gametes. Our example has two rows and two columns. Place the male gametes across the top of the Punnett square and the female gametes along the side.



Step 4. Fill in the possible genotypes of the offspring by combining the alleles of the gametes in the empty boxes.



Step 5. Determine the relative proportions of genotypes and phenotypes of the offspring. The genotypes are obtained directly from the Punnett square. These genotypes are contained within the boxes that have been filled in. In this example, the genotypes are TT , Tt , and tt in a 1:2:1 ratio. To determine the phenotypes, you must know the dominant/recessive relationship between the alleles. For plant height, T (tall) is dominant to t (short). The genotypes TT and Tt are tall, whereas the genotype tt is short. Therefore, our Punnett square shows us that the ratio of phenotypes is 3:1, or 3 tall plants : 1 short plant.

GENETIC TIPS

THE QUESTION: A pea plant that is heterozygous with regard to flower color (purple is dominant to white) is crossed to a pea plant with white flowers. What are the predicted outcomes of genotypes and phenotypes for the offspring?

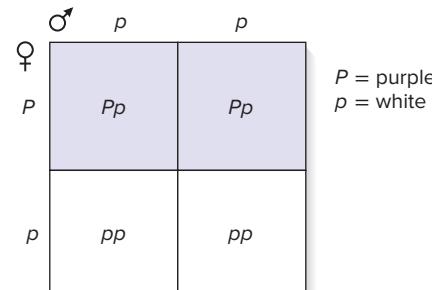
Topic: **What topic in genetics does this question address?** The topic is Mendelian inheritance. More specifically, the question is about a single-factor cross.

Information: **What information do you know based on the question and your understanding of the topic?** From the question, you know that one plant is heterozygous for flower color. If P is the purple allele and p the white allele, the genotype of this plant is Pp . The other plant exhibits the recessive phenotype, so its

genotype must be pp . From your understanding of the topic, you may remember that alleles segregate during gamete formation and each parent passes one allele to their offspring; the two alleles combine at fertilization.

P ROBLEM-SOLVING S TRATEGY: Predict the outcome.

One strategy to solve this type of problem is to use a Punnett square to predict the outcome of the cross. The Punnett square is shown next.



ANSWER: The ratio of offspring genotypes is 1 Pp : 1 pp . The ratio of the phenotypes is 1 purple : 1 white.

3.2 COMPREHENSION QUESTIONS

1. A pea plant is Tt . Which of the following statements is correct?
 - a. Its genotype is Tt , and its phenotype is short.
 - b. Its phenotype is Tt , and its genotype is short.
 - c. Its genotype is Tt , and its phenotype is tall.
 - d. Its phenotype is Tt , and its genotype is tall.
2. A Tt pea plant is crossed to a tt plant. What is the expected ratio of phenotypes for offspring from this cross?
 - a. 3 tall : 1 short
 - b. 1 tall : 1 short
 - c. 1 tall : 3 short
 - d. 2 tall : 1 short

3.3 LAW OF INDEPENDENT ASSORTMENT

Learning Outcomes:

1. Analyze Mendel's experiments involving two-factor crosses.
2. State Mendel's law of independent assortment.
3. Predict the outcome of a two-factor cross using a Punnett square.
4. Use the forked-line or multiplication method to predict the outcome of crosses involving three or more genes

Even though the experiments described in Figure 3.5 revealed important ideas regarding a hereditary law, Mendel realized

that additional insights might be uncovered if more complicated experiments were carried out. In this section, we will examine crosses in which Mendel simultaneously investigated the pattern of inheritance for two different characters. Such

two-factor crosses followed the inheritance of two different characters within the same groups of individuals. These experiments led to the formulation of a second law—the law of independent assortment.

EXPERIMENT 3B

Mendel Also Analyzed Crosses Involving Two Different Characters

To illustrate Mendel's work, we will consider an experiment in which one of the characters involved was seed shape, found in round or wrinkled variants, and the second character was seed color, which existed as yellow and green variants. In this two-factor cross, Mendel followed the inheritance pattern for both characters simultaneously.

What results are possible from a two-factor cross? One possibility is that the genes for these two different characters are always linked to each other and inherited as a single unit (**Figure 3.7a**). If this were the case, the F₁ offspring could produce only two types of gametes, RY and ry. A second possibility is the genes are not linked and can assort themselves independently into gametes (**Figure 3.7b**). If independent assortment occurred, an F₁ offspring could produce four types of gametes: RY, Ry, rY, and ry. Keep in mind that the results of Figure 3.5 have already shown us that a gamete carries only one allele for each gene.

The experimental protocol for this two-factor cross is shown in **Figure 3.8**. Mendel began with two different strains of true-breeding pea plants that were different in seed shape and seed color. One plant was produced from seeds that were round and yellow; the other plant from seeds that were wrinkled and green. When these plants were crossed, the seeds, which contain the plant embryo, are considered part of the F₁ generation. As expected, the data revealed that the F₁ seeds displayed a phenotype of round and yellow. This phenotype was observed because round and yellow are dominant traits. It is the F₂ generation that supports the independent-assortment model and refutes the linked-assortment model.

THE HYPOTHESES

The inheritance pattern for two different characters follows one or more quantitative natural laws. Two possible hypotheses are described in Figure 3.7.

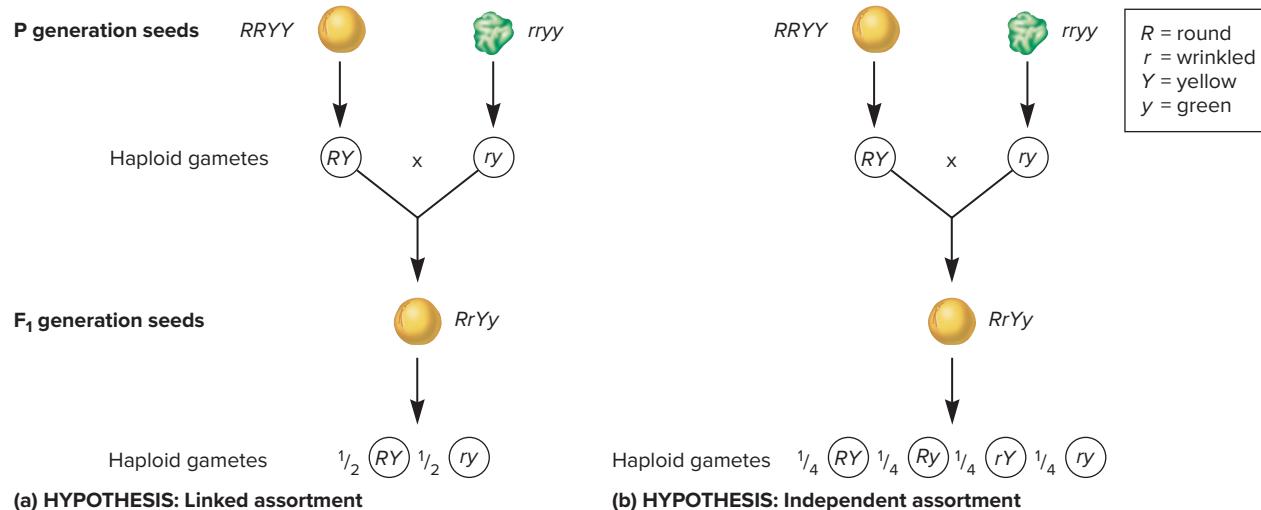
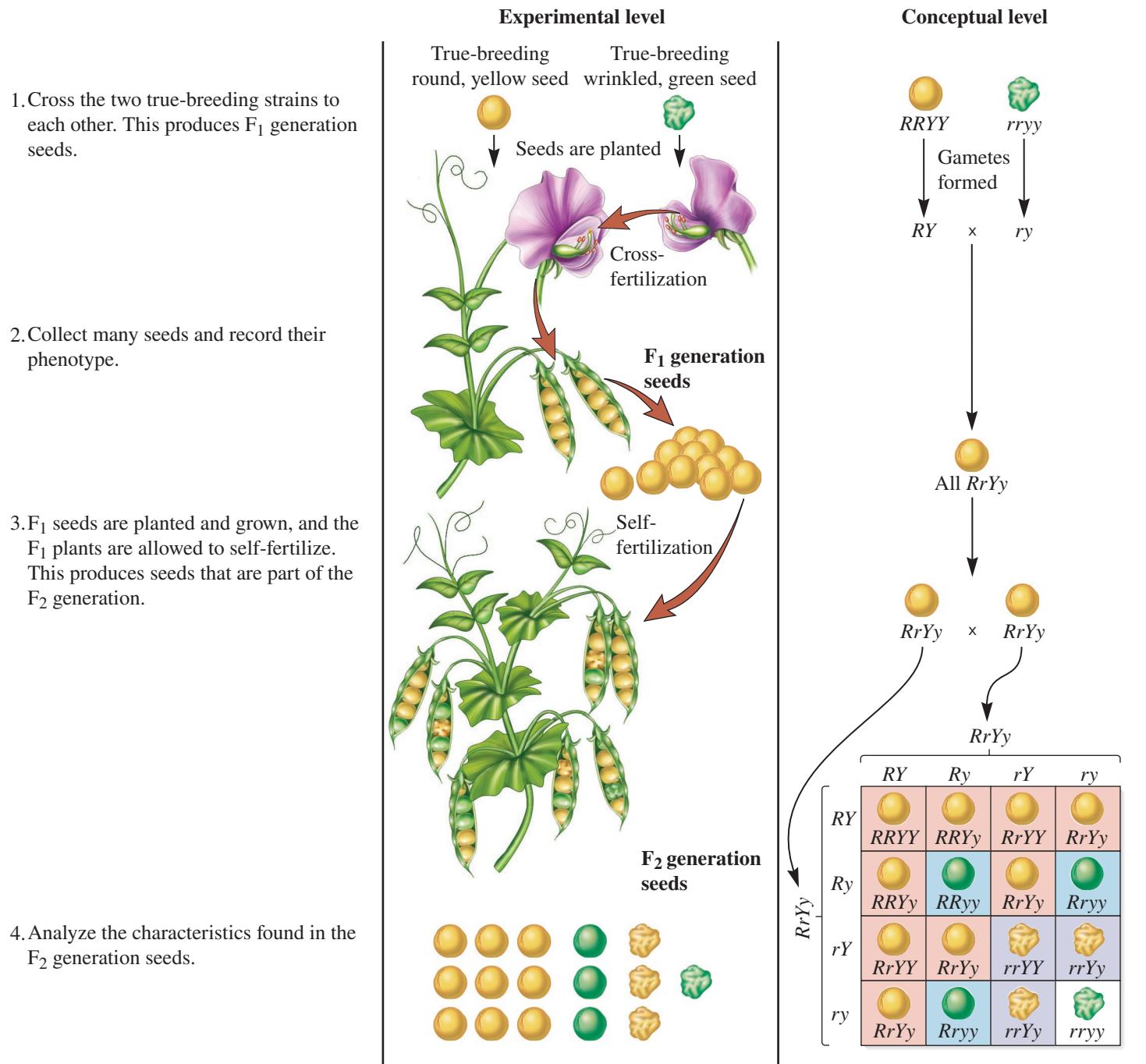


FIGURE 3.7 Two hypotheses to explain how two different genes assort during gamete formation. (a) According to the hypothesis of linked assortment, the two genes always stay associated with each other. (b) In contrast, the independent-assortment hypothesis proposes that the two different genes randomly segregate into haploid cells.

CONCEPT CHECK: According to the hypothesis of linked assortment shown here, what is linked? Are two different genes linked, or are two different alleles of the same gene linked, or both?

TESTING THE HYPOTHESES**FIGURE 3.8** Mendel's analysis of a two-factor cross.

Starting material: In this experiment, Mendel began with two types of true-breeding strains of pea plants that were different with regard to two characters. One strain produced round, yellow seeds (*RRYY*); the other strain produced wrinkled, green seeds (*rryy*).

**THE DATA**

P cross	F ₁ generation	F ₂ generation
Round, yellow seeds × wrinkled, green seeds	All round, yellow seeds	315 round, yellow seeds 108 round, green seeds 101 wrinkled, yellow seeds 32 wrinkled, green seeds

INTERPRETING THE DATA

As seen in the data, the F_2 generation had four categories of seeds. In addition to seeds that were like those of the parental generation, the F_2 generation also had seeds that were round and green and seeds that were wrinkled and yellow. These two categories of F_2 seeds are called **nonparental** because these combinations of

traits were not found in the true-breeding plants of the parental generation.

The occurrence of nonparental variants contradicts the linked-assortment hypothesis (see Figure 3.7a). According to that model, the *R* and *Y* alleles should be linked together and so should the *r* and *y* alleles. If this were the case, the F₁ plants could only

produce gametes that were *RY* or *ry*. These would combine to produce *RRYY* (round, yellow), *RrYy* (round, yellow), or *rryy* (wrinkled, green) seeds in a 1:2:1 ratio. Nonparental seeds could, therefore, not be produced. However, Mendel did not obtain this result. Instead, a phenotypic ratio of 9:3:3:1 was observed in the F₂ generation.

Mendel's Two-Factor Crosses Led to the Law of Independent Assortment

Mendel's results from many two-factor crosses rejected the linked-assortment hypothesis and, instead, supported the hypothesis that different characters assort themselves independently. Using modern terminology, **Mendel's law of independent assortment** states the following:

Two different genes will randomly assort their alleles during the process that gives rise to gametes.

In other words, the allele for one gene will be found within a resulting gamete independently of whether the allele for a different gene is found in the same gamete. In the example given in Figure 3.8, the round and wrinkled alleles are assorted into haploid gametes independently of the yellow and green alleles. Therefore, a heterozygous *RrYy* parent can produce four different gametes—*RY*, *Ry*, *rY*, and *ry*—in equal proportions.

In an F₁ self-fertilization experiment, any two gametes can combine randomly during fertilization. This allows for 4², or 16, possible offspring, although some offspring will be genetically identical to each other. As shown in **Figure 3.9**, these 16 possible

combinations result in seeds with the following phenotypes: 9 round, yellow; 3 round, green; 3 wrinkled, yellow; and 1 wrinkled, green. This 9:3:3:1 ratio is the expected outcome when a plant that is heterozygous for both genes is allowed to self-fertilize. Mendel was clever enough to realize that the data from the two-factor crosses were close to a 9:3:3:1 ratio.

As an example, let's consider the data in Figure 3.8. The F₁ generation produced F₂ seeds with the following phenotypes: 315 round, yellow; 108 round, green; 101 wrinkled, yellow; and 32 wrinkled, green. This yielded a total of 556 seeds. If you divide each phenotype by 556 (the total number of seeds) and multiply by 16 (the total number of possible genotypes), the phenotypic ratio of the F₂ generation is 9.1 : 3.1 : 2.9 : 0.9. Within experimental error, Mendel's data approximated the predicted 9:3:3:1 ratio for the F₂ generation.

The law of independent assortment held true for two-factor crosses involving all seven characters described earlier in Figure 3.4. However, in other cases, the inheritance pattern of two different genes is consistent with the linked-assortment hypothesis described in Figure 3.7a. In Chapter 6, we will examine the inheritance of genes that are linked because they are close to each other within the same chromosome. As we will see, linked genes do not assort independently.

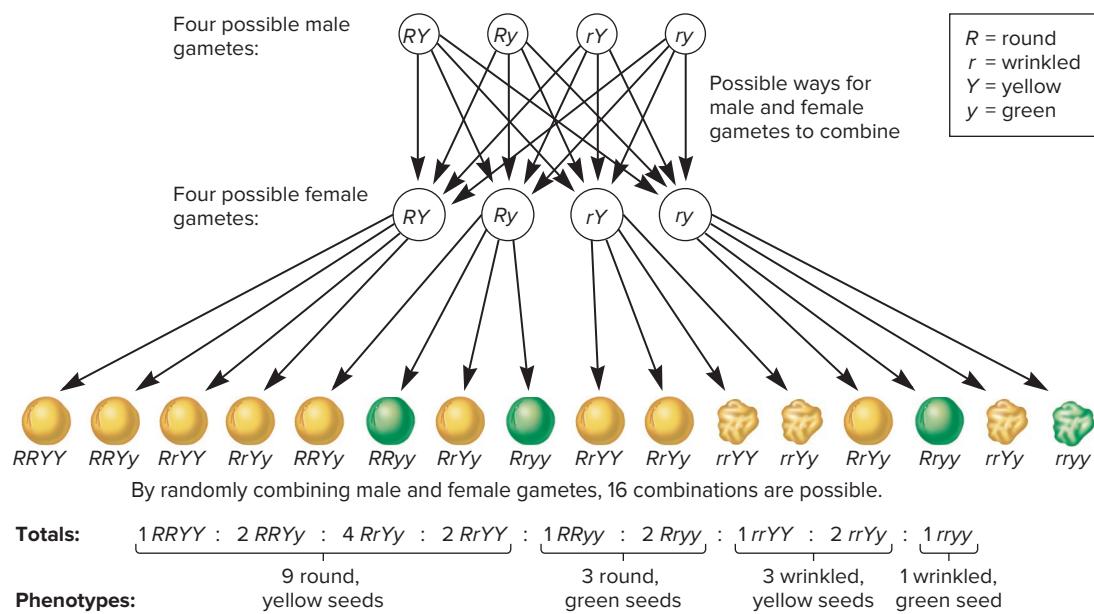


FIGURE 3.9 Mendel's law of independent assortment.

Genes→Traits This self-fertilization experiment involves a parent that is heterozygous for seed shape and seed color (*RrYy*). Four types of male gametes are possible: *RY*, *Ry*, *rY*, and *ry*. Likewise, four types of female gametes are possible: *RY*, *Ry*, *rY*, and *ry*. These four types of gametes are the result of the independent assortment of the seed shape and seed color alleles relative to each other. During fertilization, any one of the four types of male gametes can unite with any one of the four types of female gametes, resulting in 16 combinations.

CONCEPT CHECK: Why does independent assortment promote genetic variation?

Independent Assortment Promotes Genetic Diversity

An important consequence of the law of independent assortment is that a single individual can produce a vast array of genetically different gametes. As mentioned in Chapter 1, diploid species have pairs of homologous chromosomes, which may differ with respect to the alleles they carry. When an offspring receives a combination of alleles that differs from those in the parental generation, this phenomenon is termed **genetic recombination**. One mechanism that accounts for genetic recombination is independent assortment. A second mechanism, discussed in Chapter 6, is crossing over, which can reassort alleles that happen to be linked along the same chromosome.

The phenomenon of independent assortment is rooted in the random pattern in which the pairs of chromosomes assort themselves during the process of meiosis, a topic addressed in Section 3.4. When two different genes are found on different chromosomes, they randomly assort into haploid cells (look ahead to Figure 3.13). If a species contains a large number of chromosomes, this creates the potential for an enormous amount of genetic diversity.

Let's consider how independent assortment affects genetic diversity in humans. Human cells contain 23 pairs of chromosomes. These pairs separate and randomly assort into gametes during meiosis. The number of different gametes an individual can make equals 2^n , where n is the number of pairs of chromosomes. Therefore, a human can make 2^{23} , or over 8 million, possible gametes, due to independent assortment. The capacity to make so

many genetically different gametes enables a species to produce a great diversity of individuals with different combinations of traits. This variety of phenotypes allows environmental factors to select for those combinations of traits that favor reproductive success.

A Punnett Square Can Be Used to Solve Independent Assortment Problems

As depicted in Figure 3.8, we can make a Punnett square to predict the outcome of experiments involving two or more genes that assort independently. Let's see how such a Punnett square is made by considering a cross between two plants that are heterozygous for height and seed color (Figure 3.10). This cross is $TtYy \times TtYy$. When we construct a Punnett square for this cross, we must keep in mind that each gamete has a single allele for each of two genes. In this example, the four possible gametes from each parent are

TY , Ty , tY , and ty

In this two-factor cross, we need to make a Punnett square containing 16 boxes. The phenotypes of the resulting offspring are predicted to occur in a ratio of 9:3:3:1.

The Forked-Line and Multiplication Methods Can Also Be Used to Solve Independent Assortment Problems

In crosses involving three or more genes, the construction of a single large Punnett square becomes very unwieldy. For example, in a

		Cross: $TtYy \times TtYy$				T = tall t = short Y = yellow y = green
		TY	Ty	tY	ty	
TY	TY	$TTYY$ Tall, yellow	$TTYy$ Tall, yellow	$TtYY$ Tall, yellow	$TtYy$ Tall, yellow	
	Ty	$TTYy$ Tall, yellow	$TTyy$ Tall, green	$TtYy$ Tall, yellow	$Ttyy$ Tall, green	
tY	TY	$TtYY$ Tall, yellow	$TtYy$ Tall, yellow	$ttYY$ Short, yellow	$ttYy$ Short, yellow	
	Ty	$TtYy$ Tall, yellow	$Ttyy$ Tall, green	$ttYy$ Short, yellow	$ttyy$ Short, green	
Genotypes:		$1 TTYY : 2 TTYy : 4 TtYy : 2 TtYY : 1 TTyy : 2 Ttyy : 1 ttYY : 2 ttYy : 1 tyy$				
Phenotypes:		9 tall plants with yellow seeds		3 tall plants with green seeds	3 short plants with yellow seeds	1 short plant with green seeds

FIGURE 3.10 A Punnett square for a two-factor cross. The Punnett square shown here involves a cross between two pea plants that are heterozygous for height and seed color. The cross is $TtYy \times TtYy$.

CONCEPT CHECK: If a parent plant is $Ttyy$, how many different types of gametes can it make?

three-factor cross between two pea plants that are $Tt Rr Yy$, each parent can make 2^3 , or 8, possible gametes. Therefore, the Punnett square must contain $8 \times 8 = 64$ boxes. As a more reasonable alternative, we can consider each gene separately and then algebraically combine them by multiplying together the expected outcomes for each gene. Two methods for doing this kind of analysis are termed the forked-line method and the multiplication method. To illustrate these methods, let's consider the following question:

Two pea plants are heterozygous for three genes ($Tt Rr Yy$), where T = tall, t = short, R = round seeds, r = wrinkled seeds, Y = yellow seeds, and y = green seeds. If these plants are crossed to each other, what are the predicted phenotypes of the offspring, and what fraction of the offspring will have each phenotype?

You could solve this problem by constructing a large Punnett square and filling in the boxes. However, in this case, eight

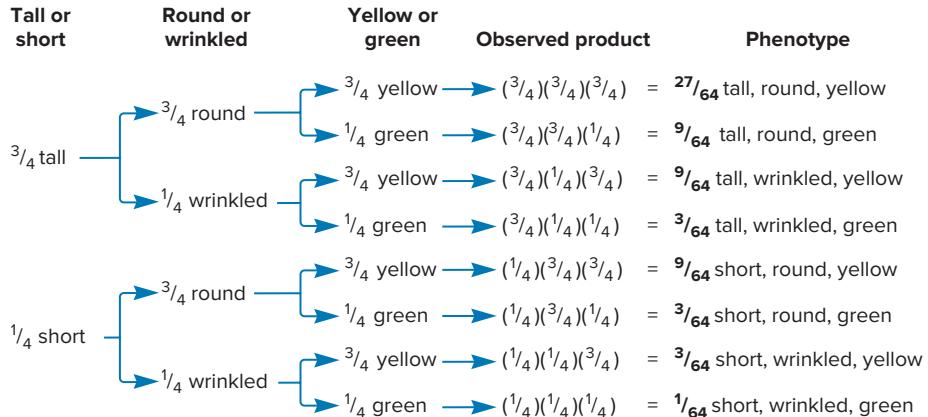
different male gametes and eight different female gametes are possible: TRY , TRy , TrY , tRY , trY , Try , tRy , and try . It would become rather time-consuming to construct and fill in this Punnett square, which would contain 64 boxes. As an alternative, we can consider each gene separately and then algebraically combine them by multiplying together the expected phenotypic outcomes for each gene. In the cross $Tt Rr Yy \times Tt Rr Yy$, a Punnett square can be made for each gene (Figure 3.11a).

In the **forked-line method**, a series of forked lines are created that connect the variants in this three-factor cross. The variants are tall or short, round or wrinkled, and yellow or green (Figure 3.11b). The genetic proportions of the 8 possible phenotype combinations are determined by multiplying the probabilities of each of the variants. For example, as shown at the top of Figure 3.11b, $3/4$ tall \times $3/4$ round \times $3/4$ yellow = $27/64$ tall, round, yellow.

An alternative to the forked-line method is the **multiplication method**. In this approach, you use the product rule (discussed

<table border="1"> <thead> <tr> <th>♂</th> <th>T</th> <th>t</th> </tr> <tr> <th>♀</th> <td>TT</td> <td>Tt</td> </tr> </thead> <tbody> <tr> <td>T</td> <td>Tall</td> <td>Tall</td> </tr> <tr> <td>t</td> <td>Tt</td> <td>tt</td> </tr> <tr> <td></td> <td>Tall</td> <td>Short</td> </tr> </tbody> </table> 3 tall : 1 short	♂	T	t	♀	TT	Tt	T	Tall	Tall	t	Tt	tt		Tall	Short	<table border="1"> <thead> <tr> <th>♂</th> <th>R</th> <th>r</th> </tr> <tr> <th>♀</th> <td>RR</td> <td>Rr</td> </tr> </thead> <tbody> <tr> <td>R</td> <td>Round</td> <td>Round</td> </tr> <tr> <td>r</td> <td>Rr</td> <td>rr</td> </tr> <tr> <td></td> <td>Round</td> <td>Wrinkled</td> </tr> </tbody> </table> 3 round : 1 wrinkled	♂	R	r	♀	RR	Rr	R	Round	Round	r	Rr	rr		Round	Wrinkled	<table border="1"> <thead> <tr> <th>♂</th> <th>Y</th> <th>y</th> </tr> <tr> <th>♀</th> <td>YY</td> <td>Yy</td> </tr> </thead> <tbody> <tr> <td>Y</td> <td>Yellow</td> <td>Yellow</td> </tr> <tr> <td>y</td> <td>Yy</td> <td>yy</td> </tr> <tr> <td></td> <td>Yellow</td> <td>Green</td> </tr> </tbody> </table> 3 yellow : 1 green	♂	Y	y	♀	YY	Yy	Y	Yellow	Yellow	y	Yy	yy		Yellow	Green
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	Yellow	Green																																													

(a) Punnett squares for each gene



(b) Forked-line method

$$P = (3 \text{ tall} + 1 \text{ short})(3 \text{ round} + 1 \text{ wrinkled})(3 \text{ yellow} + 1 \text{ green})$$

First, multiply $(3 \text{ tall} + 1 \text{ short})$ times $(3 \text{ round} + 1 \text{ wrinkled})$:

$$(3 \text{ tall} + 1 \text{ short})(3 \text{ round} + 1 \text{ wrinkled}) = 9 \text{ tall, round} + 3 \text{ tall, wrinkled} + 3 \text{ short, round} + 1 \text{ short, wrinkled}$$

Next, multiply this product by $(3 \text{ yellow} + 1 \text{ green})$:

$$P = (9 \text{ tall, round} + 3 \text{ tall, wrinkled} + 3 \text{ short, round} + 1 \text{ short, wrinkled})(3 \text{ yellow} + 1 \text{ green}) = 27 \text{ tall, round, yellow} + 9 \text{ tall, round, green} + 9 \text{ tall, wrinkled, yellow} + 3 \text{ tall, wrinkled, green} + 9 \text{ short, round, yellow} + 3 \text{ short, round, green} + 3 \text{ short, wrinkled, yellow} + 1 \text{ short, wrinkled, green}$$

(c) Multiplication method

FIGURE 3.11 Two alternative ways to predict the outcome of a three-factor cross. The cross is $Tt Rr Yy \times Tt Rr Yy$. (a) For both methods, each gene is treated separately. The three Punnett squares predict the outcome for each gene. (b) Forked-line method. (c) Multiplication method.

later in Section 3.6) and multiply the phenotypic outcomes together in three sequential pairs: (3 tall + 1 short)(3 round + 1 wrinkled)(3 yellow + 1 green) (**Figure 3.11c**). Even though the multiplication steps are rather tedious, this approach is usually faster than making a Punnett square with 64 boxes, filling them in, deducing each phenotype, and then adding them up.

3.3 COMPREHENSION QUESTIONS

1. A pea plant has the genotype $rrYy$. How many different types of gametes can it make and in what proportions?
 - a. 1 rr : 1 Yy
 - b. 1 rY : 1 ry
 - c. 3 rY : 1 ry
 - d. 1 RY : 1 rY : 1 Ry : 1 ry
2. A cross is made between a pea plant that is $RrYy$ and one that is $rrYy$. What is the predicted outcome of the seed phenotypes?
 - a. 9 round, yellow : 3 round, green : 3 wrinkled, yellow : 1 wrinkled, green
 - b. 3 round, yellow : 3 round, green : 1 wrinkled, yellow : 1 wrinkled, green
 - c. 3 round, yellow : 1 round, green : 3 wrinkled, yellow : 1 wrinkled, green
 - d. 1 round, yellow : 1 round, green : 1 wrinkled, yellow : 1 wrinkled, green
3. In a population of wild squirrels, most of them have gray fur, but an occasional squirrel is completely white. If we let P and p represent dominant and recessive alleles, respectively, of a gene that codes an enzyme necessary for pigment formation, which of the following statements do you think is most likely to be correct?
 - a. The white squirrels are pp , and the p allele is a loss-of-function allele.
 - b. The gray squirrels are pp , and the p allele is a loss-of-function allele.
 - c. The white squirrels are PP , and the P allele is a loss-of-function allele.
 - d. The gray squirrels are PP , and the P allele is a loss-of-function allele.

3.4 THE CHROMOSOME THEORY OF INHERITANCE

Learning Outcomes:

1. List the five principles of the chromosome theory of inheritance.
2. Explain the relationship between meiosis and Mendel's laws of inheritance.
3. Analyze the results of Morgan's experiment, which showed that a gene affecting eye color in fruit flies is located on the X chromosome.

The **chromosome theory of inheritance** explains the relationship between the transmission of chromosomes from parent to offspring and the transmission of traits from parent to offspring. This theory was a major breakthrough in the study of genetics because it established the framework for understanding how chromosomes carry and transmit the genetic determinants that govern the outcome of traits. In this section, we will examine the five principles of the chromosome theory of inheritance and consider how they relate to Mendel's laws of inheritance. We will also consider an experiment in fruit flies that provided evidence for this theory.

The Chromosome Theory of Inheritance Relates the Behavior of Chromosomes to the Mendelian Inheritance of Traits

This theory dramatically unfolded as a result of three lines of scientific inquiry.

- One of these concerned Mendel's breeding studies, in which the transmission of traits from parent to offspring were analyzed quantitatively.
- A second line of inquiry focused on the biochemical basis for heredity. Carl Nageli and August Weismann championed the idea that a substance found in living cells is responsible for the transmission of traits from parent to offspring. Nageli also suggested that both parents contribute equal amounts of this substance to their offspring. We now know that DNA within the chromosomes is the genetic material.
- The third line of inquiry involved the microscopic examination of the processes of meiosis and fertilization. When the work of Mendel was rediscovered, several scientists noted striking parallels between the segregation and assortment of traits noted by Mendel and the behavior of chromosomes during meiosis. Among them were Theodor Boveri and Walter Sutton, who independently proposed the chromosome theory of inheritance.

According to this theory, the inheritance patterns of traits can be explained by the transmission patterns of chromosomes during meiosis and fertilization. The chromosome theory of inheritance is based on a few fundamental principles:

1. Chromosomes contain the genetic material that is transmitted from parent to offspring and from cell to cell.
2. Chromosomes are replicated and passed along, generation after generation, from parent to offspring. They are also passed from cell to cell during the development of a multicellular organism. Each type of chromosome retains its individuality during cell division and gamete formation.
3. The nuclei of most eukaryotic cells contain chromosomes that are found in homologous pairs—the cells are diploid. One member of each pair is inherited from the female parent, the other from the male parent. At meiosis, one of the two members of each pair segregates into one daughter

cell, and its homolog segregates into the other daughter cell. Gametes contain one set of chromosomes—they are haploid.

- During the formation of haploid cells, different types of (nonhomologous) chromosomes segregate independently of each other.
- At fertilization, each parent contributes one set of chromosomes to its offspring. The maternal and paternal sets of homologous chromosomes are functionally equivalent; each set carries a full complement of genes.

The Law of Segregation Is Explained by the Separation of Homologs During Meiosis

The chromosome theory of inheritance allows us to see the relationship between Mendel's laws and chromosome transmission. As shown in **Figure 3.12**, Mendel's law of segregation can be explained by the homologous pairing and segregation of chromosomes during meiosis. This figure depicts the behavior of a pair of homologous chromosomes that carry a gene for seed color in pea plants. One of the chromosomes carries a dominant allele that confers yellow seed color, whereas the homologous chromosome carries a recessive allele that confers green color. A heterozygous individual passes only one of these alleles to each offspring. In other words, a gamete may contain the yellow allele or the green allele but not both. Because the homologs segregate during meiosis I and the sister chromatids separate during meiosis II, a gamete contains only one copy of each type of chromosome.

The Law of Independent Assortment Is Explained by the Random Alignment of Homologs During Meiosis

How is the law of independent assortment explained by the behavior of chromosomes? **Figure 3.13** considers the segregation of two types of chromosomes in a pea plant, each carrying a different gene.

- One pair of chromosomes carries the gene for seed color: The yellow (*Y*) allele is on one chromosome, and the green (*y*) allele is on the homolog.
- The other pair of (smaller) chromosomes carries the gene for seed shape: One copy has the round (*R*) allele, and the homolog carries the wrinkled (*r*) allele.
- At metaphase of meiosis I, the different types of chromosomes have randomly aligned along the metaphase plate. As shown in Figure 3.13, this can occur in more than one way. On the left, the *y* allele has sorted with the *R* allele, whereas the *Y* allele has sorted with the *r* allele. On the right, the opposite situation has occurred. Therefore, the random alignment of chromatid pairs during meiosis I can lead to an independent assortment of genes that are found on nonhomologous chromosomes.

Heterozygous (*Yy*) cell from a pea plant with yellow seeds

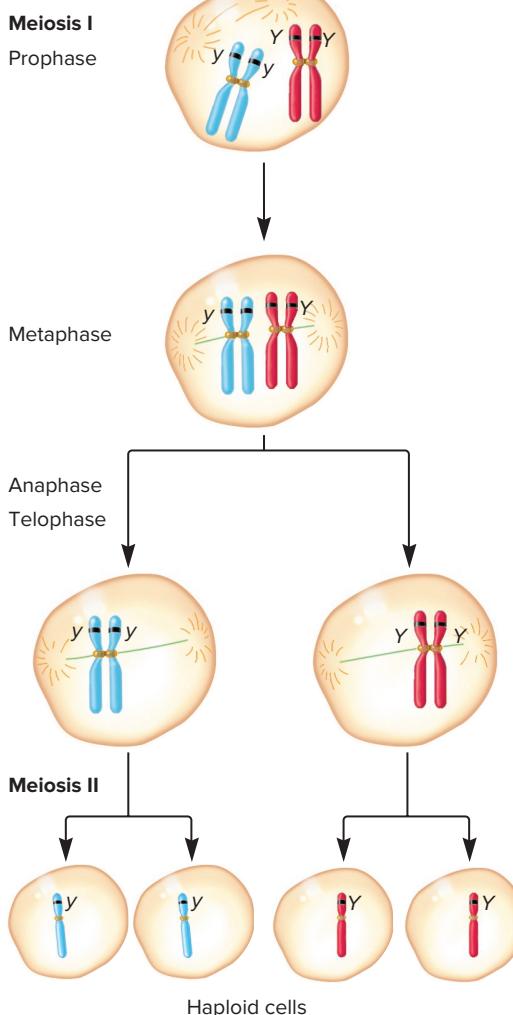


FIGURE 3.12 Mendel's law of segregation can be explained by the segregation of homologs during meiosis. The two copies of a gene are located on homologous chromosomes. In this example using pea plant seed color, the two alleles are *Y* (yellow) and *y* (green). During meiosis, the homologous chromosomes segregate from each other, leading to segregation of the two alleles into separate gametes.

Genes→Traits The gene for seed color exists in two alleles, *Y* (yellow) and *y* (green). During meiosis, the homologous chromosomes that carry these alleles segregate from each other. The resulting cells receive either the *Y* or *y* allele, but not both. When two gametes unite during fertilization, the alleles they carry determine the traits of the resulting offspring. In this case, they affect seed color, producing yellow or green seeds.

CONCEPT CHECK: At which stage of meiosis do homologous chromosomes separate from each other?

As we will see in Chapter 6, this law is violated if two different genes are located close to one another on the same chromosome.

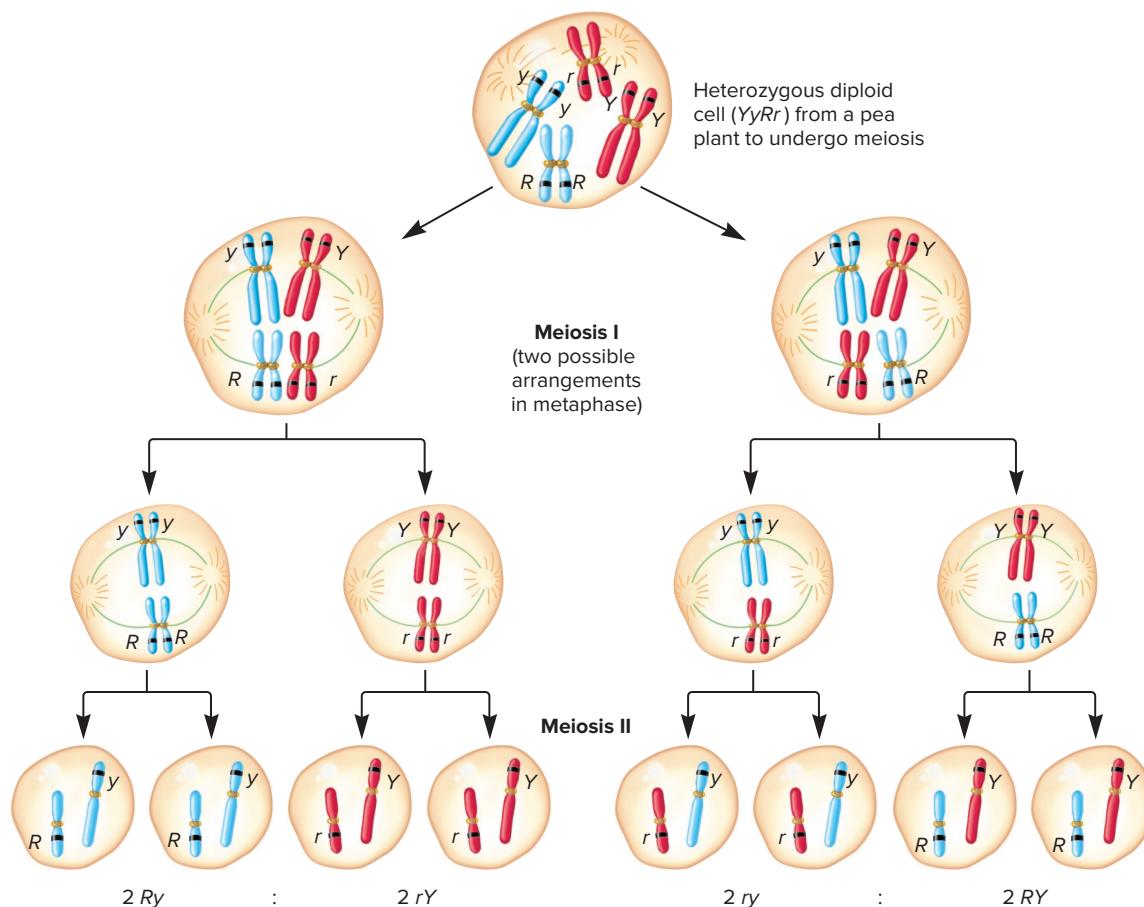


FIGURE 3.13 Mendel’s law of independent assortment can be explained by the random alignment of bivalents during metaphase of meiosis I. This figure shows the assortment of two genes located on two different chromosomes in a pea plant, using seed color and shape as an example ($YyRr$). During metaphase of meiosis I, different possible arrangements of the homologs within bivalents can lead to different combinations of the alleles in the resulting gametes. For example, on the left, the recessive y allele has sorted with the dominant R allele; on the right, the dominant Y allele has sorted with the dominant R allele.

Genes→Traits Most species have several different chromosomes that carry many different genes. In this example, the gene for seed color exists in two alleles, Y (yellow) and y (green), and the gene for seed shape is found as R (round) and r (wrinkled) alleles. The two genes are located on different (nonhomologous) chromosomes. During meiosis, the homologous chromosomes that carry these alleles segregate from each other. In addition, the chromosomes carrying the Y or y alleles will independently assort from the chromosomes carrying the R or r alleles. As shown here, this sorting process can create haploid cells with different combinations of alleles. When two gametes unite during fertilization, the alleles they carry affect the traits of the resulting offspring.

CONCEPT CHECK: Let’s suppose a pea plant is heterozygous for three genes, $Tt Yy Rr$, and each gene is on a different chromosome. How many different ways could the three pairs of homologous chromosomes line up during metaphase of meiosis I?

EXPERIMENT 3C

Morgan’s Experiments Showed a Connection Between a Genetic Trait and the Inheritance of a Sex Chromosome in *Drosophila*

Even though an examination of meiosis provided compelling evidence that Mendel’s laws could be explained by chromosome sorting, researchers still needed to correlate chromosome behavior with the inheritance of particular traits. In the early 1900s, American geneticist Thomas Hunt Morgan carried out a particularly influential study that confirmed the chromosome theory of inheritance by

showing that a gene affecting eye color in fruit flies (*Drosophila melanogaster*) is located on the X chromosome.

Within a population of red-eyed flies, Morgan identified a male fruit fly with white eyes rather than the common (wild-type) red eyes. Because this had been a true-breeding strain of flies, this white-eyed male must have arisen from a new mutation that converted a red-eye allele (denoted w^+) into a white-eye allele (denoted w). Morgan is said to have carried this fly home with him in a jar, kept it on a bedside table at night, and then took it back to the laboratory during the day!

Morgan studied the inheritance of this white-eye trait by making crosses and quantitatively analyzing their outcome (**Figure 3.14**). First, the white-eyed male was crossed to a true-breeding red-eyed female. All of the F₁ offspring had red eyes, indicating that red is dominant to white. Next, the F₁ offspring were then mated to each other to obtain an F₂ generation.

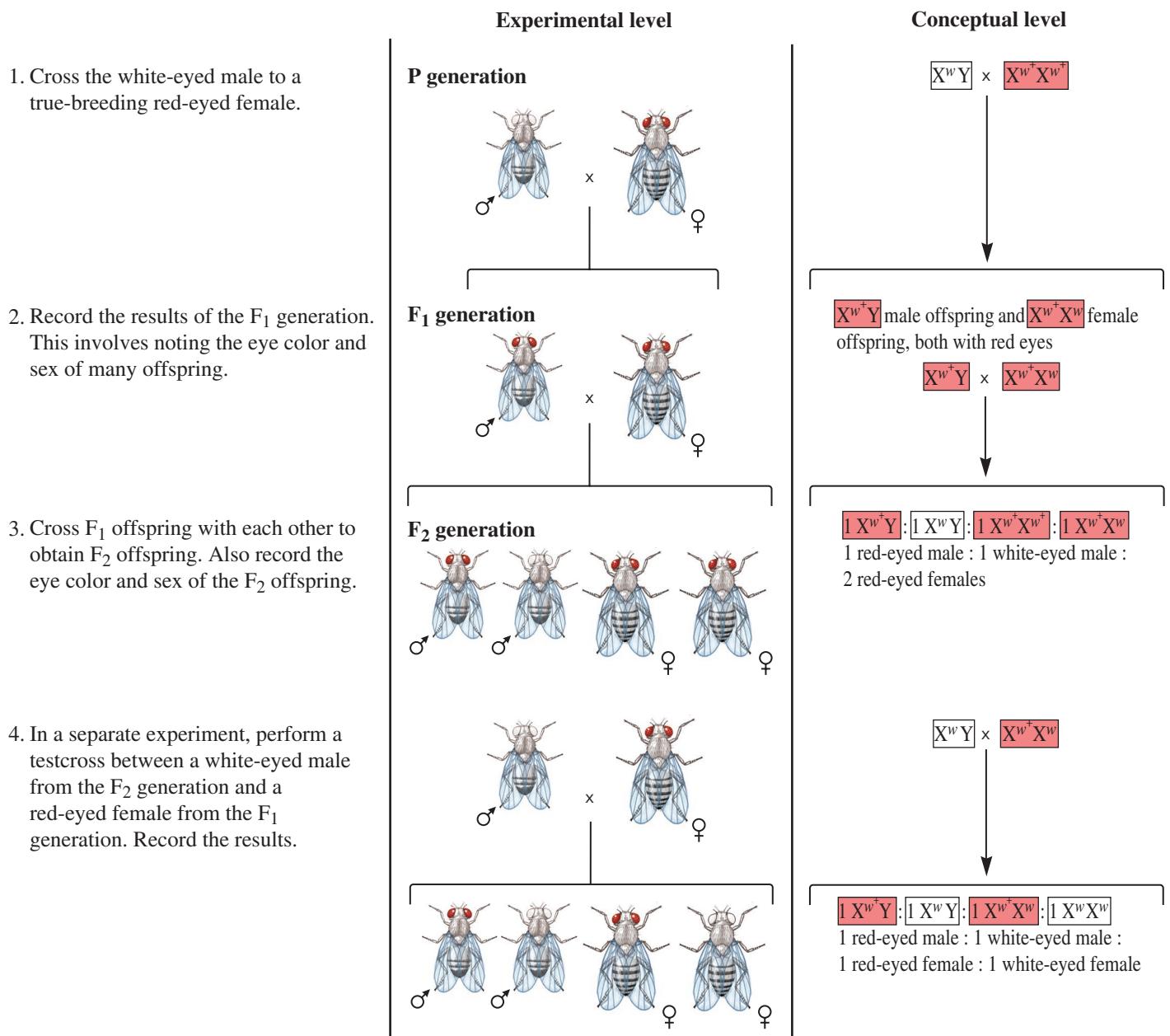
THE GOAL (DISCOVERY-BASED SCIENCE)

This is an example of discovery-based science rather than hypothesis testing. In this case, a quantitative analysis of genetic crosses may reveal the inheritance pattern for the white-eye allele.

ACHIEVING THE GOAL

FIGURE 3.14 Inheritance pattern of an X-linked trait in fruit flies.

Starting material: A true-breeding strain of red-eyed fruit flies plus one white-eyed male fly that was discovered in the population.



THE DATA

Cross	Results
Original white-eyed male to a true-breeding red-eyed female	F ₁ generation: All red-eyed flies
F ₁ male to F ₁ female	F ₂ generation: 2459 red-eyed females 1011 red-eyed males 0 white-eyed females 782 white-eyed males
F ₂ white-eyed male to F ₁ female	Testcross: 129 red-eyed females 132 red-eyed males 88 white-eyed females 86 white-eyed males

Source: Morgan, Thomas H., "Sex limited inheritance in *Drosophila*," *Science*, vol. 32, no. 812, July 22, 1910, 120–122.

INTERPRETING THE DATA

As seen in the data table, the F₂ generation consisted of 2459 red-eyed females, 1011 red-eyed males, and 782 white-eyed males. Most notably, no white-eyed female offspring were observed in the F₂ generation. These results suggested that the pattern of transmission from parent to offspring depends on the sex of the offspring and on the alleles that they carry. As shown in the Punnett square below, the data are consistent with the idea that the eye color alleles are located on the X chromosome. This phenomenon is called **X-linked inheritance**.

		Male gametes	
		♂ X ^{w+}	Y
Female gametes	X ^{w+}	X ^{w+} X ^{w+} Red, female	X ^{w+} Y Red, male
	X ^w	X ^{w+} X ^w Red, female	X ^w Y White, male

The Punnett square predicts that the F₂ generation will not have any white-eyed females. This prediction was confirmed

experimentally. These results indicated that the eye color alleles are located on the X chromosome. Genes that are physically located within the X chromosome are called **X-linked genes**, or **X-linked alleles**.

However, it should also be pointed out that the experimental ratio of red eyes to white eyes in the F₂ generation is (2459 + 1011):782, which equals 4.4:1. This ratio deviates significantly from the predicted ratio of 3:1. How can this discrepancy be explained? Later work revealed that the lower-than-expected number of white-eyed flies is due to their decreased survival rate.

Morgan also conducted a **testcross** (see step 4, Figure 3.14) in which an individual with a dominant phenotype and unknown genotype is crossed to an individual with a recessive phenotype. In this case, an F₁ red-eyed female was mated to an F₂ white-eyed male. This cross produced red-eyed males and females in approximately equal numbers, and white-eyed males and females in approximately equal numbers. The testcross data are also consistent with an X-linked pattern of inheritance. As shown in the following Punnett square, a 1:1:1:1 ratio is predicted for this testcross:

Testcross:
Male is X^wY
F₁ female is X^{w+}X^w

		Male gametes	
		X ^w	Y
Female gametes	♂ X ^{w+}	X ^{w+} X ^w Red, female	X ^{w+} Y Red, male
	X ^w	X ^w X ^w White, female	X ^w Y White, male

The observed data are 129:132:88:86, which is a ratio of 1.5:1.5:1:1. Again, the lower-than-expected numbers of white-eyed males and females can be explained by a lower survival rate for white-eyed flies. Based on these data, Morgan concluded that red eye color and X (a sex factor that is present in two copies in the female) are combined and have never existed apart. In other words, this gene for eye color is on the X chromosome. Morgan was the first geneticist to receive a Nobel Prize.

3.4 COMPREHENSION QUESTIONS

- Which of the following is *not* one of the principles of the chromosome theory of inheritance?
 - Chromosomes contain the genetic material that is transmitted from parent to offspring and from cell to cell.

- Chromosomes are replicated and passed along, generation after generation, from parent to offspring.
- Chromosome replication occurs during S phase of the cell cycle.
- Each parent contributes one set of chromosomes to its offspring.

2. A pea plant has the genotype $TtRr$. The independent assortment of these two genes occurs at _____ because chromosomes carrying the _____ alleles line up independently of the chromosomes carrying the _____ alleles.
- metaphase of meiosis I, T and t , R and r
 - metaphase of meiosis I, T and R , t and r
 - metaphase of meiosis II, T and t , R and r
 - metaphase of meiosis II, T and R , t and r

3.5 STUDYING INHERITANCE PATTERNS IN HUMANS

Learning Outcomes:

- Describe the features of a pedigree.
- Analyze a pedigree to determine if a trait or disease is dominant or recessive.

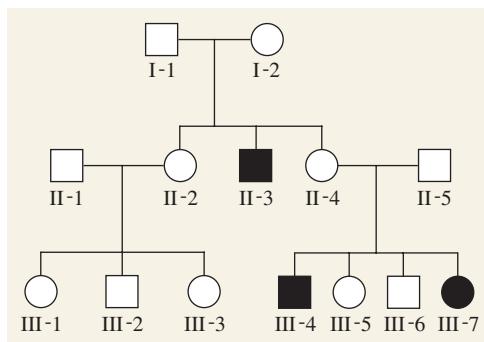
Before we end our discussion of simple Mendelian traits, let's address the question of how we can analyze inheritance patterns that occur in humans. As discussed in Sections 3.2 and 3.3, Mendel selectively made crosses and then analyzed a large number of offspring. When studying human traits, however, researchers cannot control parental crosses. Instead, they must rely on the information that is contained within family trees, or **pedigrees**, which are charts representing family relationships. This type of approach, known as **pedigree analysis**, is aimed at determining the type of inheritance pattern that a gene follows. Although this method may be less definitive than performing experiments like Mendel's, pedigree analyses often provide important clues concerning the pattern of inheritance of traits within human families. An expanded discussion of human pedigrees is found in Chapter 24, which concerns the inheritance patterns of many human diseases.

In order to discuss the applications of pedigree analysis, we need to understand the organization and symbols of a pedigree (**Figure 3.15**).

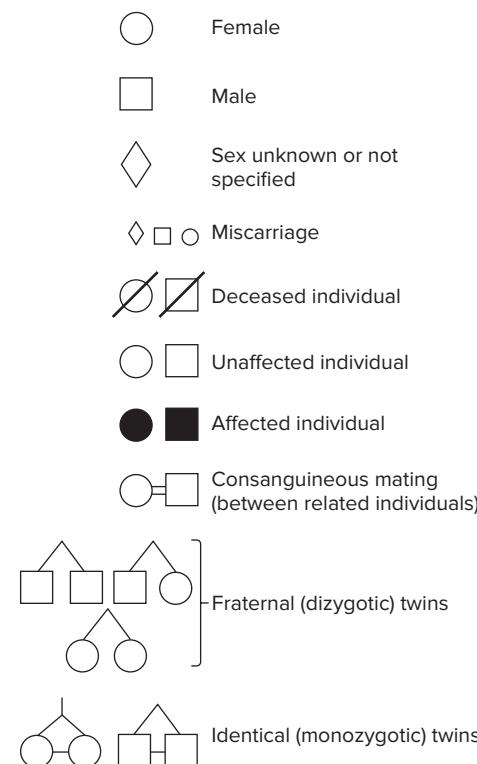
- The oldest generation is at the top of the pedigree, and the most recent generation is at the bottom.
- Vertical lines connect each succeeding generation.
- A male (square) and female (circle) who produce one or more offspring are directly connected by a horizontal line.
- A vertical line connects parents with their offspring.
- If parents produce two or more offspring, the group of siblings (male and/or female offspring) is denoted by two or more squares and/or circles projecting downward from the same horizontal line.

As discussed in Section 1.5 in Chapter 1, the terms *male* and *female* refer to an individuals' sex. These terms do not indicate gender identity.

The pedigree shown in Figure 3.15a involves the transmission of a human disorder called cystic fibrosis. Affected individuals are depicted by filled symbols (in this case, filled with



(a) Human pedigree showing cystic fibrosis



(b) Symbols used to denote phenotype in a human pedigree

FIGURE 3.15 Pedigree analysis. (a) A family pedigree in which some of the members are affected with cystic fibrosis. (b) The symbols used in a human pedigree. Note: The symbols shown here denote phenotypes, not genotypes.

CONCEPT CHECK: What are the two different meanings of horizontal lines in a pedigree?

black) that distinguish them from unaffected individuals. Each generation is given a roman numeral designation, and individuals within the same generation are numbered from left to right. A few examples of the genetic relationships in Figure 3.15a are described here:

- Individuals II-1 and II-2 are the parents of III-1, III-2, and III-3.
- Individuals I-1 and I-2 are the grandparents of III-1, III-2, III-3, III-4, III-5, III-6, and III-7.

- Individuals III-1, III-2, and III-3 are siblings.
- Individual III-4 is affected by a genetic disease.

The symbols in Figure 3.15 and those found in the problem sets at the end of the chapter indicate phenotypes. In such pedigrees, affected individuals are shown with filled symbols, and unaffected individuals, including those that might be heterozygous for a recessive disease, are depicted with unfilled symbols.

Pedigree analysis is commonly used to determine the inheritance pattern for human genetic diseases. Human geneticists are routinely interested in knowing whether a genetic disease is inherited as a recessive or dominant trait. One way to discern the dominant/recessive relationship between two alleles is by pedigree analysis. Genes that play a role in disease may exist as a common (wild-type) allele or a mutant allele that causes disease symptoms.

If the disease follows a simple Mendelian pattern of inheritance and is caused by a recessive allele, an individual must inherit two copies of the mutant allele to exhibit the disease. Therefore, a recessive pattern of inheritance makes two important predictions:

- Two heterozygous unaffected individuals will, on average, have 1/4 of their offspring affected.
- All offspring of two affected individuals will be affected.

Alternatively, with a dominant trait, affected individuals will have inherited the gene from at least one affected parent (unless a new mutation has occurred during gamete formation).

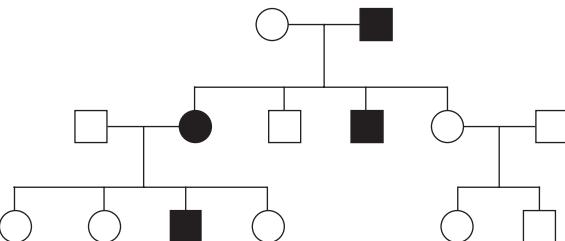
As mentioned, the pedigree in Figure 3.15a illustrates inheritance of a human genetic disease known as cystic fibrosis (CF). Among people of Northern European descent, approximately 3% of the population are heterozygous carriers of the recessive allele. In homozygotes, the disease symptoms include abnormalities of the pancreas, intestine, sweat glands, and lungs. These abnormalities are caused by an imbalance of ions across the plasma membranes of cells. In the lungs, this leads to a buildup of thick, sticky mucus. Respiratory problems may lead to early death, although modern treatments have greatly increased the life span of CF patients.

In the late 1980s, the gene for CF was identified. It codes a protein called the *cystic fibrosis transmembrane conductance regulator* (CFTR). This protein regulates ion balance across the cell membrane in tissues of the pancreas, intestine, sweat glands, and lungs. The mutant allele causing CF alters the CFTR protein in such a way that the altered protein is not correctly inserted into the plasma membrane, resulting in decreased function that causes the ion imbalance.

As seen in the pedigree, the pattern of affected and unaffected individuals is consistent with a recessive mode of inheritance. Two unaffected individuals can produce an affected offspring. Although not shown in this pedigree, a recessive mode of inheritance is also indicated by the observation that two affected individuals produce 100% affected offspring. However, for human genetic diseases that limit survival or fertility (or both), there may never be cases where two affected individuals produce offspring.

3.5 COMPREHENSION QUESTIONS

1. Which of the following would *not* be observed in a pedigree if a genetic disorder was inherited in a recessive manner?
 - a. Two unaffected parents have an affected offspring.
 - b. Two affected parents have an unaffected offspring.
 - c. One affected and one unaffected parent have an unaffected offspring.
 - d. All of the above are possible for a recessive disorder.
2. For the pedigree shown here, which pattern(s) of inheritance is/are possible? Affected individuals are shown with a filled symbol.



- a. Recessive
- b. Dominant
- c. Both recessive and dominant
- d. Neither recessive nor dominant

3.6 PROBABILITY AND STATISTICS

Learning Outcomes:

1. Define *probability*.
2. Predict the outcomes of crosses using the product rule or the binomial expansion equation.
3. Evaluate the validity of a hypothesis using a chi square test.

A powerful application of Mendel's work is that the laws of inheritance can be used to predict the outcomes of genetic crosses. In agriculture, for example, plant and animal breeders are concerned with the types of offspring resulting from their crosses. This information is used to produce commercially important crops and livestock. In addition, people are often interested in predicting the characteristics of the children they may have. This may be particularly important to individuals who carry alleles that cause inherited diseases. Of course, we cannot see into the future and definitively predict what will happen. Nevertheless, genetic counselors can help couples to predict the likelihood of having an affected child. This probability is one factor that may influence a couple's decision whether to have children.

In this section, we will see how probability calculations are used in genetic problems to predict the outcomes of crosses. We will consider two mathematical operations known as the product rule and the binomial expansion equation. These methods allow us to determine the probability that a cross between two individuals will produce a particular outcome. To apply these operations, we

must have some knowledge regarding the genotypes of the parents and the pattern of inheritance of a given trait. The following operations are used to solve certain types of problems:

- The product rule is used for problems in which the outcomes are independent of each other.
- The binomial expansion equation is used for problems having an unordered combination of outcomes.

Probability calculations can also be used in hypothesis testing. In many situations, a researcher would like to discern the genotypes and patterns of inheritance for traits that are not yet understood. A traditional approach to this type of problem is to conduct crosses and then analyze their outcomes. The proportions of offspring may provide important clues that allow the experimenter to propose a hypothesis, based on the quantitative laws of inheritance, that explains the transmission of the trait from parents to offspring. Statistical methods, such as the chi square test, can then be used to evaluate how well the observed data from crosses fit the expected data. We will end this chapter with an example that applies the chi square test to a genetic cross.

Probability Is the Likelihood That an Outcome Will Occur

The chance that an outcome will occur in the future is called the outcome's **probability**. For example, if you flip a coin, the probability is 0.50, or 50%, that the head side will be showing when the coin lands. Probability depends on the number of possible outcomes. In this case, two possible outcomes (heads or tails) are equally likely. This allows us to predict a 50% chance that a coin flip will produce heads. The general formula for probability (P) is

$$\text{Probability} = \frac{\text{Number of times a particular outcome occurs}}{\text{Total number of possible outcomes}}$$

Thus, the probability of heads for a coin flip is

$$P_{\text{heads}} = 1 \text{ heads} / (1 \text{ heads} + 1 \text{ tails}) = 1/2, \text{ or } 50\%$$

In genetic problems, we are often interested in the probability that a particular type of offspring will be produced. Recall that when two heterozygous tall pea plants (Tt) are crossed, the phenotypic ratio of the offspring is 3 tall to 1 short. This information can be used to calculate the probability for either type of offspring:

$$\text{Probability} = \frac{\text{Number of individuals with a given phenotype}}{\text{Total number of individuals}}$$

$$P_{\text{tall}} = 3 \text{ tall} / (3 \text{ tall} + 1 \text{ short}) = 3/4, \text{ or } 75\%$$

$$P_{\text{short}} = 1 \text{ short} / (3 \text{ tall} + 1 \text{ short}) = 1/4, \text{ or } 25\%$$

The probability is 75% for offspring that are tall and 25% for offspring that are short. When we add together the probabilities of all possible outcomes (tall and short), we should get a sum of 100% (here, 75% + 25% = 100%).

A probability calculation allows us to predict the likelihood that an outcome will occur in the future. The accuracy of this prediction, however, depends to a great extent on the size of the

sample. For example, if we toss a coin six times, our probability prediction suggests that 50% of the time we should get heads (i.e., three heads and three tails). With this small sample size, however, we would not be too surprised if we came up with four heads and two tails. Each time we toss a coin, there is a random chance that it will be heads or tails.

The deviation between the observed and expected outcomes is called the **random sampling error**. In a small sample of coin tosses, the error between the predicted percentage of heads and the actual percentage observed may be quite large. By comparison, if we flipped a coin 1000 times, the percentage of heads would be fairly close to the predicted 50% value. In a larger sample, we expect the random sampling error to be a much smaller percentage. For example, the fairly large data sets produced by Mendel had relatively small sampling errors (refer back to the data table following Figure 3.5).

The Product Rule Is Used to Predict the Probability of Independent Outcomes

We can use probability to make predictions regarding the likelihood of two or more independent outcomes from a genetic cross. When we say that outcomes are independent, we mean that the occurrence of one outcome does not affect the probability of another. As an example, let's consider a rare, recessive human trait known as congenital analgesia. Persons with this trait can distinguish between sharp and dull, and hot and cold, but do not perceive extremes of sensation as being painful. The first case of congenital analgesia, described in 1932, was a person who entertained the public as a "human pincushion."

For a phenotypically unaffected couple, in which each parent is heterozygous, Pp (where P is the common allele and p is the recessive allele causing congenital analgesia), we can ask, What is the probability that the couple's first three offspring will have congenital analgesia? To answer this question, the **product rule** is used. According to this rule,

The probability that two or more independent outcomes will occur is equal to the product of their individual probabilities.

A strategy for solving this type of problem is shown here.

The Cross: $Pp \times Pp$

The Question: What is the probability that this couple's first three offspring will have congenital analgesia?

Step 1. Calculate the individual probability of this phenotype.

As described previously, this is accomplished using a Punnett square. The probability of an affected offspring is 1/4.

Step 2. Multiply the individual probabilities. In this case, we are asking about the first three offspring, and so we multiply 1/4 three times.

$$1/4 \times 1/4 \times 1/4 = 1/64 = 0.016, \text{ or } 1.6\%$$

In this case, the probability that the first three offspring will have this trait is 0.016. We predict that 1.6% of the time the first three

offspring will all have congenital analgesia when both parents are heterozygotes. In this example, the phenotypes of the first, second, and third offspring are independent outcomes. The phenotype of the first offspring does not have an effect on the phenotype of the second or third offspring.

In the problem described here, we have used the product rule to determine the probability that the first three offspring will all have the same phenotype (congenital analgesia). We can also apply the rule to predict the probability of a sequence of outcomes that involves combinations of different offspring. For example, consider this question: What is the probability that the first offspring will be unaffected, the second offspring will have congenital analgesia, and the third offspring will be unaffected? Again, to solve this problem, we begin by calculating the individual probability of each phenotype.

$$\text{Unaffected} = 3/4$$

$$\text{Congenital analgesia} = 1/4$$

The probability that these three phenotypes will occur in this specified order is

$$3/4 \times 1/4 \times 3/4 = 9/64 = 0.14, \text{ or } 14\%$$

This sequence of outcomes is expected to occur 14% of the time.

The product rule can also be used to predict the outcome of a cross involving two or more genes. Let's suppose an individual with the genotype *Aa Bb CC* was crossed to an individual with the genotype *Aa bb Cc*. We could ask: What is the probability that an offspring will have the genotype *AA bb Cc*? If the three genes independently assort, the probability of inheriting alleles for each gene is independent of the probability for the two other genes. Therefore, we can separately calculate the probability of the desired outcome for each gene.

Cross: *Aa Bb CC* \times *Aa bb Cc*

$$\text{Probability that an offspring will be } AA = 1/4$$

$$\text{Probability that an offspring will be } bb = 1/2$$

$$\text{Probability that an offspring will be } Cc = 1/2$$

We can use the product rule to determine the probability that an offspring will be *AA bb Cc*:

$$P = 1/4 \times 1/2 \times 1/2 = 1/16 = 0.0625, \text{ or } 6.25\%$$

The Binomial Expansion Equation Is Used to Predict the Probability of an Unordered Combination of Outcomes

With regard to probability, unordered combinations are outcomes in which the order of a set of events does not matter. For example, a group of children in a given family might be composed of two females and one male, but the order of their births does not matter. From first to last, the order could be: female, female, male; female, male, female; or male, female, female.

With regard to genetics, the probability of an unordered combination also depends on the relative probability of each phenotype. For example, we can calculate the relative probabilities of brown-eyed and blue-eyed children, if both parents are

heterozygotes. As seen in the following Punnett square, 3/4 of the offspring have brown eyes and 1/4 have blue eyes.

♂	<i>B</i>	<i>b</i>	
♀	<i>B</i>	<i>Bb</i>	<i>BB</i>
<i>b</i>	<i>Bb</i>	<i>bb</i>	

B = brown
b = blue

With the relative probabilities of producing children with each type of eye color, we can calculate the probability of an unordered combination of offspring. In this case, we are not concerned with the order in which the offspring are born. Instead, we are only concerned with the final numbers of blue-eyed and brown-eyed offspring. To solve this type of problem, the **binomial expansion equation** can be used. This equation represents all of the possibilities for a given set of two unordered outcomes.

$$P = \frac{n!}{x!(n-x)!} p^x q^{n-x}$$

where

P = the probability that the unordered outcome will occur

n = total number of outcomes

x = number of outcomes in one category (e.g., blue eyes)

p = individual probability of *x*

q = individual probability of the other category
(e.g., brown eyes)

Note: In this case, $p + q = 1$.

The symbol ! denotes a factorial. The factorial *n*! is the product of all integers from *n* down to 1. For example, $4! = 4 \times 3 \times 2 \times 1 = 24$. An exception is $0!$, which equals 1.

The use of the binomial expansion equation is described next.

The Cross: *Bb* \times *Bb*

The Question: What is the probability that two out of five offspring will have blue eyes?

Step 1. Calculate the individual probabilities of the blue-eye and brown-eye phenotypes. If we constructed a Punnett square, we would find the probability of blue eyes is 1/4 and the probability of brown eyes is 3/4:

$$p = 1/4$$

$$q = 3/4$$

Step 2. Determine the number of outcomes in category *x* (in this case, blue eyes) versus the total number of outcomes. In this example, the number of outcomes in category *x* is two blue-eyed children among a total number of five.

$$x = 2$$

$$n = 5$$

Step 3. Substitute the values for p , q , x , and n in the binomial expansion equation.

$$P = \frac{n!}{x!(n-x)!} p^x q^{n-x}$$

$$P = \frac{5!}{2!(5-2)!} (1/4)^2 (3/4)^{5-2}$$

$$P = \frac{5 \times 4 \times 3 \times 2 \times 1}{(2 \times 1)(3 \times 2 \times 1)} (1/16) (27/64)$$

$$P = 0.26, \text{ or } 26\%$$

Thus, the probability is 0.26 that two out of five offspring will have blue eyes. In other words, 26% of the time we expect a $Bb \times Bb$ cross yielding five offspring to have two blue-eyed children and three brown-eyed children.

When more than two outcomes are possible, we use the **multinomial expansion equation** to solve a problem involving three or more types of unordered outcomes. A general expression for this equation is

$$P = \frac{n!}{a!b!c!\dots} p^a q^b r^c \dots$$

where

P = the probability that the unordered number of outcomes will occur

n = total number of outcomes

$a + b + c + \dots = n$

$p + q + r + \dots = 1$

(p is the likelihood of a , q is the likelihood of b , r is the likelihood of c , and so on)

The multinomial expansion equation can be useful for many genetic problems in which more than two combinations of offspring are possible. For example, this formula can be used to solve problems involving an unordered sequence of outcomes in a two-factor cross (see question 3 in More Genetic TIPS at the end of this chapter).

The Chi Square Test Is Used to Test the Validity of a Genetic Hypothesis

Let's now consider a different way to analyze genetic problems, namely **hypothesis testing**. Our goal here is to determine if the data from genetic crosses are consistent with a particular pattern of inheritance. For example, a geneticist may study the inheritance of body color and wing shape in fruit flies over the course of two generations. The following question may be asked about the F_2 generation: Do the observed numbers of offspring agree with the predicted numbers based on Mendel's laws of segregation and independent assortment? As we will see in Chapters 4 through 6, not all traits follow a Mendelian pattern of inheritance. Some genes do not segregate and independently assort themselves in the way that Mendel's seven characters did in pea plants.

To distinguish inheritance patterns that obey Mendel's laws from those that do not, a conventional strategy is to make crosses and then quantitatively analyze the offspring. Based on the

observed outcome, an experimenter may make a tentative hypothesis. For example, the data may seem to obey Mendel's laws. Hypothesis testing provides an objective, statistical method to evaluate whether the observed data really agree with the hypothesis. In other words, we use statistical methods to determine whether the data that have been gathered from crosses are consistent with predictions based on quantitative laws of inheritance.

The rationale behind certain types of statistical approaches is to evaluate the **goodness of fit** between the observed data from experimentation and the expected data that are predicted from a hypothesis. This predictive hypothesis is also called a **null hypothesis** because it is the hypothesis that the experimenter may or may not nullify. The null hypothesis assumes that there is no real difference between the observed and expected data. Any actual differences that occur are presumed to be due to random sampling error. In some cases, statistical methods may reveal a poor fit between hypothesis and data. In other words, a high deviation may be found between the observed and expected values. If this occurs, the null hypothesis is rejected or nullified. Hopefully, the experimenter can subsequently propose an alternative hypothesis that has a better fit with the data.

In other cases, if the observed and expected data are very similar, we conclude that the hypothesis is consistent with the observed outcome. It is reasonable to accept the hypothesis. However, it should be emphasized that statistical methods can never prove that a hypothesis is correct. They can provide insight as to whether or not the observed data seem reasonably consistent with a hypothesis. Alternative hypotheses, perhaps even ones that the experimenter has failed to realize, may also be consistent with the data.

One commonly used statistical method to determine goodness of fit is the **chi square test** (the symbol for "chi square" is χ^2). We can use the chi square test to analyze population data in which the members of the population fall into different categories. We typically have this kind of data when we evaluate the outcomes of genetic crosses, because these usually produce a population of offspring that differ with regard to phenotypes. The general formula for the chi square test is

$$\chi^2 = \Sigma \frac{(O - E)^2}{E}$$

where

O = observed data in each category

E = expected data in each category based on the experimenter's hypothesis

The symbol Σ means that the data values for each category are added together. For example, if the population data fell into two categories, the chi square calculation would be

$$\chi^2 = \frac{(O_1 - E_1)^2}{E_1} + \frac{(O_2 - E_2)^2}{E_2}$$

We can use the chi square test to determine if a genetic hypothesis is consistent with the observed outcome of a genetic cross. The strategy described next provides a step-by-step outline for applying the chi square test. In this problem, the experimenter wants to determine if a two-factor cross obeys Mendel's laws. The

experimental organism is *Drosophila melanogaster* (the common fruit fly), and the two characters involve wing shape and body color. Straight wing shape and curved wing shape are designated by c^+ and c , respectively; gray body color and ebony body color are designated by e^+ and e , respectively. Note: For certain species, such as *Drosophila melanogaster*, the convention is to designate the common (wild-type) allele with a plus sign. Recessive mutant alleles are designated with lowercase letters and dominant mutant alleles with capital letters.

The Cross: A true-breeding fly with straight wings and a gray body ($c^+c^+e^+e^+$) is crossed to a true-breeding fly with curved wings and an ebony body ($ccee$). The flies of the F_1 generation are then allowed to mate with each other to produce an F_2 generation.

The Outcome:

F_1 generation:	All offspring have straight wings and gray bodies.
F_2 generation:	193 straight wings, gray bodies 69 straight wings, ebony bodies 64 curved wings, gray bodies <u>26</u> curved wings, ebony bodies
Total:	<u>352</u>

Step 1. Propose a hypothesis that allows us to calculate the expected values based on Mendel's laws. The phenotypes of the F_1 generation suggest that the trait of straight wings is dominant to curved wings and gray body color is dominant to ebony. Looking at the F_2 generation, it appears that the data show a 9:3:3:1 ratio. If so, this is consistent with an independent assortment of the two characters.

Based on these observations, the null hypothesis is the following:

Straight (c^+) is dominant to curved (c), and gray (e^+) is dominant to ebony (e). The two characters segregate and assort independently from generation to generation.

Step 2. List the observed data, including the total number of observed offspring.

193 straight wings, gray bodies
69 straight wings, ebony bodies
64 curved wings, gray bodies
<u>26</u> curved wings, ebony bodies
352 Total

Step 3. Based on the hypothesis and the total number of observed offspring, calculate the expected values of the four phenotypes. We first need to calculate the individual probabilities of the four phenotypes. According to our hypothesis, the ratio of the F_2 generation should be 9:3:3:1. Therefore, the expected probabilities are as follows:

$$\begin{aligned} 9/16 &= \text{straight wings, gray bodies} \\ 3/16 &= \text{straight wings, ebony bodies} \end{aligned}$$

$$\begin{aligned} 3/16 &= \text{curved wings, gray bodies} \\ 1/16 &= \text{curved wings, ebony bodies} \end{aligned}$$

The observed F_2 generation contained a total of 352 individuals. Our next step is to calculate the expected numbers of each type of offspring when the total equals 352. This is accomplished by multiplying each individual probability by 352.

$$9/16 \times 352 = 198 \text{ (expected number with straight wings, gray bodies)}$$

$$3/16 \times 352 = 66 \text{ (expected number with straight wings, ebony bodies)}$$

$$3/16 \times 352 = 66 \text{ (expected number with curved wings, gray bodies)}$$

$$1/16 \times 352 = 22 \text{ (expected number with curved wings, ebony bodies)}$$

Step 4. Apply the chi square formula, using the observed data listed in step 2 and the expected values that have been calculated in step 3. In this case, the data include four categories, and thus the sum has four terms.

$$\chi^2 = \frac{(O_1 - E_1)^2}{E_1} + \frac{(O_2 - E_2)^2}{E_2} + \frac{(O_3 - E_3)^2}{E_3} + \frac{(O_4 - E_4)^2}{E_4}$$

$$\chi^2 = \frac{(193 - 198)^2}{198} + \frac{(69 - 66)^2}{66} + \frac{(64 - 66)^2}{66} + \frac{(26 - 22)^2}{22}$$

$$\chi^2 = 0.13 + 0.14 + 0.06 + 0.73 = 1.06$$

Step 5. Determine the degrees of freedom. Before we can determine the probability that this deviation occurred as a matter of random chance, we must first determine the degrees of freedom (df) in this experiment. The **degrees of freedom** indicate the number of categories that are independent of each other. When phenotype categories are derived from a Punnett square, the degrees of freedom are typically given by $n - 1$, where n equals the total number of categories. In our fruit fly problem, $n = 4$ (the categories are the phenotypes: straight wings and gray body; straight wings and ebony body; curved wings and gray body; and curved wings and ebony body); thus, the degrees of freedom equal 3.* We now have sufficient information to interpret our chi square value of 1.06.

Step 6. Determine the P value for the chi square value calculated in step 4. This is done using a chi square table and the degrees of freedom determined in step 5. We must use **Table 3.1** to determine a **P value**, which is the probability that the amount of variation indicated by a given chi square value is due to random chance alone, based on a particular hypothesis. The chi square value is 1.06 and the degrees of freedom equals 3. Begin in the left column at 3 degrees of freedom and slide to the right until you identify the range where 1.06 is located. In this case,

*If the hypothesis assumed that the law of segregation is obeyed, the degrees of freedom would be 1 (see Section 6.2).

TABLE 3.1
Chi Square Values and Probability

Degrees of Freedom	Null Hypothesis Rejected						
	P = 0.99	0.95	0.80	0.50	0.20	0.05	0.01
1	0.000157	0.00393	0.0642	0.455	1.642	3.841	6.635
2	0.020	0.103	0.446	1.386	3.219	5.991	9.210
3	0.115	0.352	1.005	2.366	4.642	7.815	11.345
4	0.297	0.711	1.649	3.357	5.989	9.488	13.277
5	0.554	1.145	2.343	4.351	7.289	11.070	15.086
6	0.872	1.635	3.070	5.348	8.558	12.592	16.812
7	1.239	2.167	3.822	6.346	9.803	14.067	18.475
8	1.646	2.733	4.594	7.344	11.030	15.507	20.090
9	2.088	3.325	5.380	8.343	12.242	16.919	21.666
10	2.558	3.940	6.179	9.342	13.442	18.307	23.209
15	5.229	7.261	10.307	14.339	19.311	24.996	30.578
20	8.260	10.851	14.578	19.337	25.038	31.410	37.566
25	11.524	14.611	18.940	24.337	30.675	37.652	44.314
30	14.953	18.493	23.364	29.336	36.250	43.773	50.892

Source: Fisher, Ronald A., and Yates, Frank, *Statistical Tables for Biological, Agricultural, and Medical Research*. London: Oliver and Boyd, 1943.

it is located between 1.005 and 2.366. If you then look up to the top of the table, 1.005 is a *P* value of 0.8 and 2.366 is 0.5. Our chi square value of 1.06 is pretty close to 1.005, so the *P* value is close to 0.8, or 80%.

Step 7. Interpret the *P* value you have obtained. As mentioned, a *P* value is the likelihood that the amount of variation indicated by a given chi square value is due to random chance alone, based on a particular hypothesis. In our example, the *P* value is approximately 0.8, or 80%. With 3 degrees of freedom, chi square values that are equal to or greater than 1.06 are expected to occur about 80% of the time when a hypothesis is correct. In other words, about 80 times out of 100 we expect that random chance alone will produce a deviation between the observed data and the expected data that is equal to or greater than 1.06. In general, such a low chi square value indicates a high probability that the observed deviations could be due to random chance alone. By comparison, if a high chi square value were obtained, an experimenter becomes suspicious that the high deviation has occurred because the hypothesis is incorrect.

A common convention is to reject the null hypothesis if the chi square value results in a probability that is less than 0.05 (less than 5%) or if the probability is less than 0.01 (less than 1%). These are called the 5% and 1% significance levels, respectively. Which level is better to choose? The choice is somewhat subjective. If you choose a 5% level rather than a 1% level, a disadvantage is that you are more likely to reject a null hypothesis that happens to be correct. Even so, choosing a 5% level

rather than a 1% level has the advantage that you are less likely to accept an incorrect null hypothesis.

For our problem involving flies with straight or curved wings and gray or ebony bodies, the calculated chi square value is 1.06, which gives a *P* value of approximately 0.80, or 80%. Because this *P* value is greater than 0.05, you accept the null hypothesis. To reject the null hypothesis at the 5% significance level, the chi square would have to be equal to or greater than 7.815 (see Table 3.1). Because it is actually far less than this value, you accept that the null hypothesis is correct. Keep in mind that the chi square test does not prove a hypothesis is correct! It is a statistical method for evaluating whether the data and hypothesis have a good fit. In other words, the chi square test provides an objective way to accept or reject a hypothesis based on the deviation between observed data and expected data.

3.6 COMPREHENSION QUESTIONS

1. A cross is made between *AA Bb Cc Dd* and *Aa Bb cc dd* individuals. Rather than making a very large Punnett square, which statistical operation could you use to solve this problem, and what would be the probability that the cross produces an offspring that is *AA bb Cc dd*?
 - a. Product rule, 1/32
 - b. Product rule, 1/4
 - c. Binomial expansion, 1/32
 - d. Binomial expansion, 1/4

- 2.** In dogs, brown fur color (*B*) is dominant to white (*b*). A cross is made between two heterozygotes for fur color. If the litter consists of six puppies, what is the probability that half of them will be white?
- 0.066, or 6.6%
 - 0.13, or 13%
 - 0.25, or 25%
 - 0.26, or 26%
- 3.** Which of the following operations could be used for hypothesis testing?
- Product rule
 - Binomial expansion equation
 - Chi square test
 - Any of the above operations could be used.

KEY TERMS

- 3.1:** gamete, sperm cell, pollen grains, anthers, egg cell, ovules, ovaries, stigma, cross, hybridization, hybrids, cross-fertilization, self-fertilization, strain, characters, trait, variant, true-breeding strain
- 3.2:** single-factor cross, monohybrids, empirical approach, parental generation (P generation), F₁ generation, F₂ generation, dominant, recessive, particulate theory of inheritance, segregate, gene, allele, Mendel's law of segregation, homozygous, heterozygous, genotype, phenotype, Punnett square
- 3.3:** two-factor crosses, nonparental, Mendel's law of independent assortment, genetic recombination, forked-line method, multiplication method

3.4: chromosome theory of inheritance, X-linked inheritance, X-linked gene, X-linked allele, testcross

3.5: pedigrees, pedigree analysis

3.6: probability, random sampling error, product rule, binomial expansion equation, multinomial expansion equation, hypothesis testing, goodness of fit, null hypothesis, chi square test, degrees of freedom, *P* value

CHAPTER SUMMARY

- Early ideas regarding inheritance of traits included pangenesis and the blending hypothesis of inheritance. These ideas were later refuted by the work of Mendel.

3.1 Mendel's Study of Pea Plants

- Sexual reproduction in pea plants occurs via pollination followed by fertilization (see Figure 3.1).
- Mendel chose pea plants as his experimental organism because it was easy to carry out cross-fertilization or self-fertilization experiments with these plants, and because pea plants were available in several varieties in which a character existed in two distinct variants (see Figures 3.2, 3.3, 3.4).

3.2 Law of Segregation

- By conducting single-factor crosses, Mendel proposed three key ideas regarding inheritance: (1) Traits may be dominant or recessive. (2) Genes are passed unaltered from generation to generation. (3) The law of segregation states the following: The two copies of a gene segregate (or separate) from each other during transmission from parent to offspring (see Figures 3.5, 3.6).
- A Punnett square is used to predict the outcome of single-factor crosses and self-fertilization experiments.

3.3 Law of Independent Assortment

- By conducting two-factor crosses, Mendel formulated the law of independent assortment: Two different genes will randomly

assort their alleles during the formation of haploid cells (see Figures 3.7, 3.8, 3.9).

- Independent assortment promotes genetic diversity.
- A Punnett square can be used to predict the outcomes of two-factor crosses (see Figure 3.10).
- The multiplication and forked-line methods are used to solve the outcomes of crosses involving three or more genes (see Figure 3.11).

3.4 The Chromosome Theory of Inheritance

- The chromosome theory of inheritance describes how the transmission of chromosomes can explain Mendel's laws. This theory is based on five fundamental principles.
- Mendel's law of segregation is explained by the separation of homologs during meiosis (see Figure 3.12).
- Mendel's law of independent assortment is explained by the random alignment of bivalents during metaphase of meiosis I (see Figure 3.13).
- Morgan's work provided strong evidence for the chromosome theory of inheritance by showing that a gene affecting eye color in fruit flies is located on the X chromosome (see Figure 3.14).

3.5 Studying Inheritance Patterns in Humans

- Human inheritance patterns are determined by analyzing charts that represent family relationships and are known as pedigrees (see Figure 3.15).

3.6 Probability and Statistics

- Probability is the number of times an outcome occurs divided by the total number of outcomes.
- According to the product rule, the probability that two or more independent outcomes will occur is equal to the product of their

- individual probabilities. This rule can be used to predict the outcome of crosses involving two or more genes.
- The binomial expansion equation is used to predict the probability of a given set of two unordered outcomes.
- The chi square test is used to test the validity of a hypothesis (see Table 3.1).

PROBLEM SETS & INSIGHTS

MORE GENETIC TIPS

1. In dogs, black fur color is dominant to white. Two heterozygous black dogs are mated. What is the probability of the following combinations of offspring?

- A litter of six pups, four with black fur and two with white fur
- A first litter of six pups, four with black fur and two with white fur, and then a second litter of seven pups, five with black fur and two with white fur

T OPIC: *What topic in genetics does this question address?* The topic is Mendelian inheritance. More specifically, the question is about a single-factor cross involving fur color in dogs.

I NFORMATION: *What information do you know based on the question and your understanding of the topic?* From the question, you know that black fur is dominant to white fur and that the parents are heterozygotes. If *B* is the black allele and *b* is the white allele, the genotype of each parent must be *Bb*. From your understanding of the topic, you may remember how to use a Punnett square to predict the outcome of a cross. You may also realize that each litter is an unordered combination of two different outcomes and, therefore, the binomial expansion can be used to calculate the probability of each litter.

P ROBLEM-SOLVING **S TRATEGIES:** *Predict the outcome.* **Make a calculation.** To begin to solve this problem, you need to know the probabilities of producing black offspring and white offspring. These can be deduced from a Punnett square, which is shown next.

	♂	B	b
♀			
<i>B</i>	<i>BB</i>	<i>Bb</i>	
<i>b</i>	<i>Bb</i>	<i>bb</i>	

$B = \text{black}$
 $b = \text{white}$

For part A of the question, you can derive probabilities for black and white fur from the Punnett square, and then use those values in the binomial expansion equation. For part B, you need two types of calculations. To determine the probability of each litter

occurring, you can use the binomial expansion equation. Because each litter is an independent outcome, you multiply the probability of the first litter times the probability of the second litter to get the probability of both litters occurring in this order.

ANSWER: From the Punnett square, you can deduce that the probability of black fur is $3/4$, or 0.75, and the probability of white fur is $1/4$, or 0.25.

A. Because this is an unordered combination of outcomes, you use the binomial expansion equation, where $n = 6$, $x = 4$, $p = 0.75$ (probability of black), and $q = 0.25$ (probability of white).

The answer is that such a litter will occur 0.297, or 29.7%, of the time.

B. The two litters occur in a row, so they are independent outcomes. Therefore, you use the product rule and multiply the probability of the first litter times the probability of the second litter. You need to use the binomial expansion equation for each litter: The result from this equation for the first litter is multiplied by the result for the second litter.

For the first litter, $n = 6$, $x = 4$, $p = 0.75$, $q = 0.25$. For the second litter, $n = 7$, $x = 5$, $p = 0.75$, $q = 0.25$.

The answer is that two such litters will occur in this order 0.092, or 9.2%, of the time.

2. A pea plant is heterozygous for three genes (*Tt Rr Yy*), where *T* = tall, *t* = short, *R* = round seeds, *r* = wrinkled seeds, and *Y* = yellow seeds, *y* = green seeds. Tall, round, and yellow are the dominant traits. What is the probability that an offspring from self-fertilization of this plant will be tall with wrinkled, yellow seeds?

T OPIC: *What topic in genetics does this question address?* The topic is Mendelian inheritance. More specifically, the question is about a three-factor self-fertilization experiment involving a pea plant.

I NFORMATION: *What information do you know based on the question and your understanding of the topic?* In the question, you are given the genotype of a pea plant and told that it is self-fertilized. From your understanding of the topic, you may remember how to use a Punnett square to predict the outcome of a self-fertilization experiment. You may also realize that the outcome for each gene can be considered an independent outcome and the product rule can be used to solve this type of problem.

P ROBLEM-SOLVING **S TRATEGIES:** *Predict the outcome.* **Make a calculation.** Instead of constructing a large, 64-box

Punnett square, you can make smaller Punnett squares to determine the probability of offspring inheriting each of the three genes and having particular phenotypes.

	♂	T	t
♀	T	TT	Tt
		Tall	Tall
t	t	Tt	tt
		Tall	Short

3 tall : 1 short

	♂	R	r
♀	R	RR	Rr
		Round	Round
r	r	Rr	rr
		Round	Wrinkled

3 round : 1 wrinkled

	♂	Y	y
♀	Y	YY	Yy
		Yellow	Yellow
y	y	Yy	yy
		Yellow	Green

3 yellow : 1 green

Next, you use the product rule. Multiply the specified combinations together. In this case, tall = 3/4, wrinkled = 1/4, and yellow = 3/4.

ANSWER: The probability of an offspring being tall with wrinkled, yellow seeds is

$$3/4 \times 1/4 \times 3/4 = 9/64 = 0.14, \text{ or } 14\%$$

3. A pea plant that is ($RrYy$) is allowed to self-fertilize. Round seed (R) is dominant to wrinkled (r), and yellow seed (Y) is dominant to green (y). What is the probability of producing the following group of five seeds: two round, yellow; one round, green; one wrinkled, yellow; and one wrinkled, green?

T OPIC: *What topic in genetics does this question address?* The topic is Mendelian inheritance. More specifically, the question is about a two-factor self-fertilization experiment involving a pea plant.

I NFORMATION: *What information do you know based on the question and your understanding of the topic?* In the question, you are given the genotype of a pea plant and told that it is self-fertilizing. From your understanding of the topic, you may remember how to use a Punnett square to predict the outcome of a self-fertilization experiment. You may also recall how to use the multinomial expansion equation to predict the probability of an unordered combination of offspring having more than two phenotypes.

P ROBLEM-SOLVING S TRATEGIES: *Predict the outcome.*

Make a calculation. To begin to solve this problem, you need to know the probability of producing the four types of offspring described in the question. As shown at the bottom of the Conceptual level in Figure 3.8, this can be determined from a Punnett square. The phenotypic ratio is: 9 round, yellow; 3 round, green; 3 wrinkled, yellow; and 1 wrinkled, green.

The probability of a round, yellow seed: $p = 9/16$

The probability of a round, green seed: $q = 3/16$

The probability of a wrinkled, yellow seed: $r = 3/16$

The probability of a wrinkled, green seed: $s = 1/16$

For the values in the multinomial expansion equation, you have

$$n = 5, a = 2, b = 1, c = 1, d = 1$$

ANSWER: Substitute the values in the multinomial expansion equation.

$$\begin{aligned} P &= \frac{n!}{a!b!c!d!} p^a q^b r^c s^d \\ P &= \frac{5!}{2!1!1!1!} (9/16)^2 (3/16)^1 (3/16)^1 (1/16)^1 \\ P &= 0.04, \text{ or } 4\% \end{aligned}$$

This means that 4% of the time you can expect to obtain five offspring with the phenotypes described in the question.

4. A cross was made between a hyacinth plant that has blue flowers and purple seeds and another hyacinth plant with white flowers and green seeds. The F_1 generation was then allowed to self-fertilize. The following data were obtained:

F_1 generation: All offspring have blue flowers with purple seeds.

F_2 generation: 208 offspring with blue flowers, purple seeds; 13 with blue flowers, green seeds; 19 with white flowers, purple seeds; and 60 with white flowers, green seeds. Total = 300 offspring.

Start with the hypothesis that blue flowers and purple seeds are dominant traits and that the two genes assort independently. Calculate a chi square value. What does this value mean with regard to your hypothesis? If you decide to reject the hypothesis, which aspect of the hypothesis do you think is incorrect (i.e., that blue flowers and purple seeds are dominant traits, or that the two genes assort independently)?

T OPIC: *What topic in genetics does this question address?* The topic is hypothesis testing. More specifically, the question is about evaluating the dominant and recessive relationships of two genes and determining if they are obeying the law of independent assortment.

I NFORMATION: *What information do you know based on the question and your understanding of the topic?* From the question, you know the outcome of a two-factor cross. You are given a starting hypothesis. From your understanding of the topic, you may remember that this type of experiment should produce a 9:3:3:1 ratio of the four types of offspring in the F₂ generation, according to the law of independent assortment. Alternatively, you could set up a Punnett square and deduce the outcome for the F₂ generation. You may also remember that the chi square test can be used to evaluate the validity of a hypothesis.

P ROBLEM-SOLVING **S** TRATEGY: *Analyze data.* One strategy is to analyze the data by carrying out a chi square test. According to the hypothesis, the F₂ generation should display a ratio of 9 offspring with blue flowers, purple seeds : 3 with blue flowers, green seeds : 3 with white flowers, purple seeds : 1 with white flowers, green seeds. Because a total of 300 offspring were produced, the expected numbers are as follows:

$$9/16 \times 300 = 169 \text{ blue flowers, purple seeds}$$

$$3/16 \times 300 = 56 \text{ blue flowers, green seeds}$$

$$3/16 \times 300 = 56 \text{ white flowers, purple seeds}$$

$$1/16 \times 300 = 19 \text{ white flowers, green seeds}$$

ANSWER: In this case, the data include four categories, and thus the sum for calculating the chi square value has four terms.

$$\chi^2 = \frac{(O_1 - E_1)^2}{E_1} + \frac{(O_2 - E_2)^2}{E_2} + \frac{(O_3 - E_3)^2}{E_3} + \frac{(O_4 - E_4)^2}{E_4}$$

$$\chi^2 = \frac{(208 - 169)^2}{169} + \frac{(13 - 56)^2}{56} + \frac{(19 - 56)^2}{56} + \frac{(60 - 19)^2}{19}$$

$$\chi^2 = 154.9$$

Looking up this value in the chi square table under 3 degrees of freedom, you see that it is much higher than would be expected 1% of the time by chance alone. Therefore, you reject the hypothesis. The idea that the two genes are assorting independently seems to be incorrect. The outcome for the F₁ generation supports the idea that blue flowers and purple seeds are dominant traits.

Note: We will discuss why independent assortment may not occur in Chapter 6.

5. Calvin Bridges, who worked in the lab of Morgan, made crosses to study the inheritance of X-linked traits in fruit flies. One of Bridges' experiments concerned two different X-linked genes affecting eye color and wing length. For the eye color gene, the red-eye allele (*w*⁺) is dominant to the white-eye allele (*w*). A second X-linked trait is wing length; the allele called *miniature* is recessive to the wild-type allele, which is called *long*. In this case, *m* represents the miniature allele and *m*⁺ the long allele. A male fly carrying a miniature allele on its single X chromosome has small (miniature) wings. A female must be homozygous, *mm*, in order to have miniature wings.

Bridges made a cross between X^{w,m+}X^{w,m+} female flies (white eyes and long wings) and X^{w+,m}Y male flies (red eyes and

miniature wings). Thousands of offspring were then examined with regard to their eye color, wing length, and sex. As expected, most of the offspring were females with red eyes and long wings or males with white eyes and long wings. On rare occasions (approximately 1 out of 1700 flies), however, female offspring with white eyes or males with red eyes were obtained. The wing length in these flies was also noted and then their chromosome composition was examined using a microscope. The following results were obtained:

Offspring	Eye Color	Wing Length	Sex Chromosomes
Expected females	Red	Long	XX
Expected males	White	Long	XY
Unexpected females (rare)	White	Long	XXY
Unexpected males (rare)	Red	Miniature	X0

Source: Bridges, Calvin B., "Non-disjunction as Proof of the Chromosome Theory of Heredity," *Genetics*, vol. 1, no. 2, March, 1916, 107–163.

Explain how the unexpected female and male offspring were produced.

T OPIC: *What topic in genetics does this question address?* The topic is X-linked inheritance—more specifically, the question is about X-linked inheritance and its relationship to abnormalities in chromosome number.

I NFORMATION: *What information do you know based on the question and your understanding of the topic?* From the question, you know the outcome of a cross involving X^{w,m+}X^{w,m+} female flies and X^{w+,m}Y male flies. From your understanding of the topic, you may remember that females transmit an X chromosome to both daughters and sons, whereas males transmit an X to their daughters and a Y to their sons. In fruit flies, sex is determined by the ratio of the number of X chromosomes to the number of sets of autosomes. It is not determined by the presence of the Y chromosome (see Figure 2.15).

P ROBLEM-SOLVING **S** TRATEGY: *Compare and contrast.* One strategy to solve this problem is to compare and contrast the outcomes of this cross if the female transmits the wrong number of chromosomes or if the male transmits the wrong number.

The cross is X^{w,m+}X^{w,m+} × X^{w+,m}Y.

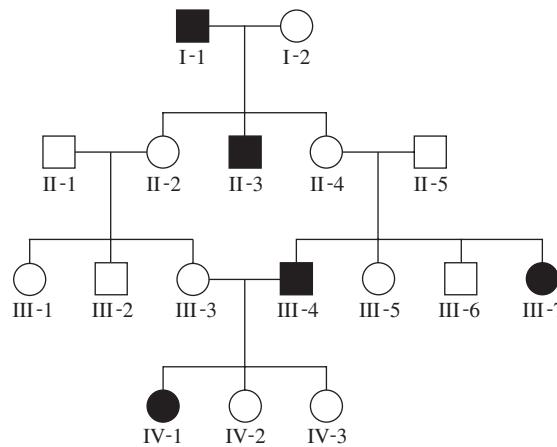
Female Transmits	Male Transmits	Offspring's Genotype	Offspring's Phenotype
X ^{w,m+} X ^{w,m+}	Y	X ^{w,m+} X ^{w,m+} Y	White eyes, long wings, female
X ^{w,m+} X ^{w,m+}	X ^{w+,m}	X ^{w,m+} X ^{w,m+} X ^{w+,m}	Red eyes, long wings, female
No sex chromosomes	Y	Y	Inviabie
No sex chromosomes	X ^{w+,m}	X ^{w+,m}	Red eyes, miniature wings, male
X ^{w,m+}	X ^{w+,m} Y	X ^{w,m+} X ^{w+,m} Y	Red eyes, long wings, female
X ^{w,m+}	No sex chromosomes	X ^{w,m+}	White eyes, long wings, male

ANSWER: The white-eyed female flies were due to the union between an abnormal XX female gamete and a normal Y male gamete. The unexpected male offspring had only one X chromosome and no Y. These male offspring were due to the union between an abnormal egg without any X chromosome and a normal sperm

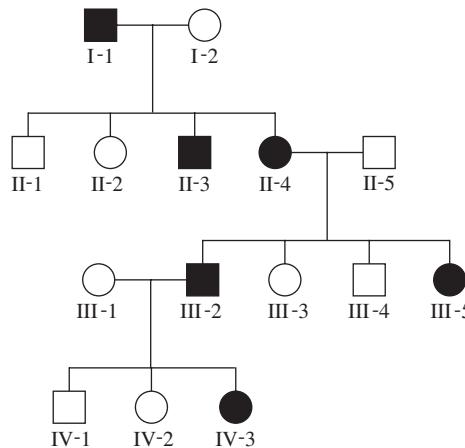
containing one X chromosome. The wing size of the unexpected males was a particularly significant result. The red-eyed males showed a miniature wing size. As noted by Bridges, this means that they inherited their X chromosome from their male parent rather than their female parent.

Conceptual Questions

- C1. Why did Mendel's work refute the blending hypothesis of inheritance?
- C2. What is the difference between cross-fertilization and self-fertilization?
- C3. Explain the difference between genotype and phenotype. Give three examples. Is it possible for two individuals to have the same phenotype but different genotypes?
- C4. With regard to genotypes, what is a true-breeding organism?
- C5. How can you determine whether an organism is heterozygous or homozygous for a dominant trait?
- C6. In your own words, describe Mendel's law of segregation. Do not use the word *segregation* in your answer.
- C7. With regard to genes in pea plants that we have considered in this chapter, which statement(s) is/are *not* correct?
 - A. The gene causing tall plants is an allele of the gene causing short plants.
 - B. The gene causing tall plants is an allele of the gene causing purple flowers.
 - C. The alleles causing tall plants and purple flowers are dominant.
- C8. For a cross between a heterozygous tall pea plant and a short pea plant, predict the ratios of the offspring's genotypes and phenotypes.
- C9. Do you know the genotype of an individual exhibiting a recessive trait or of an individual exhibiting a dominant trait? Explain your answer.
- C10. A cross is made between a pea plant that has constricted pods (a recessive trait; smooth is dominant) and is heterozygous for seed color (yellow is dominant to green) and a pea plant that is heterozygous for both pod texture and seed color. Construct a Punnett square that depicts this cross. What are the predicted outcomes of genotypes and phenotypes of the offspring?
- C11. A pea plant that is heterozygous with regard to seed color (yellow is dominant to green) is allowed to self-fertilize. What are the predicted outcomes of genotypes and phenotypes of the offspring?
- C12. Describe the significance of nonparental combinations of traits with regard to the law of independent assortment. In other words, explain how the appearance of nonparental combinations refutes the hypothesis of linked assortment.
- C13. From the following pedigrees, describe what is the likely inheritance pattern (dominant or recessive). Explain your reasoning. Filled (black) symbols indicate affected individuals.



(a)



(b)

- C14. Ectrodactyly is a recessive disorder in humans that affects the structure of the hands. If a phenotypically unaffected couple produces an offspring with ectrodactyly, what are the following probabilities?
 - A. Both parents are heterozygotes.
 - B. The next offspring is a heterozygote.
 - C. The next three offspring will be phenotypically unaffected.
 - D. Any two out of the next three offspring will be phenotypically unaffected.
- C15. Identical twins are produced from the same sperm and egg. Sometime after the first mitotic division, the cells detach from each

- other and develop into distinct individuals. In contrast, fraternal twins are produced from separate sperm and separate egg cells. If two parents with brown eyes (a dominant trait) produce one twin child with blue eyes, what are the probabilities of the following?
- The other twin, who is an identical twin, has blue eyes.
 - The other twin, who is a fraternal twin, has blue eyes.
 - If the other twin is fraternal, this twin will transmit the blue eye allele to an offspring.
 - The parents are both heterozygotes.
- C16. In cocker spaniels, solid coat color is dominant over spotted coat color. If two heterozygous dogs were crossed to each other, what would be the probability of the following combinations of offspring?
- A litter of five pups, four with solid fur and one with spotted fur
 - A first litter of six pups, four with solid fur and two with spotted fur, and then a second litter of five pups, all with solid fur
 - A first litter of five pups, the firstborn with solid fur, and then among the next four, three with solid fur and one with spotted fur, and then a second litter of seven pups in which the first-born is spotted, the second born is spotted, and the remaining five are composed of four solid and one spotted animal
 - A litter of six pups, the firstborn with solid fur, the second born spotted, and among the remaining four pups, two with spotted fur and two with solid fur
- C17. Crosses were made between a white male dog and two different black females. The first female gave birth to eight black pups, and the second female gave birth to four white and three black pups. What are the likely genotypes of the male parent and the two female parents? Explain whether you are uncertain about any of the genotypes.
- C18. In humans, the allele for brown eye color (*B*) is dominant to that for blue eye color (*b*). If two parents who are heterozygous for eye color produce children, what are the following probabilities for those offspring?
- The first two children have blue eyes.
 - Among a total of four children, two have blue eyes and the other two have brown eyes.
 - The first child has blue eyes, and the next two have brown eyes.
- C19. Albinism, a condition characterized by a partial or total lack of skin pigment, is a recessive human trait. If a phenotypically unaffected couple produce a child with albinism, what is the probability that their next child will have albinism?
- C20. A true-breeding tall plant was crossed to a short plant. Tallness is a dominant trait. The F_1 individuals were allowed to self-fertilize. What are the following probabilities for the F_2 generation?
- The first plant is short.
 - The first plant is short or tall.
 - The first three plants are tall.
 - For any seven plants, three are tall and four are short.
 - The first plant is tall, and then among the next four, two are tall and the other two are short.
- C21. For pea plants with the following genotypes, list the possible gametes that each plant can make.
- $TT\ Yy\ Rr$
 - $Tt\ YY\ rr$
 - $Tt\ Yy\ Rr$
 - $tt\ Yy\ rr$
- C22. An individual has the genotype $Aa\ Bb\ Cc$ and makes an abnormal gamete with the genotype $AaBc$. Does this gamete violate the law of independent assortment or the law of segregation (or both)? Explain your answer.
- C23. In people with maple syrup urine disease, the body is unable to metabolize the amino acids leucine, isoleucine, and valine. One of the symptoms is that the urine smells like maple syrup. An unaffected couple produced six children in the following order: unaffected female, affected female, unaffected male, unaffected male, affected male, and unaffected male. The youngest unaffected male in this family and an unrelated unaffected female have three children in the following order: affected female, unaffected female, and unaffected male. Draw a pedigree that represents this family. What type of inheritance (dominant or recessive) would you propose to explain maple syrup urine disease?
- C24. Marfan syndrome is a rare inherited human disorder characterized by unusually long limbs and digits plus defects in the heart (especially the aorta) and the eyes, among other symptoms. Following is a pedigree for this disorder in a certain family. Affected individuals are shown with filled (black) symbols. What type of inheritance pattern do you think is more likely?
-
- C25. A true-breeding pea plant with round and green seeds was crossed to a true-breeding pea plant with wrinkled and yellow seeds. Round and yellow seeds are the dominant traits. The F_1 plants were allowed to self-fertilize. What are the following probabilities for the F_2 generation?
- An F_2 plant with wrinkled, yellow seeds
 - Three out of three F_2 plants with round, yellow seeds
 - Five F_2 plants in the following order: two have round, yellow seeds; one has round, green seeds; and two have wrinkled, green seeds
 - An F_2 plant with either round, green seeds, wrinkled, yellow seeds, or wrinkled, green seeds
- C26. A true-breeding tall pea plant was crossed to a true-breeding short pea plant. What is the probability that an F_1 individual will be true-breeding? What is the probability that an F_1 individual will be a true-breeding tall plant?
- C27. What are the expected phenotypic ratios from the following cross: $Tt\ Rr\ yy\ Aa \times Tt\ rr\ YY\ Aa$, where $T =$ tall, $t =$ short, $R =$ round, $r =$ wrinkled, $Y =$ yellow, $y =$ green, and $A =$ axial, $a =$ terminal; T , R , Y , and A are dominant alleles. Hint: Consider using the multiplication method in answering this problem.

- C28. On rare occasions, an organism may have three copies of a chromosome and therefore three copies of the genes on that chromosome (instead of the usual number of two copies). The alleles for each gene usually segregate so that a gamete will contain one or two copies of the gene. Let's suppose that a rare pea plant has three copies of the chromosome that carries the height gene. Its genotype is TTt . The plant is also heterozygous for the seed color gene, Yy , which is found on a different chromosome. With regard to both genes, how many types of gametes can this plant make, and in what proportions? (Assume that it is equally likely that a gamete will contain one or two copies of the height gene.)
- C29. Honeybees are unusual in that male bees (drones) have only one copy of each gene, but female bees have two copies of their genes. This difference arises because drones develop from eggs that have not been fertilized by sperm cells. In bees, the trait of long wings is dominant over short wings, and the trait of black eyes is dominant over white eyes. If a drone with short wings and black eyes was mated to a queen bee that is heterozygous for both genes, what are the predicted genotypes and phenotypes of male and female offspring? What are the phenotypic ratios if we assume an equal number of male and female offspring?
- C30. A pea plant that is short with green, wrinkled seeds is crossed to a true-breeding pea plant that is tall with yellow, round seeds. The F_1 generation is then allowed to self-fertilize. What types of gametes, and in what proportions, will the F_1 generation make? What will be the ratios of genotypes and phenotypes of the F_2 generation?
- C31. A true-breeding pea plant with round and green seeds is crossed to a true-breeding pea plant with wrinkled and yellow seeds. The F_1 plants are then allowed to self-fertilize. What is the probability of obtaining the following plants in the F_2 generation: two that have round, yellow seeds; one with round, green seeds; and two with wrinkled, green seeds?
- C32. Wooly hair is a rare dominant trait found in people of Scandinavian descent; their hair resembles the wool of a sheep. A male with wooly hair, who has a female parent with straight hair, moves to an island that is inhabited by people who are not of Scandinavian descent. Assuming that no other Scandinavians immigrate to the island, what is the probability that a great-grandchild of this male will have wooly hair? (Hint: You may want to draw a pedigree to help you figure this out.) If this wooly-haired male has eight great-grandchildren, what is the probability that one out of eight will have wooly hair?
- C33. Huntington disease is a rare dominant disorder that causes neurodegeneration later in life. A 34-year old person named Alonzo already has three children. One of Alonzo's parents has recently developed Huntington disease though the other parent is unaffected. If you assume that the unaffected parent does not carry the allele causing Huntington disease, what are the following probabilities?
- Alonzo will develop Huntington disease.
 - Alonzo's first child will develop Huntington disease.
 - One out of three of Alonzo's children will develop Huntington disease.
- C34. Brown eyes are caused by a dominant allele (B), whereas blue eyes are recessive (b). A person with brown eyes has seven children, all of whom have brown eyes. The other parent has blue eyes.
- What is the probability of producing such a family if the brown-eyed parent is a heterozygote?
 - What is the probability that the brown-eyed parent is a homozygote if an eighth child has blue eyes?

Experimental Questions

- E1. List three advantages of using pea plants as an experimental organism.
- E2. Explain the technical difference between a cross-fertilization experiment and a self-fertilization experiment.
- E3. How long did it take Mendel to complete the experiment in Figure 3.5?
- E4. For all seven characters described in the data table for Figure 3.5, Mendel allowed the F_2 plants to self-fertilize. When F_2 plants with recessive traits were allowed to self-fertilize, they always bred true. However, when F_2 plants with dominant traits were allowed to self-fertilize, some bred true but others did not. A summary of Mendel's results is shown in the following table.

F2 Parents	True-Breeding	Non-True-Breeding	Ratio
Round	193	372	1:1.9
Yellow	166	353	1:2.1
Gray	36	64	1:1.8
Smooth	29	71	1:2.4
Green	40	60	1:1.5
Axial	33	67	1:2.0
Tall	28	72	1:2.6
TOTAL:	525	1059	1:2.0

When considering the data in this table, keep in mind that they describe the F_3 generation that was produced from F_2 individuals with a dominant phenotype. These data were deduced by analyzing the outcome of the F_3 generation. Based on Mendel's laws, explain why the ratios are approximately 1:2.

- E5. From the point of view of crosses and data collection, what are the experimental differences between a single-factor and a two-factor cross?
- E6. As in many animals, albino coat color is a recessive trait in guinea pigs. Researchers removed the ovaries from an albino female guinea pig and then transplanted ovaries from a true-breeding black guinea pig. They then mated this albino female (with the transplanted ovaries) to an albino male. The albino female produced three offspring. What were their coat colors? Explain the results.
- E7. The fungus *Melampsora lini* causes a disease known as flax rust. Different strains of *M. lini* cause varying degrees of the disease. Conversely, different strains of flax are resistant or sensitive to the various varieties of the fungus. The Bombay variety of flax is resistant to *M. lini* strain 22 but sensitive to *M. lini* strain 24. A strain of flax called 770B has the opposite characteristics; it is resistant to strain 24 but sensitive to strain 22. When 770B was crossed to Bombay, all F_1 individuals were resistant to both strain 22 and

strain 24. When F_1 individuals were self-fertilized, the following data were obtained:

- 43 resistant to strain 22 but sensitive to strain 24
- 9 sensitive to strain 22 and strain 24
- 32 sensitive to strain 22 but resistant to strain 24
- 110 resistant to strain 22 and strain 24

Explain the inheritance pattern for flax resistance and sensitivity to *M. lini* strains.

- E8. Using Mendel's data from the experiment in Figure 3.8, conduct a chi square test to determine if the data agree with Mendel's law of independent assortment.
 - E9. Would it be possible to deduce the law of independent assortment from a single-factor cross? Explain your answer.
 - E10. In fruit flies, curved wings are recessive to straight wings, and ebony body is recessive to gray body. A cross was made between true-breeding flies with curved wings and gray bodies and flies with straight wings and ebony bodies. The F_1 offspring were then mated to flies with curved wings and ebony bodies to produce an F_2 generation.
 - A. Describe the genotypes of this cross, starting with the parental generation and ending with the F_2 generation.
 - B. What is the predicted phenotypic ratio of the F_2 generation?
 - C. Let's suppose the following data were obtained for the F_2 generation:
 - 114 curved wings, ebony body
 - 105 curved wings, gray body
 - 111 straight wings, gray body
 - 114 straight wings, ebony body
- Conduct a chi square test to determine if the experimental data are consistent with the expected outcome based on Mendel's laws.
- E11. A recessive allele in mice results in an unusually long neck. Sometimes, during early embryonic development, the long neck causes the embryo to die. An experimenter began with a population of

true-breeding mice with normal necks and true-breeding mice with long necks. Crosses were made between these two populations to produce an F_1 generation of mice with normal necks. The F_1 mice were then mated to each other to obtain an F_2 generation. For the mice that were born alive, the following data were obtained:

522 mice with normal necks

62 mice with long necks

What percentage of homozygous mice (that would have had long necks if they had survived) died during embryonic development?

- E12. The data with Figure 3.5 show the results of the F_2 generation for seven of Mendel's experiments. Conduct a chi square test to determine if these data are consistent with the law of segregation.
- E13. Let's suppose you conducted an experiment involving genetic crosses and calculated a chi square value of 1.005. There were four categories of offspring (i.e., the degrees of freedom equaled 3). Explain what the 1.005 value means. Your answer should include the phrase "80% of the time."
- E14. In Morgan's experiments, which result do you think is the most convincing piece of evidence pointing to X-linkage of the eye color gene? Explain your answer.
- E15. In the original studies presented in Figure 3.14, Morgan first suggested that the original white-eyed male had two copies of the white-eye allele. In this problem, let's assume that this means the fly was X^wY^w instead of X^wY . Are the data in Figure 3.14 consistent with this hypothesis? What crosses would need to be made to rule out the possibility that the Y chromosome carries a copy of the eye color gene?
- E16. White-eyed flies have a lower survival rate than red-eyed flies. Based on the data in Figure 3.14, what percentage of white-eyed flies survived compared with red-eyed flies, assuming 100% survival of red-eyed flies?
- E17. Discuss why crosses (i.e., the experiments of Mendel) and the microscopic observations of chromosomes during mitosis and meiosis were both needed to deduce the chromosome theory of inheritance.

Questions for Student Discussion/Collaboration

1. Consider this cross of pea plants: $TtRryyAa \times TtrryyAa$, where T = tall, t = short, R = round, r = wrinkled, Y = yellow, y = green, and A = axial, a = terminal. What is the expected phenotypic outcome of this cross? One group of students should solve this problem by making one big Punnett square, and another group should solve it by making four single-gene Punnett squares and using the forked-line method. Time each other to see who gets done first.
2. A cross was made between two pea plants, $TtAa$ and $Ttaa$, where T = tall, t = short, and A = axial, a = terminal. What is the probability that the first three offspring will be tall with axial flowers or short with terminal flowers and the fourth offspring will be tall

with axial flowers? Discuss what operation(s) (e.g., product rule and/or binomial expansion equation) you used and in what order you used them.

3. Discuss the principles of the chromosome theory of inheritance. Which principles were deduced via light microscopy, and which were deduced from crosses? What modern techniques could be used to support the chromosome theory of inheritance?

Note: All answers are available for the instructor in Connect; the answers to the even-numbered questions and all of the Concept Check and Comprehension Questions are in Appendix B.