PowerPoint to accompany

Genetics: From Genes to Genomes

Fourth Edition

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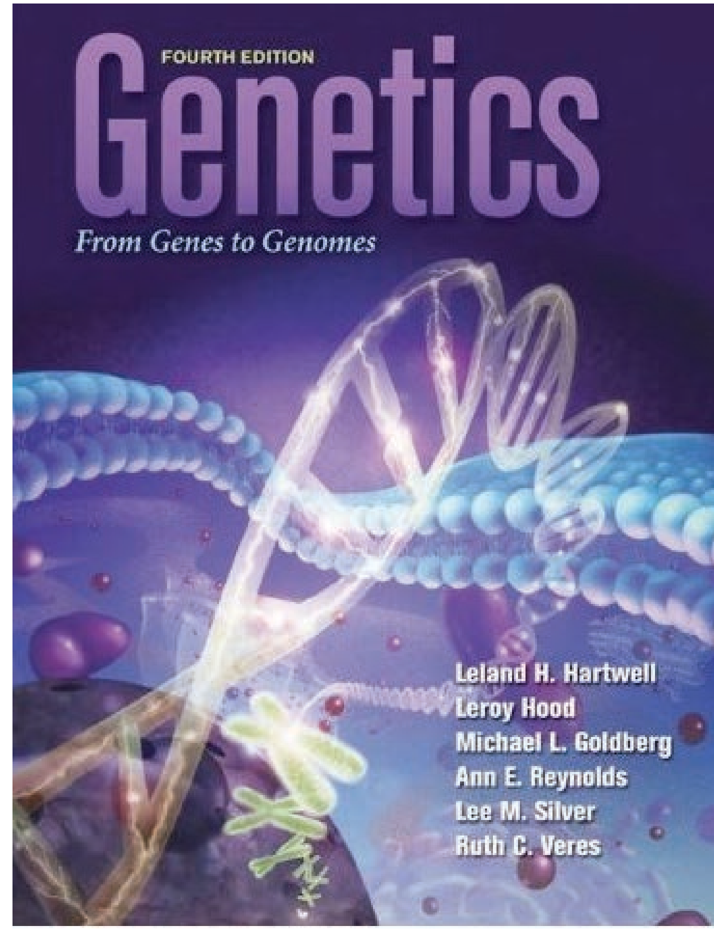
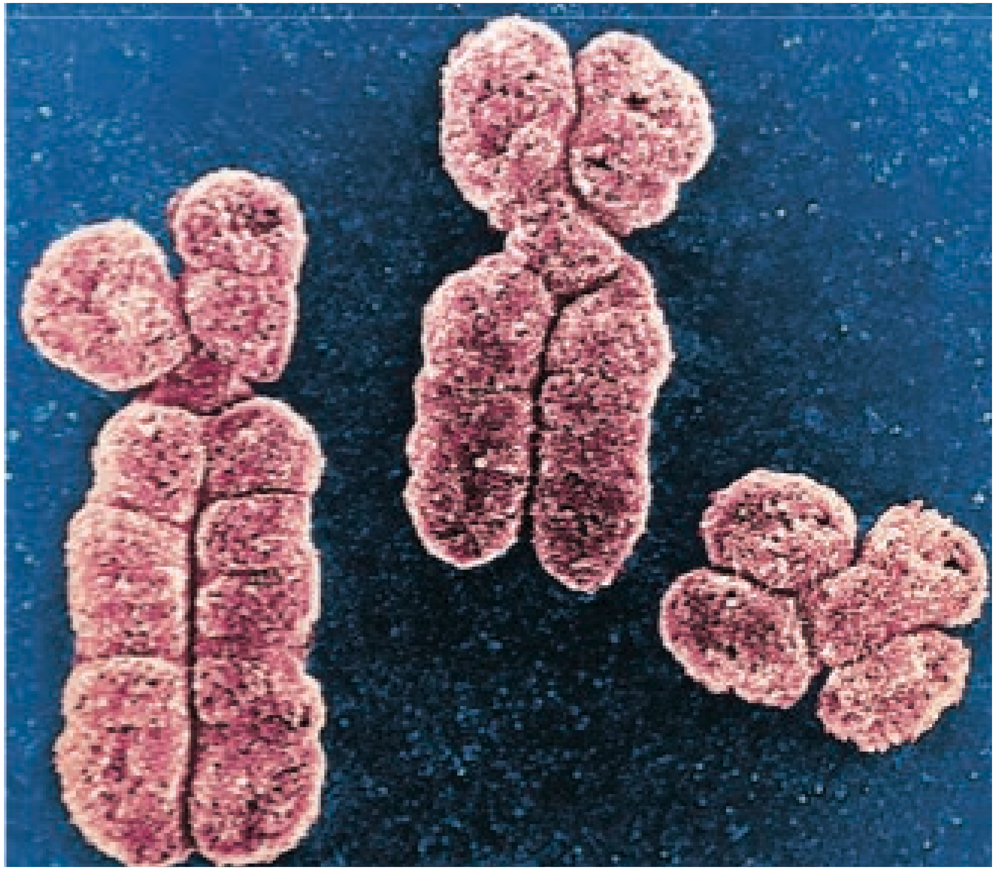
Prepared by Mary A. Bedell
University of Georgia



The Chromosome Theory of Inheritance



CHAPTER OUTLINE

- **4.1 Chromosomes: The Carriers of Genes**
- **Cell Division**
  - **4.2 Mitosis: Cell Division That Preserves Chromosome Number**
  - **4.3 Meiosis: Cell Divisions That Halve Chromosome Number**
- **4.4 Gametogenesis**
- **4.5 Validation of the Chromosome Theory**

Chromosomes are cellular structures that transmit genetic information

- **Breeding experiments and microscopy provided evidence for the <u>Chromosome Theory of Inheritance</u>**

- **Proper development relies on accurate: (i) transmission of genes; (ii) maintenance of chromosome number**

- **The abstract idea of a gene was changed to a physical reality by the Chromosome Theory of Inheritance**

Evidence that genes reside in the nucleus

1667 - Anton Van Leeuwenhoek

- Microscopy revealed that semen contain spermatozoa ("sperm animals")
- Hypothesized that sperm may enter egg to achieve fertilization

1854 – 1874

- Direct observations of fertilization through union of nuclei of eggs and sperm (frog and sea urchin)
- Conclusion: something in the nucleus must contain the hereditary material

Two general types of cells in plants and animals

- Somatic cells make up vast majority of cells in the organism
  - In G_0 or are actively going through mitosis
- Germ cells are precursors to gametes
  - Set aside from somatic cells during embryogenesis
  - Become incorporated into reproductive organs
  - Only cells that undergo meiosis produce haploid gametes

Evidence that genes reside in chromosomes

- 1880s – improved microscopy and staining techniques
  - Long, threadlike, colored bodies (chromosomes) visualized in the nucleus
  - Movement of these bodies followed through cell division

- MITOSIS -nuclear division that generates two daughter cells containing the same number and type of chromosomes as parent cell

- MEIOSIS -nuclear division that generates gametes (egg and sperm) containing half the number of chromosomes found in other cells

Diploid versus haploid: 2*n* versus *n*

- **Most body cells are diploid (each chromosome pair has 1: maternal and paternal copy)**
- **Meiosis →haploid (*n*) gametes**
- **In Drosophila, 2*n* = 8, *n* = 4**
- **In humans , 2*n* = 46 and *n* = 23**

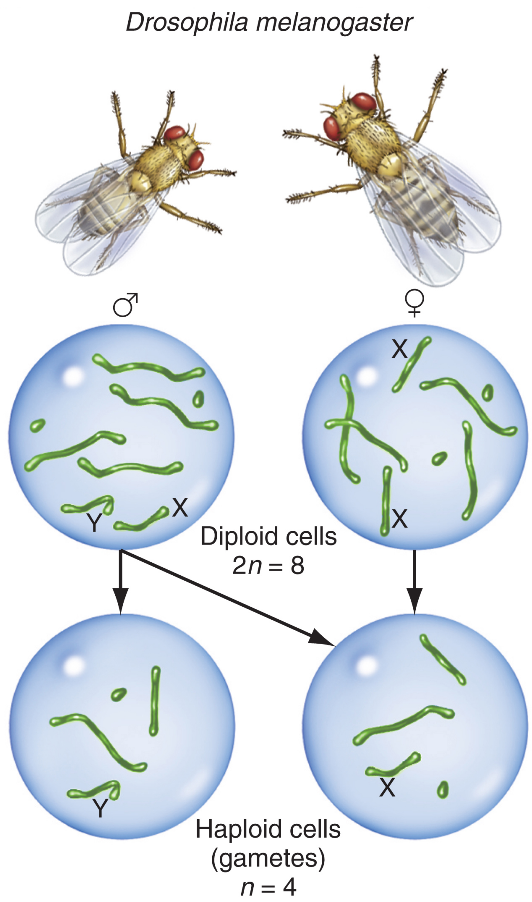


Fig. 4.2

Fertilization is the union of haploid gametes to produce diploid zygotes

- **Fertilized eggs carry matching sets of chromosomes: one set from <u>maternal gamete</u> and one set from <u>paternal gamete</u>**
- **Gametes are haploid (*n*) – carry only a single set of chromosomes**
- **Zygotes are diploid (*2n*) – carry two matching set of chromosome**
- **Mitosis ensures that all cells of developing individuals have identical *2n* chromosome sets**

Metaphase chromosomes can be classified by centromere position

Metacentric chromosome –centromere is in the middle

Acrocentric chromosome –centromere is near one end

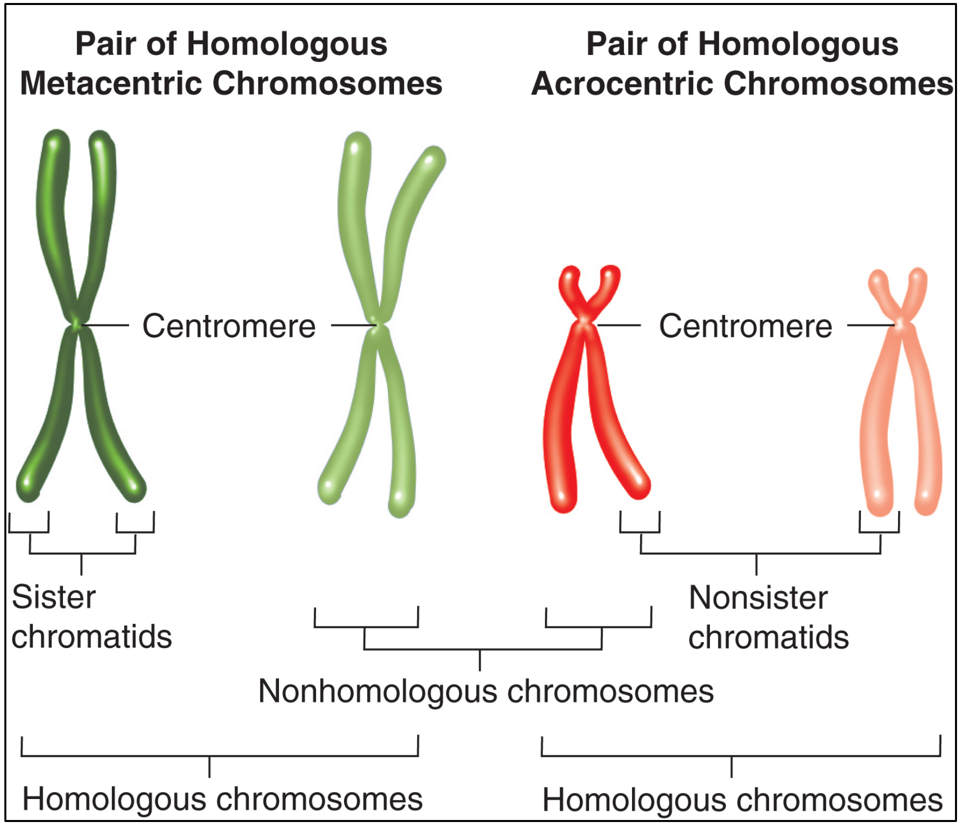


Fig. 4.3

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Homologous chromosomes are matched in size, shape, and banding patterns

- **Homologs** contain the same set of genes, but can have different alleles for some genes
- Non-homologs carry completely unrelated sets of genes
- Cells of each species have a characteristic diploid number of chromosomes
  - e.g. *D. melanogaster*, $2n = 8$; *D. obscura*, $2n = 10$; *D. virilis*, $2n = 12$; sweet peas, $2n = 14$; goldfish, $2n = 94$; dogs, $2n = 78$
  - **Sex chromosomes** –unpaired X and Y chromosome
  - **Autosomes** –all chromosomes except X and Y
- **Karyotype** –micrograph of stained chromosomes arranged in homologous pairs (see Fig 4.4)

Karyotype of a Human Male

- Photos of metaphase human chromosomes ($2n$ = 46, n = 23)
- Each homologous pair arranged in order of decreasing size

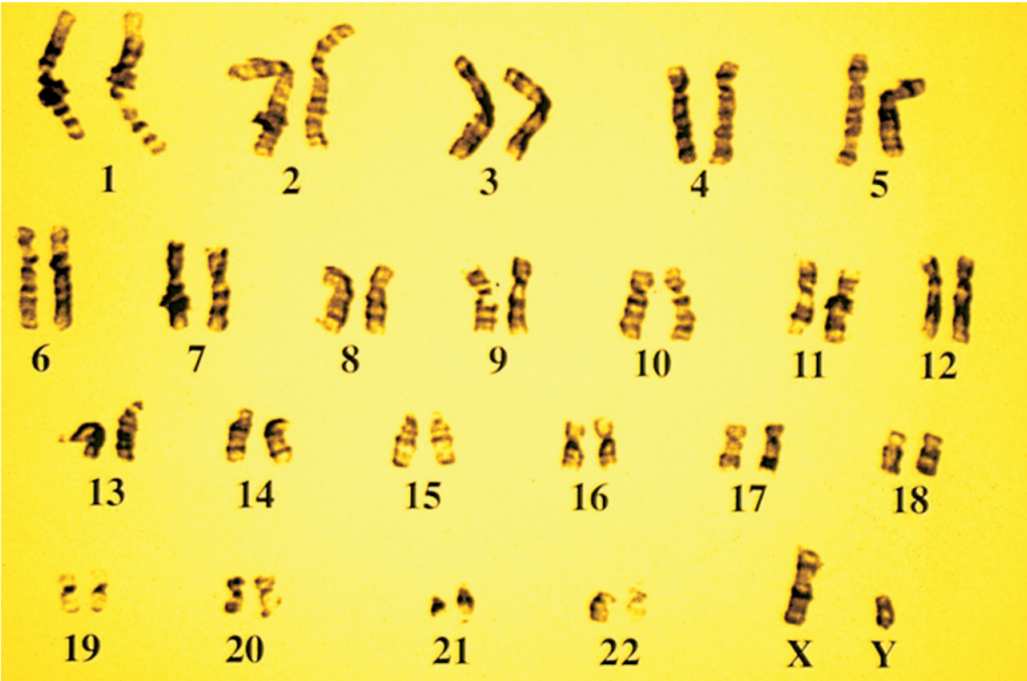

Fig. 4.4

One chromosome pair determines sex in grasshoppers

- W. S. Sutton studied meiosis in great lubber grasshoppers
- Before meiosis: testes cells had 24 chromosomes
  - 22 in matched pairs (autosomes) and 2 unmatched (large = X and smaller = Y)
- After meiosis: two types of sperm were formed
  - 1/2 of sperm had 11 chromosomes and an X
  - 1/2 of sperm had 11 chromosomes and a Y
- After meiosis: only one type of egg was produced
  - All had 11 chromosomes plus an X

The great lubber grasshopper

- Fertilization of egg with sperm carrying an X → XX female
- Fertilization of egg with sperm carrying a Y → XY male
- Sutton concluded that the X and Y chromosomes determine sex

Fig. 4.5

The X and Y chromosomes determine sex in humans

- Children receive an X chromosome from their mother, but either an X or Y chromosome from their father
- Results in 1:1 ratio of females-to-males

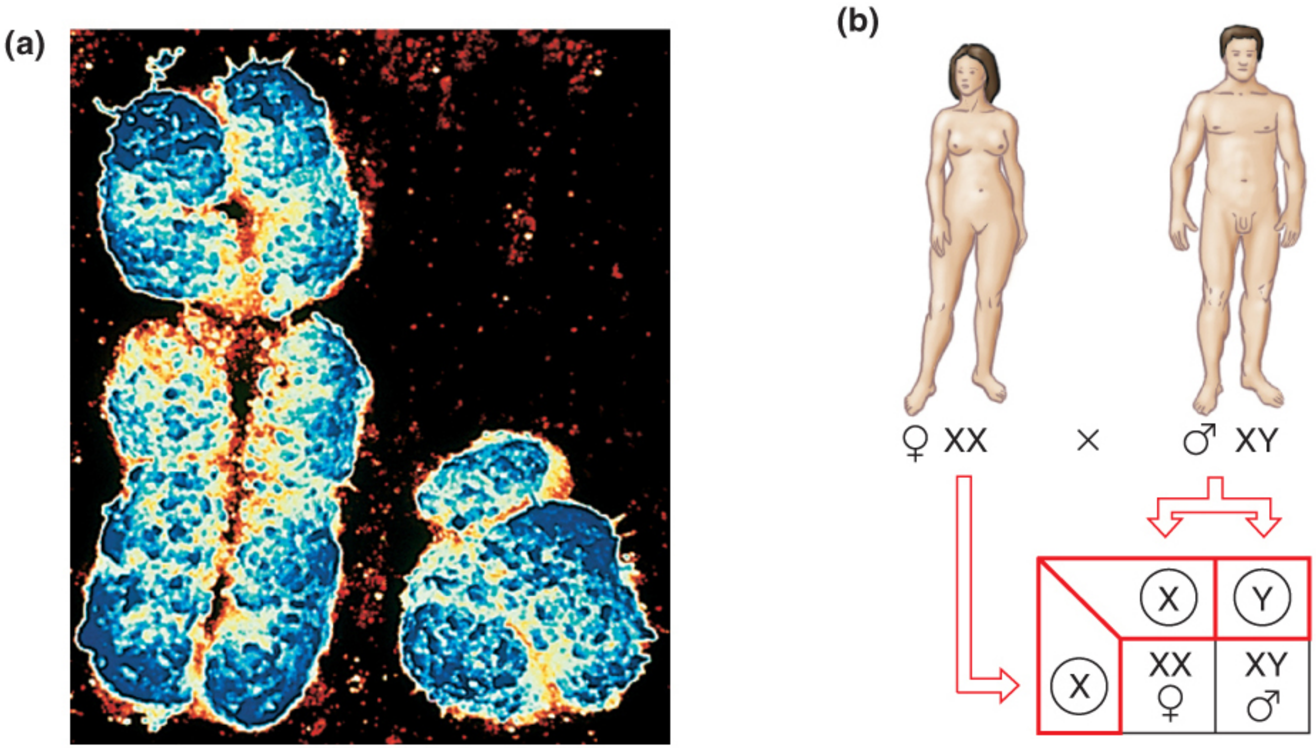

Fig. 4.6

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Sex determination in fruit flies and humans

- Drosophila: ratio of X chromosomes to autosomes determines gender
- Humans: presence or absence of Y chromosome determines gender
- Abnormal numbers of X or Y chromosomes have different effects in humans and flies

	Complement of Sex Chromosomes						
	XXX	XX	XXY	XO	XY	XYY	OY
Drosophila	Dies	Normal female	Normal female	Sterile male	Normal male	Normal male	Dies
Humans	Nearly normal female	Normal female	Klinefelter male (sterile); tall, thin	Turner female (sterile); webbed neck	Normal male	Normal or nearly normal male	Dies

Table 4.1

Mechanisms of sex determination differ between species

- **Heterogametic sex** –gender with two different kinds of gametes
- **Homogametic sex** –gender with one type of gamete
- In some species, gender is determined by environment (e.g. temperature)

	♀	♂
Humans and *Drosophila*	XX	XY
Moths and *C. elegans*	XX (hermaphrodites in *C. elegans*)	XO
Birds and Butterflies	ZW	ZZ
Bees and Wasps	Diploid	Haploid
Lizards and Alligators	Cool temperature	Warm temperature
Tortoises and Turtles	Warm temperature	Cool temperature
Anemone Fish	Older adults	Young adults

Table 4.2

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- 4.4 Gametogenesis
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The cell cycle is a repeating pattern of cell growth and division

- Nuclear division during mitosis apportions chromosomes in equal fashion to two genetically identical daughter cells
- Interphase has three parts - gap 1 (G_1) phase, synthesis (S) phase, and gap 2 (G_2) phase
  - Period of cell growth and chromosome duplication between divisions
  - Formation of microtubules in cytoplasm
    - Centrosome – microtubule organizing center near the nuclear envelope
    - Centrioles – core of centrosome, not found in plant cells

The cell cycle: An alternation between interphase and mitosis

- Most of cell growth occurs during G_1 and G_2 phases
- Some terminally differentiated cells stop dividing and arrest in G_0 stage
- Chromosomes replicate to form sister chromatids during S phase

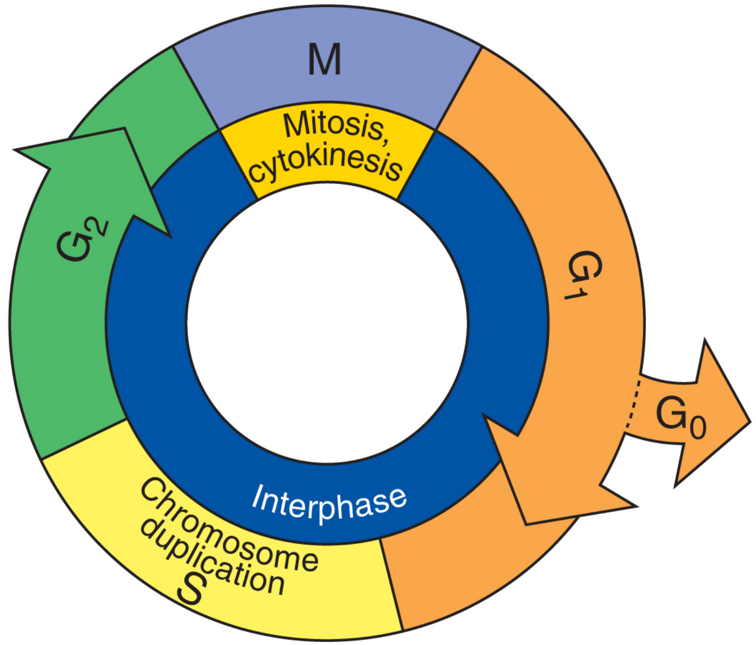

Fig. 4.7a

Chromosomes replicate during S phase

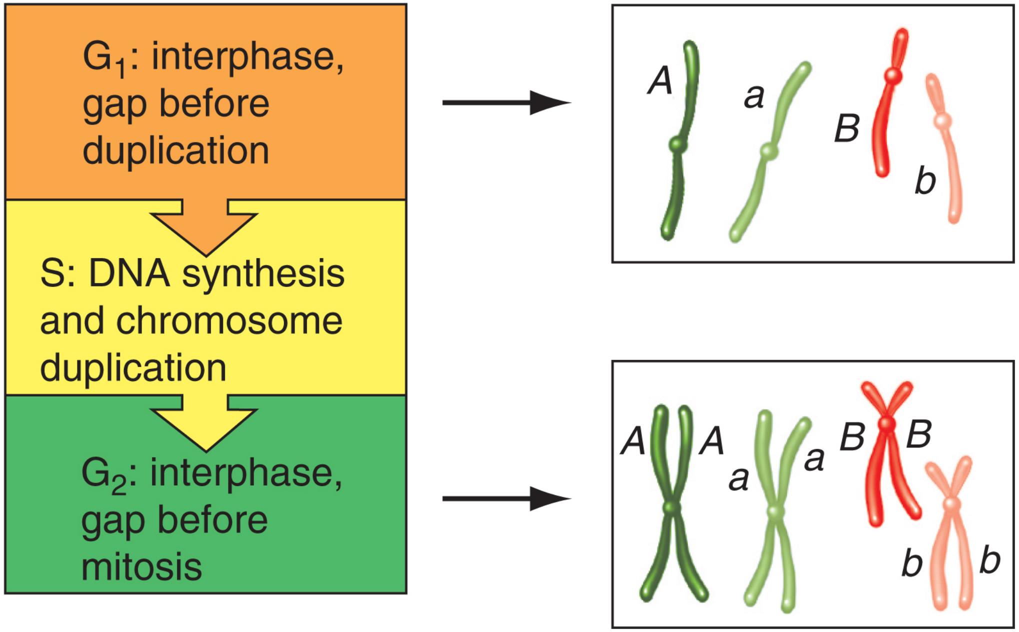

Fig. 4.7b

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Mitosis has five stages that have distinct cytological characteristics

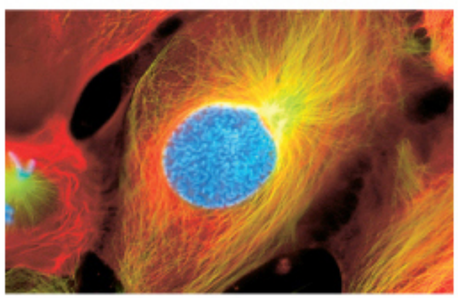
- The five stages of mitosis and their major events
  - **Prophase** -chromosomes condense and become visible
  - **Prometaphase** –spindle forms and sister chromatids attach to microtubules from opposite centrosomes
  - **Metaphase** –chromosome align at the cell's equator
  - **Anaphase** – sister chromatids separate and move to opposite poles
  - **Telophase** –chromosomes decondense and are enclosed in two nuclei

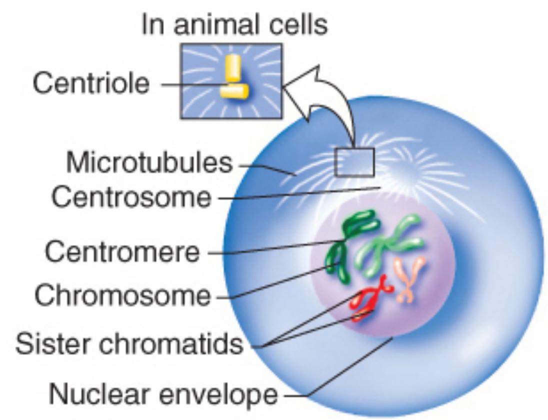
Stages of mitosis: prophase

Chromosomes condense and become visible

Centrosomes move apart toward opposite poles

Nucleoli begin to disappear





(left): Photographs by Dr. Conly L. Rieder, Division of Molecular Medicine, Wadsworth Center, NYS Dept. Of Health, Albany, NY

Figure 4.8a

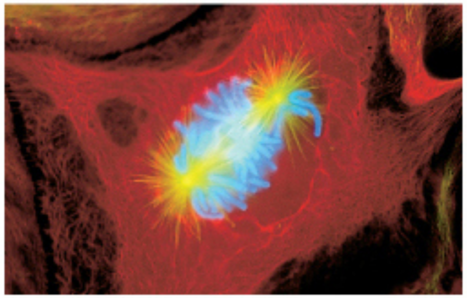
Stages of mitosis: prometaphase

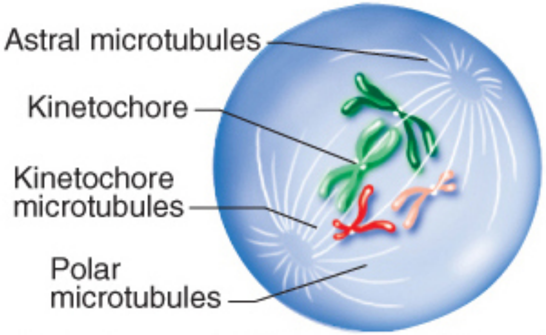
Nuclear envelope breaks down

Microtubules from centrosomes invade the nucleus and connect to kinetochores in centromere of each chromatid

- Sister chromatids attach to microtubules from opposite poles
- Mitotic spindle forms from three kinds of microtubules (astral, kinetochore, and polar)

Figure 4.8b



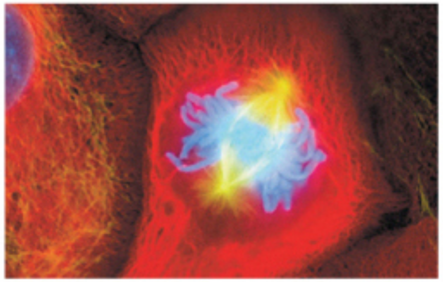


(left): Photographs by Dr. Conly L. Rieder, Division of Molecular Medicine, Wadsworth Center, NYS Dept. Of Health, Albany, NY

Stages of mitosis: metaphase

Chromosomes align on the metaphase plate with sister chromatids facing opposite poles

Forces pushing and pulling chromosomes to or from each pole are in balanced equilibrium



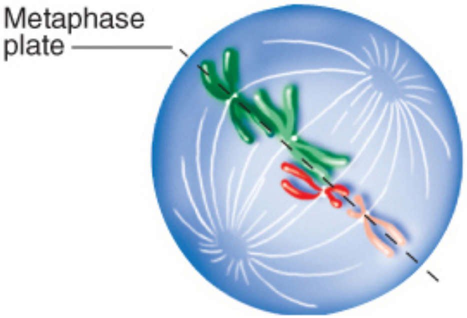


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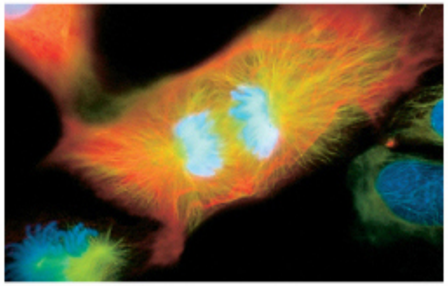
Figure 4.8c

Stages of mitosis: anaphase

Centromeres of all chromosomes divide simultaneously

Kinetochore microtubules shorten and pull separated sister chromatids to opposite poles (characteristic V shape)



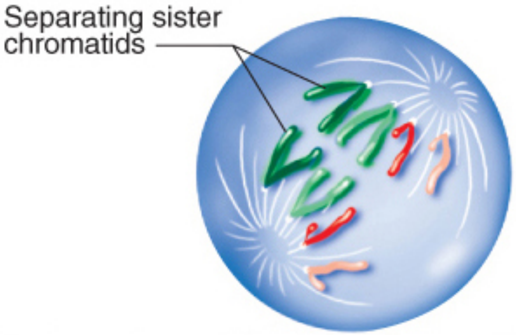


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Figure 4.8d

Stages of mitosis: telophase

Rewind of prophase

Nuclear envelope forms around each group of chromatids

- **Nucleoli re-form**
- **Spindle fibers disperse**
- **Chromosomes decondense**

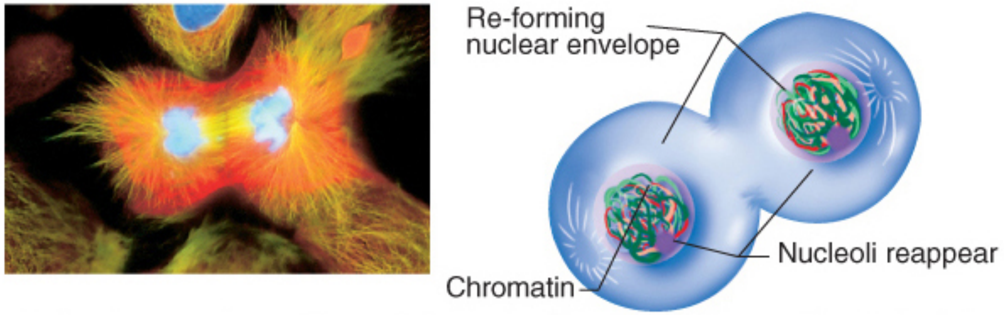

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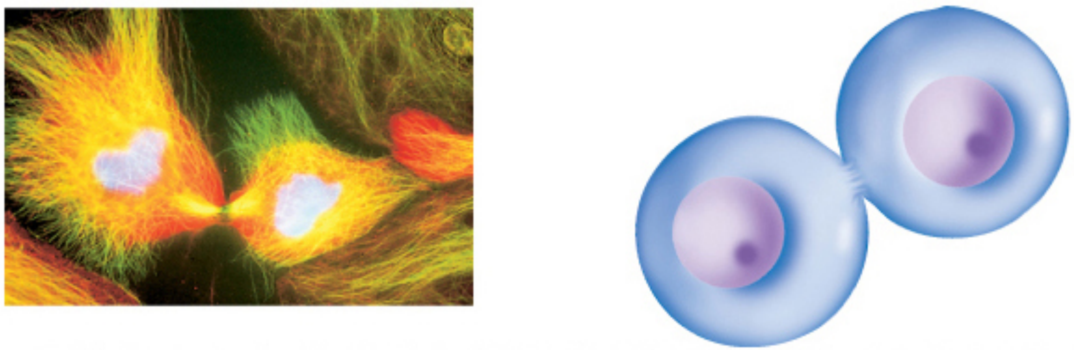
Figure 4.8e

Cytokinesis is the final stage of cell division

Begins during anaphase but not completed until after telophase

Parent cells split into two daughter cells with identical nuclei



(left): Photographs by Dr. Conly L. Rieder, Division of Molecular Medicine, Wadsworth Center, NYS Dept. Of Health, Albany, NY

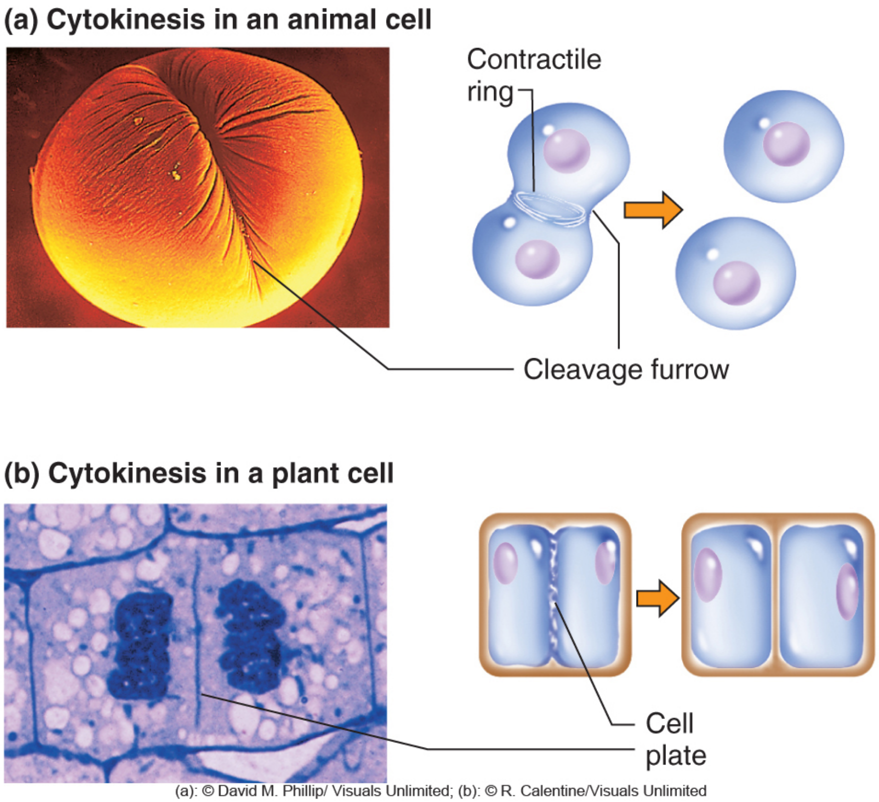
Figure 4.8f

Cytokinesis: The cytoplasm divides and produces two daughter cells

Animals have contractile ring that contracts to form cleavage furrow

Plants have cell plate that forms near equator of cell

Organelles (e.g. ribosomes, mitochondria, Golgi bodies) are distributed to each daughter cell



(a): © David M. Phillip/ Visuals Unlimited; (b): © R. Calentine/Visuals Unlimited

Fig. 4.9

Cytokinesis does not always occur after mitosis

- **In fertilized Drosophila eggs, 13 rounds of mitosis occur without cytokinesis**
- **Results in syncytial embryo with thousands of nuclei within a single cell**

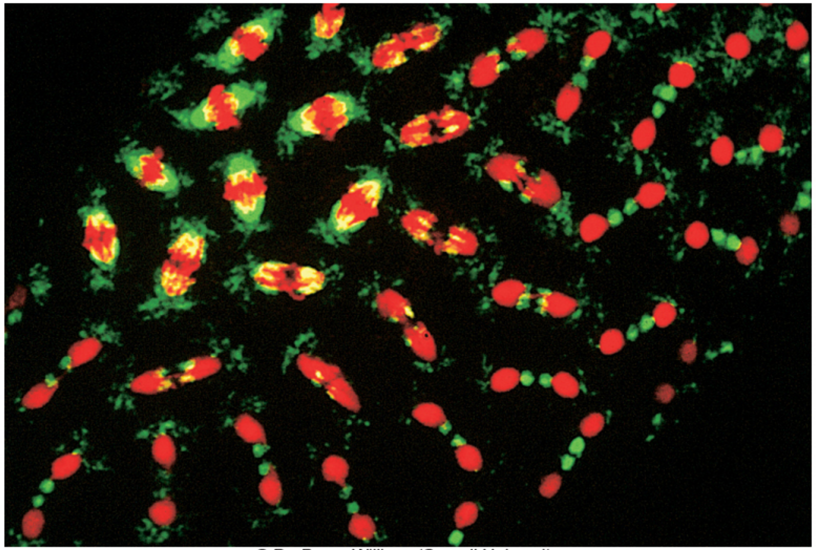


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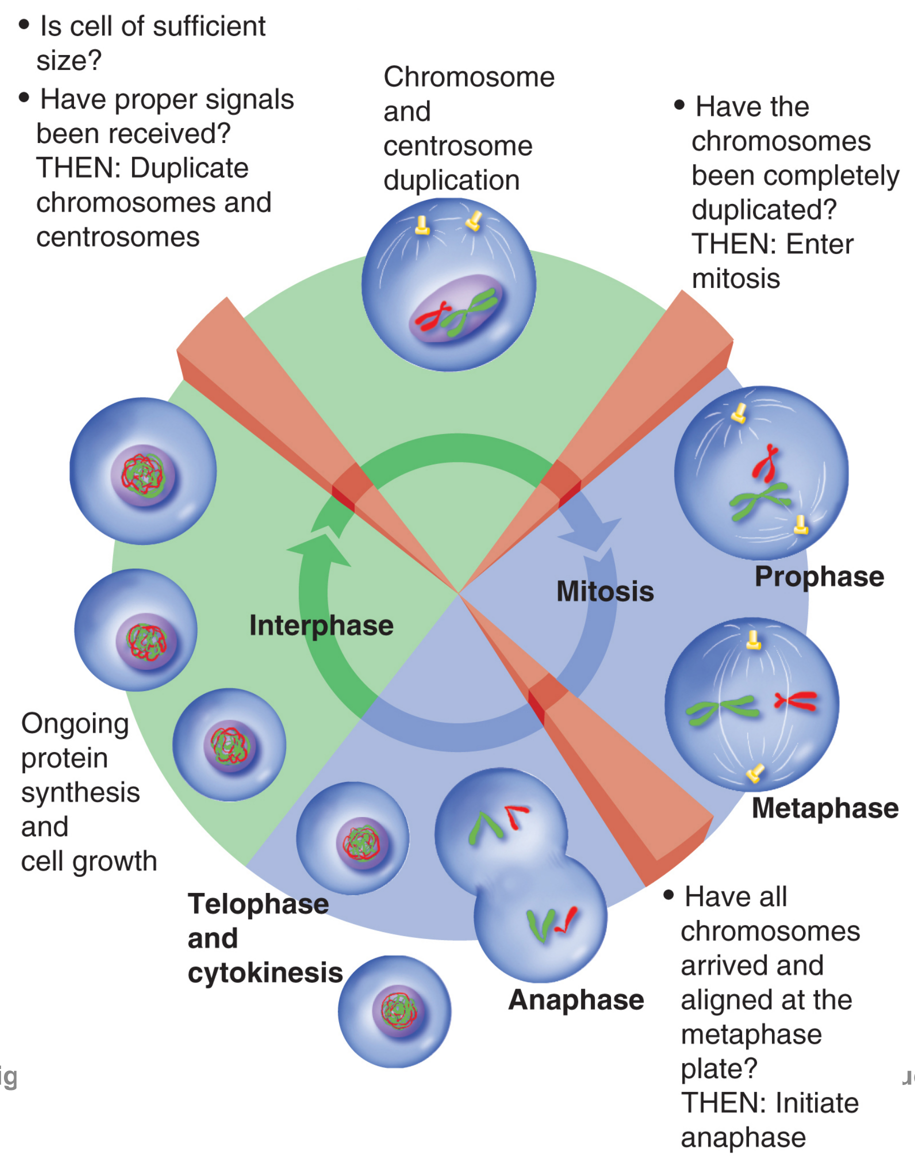
Fig. 4.10

Checkpoints help regulate the cell cycle



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Overview of meiosis

Two rounds of meiosis

Chromosomes duplicate once

Nuclei divide twice

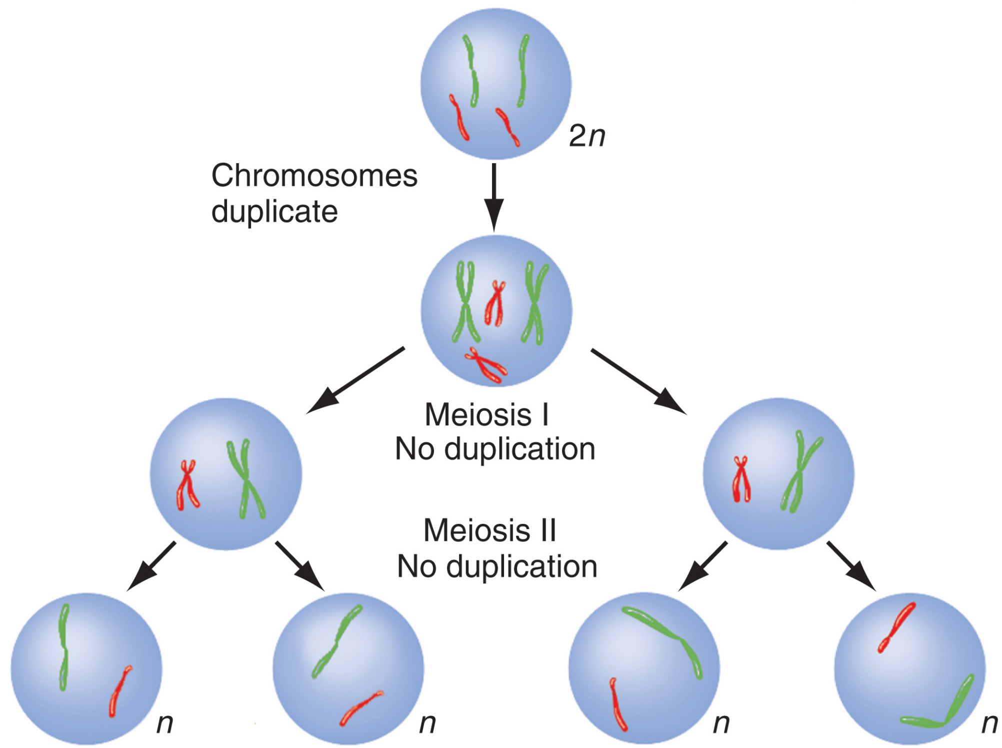


Fig. 4.12

Overview of meiosis I

Homologs pair, exchange parts, and then segregate

Sister chromatids remain intact throughout meiosis I

Maternal and paternal homologs recombine and create new combinations of alleles

After recombination, homologs segregate to different daughter cells

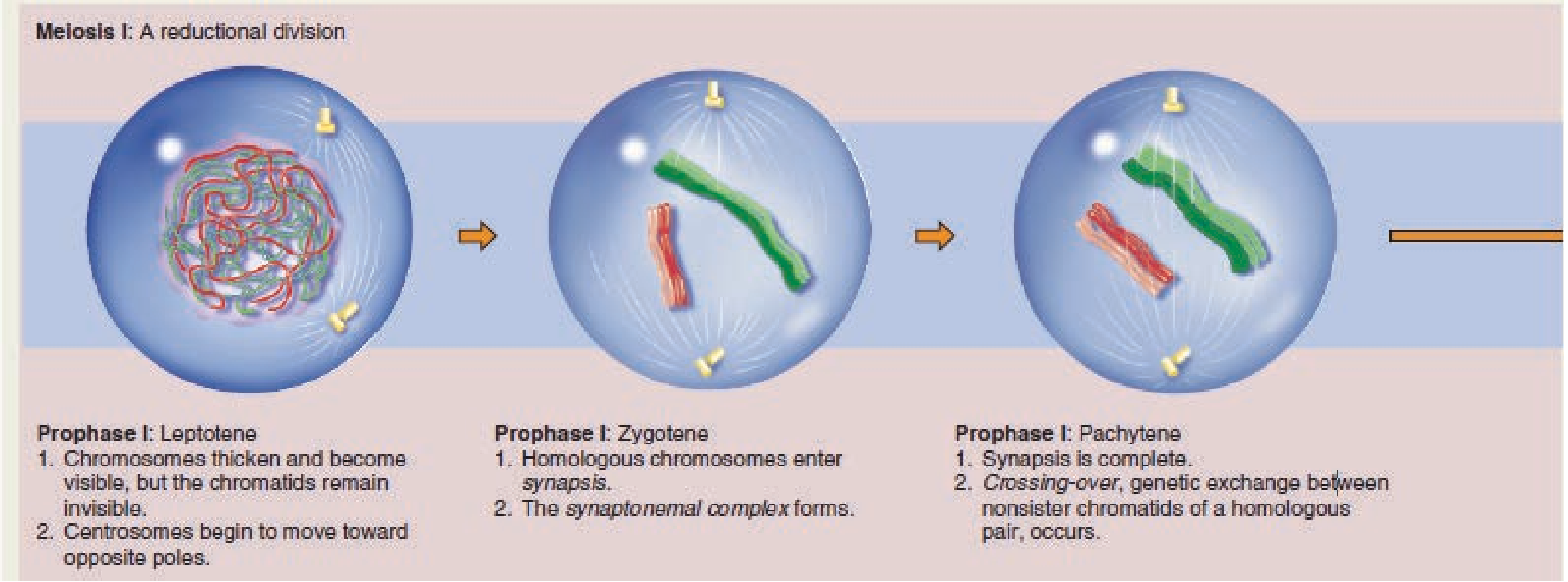
Five substages to prophase I – leptotene, zygotene, pachytene, diplotene, and diakinesis

- Depending on the species, length of time in prophase I can be short or very long

The first three substages of prophase I: Leptotene, zygotene, and pachytene

Homologs pair and are held together by synaptonemal complex

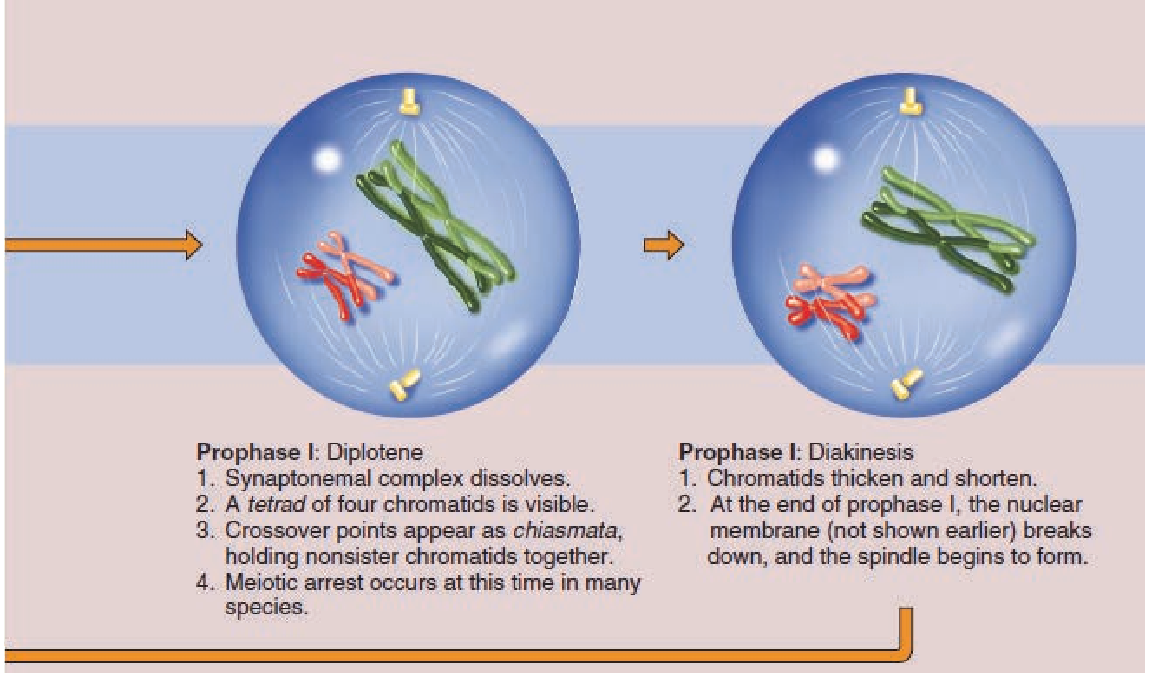
Crossing-over (recombination) occurs during prophase I



Feature Fig. 4.13

The last two substages of prophase : Diplotene and diakinesis

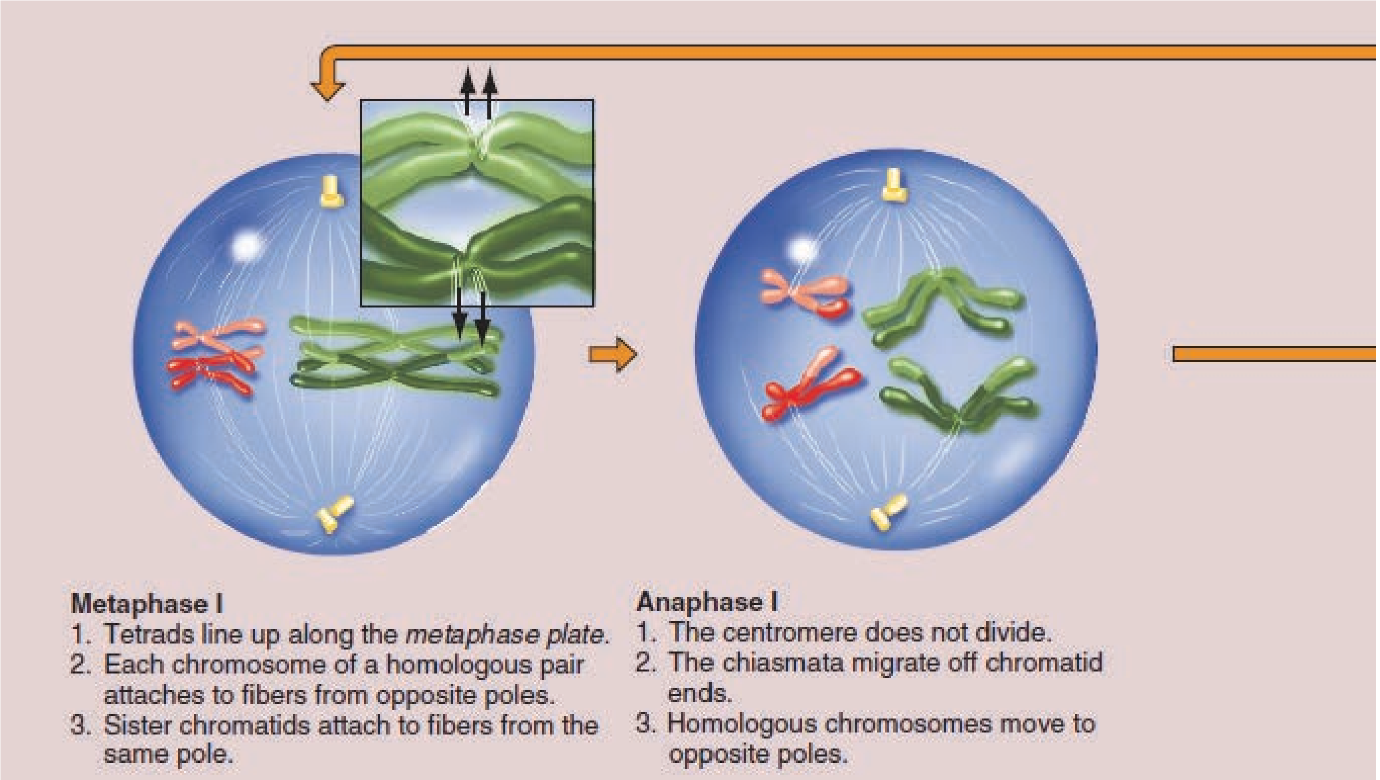
Synaptonemal complex dissolves and chromatids in each tetrad become visible



Feature Fig. 4.13

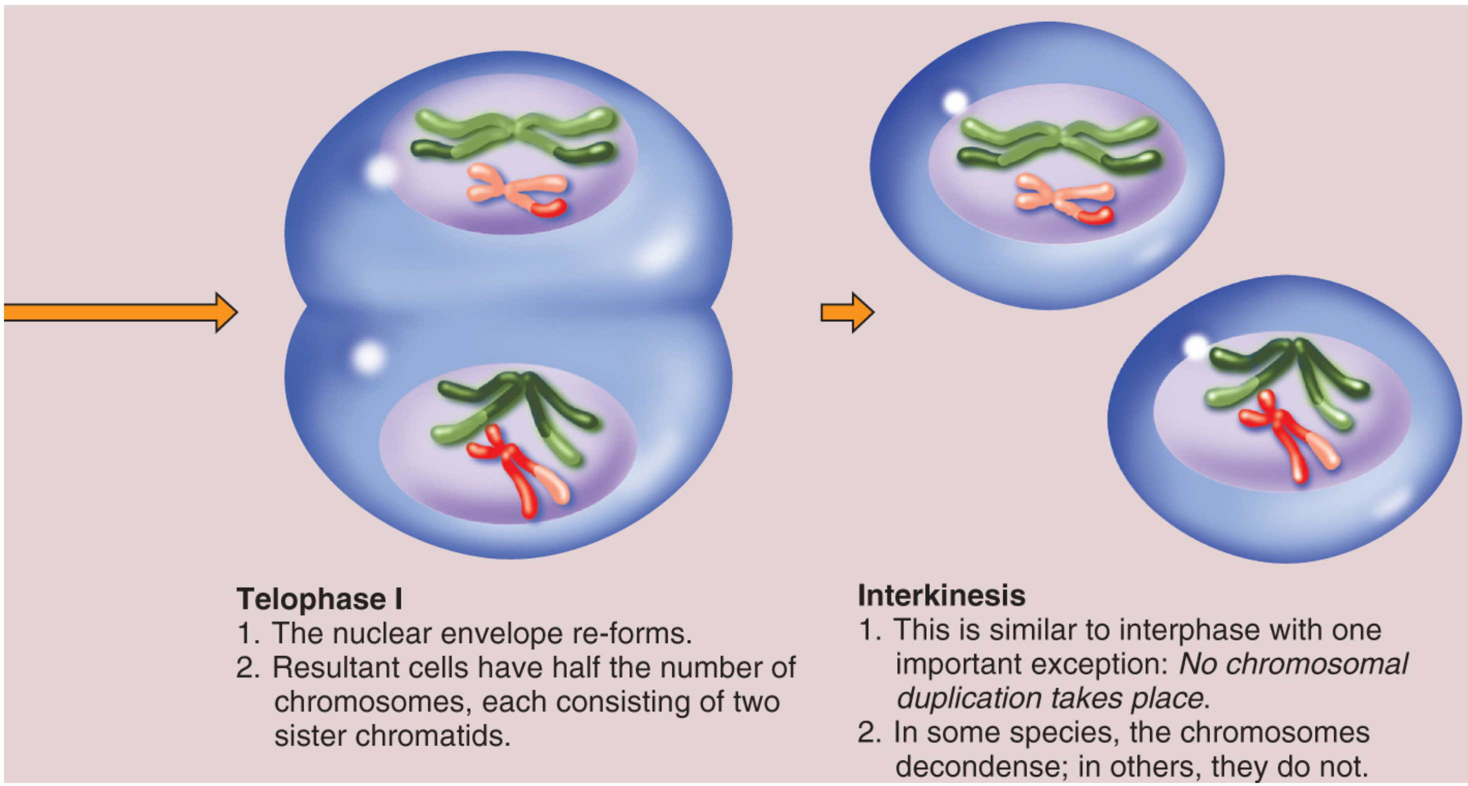
In metaphase I and anaphase I, homologs move to opposite poles

Note that the centromeres do not divide and sister chromatids are not separated



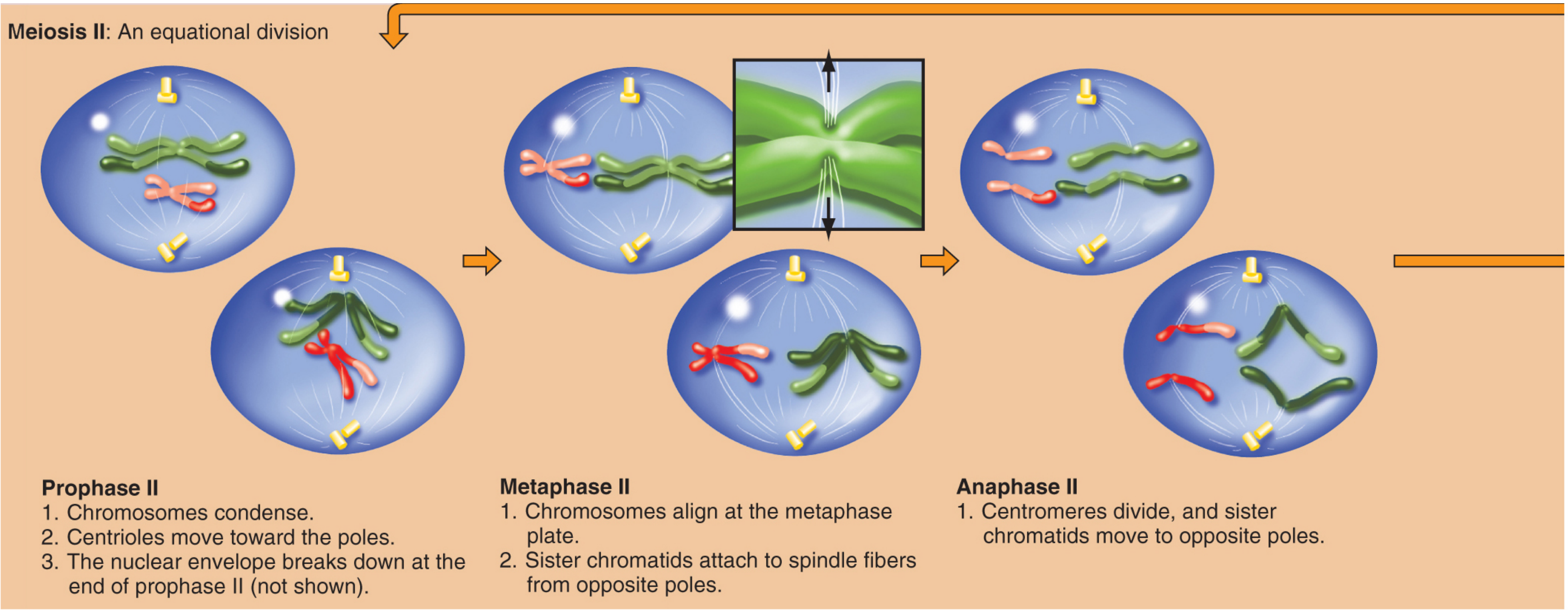
Feature Fig. 4.13

Meiosis I is a reductional division



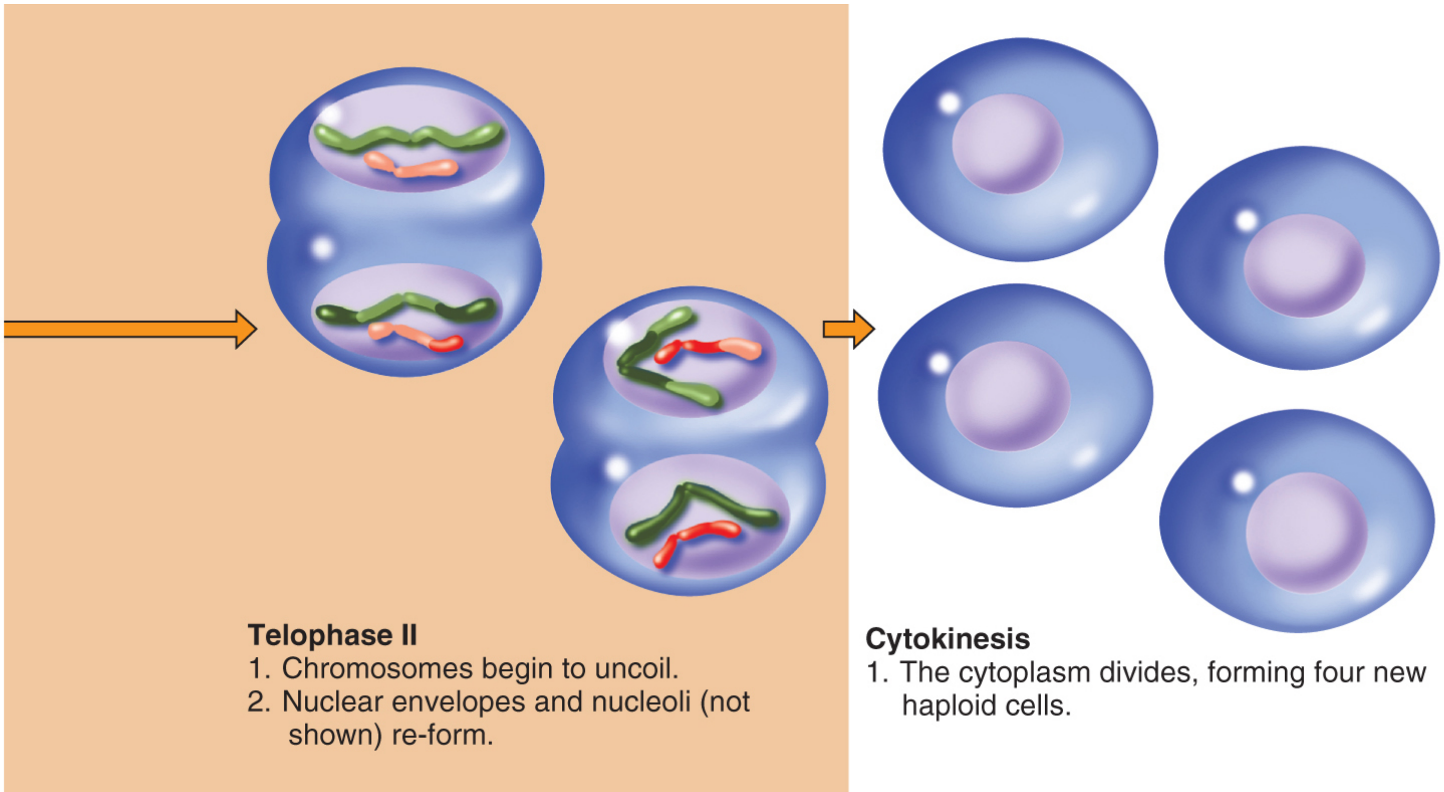
Feature Fig. 4.13

During meiosis II, sister chromatids separate and move to opposite poles



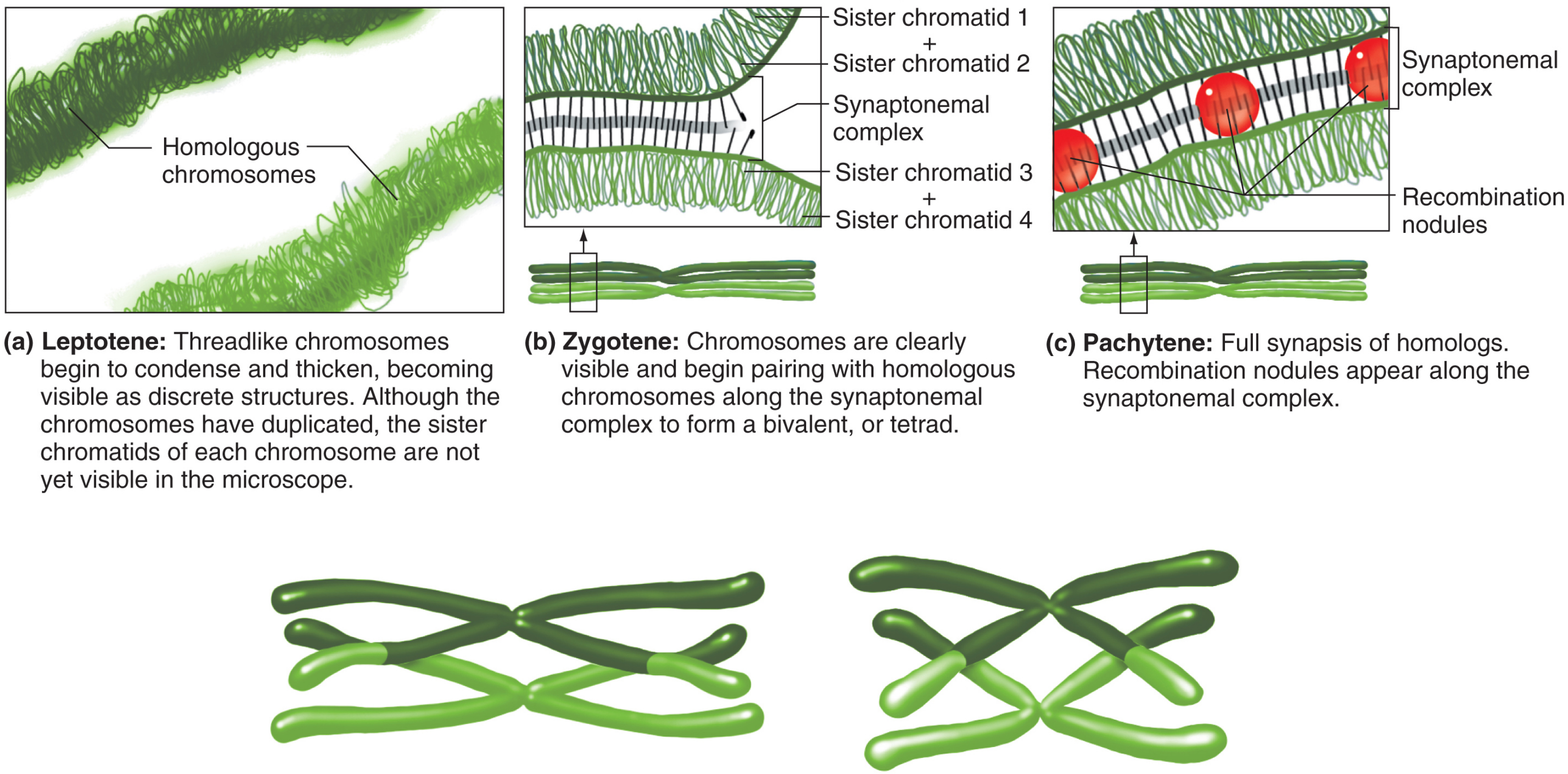
Feature Fig. 4.13

Meiosis II is an equational division



Feature Fig. 4.13

Prophase I of meiosis at very high magnification



(a) Leptotene: Threadlike chromosomes begin to condense and thicken, becoming visible as discrete structures. Although the chromosomes have duplicated, the sister chromatids of each chromosome are not yet visible in the microscope.

(b) Zygotene: Chromosomes are clearly visible and begin pairing with homologous chromosomes along the synaptonemal complex to form a bivalent, or tetrad.

(c) Pachytene: Full synapsis of homologs. Recombination nodules appear along the synaptonemal complex.

(d) Diplotene: Bivalent appears to pull apart slightly but remains connected at crossover sites, called chiasmata.

(e) Diakinesis: Further condensation of chromatids. Nonsister chromatids that have exchanged parts by crossing-over remain closely associated at chiasmata.

Fig. 4.14

Mistakes in meiosis produce defective gametes

Nondisjunction – mistakes in chromosome segregation during meiosis I or II

- May result in inviable gametes or embryos
- Can also result in abnormal chromosome numbers in viable individuals (e.g. trisomy 21, Down syndrome; or XXY, Klinefelter syndrome)

Many hybrids between species (i.e. donkey x horse → mule) are sterile because chromosomes cannot pair properly (hybrid sterility, see Figure 4.15)

Meiosis contributes to genetic diversity in two ways

Independent assortment of nonhomologs creates different combinations of alleles

Crossing-over between homologs creates different combinations of alleles within each chromosome

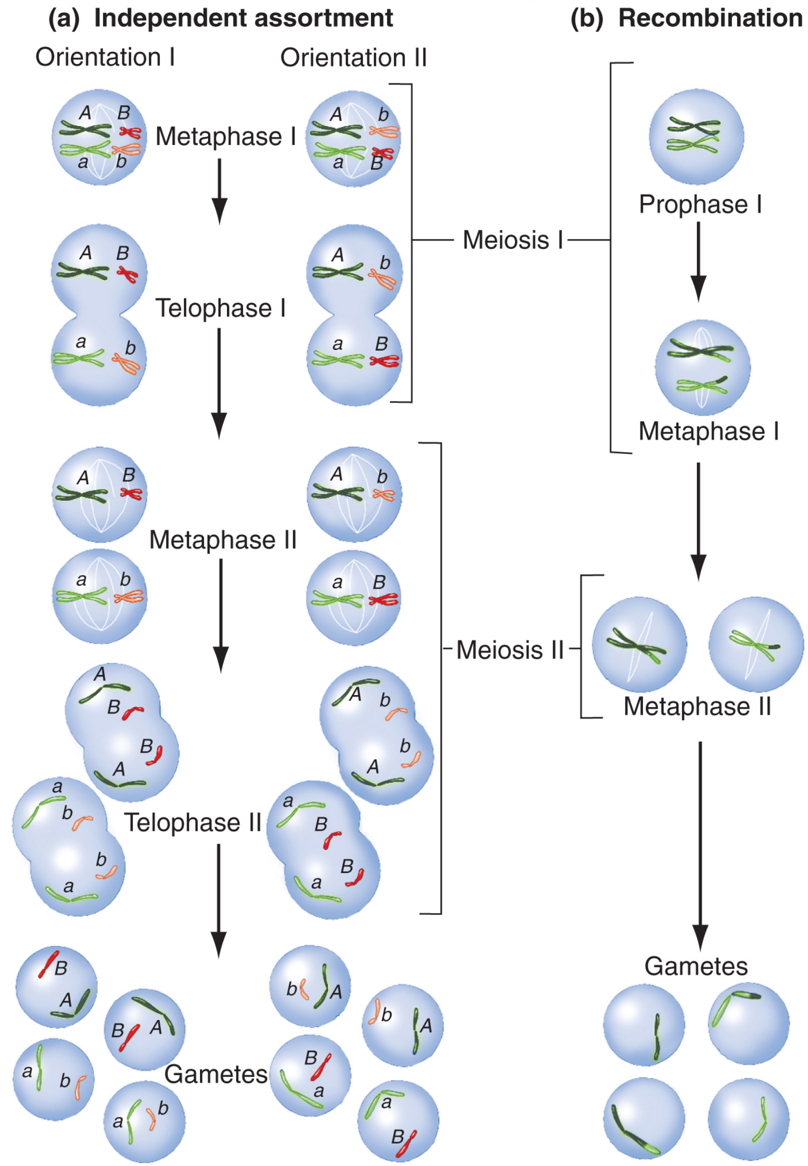


Fig. 4.16

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Comparison of mitosis and meiosis

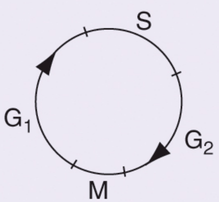
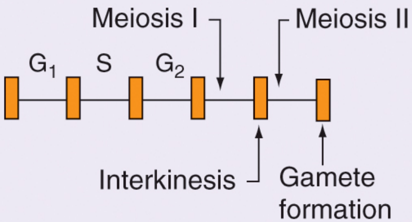
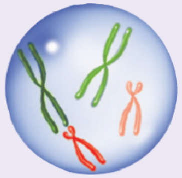
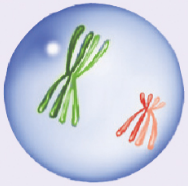
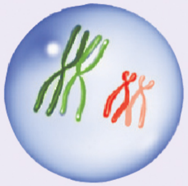
Mitosis	Meiosis
Occurs in somatic cells Haploid and diploid cells can undergo mitosis One round of division	Occurs in germ cells as part of the sexual cycle Two rounds of division, meiosis I and meiosis II Only diploid cells undergo meiosis
 Mitosis is preceded by S phase (chromosome duplication).	 Chromosomes duplicate prior to meiosis I but not before meiosis II.
 Homologous chromosomes do not pair.	 During prophase of meiosis I, homologous chromosomes pair (synapse) along their length.
Genetic exchange between homologous chromosomes is very rare.	 Crossing-over occurs between homologous chromosomes during prophase of meiosis I.

Table 4.3

Comparison of mitosis and meiosis (continued)

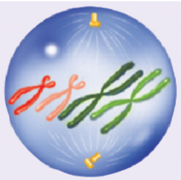
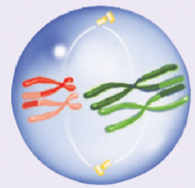
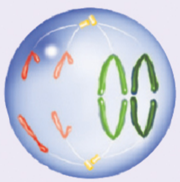
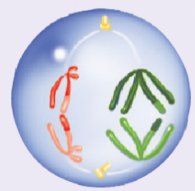
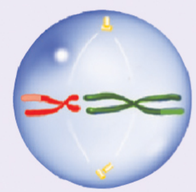
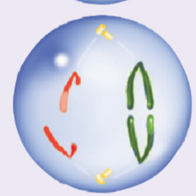
Mitosis		Meiosis	
	Sister chromatids attach to spindle fibers from opposite poles during metaphase.		Homologous chromosomes (not sister chromatids) attach to spindle fibers from opposite poles during metaphase I.
	The centromere splits at the beginning of anaphase.		The centromere does not split during meiosis I.
			Sister chromatids attach to spindle fibers from opposite poles during metaphase II.
			The centromere splits at the beginning of anaphase II.

Table 4.3

CHAPTER OUTLINE

- 4.1 Chromosomes: The Carriers of Genes
- Cell Division
  - 4.2 Mitosis: Cell Division That Preserves Chromosome Number
  - 4.3 Meiosis: Cell Divisions That Halve Chromosome Number
- **4.4 Gametogenesis**
- 4.5 Validation of the Chromosome Theory

Gametogenesis in sexually reproducing animals

Germ line – specialized diploid cells set aside during embryogenesis

Gametogenesis – the formation of gametes

- Involves meiosis as well as specialized events before and after meiosis
- Different types of animals have variations on general aspects of this process
- In humans, oogenesis produces one ovum from each primary oocyte
- In humans, spermatogenesis produces four sperm from each primary spermatocyte

Oogenesis in humans

Oogonia – diploid germ cells in ovaries of female embryos

- Divide by mitosis and enter meiosis I to become primary oocytes
- Primary oocytes arrest in diplotene stage of meiosis I until after birth

At puberty, one oocyte per month resumes meiosis

- At ovulation, completion of meiosis I produces a secondary oocyte and first polar body
- Secondary oocyte arrests in metaphase of meiosis II
- If oocyte is fertilized, meiosis II is completed and produces a mature ovum and second polar body

In humans, egg formation begins in the fetal ovaries and arrests during prophase of meiosis I

One ovum and 2 – 3 nonfunctional polar bodies produced by asymmetrical meiosis

Long meiotic arrest may contribute to chromosome segregation errors (e.g. trisomies)

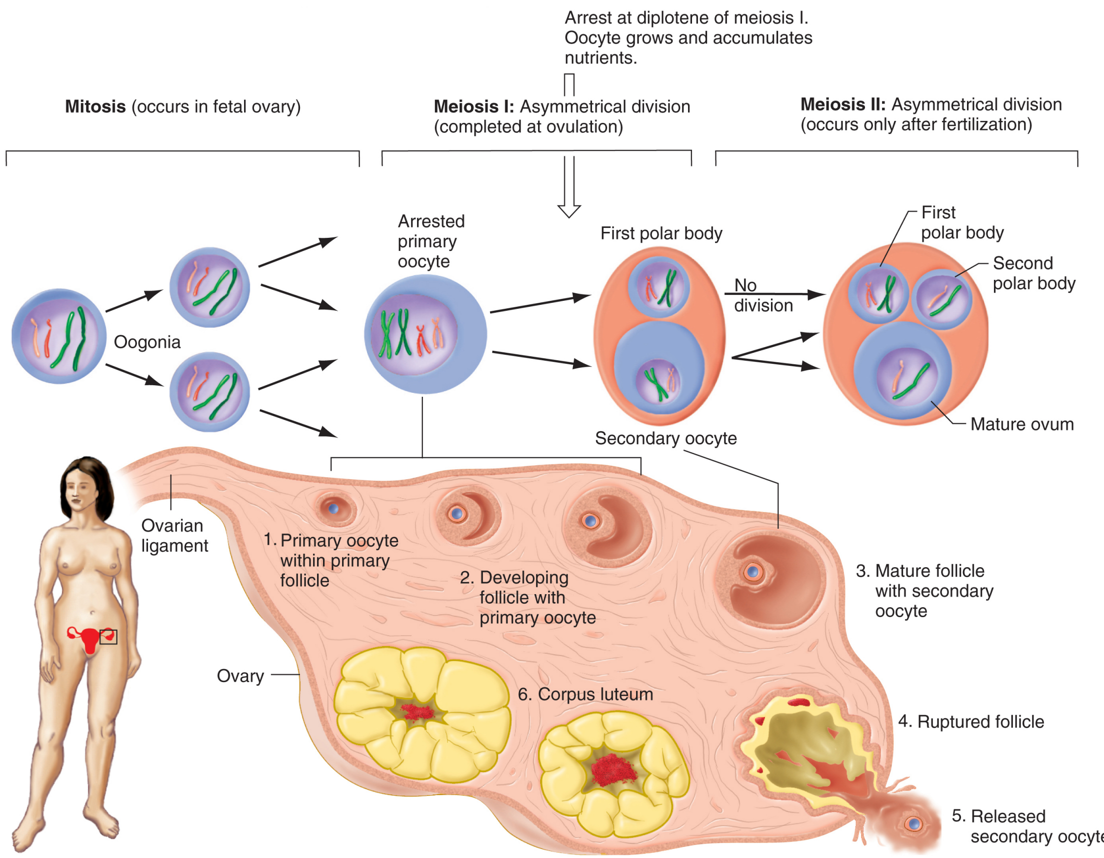


Fig. 4.17

Hartwell et al., 4th ed., Chapter 4

Spermatogenesis in humans

Spermatogonia – diploid germ cells found only in testis

- Divide by mitosis throughout lifespan of individual

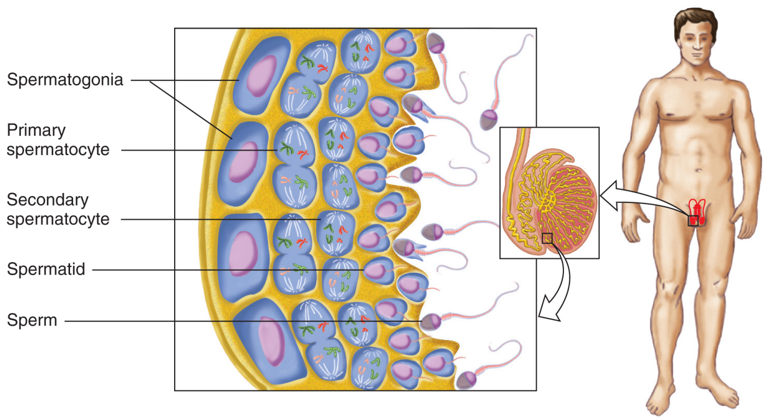
After birth, meiosis begins and spermatogonia become **primary spermatocytes**

- Primary spermatocytes undergo symmetrical division at meiosis I to produce two **secondary spermatoctyes**
- Secondary spermatocytes undergo symmetrical division at meiosis II to produce two **spermatids**
- Spermatids mature to become **sperm**
- Equal numbers of X and Y sperm are produced

Human sperm form continuously in the testes after puberty

Four haploid sperm produced by symmetrical meiosis of each spermatocyte

Mitosis and meiosis occur throughout adult life



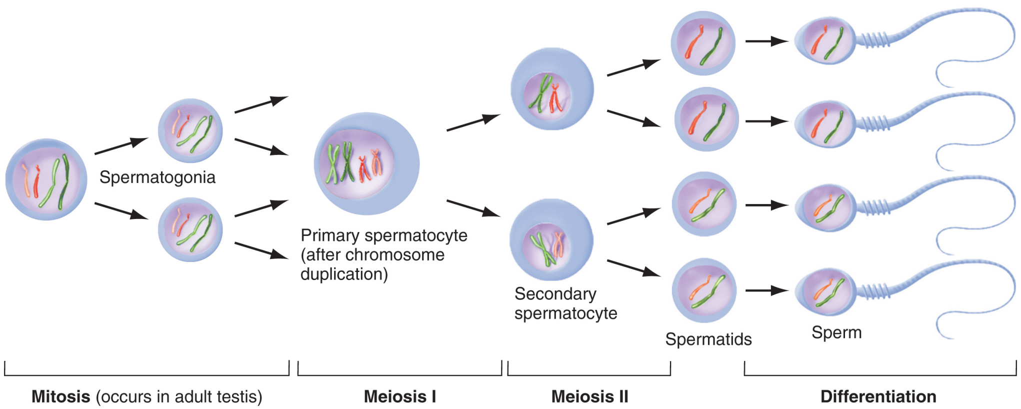


Fig. 4.18

CHAPTER OUTLINE

- 4.1 Chromosomes: The Carriers of Genes
- Cell Division
  - 4.2 Mitosis: Cell Division That Preserves Chromosome Number
  - 4.3 Meiosis: Cell Divisions That Halve Chromosome Number
- 4.4 Gametogenesis
- **4.5 Validation of the Chromosome Theory**

The chromosome theory of inheritance

Walter Sutton – 1903, chromosomes carry Mendel's units of heredity

1. **Two copies of each kind of chromosome**
2. **Chromosome complement is unchanged during transmission to progeny**
3. **Homologous chromosomes separate to different gametes**
4. **Maternal and paternal chromosomes move to opposite poles**
5. **Fertilization of eggs by random encounter with sperm**
6. **In all cells derived from fertilized egg, half of chromosomes are maternal and half are paternal**

How the chromosome theory of inheritance explains Mendel's law of segregation

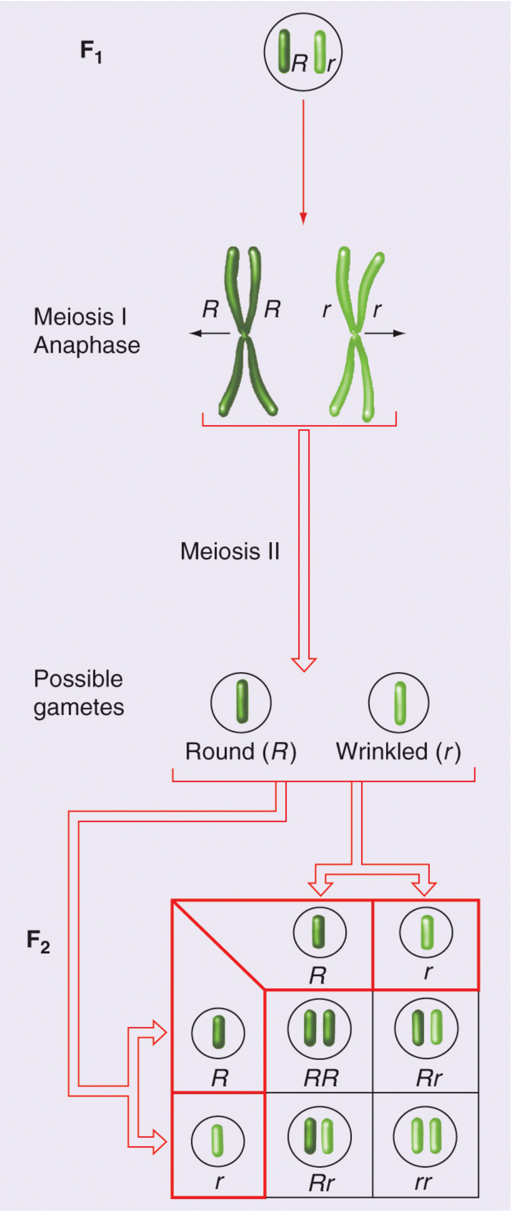


Table 4.4a

How the chromosome theory of inheritance explains Mendel's law of independent assortment

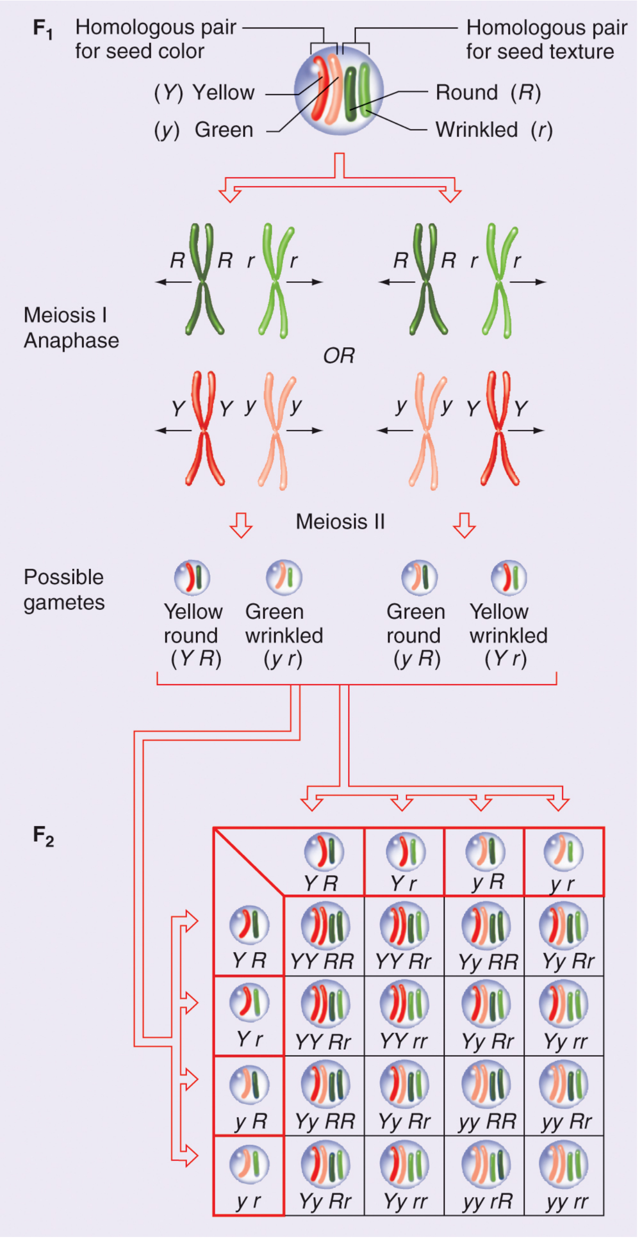


Table 4.4b

Validation of the chromosome theory

Prior to 1910, the chromosome theory of inheritance was supported by two circumstantial lines of evidence

1. Sex determination associates with inheritance of particular chromosomes
2. Events in mitosis, meiosis, and gametogenesis ensure constant numbers of chromosomes in somatic cells

This theory confirmed and validated by:

1. Inheritance of genes and chromosomes correspond in every detail
2. Transmission of particular chromosome coincides with transmission of traits other than for sex determination

The *Drosophila white* gene is located on the X chromosome

T. H. Morgan (1910) discovered a white-eyed *Drosophila* mutant and did a series of crosses

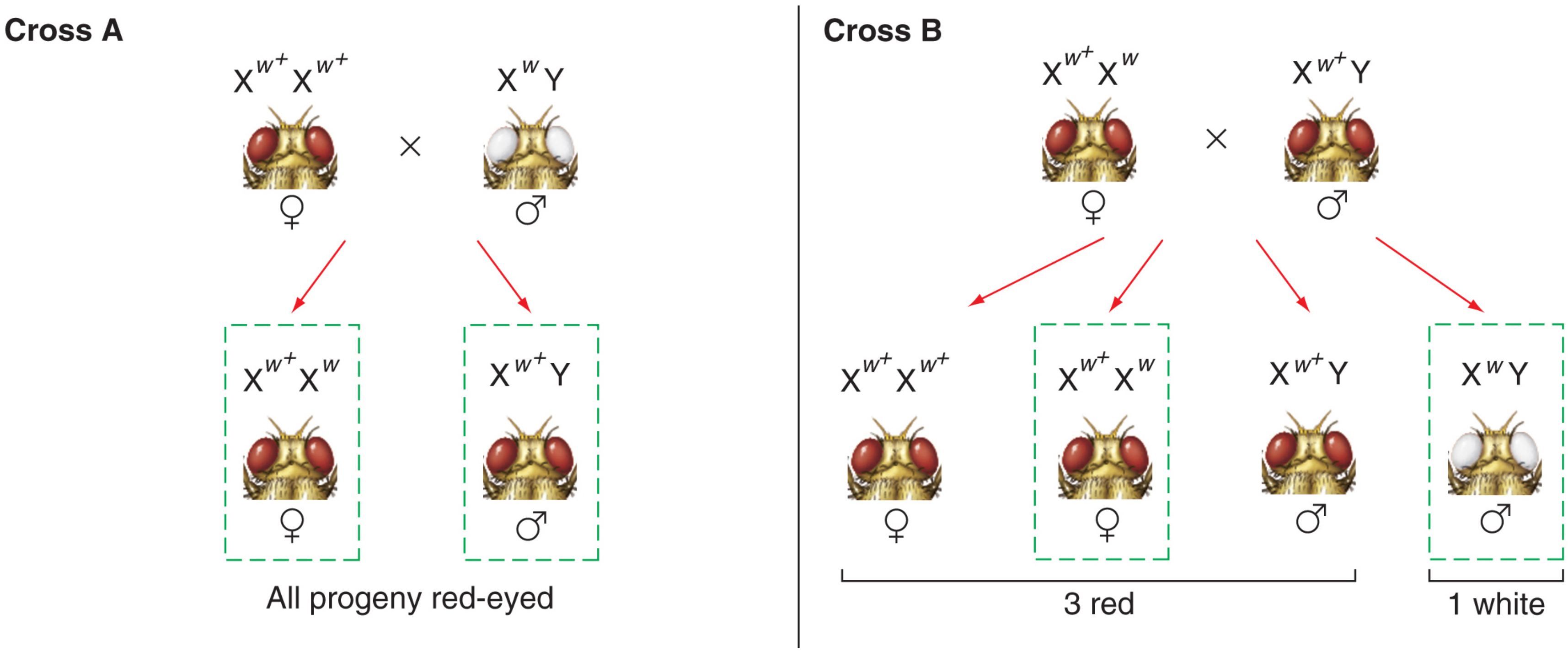


Fig. 4.19

Hartwell et al., 4th ed., Chapter 4

Crisscross inheritance occurs with X-linked recessive traits

See cross D – daughters inherit the phenotype of their fathers, sons inherit the phenotype of their mothers

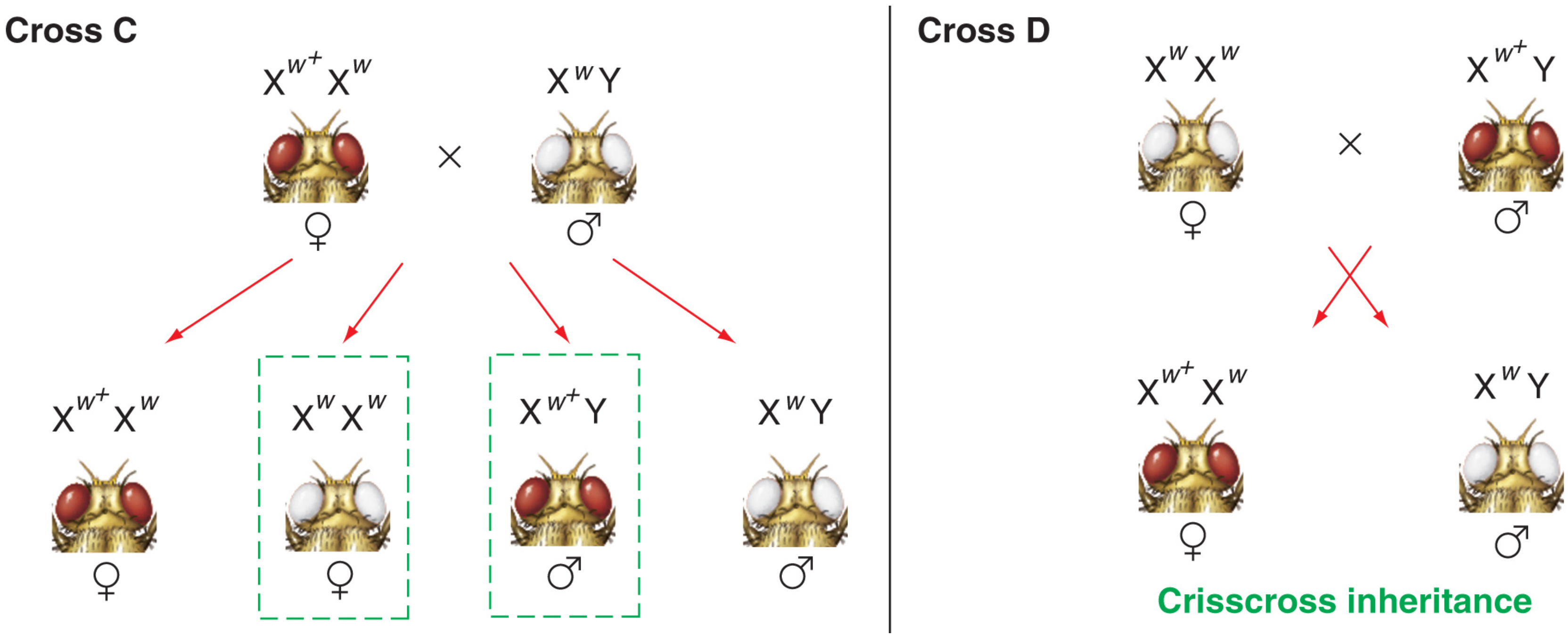


Fig. 4.19

Hartwell et al., 4th ed., Chapter 4

Rare mistakes in meiosis helped confirm the chromosome theory

C. Bridges found 1/2000 male progeny of white females have red eyes

Hypothesized that red-eyed males arise from mistakes in chromosome segregation (nondisjunction) during meiosis in white-eyed females

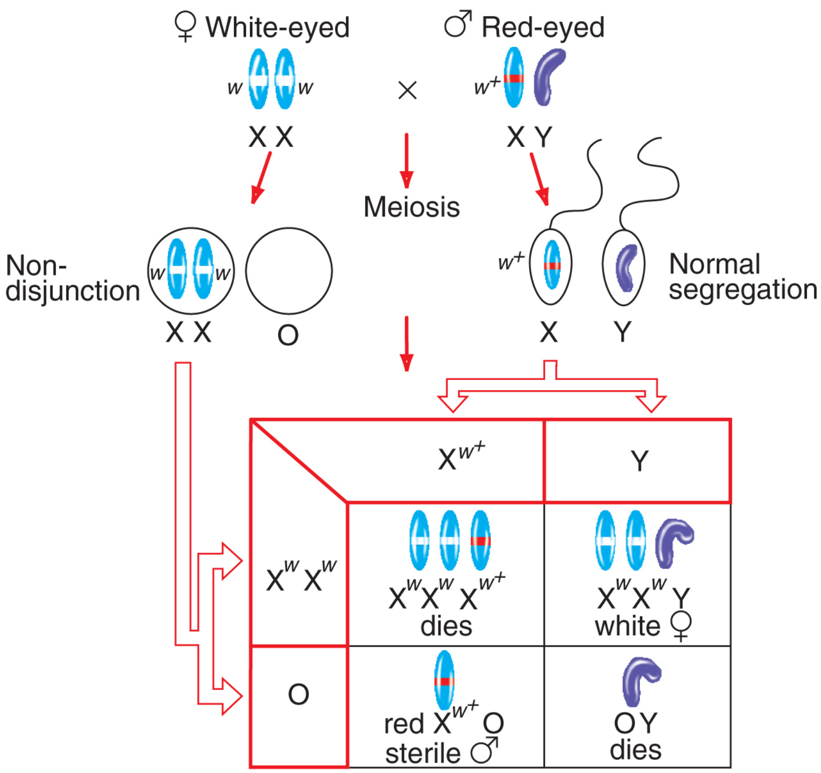


Fig. 4.20a

Hartwell et al., 4th ed., Chapter 4

Rare mistakes in meiosis helped confirm the chromosome theory (cont)

Chromosome segregation in an XXY female

The three sex chromosomes pair and segregate in two ways, producing progeny with unusual sex chromosome complements

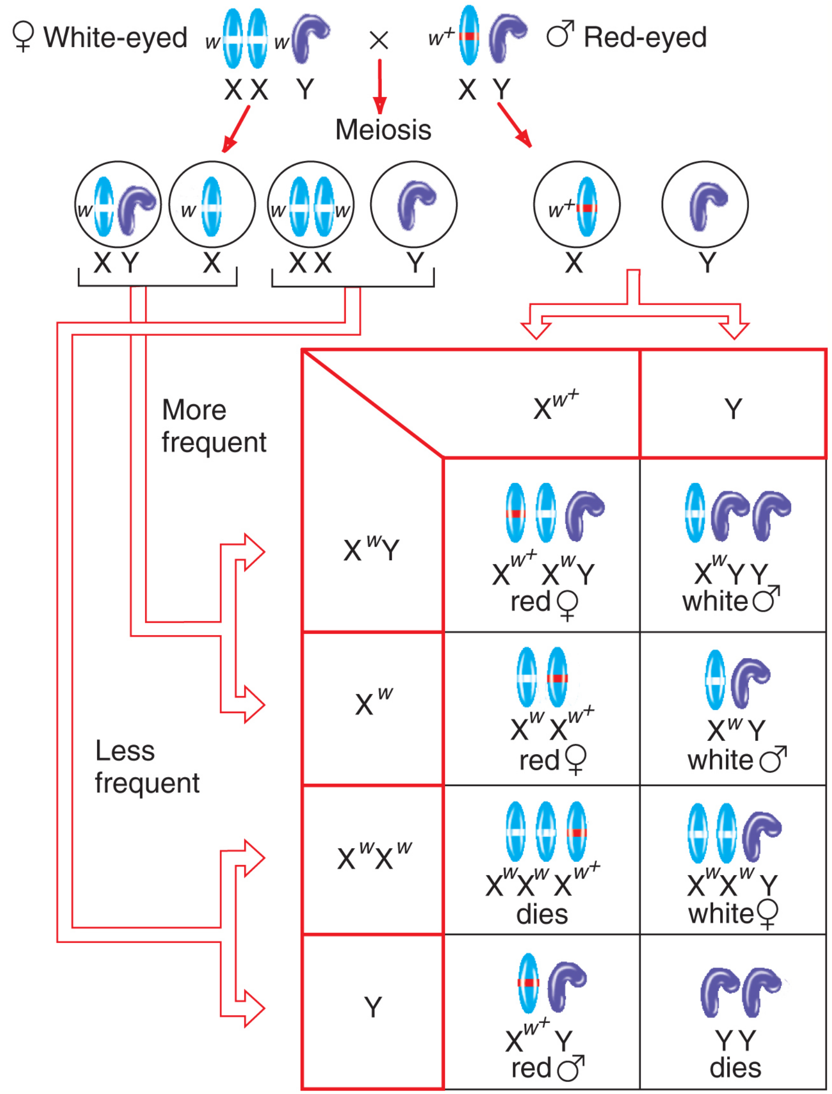


Fig. 4.20b

Example of an X-linked trait in humans

(Top) View of the world to a person with normal color vision

(Bottom) View of the world to a person with red-green colorblindness

E. B. Wilson – 1911, assigned gene for this trait to the X chromosome

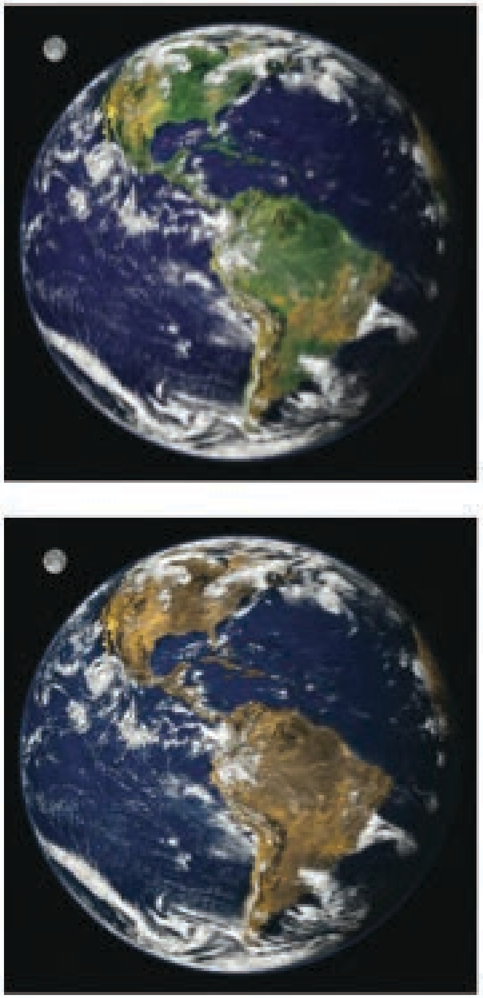


Fig. 4.21

An example of a pedigree for an X-linked recessive trait: Hemophilia

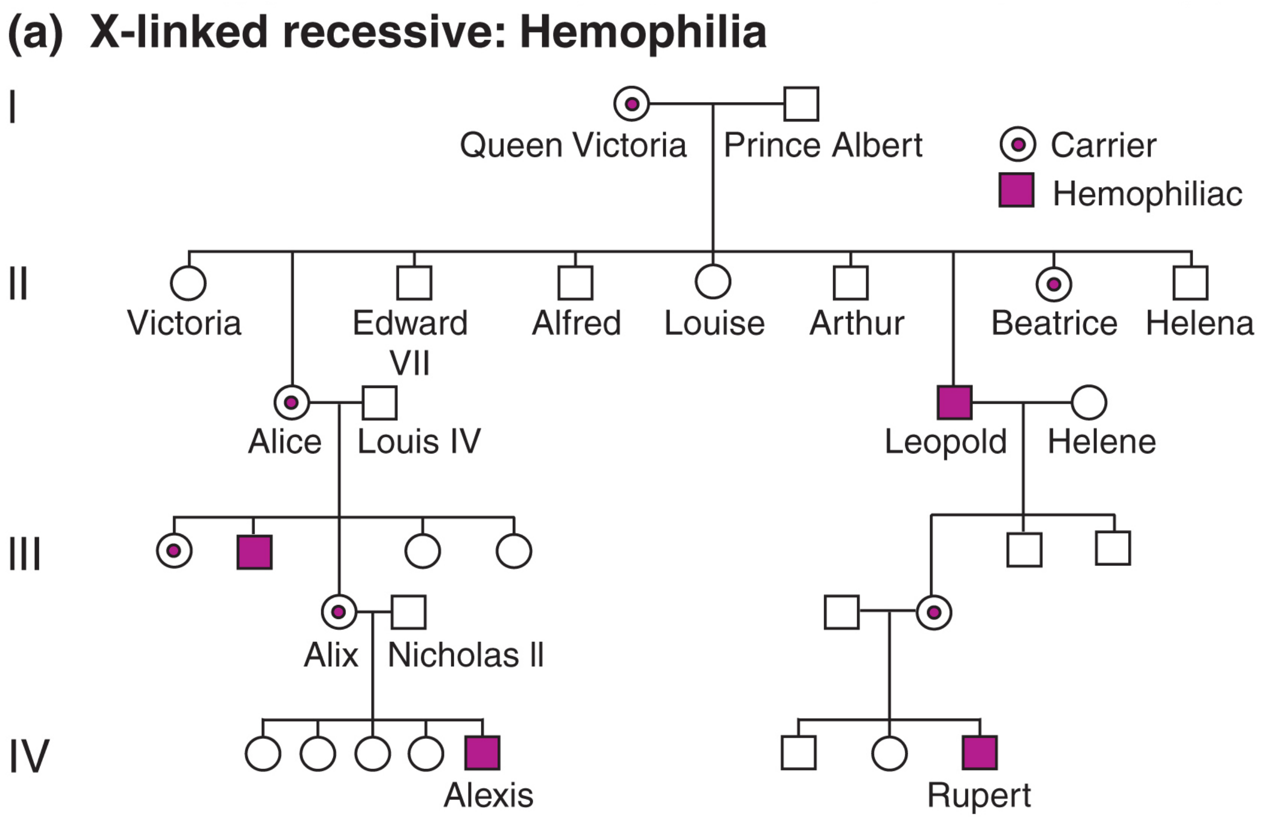


Fig. 4.22a

Chapter 4 Review Questions