11

Mendel and the Gene Idea

Lecture Presentations by Kathleen Fitzpatrick and Nicole Tunbridge, Simon Fraser University

Overview: Drawing from the Deck of Genes

- What genetic principles account for the passing of traits from parents to offspring?
- The “blending” hypothesis is the idea that genetic material from the two parents blends together (the way blue and yellow paint blend to make green)

- The “particulate” hypothesis is the idea that parents pass on discrete heritable units (genes)
- Mendel documented a particulate mechanism through his experiments with garden peas

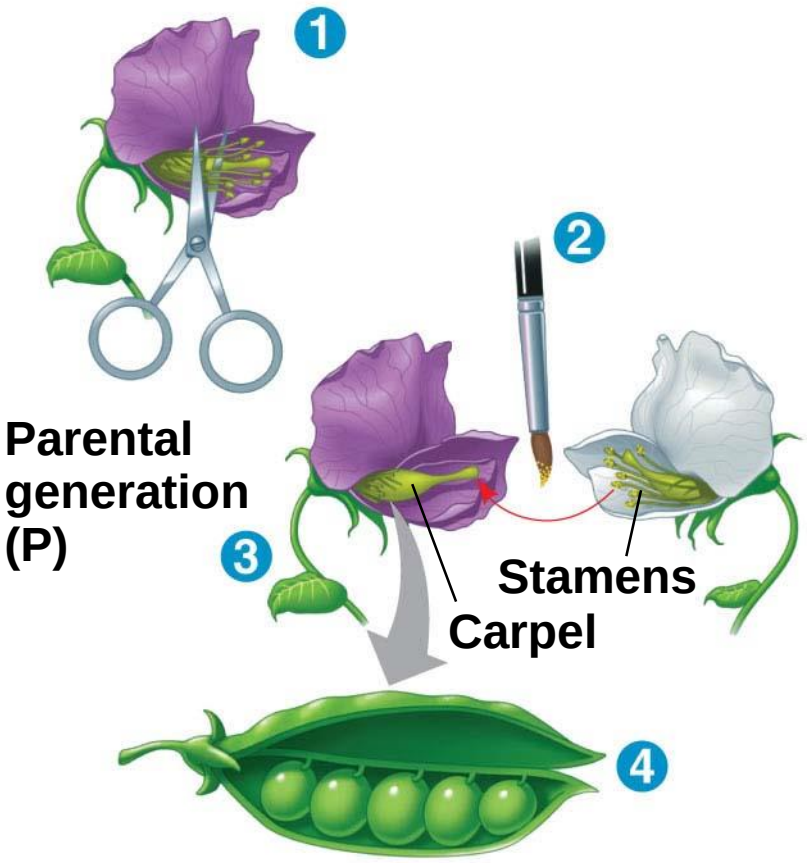
Concept 11.1: Mendel used the scientific approach to identify two laws of inheritance

- Mendel discovered the basic principles of heredity by breeding garden peas in carefully planned experiments

Mendel's Experimental, Quantitative Approach

- Mendel probably chose to work with peas because
  - There are many varieties with distinct heritable features, or **characters** (such as flower color); character variants (such as purple or white flowers) are called **traits**
  - He could control mating between plants

Figure 11.2



- Mendel chose to track only characters that occurred in two distinct alternative forms
- He also used varieties that were **true-breeding** (plants that produce offspring of the same variety when they self-pollinate)

- In a typical experiment, Mendel mated two contrasting, true-breeding varieties, a process called **hybridization**
- The true-breeding parents are the **P generation**
- The hybrid offspring of the P generation are called the **F_1 generation**
- When F_1 individuals self-pollinate or cross-pollinate with other F_1 hybrids, the **F_2 generation** is produced

The Law of Segregation

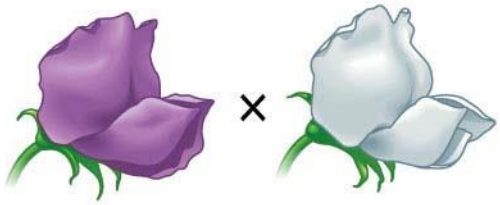
- When Mendel crossed contrasting, true-breeding white- and purple-flowered pea plants, all of the F_1 hybrids were purple
- When Mendel crossed the F_1 hybrids, many of the F_2 plants had purple flowers, but some had white
- Mendel discovered a ratio of about three to one, purple to white flowers, in the F_2 generation

Figure 11.3-s1

Experiment

P Generation

(true-breeding parents)



Purple flowers × **White flowers**

Figure 11.3-s2

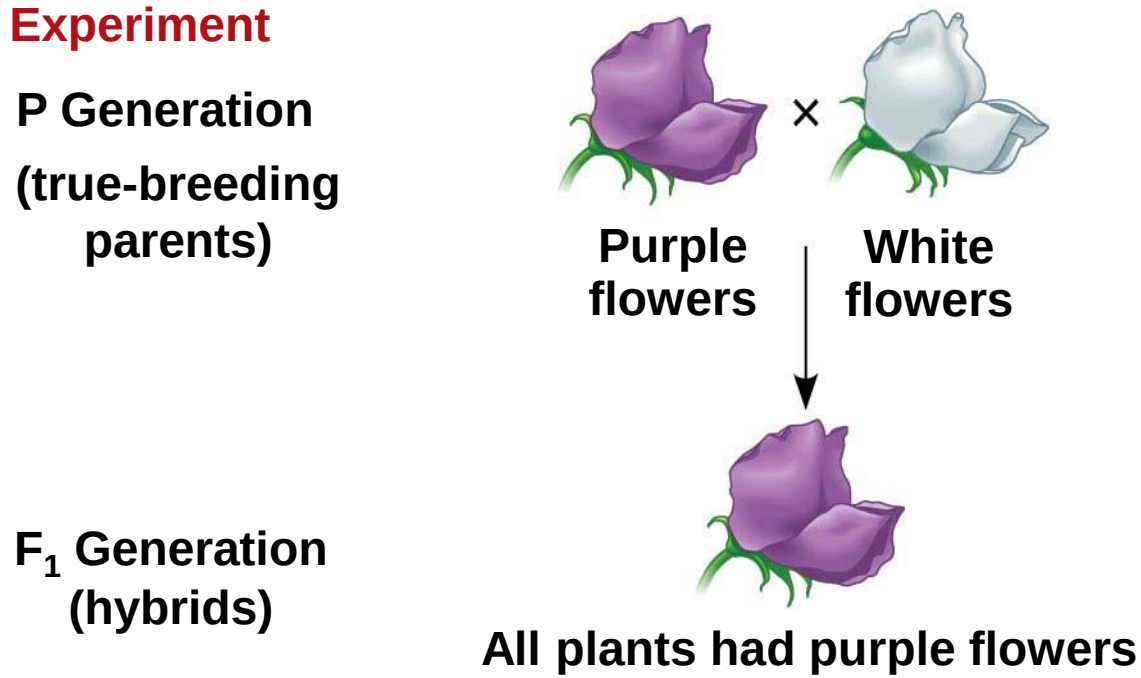
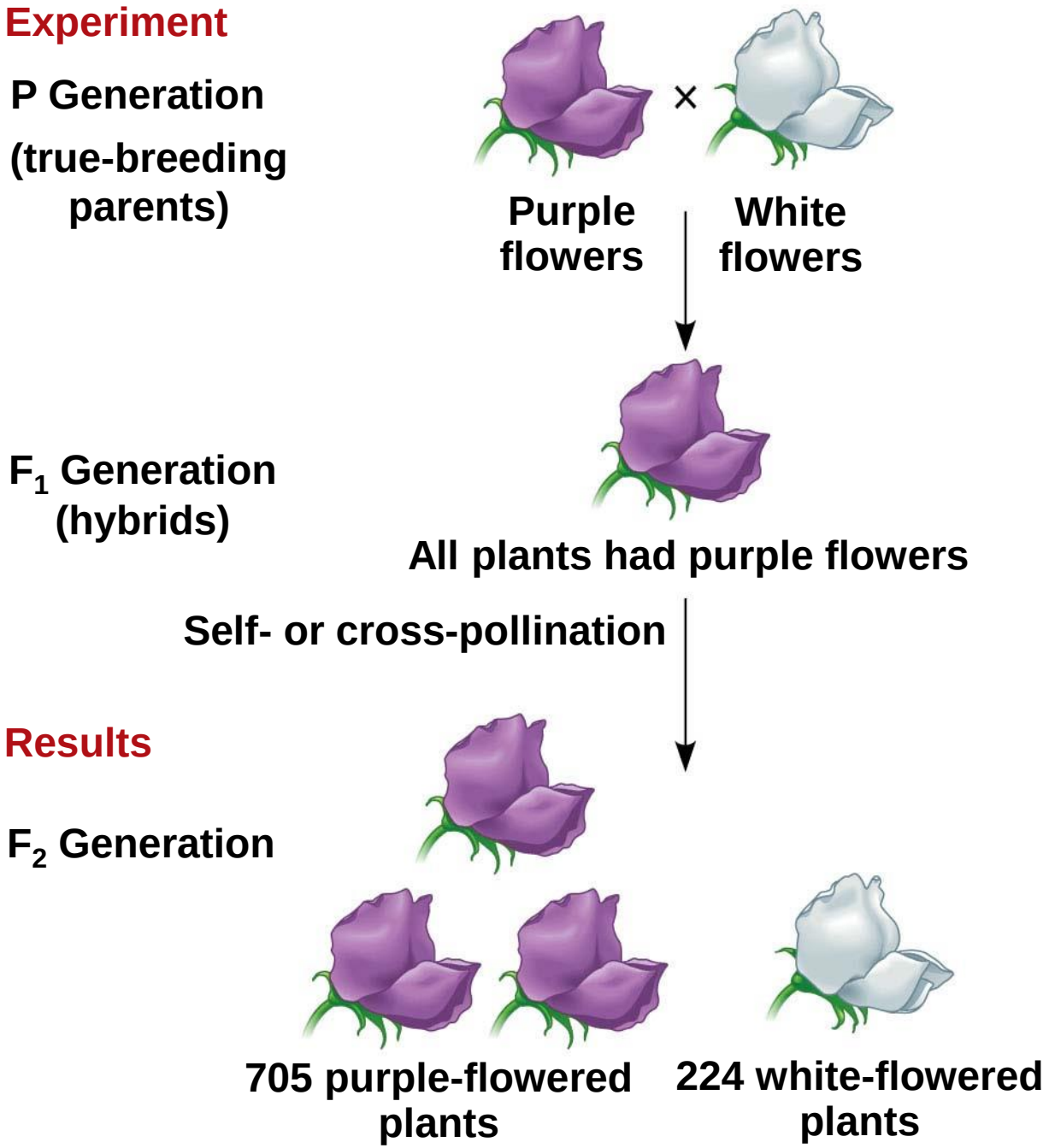


Figure 11.3-s3



- Mendel reasoned that in the F_1 plants, the heritable factor for white flowers was hidden or masked in the presence of the purple-flower factor
- He called the purple flower color a dominant trait and the white flower color a recessive trait
- The factor for white flowers was not diluted or destroyed because it reappeared in the F_2 generation

- Mendel observed the same pattern of inheritance in six other pea plant characters, each represented by two traits
- What Mendel called a “heritable factor” is what we now call a gene

Table 11.1

Table 11.1 The Results of Mendel's F_1 Crosses for Seven Characters in Pea Plants

Character	Dominant Trait	×	Recessive Trait	F_2 Generation Dominant: Recessive	Ratio
Flower color	Purple 	×	White 	705:224	3.15:1
Seed color	Yellow 	×	Green 	6,022:2,001	3.01:1
Seed shape	Round 	×	Wrinkled 	5,474:1,850	2.96:1
Pod shape	Inflated 	×	Constricted 	882:299	2.95:1
Pod color	Green 	×	Yellow 	428:152	2.82:1
Flower position	Axial 	×	Terminal 	651:207	3.14:1
Stem length	Tall 	×	Dwarf 	787:277	2.84:1

Table 11.1-1

Table 11.1 The Results of Mendel's F_1 Crosses for Seven Characters in Pea Plants

Character	Dominant Trait	×	Recessive Trait	F_2 Generation Dominant: Recessive	Ratio
Flower color	Purple 	×	White 	705:224	3.15:1
Seed color	Yellow 	×	Green 	6,022:2,001	3.01:1
Seed shape	Round 	×	Wrinkled 	5,474:1,850	2.96:1
Pod shape	Inflated 	×	Constricted 	882:299	2.95:1

Table 11.1-2

Table 11.1 The Results of Mendel's F_1 Crosses for Seven Characters in Pea Plants

Character	Dominant Trait	×	Recessive Trait	F_2 Generation Dominant: Recessive	Ratio
Pod color	Green 	×	Yellow 	428:152	2.82:1
Flower position	Axial 	×	Terminal 	651:207	3.14:1
Stem length	Tall 	×	Dwarf 	787:277	2.84:1

Mendel's Model

- Mendel developed a model to explain the 3:1 inheritance pattern he observed in F_2 offspring
- Four related concepts make up this model

- First, *alternative versions of genes account for variations in inherited characters*
- For example, the gene for flower color in pea plants exists in two versions, one for purple flowers and the other for white flowers
- These alternative versions of a gene are now called **alleles**
- Each gene resides at a specific locus on a specific chromosome

Figure 11.4

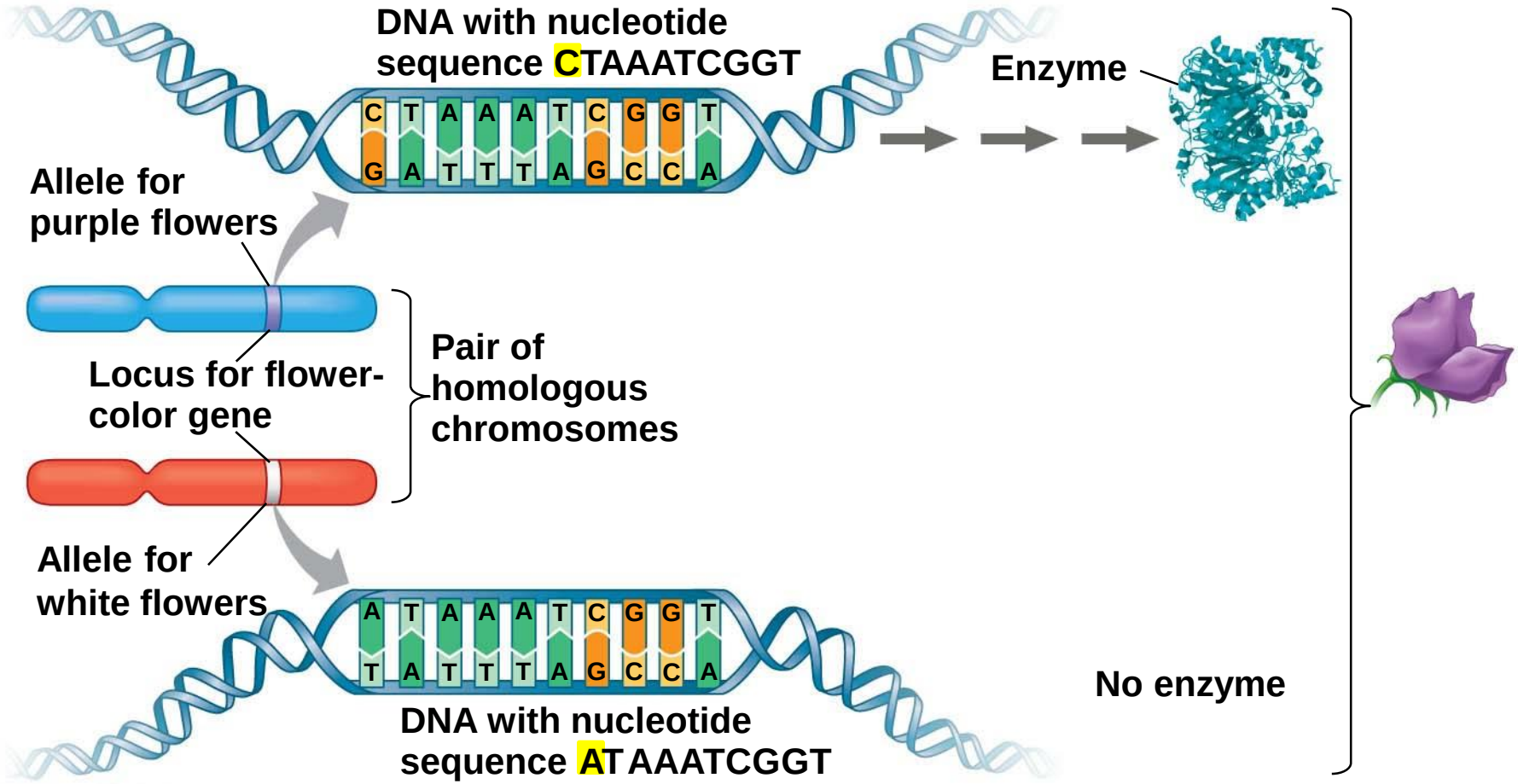


Figure 11.4-1

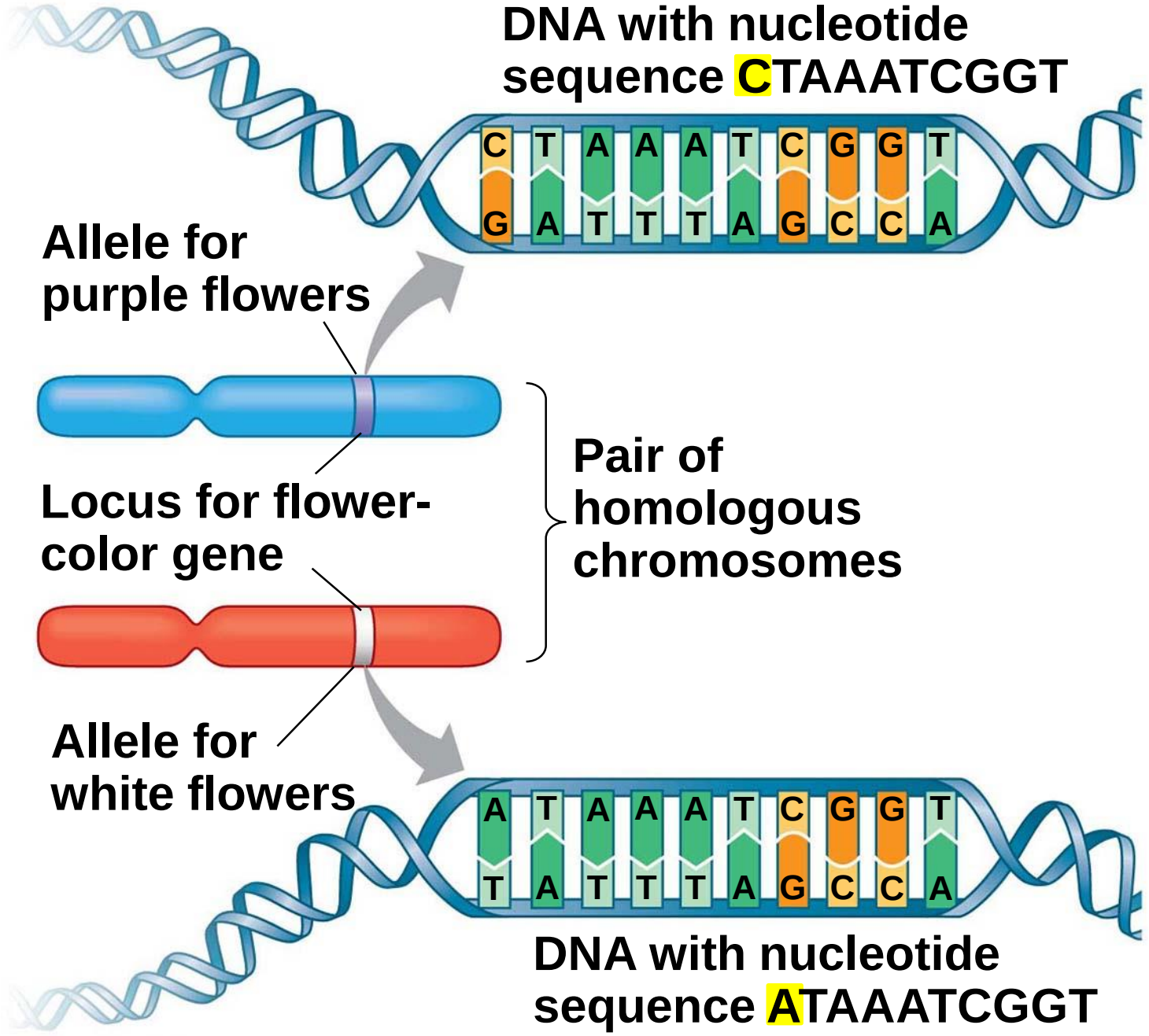
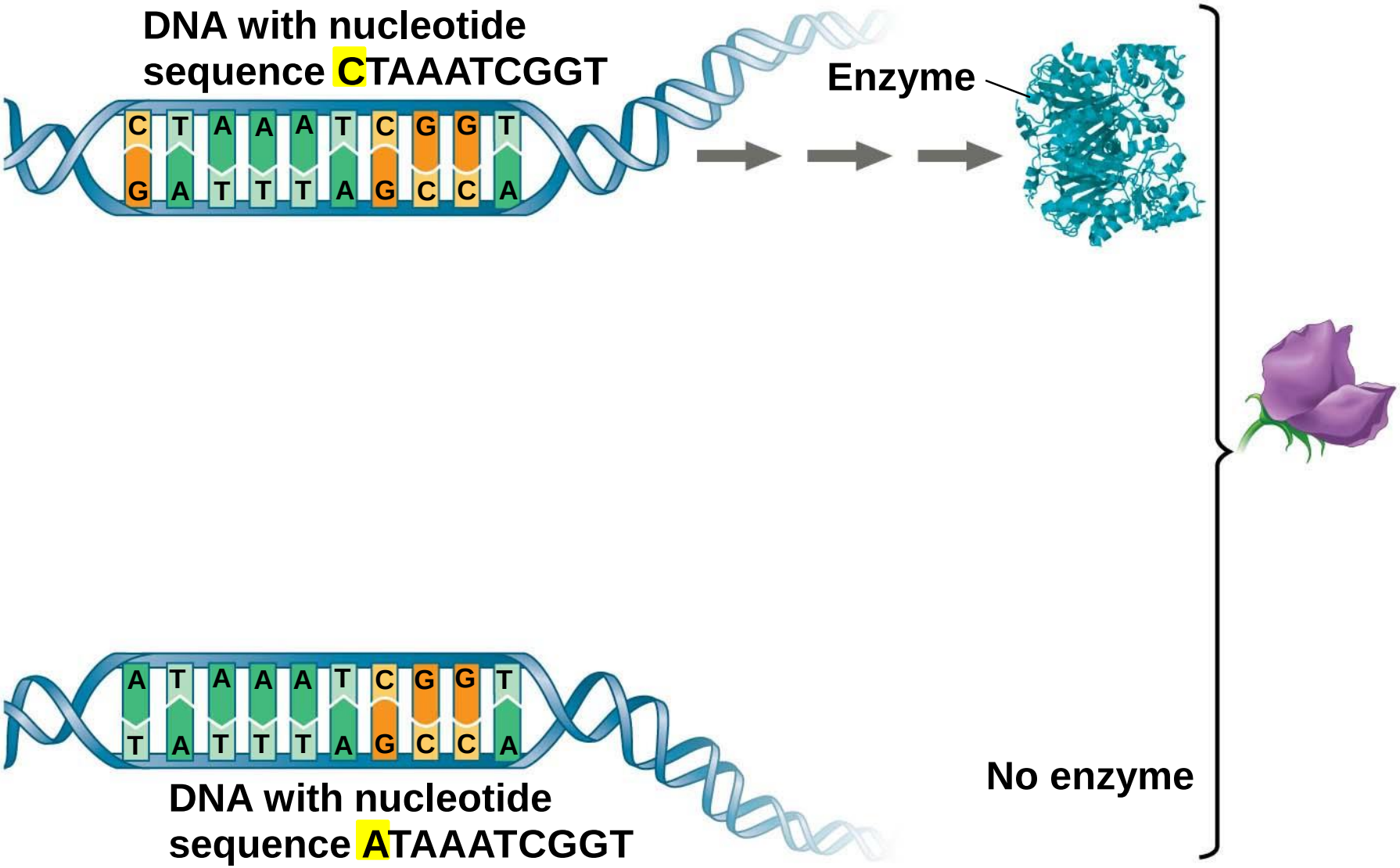


Figure 11.4-2



- Second, *for each character, an organism inherits two alleles, one from each parent*
- Mendel made this deduction without knowing about the existence of chromosomes
- Two alleles at a particular locus may be identical, as in the true-breeding plants of Mendel's P generation
- Alternatively, the two alleles at a locus may differ, as in the F_1 hybrids

- Third, *if the two alleles at a locus differ, then one* (*the* ***dominant allele***) *determines the organism's appearance, and the other* (*the* ***recessive allele***) *has no noticeable effect on appearance*
- In the flower-color example, the F_1 plants had purple flowers because the allele for that trait is dominant

- Fourth (the **law of segregation**), *the two alleles for a heritable character separate* (*segregate*) *during gamete formation and end up in different gametes*
- Thus, an egg or a sperm gets only one of the two alleles that are present in the organism
- This segregation of alleles corresponds to the distribution of homologous chromosomes to different gametes in meiosis

- Mendel's segregation model accounts for the 3:1 ratio he observed in the F_2 generation of his crosses
- Possible combinations of sperm and egg can be shown using a **Punnett square** to predict the results of a genetic cross between individuals of known genetic makeup
- A capital letter represents a dominant allele, and a lowercase letter represents a recessive allele
- For example, *P* is the purple-flower allele and *p* is the white-flower allele

Figure 11.5-s1

P Generation

×

Appearance: **Purple flowers** **White flowers**

Genetic makeup: ***PP*** ***pp***

Gametes: ***P*** ***p***

Figure 11.5-s2

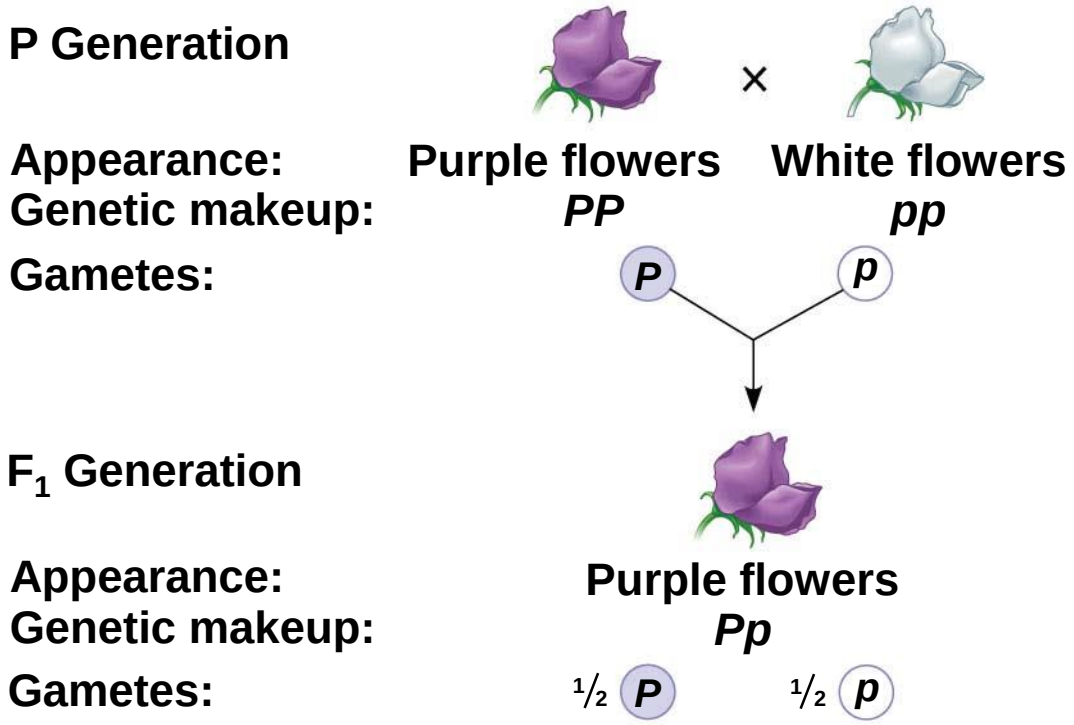
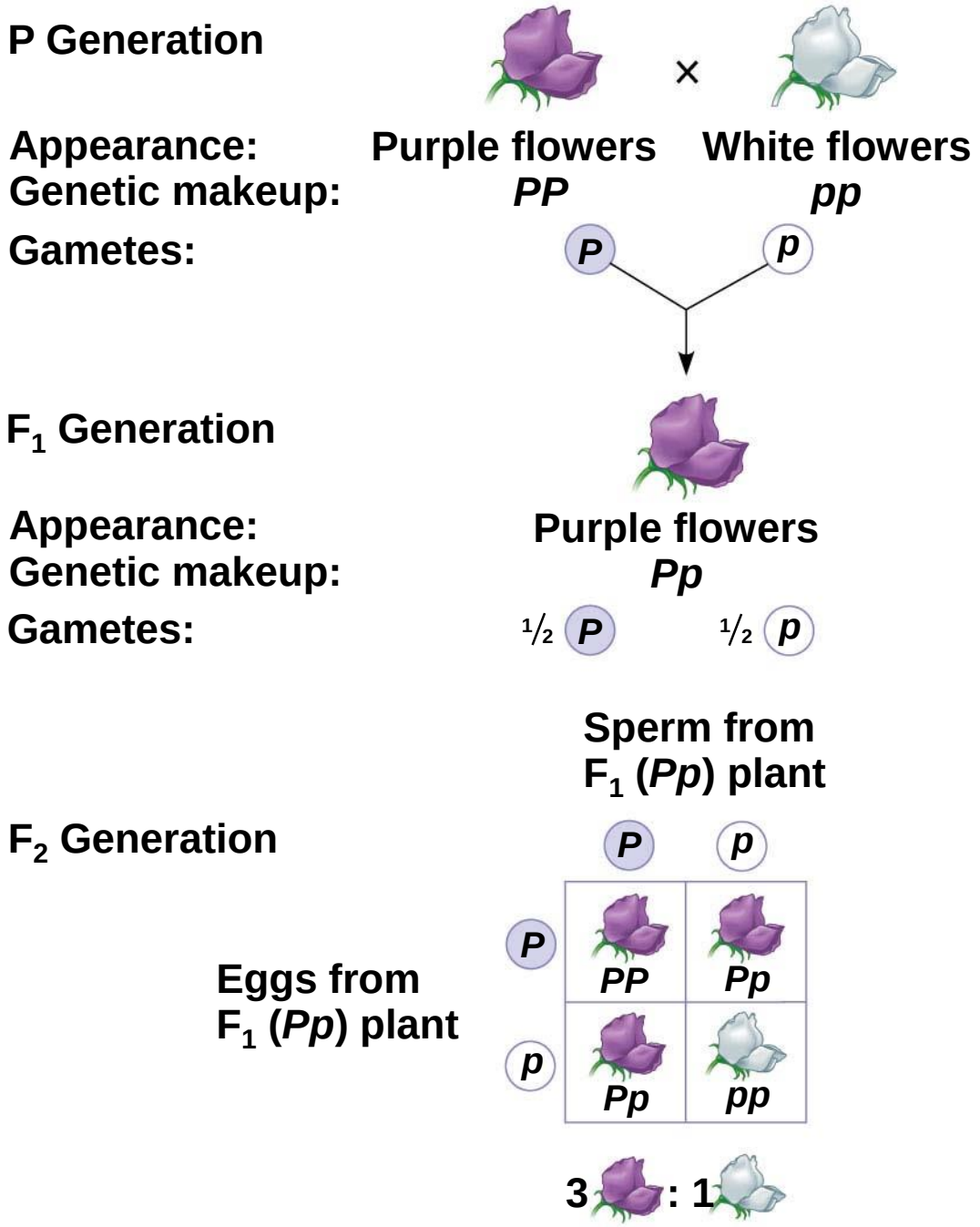


Figure 11.5-s3

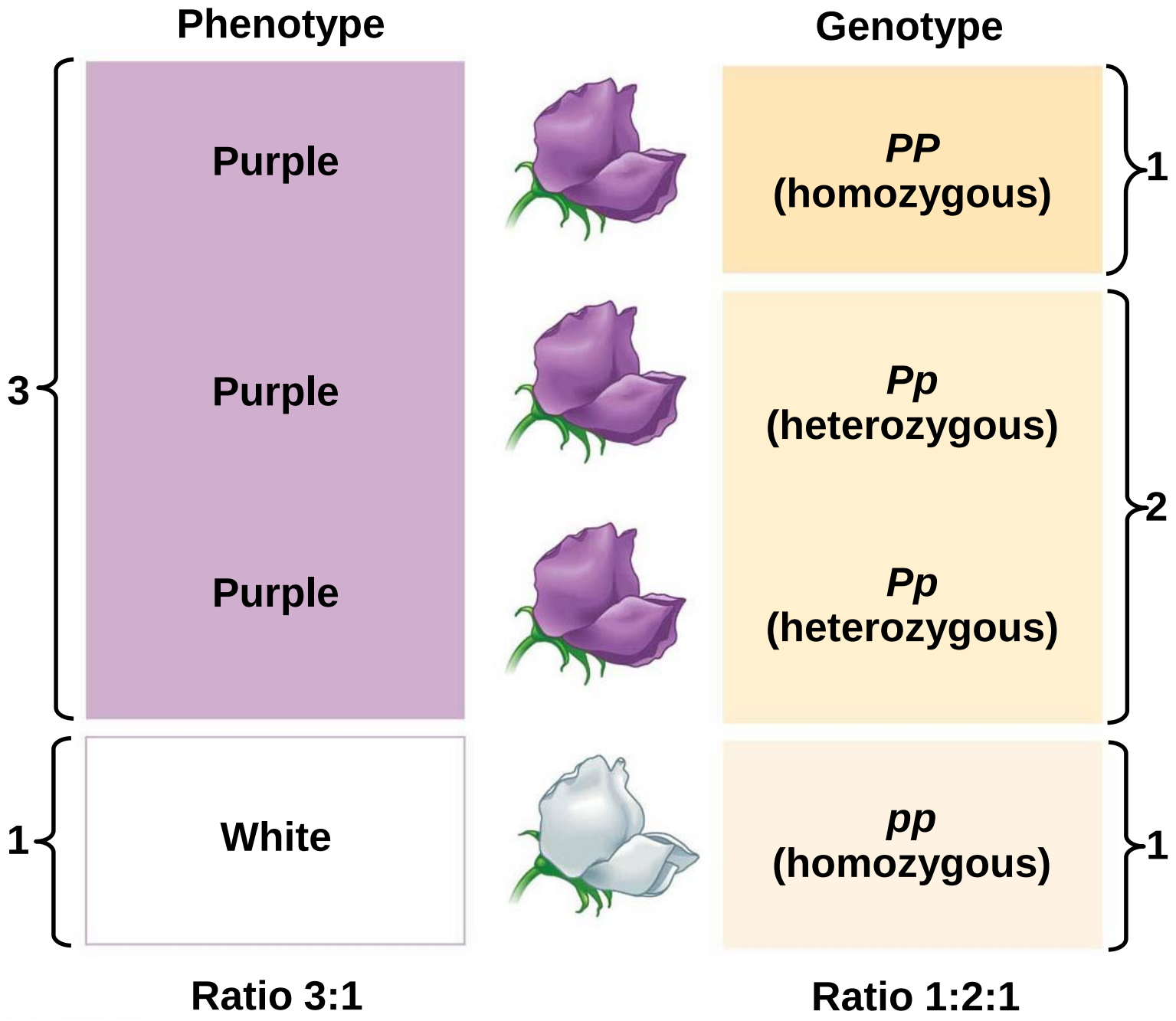


Useful Genetic Vocabulary

- An organism with two identical alleles for a character is said to be **homozygous** for the gene controlling that character
- An organism that has two different alleles for a gene is said to be **heterozygous** for the gene controlling that character
- Unlike **homozygotes**, **heterozygotes** are not true-breeding

- Because of the effects of dominant and recessive alleles, an organism's traits do not always reveal its genetic composition
- Therefore, we distinguish between an organism's **phenotype**, or physical appearance, and its **genotype**, or genetic makeup
- In the example of flower color in pea plants, *PP* and *Pp* plants have the same phenotype (purple) but different genotypes

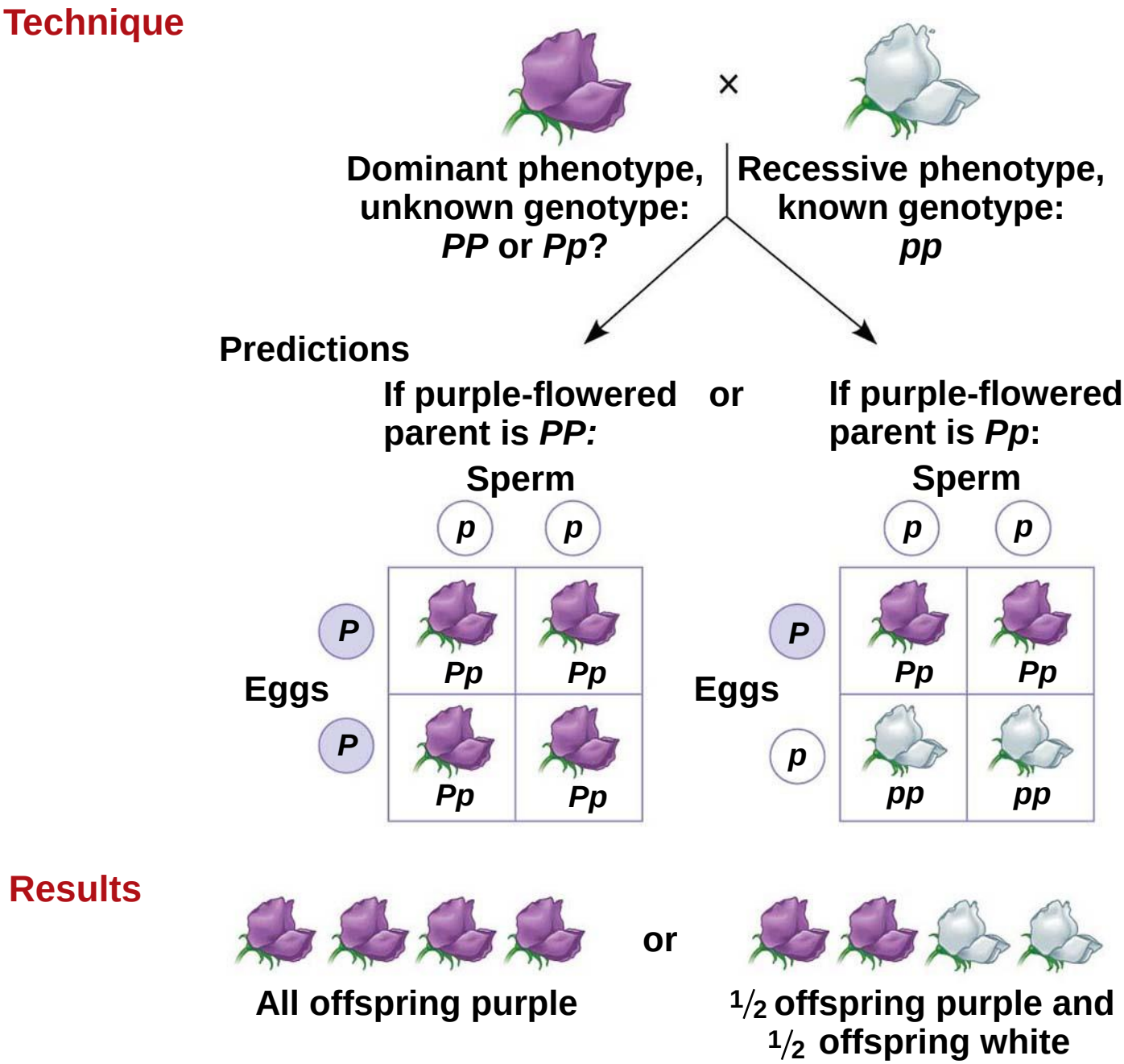
Figure 11.6



The Testcross

- How can we tell the genotype of an individual with the dominant phenotype?
- Such an individual could be either homozygous dominant or heterozygous
- The answer is to carry out a **testcross**: breeding the mystery individual with a homozygous recessive individual
- If any offspring display the recessive phenotype, the mystery parent must be heterozygous

Figure 11.7



The Law of Independent Assortment

- Mendel derived the law of segregation by following a single character
- The F_1 offspring produced in this cross were **monohybrids**, individuals that are heterozygous for one character
- A cross between such heterozygotes is called a **monohybrid cross**

- Mendel identified his second law of inheritance by following two characters at the same time
- Crossing two true-breeding parents differing in two characters produces **dihybrids** in the F_1 generation, heterozygous for both characters
- A **dihybrid cross**, a cross between F_1 dihybrids, can determine whether two characters are transmitted to offspring as a package or independently

Figure 11.8

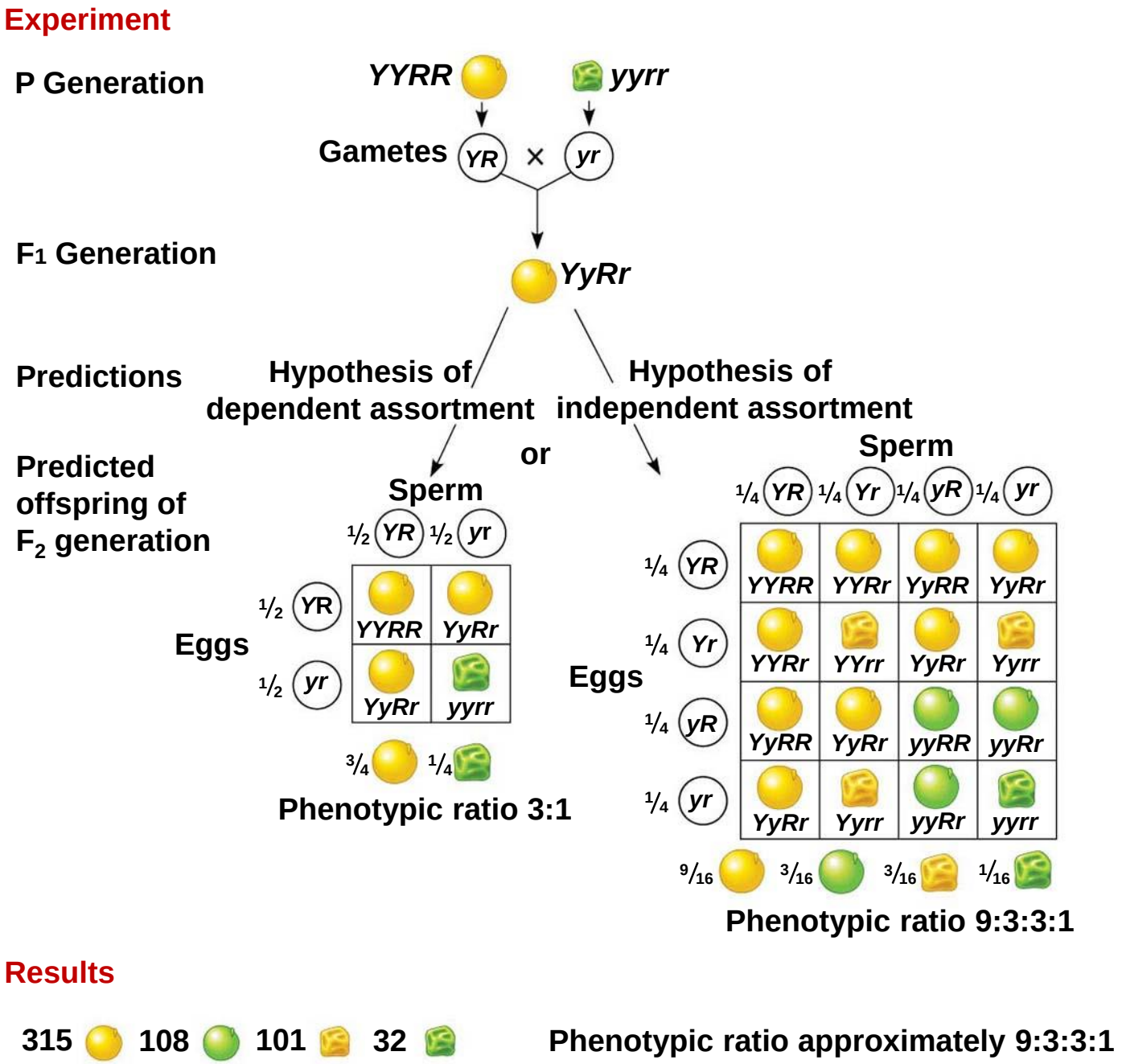
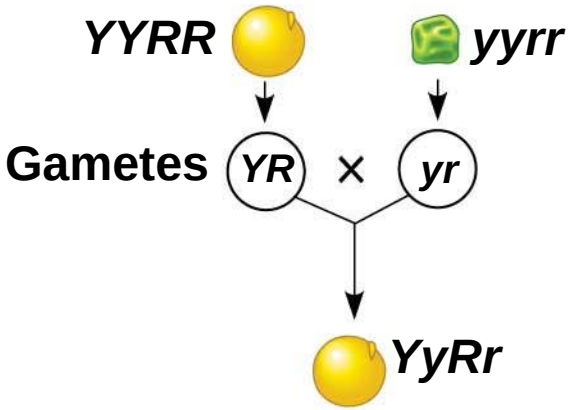


Figure 11.8-1

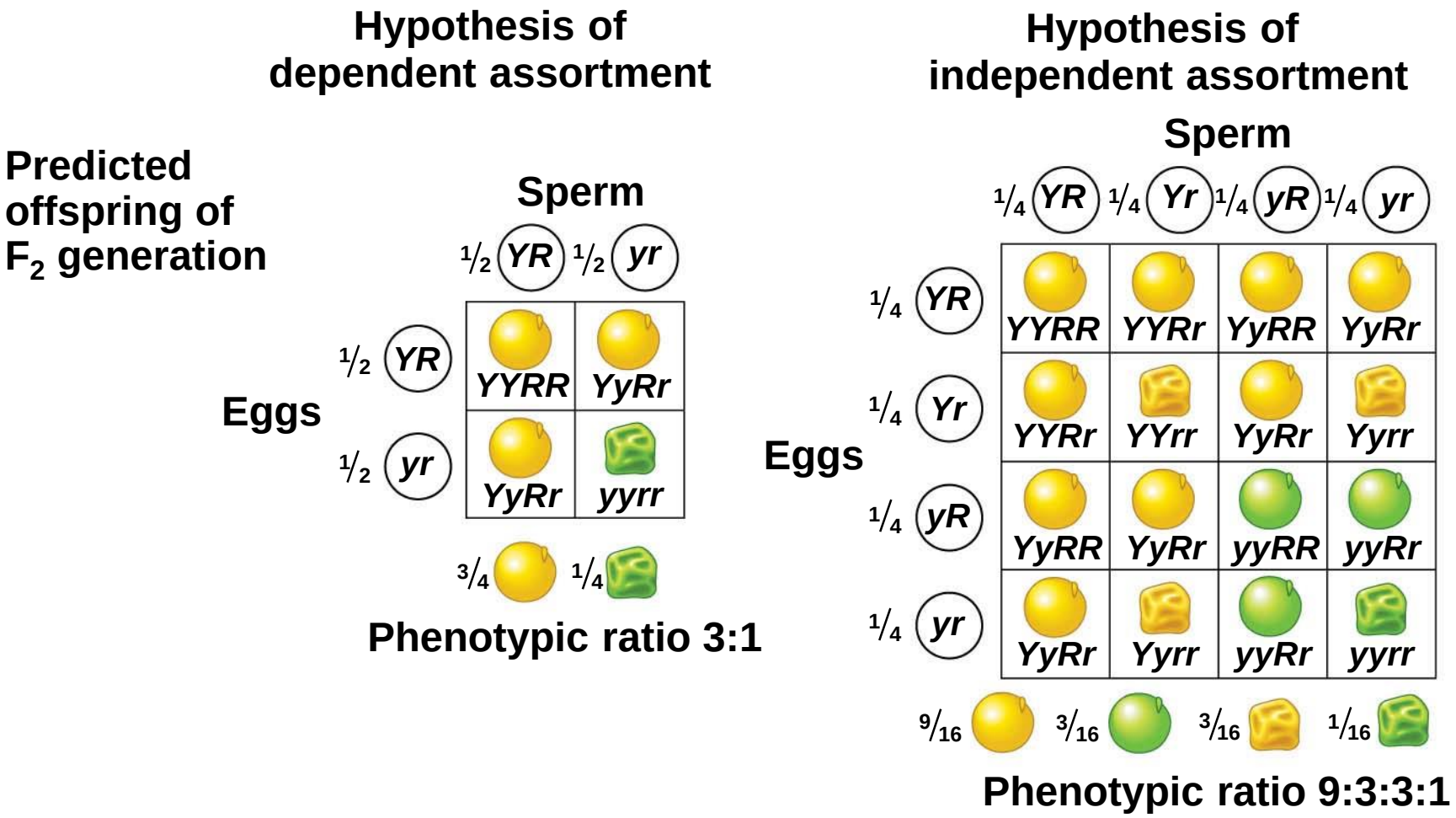
Experiment

P Generation



F_1 Generation

Figure 11.8-2



Results

315 108 101 32

Phenotypic ratio approximately 9:3:3:1

- The results of Mendel's dihybrid experiments are the basis for the **law of independent assortment**
- It states that *each pair of alleles segregates independently of any other pair during gamete formation*
- This law applies to genes on chromosomes that are not homologous, or those far apart on the same chromosome
- Genes located near each other on the same chromosome tend to be inherited together

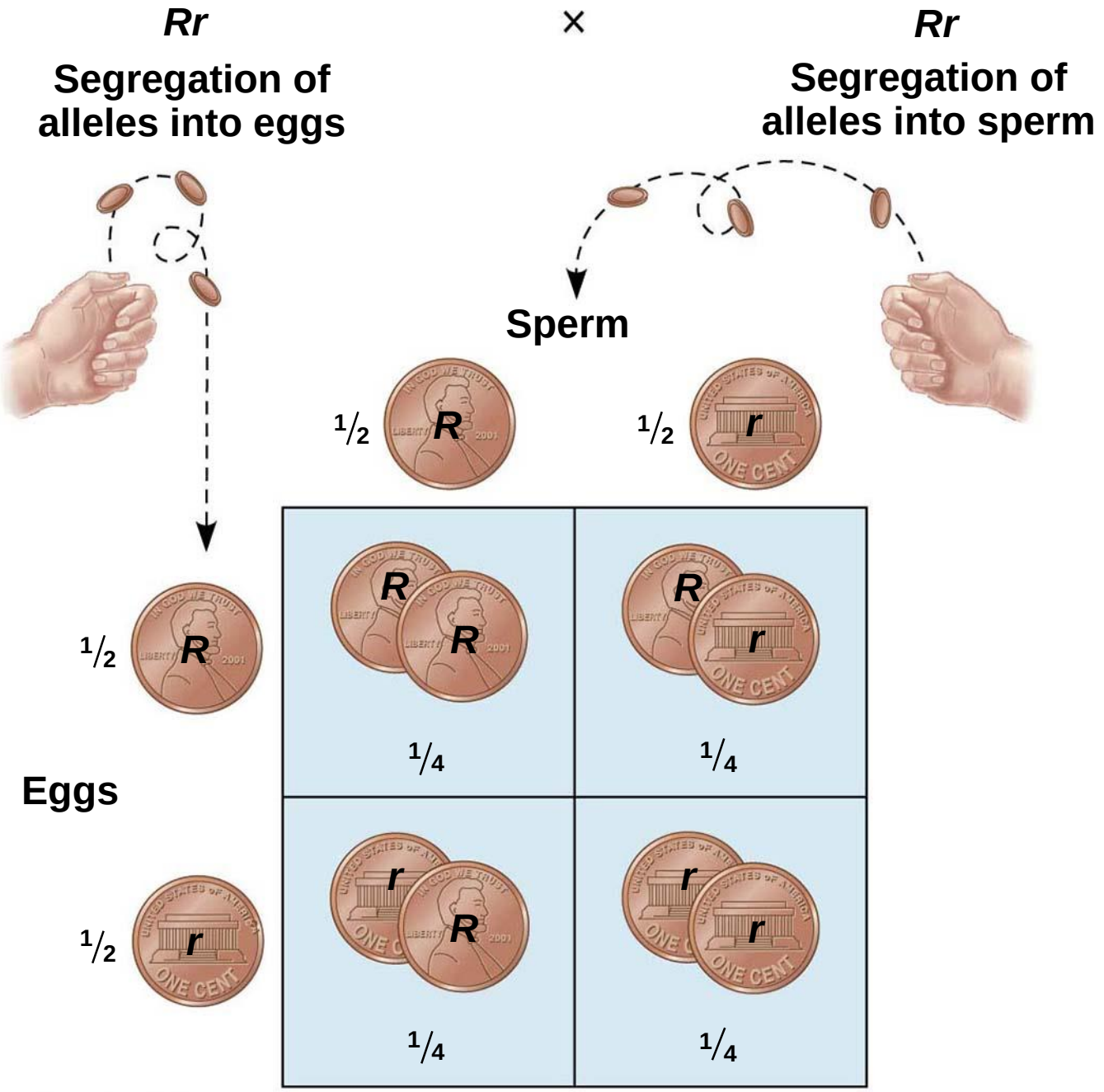
Concept 11.2: Probability laws govern Mendelian inheritance

- Mendel's laws of segregation and independent assortment reflect the rules of probability
- The outcome of one coin toss has no impact on the outcome of the next toss
- In the same way, the alleles of one gene segregate into gametes independently of another gene's alleles

The Multiplication and Addition Rules Applied to Monohybrid Crosses

- The **multiplication rule** states that the probability that two or more independent events will occur together is the product of their individual probabilities
- This can be applied to an F_1 monohybrid cross
- Segregation in a heterozygous plant is like flipping a coin: Each gamete has a ½ chance of carrying the dominant allele and a ½ chance of carrying the recessive allele

Figure 11.9



- The **addition rule** states that the probability that any one of two or more mutually exclusive events will occur is calculated by adding together their individual probabilities
- It can be used to figure out the probability that an F_2 plant from a monohybrid cross will be heterozygous rather than homozygous

Solving Complex Genetics Problems with the Rules of Probability

- We can apply the rules of probability to predict the outcome of crosses involving multiple characters
- A dihybrid or other multicharacter cross is equivalent to two or more independent monohybrid crosses occurring simultaneously
- In calculating the chances for various genotypes, each character is considered separately, and then the individual probabilities are multiplied

- For example, if we cross F_1 heterozygotes of genotype *YyRr*, we can calculate the probability of different genotypes among the F_2 generation

Probability of *YYRR* = ¼ (probability of *YY*) × ¼ (*RR*) = ¹⁄₁₆

Probability of *YyRR* = ½ (*Yy*) × ¼ (*RR*) = ⅛

- For example, for the cross *PpYyRr* × *Ppyyrr*, we can calculate the probability of offspring showing at least two recessive traits

ppyyRr	**¼ (probability of *pp*) × ½ (*yy*) × ½ (*Rr*)**	**= 1/16**
ppYyrr	¼ × ½ × ½	= 1/16
Ppyyrr	½ × ½ × ½	= 2/16
PPyyrr	¼ × ½ × ½	= 1/16
ppyyrr	¼ × ½ × ½	= 1/16
Chance of *at least two* recessive traits		**= 6/16 or 3/8**

Concept 11.3: Inheritance patterns are often more complex than predicted by simple Mendelian genetics

- Not all heritable characters are determined as simply as the traits Mendel studied
- However, the basic principles of segregation and independent assortment apply even to more complex patterns of inheritance

Extending Mendelian Genetics for a Single Gene

- Inheritance of characters by a single gene may deviate from simple Mendelian patterns in the following situations
  - When alleles are not completely dominant or recessive
  - When a gene has more than two alleles
  - When a single gene produces multiple phenotypes

Degrees of Dominance

- **Complete dominance** occurs when phenotypes of the heterozygote and dominant homozygote are identical
- In **incomplete dominance**, the phenotype of F_1 hybrids is somewhere between the phenotypes of the two parental varieties
- In **codominance**, two dominant alleles affect the phenotype in separate, distinguishable ways

Figure 11.10-s1

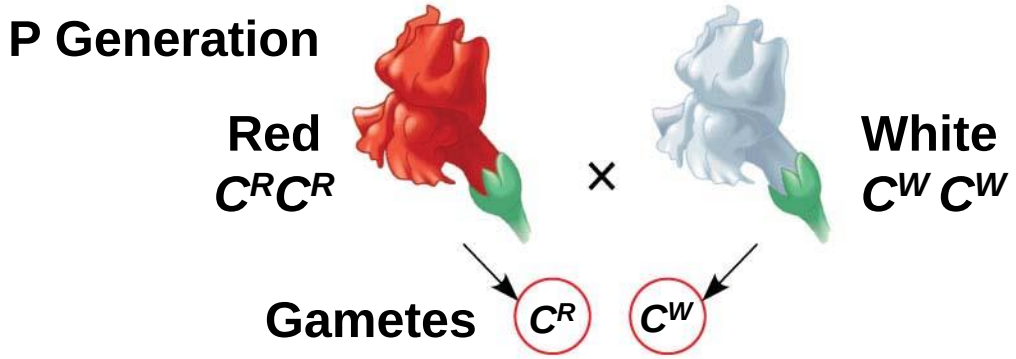


Figure 11.10-s2

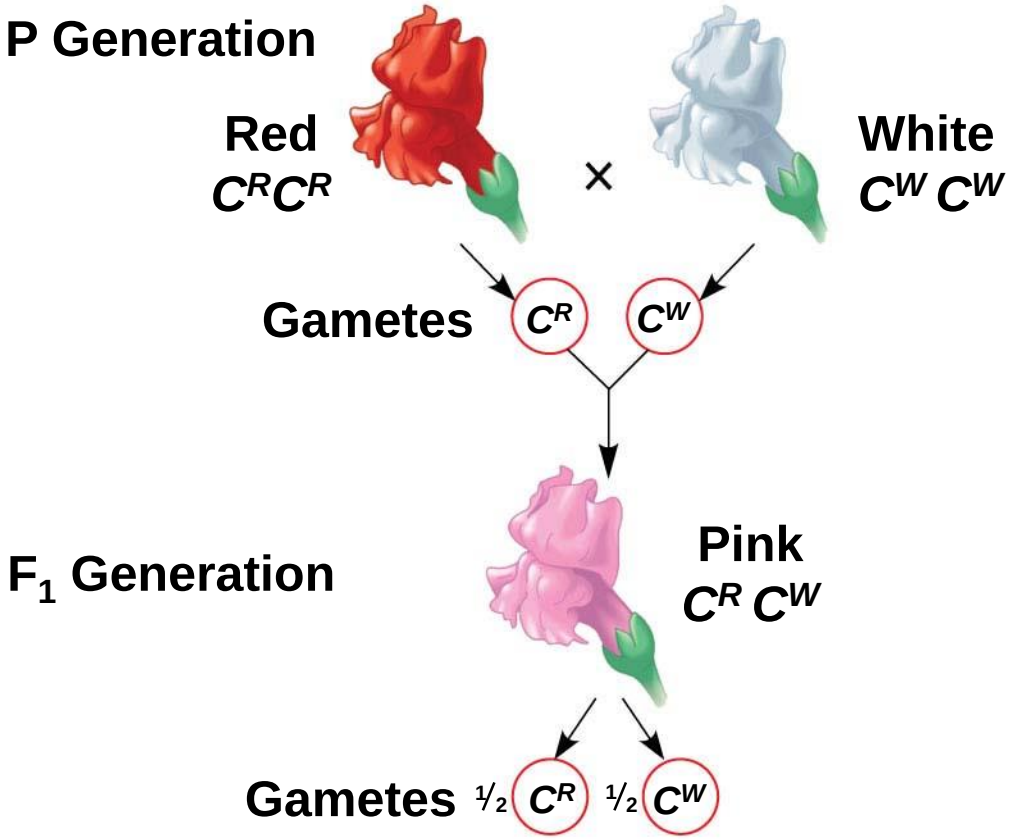
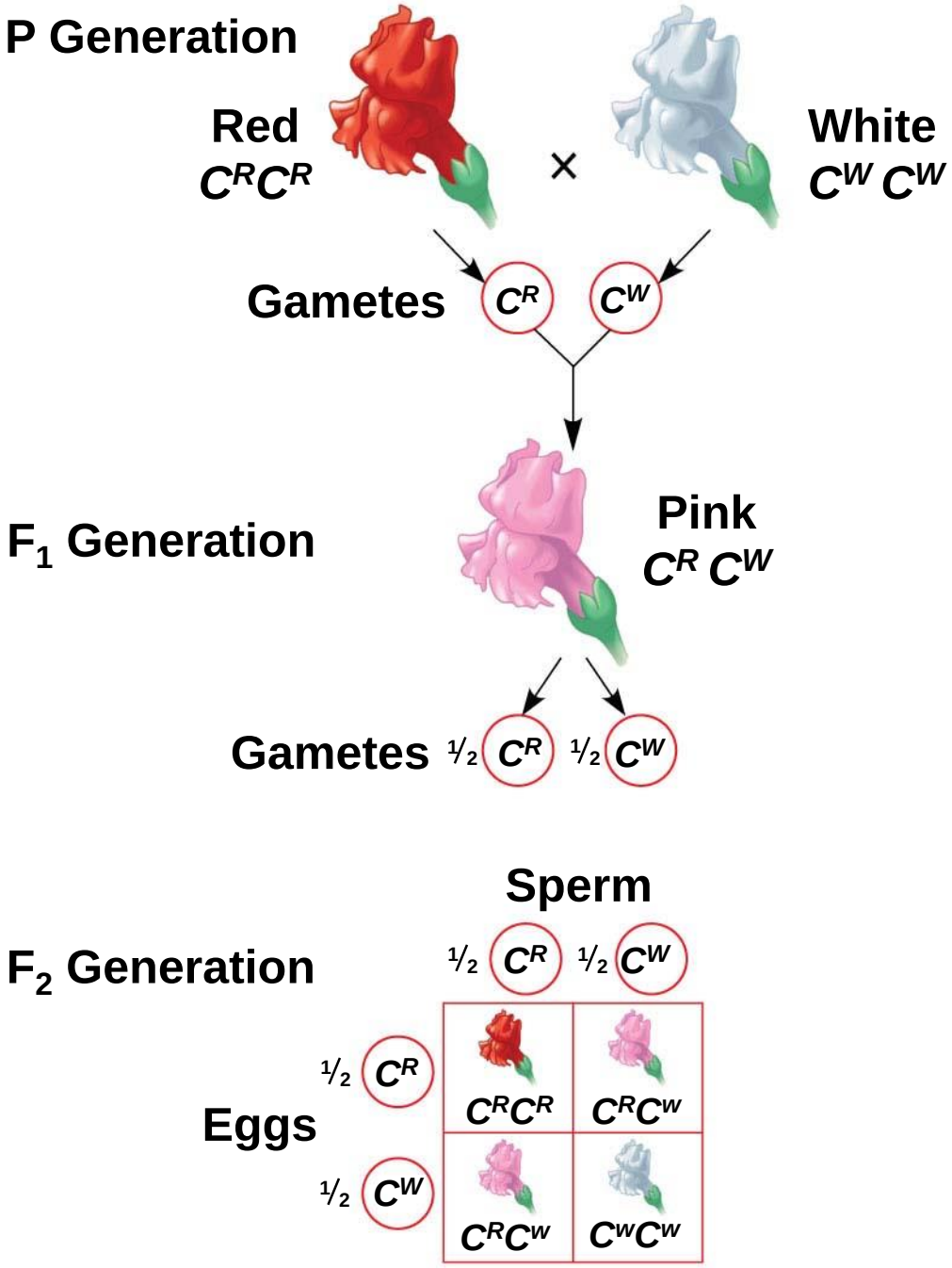


Figure 11.10-s3



The Relationship Between Dominance and Phenotype

- Alleles are simply variations in a gene's nucleotide sequence
- When a dominant allele coexists with a recessive allele in a heterozygote, they do not actually interact at all
- For any character, dominant/recessive relationships of alleles depend on the level at which we examine the phenotype

- **Tay-Sachs disease** is fatal; a dysfunctional enzyme causes an accumulation of lipids in the brain
  - At the *organismal* level, the allele is recessive
  - At the *biochemical* level, the phenotype (i.e., the enzyme activity level) is incompletely dominant
  - At the *molecular* level, the alleles are codominant

Frequency of Dominant Alleles

- Dominant alleles are not necessarily more common in populations than recessive alleles
- For example, one baby out of 400 in the United States is born with extra fingers or toes, a dominant trait called polydactyly

Multiple Alleles

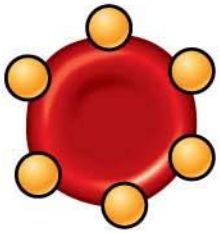
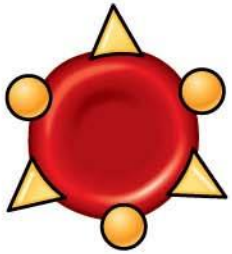
- Most genes exist in populations in more than two allelic forms
- For example, the four phenotypes of the ABO blood group in humans are determined by three alleles of the gene: I^A, I^B, and i.
- The enzyme (I) adds specific carbohydrates to the surface of blood cells
- The enzyme encoded by I^A adds the A carbohydrate, and the enzyme encoded by I^B adds the B carbohydrate; the enzyme encoded by the i allele adds neither

Figure 11.11

(a) The three alleles for the ABO blood groups and their carbohydrates

Allele	I^A	I^B	i
Carbohydrate	A 	B 	none

(b) Blood group genotypes and phenotypes

Genotype	$I^A I^A$ or $I^A i$	$I^B I^B$ or $I^B i$	$I^A I^B$	ii
Red blood cell appearance				
Phenotype (blood group)	A	B	AB	O

Pleiotropy

- Most genes have multiple phenotypic effects, a property called **pleiotropy**
- For example, pleiotropic alleles are responsible for the multiple symptoms of certain hereditary diseases, such as cystic fibrosis and sickle-cell disease

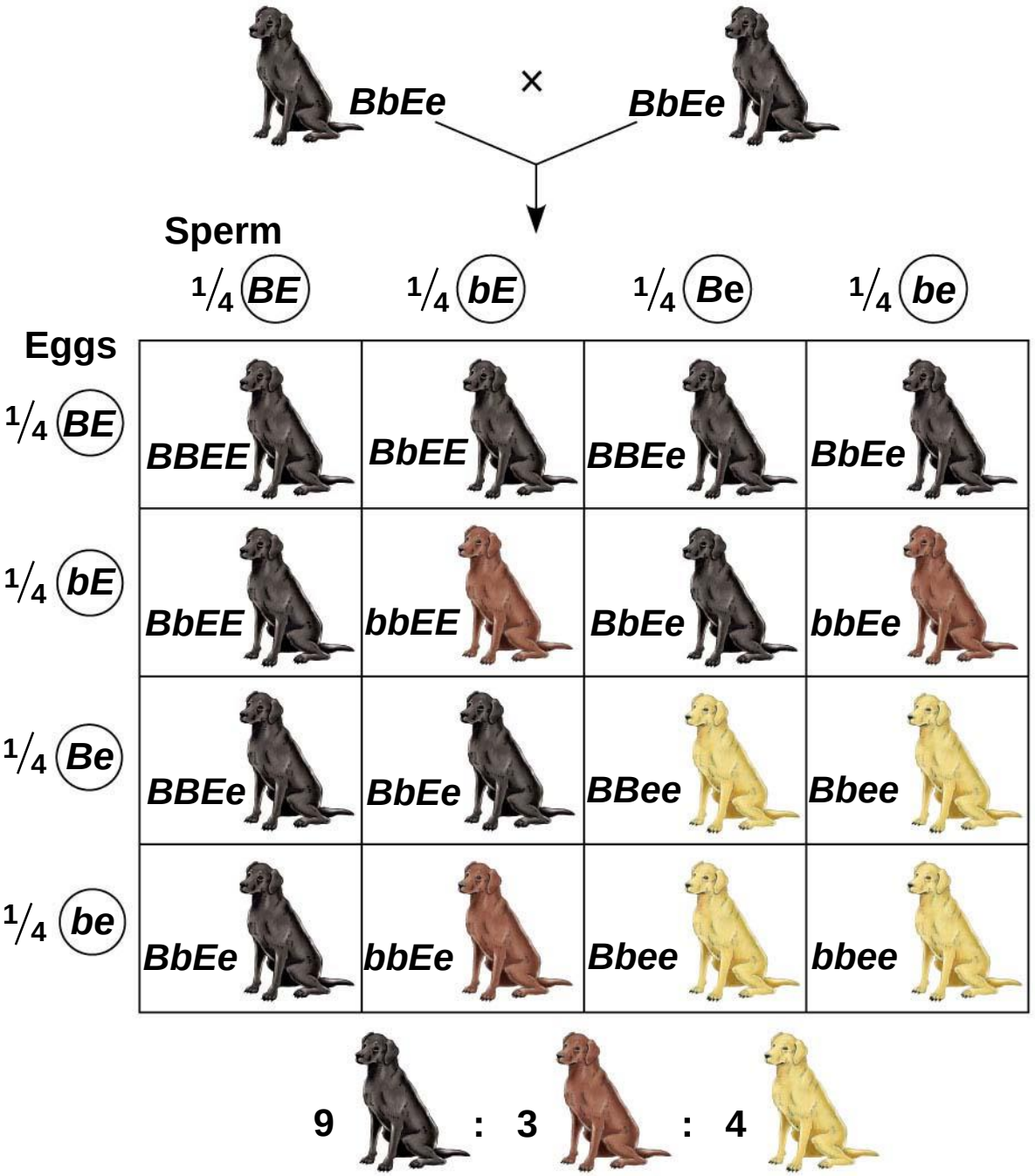
Extending Mendelian Genetics for Two or More Genes

- Some traits may be determined by two or more genes
- The gene products may interact
- Alternatively, multiple genes could independently affect a single trait

Epistasis

- In **epistasis**, a gene at one locus alters the phenotypic expression of a gene at a second locus
- For example, in Labrador retrievers and many other mammals, coat color depends on two genes
- One gene determines the pigment color (with alleles *B* for black and *b* for brown)
- The other gene (with alleles *C* for color and *c* for no color) determines whether the pigment will be deposited in the hair

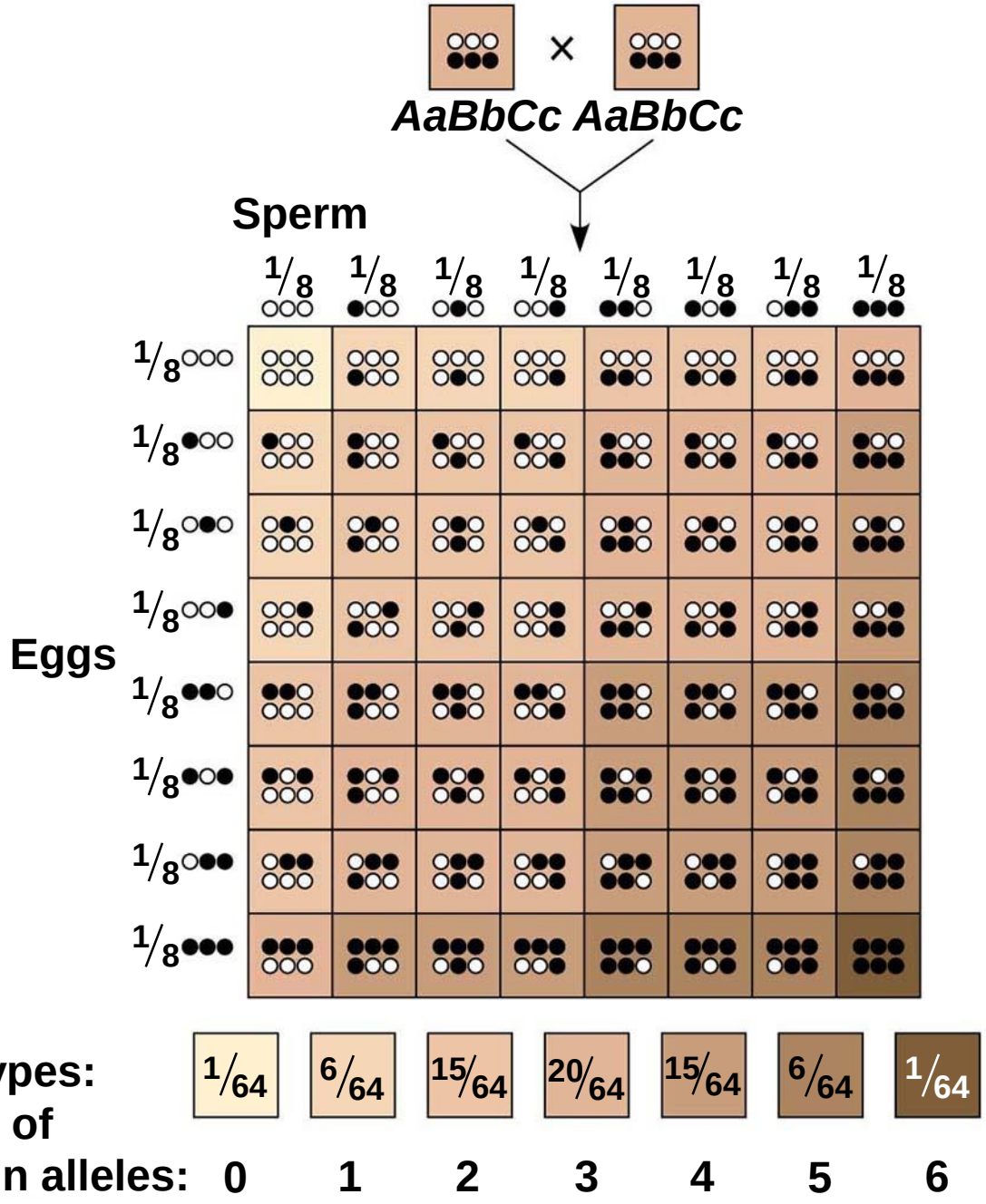
Figure 11.12



Polygenic Inheritance

- **Quantitative characters** are those that vary in the population along a continuum
- Quantitative variation usually indicates **polygenic inheritance**, an additive effect of two or more genes on a single phenotype
- Skin color in humans is an example of polygenic inheritance

Figure 11.13



Nature and Nurture: The Environmental Impact on Phenotype

- Another departure from Mendelian genetics arises when the phenotype for a character depends on environment as well as genotype
- The norm of reaction is the phenotypic range of a genotype influenced by the environment

- The phenotypic range is generally broadest for polygenic characters
- Such characters are called **multifactorial** because genetic and environmental factors collectively influence phenotype

A Mendelian View of Heredity and Variation

- An organism's phenotype includes its physical appearance, internal anatomy, physiology, and behavior
- An organism's phenotype reflects its overall genotype and unique environmental history

Concept 11.4: Many human traits follow Mendelian patterns of inheritance

- Humans are not good subjects for genetic research
  - Generation time is too long
  - Parents produce relatively few offspring
  - Breeding experiments are unacceptable
- However, basic Mendelian genetics endures as the foundation of human genetics

Pedigree Analysis

- A **pedigree** is a family tree that describes the interrelationships of parents and children across generations
- Inheritance patterns of particular traits can be traced and described using pedigrees

- Pedigrees can also be used to make predictions about future offspring
- We can use the multiplication and addition rules to predict the probability of specific phenotypes

Figure 11.14

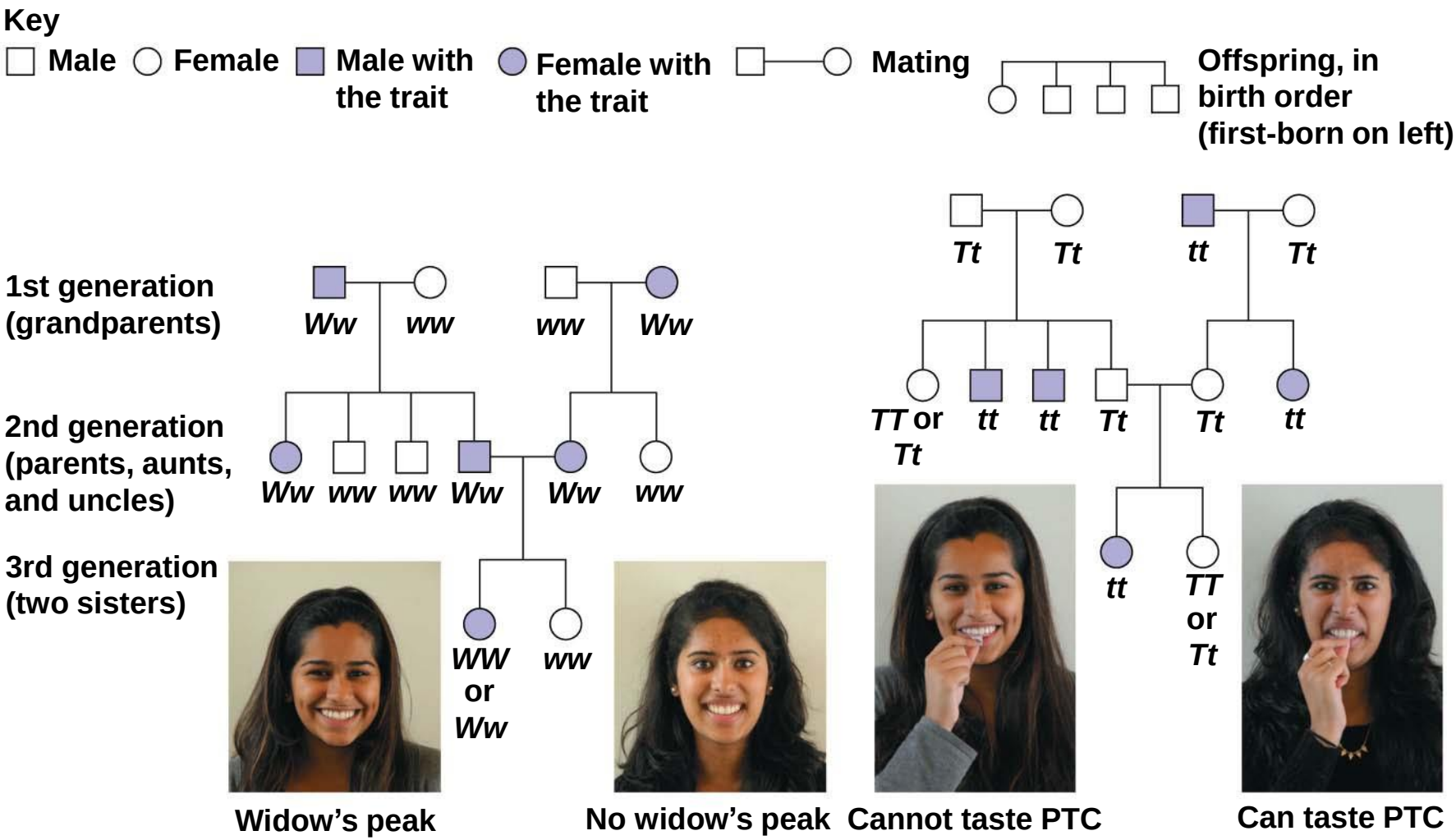
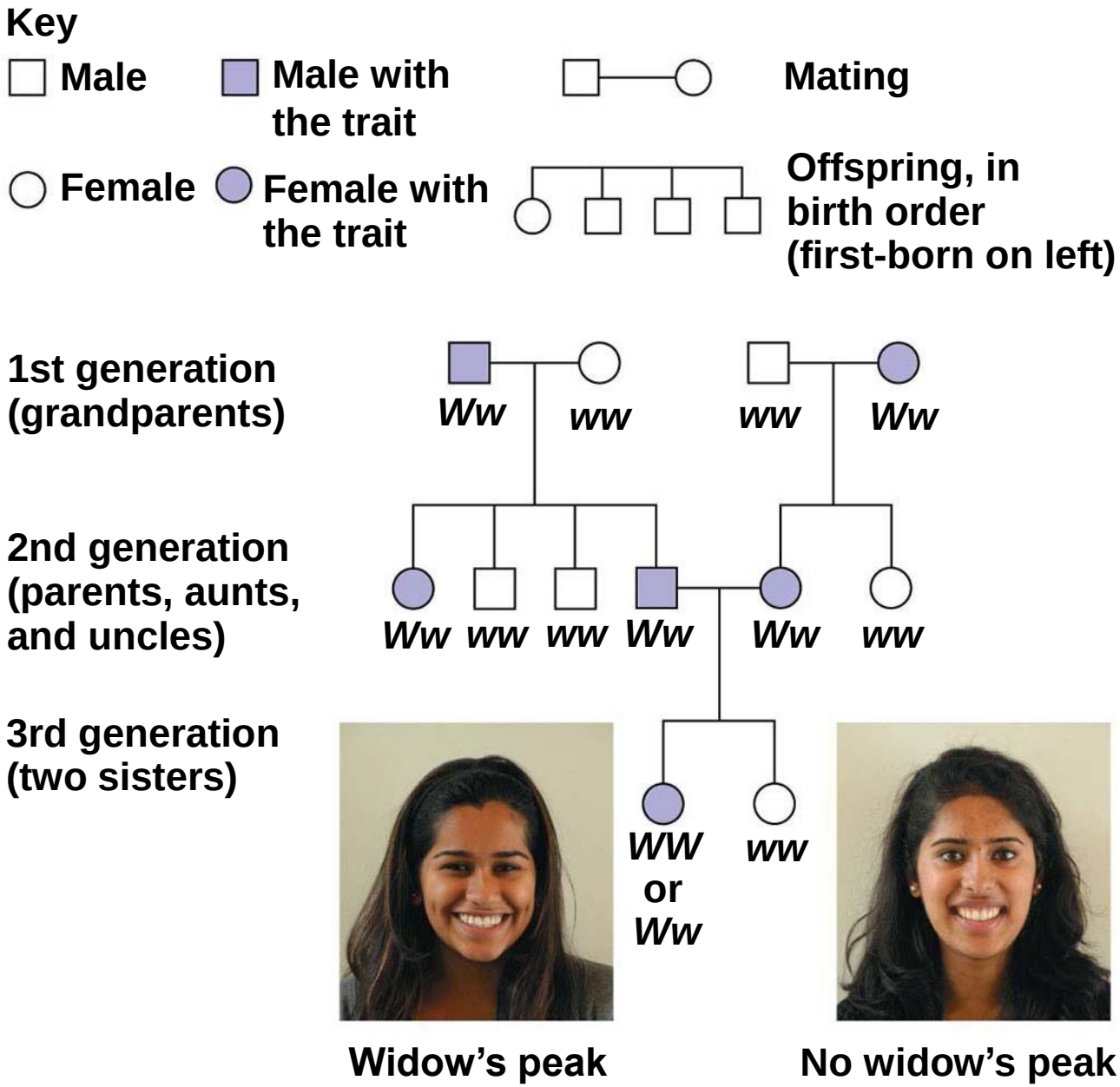
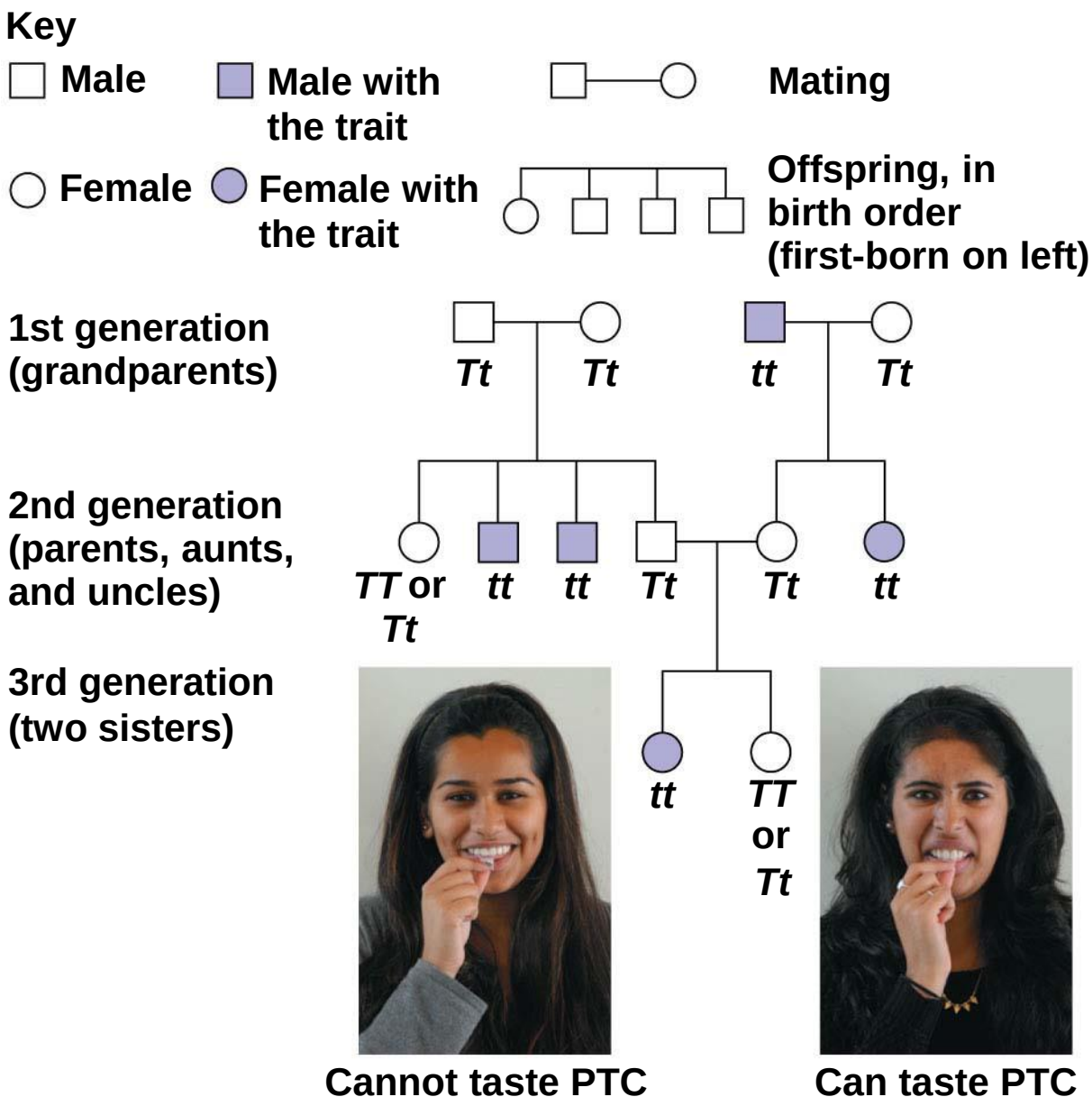


Figure 11.14-1



(a) Is a widow's peak a dominant or recessive trait?

Figure 11.14-2



(b) Is the inability to taste a chemical called PTC a dominant or recessive trait?

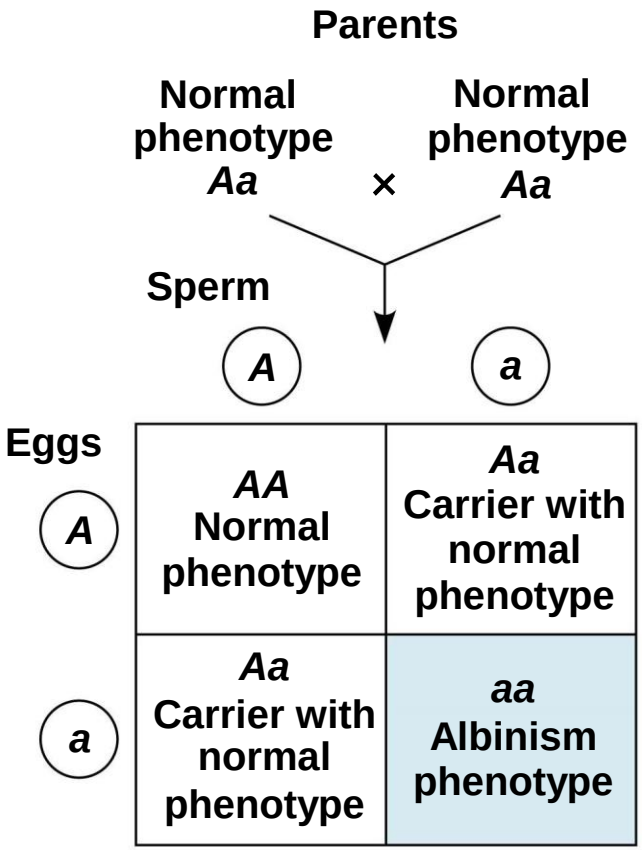
Recessively Inherited Disorders

- Many genetic disorders are inherited in a recessive manner
- These range from relatively mild to life-threatening

The Behavior of Recessive Alleles

- Recessively inherited disorders show up only in individuals homozygous for the allele
- **Carriers** are heterozygous individuals who carry the recessive allele but are phenotypically normal
- Most people who have recessive disorders are born to parents who are carriers of the disorder

Figure 11.15



- If a recessive allele that causes a disease is rare, then the chance of two carriers meeting and mating is low
- Consanguineous (between close relatives) matings increase the chance of mating between two carriers of the same rare allele
- Most societies and cultures have laws or taboos against marriages between close relatives

Cystic Fibrosis

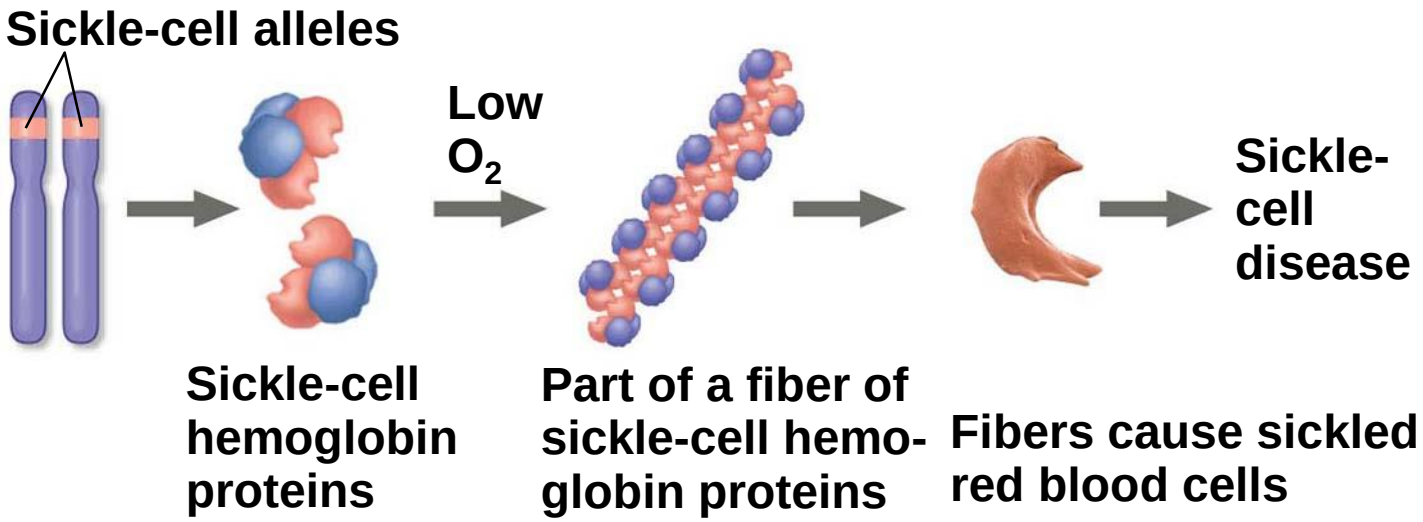
- **Cystic fibrosis** is the most common lethal genetic disease in the United States, striking one out of every 2,500 people of European descent
- The cystic fibrosis allele results in defective or absent chloride transport channels in plasma membranes leading to a buildup of chloride ions outside the cell
- Symptoms include mucus buildup in some internal organs and abnormal absorption of nutrients in the small intestine

Sickle-Cell Disease: A Genetic Disorder with Evolutionary Implications

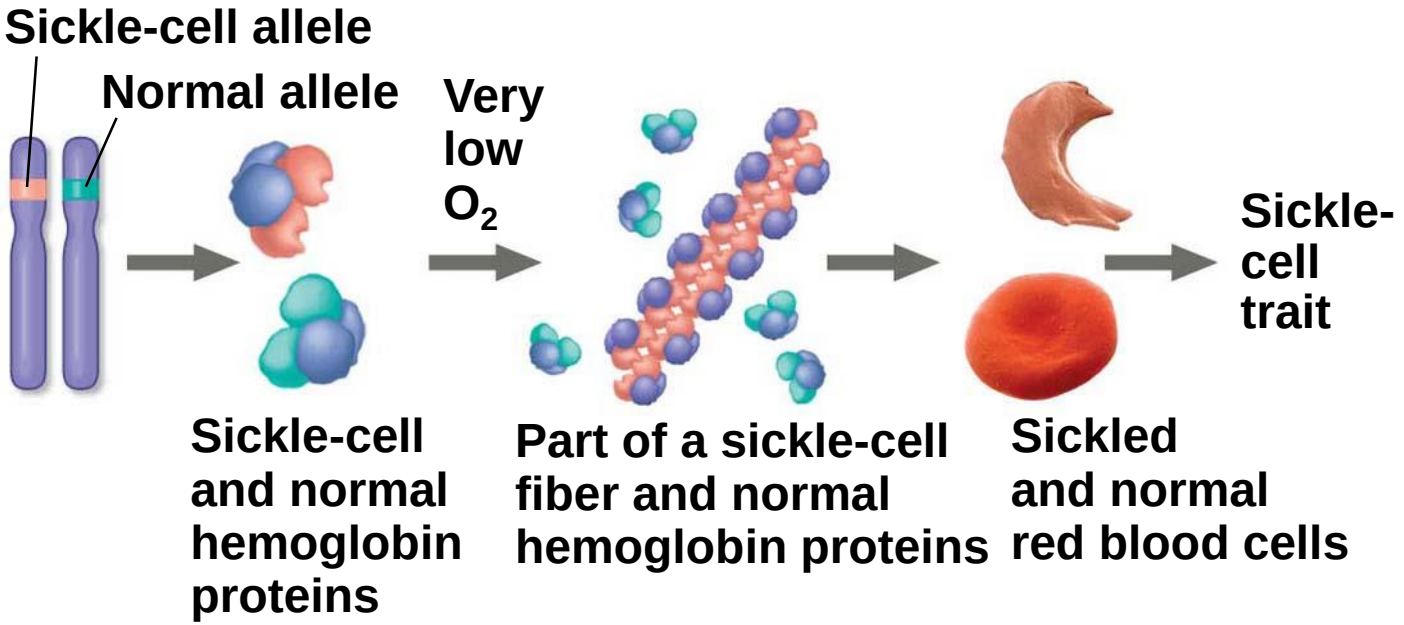
- **Sickle-cell disease** affects one out of 400 African-Americans
- The disease is caused by the substitution of a single amino acid in the hemoglobin protein in red blood cells
- In homozygous individuals, all hemoglobin is abnormal (sickle-cell)
- Symptoms include physical weakness, pain, organ damage, and even stroke and paralysis

- Heterozygotes (said to have sickle-cell trait) are usually healthy but may suffer some symptoms
- About one out of ten African-Americans has sickle-cell trait, an unusually high frequency of an allele with detrimental effects in homozygotes
- Heterozygotes are less susceptible to the malaria parasite, so there is an advantage to being heterozygous

Figure 11.16



(a) Homozygote with sickle-cell disease

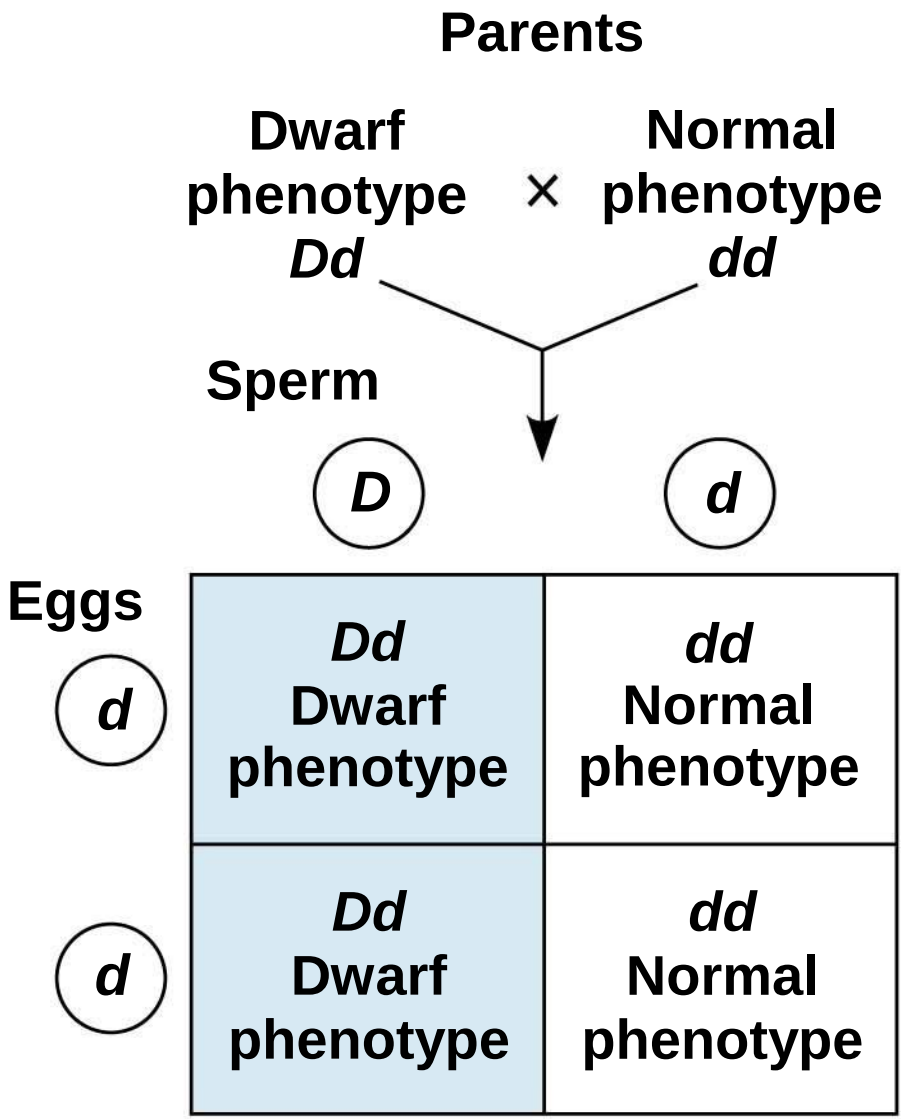


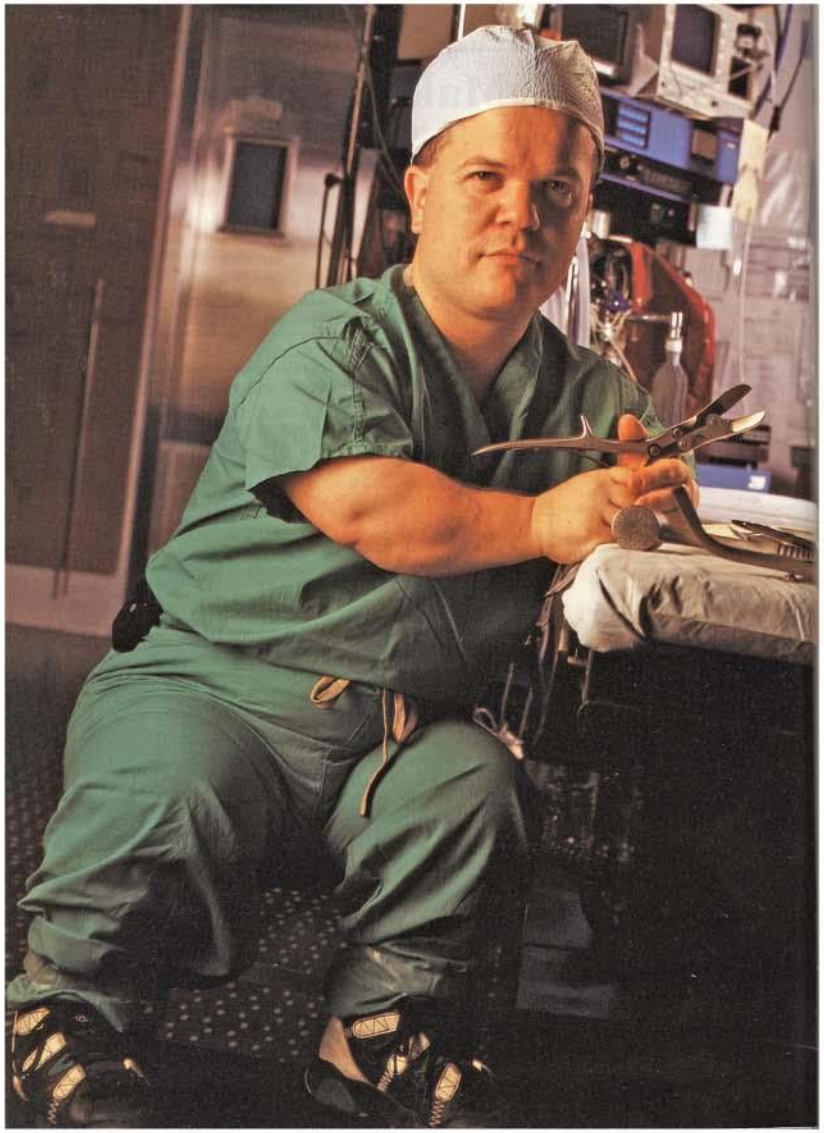
(b) Heterozygote with sickle-cell trait

Dominantly Inherited Disorders

- Some human disorders are caused by dominant alleles
- Dominant alleles that cause a lethal disease are rare and arise by mutation
- Achondroplasia is a form of dwarfism caused by a rare dominant allele

Figure 11.17





- The timing of onset of a disease significantly affects its inheritance
- **Huntington's disease** is a degenerative disease of the nervous system
- The disease has no obvious phenotypic effects until the individual is about 35 to 45 years of age
- Once the deterioration of the nervous system begins the condition is irreversible and fatal

Multifactorial Disorders

- Many diseases, such as heart disease, diabetes, alcoholism, mental illnesses, and cancer, have both genetic and environmental components
- Lifestyle has a tremendous effect on phenotype for cardiovascular health and other multifactorial characters

Genetic Counseling Based on Mendelian Genetics

- Genetic counselors can provide information to prospective parents concerned about a family history for a specific disease
- Each child represents an independent event in the sense that its genotype is unaffected by the genotypes of older siblings

Figure 11.UN03-1

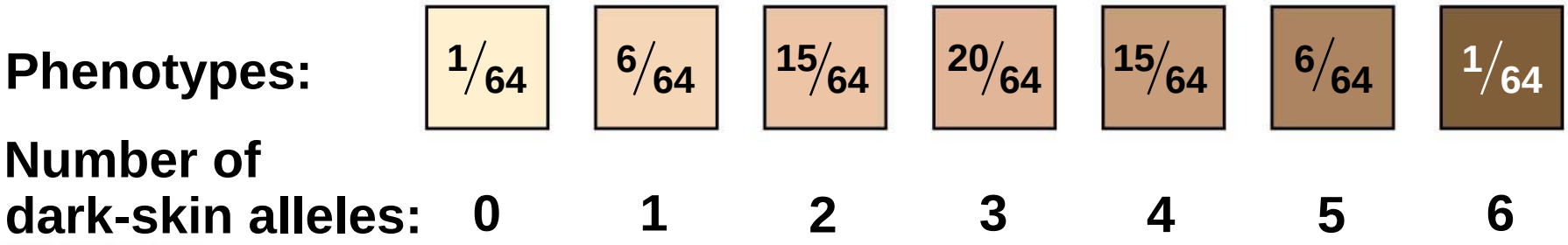
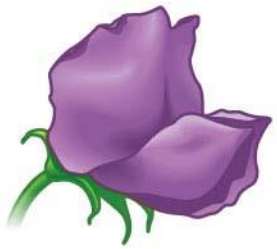
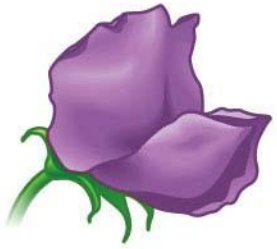


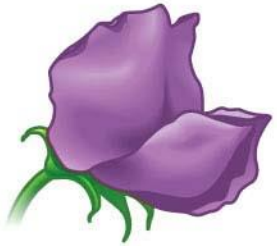
Figure 11.UN04



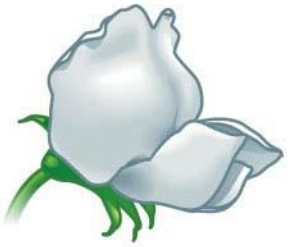
PP
(homozygous)



Pp
(heterozygous)



Pp
(heterozygous)



pp
(homozygous)

Figure 11.UN05

Relationship among alleles of a single gene	Description	Example
Complete dominance of one allele	Heterozygous phenotype same as that of homozygous dominant	*PP*  *Pp* 
Incomplete dominance of either allele	Heterozygous phenotype intermediate between the two homozygous phenotypes	 $C^R C^R$ $C^R C^W$ $C^W C^W$
Codominance	Both phenotypes expressed in heterozygotes	$I^A I^B$ 
Multiple alleles	In the population, some genes have more than two alleles	ABO blood group alleles I^A, I^B, i
Pleiotropy	One gene affects multiple phenotypic characters	Sickle-cell disease

Figure 11.UN06

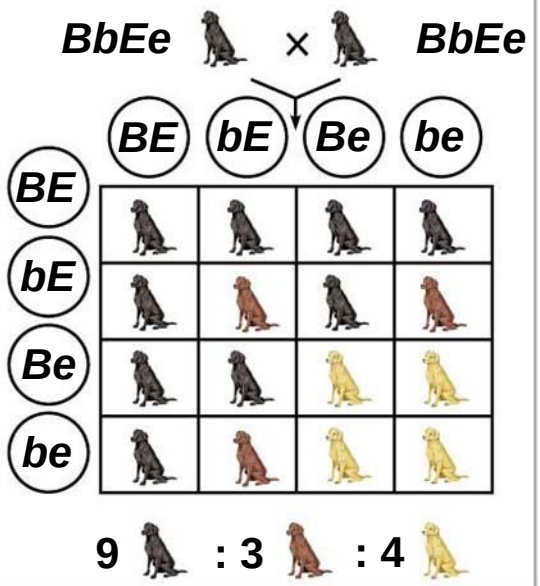
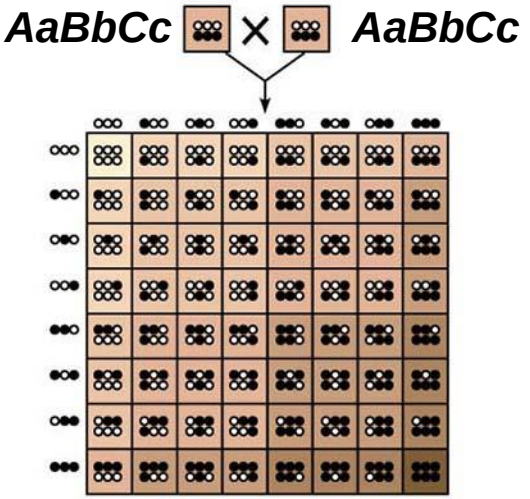
Relationship among two or more genes	Description	Example
Epistasis	**The phenotypic expression of one gene affects the expression of another gene**	
Polygenic inheritance	**A single phenotypic character is affected by two or more genes**	

Figure 11.UN07

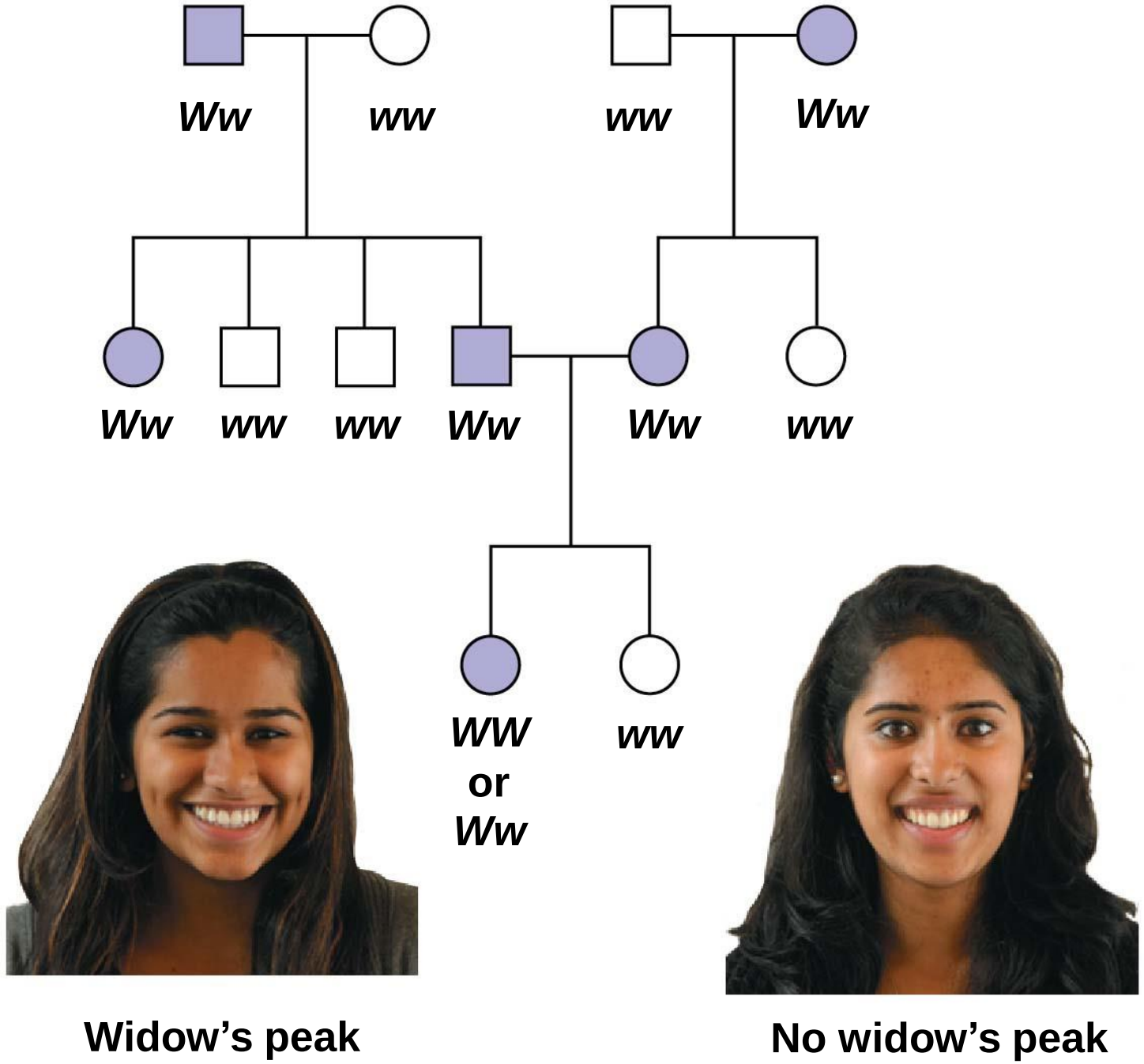


Figure 11.UN08

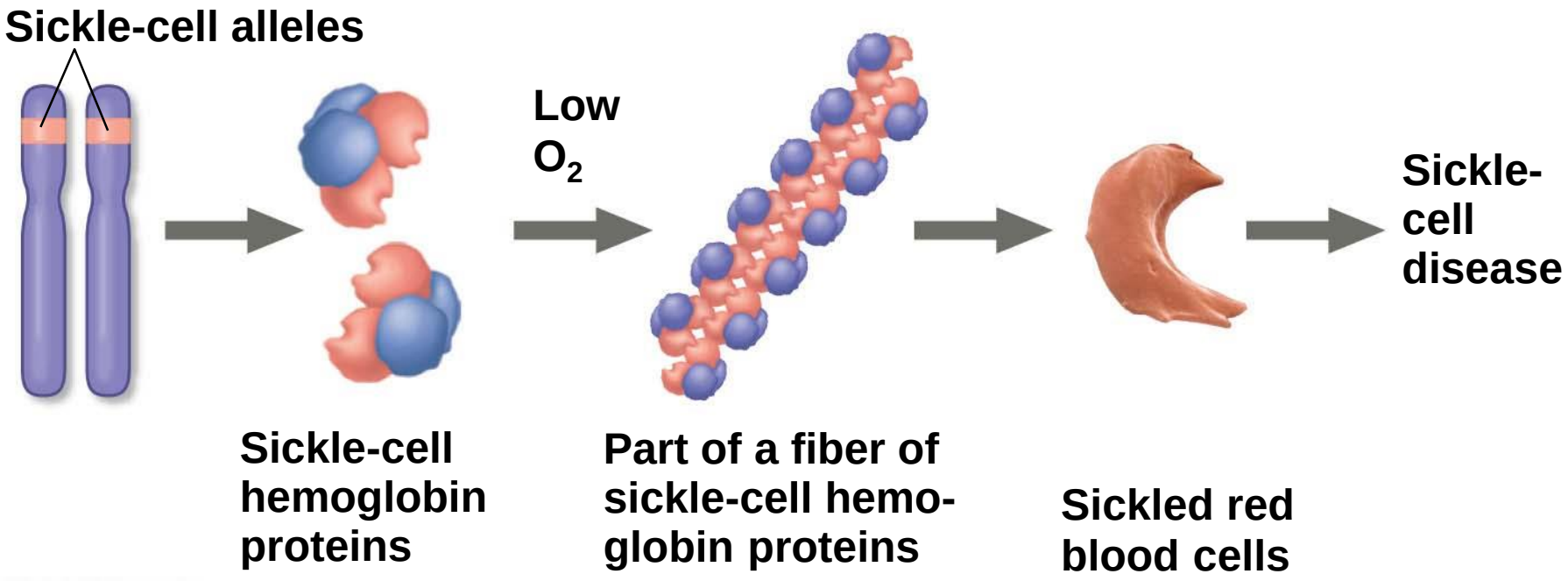


Figure 11.UN10