CAMPBELL BIOLOGY IN FOCUS

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12

The Chromosomal Basis of Inheritance

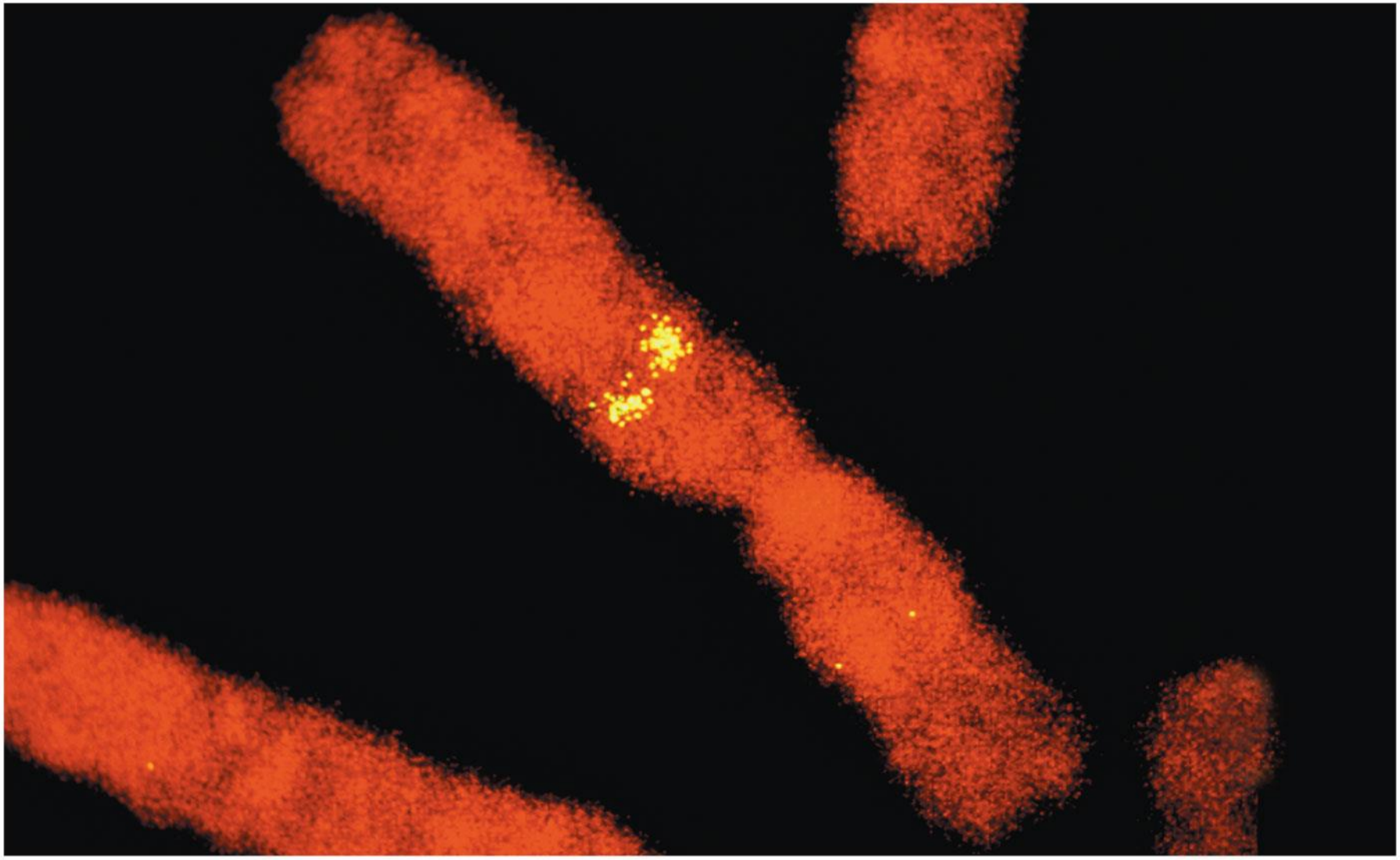
Lecture Presentations by Kathleen Fitzpatrick and Nicole Tunbridge, Simon Fraser University

SECOND EDITION

Overview: Locating Genes Along Chromosomes

- Mendel's "hereditary factors" were genes
- Today we know that genes are located on chromosomes
- The location of a particular gene can be seen by tagging isolated chromosomes with a fluorescent dye that highlights the gene

Figure 12.1



- Mitosis and meiosis were first described in the late 1800s
- The **chromosome theory of inheritance** states
  - Mendelian genes have specific loci (positions) on chromosomes
  - Chromosomes undergo segregation and independent assortment
- The behavior of chromosomes during meiosis can account for Mendel's laws of segregation and independent assortment

Figure 12.2

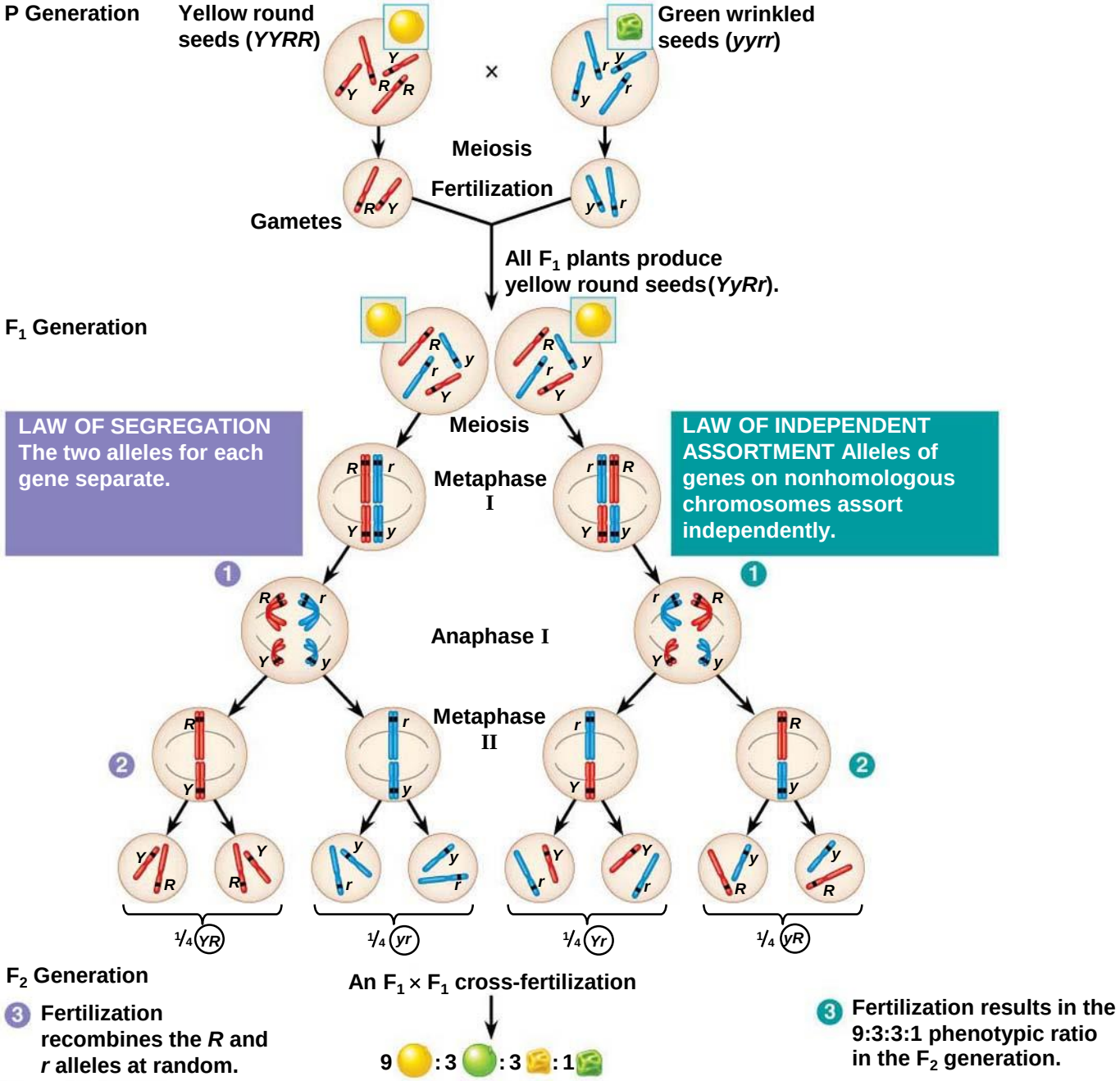


Figure 12.2-1

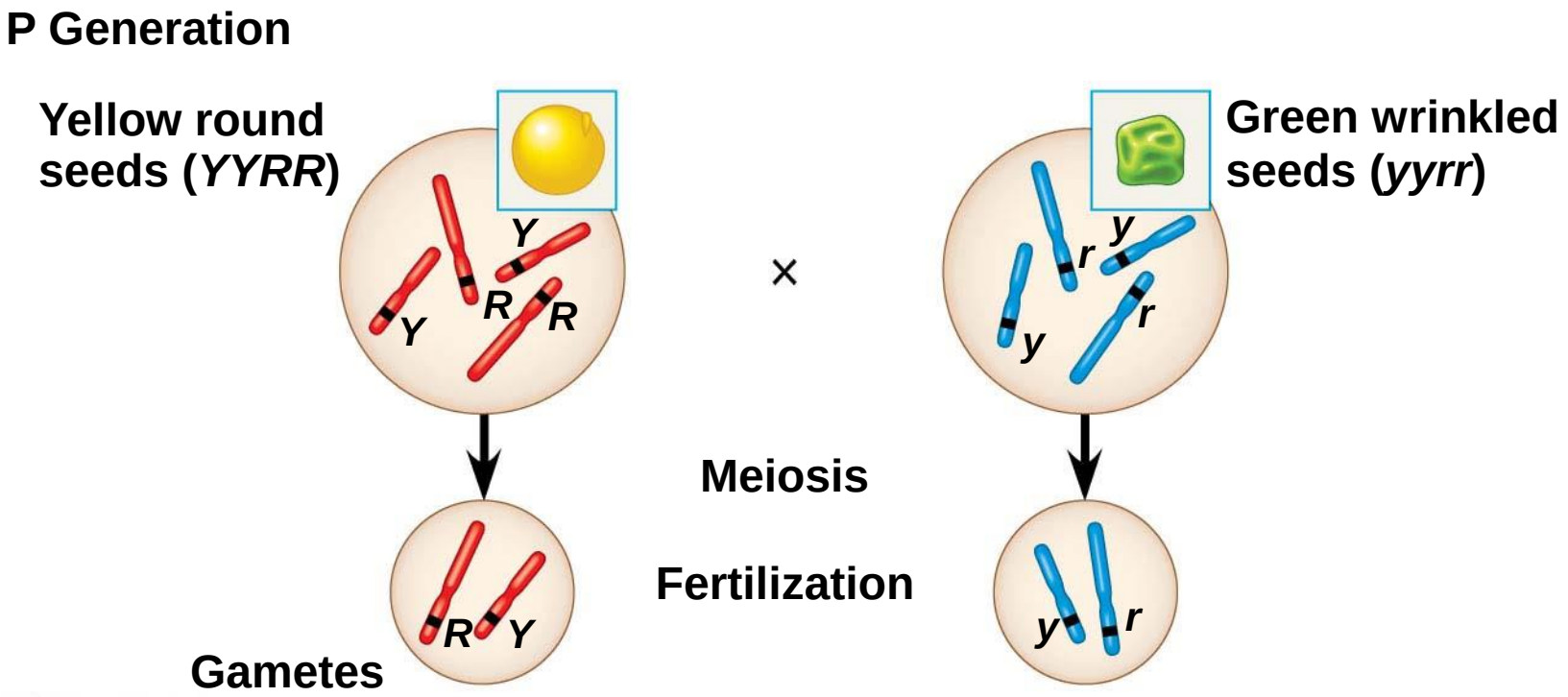


Figure 12.2-2

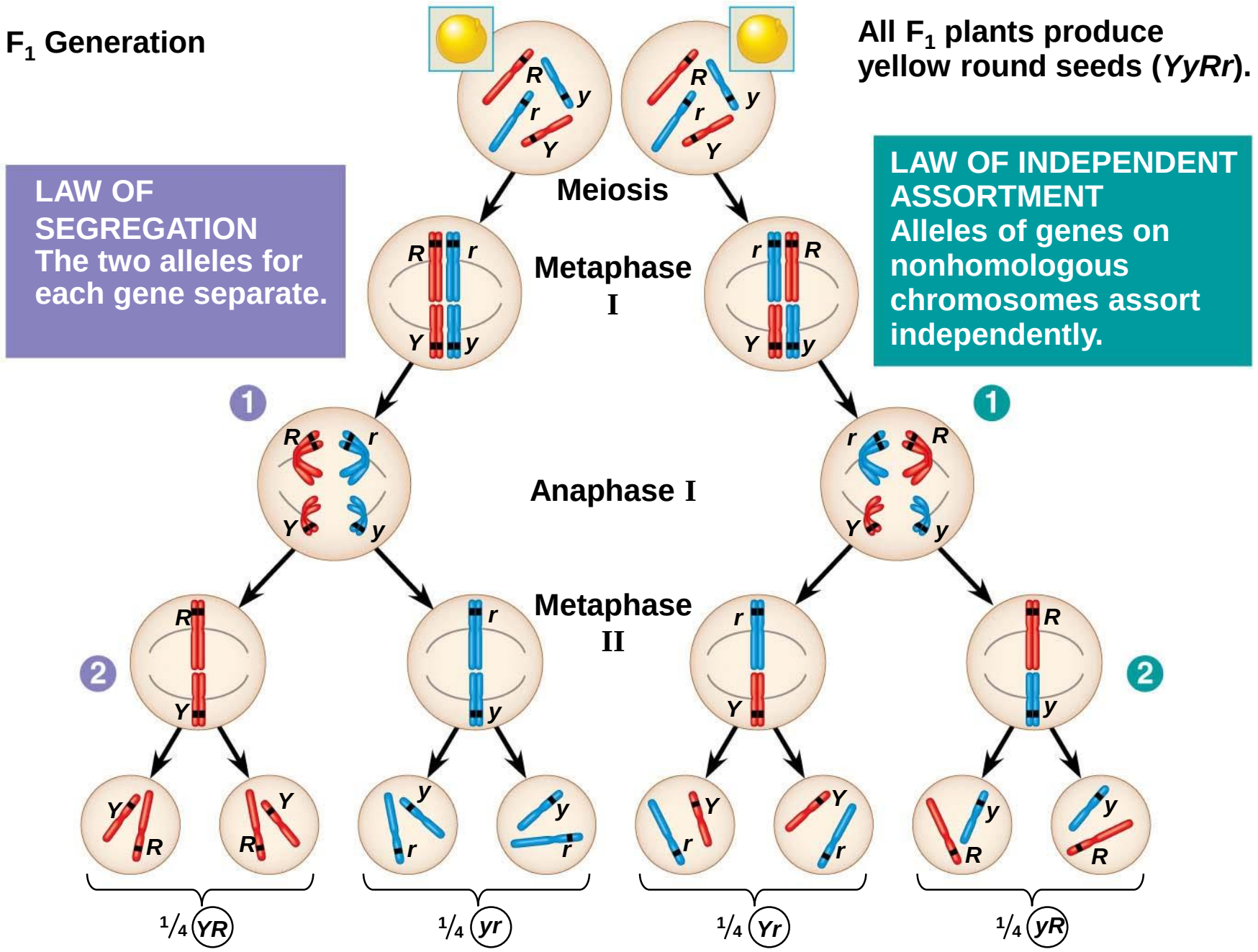


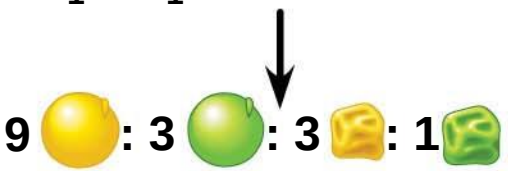
Figure 12.2-3

LAW OF SEGREGATION

F_2 Generation

3 **Fertilization recombines the *R* and *r* alleles at random.**

An $F_1 \times F_1$ cross-fertilization



LAW OF INDEPENDENT ASSORTMENT

3 **Fertilization results in the 9:3:3:1 phenotypic ratio in the F_2 generation.**

Concept 12.1: Morgan showed that Mendelian inheritance has its physical basis in the behavior of chromosomes: *scientific inquiry*

- The first solid evidence associating a specific gene with a specific chromosome came from the work of Thomas Hunt Morgan in the early 1900s

Morgan's Choice of Experimental Organism

- Morgan selected a species of fruit fly, *Drosophila melanogaster*, as his research organism
- Several characteristics make fruit flies a convenient organism for genetic studies
  - They produce many offspring
  - A generation can be bred every two weeks
  - They have only four pairs of chromosomes

- Morgan noted **wild-type**, or normal, phenotypes that were common in the fly populations
- Traits alternative to the wild type are called mutant phenotypes
- The first mutant phenotype he discovered was a fly with white eyes instead of the wild type red

Figure 12.3

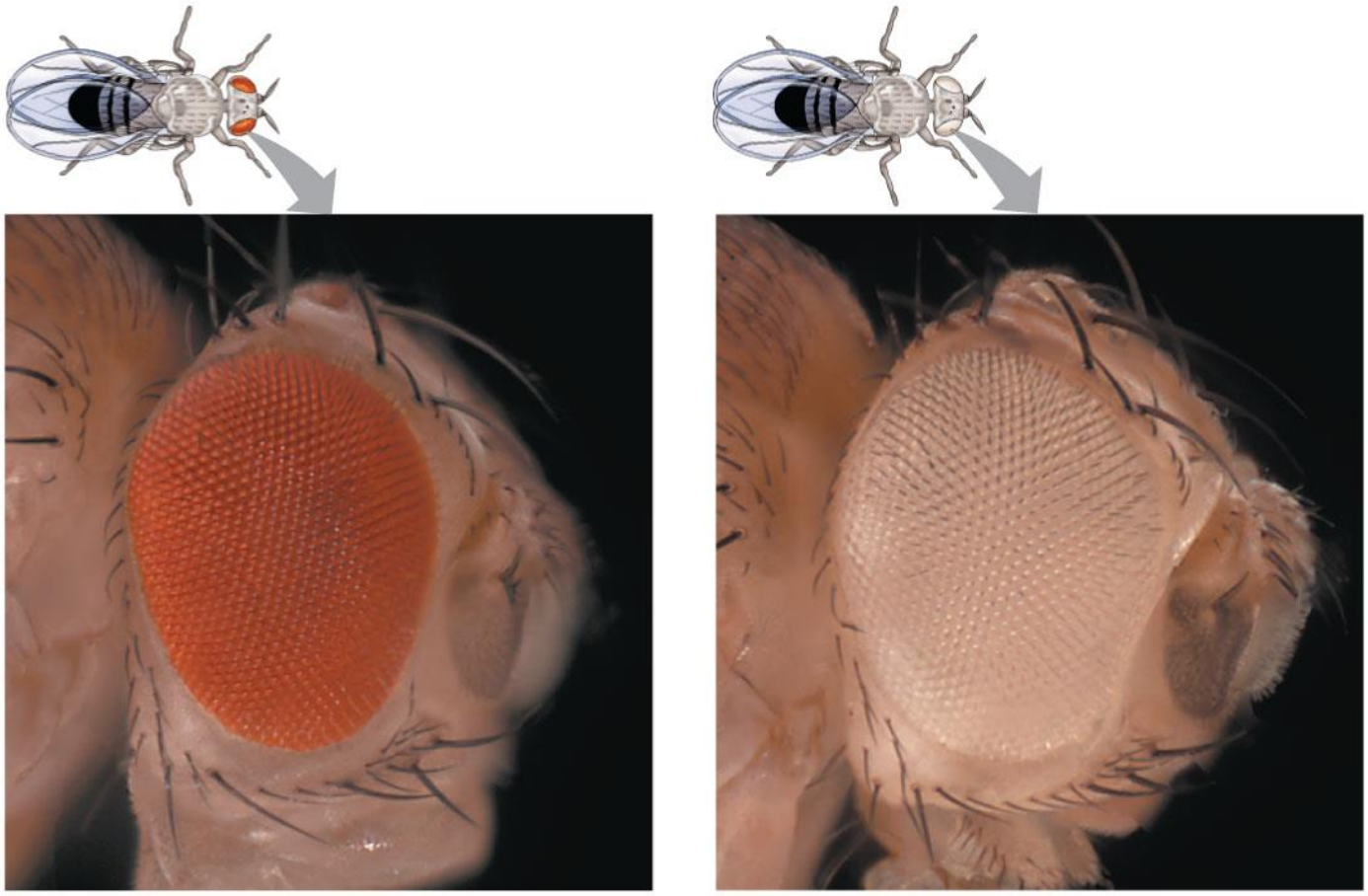


Figure 12.3-1

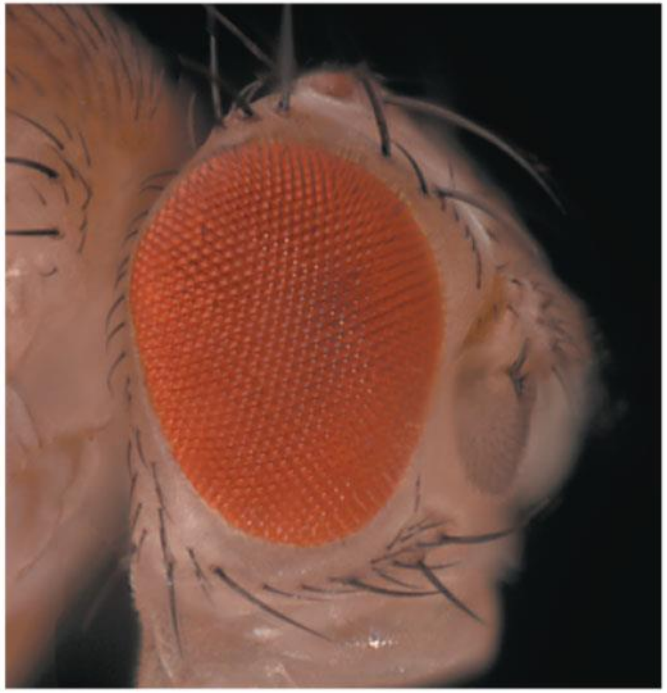


Figure 12.3-2

Correlating Behavior of a Gene's Alleles with Behavior of a Chromosome Pair

- In one experiment, Morgan mated male flies with white eyes (mutant) with female flies with red eyes (wild type)
  - The F_1 generation all had red eyes
  - The F_2 generation showed the classical 3:1 red:white ratio, but only males had white eyes
- Morgan concluded that the eye color was related to the sex of the fly

- Morgan determined that the white-eyed mutant allele must be located on the X chromosome
- Morgan's finding supported the chromosome theory of inheritance

Figure 12.4

Experiment

P Generation

♀ × ♂

F_1 Generation

All offspring had red eyes.

Results

F_2 Generation

♀ ♀ ♂ ♂

Conclusion

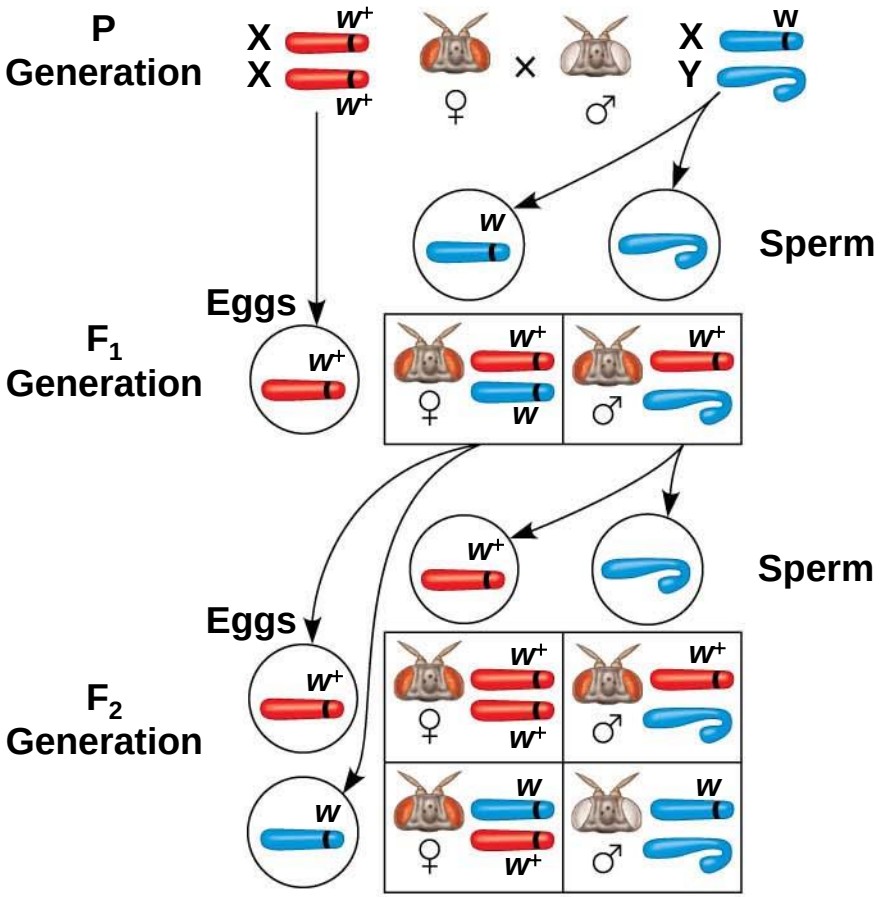


Figure 12.4-1

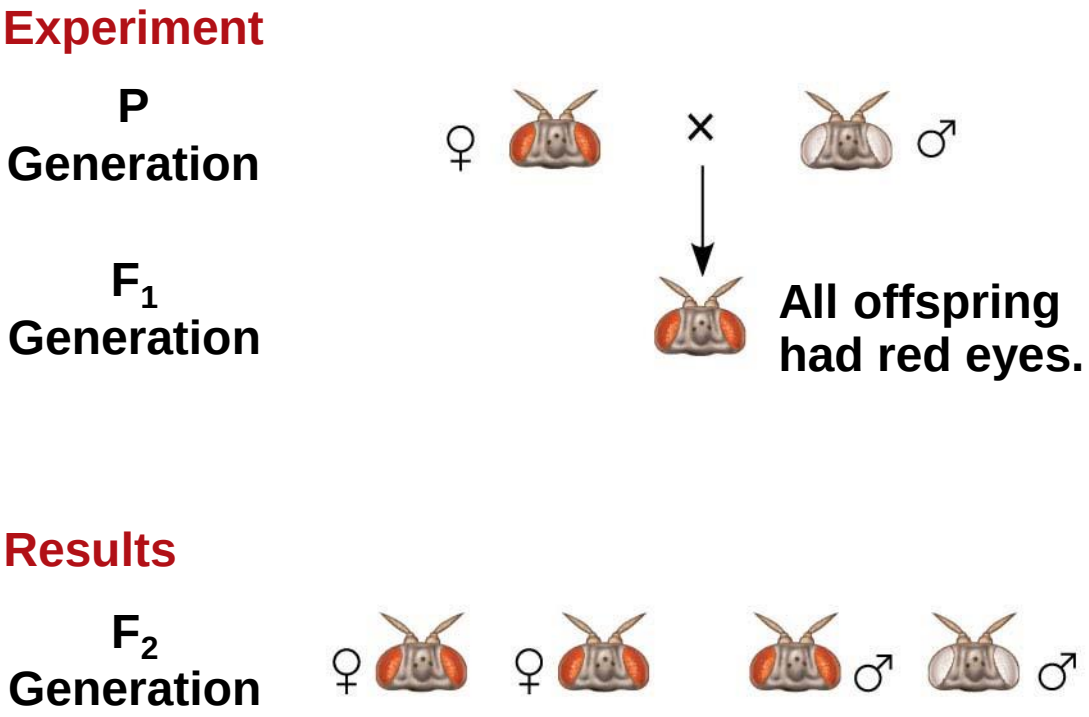
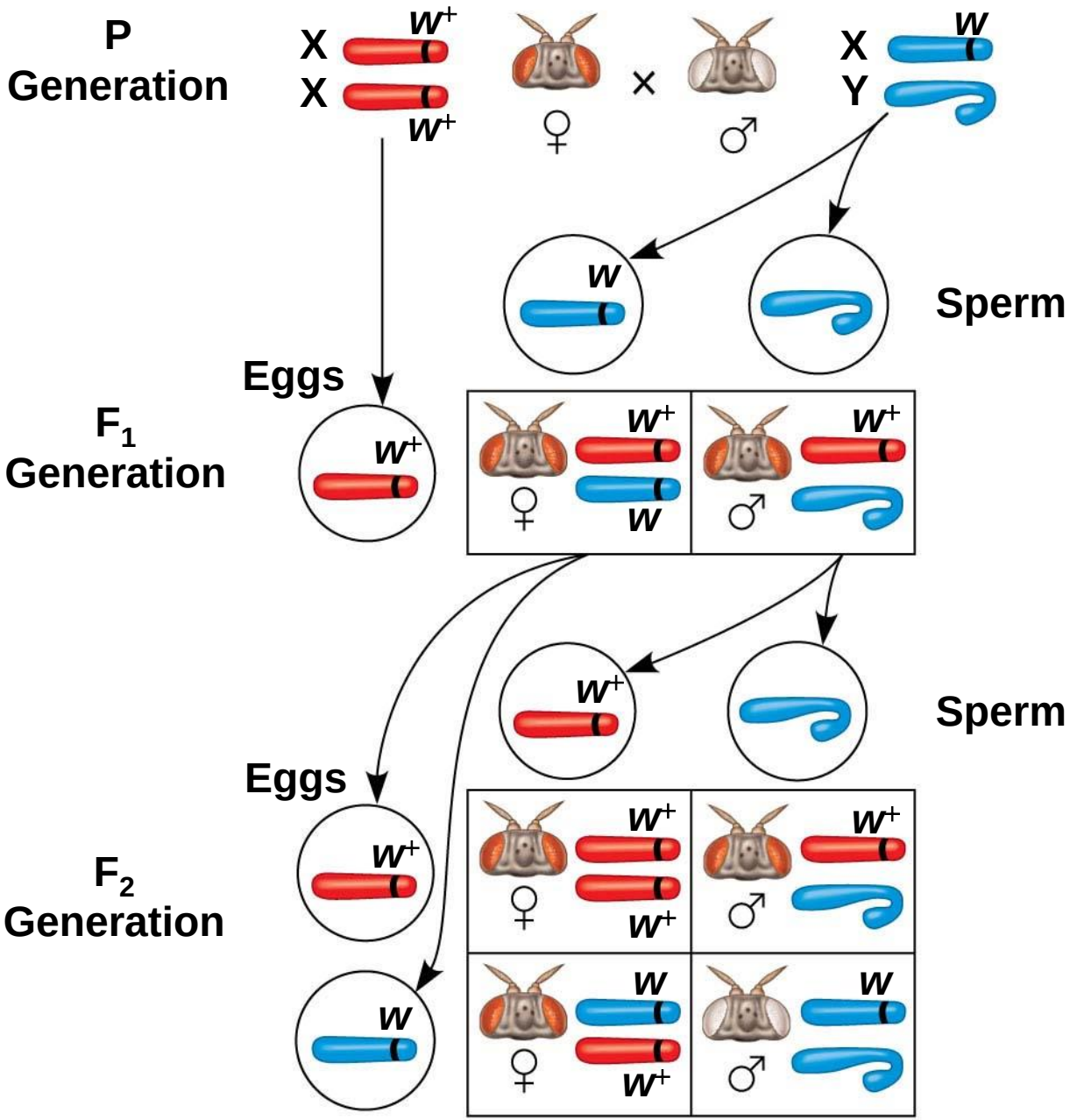


Figure 12.4-2



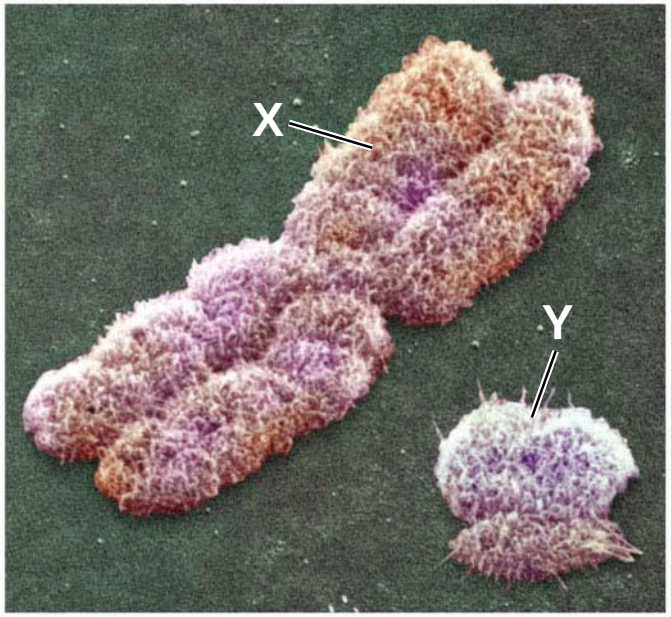
Concept 12.2: Sex-linked genes exhibit unique patterns of inheritance

- The behavior of the members of the pair of sex chromosomes can be correlated with the behavior of the two alleles of the eye-color gene *white*

The Chromosomal Basis of Sex

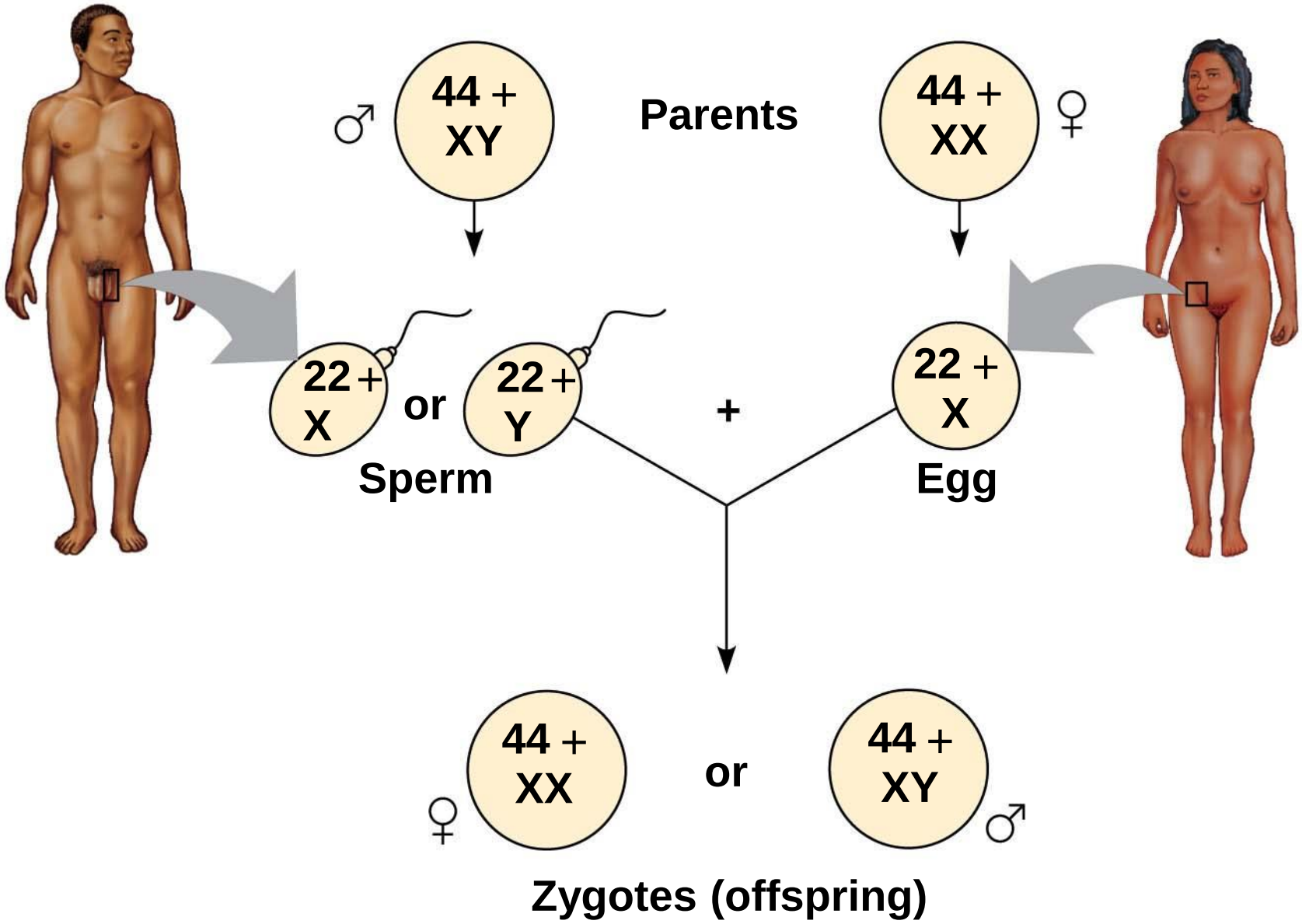
- Humans and other mammals have two types of sex chromosomes: a larger X chromosome and a smaller Y chromosome
- Only the ends of the Y chromosome have regions that are homologous with corresponding regions of the X chromosome
- The *SRY* gene on the Y chromosome is required for the developments of testes

Figure 12.5



- Females are XX, and males are XY
- Each ovum contains an X chromosome, while a sperm may contain either an X or a Y chromosome
- Other animals have different methods of sex determination

Figure 12.6



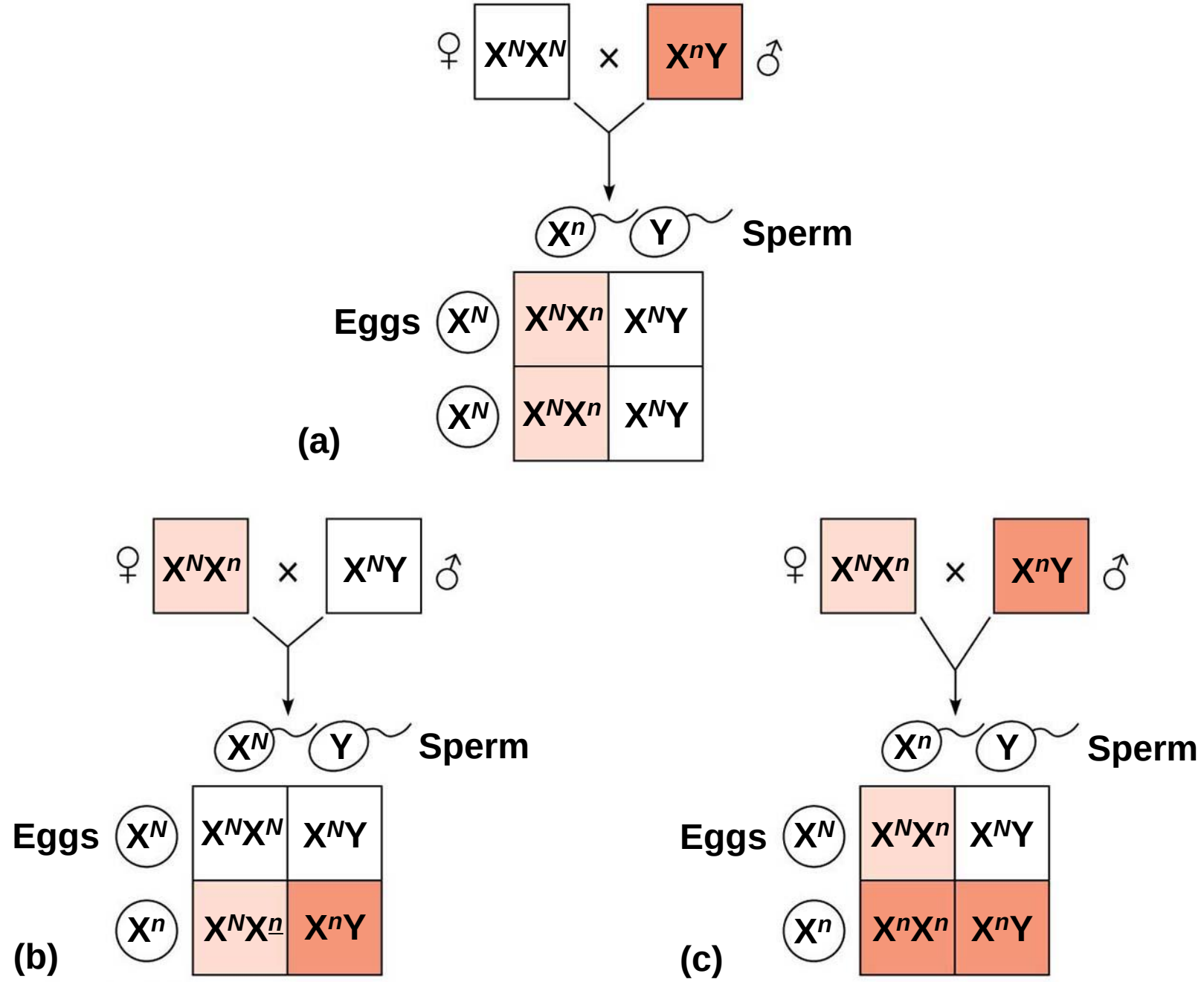
- A gene that is located on either sex chromosome is called a **sex-linked gene**
- Genes on the Y chromosome are called Y-linked genes; there are few of these
- Genes on the X chromosome are called **X-linked genes**

Inheritance of X-Linked Genes

- Most Y-linked genes help determine sex
- The X chromosomes have genes for many characters unrelated to sex

- X-linked genes follow specific patterns of inheritance
- For a recessive X-linked trait to be expressed
  - A female needs two copies of the allele (homozygous)
  - A male needs only one copy of the allele (hemizygous)
- X-linked recessive disorders are much more common in males than in females

Figure 12.7



- Some disorders caused by recessive alleles on the X chromosome in humans:
  - Color blindness (mostly X-linked)
  - **Duchenne muscular dystrophy**
  - **Hemophilia**

X Inactivation in Female Mammals

- In mammalian females, one of the two X chromosomes in each cell is randomly inactivated during embryonic development
- The inactive X condenses into a **Barr body**
- If a female is heterozygous for a particular gene located on the X chromosome, she will be a mosaic for that character

Figure 12.8

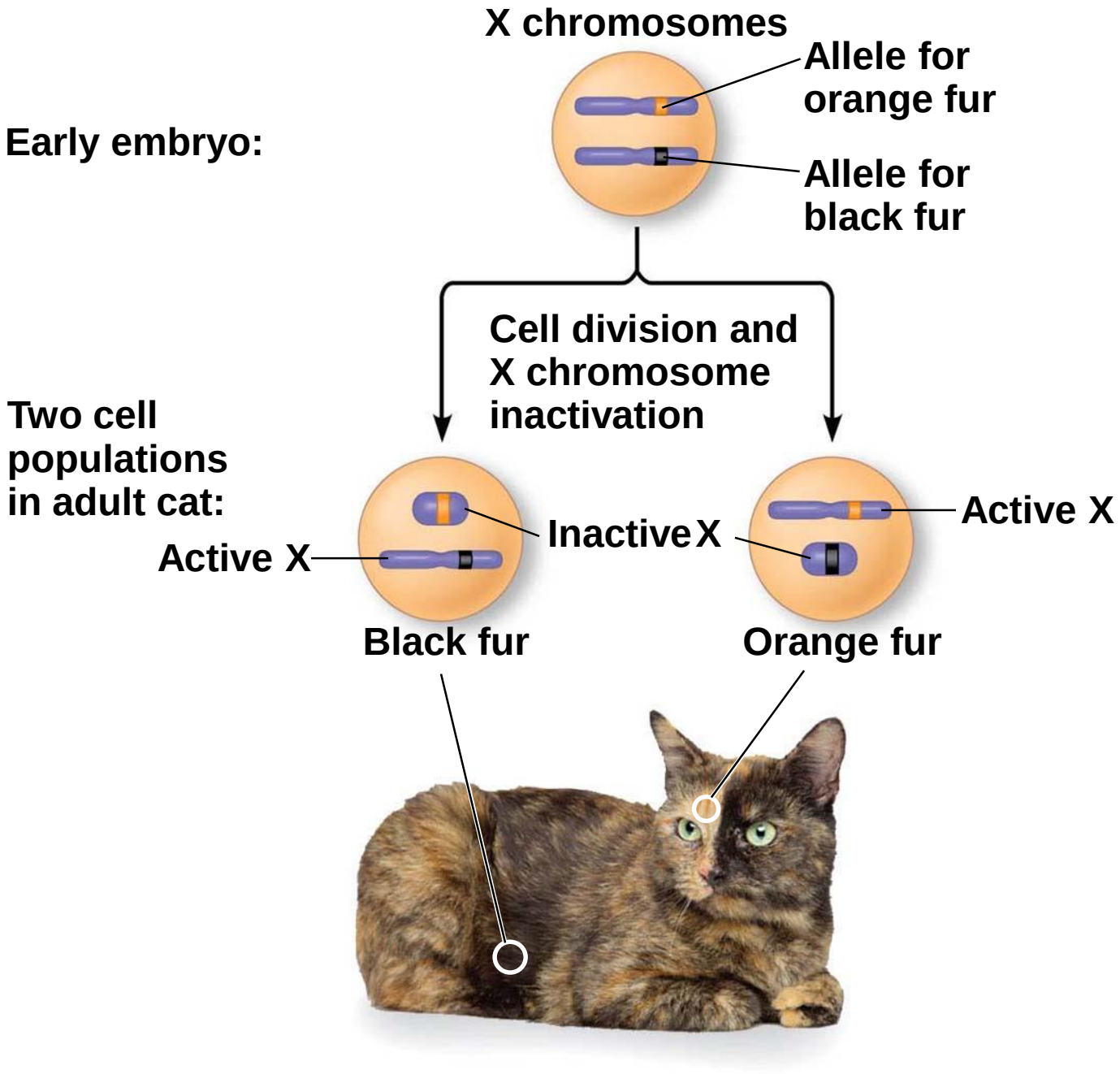


Figure 12.8-1

Concept 12.3: Linked genes tend to be inherited together because they are located near each other on the same chromosome

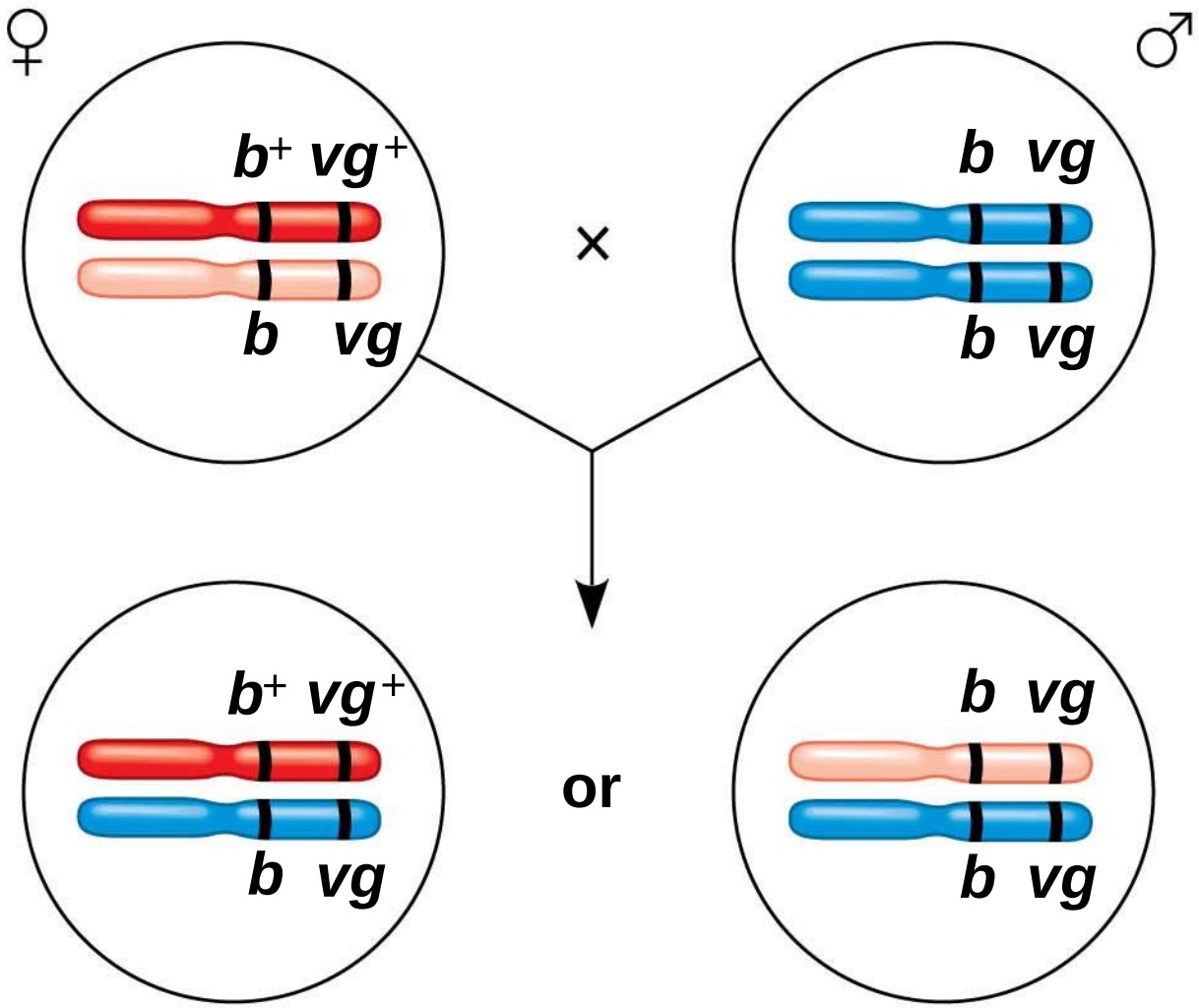
- Each chromosome has hundreds or thousands of genes (except the Y chromosome)
- Genes located on the same chromosome that tend to be inherited together are called **linked genes**

How Linkage Affects Inheritance

- Morgan did experiments with fruit flies that show how linkage affects inheritance of two characters
- Morgan crossed flies that differed in traits of body color and wing size

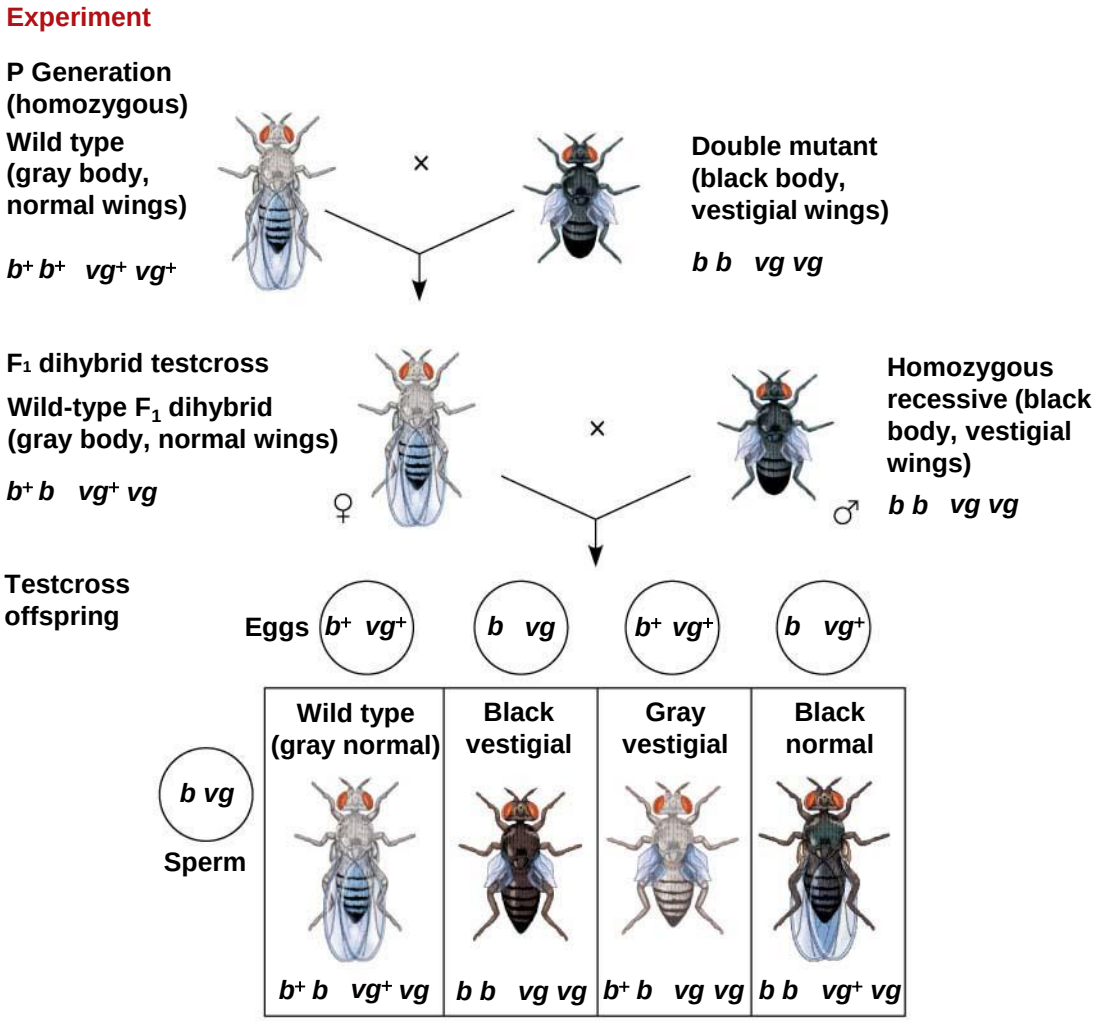
- Morgan found that body color and wing size are usually inherited together in specific combinations (parental phenotypes)
- He reasoned that since these genes did not assort independently, they were on the same chromosome

Figure 12.UN01



- However, nonparental phenotypes were also produced
- Understanding this result involves exploring **genetic recombination**, the production of offspring with combinations of traits differing from either parent

Figure 12.9



PREDICTED RATIOS

Genes on different chromosomes:	1	:	1	:	1	: 1
Genes on same chromosome:	1	:	1	:	0	: 0
Results	965	:	944	:	206	: 185

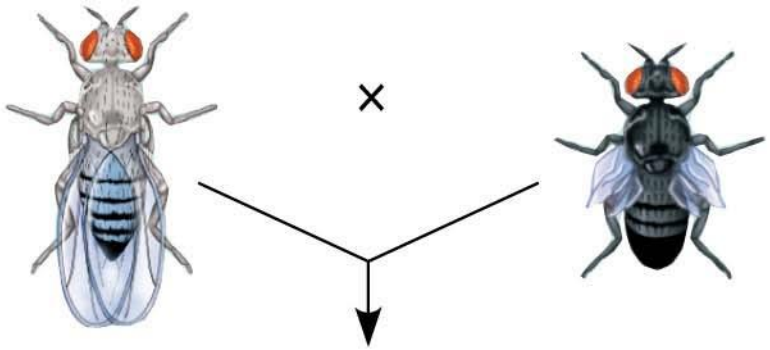
Figure 12.9-1

Experiment

P Generation (homozygous)

Wild type (gray body, normal wings)

***b*⁺ *b*⁺ *vg*⁺ *vg*⁺**



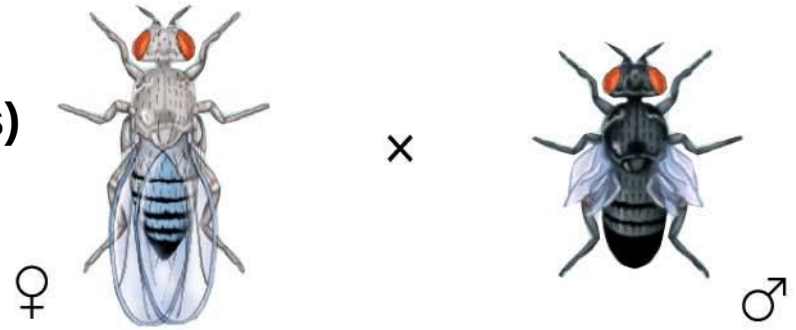
Double mutant (black body, vestigial wings)

b b vg vg

F_1 dihybrid testcross

Wild-type F_1 dihybrid (gray body, normal wings)

b*⁺ *b* *vg*⁺ *vg



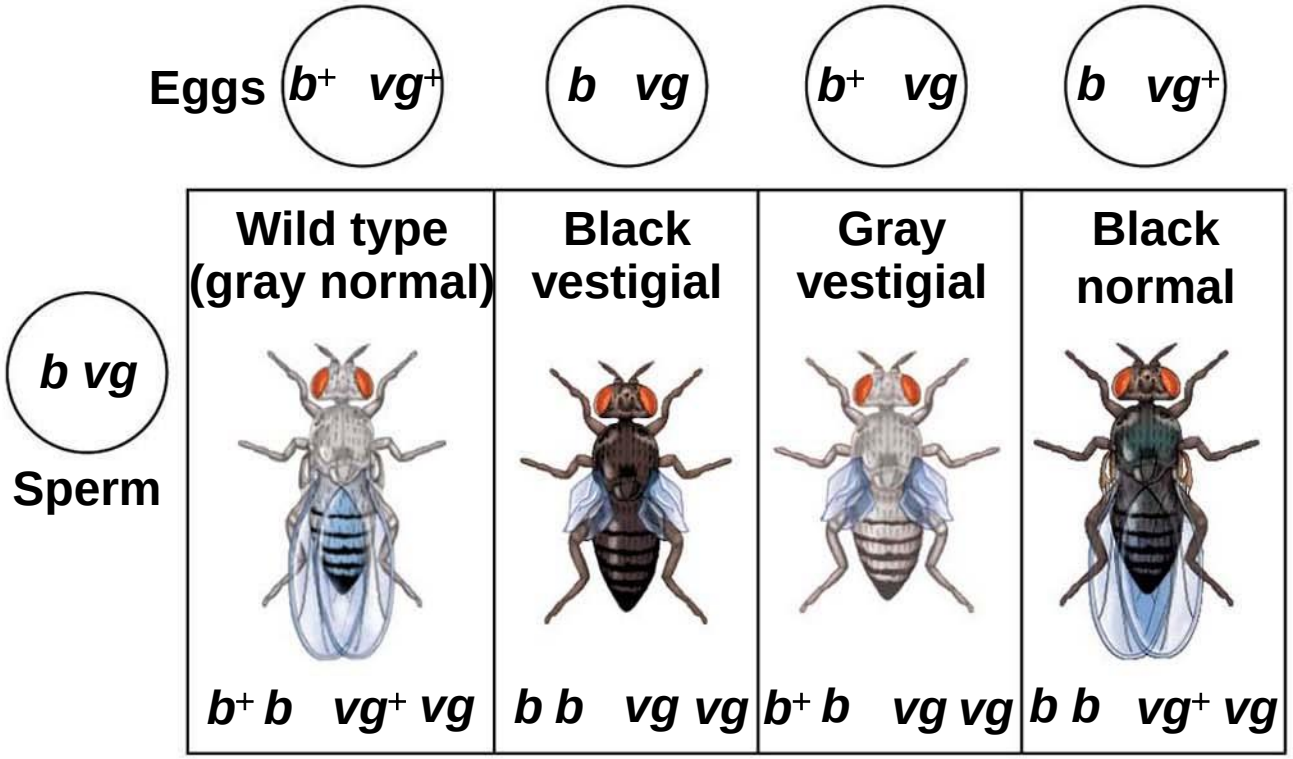
Homozygous recessive (black body, vestigial wings)

b b vg vg

Figure 12.9-2

Experiment

Testcross offspring



PREDICTED RATIOS

Genes on different chromosomes:	**1**	**:**	**1**	**:**	**1**	**:**	**1**
Genes on same chromosome:	**1**	**:**	**1**	**:**	**0**	**:**	**0**
Results	**965**	**:**	**944**	**:**	**206**	**:**	**185**

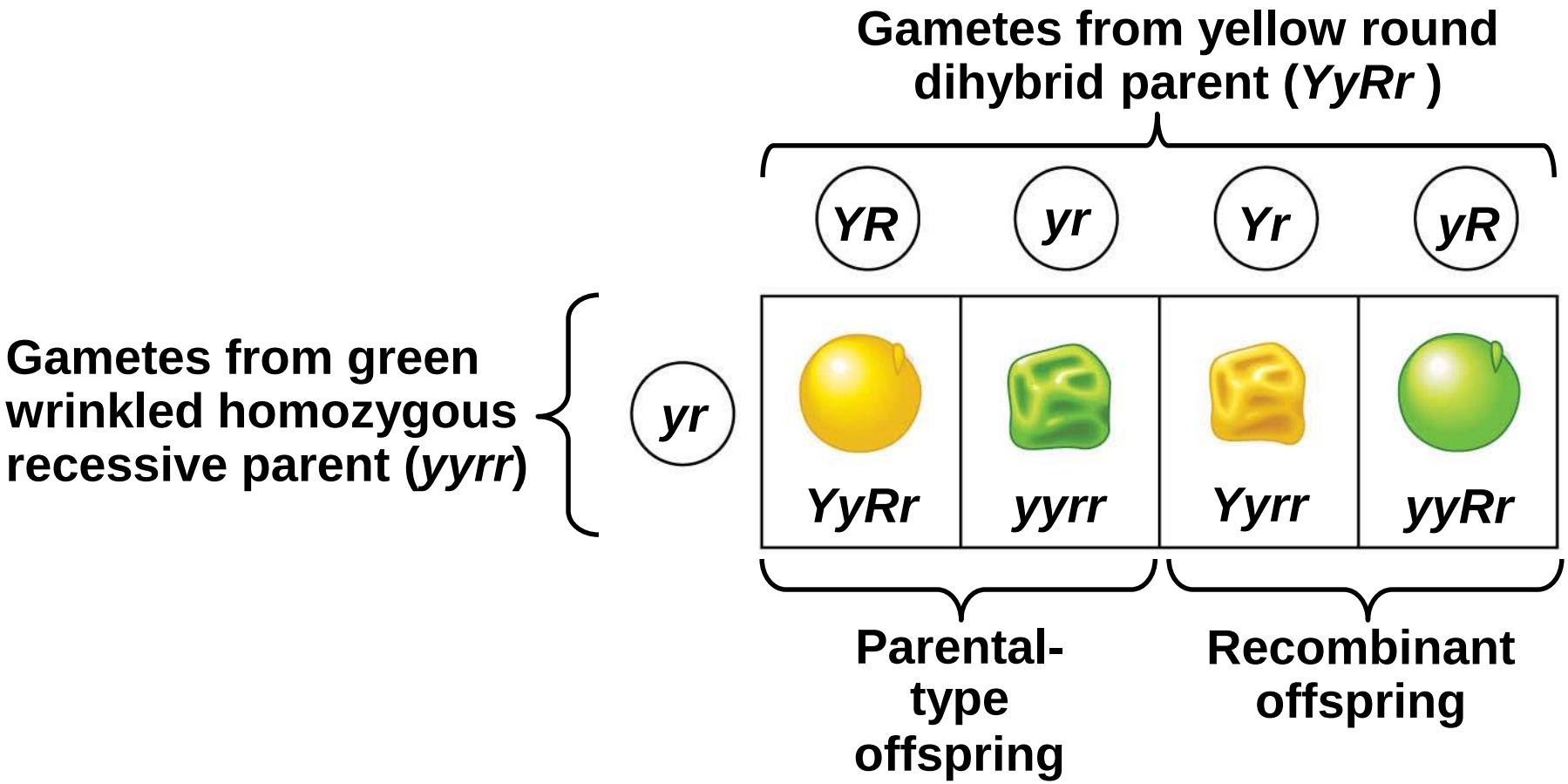
Genetic Recombination and Linkage

- The genetic findings of Mendel and Morgan relate to the chromosomal basis of recombination

Recombination of Unlinked Genes: Independent Assortment of Chromosomes

- Mendel observed that combinations of traits in some offspring differ from either parent
- Offspring with a phenotype matching one of the parental phenotypes are called **parental types**
- Offspring with nonparental phenotypes (new combinations of traits) are called **recombinant types**, or **recombinants**
- A 50% frequency of recombination is observed for any two genes on different chromosomes

Figure 12.UN02



Recombination of Linked Genes: Crossing Over

- Morgan discovered that even when two genes were on the same chromosome, some recombinant phenotypes were observed
- He proposed that some process must occasionally break the physical connection between genes on the same chromosome
- That mechanism was the **crossing over** between homologous chromosomes

Animation: Crossing Over

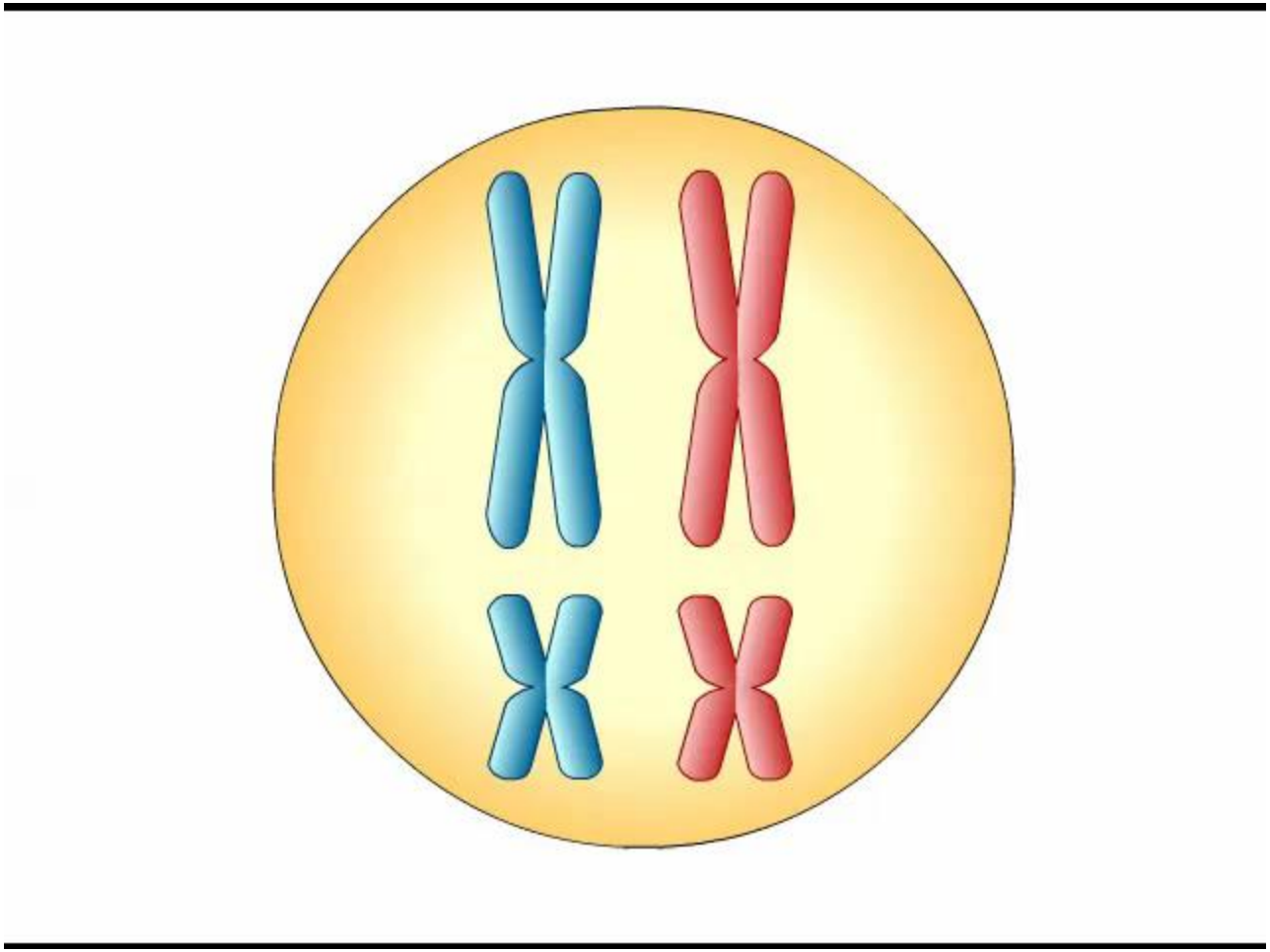


Figure 12.10

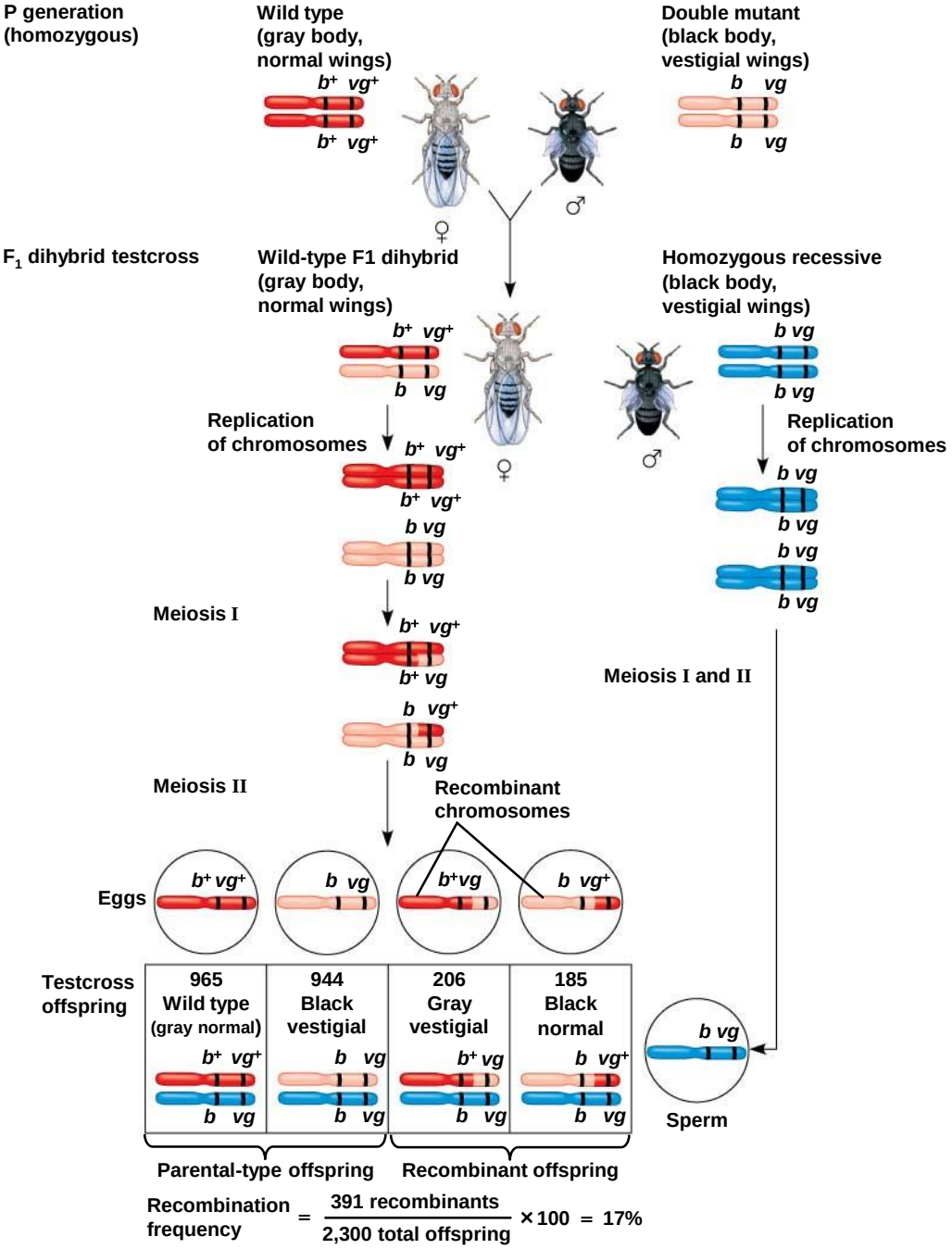


Figure 12.10-1

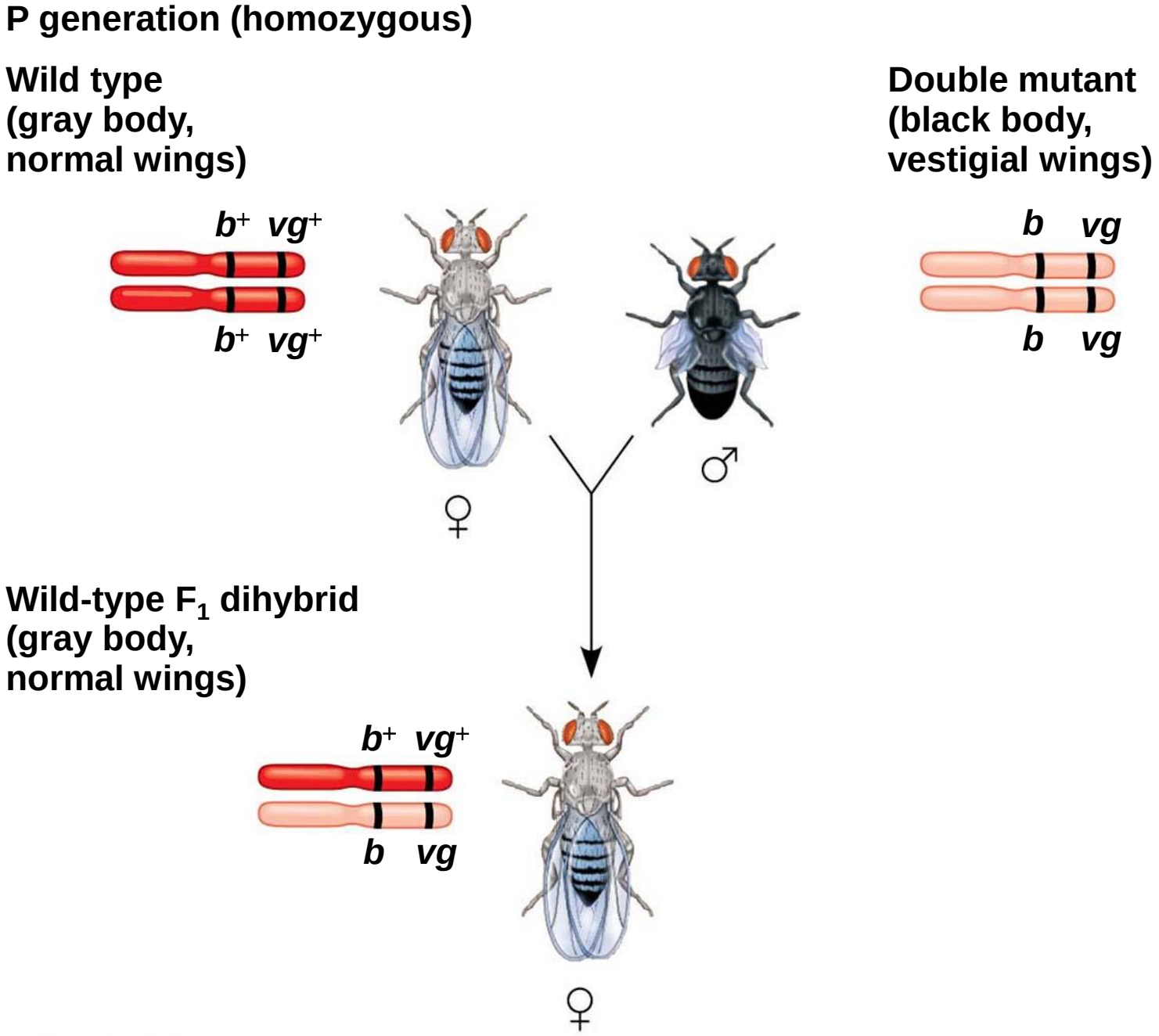


Figure 12.10-2

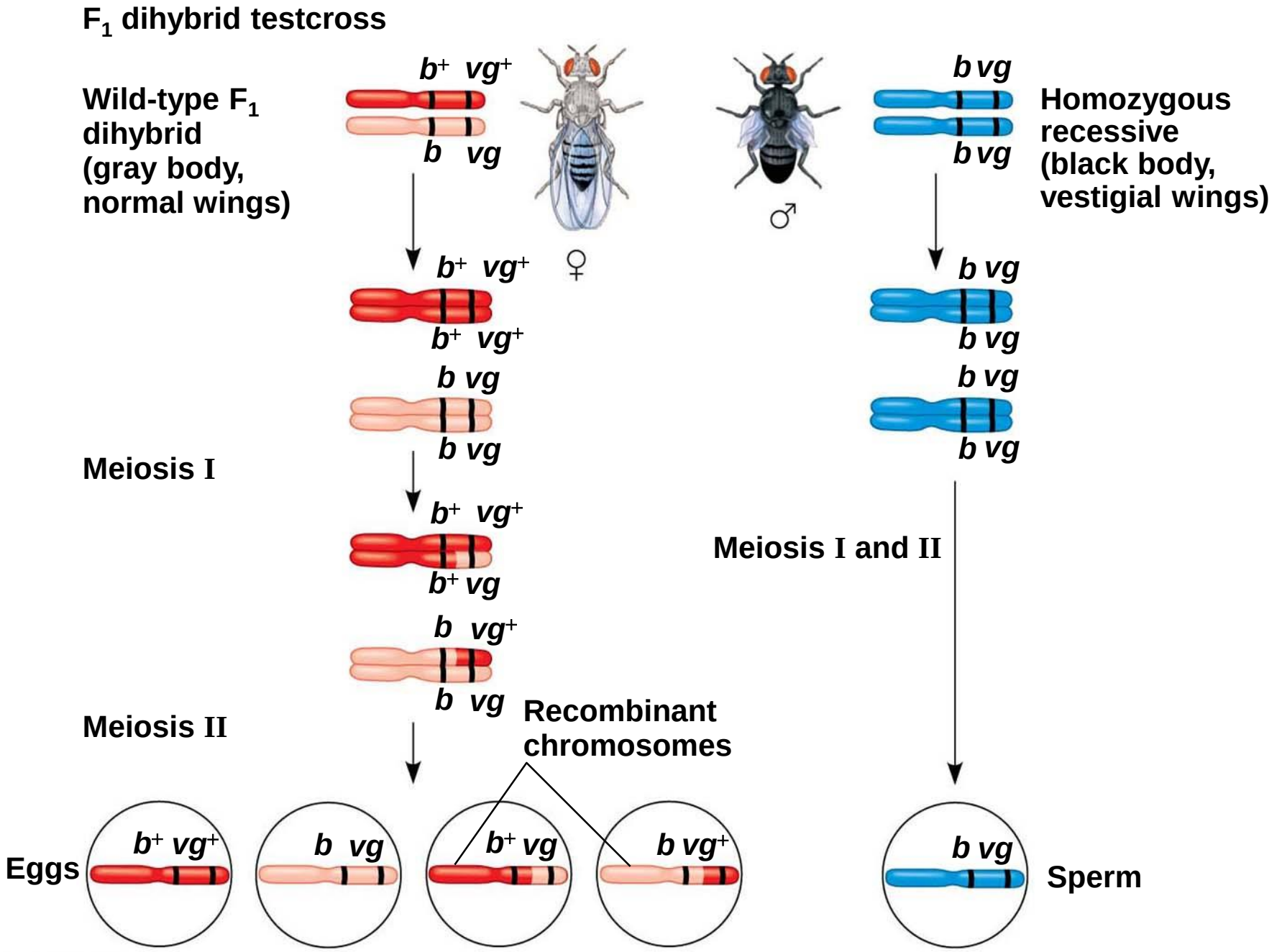
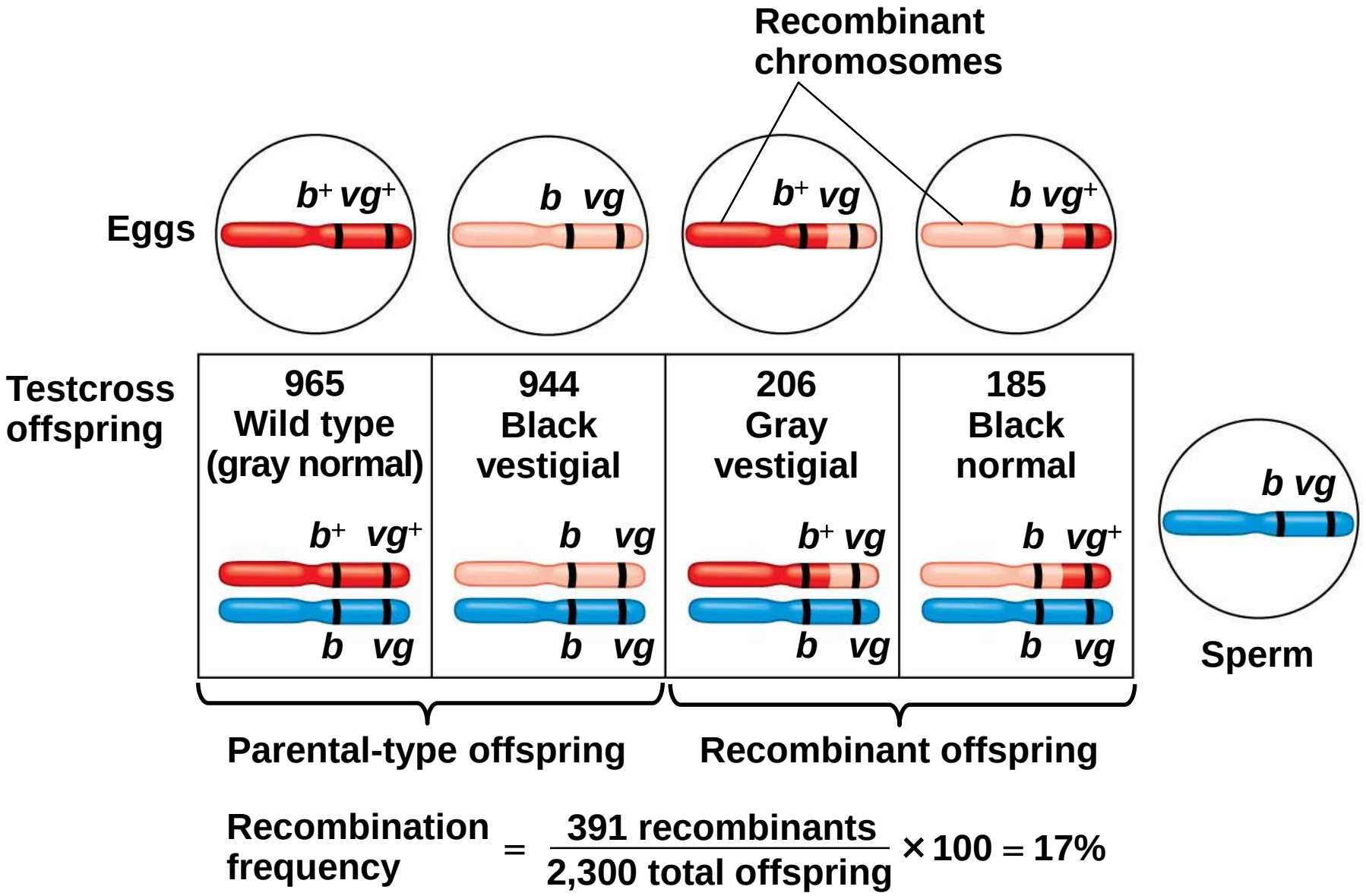


Figure 12.10-3



New Combinations of Alleles: Variation for Natural Selection

- Recombinant chromosomes bring alleles together in new combinations in gametes
- Random fertilization increases even further the number of variant combinations that can be produced
- This abundance of genetic variation is the raw material upon which natural selection works

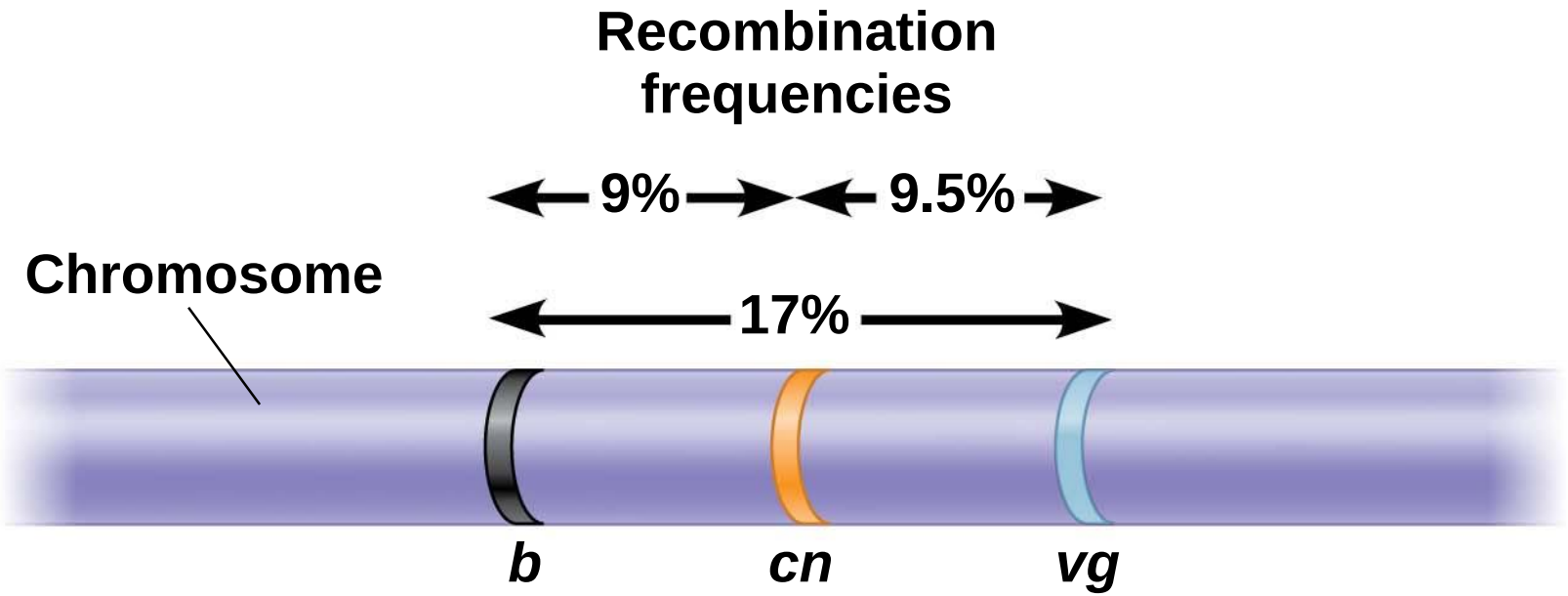
Mapping the Distance Between Genes Using Recombination Data: *Scientific Inquiry*

- Alfred Sturtevant, one of Morgan's students, constructed a **genetic map**, an ordered list of the genetic loci along a particular chromosome
- Sturtevant predicted that *the farther apart two genes are, the higher the probability that a crossover will occur between them and therefore the higher the recombination frequency*

- A **linkage map** is a genetic map of a chromosome based on recombination frequencies
- Distances between genes can be expressed as **map units**; one map unit represents a 1% recombination frequency

Figure 12.11

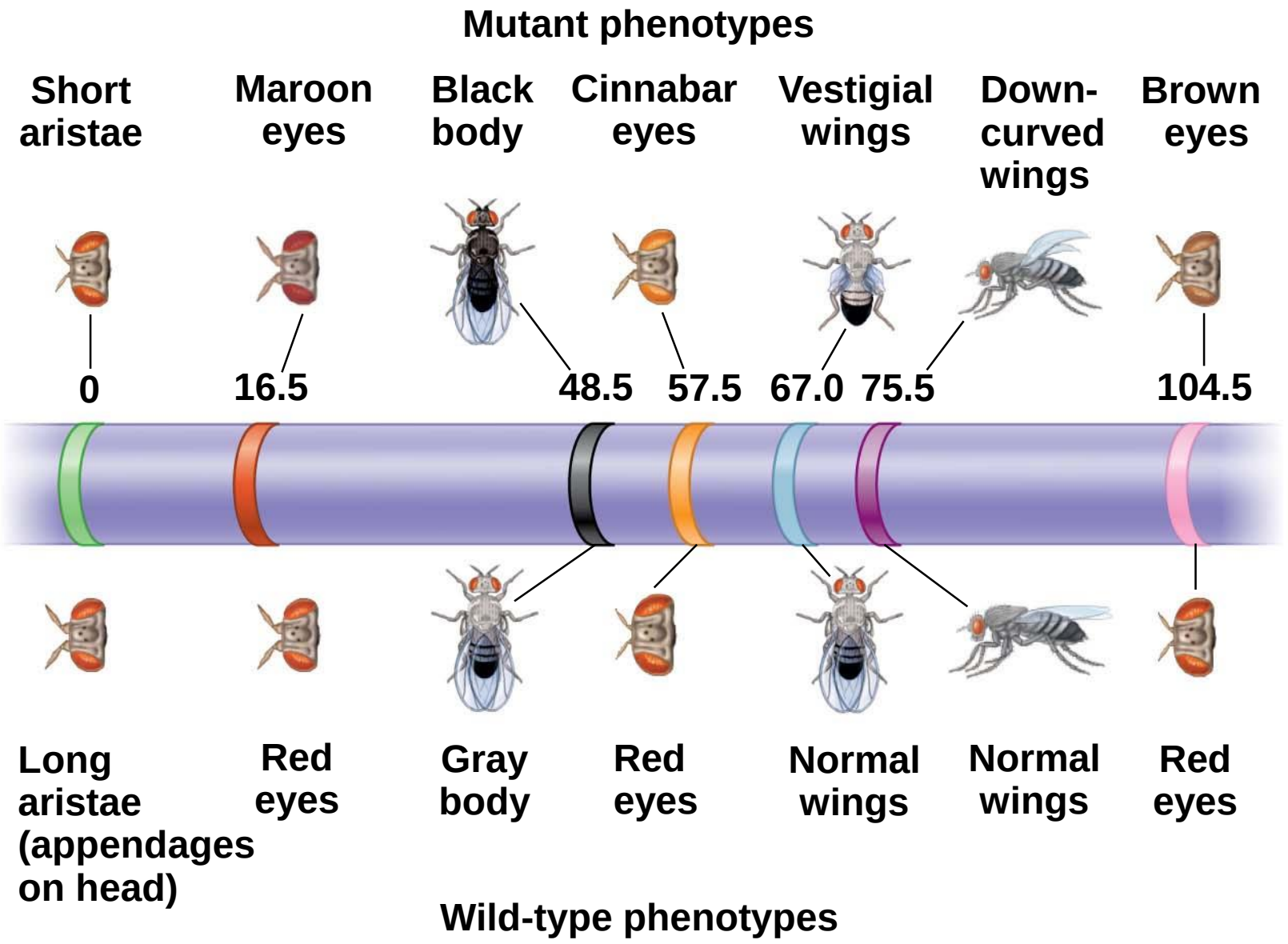
Results



- Genes that are far apart on the same chromosome can have a recombination frequency near 50%
- Such genes are physically connected, but genetically unlinked

- Sturtevant used recombination frequencies to make linkage maps of fruit fly genes
- Using methods like chromosomal banding, geneticists can develop cytogenetic maps of chromosomes
- **Cytogenetic maps** indicate the positions of genes with respect to chromosomal features

Figure 12.12



Concept 12.4: Alterations of chromosome number or structure cause some genetic disorders

- Large-scale chromosomal alterations in humans and other mammals often lead to spontaneous abortions (miscarriages) or cause a variety of developmental disorders
- Plants tolerate such genetic changes better than animals do

Abnormal Chromosome Number

- In **nondisjunction**, pairs of homologous chromosomes do not separate normally during meiosis
- As a result, one gamete receives two of the same type of chromosome, and another gamete receives no copy

Video: Nondisjunction

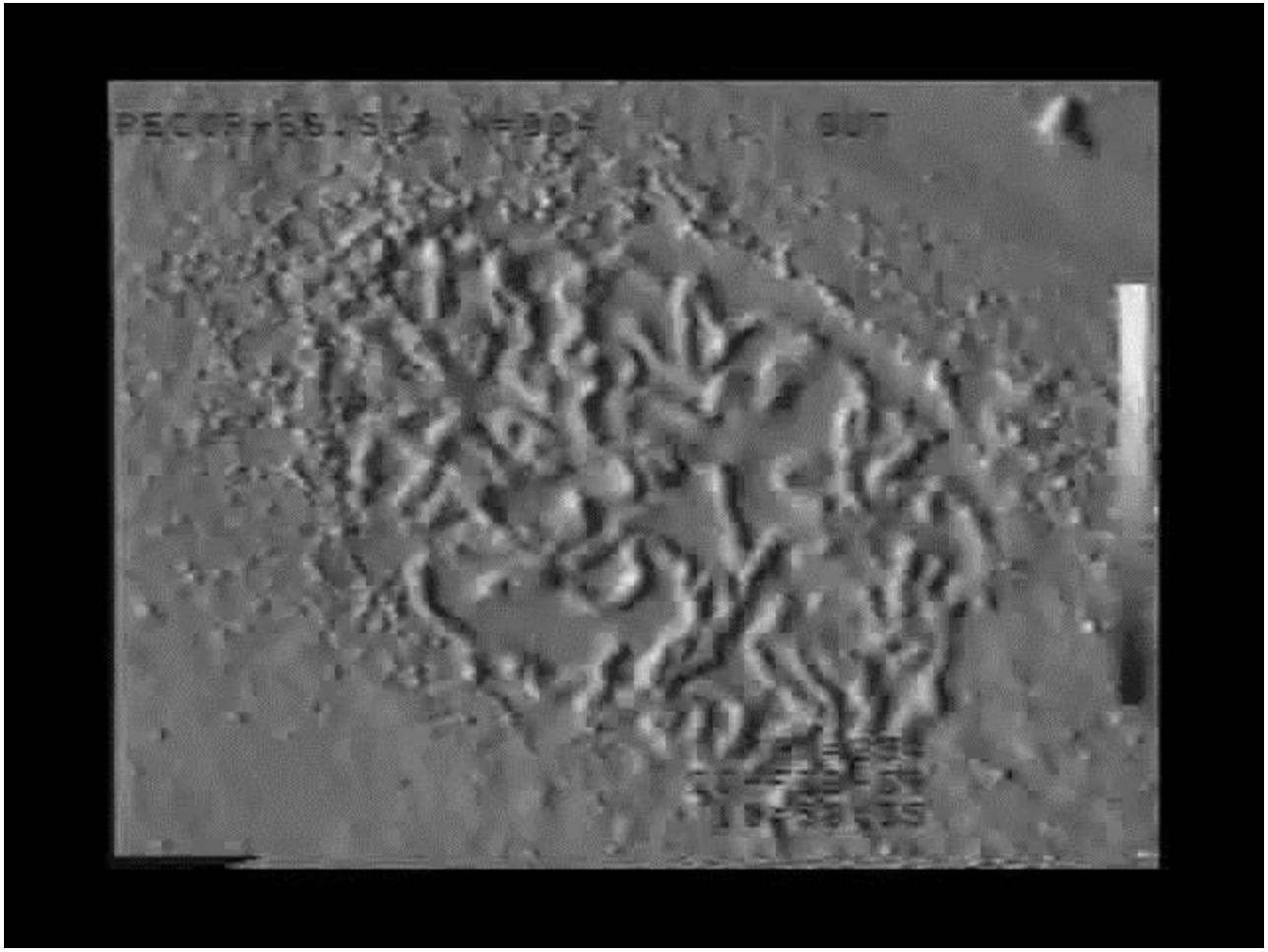


Figure 12.13-s1

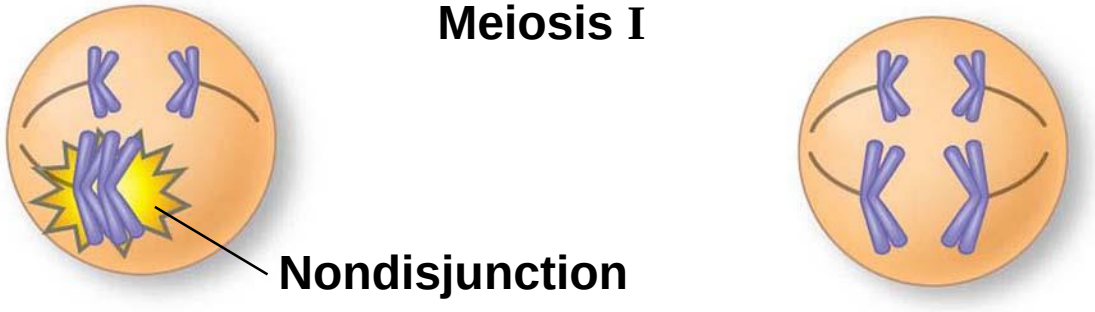


Figure 12.13-s2

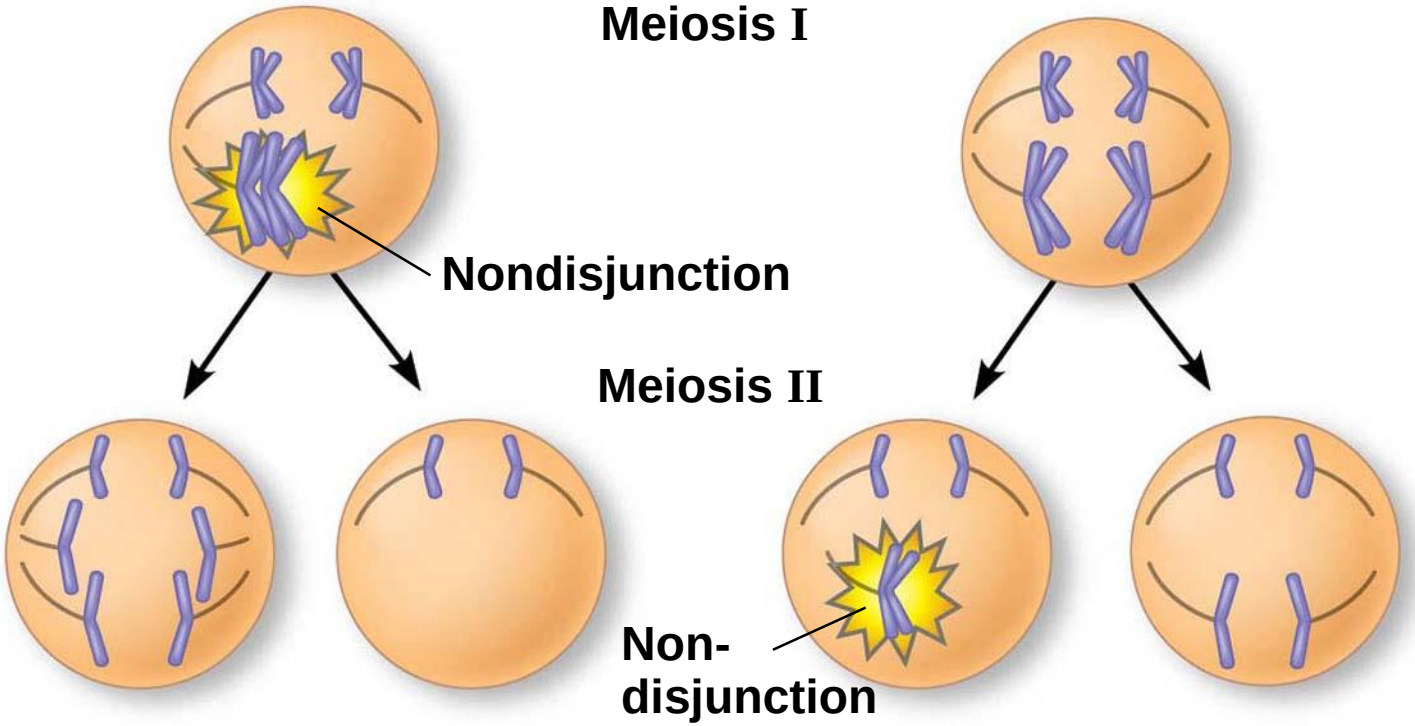
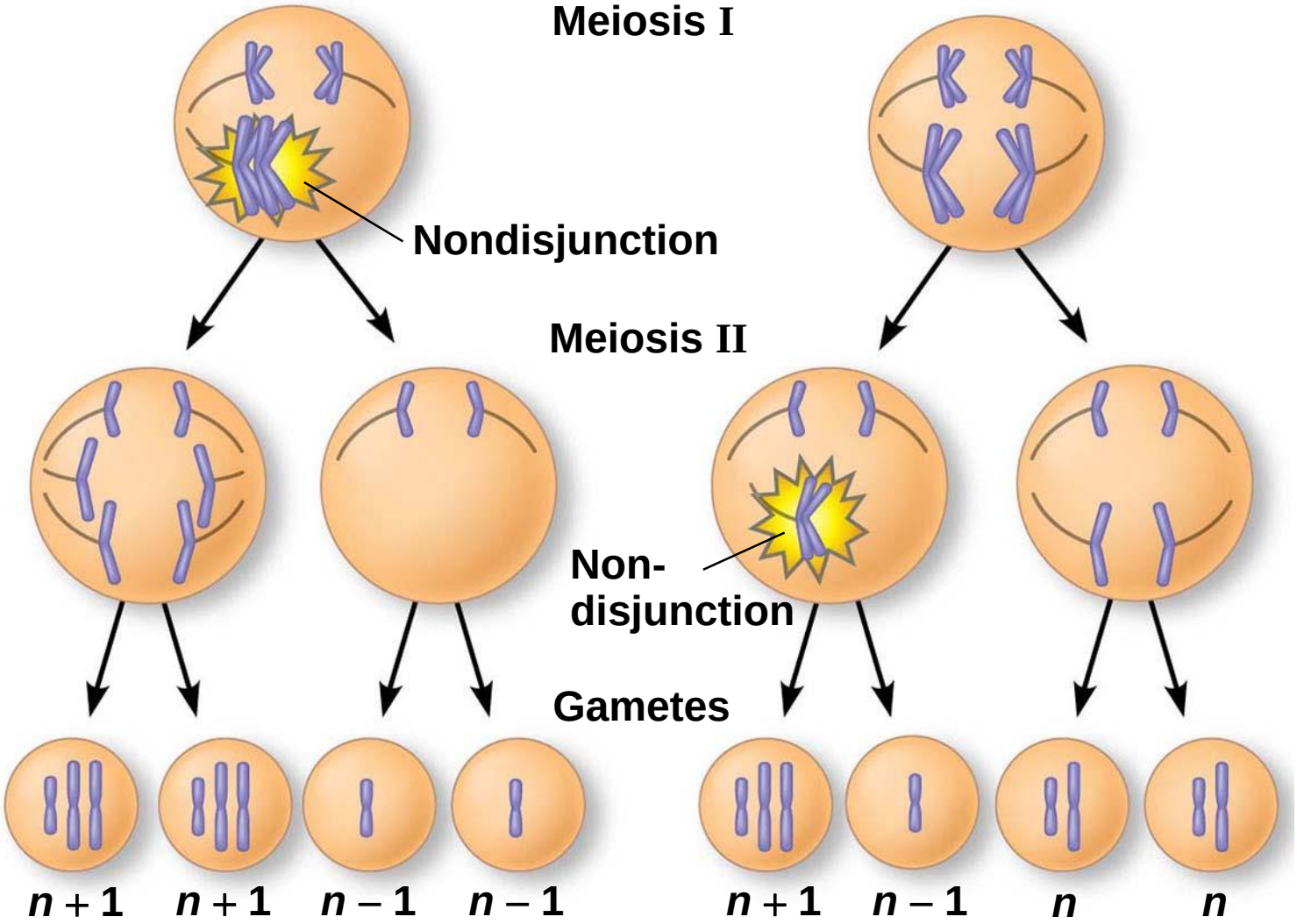


Figure 12.13-s3



(a) Nondisjunction of homologous chromosomes in meiosis I

(b) Nondisjunction of sister chromatids in meiosis II

- **Aneuploidy** results from fertilization involving gametes in which nondisjunction occurred
- Offspring with this condition have an abnormal number of a particular chromosome

- A **monosomic** zygote has only one copy of a particular chromosome
- A **trisomic** zygote has three copies of a particular chromosome

- **Polyploidy** is a condition in which an organism has more than two complete sets of chromosomes
  - Triploidy (3*n*) is three sets of chromosomes
  - Tetraploidy (4*n*) is four sets of chromosomes
- Polyploidy is common in plants, but not animals
- Polyploids are more normal in appearance than aneuploids

Alterations of Chromosome Structure

- Breakage of a chromosome can lead to four types of changes in chromosome structure
  - **Deletion** removes a chromosomal segment
  - **Duplication** repeats a segment
  - **Inversion** reverses orientation of a segment within a chromosome
  - **Translocation** moves a segment from one chromosome to another

Figure 12.14

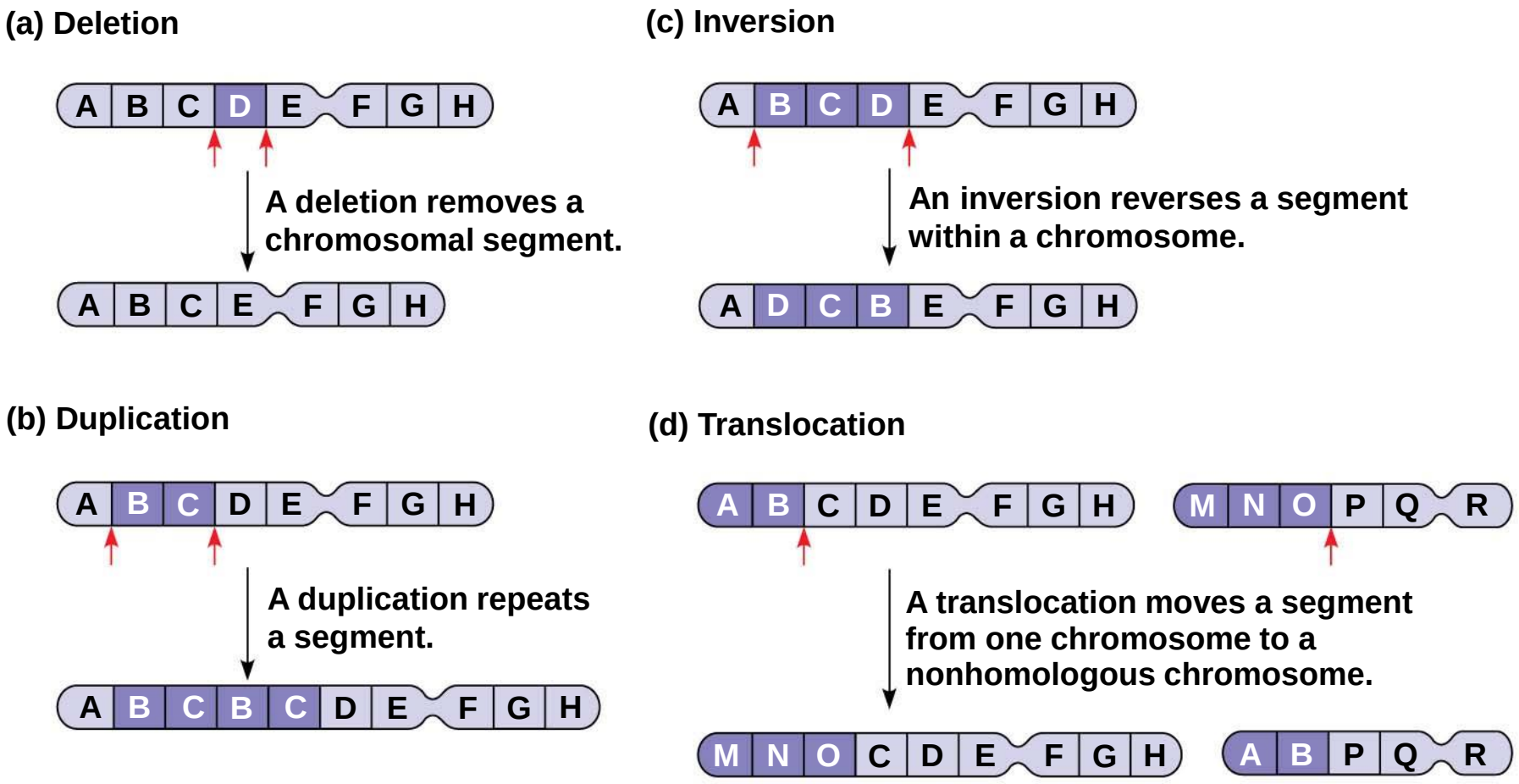


Figure 12.14-1

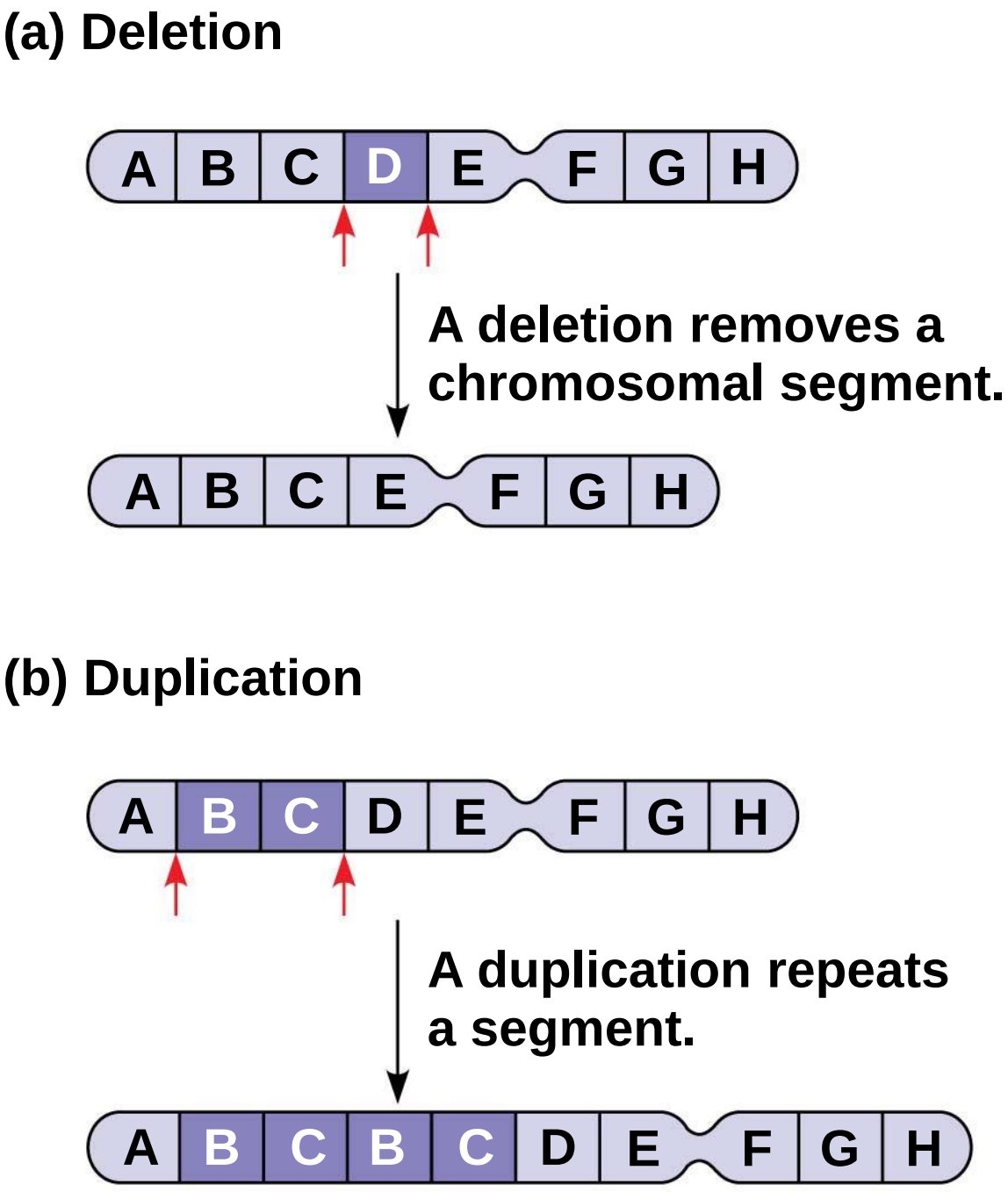
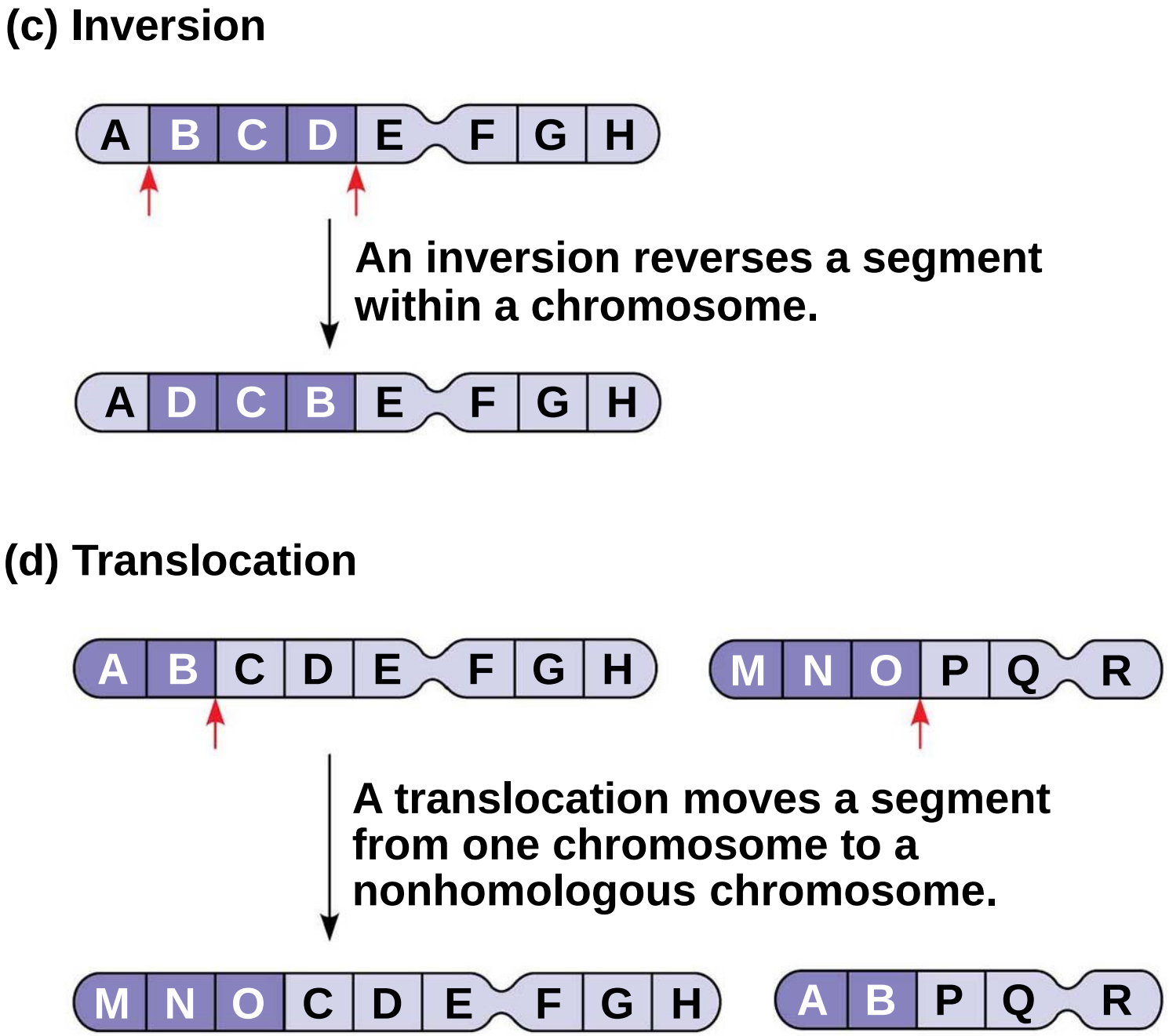


Figure 12.14-2



- A diploid embryo that is homozygous for a large deletion is likely missing a number of essential genes; such a condition is generally lethal
- Duplications and translocations also tend to be harmful
- In inversions, the balance of genes is normal but phenotype may be influenced if the expression of genes is altered

Human Disorders Due to Chromosomal Alterations

- Alterations of chromosome number and structure are associated with some serious disorders
- Some types of aneuploidy upset the genetic balance less than others, resulting in individuals surviving to birth and beyond
- These surviving individuals have a set of symptoms, or syndrome, characteristic of the type of aneuploidy

Down Syndrome (Trisomy 21)

- **Down syndrome** is an aneuploid condition that results from three copies of chromosome 21
- It affects about one out of every 830 children born in the United States
- The frequency of Down syndrome increases with the age of the mother, a correlation that has not been explained

Figure 12.15

Figure 12.15-1

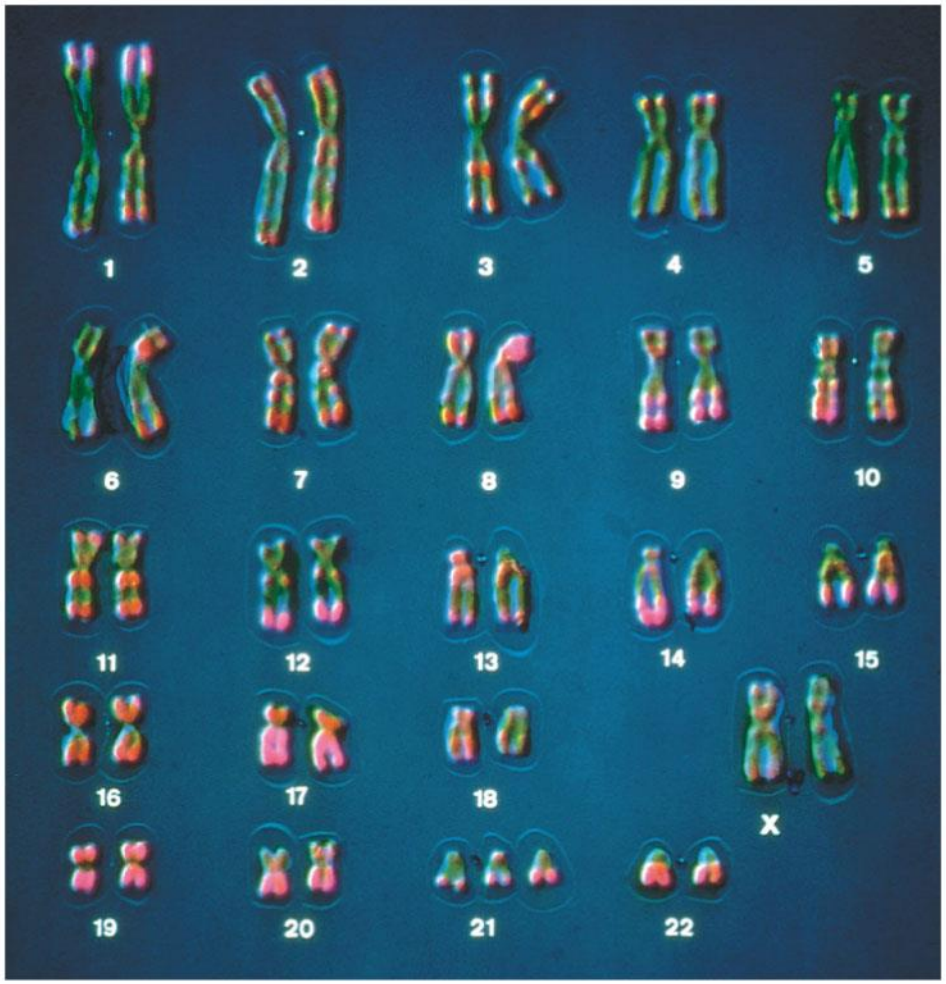


Figure 12.15-2

Aneuploidy of Sex Chromosomes

- Nondisjunction of sex chromosomes produces a variety of aneuploid conditions
- Klinefelter syndrome is the result of an extra chromosome in a male, producing XXY individuals
- About one in every 1,000 males is born with an extra Y chromosome (XYY) and does not exhibit any defined syndrome
- Females with trisomy X (XXX) have no unusual physical features except being slightly taller than average

- Monosomy X, called Turner syndrome, produces X0 females, who are sterile
- It is the only known viable monosomy in humans

Disorders Caused by Structurally Altered Chromosomes

- The syndrome *cri du chat* (“cry of the cat”) results from a specific deletion in chromosome 5
- A child born with this syndrome is severely intellectually disabled and has a catlike cry; individuals usually die in infancy or early childhood
- Certain cancers, including *chronic myelogenous leukemia* (CML), are caused by translocations of chromosomes

Figure 12.16

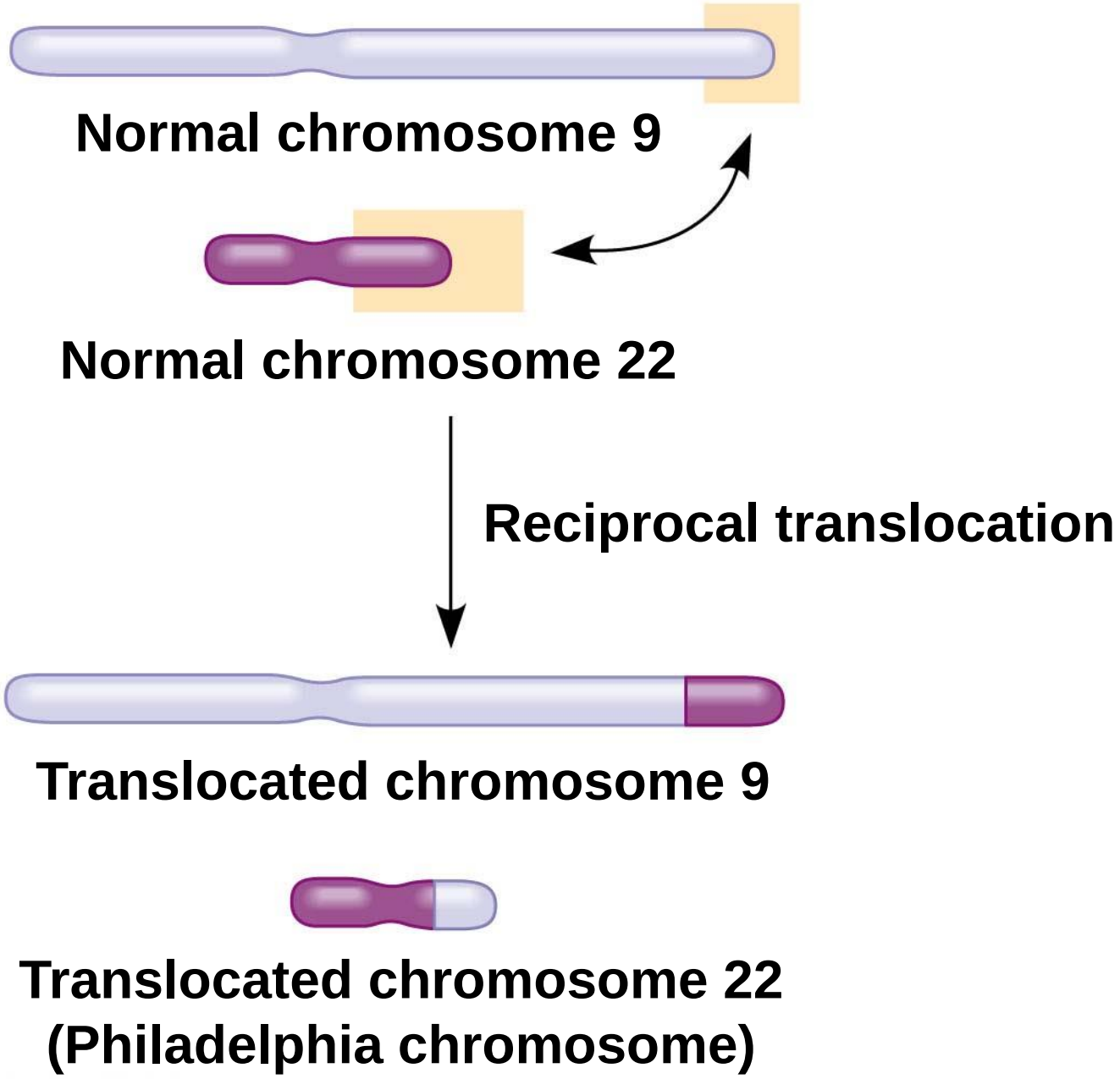


Figure 12.UN03-1

Offspring from testcross of *AaBb* (F_1) × *aabb*	Purple stem/short petals (*A–B–*)	Green stem/short petals (*aaB–*)	Purple stem/long petals (*A–bb*)	Green stem/long petals (*aabb*)
Expected ratio if the genes are unlinked	1	1	1	1
Expected number of offspring (of 900)				
Observed number of offspring (of 900)	220	210	231	239

Figure 12.UN03-2

Testcross offspring	Expected (e)	Observed (o)	Deviation ($o - e$)	$(o - e)^2$	$(o - e)^2/e$
(*A–B–*)		220			
(*aaB–*)		210			
(*A–bb*)		231			
(*aabb*)		239			
				χ^2 = Sum	

Figure 12.UN03-3

Figure 12.UN04

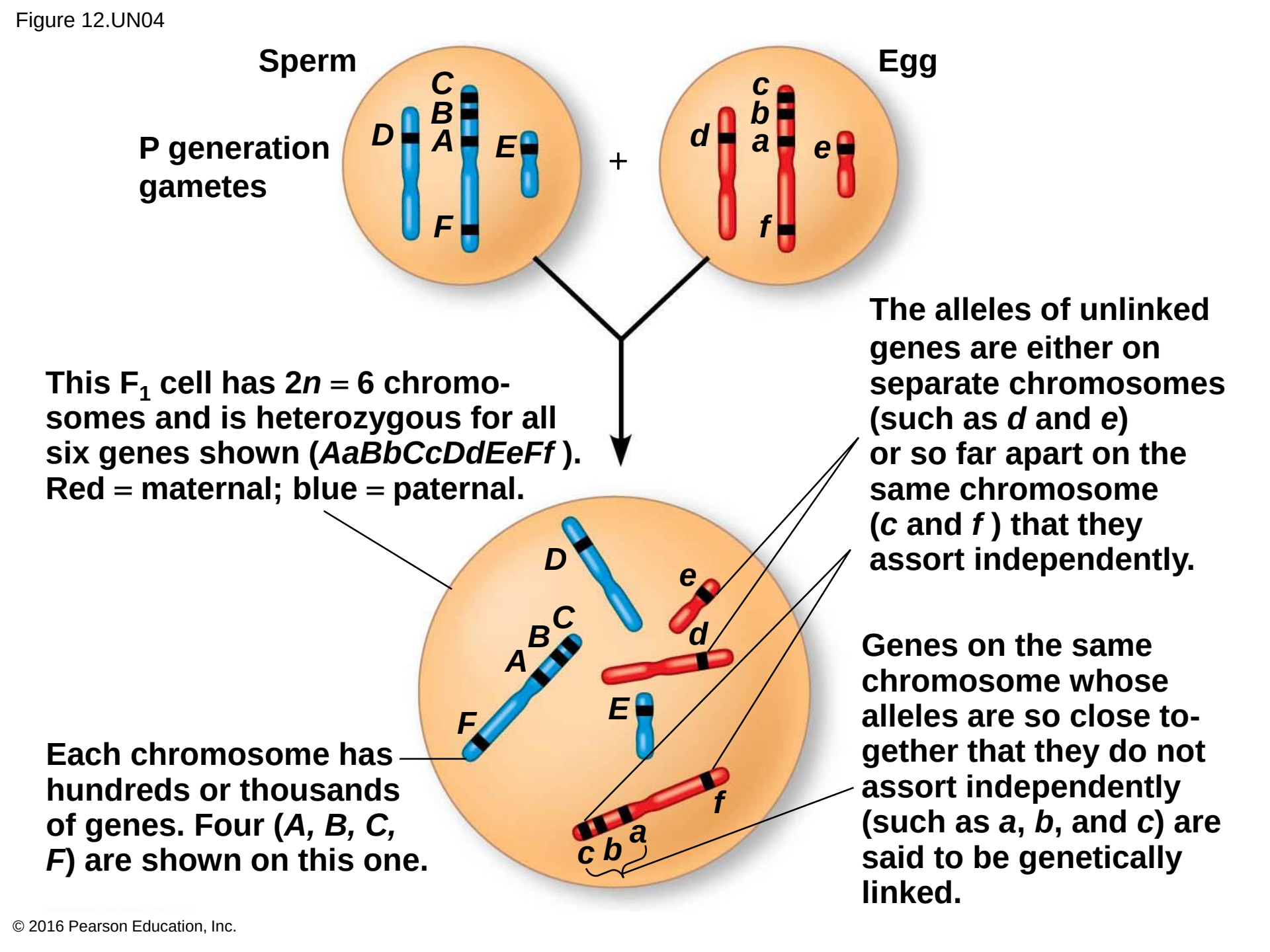


Figure 12.UN05