

## CHAPTER OUTLINE

- 2.1 Mendel's Study of Pea Plants
- 2.2 Law of Segregation
- 2.3 Law of Independent Assortment
- 2.4 Studying Inheritance Patterns in Humans
- 2.5 Probability and Statistics

## 2

*The garden pea, studied by Mendel.*



## MENDELIAN INHERITANCE

An appreciation for the concept of heredity can be traced far back in human history. Hippocrates, a famous Greek physician, was the first person to provide an explanation for hereditary traits (ca. 400 B.C.E.). He suggested that “seeds” are produced by all parts of the body, which are then collected and transmitted to the offspring at the time of conception. Furthermore, he hypothesized that these seeds 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.

For the next 2000 years, the ideas of Hippocrates were accepted by some and rejected by many. After the invention of the microscope in the late seventeenth century, some people observed sperm and thought they could see a tiny creature inside, which they termed a homunculus (little man). This homunculus was hypothesized to be a miniature human waiting to develop within the womb of its mother. Those who held that thought, known as spermists, suggested that only the father was responsible for creating future generations and that any resemblance between mother and offspring was due to influences within the womb. During the same time, an opposite school of thought also developed. According to the ovists, the egg was solely responsible for human characteristics. The only role of the sperm was to

stimulate the egg onto its path of development. Of course, neither of these ideas was correct.

The first systematic studies of genetic crosses were carried out by Joseph Kölreuter from 1761 to 1766. In crosses between different strains of tobacco plants, he found that the offspring were usually intermediate in appearance between the two parents. This led Kölreuter to conclude that both parents make equal genetic contributions to their offspring. Furthermore, his observations were consistent with the blending hypothesis of inheritance. According to this idea, the factors that dictate hereditary traits can blend together from generation to generation. The blended traits would then be passed to the next generation. The popular view before the 1860s, 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. However, the pioneering work of Gregor Mendel would prove instrumental in refuting this viewpoint.

In Chapter 2, we will first examine the outcome of Mendel's crosses in pea plants. We begin our inquiry into genetics here because the inheritance patterns observed in peas are fundamentally related to inheritance patterns found in other eukaryotic species, such as corn, fruit flies, mice, and humans. We will discover how Mendel's insights into the patterns of inheritance in

pea plants revealed some simple rules that govern the process of inheritance. In Chapters 3 through 8, we will explore more complex patterns of inheritance and also consider the role that chromosomes play as the carriers of the genetic material.

In the last part 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 learn how to use statistics to test the validity of genetic hypotheses that attempt to explain the inheritance patterns of traits.

## 2.1 MENDEL'S STUDY OF PEA PLANTS

### Learning Outcomes:

1. Explain 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. List the seven characteristics of pea plants that Mendel chose to study.

Gregor Johann Mendel, born in 1822, is now remembered as the father of genetics (**Figure 2.1**). He grew up on a small farm in Hyncice (formerly Heinzendorf) in northern Moravia, which was then a part of Austria and is now a part of the Czech Republic. As a young boy, he worked with his father grafting trees to improve the family orchard. Undoubtedly, his success at grafting taught him that precision and attention to detail are important elements of success. These qualities would later be important in his experiments as an adult scientist. Instead of farming, however, Mendel was accepted into the Augustinian monastery of St. Thomas, completed his studies for the priesthood, and was ordained in 1847. Soon after becoming a priest, Mendel worked for a short time as a substitute teacher. To continue that role, he needed to obtain a teaching license from the government. Surprisingly, he failed the licensing exam due to poor answers in the areas of physics and natural history. Therefore, Mendel then enrolled at the University of Vienna to expand his knowledge in these two areas. Mendel's training in physics and mathematics taught him to perceive the world as an orderly place, governed by natural laws. In his studies, Mendel learned that these natural laws could be stated as simple mathematical relationships.

In 1856, Mendel began his historic studies on pea plants. For 8 years, he grew and crossed thousands of pea plants in a small 23- by 115-foot garden. He kept meticulously accurate records that included quantitative data concerning the outcome of his crosses. He published his work, entitled *Experiments on Plant Hybrids*, in 1866. This paper was largely ignored by scientists at that time, possibly because of its title, which did not reveal the key observations he made. Another reason his work went unrecognized could be tied



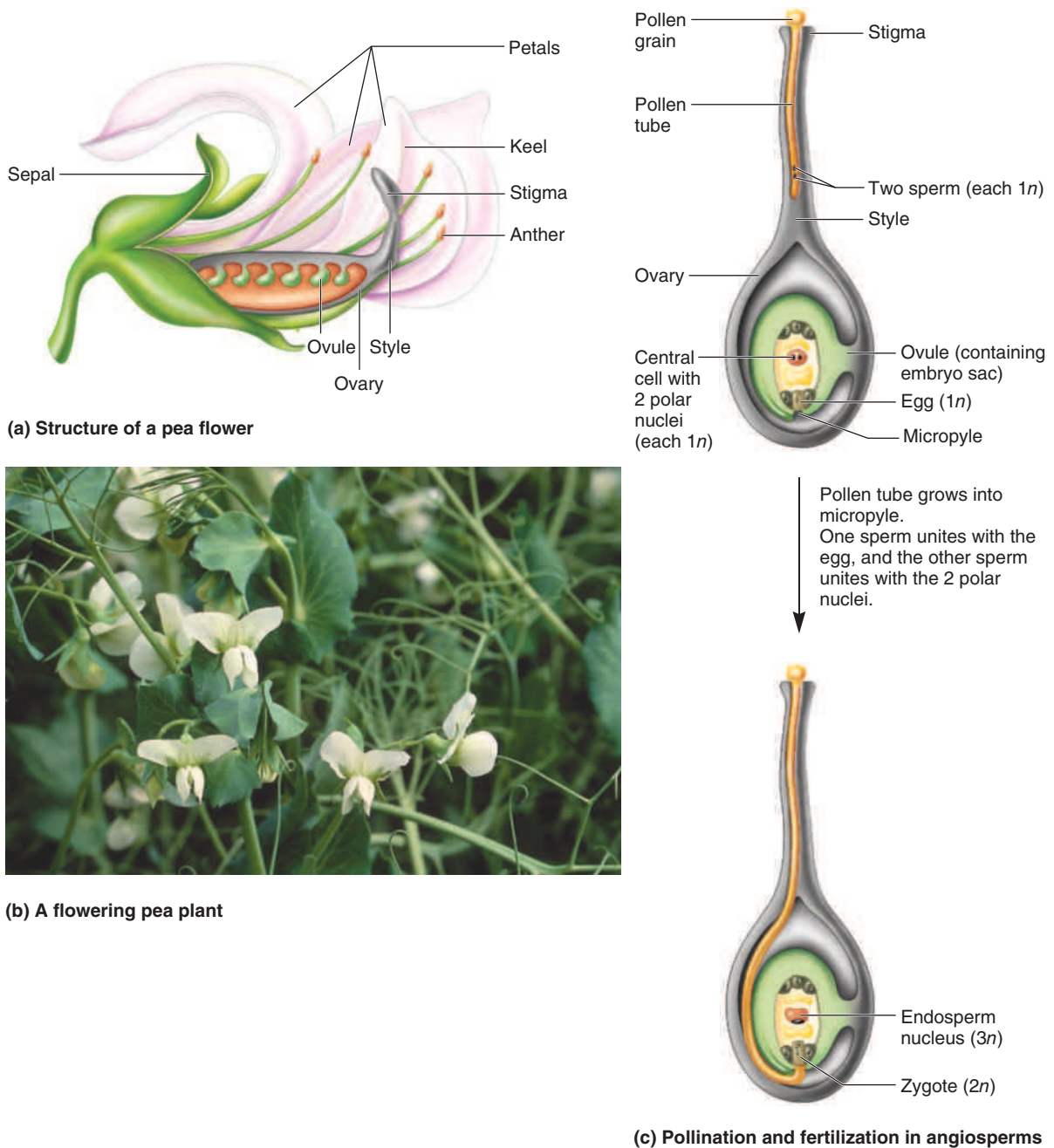
**FIGURE 2.1** Gregor Johann Mendel, the father of genetics.

to a lack of understanding of chromosomes and their transmission, a topic we will discuss in Chapter 3. Nevertheless, Mendel's groundbreaking work allowed him to propose the natural laws that now provide a framework for our understanding of genetics.

Prior to his death in 1884, 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." Sixteen years later, in 1900, the work of Mendel was independently rediscovered by three biologists with an interest in plant genetics: Hugo de Vries of Holland, Carl Correns of Germany, and Erich von Tschermak of Austria. Within a few years, the influence of Mendel's studies was felt around the world. In this section, we will examine Mendel's experimental approach.

### Mendel Chose Pea Plants as His Experimental Organism

Mendel's study of genetics grew out of his interest in ornamental flowers. Prior to his work with pea plants, many plant breeders had conducted experiments aimed at obtaining flowers with new varieties of colors. When two distinct individuals with different characteristics are bred to each other, this is called a **cross**, or a **hybridization** experiment, 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. Mendel was particularly intrigued by the consistency with which



**FIGURE 2.2 Flower structure and pollination in pea plants.** (a) The pea flower can produce 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 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 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 provides a nutritive material for the developing embryo.

**CONCEPT CHECK:** Prior to fertilization, where is the male gamete located?

offspring of subsequent generations showed characteristics of one or the other parent. His educational training in physics and the natural sciences led him to consider that this regularity might be rooted in natural laws that could be expressed mathematically. To uncover these laws, he realized that he needed to carry out quantitative experiments in which the numbers of offspring carrying certain traits were carefully recorded and analyzed.

Mendel chose the garden pea, *Pisum sativum*, to investigate the natural laws that govern plant hybrids. The morphological features of this plant are shown in **Figure 2.2a** and **2.2b**. Several properties of this species were particularly advantageous for studying plant hybridization. First, the species was available in several varieties, which varied in height and in the appearance of their flowers, seeds, and pods.

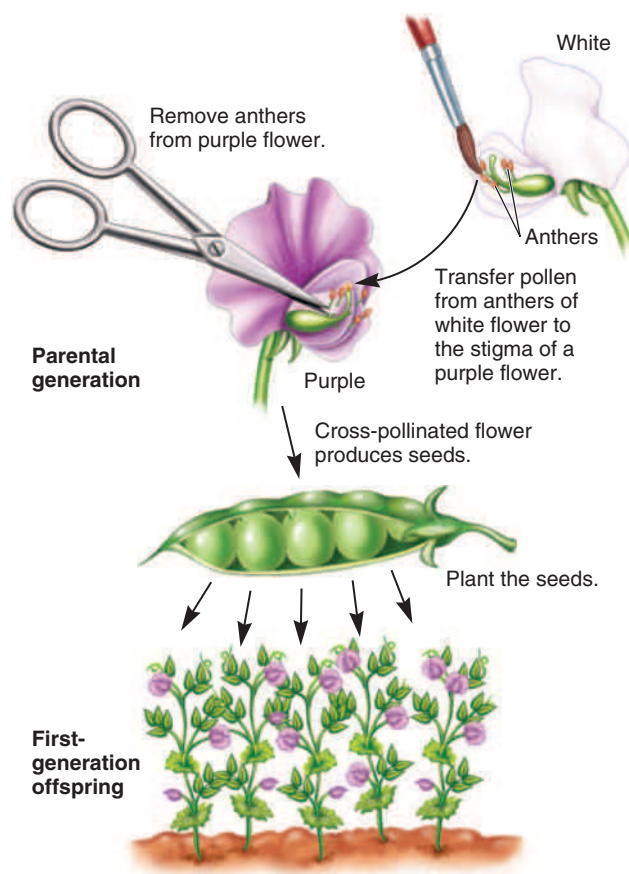
A second important issue is the ease of making crosses. The term **gamete** is used to describe the haploid reproductive cells that fuse to form a zygote. In flowering plants, reproduction occurs by a pollination event (**Figure 2.2c**). Male gametes (**sperm**) are produced within **pollen grains** that form in the **anthers**, and the female gametes (**eggs**) are produced within **ovules** that form in the **ovaries**. For fertilization to occur, a pollen grain lands on the **stigma**, which stimulates the growth of a pollen tube. This enables sperm cells to enter the stigma and migrate toward an ovule. Fertilization takes place when a sperm enters the micropyle, an opening in the ovule wall, and fuses with an egg cell.

In some experiments, Mendel wanted to carry out **self-fertilization**, which means that the pollen and egg are derived from the same plant. In peas, two modified petals are fused to form a keel that encloses the reproductive structures of the plant. Because of this covering, pea plants naturally reproduce by self-fertilization. Usually, pollination occurs even before the flower opens. In other experiments, however, Mendel wanted to make crosses between different plants. How did he accomplish this goal? Fortunately, pea plants contain relatively large flowers that are easy to manipulate, making it possible to cross two particular plants and study the outcomes. This process, known as **cross-fertilization**, requires that the pollen from one plant be placed on the stigma of another plant. This procedure is shown in **Figure 2.3**. Mendel was able to pry open immature flowers and remove the anthers before they produced pollen. Therefore, these flowers could not self-fertilize. He then obtained pollen from another plant by gently touching its mature anthers with a paintbrush. Mendel applied this pollen to the stigma of the flower that already had its anthers removed. In this way, he was able to cross-fertilize his pea plants, thereby obtaining any type of hybrid he wanted.

### Mendel Studied Seven Characteristics That Bred True

When he initiated his studies, Mendel obtained several varieties of peas that were considered to be distinct. These plants had many different morphological characteristics. The general characteristics of an organism are called **characters**. The terms **trait** or **variant** are typically used to describe the specific properties of a character. For example, eye color is a character of humans and blue eyes is the trait (or variant) found in some people. Over the course of 2 years, Mendel tested his pea strains to determine if their characteristics bred true. This means that a trait did 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 variety that continues to produce the same trait after several generations of self-fertilization is called a **true-breeding strain**, or **true-breeding line**.

Mendel next concentrated his efforts on the analysis of characters that were clearly distinguishable between different true-breeding lines. **Figure 2.4** illustrates the seven characters that Mendel eventually chose to follow in his breeding experiments. All seven were found in two variants. For example, one character he followed was height, which was found in two variants: tall and dwarf plants.

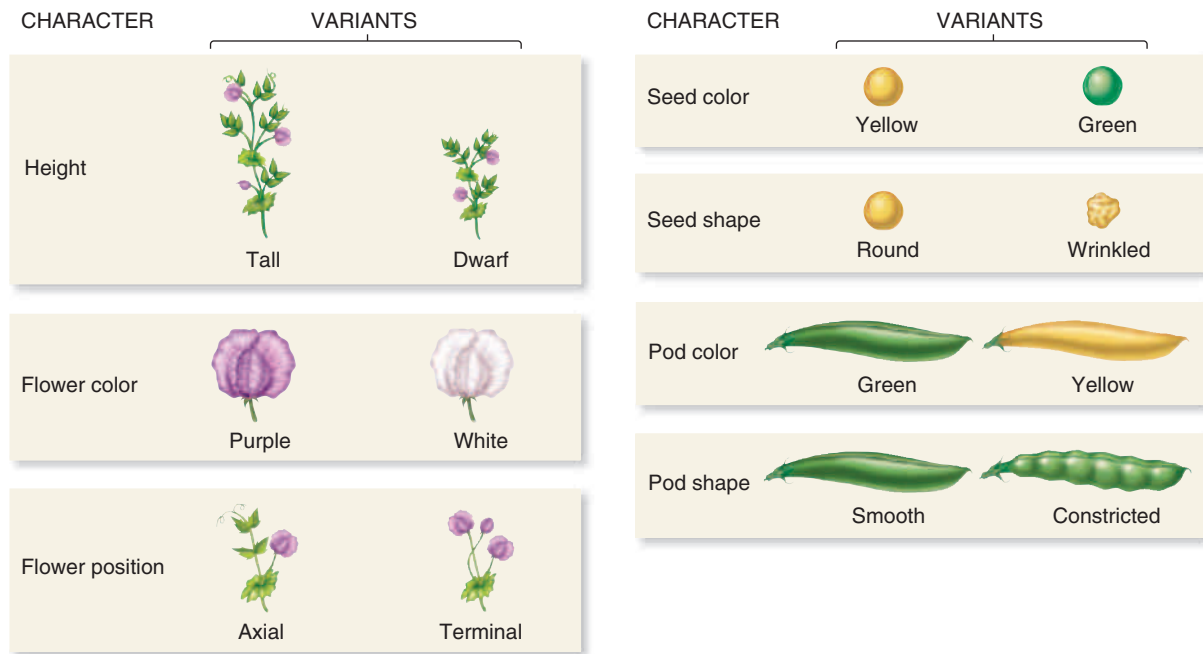


**FIGURE 2.3** How Mendel cross-fertilized pea plants. This illustration depicts a cross between one plant with purple flowers and another with white flowers. The offspring from this cross are the result of pollination of the purple flower using pollen from a white flower.

**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?

## 2.1 COMPREHENSION QUESTIONS

- Experimental advantages of using pea plants include which of the following?
  - They came in several different varieties.
  - They were capable of self-fertilization.
  - They were easy to cross.
  - All of the above were advantages.
- The term “cross” refers to an experiment in which
  - the gametes come from different individuals.
  - the gametes come from a single flower of the same individual.
  - the gametes come from different flowers of the same individual.
  - both a and c.
- To avoid self-fertilization in his pea plants, Mendel had to
  - spray the plants with a chemical that damaged the pollen.
  - remove the anthers from immature flowers.
  - grow the plants in a greenhouse that did not contain pollinators (e.g., bees).
  - do all of the above.



**FIGURE 2.4** 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?

## 2.2 LAW OF SEGREGATION

### Learning Outcomes:

1. Analyze Mendel's experiments involving single-factor crosses.
2. Define the law of segregation and explain how it is related to gamete formation and fertilization.
3. Predict the outcome of single-factor crosses using a Punnett square.

As discussed in the previous section, Mendel carried out self-fertilization or cross-fertilization experiments with his pea plants. In this section, we will examine how he studied the inheritance of characters by crossing the 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 2A

### Mendel Followed the Outcome of a Single Character for Two Generations

Prior to conducting his studies, Mendel did not already have a hypothesis to explain the formation of hybrids. However, his educational background caused him to realize that a quantitative analysis of crosses may uncover mathematical relationships that would otherwise be mysterious. His experiments were designed to determine the relationships that govern hereditary traits. 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 2.5**. He 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 the offspring that constitute the **F<sub>1</sub> generation**, for first filial generation. As seen in the data, all plants of the F<sub>1</sub> 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 F<sub>1</sub> generation were allowed to self-fertilize to produce a second generation called the **F<sub>2</sub> generation**, for 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 2.5 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 (see Figure 2.4).

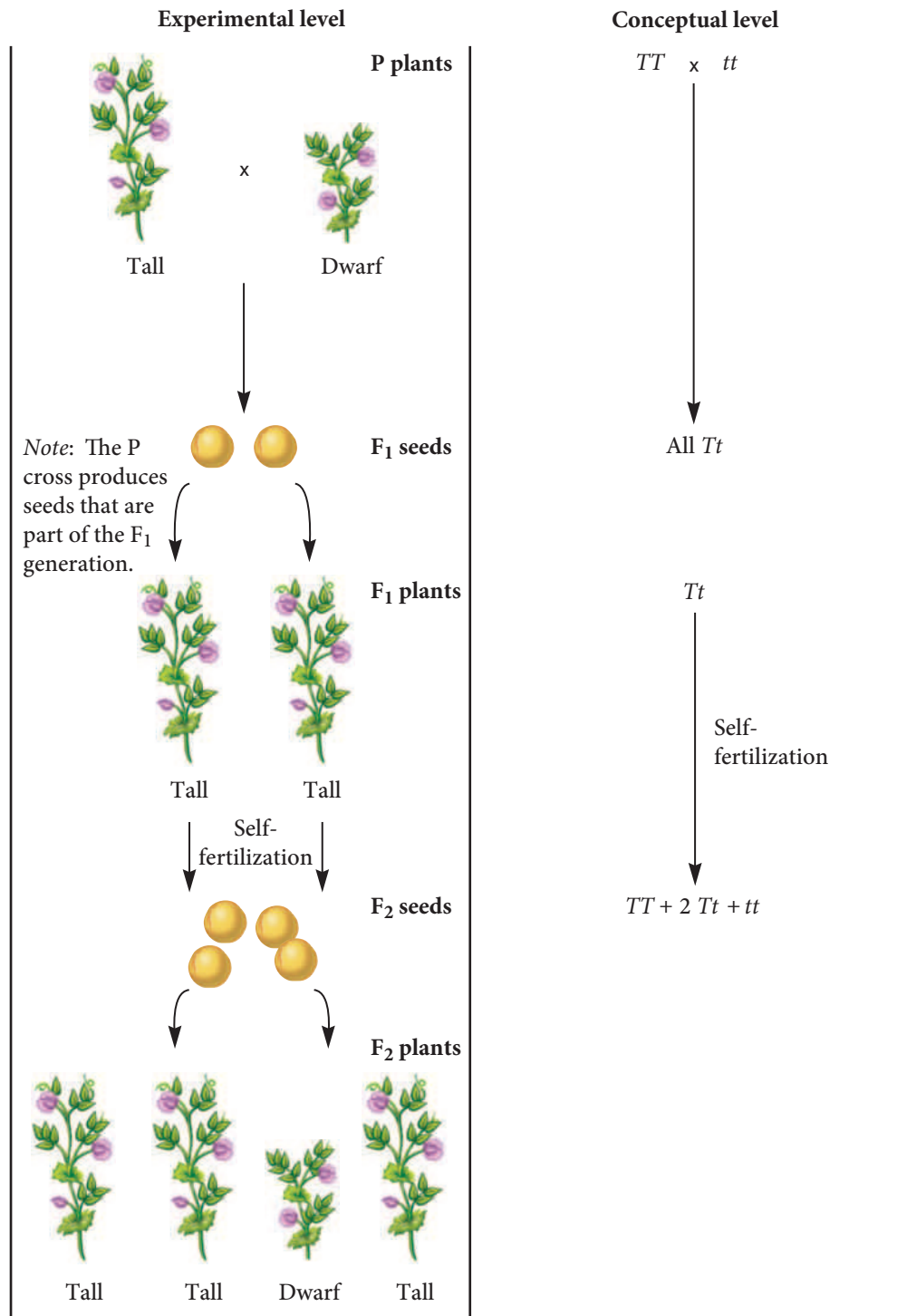
1. For each of seven characters, Mendel cross-fertilized two different true-breeding strains. Keep in mind that each cross involved two plants that differed in regard to only one of the seven characters studied. The illustration at the right shows one cross between a tall and dwarf plant. This is called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

2. Collect the F<sub>1</sub> generation seeds. The following spring, plant the seeds and allow the plants to grow. These are the plants of the F<sub>1</sub> generation.

3. Allow the F<sub>1</sub> generation plants to self-fertilize. This produces seeds that are part of the F<sub>2</sub> generation.

4. Collect the F<sub>2</sub> generation seeds and plant them the following spring to obtain the F<sub>2</sub> generation plants.

5. Analyze the traits found in each generation.



## THE DATA

<i>P</i> cross	<i>F</i> <sub>1</sub> generation	<i>F</i> <sub>2</sub> generation	Ratio
Tall × dwarf stem	All tall	787 tall, 277 dwarf	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

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

## INTERPRETING THE DATA

The data shown in Figure 2.5 are the results of producing an *F*<sub>1</sub> generation via cross-fertilization and an *F*<sub>2</sub> generation via self-fertilization of the *F*<sub>1</sub> plants. A quantitative analysis of these data allowed Mendel to propose three important ideas:

1. Mendel's data argued strongly against a blending mechanism of heredity. In all seven cases, the *F*<sub>1</sub> generation displayed characteristics that were distinctly like one of the two parents

rather than traits intermediate in character. His first proposal was that one variant for a particular character is **dominant** over 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 dwarf stems 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 *F*<sub>1</sub> generation. In the *F*<sub>2</sub> 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 *F*<sub>2</sub> generation, he made a second proposal—the genetic determinants of traits are passed along as “unit factors” from generation to generation. His data were consistent with a **particulate theory of inheritance**, in which the genetic determinants 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.
3. When Mendel compared the numbers of dominant and recessive traits in the *F*<sub>2</sub> generation, he noticed a recurring pattern. Within experimental variation, he always observed approximately a 3:1 ratio between the dominant and the recessive trait. As described next, this quantitative approach allowed him to make a third proposal—genes **segregate** from each other during the process that gives rise to gametes.

**A self-help quiz involving this experiment can be found at [www.mhhe.com/brookergenetics5e](http://www.mhhe.com/brookergenetics5e).**

### Mendel's 3:1 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 the Danish botanist Wilhelm Johannsen in 1909. A **gene** is defined as a “unit of heredity” that may influence the outcome of an organism's traits. Each of the seven characters that Mendel studied is influenced by a different gene.

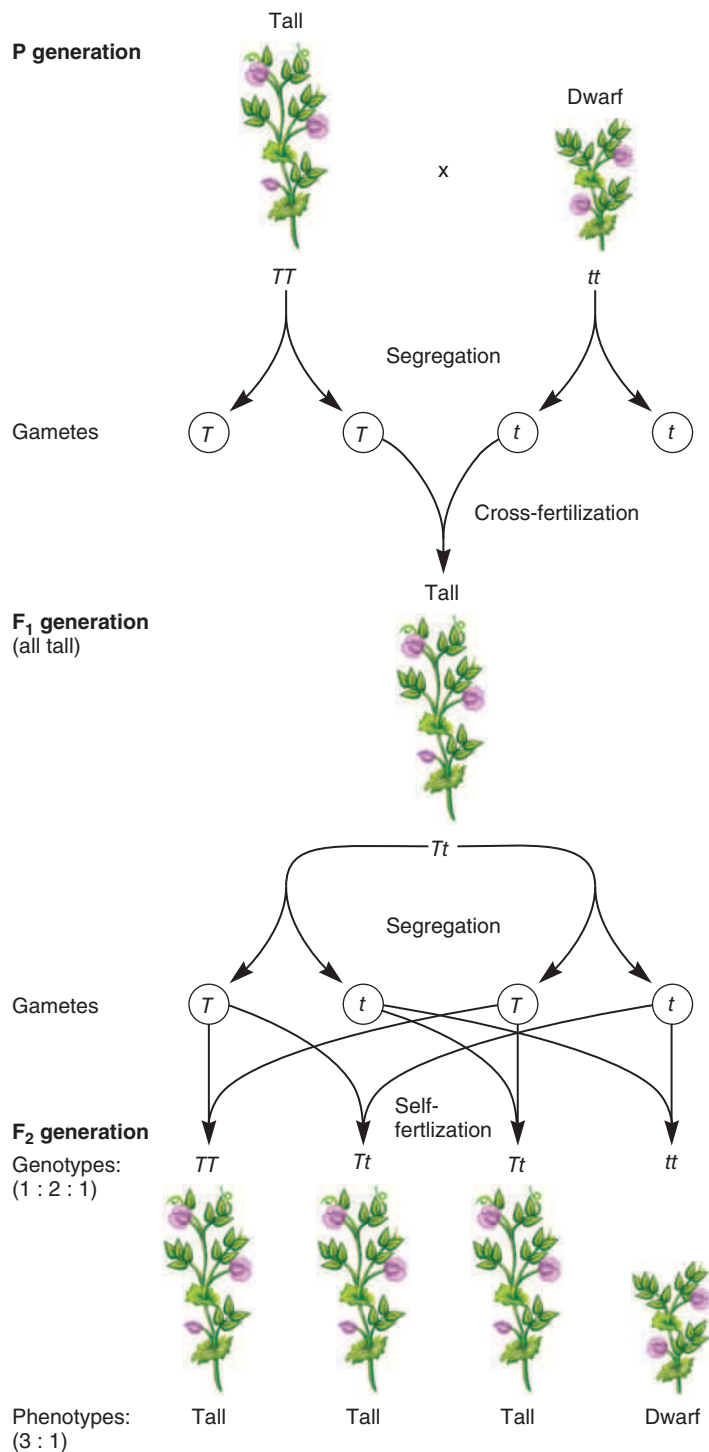
Most eukaryotic species, such as pea plants and humans, have their genetic material organized into pairs of chromosomes. For this reason, eukaryotes have two copies of most genes. These

copies may be the same or they may differ. The term **allele** (from the Latin *alius* meaning other) refers to an alternative version of a particular gene. For example, the height gene in pea plants is found as a tall allele and a dwarf allele. With this modern knowledge, the results shown in Figure 2.5 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 transmission from parent to offspring.*

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 dwarf pea plants to illustrate how alleles are passed from parents to offspring (**Figure 2.6**). The letters *T* and *t* are used to represent the alleles



**FIGURE 2.6** Mendel's law of segregation.

This illustration shows a cross between a true-breeding tall plant and a true-breeding dwarf plant and the subsequent segregation of the tall ( $T$ ) and dwarf ( $t$ ) alleles in the  $F_1$  and  $F_2$  generations.

**CONCEPT CHECK:** With regard to the  $T$  and  $t$  alleles, explain what the word "segregation" means.

of the gene that determines plant height. By convention, the uppercase letter represents the dominant allele ( $T$  for tall height, in this case), and the recessive allele is represented by the same letter in lowercase ( $t$ , for dwarf height). For the P cross, both parents are true-breeding plants. 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 for the tall allele  $T$ , and the dwarf plant is homozygous for the dwarf allele  $t$ . In contrast, the  $F_1$  generation is **heterozygous**, with the genotype  $Tt$ , because every individual carries one copy of the tall allele and one copy of the dwarf allele. A heterozygous individual carries different alleles of a gene. (The prefix *hetero-* means different.)

The term **genotype** refers to the genetic composition of an individual.  $TT$  and  $tt$  are the genotypes of the P generation in this experiment. The term **phenotype** refers to an observable characteristic of an organism. In the P generation, the plants exhibit a phenotype that is either tall or dwarf. In some cases, plants have different genotypes yet the same phenotype. For example, both  $TT$  and  $Tt$  plants are tall.

The law of segregation predicts that the phenotypes of the  $F_2$  generation will be tall and dwarf in a ratio of 3:1 (see Figure 2.6). The parents of the  $F_2$  generation are heterozygous. Due to segregation, their gametes can carry either a  $T$  allele or a  $t$  allele, but not both. Following self-fertilization,  $TT$ ,  $Tt$ , and  $tt$  are the possible genotypes of the  $F_2$  generation (note that the genotype  $Tt$  is the same as  $tT$ ). By randomly combining these alleles, the genotypes are produced in a 1:2:1 ratio. Because  $TT$  and  $Tt$  both produce tall phenotypes, a 3:1 phenotypic ratio is observed in the  $F_2$  generation.

### A Punnett Square Can Be Used to Predict the Outcome of Crosses

An easy way to predict the outcome of simple genetic crosses is to use a **Punnett square**, a method originally proposed by British geneticist 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. We will follow a step-by-step description of the Punnett square approach using a cross of heterozygous tall plants as an example.

**Step 1.** Write down the genotypes of both parents. In this example, a heterozygous tall plant is crossed to another heterozygous tall plant. The plant providing the pollen is the male parent and the plant providing the eggs, the female parent.

Male parent:  $Tt$

Female parent:  $Tt$

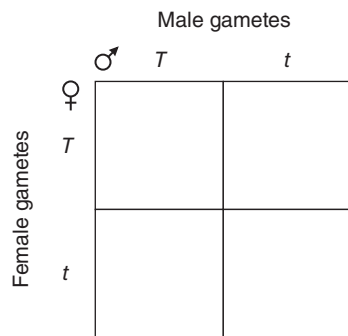


**Step 2.** Write down the possible gametes that each parent can make. Remember that the law of segregation tells us that a gamete carries only one copy of each gene.

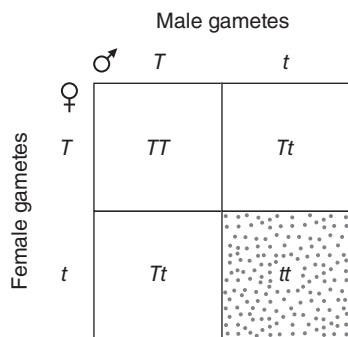
Male gametes:  $T$  or  $t$

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 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. They 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  $t$  (dwarf). The genotypes  $TT$  and  $Tt$  are tall, whereas the genotype  $tt$  is dwarf. Therefore, our Punnett square shows us that the ratio of phenotypes is 3:1, or 3 tall plants : 1 dwarf plant.

## 2.2 COMPREHENSION QUESTIONS

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

## 2.3 LAW OF INDEPENDENT ASSORTMENT

### Learning Outcomes:

- Analyze Mendel's experiments involving two-factor crosses.
- Define the law of independent assortment.
- Predict the outcome of two-factor crosses using a Punnett square.
- Define a loss-of-function allele and explain why such alleles are useful to study.

Though his experiments described in Figure 2.5 revealed important ideas regarding a hereditary law, Mendel realized that additional insights might be uncovered if he conducted more complicated experiments. In this section, we will examine how he conducted crosses in which he simultaneously investigated the pattern of inheritance for two different characters. In other words, he carried out **two-factor crosses** in which he 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 2B

## Mendel Also Analyzed Crosses Involving Two Different Characters

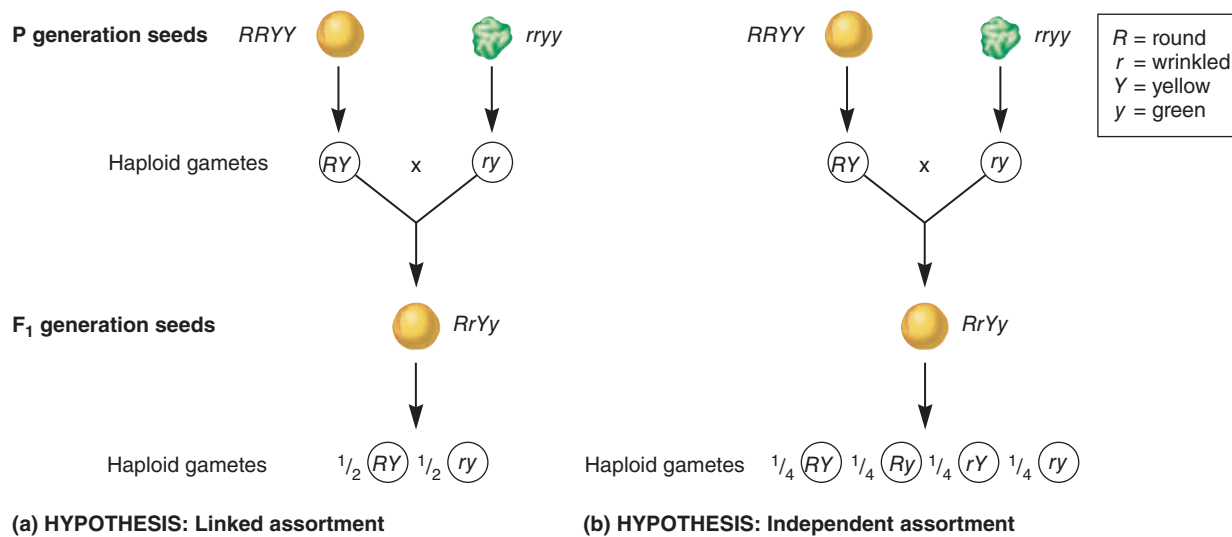
To illustrate Mendel's work, we will consider an experiment in which one of the characters was seed shape, found in round or wrinkled variants; the second character was seed color, which existed as yellow and green variants. In this two-factor cross, Mendel followed the inheritance pattern for both characters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

What results are possible from a two-factor cross? One possibility is that the genetic determinants for these two different characters are always linked to each other and inherited as a single unit (Figure 2.7a). If this were the case, the  $F_1$  offspring could produce only two types of gametes,  $RY$  and  $ry$ . A second possibility is that they are not linked and can assort themselves independently into gametes (Figure 2.7b). According to independent assortment, an  $F_1$  offspring could produce four types of gametes,  $RY$ ,  $Ry$ ,  $rY$ , and  $ry$ . Keep in mind that the results of Figure 2.5 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 2.8. 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  $F_1$  generation. As expected, the data revealed that the  $F_1$  seeds displayed a phenotype of round and yellow. This was observed because round and yellow are dominant traits. It is the  $F_2$  generation that supports the independent-assortment model and refutes the linkage model.

## THE HYPOTHESES

The inheritance pattern for two different characters follows one or more quantitative natural laws. Two possible hypotheses are described in Figure 2.7.



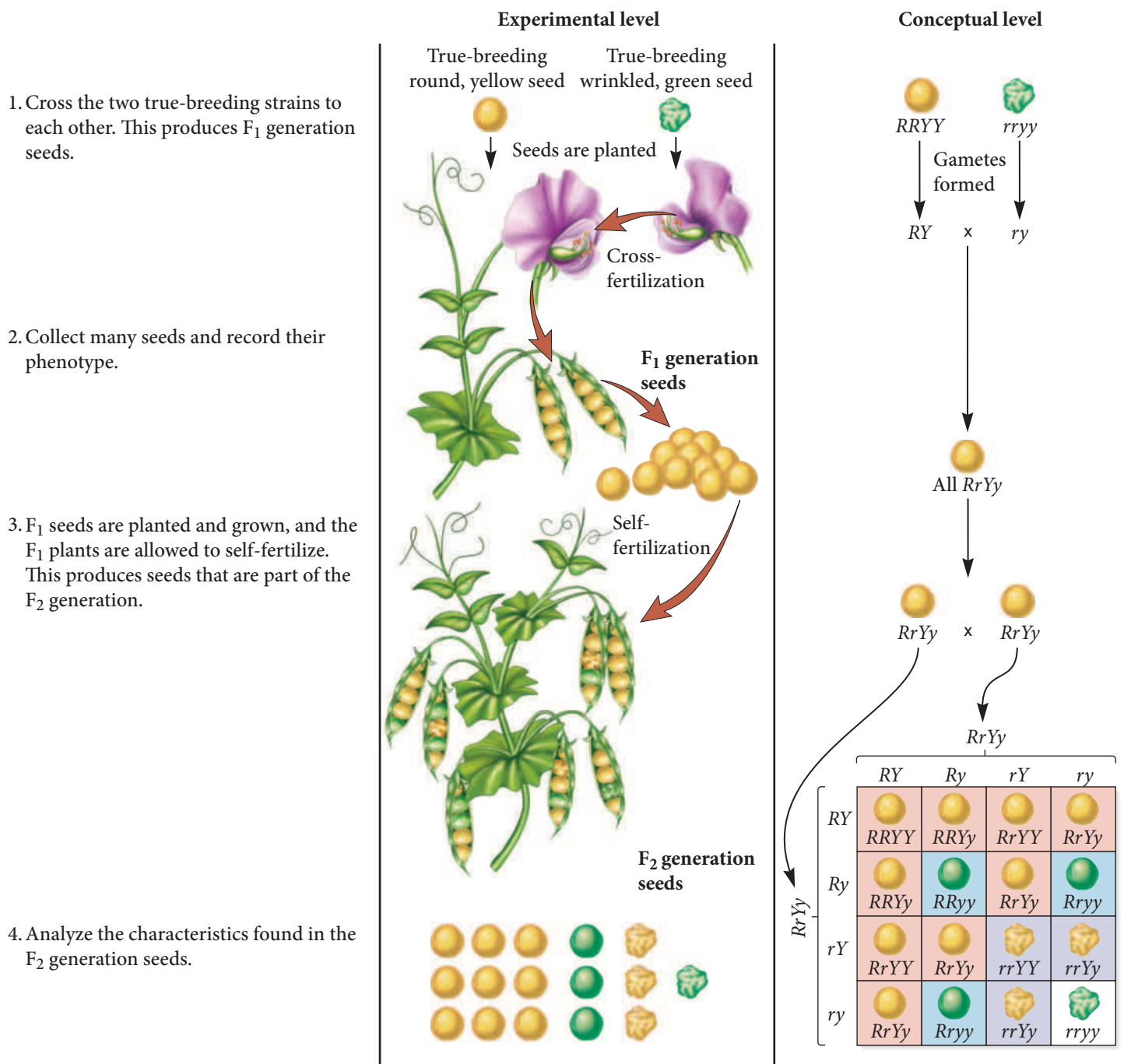
**FIGURE 2.7** Two hypotheses to explain how two different genes assort during gamete formation. (a) According to the linked hypothesis, the two genes always stay associated with each other. (b) In contrast, the independent assortment hypothesis proposes that the two different genes randomly segregate into haploid cells.

**CONCEPT CHECK:** According to the linkage hypothesis 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 2.8 Mendel's analysis of two-factor crosses.

**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 × wrinkled, green seeds	All round, yellow	315 round, yellow seeds 108 round, green seeds 101 wrinkled, yellow seeds 32 wrinkled, green seeds

## INTERPRETING THE DATA

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 **nonparentals** because these combinations of traits were not found in the true-breeding plants of the parental generation. The occurrence of nonparental variants

contradicts the linkage model (see Figure 2.7a). According to the linkage model, the  $R$  and  $Y$  alleles should be linked together and so should the  $r$  and  $y$  alleles. If this were the case, the  $F_1$  plants could produce gametes that are only  $RY$  or  $ry$ . These would combine to produce  $RRYY$  (round, yellow),  $RrYy$  (round, yellow), or  $rryy$  (wrinkled, green) in a 1:2:1 ratio. Nonparental seeds could, therefore, not be produced. However, Mendel did not obtain this result. Instead, he observed a phenotypic ratio of 9:3:3:1 in the  $F_2$  generation.

Mendel's results from many two-factor crosses rejected the hypothesis of linked assortment 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 formation of haploid cells.*

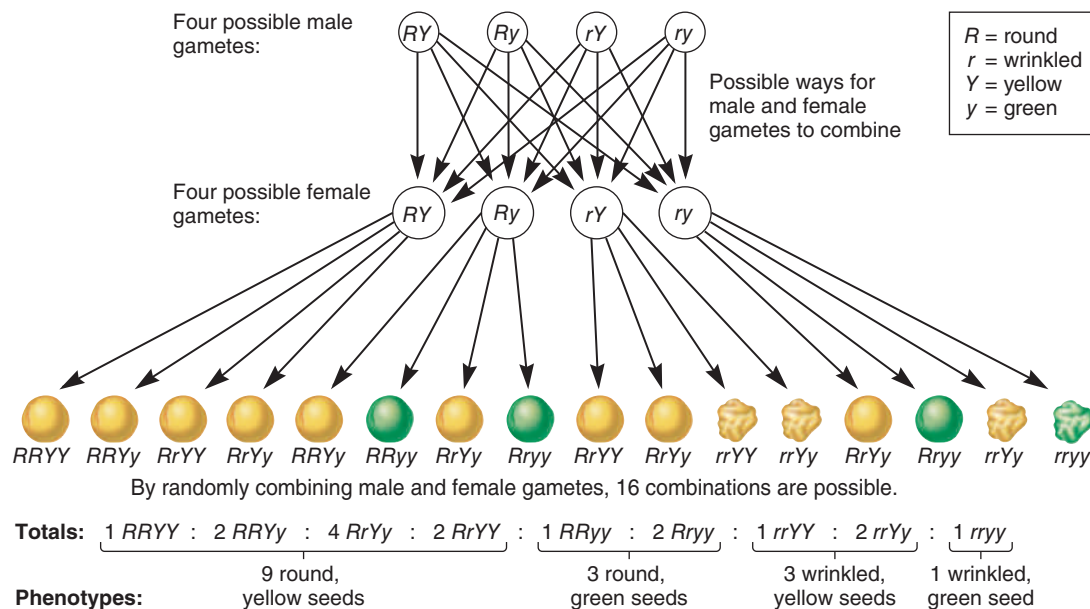
In other words, the allele for one gene will be found within a resulting gamete independently of whether the allele for a different gene is found in the same gamete. In the example given in Figure 2.8, the round and wrinkled alleles are assorted into haploid gametes independently of the yellow and green alleles. Therefore, a heterozygous  $RrYy$  parent can produce four different gametes— $RY$ ,  $Ry$ ,  $rY$ , and  $ry$ —in equal proportions.

In an  $F_1$  self-fertilization experiment, any two gametes can combine randomly during fertilization. This allows for  $4^2$ , or 16, possible offspring, although some offspring will be genetically identical to each other. As shown in **Figure 2.9**, 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 for his two-factor experiments were close to a 9:3:3:1 ratio. In Figure 2.8, for example, his  $F_1$  generation produced  $F_2$  seeds with the following characteristics: 315 round, yellow seeds; 108 round, green seeds; 101 wrinkled, yellow seeds; and 32 wrinkled, green seeds. If we divide each of these numbers by 32 (the number of plants with wrinkled, green seeds), the phenotypic ratio of the  $F_2$  generation is 9.8 : 3.4 : 3.2 : 1.0. Within experimental error, Mendel's data approximated the predicted 9:3:3:1 ratio for the  $F_2$  generation.

The law of independent assortment held true for two-factor crosses involving all of the characters that Mendel studied in pea plants. However, in other cases, the inheritance pattern of two different genes is consistent with the linkage model described earlier in Figure 2.7a. 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.

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**.



**FIGURE 2.9** Mendel's law of independent assortment.

**Genes→Traits** The cross is between two parents that are heterozygous for seed shape and seed color ( $RrYy \times RrYy$ ). 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 combine with any one of the four types of female gametes. This results in 16 types of offspring, each one containing two copies of the seed shape gene and two copies of the seed color gene.

**CONCEPT CHECK:** Why does independent assortment promote genetic variation?



INTERACTIVE  
EXERCISE

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 by which the pairs of chromosomes assort themselves during the process of meiosis, a topic addressed in Chapter 3. When two different genes are found on different chromosomes, they randomly assort into haploid cells (look ahead to Figure 3.16). If a species contains a large number of chromosomes, this creates the potential for an enormous amount of genetic diversity. For

example, 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, humans 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.

**A self-help quiz involving this experiment can be found at [www.mhhe.com/brookergenetics5e](http://www.mhhe.com/brookergenetics5e).**

### A Punnett Square Can Also Be Used to Solve Independent Assortment Problems

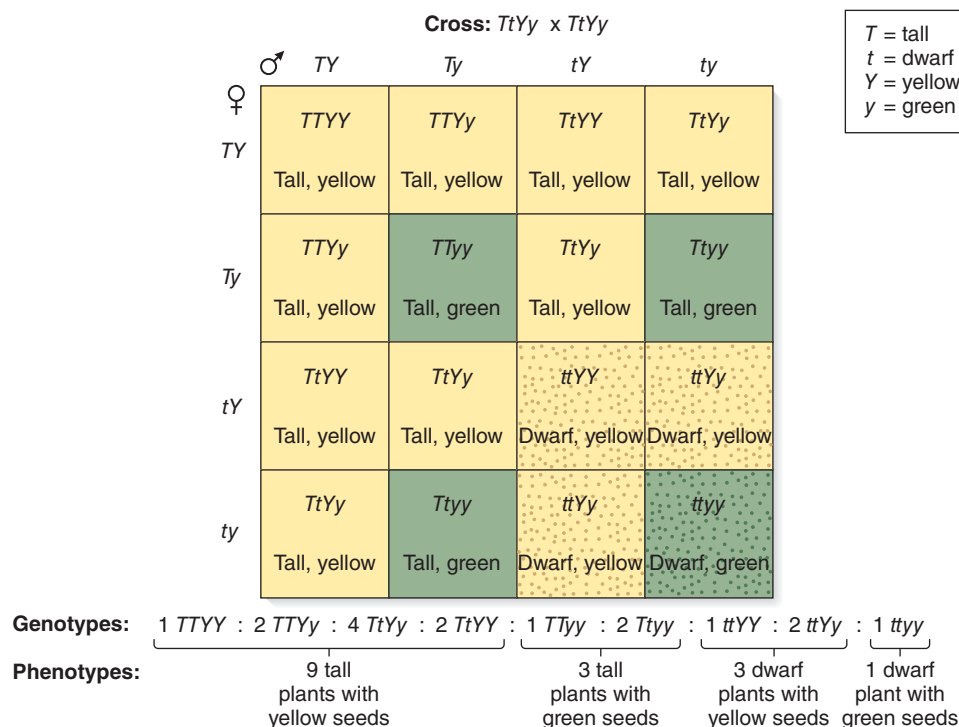
As already depicted in Figure 2.8, we can make a Punnett square to predict the outcome of crosses involving two or more genes that assort independently. Let's see how such a Punnett square is made by considering a cross between two plants that are heterozygous for height and seed color (Figure 2.10). 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.

In crosses involving three or more genes, the construction of a single large Punnett square to predict the outcome of crosses becomes very unwieldy. For example, in a three-factor cross



**FIGURE 2.10** 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 is  $Ttyy$ , how many different types of gametes can it make?

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 such methods, termed the **multiplication method** and the **forked-line method**, are shown in solved problem S3 at the end of this chapter.

Independent assortment is also revealed by a **dihybrid testcross**. In this type of experiment, individuals that are heterozygous for two genes are crossed to individuals that are homozygous recessive for the same two genes. For example, individuals with a  $TtYy$  genotype could be crossed to  $ttyy$  plants. As shown below, independent assortment predicts a 1:1:1:1 ratio among the resulting offspring:

	$TY$	$Ty$	$tY$	$ty$
$ty$	$TtYy$ Tall, yellow	$Ttyy$ Tall, green	$tTYy$ Dwarf, yellow	$ttyy$ Dwarf, green

### Modern Geneticists Are Often Interested in the Relationship Between the Molecular Expression of Genes and the Outcome of Traits

Mendel's work with pea plants was critically important because his laws of inheritance pertain to most eukaryotic organisms. These include corn, fruit flies, roundworms, mice, humans, and many others that transmit their genes through sexual reproduction. During the past several decades, many researchers have focused their attention on the relationship between the molecular expression of genes and the phenotypic appearance of traits. This theme will recur throughout the textbook (and we will draw attention to it by designating certain figure legends with a "Genes  $\rightarrow$  Traits" label). As mentioned in Chapter 1, most genes encode proteins that function within living cells. The specific function of individual proteins affects the outcome of an individual's traits. A genetic approach can help us understand the relationship between a protein's function and its effect on phenotype. Most commonly, a geneticist will try to identify an individual that has a defective copy of a gene to see how that will affect the phenotype of the organism. These defective genes are called **loss-of-function alleles**, and they provide geneticists with a great amount of information. Unknowingly, Gregor Mendel had studied seven loss-of-function alleles among his strains of plants. The recessive characteristics in his pea plants were due to genes that had been rendered defective by a mutation. Such alleles are often inherited in a recessive manner, though this is not always the case.

How are loss-of-function alleles informative? In many cases, such alleles provide critical clues concerning the purpose of the protein's function within the organism. For example, we expect the gene affecting flower color (purple versus white) to encode a protein that is necessary for pigment production. This

protein may function as an enzyme that is necessary for the synthesis of purple pigment. Furthermore, a reasonable guess is that the white allele is a loss-of-function allele that is unable to express this protein and therefore cannot make the purple pigment. To confirm this idea, a biochemist could analyze the petals from purple and white flowers and try to identify the protein that is defective or missing in the white petals but functionally active in the purple ones. The identification and characterization of this protein would provide a molecular explanation for this phenotypic characteristic.

## 2.3 COMPREHENSION QUESTIONS

- A pea plant has the genotype  $rrYy$ . How many different types of gametes can it make and in what proportions?
  - $1 rr : 1 Yy$
  - $1 rY : 1 ry$
  - $3 rY : 1 ry$
  - $1 RY : 1 rY : 1 Ry : 1 ry$
- A cross is made between a plant that is  $RrYy$  to a plant that is  $rrYy$ . What is the predicted outcome of the seed phenotypes?
  - 9 round, yellow : 3 round, green : 3 wrinkled, yellow : 1 wrinkled, green
  - 3 round, yellow : 3 round, green : 1 wrinkled, yellow : 1 wrinkled, green
  - 3 round, yellow : 1 round, green : 3 wrinkled, yellow : 1 wrinkled, green
  - 1 round, yellow : 1 round, green : 1 wrinkled, yellow : 1 wrinkled, green
- 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 encodes an enzyme necessary for pigment formation, which of the following statements do you think is most likely to be correct?
  - The white squirrels are  $pp$ , and the  $p$  allele is a loss-of-function allele.
  - The gray squirrels are  $pp$ , and the  $p$  allele is a loss-of-function allele.
  - The white squirrels are  $PP$ , and the  $P$  allele is a loss-of-function allele.
  - The gray squirrels are  $PP$ , and the  $P$  allele is a loss-of-function allele.

## 2.4 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 among humans. In his experiments, 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 will follow. Although this method may be less definitive than the results described in Mendel's experiments, 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 different human diseases.

In order to discuss the applications of pedigree analyses, we need to understand the organization and symbols of a pedigree (**Figure 2.11**). 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 man (square) and woman (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 (brothers and sisters) is denoted by two or more individuals projecting from the same horizontal line.

When a pedigree involves the transmission of a human trait or disease, affected individuals are depicted by filled symbols (in this case, 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 2.11a are described here:

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.

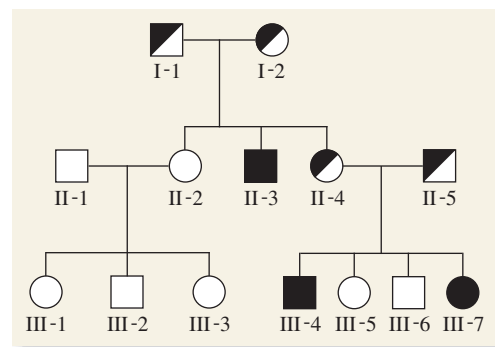
Individuals III-1, III-2, and III-3 are brother and sisters.

Individual III-4 is affected by a genetic disease.

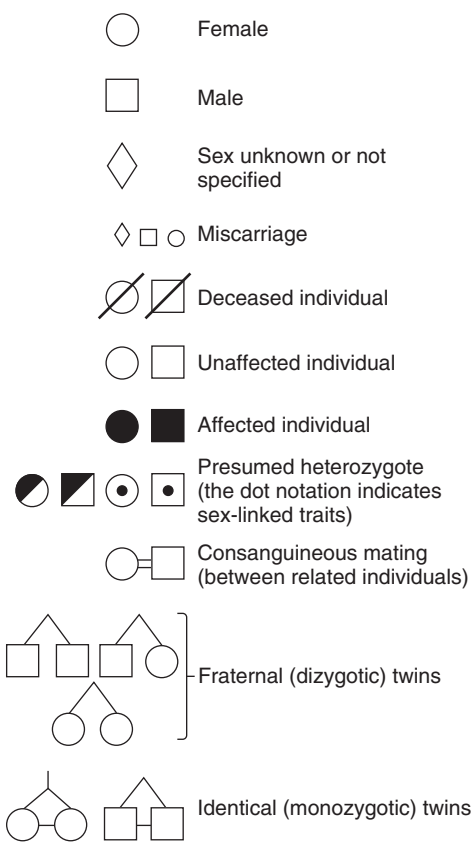
The symbols shown in Figure 2.11 depict certain individuals, such as I-1, I-2, II-4, and II-5, as presumed heterozygotes because they are unaffected with a disease but produce homozygous offspring that are affected with a recessive genetic disease. However, in many pedigrees, such as those found in the problem sets at the end of the chapter, the inheritance pattern may not be known, so the symbols reflect only phenotypes. In most 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 normal 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



(a) Human pedigree showing cystic fibrosis



(b) Symbols used in a human pedigree

**FIGURE 2.11 Pedigree analysis.** (a) A family pedigree in which some of the members are affected with cystic fibrosis. Individuals I-1, I-2, II-4, and II-5 are depicted as presumed heterozygotes because they produce affected offspring. (b) The symbols used in pedigree analysis. Note: In most pedigrees shown in this textbook, such as those found in the problem sets, the heterozygotes are not shown as half-filled symbols. Most pedigrees throughout the book show individuals' phenotypes—unfilled symbols are unaffected individuals and filled symbols are affected individuals.

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

important predictions. First, two heterozygous normal individuals will, on average, have 1/4 of their offspring affected. Second, all offspring of two affected individuals will be affected. Alternatively, a dominant trait predicts that affected individuals will have inherited the gene from at least one affected parent (unless a new mutation has occurred during gamete formation).

The pedigree in Figure 2.11a concerns a human genetic disease known as cystic fibrosis (CF). Among people of Northern European descent, approximately 3% of the population are heterozygous carriers of this recessive allele. In homozygotes, the disease symptoms include abnormalities of the pancreas, intestine, sweat glands, lungs, and reproductive organs. These abnormalities are caused by an imbalance of ions across the plasma membrane. 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 encodes a protein called the cystic fibrosis transmembrane conductance regulator (CFTR). This protein regulates the ion balance across the cell membrane in tissues of the pancreas, intestine, sweat glands, and lungs. The mutant allele causing CF alters the encoded CFTR protein. The altered CFTR protein is not correctly inserted into the plasma membrane, resulting in a decreased function that causes the ionic 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 characterized by the observation that two affected individuals will 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.

- Recessive
- Dominant
- Both recessive and dominant
- Neither recessive nor dominant

## 2.5 PROBABILITY AND STATISTICS

### Learning Outcomes:

- Define probability.
- Predict the outcome of crosses using the product rule and binomial expansion equation.
- 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 outcome 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.

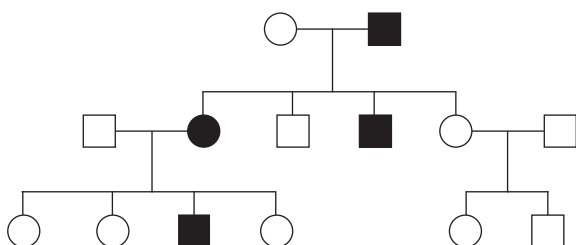
In this section, we will see how probability calculations are used in genetic problems to predict the outcome of crosses. We will consider two mathematical operations known as the product rule and the binomial expansion equation. These methods allow us to determine the probability that a cross between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

- The product rule is used in problems in which the outcomes are independent of each other.
- The binomial expansion is used in 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 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 parent 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.

## 2.4 COMPREHENSION QUESTIONS

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





## 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

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

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

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 dwarf. This information can be used to calculate the probability for either type of offspring.

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

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

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

The probability is 75% of obtaining a tall plant and 25% of obtaining a dwarf plant. When we add together the probabilities of all possible outcomes (tall and dwarf), 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). In 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, 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 a relatively small sampling error (refer back to Figure 2.5.)

## 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 man who made his living entertaining the public as a "human pincushion."

For a phenotypically unaffected couple, each being heterozygous for the recessive allele causing congenital analgesia, we can ask the question, 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:**  $Pp \times Pp$  (where  $P$  is the common allele and  $p$  is the recessive congenital analgesia allele)

**The Question:** What is the probability that the 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 (25%).

**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.

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

Thus, the probability that the first three offspring will have this trait is 0.016. In other words, we predict that 1.6% of the time the first three offspring of a couple, each heterozygous for the recessive allele, will all have congenital analgesia. In this example, the phenotypes of the first, second, and third offspring are independent outcomes. In other words, 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 the 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, 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 the question, 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 other two genes. Therefore, we can separately calculate the probability of the desired outcome for each gene.

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

Probability that an offspring will be  $AA = 1/4$

Probability that an offspring will be  $bb = 1/2$

Probability that an offspring will be  $Cc = 1/2$

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

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

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

A second type of prediction in genetics is to determine the probability that a certain proportion of offspring will be produced with particular characteristics; here they can be produced in an unspecified order. For example, we can consider a group of children produced by two heterozygous brown-eyed ( $Bb$ ) individuals. We can ask the question, What is the probability that two out of five children will have blue eyes?

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 question, the **binomial expansion equation** can be used. This equation represents all of the possibilities for a given set of 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.  $n!$  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 contain two blue-eyed children and three brown-eyed children.

When more than two outcomes are possible, we use a **multinomial expansion equation** to solve a problem involving an unordered number of 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 in many genetic problems where 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 solved problem S6 at the end of this chapter).

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

We now look at a different issue in 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 3 through 8, not all traits follow a simple Mendelian pattern of inheritance. Some genes do not segregate and independently assort themselves the same 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, it may seem that the data are obeying 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 a statistical approach is to evaluate the **goodness of fit** between the observed data and the data that are predicted from a hypothesis. This is sometimes called a **null hypothesis** because it assumes there is no real difference between the observed and expected values. Any actual differences that occur are presumed to be due to random sampling error. If the observed and predicted data are very similar, we conclude that the hypothesis is consistent with the observed outcome. In this case, it is reasonable to accept the hypothesis. However, it should be emphasized that this does not prove that a hypothesis is correct. 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 the hypothesis. Alternative hypotheses, perhaps even ones that the experimenter has failed to realize, may also be consistent with the data. In some cases, statistical methods may reveal a poor fit between hypothesis and data. In other words, a high deviation would be found between the observed and expected values. If this occurs, the hypothesis is rejected. Hopefully, the experimenter can subsequently propose an alternative hypothesis that has a better fit with the data.

One commonly used statistical method to determine goodness of fit is the **chi square test** (often written  $\chi^2$ ). We can use the chi square test to analyze population data in which the members of the population fall into different categories. This is the kind of data we have when we evaluate the outcome 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

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

where

$O$  = observed data in each category

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

$\Sigma$  means to sum this calculation for each category. 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 testing method. In this problem, the experimenter wants to determine if a two-factor cross is obeying 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: In 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 ( $cc ee$ ). 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 curved wings, ebony bodies</u>
Total:	352

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

Based on these observations, the 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.** Based on the hypothesis, calculate the expected values of the four phenotypes. We first need to calculate the individual

TABLE 2.1

## 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

From Fisher, R. A., and Yates, F. (1943) *Statistical Tables for Biological, Agricultural, and Medical Research*. Oliver and Boyd, London.

probabilities of the four phenotypes. According to our hypothesis, there should be a 9:3:3:1 ratio in the  $F_2$  generation. Therefore, the expected probabilities are as follows:

9/16 = straight wings, gray bodies

3/16 = straight wings, ebony bodies

3/16 = curved wings, gray bodies

1/16 = curved wings, ebony bodies

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.

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

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

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

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

**Step 3.** Apply the chi square formula, using the data for the expected values that have been calculated in step 2. 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 4.** Interpret the calculated chi square value. This is done using a chi square table.

Before interpreting the chi square value we obtained, we must understand how to use **Table 2.1**. The probabilities, called **P values**, listed in the chi square table allow us to determine 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. For example, let's consider a value (0.00393) listed in row 1. (The meaning of the rows will be explained shortly.) Chi square values that are equal to or greater than 0.00393 are expected to occur 95% of the time when a hypothesis is correct. In other words, 95 out of 100 times we would expect that random chance alone would produce a deviation between the experimental data and hypothesized model that is equal to or greater than 0.00393. A low chi square value indicates a high probability that the observed deviations could be due to random chance alone. By comparison, chi square values that are equal to or greater than 3.841 are expected to occur less than 5% of the time due to random sampling error. If a high chi square value is 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 sometimes 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.

In our problem involving flies with straight or curved wings and gray or ebony bodies, we have calculated a chi square value of 1.06. Before we can determine the probability that this deviation would have occurred as a matter of random chance, we must first determine the degrees of freedom (*df*) in this experiment. The **degrees of freedom** is a measure of the number of categories that are independent of each other. When phenotype categories are derived from a Punnett square, it is typically  $n - 1$ , where  $n$  equals the total number of categories. In the preceding 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 equals 3.\* We now have sufficient information to interpret our chi square value of 1.06.

With  $df = 3$ , the chi square value of 1.06 we have obtained is slightly greater than 1.005, which gives a  $P$  value of 0.80, or 80%. What does this  $P$  value mean? If the hypothesis is correct, chi square values equal to or greater than 1.005 are expected to occur 80% of the time based on random chance alone. To reject the null hypothesis at the 5% significance level, the chi square would have

to be greater than 7.815. Because it was actually far less than this value, we are inclined to accept that the null hypothesis is correct.

We must 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.

## 2.5 COMPREHENSION QUESTIONS

- 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 of an offspring that is  $AA bb Cc dd$ ?
  - Product rule, 1/32
  - Product rule, 1/4
  - Binomial expansion, 1/32
  - Binomial expansion, 1/4
- In dogs, brown fur color ( $B$ ) is dominant to white ( $b$ ). A cross is made between two heterozygotes. If a litter contains six pups, 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%
- Which of the following operations could be used for hypothesis testing?
  - Product rule
  - Binomial expansion
  - Chi square test
  - All of the above

## KEY TERMS

**Page 18.** cross, hybridization, hybrids

**Page 20.** gamete, sperm, pollen grains, anthers, eggs, ovules, ovaries, stigma, self-fertilization, cross-fertilization, characters, trait, variant, true-breeding strain, true-breeding line

**Page 21.** single-factor cross, monohybrids, empirical approach, parental generation, P generation,  $F_1$  generation,  $F_2$  generation

**Page 23.** dominant, recessive, particulate theory of inheritance, segregate, gene, allele, Mendel's law of segregation

**Page 24.** homozygous, heterozygous, genotype, phenotype, Punnett square

**Page 25.** two-factor crosses

**Page 27.** nonparentals

**Page 28.** Mendel's law of independent assortment, genetic recombination

**Page 30.** multiplication method, forked-line method, dihybrid testcross, loss-of-function alleles

**Page 31.** pedigrees, pedigree analysis

**Page 33.** probability, random sampling error, product rule

**Page 34.** binomial expansion equation, multinomial expansion equation

**Page 35.** hypothesis testing, goodness of fit, null hypothesis, chi square test

**Page 36.**  $P$  values

**Page 37.** degrees of freedom

## CHAPTER SUMMARY

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

### 2.1 Mendel's Study of Pea Plants

- Mendel chose pea plants as his experimental organism because it was easy to carry out self-fertilization or cross-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 2.1, 2.2, 2.3, 2.4).

\*If our hypothesis already assumed that the law of segregation is obeyed, the degrees of freedom would be 1 (see Chapter 6).

## 2.2 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 2.5, 2.6).
- A Punnett square is used to deduce the outcome of single-factor crosses.

## 2.3 Law of Independent Assortment

- By conducting two-factor crosses, Mendel proposed the law of independent assortment: Two different genes will randomly assort their alleles during the formation of haploid cells (see Figures 2.8, 2.9).
- A Punnett square is used to predict the outcome of two-factor crosses (see Figure 2.10).

## 2.4 Studying Inheritance Patterns in Humans

- Human inheritance patterns are determined by analyzing family trees known as pedigrees (see Figure 2.11).

## 2.5 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 of two or more independent outcomes 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 is used to predict the probability of an unordered combination of outcomes.
- The chi square test is used to test the validity of a hypothesis (see Table 2.1).

## PROBLEM SETS & INSIGHTS

### Solved Problems

- S1. As described in this chapter, a human disease known as cystic fibrosis is inherited as a recessive trait. Two unaffected individuals have a first child with the disease. What is the probability that their next two children will not have the disease?

**Answer:** An unaffected couple has already produced an affected child. To be affected, the child must be homozygous for the disease allele and thus has inherited one copy from each parent. Therefore, because the parents are unaffected with the disease, we know that both of them must be heterozygous carriers for the recessive disease-causing allele. With this information, we can calculate the probability that they will produce an unaffected offspring. Using a Punnett square, this couple should produce a ratio of 3 unaffected : 1 affected offspring.

	♂	N	n	
♀				
	N	NN	Nn	N = common allele n = cystic fibrosis allele
	n	Nn	nn	

The probability of a single unaffected offspring is

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

To obtain the probability of getting two unaffected offspring in a row (i.e., in a specified order), we must apply the product rule.

$$3/4 \times 3/4 = 9/16 = 0.56, \text{ or } 56\%$$

The chance that their next two children will be unaffected is 56%.

- S2. A cross was made between two heterozygous pea plants,  $TtYy \times TtYy$ . The following Punnett square was constructed:

	♂	TT	Tt	Tt	tt
♀					
	YY	TTYT	TtYT	TtYT	ttYT
	Yy	TTYy	TtYy	TtYy	ttYy
	Yy	TTYy	TtYy	TtYy	ttYy
	yy	Ttyy	Ttyy	Ttyy	ttyy

Phenotypic ratio:

9 tall, yellow seeds : 3 tall, green seeds : 3 dwarf, yellow seeds : 1 dwarf, green seed

What is wrong with this Punnett square?

**Answer:** The outside of the Punnett square is supposed to contain the possible types of gametes. A gamete should contain one copy of each type of gene. Instead, the outside of this Punnett square contains two

copies of one gene and zero copies of the other gene. The outcome happens to be correct (i.e., it yields a 9:3:3:1 ratio), but this is only a coincidence. The outside of the Punnett square must contain one copy of each type of gene. In this example, the correct possible types of gametes are  $TY$ ,  $Ty$ ,  $tY$ , and  $ty$  for each parent.

S3. A pea plant is heterozygous for three genes ( $Tt Rr Yy$ ), where  $T$  = tall,  $t$  = dwarf,  $R$  = round seeds,  $r$  = wrinkled seeds,  $Y$  = yellow seeds, and  $y$  = green seeds. If this plant is self-fertilized, what are the predicted phenotypes of the offspring, and what fraction of the offspring will occur in each category?

**Answer:** 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 tiresome 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  $Tt Rr Yy \times Tt Rr Yy$ , the following Punnett squares can be made for each gene:

♂	$T$	$t$
♀	$T$	$t$
	$TT$ Tall	$Tt$ Tall
	$Tt$ Tall	$tt$ Dwarf

3 tall : 1 dwarf

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

3 round : 1 wrinkled

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

3 yellow : 1 green

cross. In the multiplication method, we simply multiply these three combinations together:

$$(3 \text{ tall} + 1 \text{ dwarf})(3 \text{ round} + 1 \text{ wrinkled})(3 \text{ yellow} + 1 \text{ green})$$

This multiplication operation can be done in a stepwise manner. First, multiply  $(3 \text{ tall} + 1 \text{ dwarf})$  by  $(3 \text{ round} + 1 \text{ wrinkled})$ .

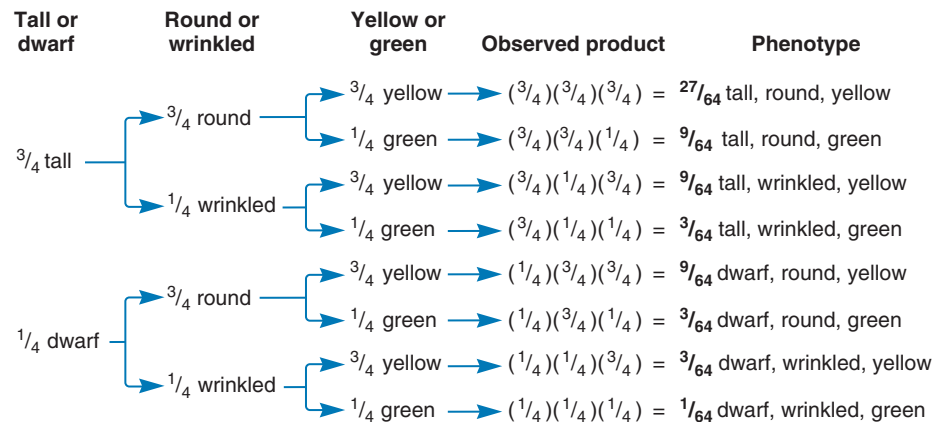
$$(3 \text{ tall} + 1 \text{ dwarf})(3 \text{ round} + 1 \text{ wrinkled}) = 9 \text{ tall, round} + 3 \text{ tall, wrinkled} + 3 \text{ dwarf, round} + 1 \text{ dwarf, wrinkled}$$

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

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

Even though the multiplication steps are also somewhat tedious, this approach is much easier than making a Punnett square with 64 boxes, filling them in, deducing each phenotype, and then adding them up!

A second approach that is analogous to the multiplication method is the forked-line method. In this case, the genetic proportions are determined by multiplying together the probabilities of each phenotype.



S4. For an individual expressing a dominant trait, how can you tell if it is a heterozygote or a homozygote?

**Answer:** One way is to conduct a testcross with an individual that expresses the recessive version of the same character. If the individual is heterozygous, half of the offspring will show the recessive trait, but if the individual is homozygous, none of the offspring will express the recessive trait.

$$\begin{array}{ccc}
 Dd \times dd & & \text{or} & DD \times dd \\
 \downarrow & & & \downarrow \\
 1Dd & : & 1dd & \text{All } Dd \\
 (\text{dominant trait}) & & (\text{recessive trait}) & (\text{dominant trait})
 \end{array}$$

Another way to determine heterozygosity involves a more careful examination of the individual at the cellular or molecular level. At the cellular level, the heterozygote may not look exactly like the homozygote. This phenomenon is described in Chapter 4. Also, gene cloning methods described in Chapter 20 can be used to distinguish between heterozygotes and homozygotes.

Instead of constructing a large, 64-box Punnett square, we can use two similar ways to determine the phenotypic outcome of this three-factor

S5. In dogs, black fur color is dominant to white. Two heterozygous black dogs are mated. What would be the probability of the following combinations of offspring?

- A litter of six pups, four with black fur and two with white fur.
- A litter of six pups, the firstborn with white fur, and among the remaining five pups, two with white fur and three with black 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.
- A first litter of five pups, four with black fur and one with white fur, and then a second litter of seven pups in which the first-born is homozygous, the second born is black, and the remaining five pups are three black and two white.

**Answer:**

A. Because this is an unordered combination of outcomes, we 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 0.297, or 29.7%, of the time.

B. We use the product rule because the order is specified. The first pup is white and then the remaining five are born later. We also need to use the binomial expansion equation to determine the probability of the remaining five pups.

(probability of a white pup)(binomial expansion for the remaining five pups)

The probability of the white pup is 0.25. In the binomial expansion equation,  $n = 5$ ,  $x = 2$ ,  $p = 0.25$ , and  $q = 0.75$ .

The answer is 0.066, or 6.6%, of the time.

C. The order of the two litters is specified, so we need to use the product rule. We multiply the probability of the first litter times the probability of the second litter. We need to use the binomial expansion equation for each litter.

(binomial expansion of the first litter)(binomial expansion of 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 0.092, or 9.2%, of the time.

D. The order of the litters is specified, so we need to use the product rule to multiply the probability of the first litter times the probability of the second litter. We use the binomial expansion equation to determine the probability of the first litter. The probability of the second litter is a little more complicated. The firstborn is homozygous. The probability of the first pup equals  $0.25 + 0.25 = 0.5$ . The probability of the second pup is 0.75, and we use the binomial expansion equation to determine the probability of the remaining pups.

(binomial expansion of first litter)([0.5][0.75]  
[binomial expansion of second litter])

For the first litter,  $n = 5$ ,  $x = 4$ ,  $p = 0.75$ ,  $q = 0.25$ . For the last five pups in the second litter,  $n = 5$ ,  $x = 3$ ,  $p = 0.75$ ,  $q = 0.25$ .

The answer is 0.039, or 3.9%, of the time.

S6. A cross is made between two heterozygous tall plants with axial flowers ( $TtAa$ ), where tall is dominant to dwarf and axial is dominant to terminal flowers. What is the probability that a group of five offspring will be composed of two tall plants with axial flowers, one tall plant with terminal flowers, one dwarf plant with axial flowers, and one dwarf plant with terminal flowers?

**Answer:**

**Step 1.** Calculate the individual probabilities of each phenotype. This can be accomplished using a Punnett square.

The phenotypic ratios are 9 tall with axial flowers, 3 tall with terminal flowers, 3 dwarf with axial flowers, and 1 dwarf with terminal flowers.

The probability of a tall plant with axial flowers is  $9/(9 + 3 + 3 + 1) = 9/16$ .

The probability of a tall plant with terminal flowers is  $3/(9 + 3 + 3 + 1) = 3/16$ .

The probability of a dwarf plant with axial flowers is  $3/(9 + 3 + 3 + 1) = 3/16$ .

The probability of a dwarf plant with terminal flowers is  $1/(9 + 3 + 3 + 1) = 1/16$ .

$$p = 9/16 \quad r = 3/16$$

$$q = 3/16 \quad s = 1/16$$

**Step 2.** Determine the number of each type of outcome versus the total number of outcomes.

$$n = 5$$

$$a = 2$$

$$b = 1$$

$$c = 1$$

$$d = 1$$

**Step 3.** Substitute the values in the multinomial expansion equation.

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

$$P = \frac{5!}{2!1!1!1!} (9/16)^2 (3/16)^1 (3/16)^1 (1/16)^1$$

$$P = 0.04, \text{ or } 4\%$$

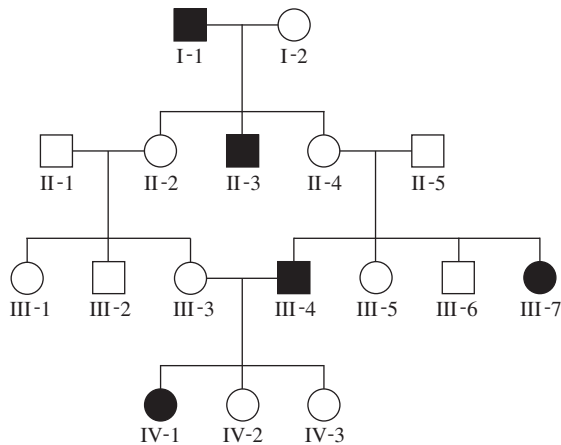
This means that 4% of the time we would expect to obtain five offspring with the phenotypes described in the question.

## Conceptual Questions

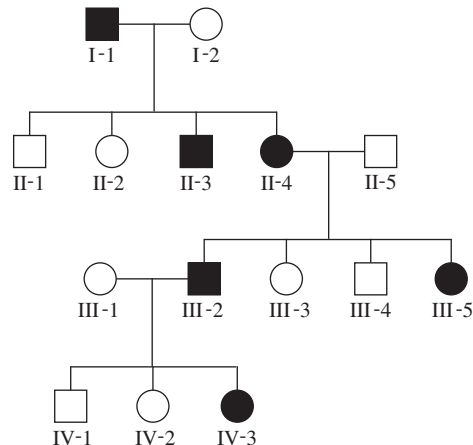
- Why did Mendel's work refute the idea of blending inheritance?
- What is the difference between cross-fertilization and self-fertilization?
- Describe the difference between genotype and phenotype. Give three examples. Is it possible for two individuals to have the same phenotype but different genotypes?
- With regard to genotypes, what is a true-breeding organism?
- How can you determine whether an organism is heterozygous or homozygous for a dominant trait?
- In your own words, describe Mendel's law of segregation. Do not use the word "segregation" in your answer.



- C7. Based on genes in pea plants that we have considered in this chapter, which statement(s) is/are not correct?
- The gene causing tall plants is an allele of the gene causing dwarf plants.
  - The gene causing tall plants is an allele of the gene causing purple flowers.
  - The alleles causing tall plants and purple flowers are dominant.
- C8. In a cross between a heterozygous tall pea plant and a dwarf plant, predict the ratios of the offspring's genotypes and phenotypes.
- C9. Do you know the genotype of an individual with a recessive trait and/or 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 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 nonparentals with regard to the law of independent assortment. In other words, explain how the appearance of nonparentals refutes a linkage hypothesis.
- C13. For the following pedigrees, describe what you think is the most likely inheritance pattern (dominant versus recessive). Explain your reasoning. Filled (black) symbols indicate affected individuals.



(a)



(b)

- C14. Ectrodactyly, also known as "lobster claw syndrome," is a recessive disorder in humans. If a phenotypically unaffected couple produces an affected offspring, what are the following probabilities?
- Both parents are heterozygotes.
  - An offspring is a heterozygote.
  - The next three offspring will be phenotypically unaffected.
  - Any two out of the next three offspring will be phenotypically unaffected.
- C15. Identical twins are produced from the same sperm and egg (which splits after the first mitotic division), whereas fraternal twins are produced from separate sperm and separate egg cells. If two parents with brown eyes (a dominant trait) produce one twin boy with blue eyes, what are the following probabilities?
- If the other twin is identical, he will have blue eyes.
  - If the other twin is fraternal, he or she will have blue eyes.
  - If the other twin is fraternal, he or she will transmit the blue eye allele to his or her 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 firstborn 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. A cross was 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 blue eye color (*b*). If two heterozygous parents produce children, what are the following probabilities?
- The first two children have blue eyes.
  - A total of four children, two with blue eyes and the other two with 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 an albino child, what is the probability that their next child will be albino?

C20. A true-breeding tall plant was crossed to a dwarf 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 dwarf.
- The first plant is dwarf or tall.
- The first three plants are tall.
- For any seven plants, three are tall and four are dwarf.
- The first plant is tall, and then among the next four, two are tall and the other two are dwarf.

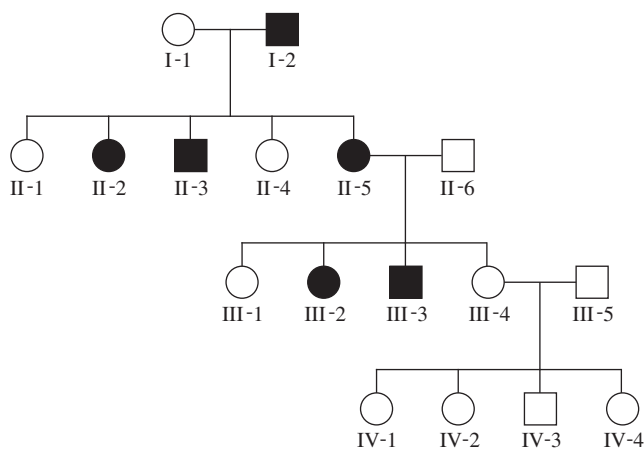
C21. For pea plants with the following genotypes, list the possible gametes that the plant can make:

- $TT Yy Rr$
- $Tt YY rr$
- $Tt Yy Rr$
- $tt Yy rr$

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 daughter, affected daughter, unaffected son, affected son, affected son, and unaffected son. The youngest unaffected son marries an unaffected woman and has three children in the following order: affected daughter, unaffected daughter, and unaffected son. Draw a pedigree that describes 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. Affected individuals are shown with filled (black) symbols. What type of inheritance pattern do you think is the most likely?



C25. A true-breeding pea plant with round and green seeds was crossed to a true-breeding 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 will not have round, yellow seeds.

C26. A true-breeding tall pea plant was crossed to a true-breeding dwarf 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,  $t$  = dwarf,  $R$  = round,  $r$  = wrinkled,  $Y$  = yellow,  $y$  = green,  $A$  = axial,  $a$  = terminal;  $T$ ,  $R$ ,  $Y$ , and  $A$  are dominant alleles. Note: See solved problem S3 for help in answering this problem.

C28. When an abnormal organism has three copies of a chromosome and therefore contains three copies of the genes on that chromosome (instead of the normal 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 an abnormal 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. That is 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 dwarf with green, wrinkled seeds was crossed to a true-breeding plant that is tall with yellow, round seeds. The  $F_1$  generation was allowed to self-fertilize. What types of gametes, and in what proportions, would the  $F_1$  generation make? What would be the ratios of genotypes and phenotypes of the  $F_2$  generation?

C31. A true-breeding plant with round and green seeds was crossed to a true-breeding plant with wrinkled and yellow seeds. The  $F_1$  plants were 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. Woolly hair is a rare dominant trait found in people of Scandinavian descent in which the hair resembles the wool of a sheep. A male with woolly hair, who has a mother 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 woolly hair? (Hint: You may want to draw a pedigree to help you figure this out.) If this woolly-haired male has eight

great-grandchildren, what is the probability that one out of eight will have woolly hair?

- C33. Huntington disease is a rare dominant trait that causes neurodegeneration later in life. A man in his thirties, who already has three children, discovers that his mother has Huntington disease though his father is unaffected. What are the following probabilities?
- That the man in his thirties will develop Huntington disease.
  - That his first child will develop Huntington disease.
  - That one out of three of his children will develop Huntington disease.

- C34. A woman with achondroplasia (a dominant form of dwarfism) and a phenotypically unaffected man have seven children, all of whom have achondroplasia. What is the probability of producing such a family if this woman is a heterozygote? What is the probability that the woman is a heterozygote if her eighth child does not have this disorder?

## Experimental Questions

- Describe three advantages of using pea plants as an experimental organism.
- Explain the technical differences between a cross-fertilization experiment versus a self-fertilization experiment.
- How long did it take Mendel to complete the experiment in Figure 2.5?
- For all seven characters described in the data of Figure 2.5, Mendel allowed the  $F_2$  plants to self-fertilize. He found that when  $F_2$  plants with recessive traits were crossed to each other, they always bred true. However, when  $F_2$  plants with dominant traits were crossed, some bred true but others did not. A summary of Mendel's results is shown here.

### The Ratio of True-Breeding and Non-True-Breeding Parents of the $F_2$ Generation

$F_2$ Parents	True-Breeding	Non-True-Breeding	Ratio
Round	193	372	1:1.93
Yellow	166	353	1:2.13
Gray	36	64	1:1.78
Smooth	29	71	1:2.45
Green	40	60	1:1.5
Axial	33	67	1:2.08
Tall	28	72	1:2.57
TOTAL:	525	1059	1:2.02

When considering the data in this table, keep in mind that it describes the characteristics of the  $F_2$  generation parents that had displayed a dominant phenotype. These data were deduced by analyzing the outcome of the  $F_3$  generation. Based on Mendel's laws, explain the 1:2 ratio obtained in these data.

- From the point of view of crosses and data collection, what are the experimental differences between a single-factor and a two-factor cross?
- 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.

- The fungus *Melampsora lini* causes a disease known as flax rust. Different strains of *M. lini* cause varying degrees of the rust disease. Conversely, different strains of flax are resistant or sensitive to the various varieties of rust. 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 is just the opposite; 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.

- For Mendel's data shown in Figure 2.8, conduct a chi square analysis to determine if the data agree with Mendel's law of independent assortment.
- Would it be possible to deduce the law of independent assortment from a single-factor cross? Explain your answer.
- 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 to 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. Diagram the genotypes of this cross, starting with the parental generation and ending with the  $F_2$  generation.

B. What are the predicted phenotypic ratios 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 analysis 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 abnormally long neck. Sometimes, during early embryonic development, the abnormal neck causes the embryo to die. An experimenter began with a population of true-breeding normal mice 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 in Figure 2.5 show the results of the  $F_2$  generation for seven of Mendel's crosses. Conduct a chi square analysis 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. A tall pea plant with axial flowers was crossed to a dwarf plant with terminal flowers. Tall plants and axial flowers are dominant traits. The following offspring were obtained: 27 tall, axial flowers; 23 tall, terminal flowers; 28 dwarf, axial flowers; and 25 dwarf, terminal flowers. What are the genotypes of the parents?

E15. A cross was made between two strains of plants that are agriculturally important. One strain was disease-resistant but herbicide-sensitive; the other strain was disease-sensitive but herbicide-resistant. A plant breeder crossed the two plants and then allowed the  $F_1$  generation to self-fertilize. The following data were obtained:

$F_1$  generation: All offspring are disease-sensitive and herbicide-resistant

$F_2$  generation: 157 disease-sensitive, herbicide-resistant  
57 disease-sensitive, herbicide-sensitive  
54 disease-resistant, herbicide-resistant  
20 disease-resistant, herbicide-sensitive

Total: 288

Formulate a hypothesis that you think is consistent with the observed data. Test the goodness of fit between the data and your hypothesis using a chi square test. Explain what the chi square results mean.

E16. A cross was made between a plant that has blue flowers and purple seeds to a plant with white flowers and green seeds. The following data were obtained:

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

$F_2$  generation: 103 blue flowers, purple seeds  
49 blue flowers, green seeds  
44 white flowers, purple seeds

104 white flowers, green seeds

Total: 300

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 your hypothesis, which aspect of the hypothesis do you think is incorrect (i.e., the idea that blue flowers and purple seeds are dominant traits, or the idea that the two genes assort independently)?

## Questions for Student Discussion/Collaboration

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

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

3. Consider this four-factor cross:  $Tt Rr yy Aa \times Tt RR Yy aa$ , where  $T$  = tall,  $t$  = dwarf,  $R$  = round,  $r$  = wrinkled,  $Y$  = yellow,  $y$  = green,  $A$  = axial,  $a$  = terminal. What is the probability that the first three plants will have round seeds? What is the easiest way to solve this problem?

*Note: All answers appear at the website for this textbook; the answers to the even-numbered questions and all of the Concept Check and Comprehension Questions are in the back of the book.*

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