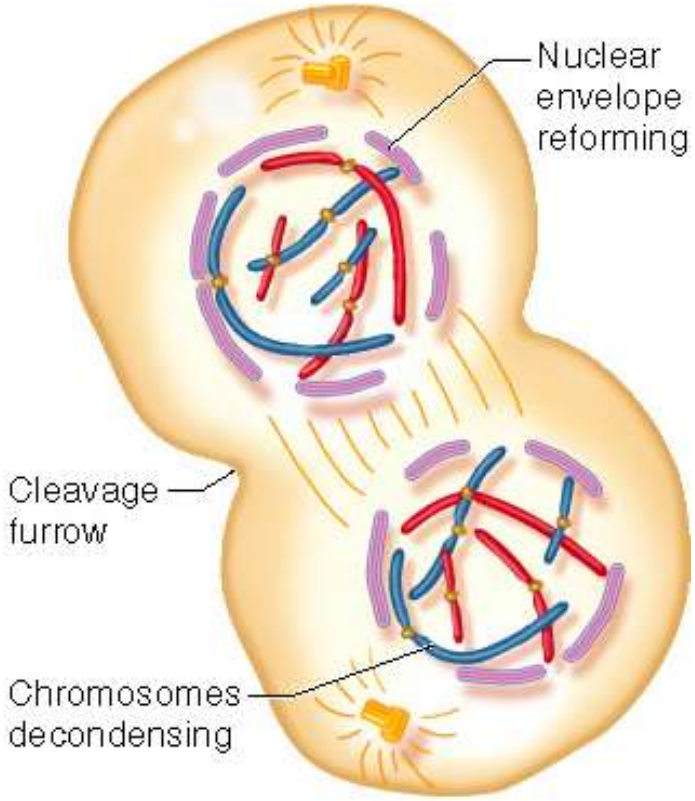
REPRODUCTION AND CHROMOSOME TRANSMISSION



INTRODUCTION

- In this chapter we will survey reproduction at the level of chromosomes (cellular level) rather than at the molecular level
- Chromosomes are large enough to be visible by light microscopy
  - This examination provides us with insights to understand the inheritance patterns of traits

3.1 GENERAL FEATURES OF CHROMOSOMES

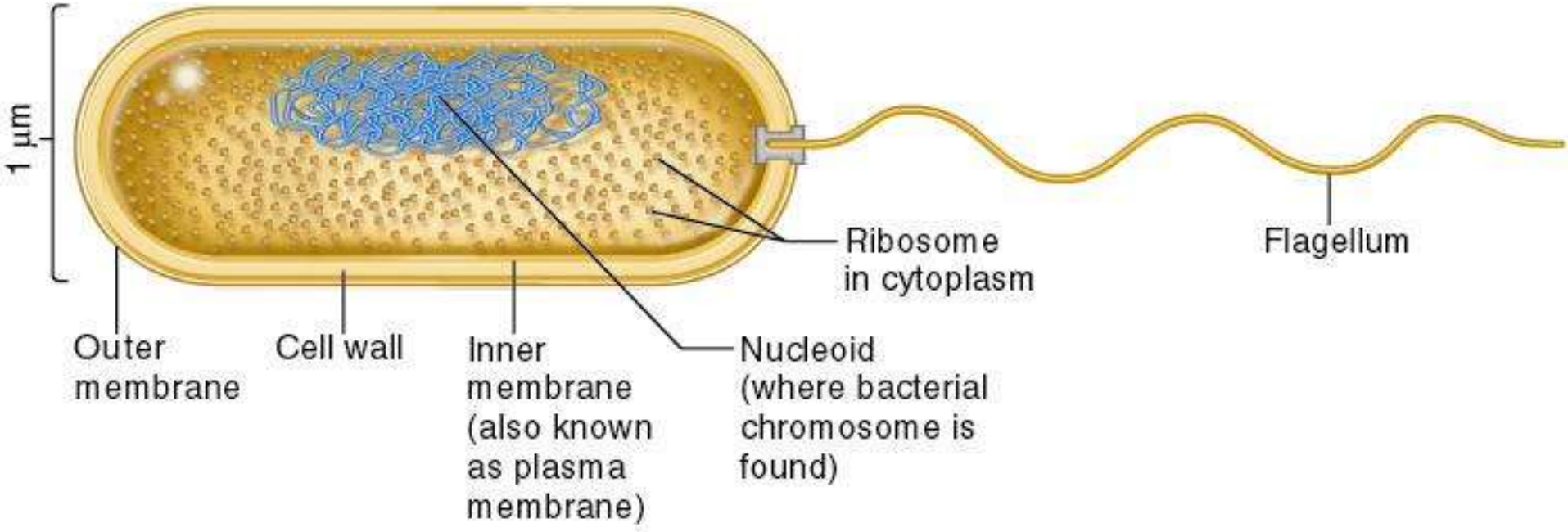
- Chromosomes are structures within living cells that contain the genetic material
  - They contain the genes
- Biochemically, chromosomes are composed of
  - DNA, which is the genetic material
  - Proteins, which provide an organized structure for carrying and transmitting the genes to daughter cells

3.1 GENERAL FEATURES OF CHROMOSOMES

- First, let's review the distinctive cellular differences between the two types of cells
  - 1. Prokaryotes
  - 2. Eukaryotes

- Prokaryotes
  - Do not contain a nucleus
  - Usually contain a single type of circular chromosome
    - Found in the nucleoid
  - Contain a cell membrane
    - For nutrient uptake and waste excretion
  - Contain a rigid cell wall
    - For protection
  - May contain other structures
    - Outer membrane
    - Flagella

Figure 3.1 (a) Bacterial cell



This example is typical of bacteria such as *Escherichia coli*, which has an outer membrane and flagella.

- Eukaryotes
  - Have a nucleus
    - Contains two or more linear chromosomes
  - Have membrane-bounded organelles with specific functions
    - These include
    - Mitochondria
      - Play a role in ATP synthesis
      - Contain their own DNA
    - Lysosomes
      - Play a role in degradation of macromolecules
    - ER/Golgi apparatus
      - Plays a role in protein modification and trafficking

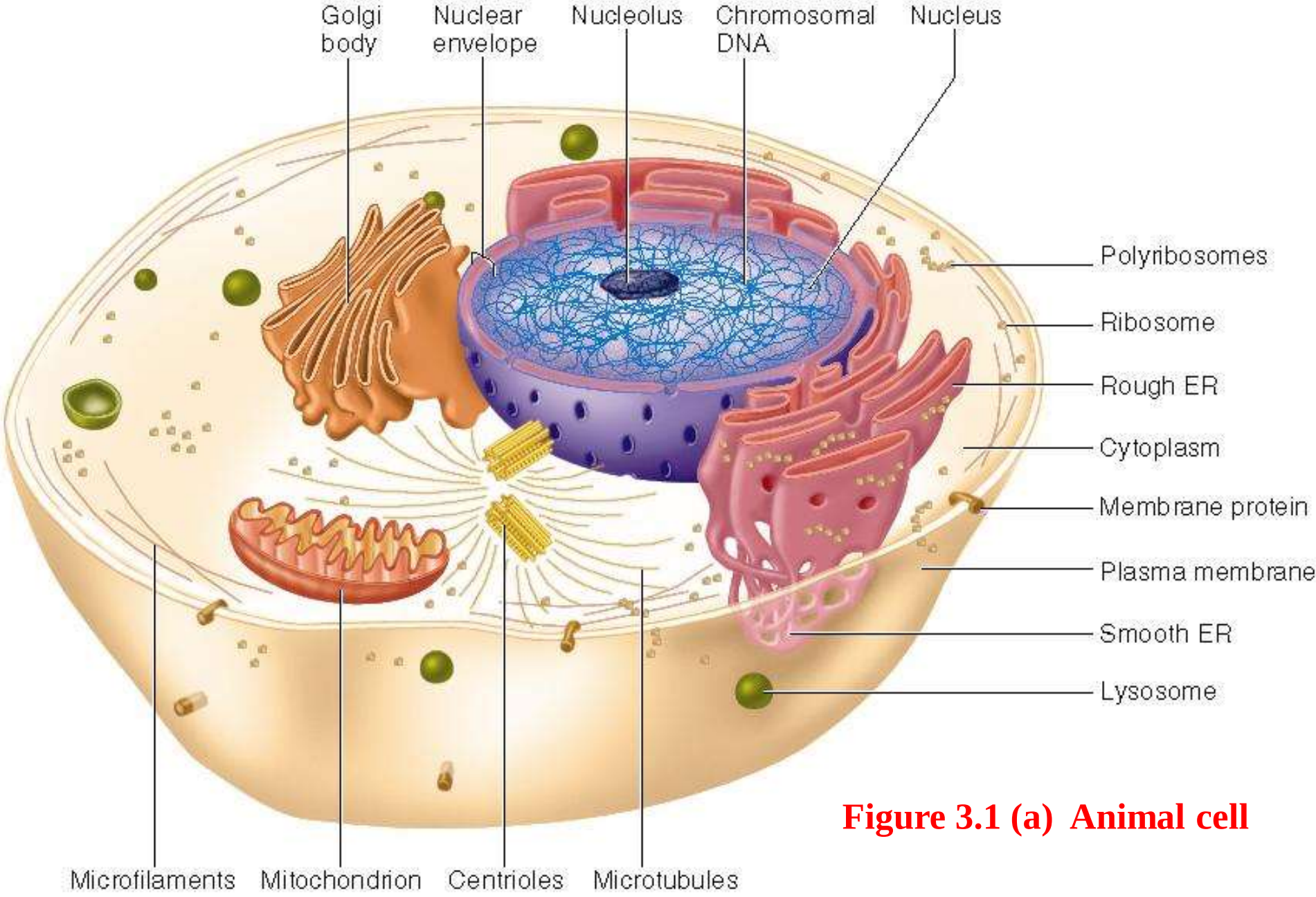


Figure 3.1 (a) Animal cell

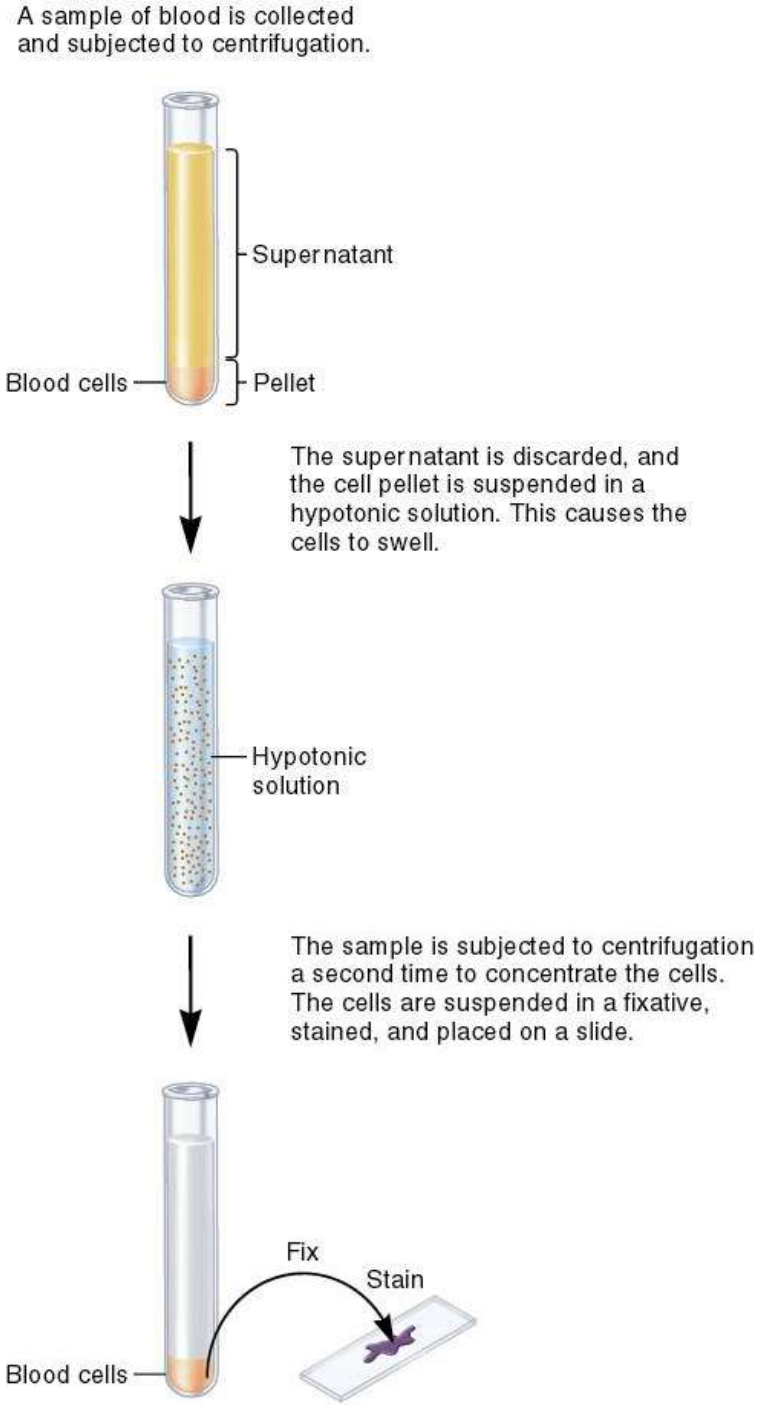
Cytogenetics

- The field of genetics involves the microscopic examination of chromosomes and their behavior
- A cytogeneticist typically examines the chromosomal composition of a particular cell or organism
  - This allows the detection of individuals with abnormal chromosome number or structure
  - This also provides a way to distinguish between two closely-related species

Cytogenetics

- Animal cells are of two types
  - Somatic cells
    - Body cells, other than gametes
      - Blood cells, for example
  - Germ cells
    - Gametes
      - Sperm and egg cells
- Figure 3.2 shows the general procedure for viewing chromosomes from a eukaryotic (somatic) cell

Figure 3.2


A sample of blood is collected and subjected to centrifugation.
Supernatant
Blood cells
Pellet
The supernatant is discarded, and the cell pellet is suspended in a hypotonic solution. This causes the cells to swell.
Hypotonic solution
The sample is subjected to centrifugation a second time to concentrate the cells. The cells are suspended in a fixative, stained, and placed on a slide.
Fix
Stain
Blood cells

Cytogenetics

- In a cytogenetics laboratory, the microscopes are equipped with a camera
- Microscopic images can now be scanned into a computer
- There, the chromosomes in the images can be organized in a standard way, usually from largest to smallest
- A karyotype is the photographic representation of the chromosomes within a cell
- Refer to Figure 3.2

Eukaryotic Chromosomes Are Inherited in Sets

- Most eukaryotic species are diploid
  - Have two complete sets of chromosomes
- For example
  - Humans
    - 46 total chromosomes (23 per set)
  - Dogs
    - 78 total chromosomes (39 per set)
  - Fruit fly
    - 8 total chromosomes (4 per set)

Eukaryotic Chromosomes Are Inherited in Sets

- Members of a pair of chromosomes are called homologues
  - The two homologues form a homologous pair
- The two chromosomes in a homologous pair
  - Are nearly identical in size
  - Have the same banding pattern and centromere location
  - Have the same genes
    - But not necessarily the same alleles

Eukaryotic Chromosomes Are Inherited in Sets

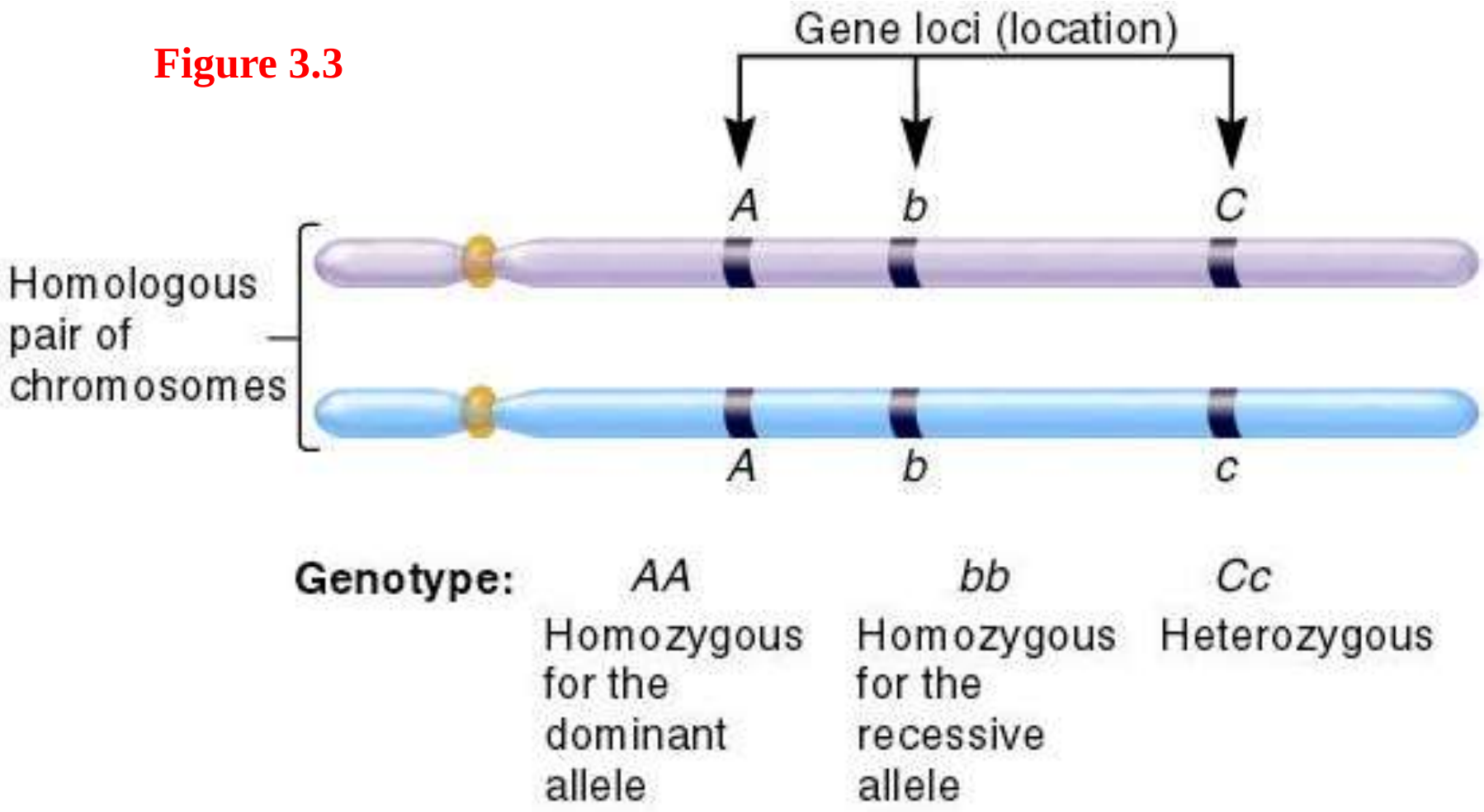
- The DNA sequences on homologous chromosomes are also very similar
  - There is usually less than 1% difference between homologues (on average, about 0.1%)
- Nevertheless, these slight differences in DNA sequence provide the allelic differences in genes
  - Eye color gene
    - Blue allele *vs* brown allele

Eukaryotic Chromosomes Are Inherited in Sets

- The sex chromosomes (X and Y) are not strictly homologous, though they behave as homologues during meiosis
  - They differ in size and genetic composition
- They do have short regions of homology, especially at the tips
- Figure 3.3 considers two homologous chromosomes labeled with 3 different genes

The physical location of a gene on a chromosome is called its locus.

Figure 3.3



3.2 CELLULAR DIVISION

- One purpose of cell division is asexual reproduction
  - This is the means by which some unicellular organisms produce the next generation of the organism
  - Examples
    - Bacteria
    - Amoeba
    - Yeast
      - *Saccharomyces cerevisiae* (Baker's yeas

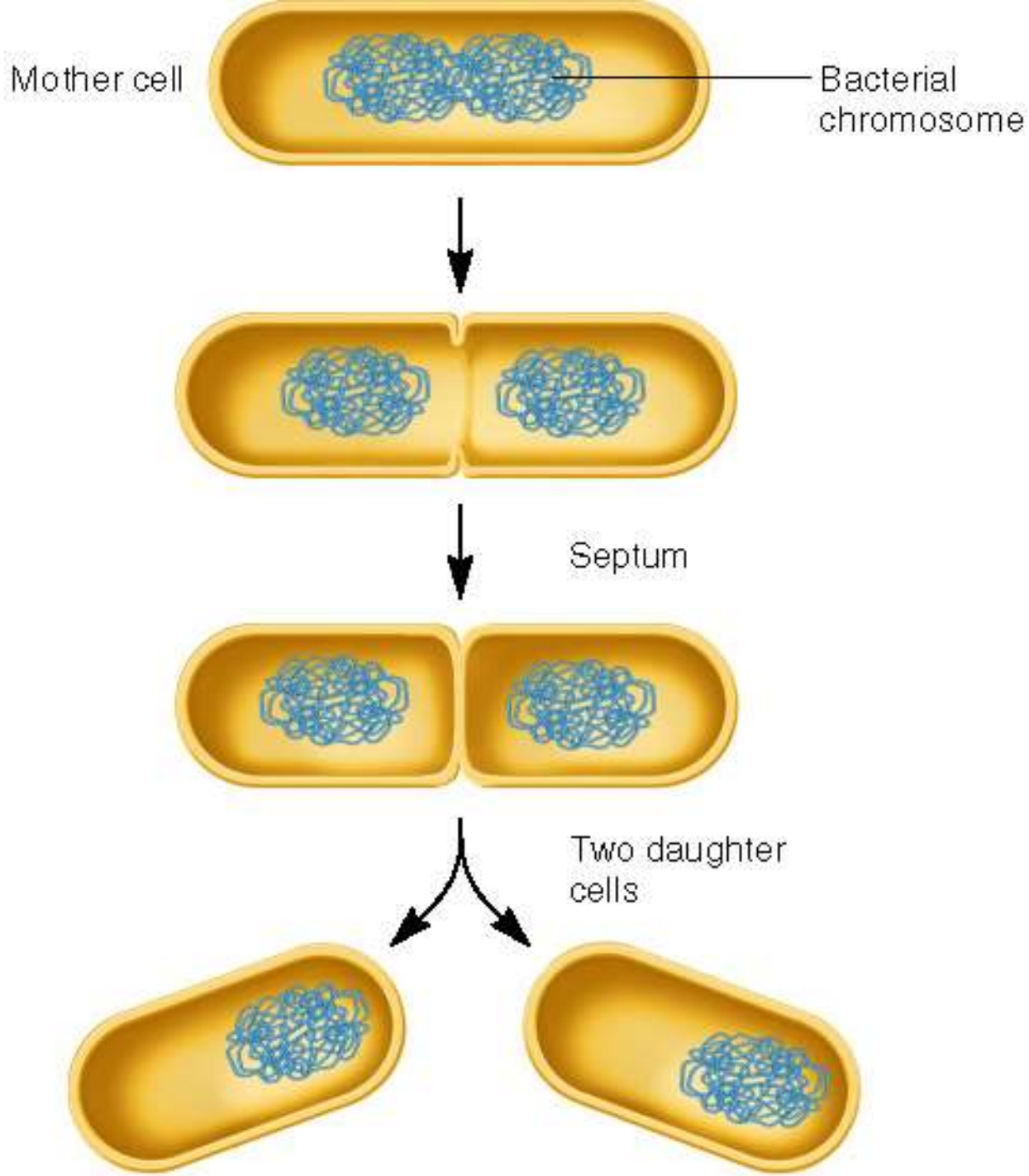
3.2 CELLULAR DIVISION

- A second purpose for asexual reproduction is to produce multi-celled organisms and to enable these organisms to grow and repair damaged tissue
  - Plants, animals and certain fungi are derived from a single cell that has undergone repeated asexual cell divisions
  - For example
    - Humans start out as a single fertilized egg
    - End up as an adult with several trillion cells

Prokaryotes Reproduce Asexually by Binary Fission

- The capacity of bacteria to divide is really quite astounding
  - *Escherichia coli*, for example, can divide every 20 minutes
- Prior to division, the bacterial cell replicates its chromosome
- Then the cell divides into two daughter cells by a process termed binary fission

Figure 3.4


Mother cell
Bacterial chromosome
Septum
Two daughter cells

Prokaryotes Reproduce Asexually by Binary Fission

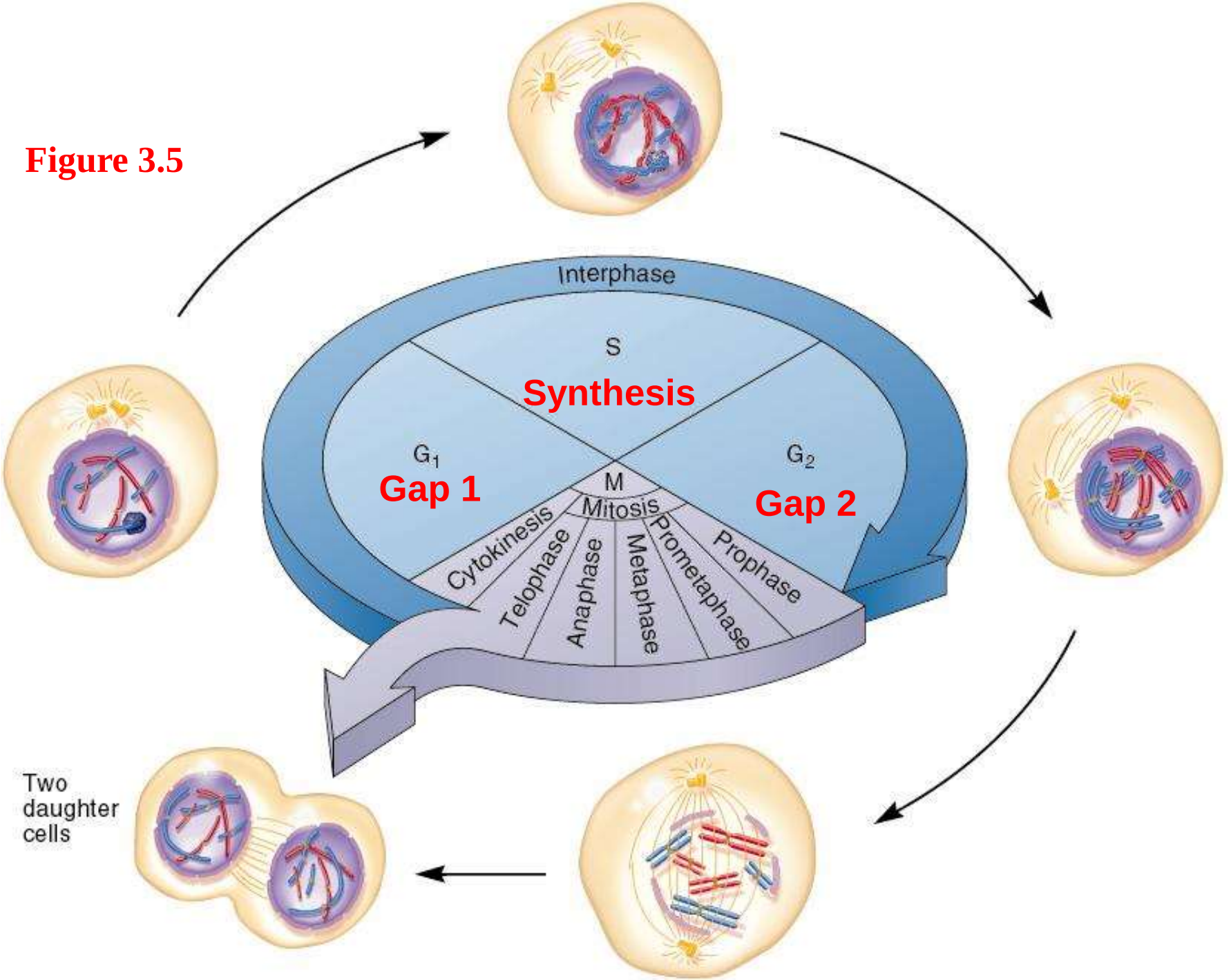
- Binary fission does not involve genetic contributions from two different gametes; it’s just nature’s way of cloning bacterial cells

MITOSIS

- Asexual cell division in eukaryotes requires a replication and sorting process that is more complicated than simple binary fission

- Eukaryotic cells that are destined to divide progress through a series of stages known as the cell cycle
  - Refer to Figure 3.5

Figure 3.5


Interphase
S
Synthesis
G1
Gap 1
G2
Gap 2
M
Mitosis
Prophase
Prometaphase
Metaphase
Anaphase
Telophase
Cytokinesis
Two daughter cells

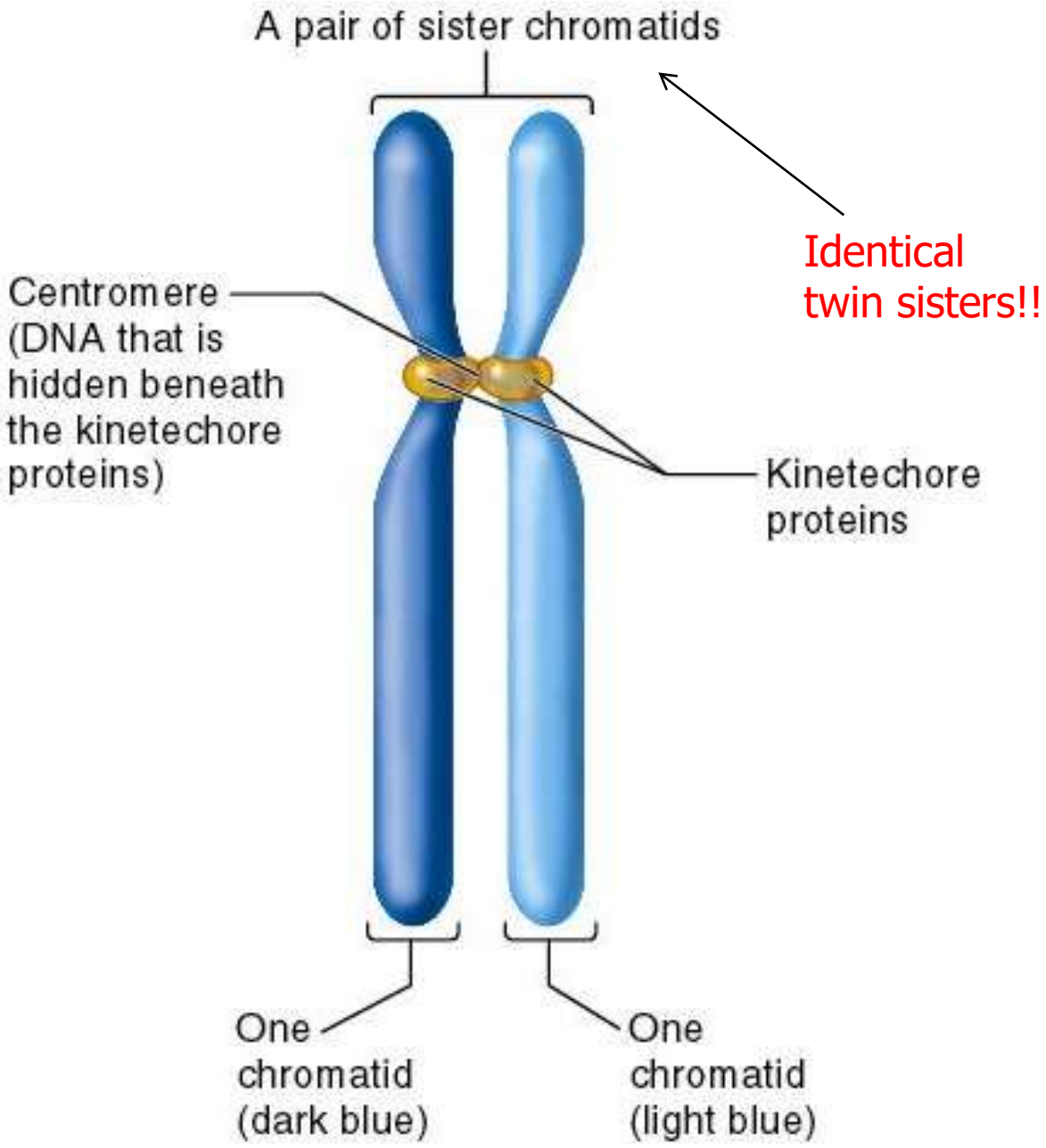
MITOSIS

- G_1, S and G_2 are collectively known as interphase
- A cell may remain for long periods of time in the G_0 phase
  - A cell in this phase has
    - Either postponed making a decision to divide
    - Or made the decision to never divide again
      - Terminally differentiated cells (e.g. nerve cells)

MITOSIS

- During the G_1 phase, a cell prepares to divide
- The cell reaches a restriction point and is committed on a pathway to cell division
- Then the cell advances to the S phase, where chromosomes are replicated
  - The two copies of a replicated chromosome are termed chromatids
  - They are joined at the centromere to form a pair of sister chromatids

Figure 3.6 (b)


A pair of sister chromatids
Identical twin sisters!!
Centromere (DNA that is hidden beneath the kinetechore proteins)
Kinetechore proteins
One chromatid (dark blue)
One chromatid (light blue)

- Note that at the end of S phase, a cell has twice as many chromatids as there are chromosomes in the G_1 phase
  - A human cell for example has
    - 46 distinct chromosomes in G_1 phase
    - 46 pairs of sister chromatids in S phase
- Therefore the term *chromosome* is relative
  - In G_1 and late in the M phase, it refers to the equivalent of one chromatid
  - In G_2 and early in the M phase, it refers to a pair of sister chromatids

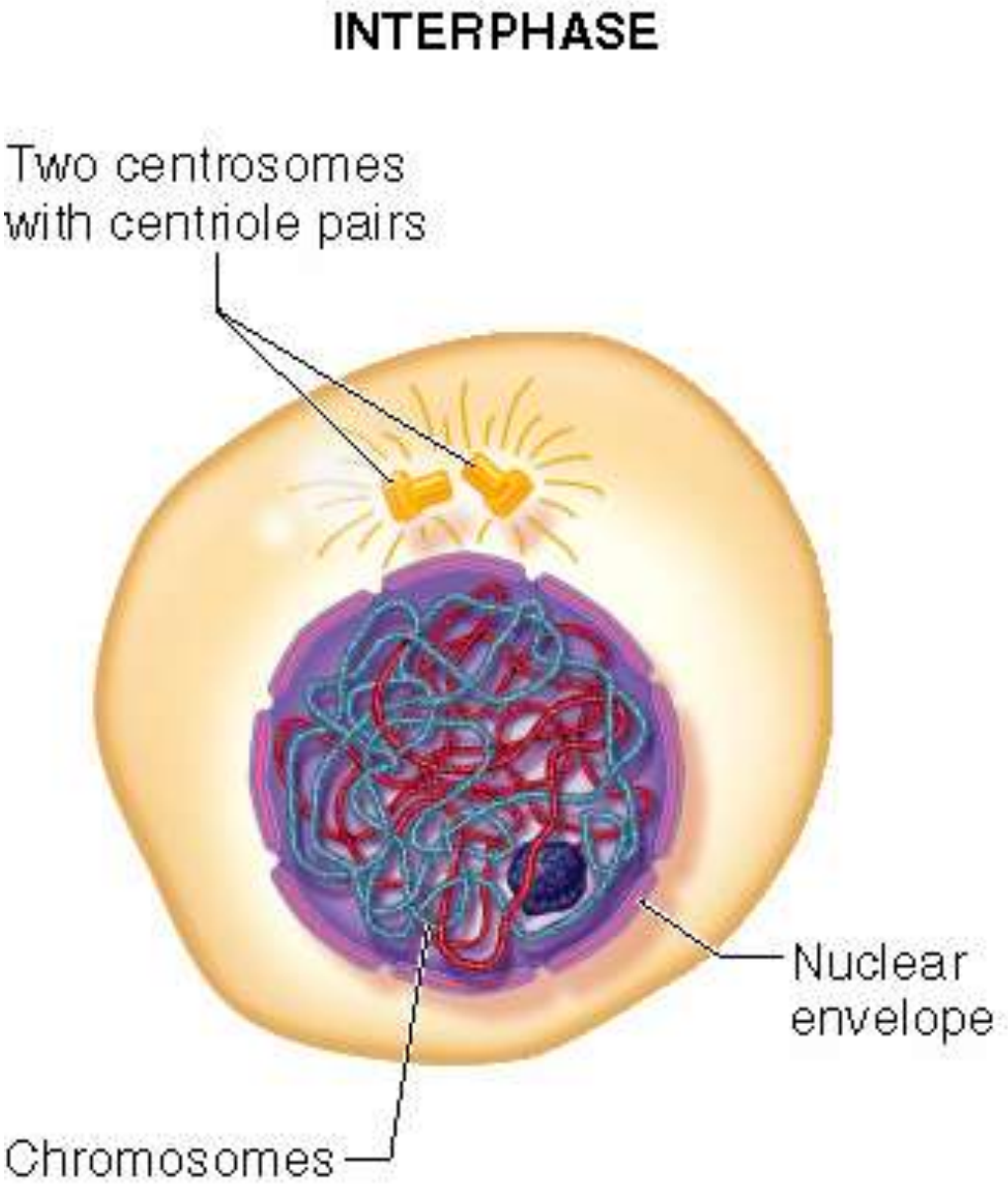
- During the G_2 phase, the cell accumulates the materials that are necessary for nuclear and cell division
- It then progresses into the M phase of the cycle where mitosis occurs
- The primary purpose of mitosis is to distribute the replicated chromosomes to the two daughter cells
  - In humans for example,
    - The 46 pairs of sister chromatids are separated and sorted
    - Each daughter cell thus receives 46 chromosomes

- Mitosis was first observed microscopically in the 1870s by the German biologist, Walter Flemming
  - He coined the term *mitosis*
    - From the Greek *mitos,* meaning thread
- The process of mitosis is shown in Figure 3.7
- The original mother cell is diploid (2n)
  - It contains a total of six chromosomes
  - Three per set (n = 3)
    - One set is shown in blue and the homologous set in red

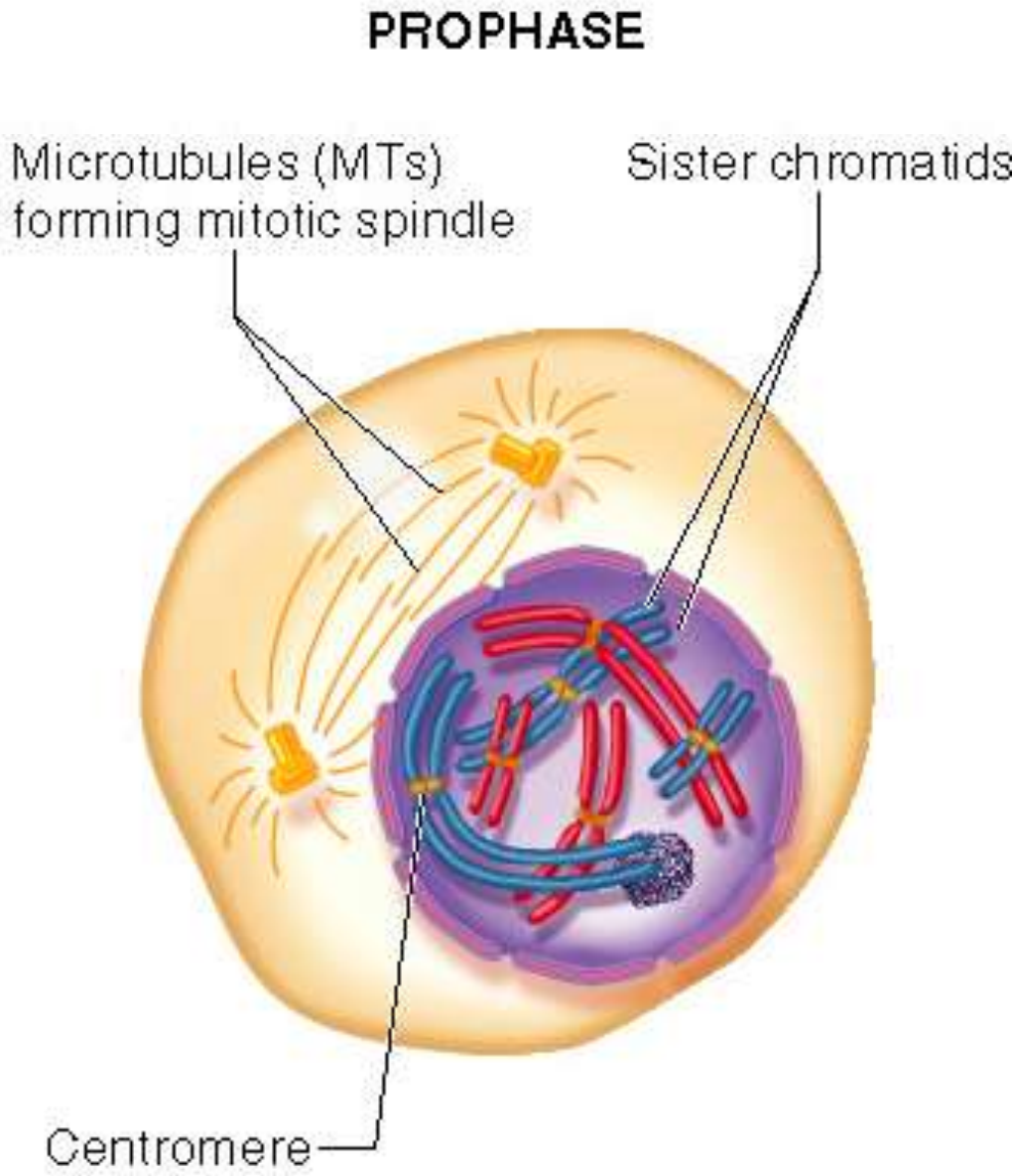
- Mitosis is subdivided into five phases
  - Prophase
  - Prometaphase
  - Metaphase
  - Anaphase
  - Telophase

- Refer to Figure 3.7

- Chromosomes are decondensed
- By the end of this phase, the chromosomes have already replicated
  - But the six pairs of sister chromatids are not seen until prophase
- The centrosome divides



- Nuclear envelope dissociates into smaller vesicles
- Centrosomes separate to opposite poles
- The mitotic spindle apparatus is formed
  - Composed of mircotubules (MTs)



- Microtubules are formed by rapid polymerization of tubulin proteins

- There are three types of spindle microtubules
  - 1. Aster microtubules
    - Important for positioning of the spindle apparatus
  - 2. Polar microtubules
    - Help to “push” the poles away from each other
  - 3. Kinetochore microtubules
    - Attach to the kinetochore , which is bound to the centromere of each individual chromosome
  - Refer to Figure 3.8

Contacts the centromere

Contacts the other two

Contacts the kinetochore microtubule

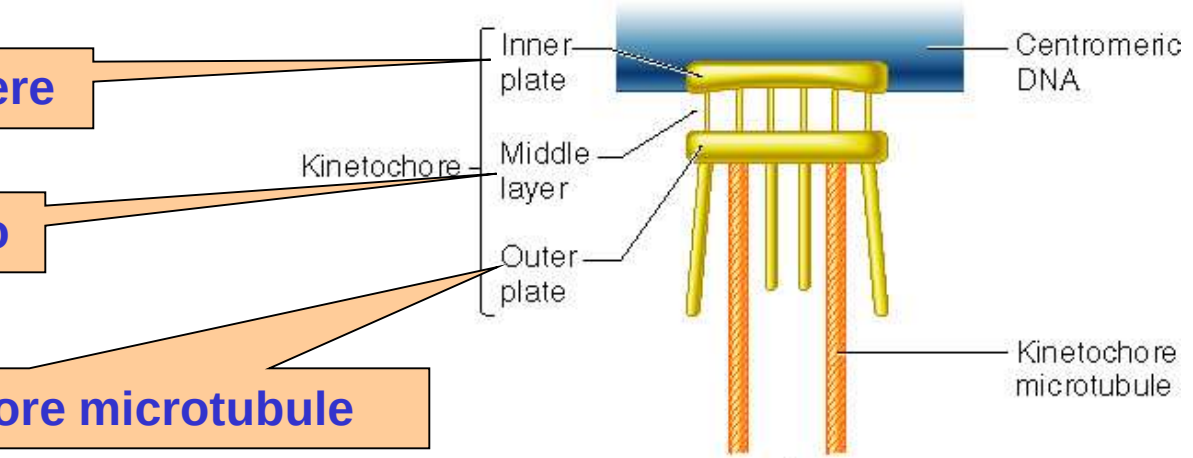
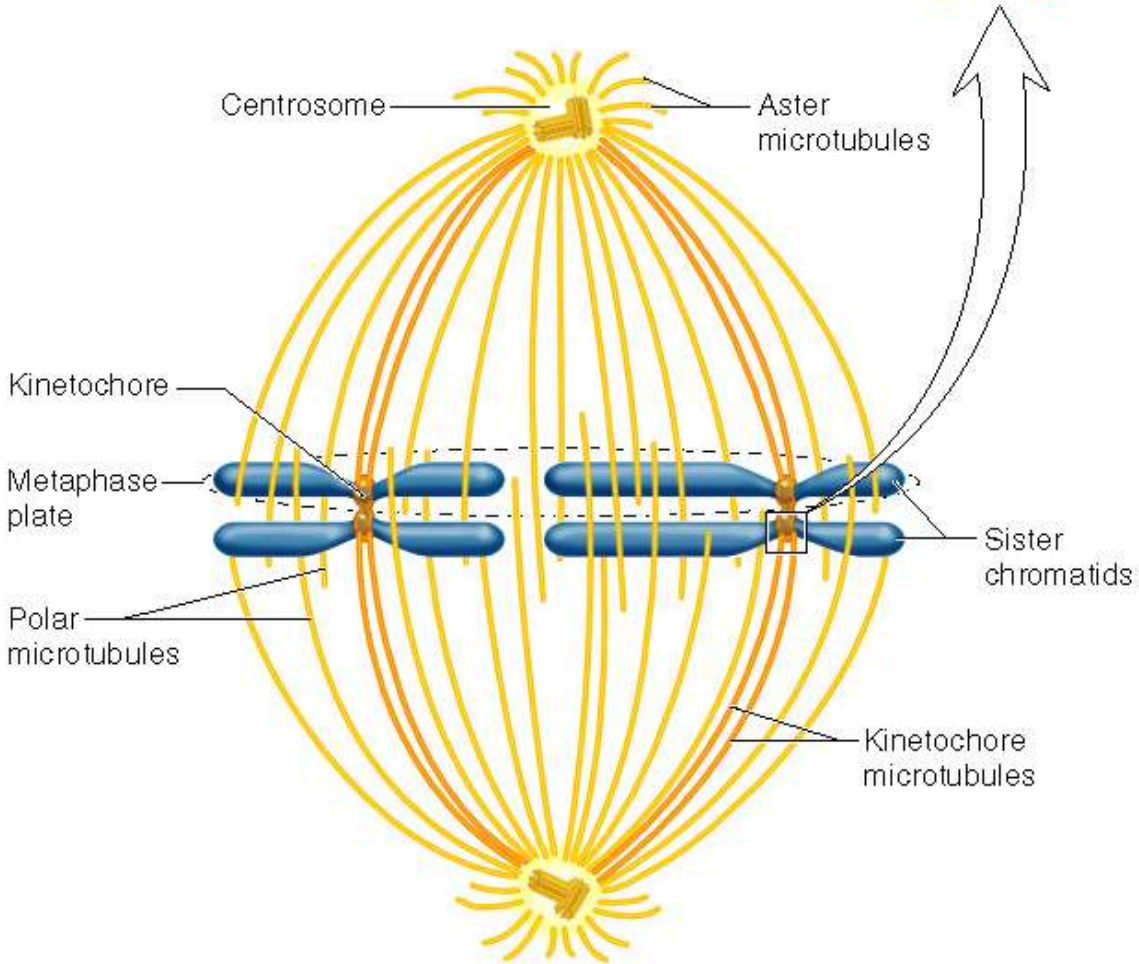
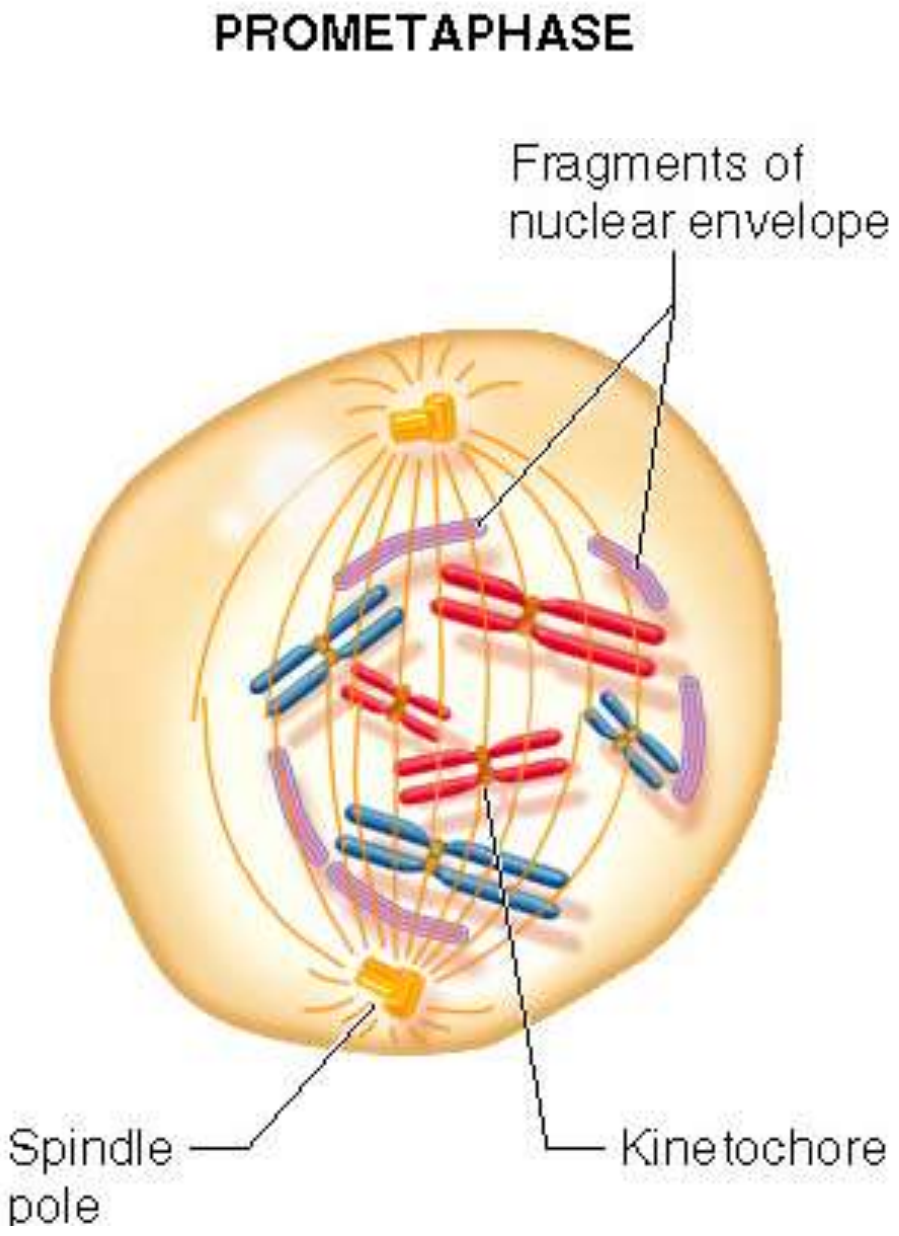


Figure 3.8



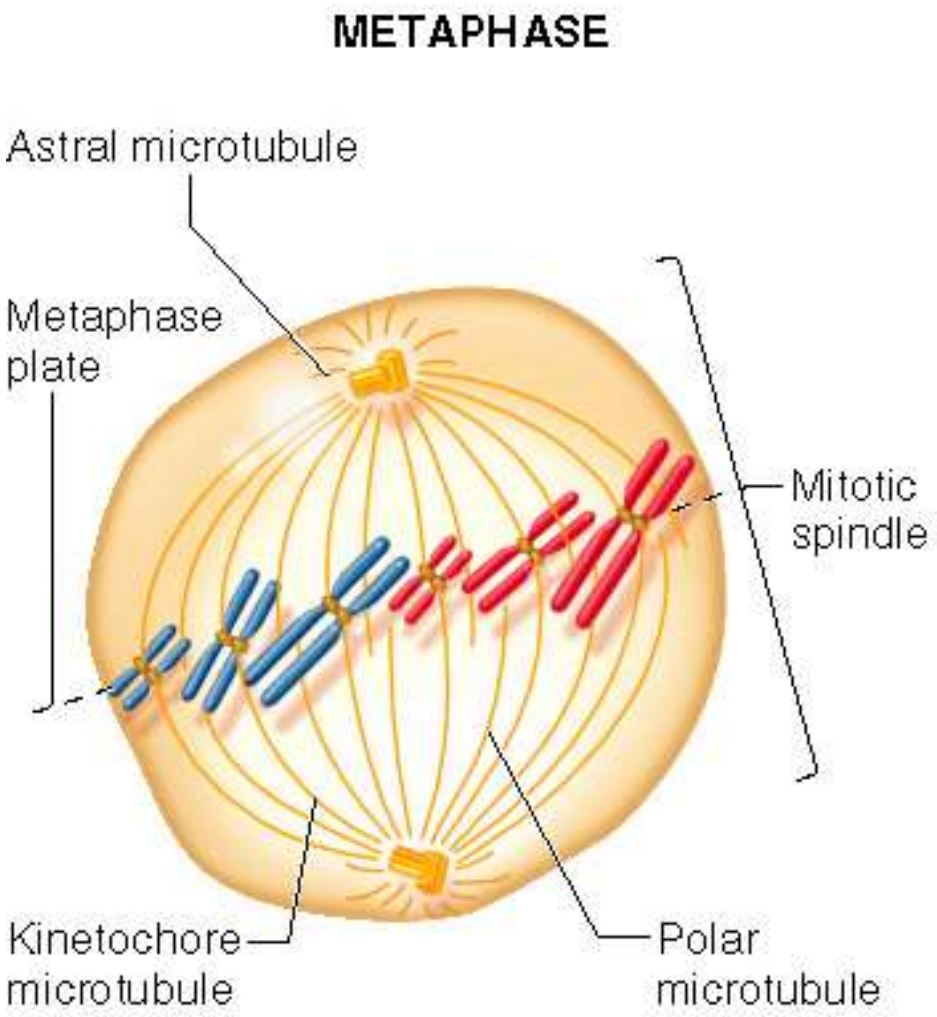
- Spindle fibers interact with the sister chromatids

- Kinetochore microtubules grow from the two poles
  - If they make contact with a kinetochore, the sister chromatid is “captured”
  - If not, the microtubule depolymerizes and retracts to the centrosome
- The two kinetochores on a pair of sister chromatids are attached to kinetochore MTs on opposite poles

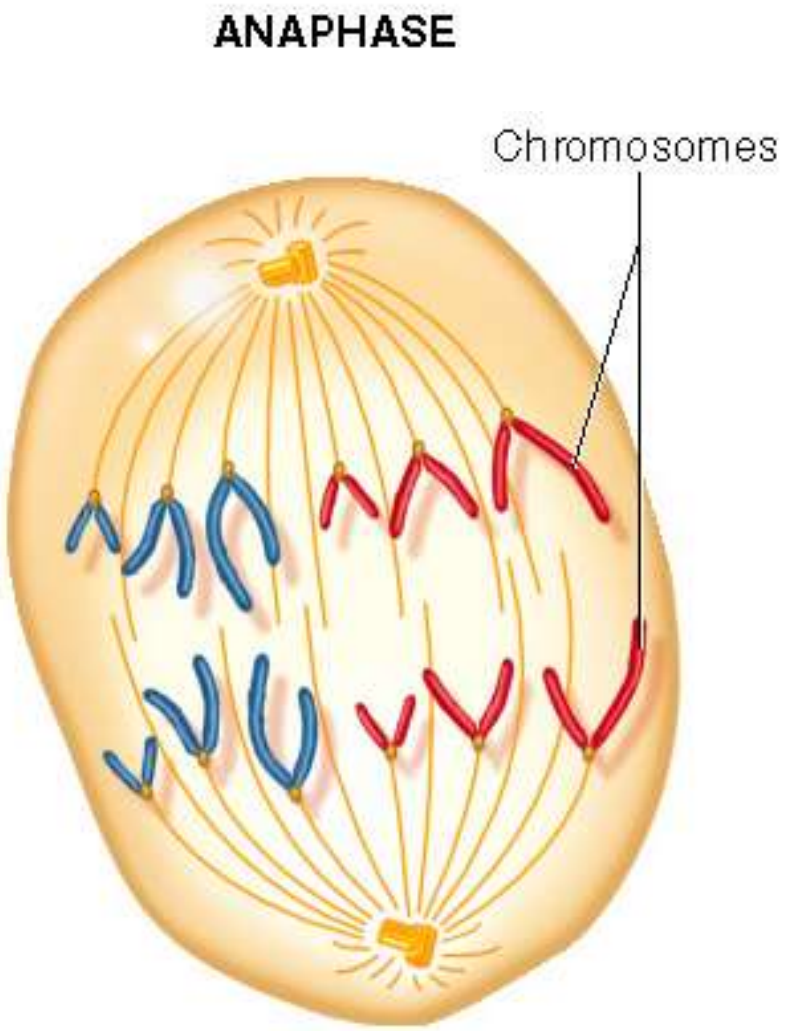


- Pairs of sister chromatids align themselves along a plane called the metaphase plate

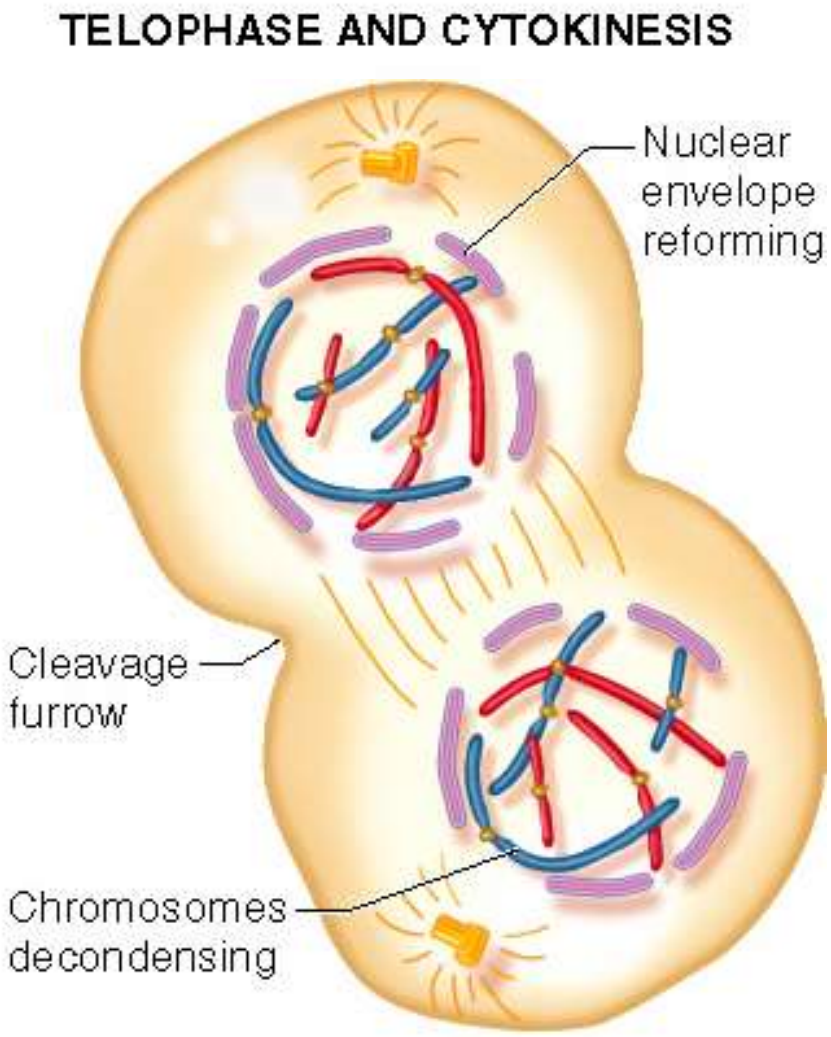
- Each pair of chromatids is attached to both poles by kinetochore microtubules



- The connection holding the sister chromatids together is broken
- Each chromatid, now an individual chromosome, is linked to only one pole
- As anaphase proceeds
  - Kinetochore MTs shorten
    - Chromosomes move to opposite poles
  - Polar MTs lengthen
    - Poles themselves move further away from each other



- Chromosomes reach their respective poles and decondense
- Nuclear membrane reforms to form two separate nuclei
- In most cases, mitosis is quickly followed by cytokinesis
  - In animals
    - Formation of a cleavage furrow
  - In plants
    - Formation of a cell plate
    - Refer to Figure 3.9



- Mitosis and cytokinesis ultimately produce two daughter cells having the same number of chromosomes as the mother cell
- The two daughter cells are genetically identical to each other
  - Barring rare mutations
- Thus, mitosis ensures genetic consistency from one cell to the next
- The development of multicellularity relies on the repeated process of mitosis and cytokinesis

3.3 SEXUAL REPRODUCTION

- Sexual reproduction is the most common way for eukaryotic organisms to produce offspring (the next generation)
  - Parents make gametes with half the amount of genetic material
    - These gametes fuse with each other during fertilization to begin the life of a new organism

- Some simple eukaryotic species are isogamous
  - They produce gametes that are morphologically similar
    - Example: Many species of fungi and algae
- Most eukaryotic species are heterogamous
  - These produce gametes that are morphologically different
    - Sperm cells
      - Relatively small and mobile
    - Egg cell or ovum
      - Usually large and nonmobile
      - Stores a large amount of nutrients, in animal species

- Gametes are typically haploid
  - They contain a single set of chromosomes
- Gametes are 1*n*, while diploid cells are 2*n*
  - A diploid human cell contains 46 chromosomes
  - A human gamete only contains 23 chromosomes
- During meiosis, haploid cells are produced from diploid cells
  - Thus, the chromosomes must be correctly sorted and distributed to reduce the chromosome number to half its original value
    - In humans, for example, a gamete must receive one chromosome from each of the 23 pairs

MEIOSIS

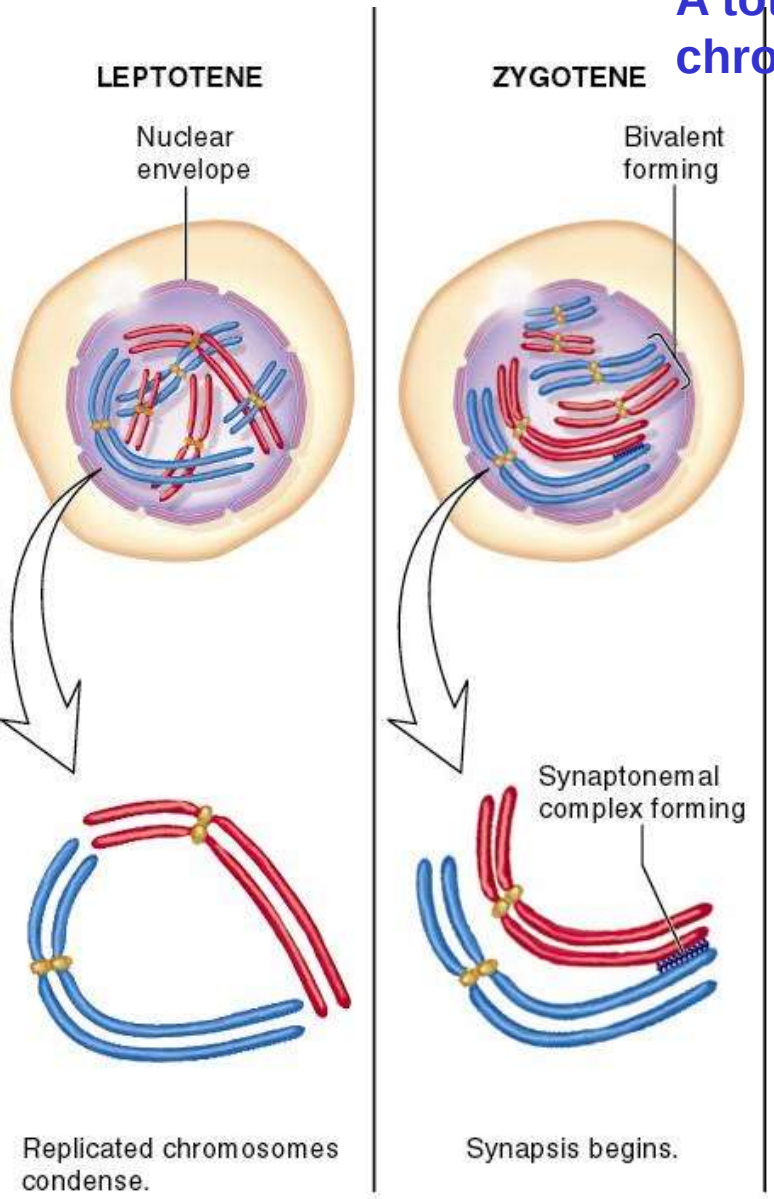
- Like mitosis, meiosis begins after a cell has progressed through interphase of the cell cycle
- Unlike mitosis, meiosis involves two successive divisions
  - These are termed Meiosis I and II
  - Each of these is subdivided into
    - Prophase
    - Prometaphase
    - Metaphase
    - Anaphase
    - Telophase

MEIOSIS

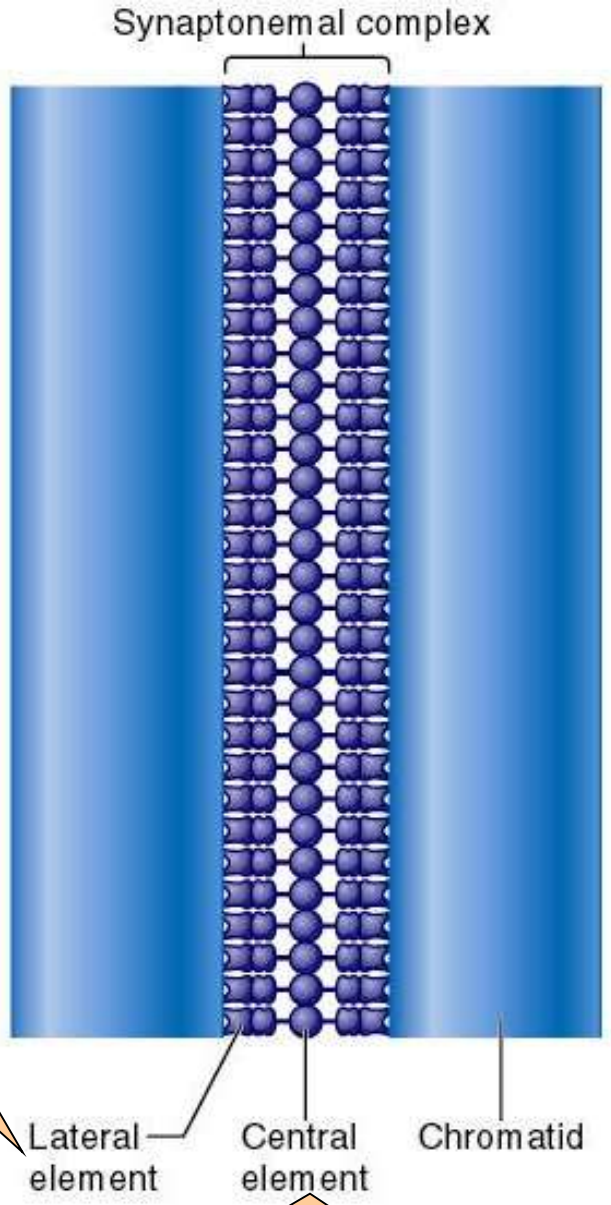
- Prophase I is further subdivided into periods known as
  - Leptotena
  - Zygotena
  - Pachytena
  - Diplotena
  - Diakinesis

  - Refer to Figure 3.10

A total of 4 chromatids



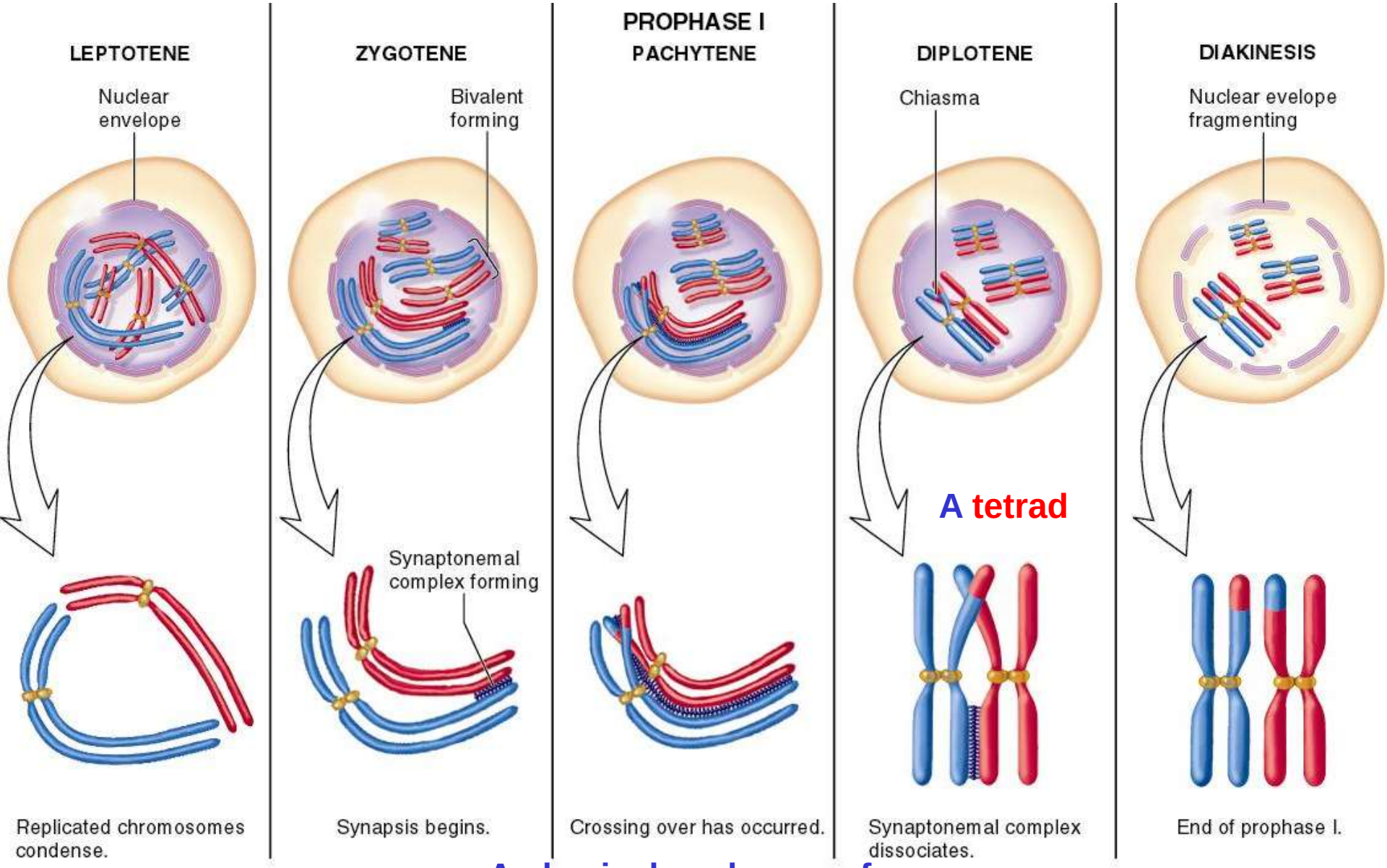
A recognition process



Bound to chromosomal DNA of homologous chromatids

Provides link between lateral elements

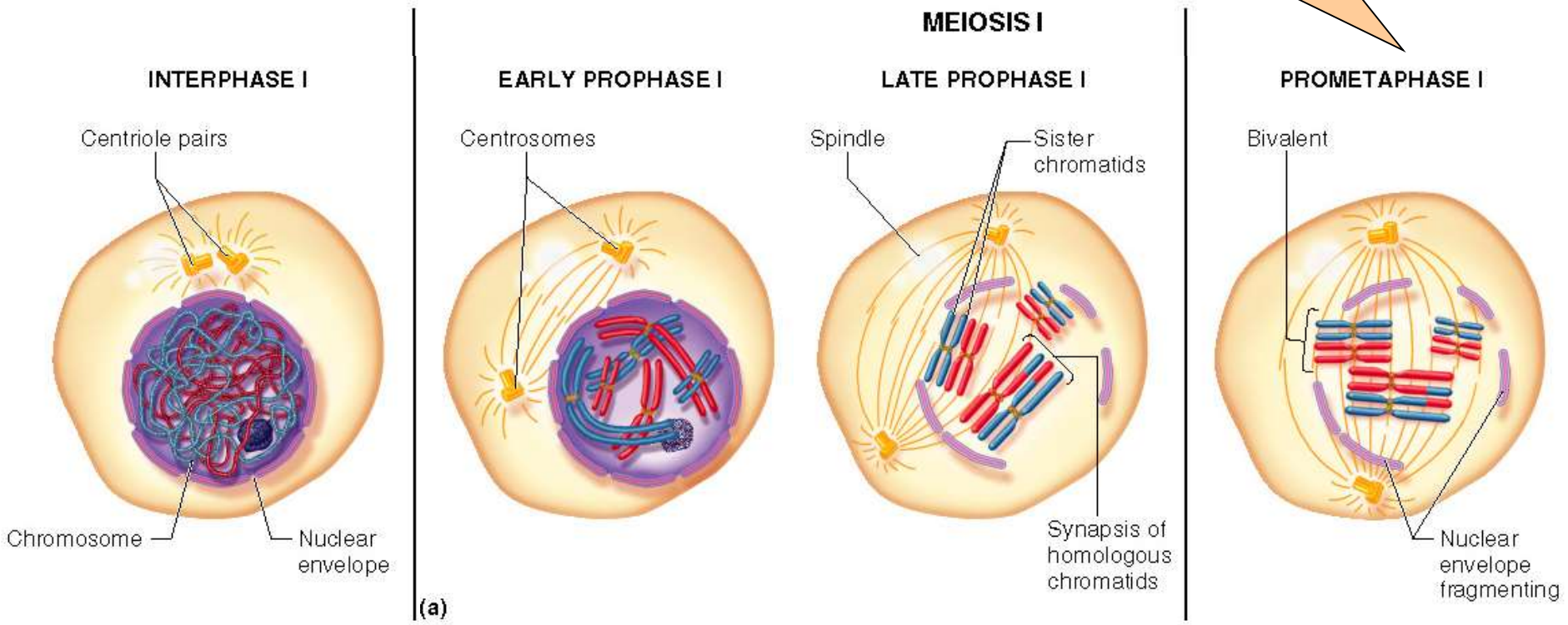
Figure 3.11 (b)



A physical exchange of chromosome pieces

Spindle apparatus complete
Chromatids attached via
kinetochore microtubules

Figure 3.12



- Bivalents are organized along the metaphase plate
  - Pairs of sister chromatids are aligned in a double row, rather than a single row (as in mitosis)
    - The arrangement is random with regards to the (blue and red) homologues
  - Furthermore
    - A pair of sister chromatids is linked to one of the poles
    - And the homologous pair is linked to the opposite pole

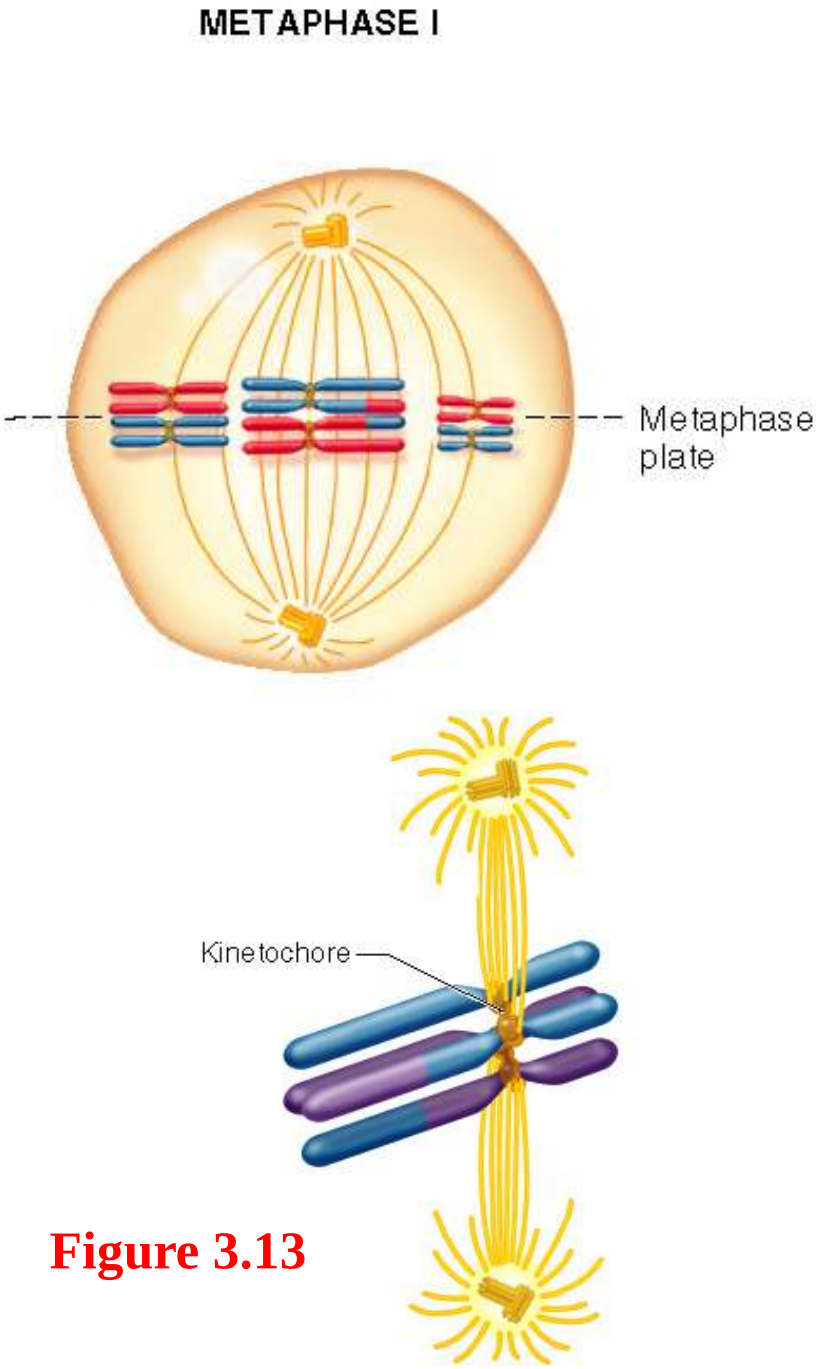
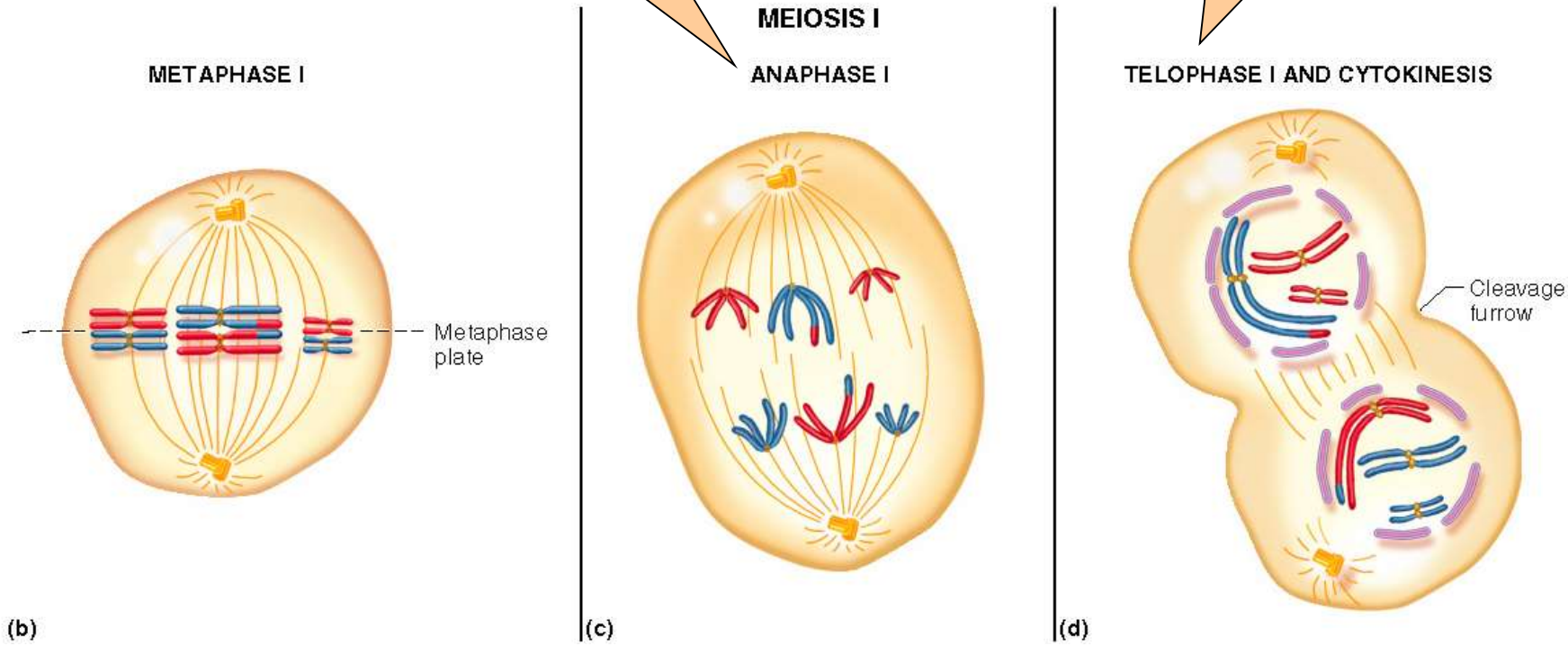


Figure 3.13

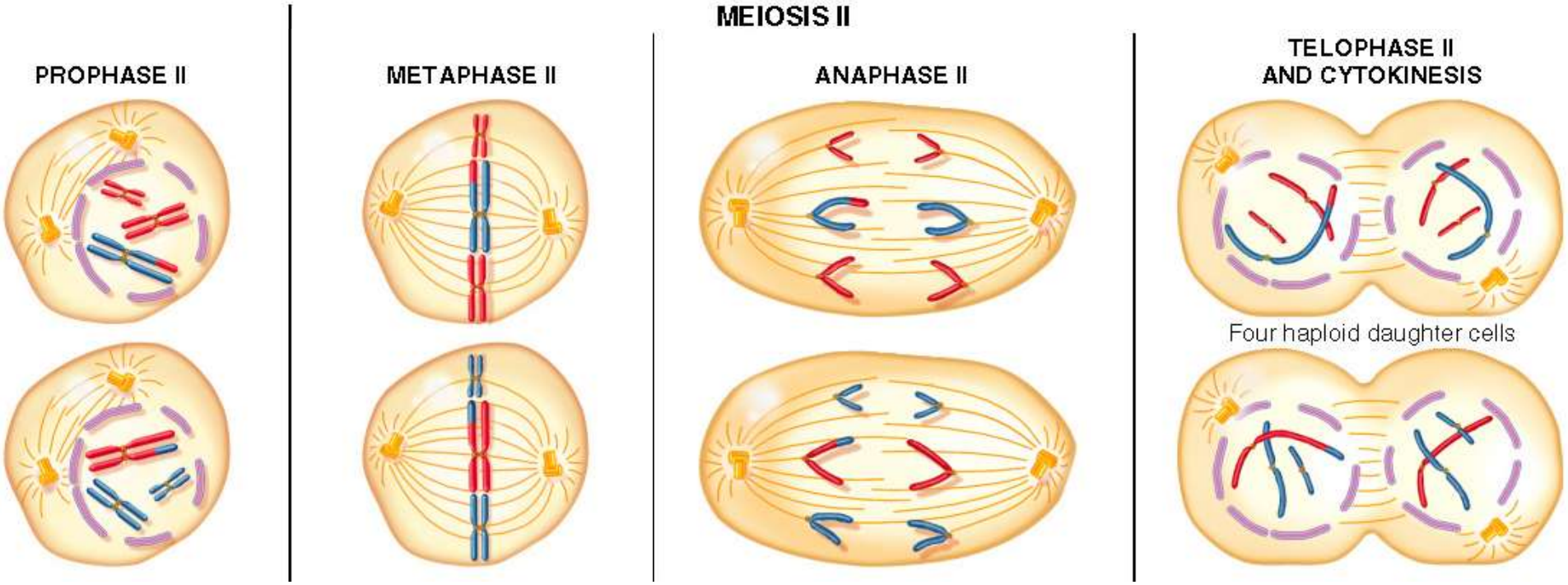
The two pairs of sister chromatids separate from each other
However, the connection that holds sister chromatids together does not break

Sister chromatids reach their respective poles and decondense
Nuclear envelope reforms to produce two separate nuclei



- Meiosis I is followed by cytokinesis and then meiosis II
- The sorting events that occur during meiosis II are similar to those that occur during mitosis
- However the starting point is different
  - For a diploid organism with six chromosomes
    - Mitosis begins with 12 chromatids joined as six pairs of sister chromatids
    - Meiosis II begins with 6 chromatids joined as three pairs of sister chromatids

MEIOSIS II


PROPHASE II
METAPHASE II
ANAPHASE II
TELOPHASE II
AND CYTOKINESIS
Four haploid daughter cells

- Mitosis *vs* Meiosis
  - Mitosis produces two diploid daughter cells
  - Meiosis produce four haploid daughter cells

  - Mitosis produces daughter cells that are genetically identical
  - Meiosis produces daughter cells that are not genetically identical
    - The daughter cells contain only one homologous chromosome from each pair

Spermatogenesis

- The production of sperm
- In male animals, it occurs in the testes
- A diploid spermatogonium cell divides mitotically to produce two cells
  - One remains a spermatogonial cell
  - The other becomes a primary spermatocyte
- The primary spermatocyte progresses through meiosis I and II
  - Refer to Figure 3.14*a*

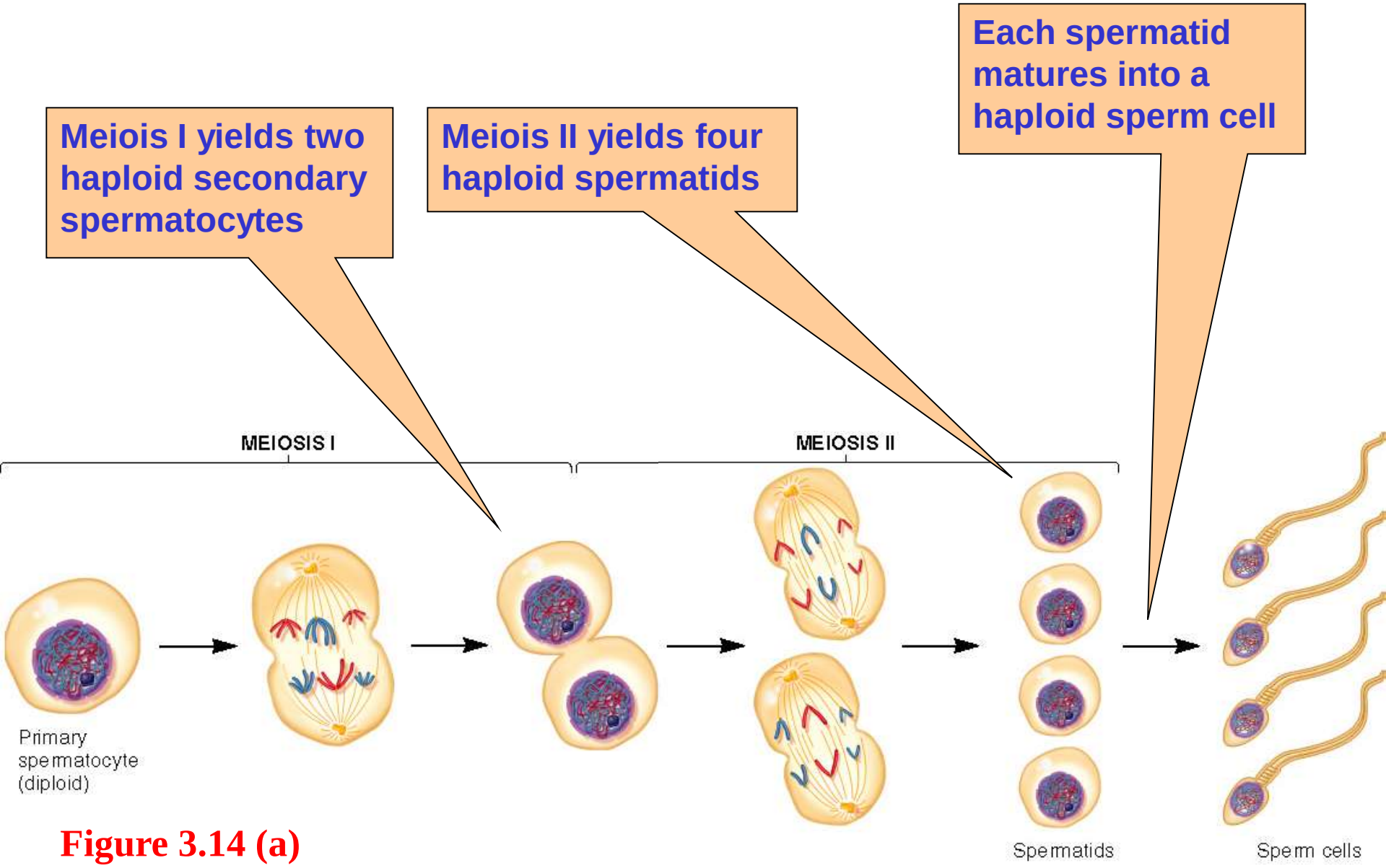
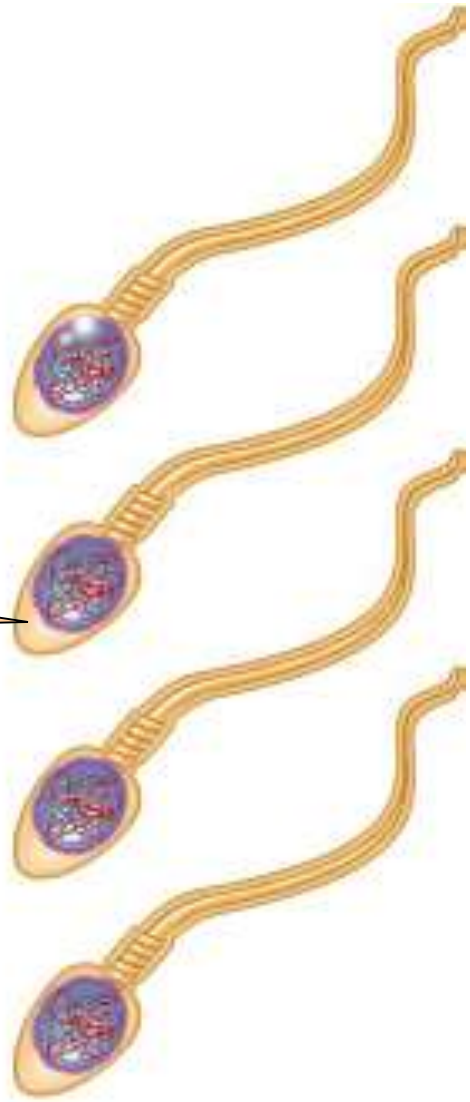


Figure 3.14 (a)

- The structure of a sperm includes
  - A long flagellum
  - A head
- The head contains a haploid nucleus
  - Capped by the acrosome

The acrosome contains digestive enzymes
- Enable the sperm to penetrate the protective layers of the egg



Sperm cells

- In human males, spermatogenesis is a continuous process
  - A mature human male produces several hundred million sperm per day

Oogenesis

- The production of egg cells
- In female animals, it occurs in the ovaries
- Early in development, diploid oogonia produce diploid primary oocytes
  - In humans, for example, about 1 million primary occytes per ovary are produced before birth

- The primary oocytes initiate meiosis I
- However, they enter into a dormant phase
  - They are arrested in prophase I until the female becomes sexually mature
- At puberty, primary oocytes are periodically activated to progress through meiosis I
  - In humans, one oocyte per month is activated
- The division in meiosis I is asymmetric producing two haploid cells of unequal size
  - A large secondary oocyte
  - A small polar body

- The secondary oocyte enters meiosis II but is quickly arrested in it
- It is released into the oviduct
  - An event called ovulation
- If the secondary oocyte is fertilized
  - Meiosis II is completed
  - A haploid egg and a second polar body are produced
- The haploid egg and sperm nuclei then fuse to created the diploid nucleus of a new individual

- Refer to Figure 3.14*b*

Unlike spermatogenesis, the divisions in oogenesis are *asymmetric*

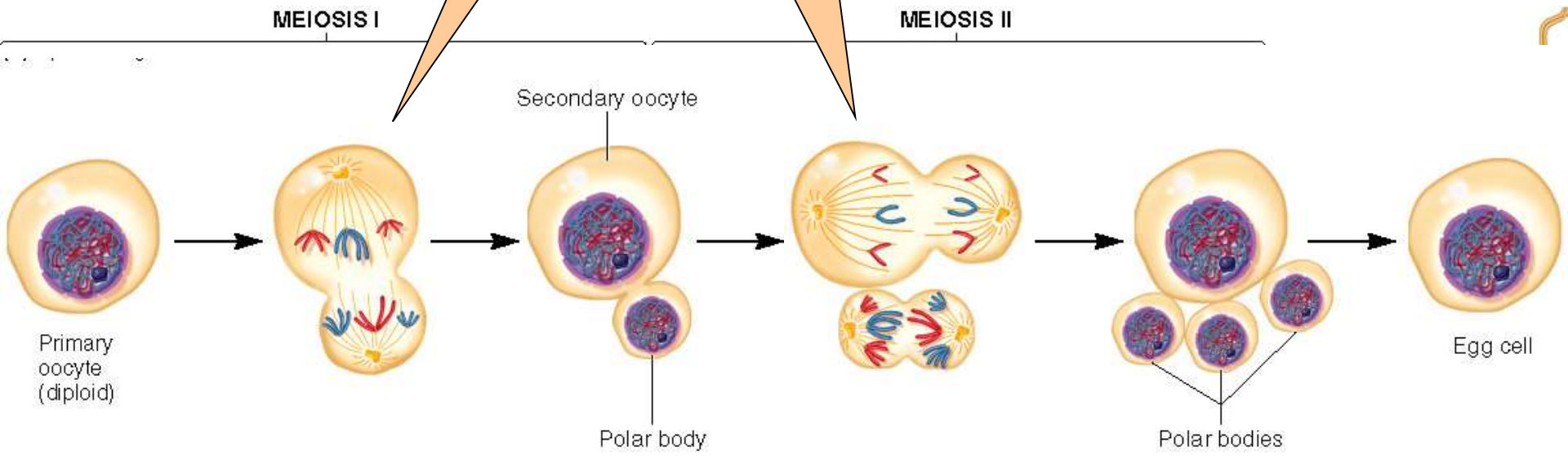


Figure 3.14 (b)

3.4 THE CHROMOSOME THEORY OF INHERITANCE AND SEX CHROMOSOMES

- The chromosome theory of inheritance describes how the transmission of chromosomes account for the Mendelian patterns of inheritance
- This theory was independently proposed in 1902-03 by
  - Theodore Boveri, a German
  - Walter Sutton, an American

- The chromosome theory of inheritance dramatically unfolded as a result of three lines of scientific inquiry
  - 1. Analysis of the transmission of traits from parent to offspring
    - Mendel's plant hybridization studies
  - 2. Inquiry into the material basis of heredity
    - Contributions by many, including
      - Carl Nägeli, a Swiss botanist, and August Weismann, a German biologist
  - 3. Microscopic examination of the processes of mitosis, meiosis and fertilization
    - Chief contributions by Boveri and Sutton

- Refer to Table 3.1

TABLE 3.1

Chronology for the Development and Proof of the Chromosome Theory of Inheritance

1866	Gregor Mendel: analyzed the transmission of traits from parents to offspring and showed that it follows a pattern of segregation and independent assortment.
1876–77	Oscar Hertwig and Hermann Fol: observed that the nucleus of the sperm enters the egg during animal cell fertilization.
1877	Eduard Strasburger: observed that the sperm nucleus of plants (and no detectable cytoplasm) enters the egg during plant fertilization.
1878	Walter Flemming: described mitosis in careful detail.
1883	Carl Nägeli and August Weismann: proposed the existence of a genetic material, which Nägeli called idioplasm and Weismann called germ plasm.
1883	Wilhelm Roux: proposed that the most important event of mitosis is the equal partitioning of "nuclear qualities" to the daughter cells.

TABLE 3.1

Chronology for the Development and Proof of the Chromosome Theory of Inheritance

1884–85	Hertwig, Strausburger, and Weismann: proposed that chromosomes are carriers of the genetic material.
1889	Theodore Boveri: showed that enucleated sea urchin eggs that are fertilized by sperm from a different species develop into larva that have characteristics that coincide with the sperm's species.
1900	Hugh de Vries, Carl Correns, and Erich von Tschermak: rediscovered Mendel's work.
1901	Thomas Montgomery: maternal and paternal chromosomes pair with each other during meiosis.
1901	C. E. McClung: sex determination in insects is related to differences in chromosome composition.
1902	Boveri: showed that when sea urchin eggs were fertilized by two sperm, the abnormal development of the embryo was related to an abnormal number of chromosomes.

TABLE 3.1

Chronology for the Development and Proof of the Chromosome Theory of Inheritance

1903	Walter Sutton: showed that even though the chromosomes seem to disappear during interphase, they do not actually disintegrate. Instead, he argued that chromosomes must retain their continuity and individuality from one cell division to the next.
1902–3	Boveri and Sutton: independently proposed tenets of the chromosome theory of inheritance. Some historians primarily credit this theory to Sutton.
1910	Thomas Hunt Morgan: showed that a genetic trait (i.e., white-eyed phenotype in *Drosophila*) was linked to a particular chromosome.
1913	E. Eleanor Carothers: demonstrated that homologous pairs of chromosomes show independent assortment.
1916	Calvin Bridges: studied nondisjunction as a way to prove the chromosome theory of inheritance.

For a description of these experiments, the student is encouraged to read: Voeller, B. R. (1968) *The Chromosome Theory of Inheritance. Classic Papers in Development and Heredity*. New York: Appleton-Century-Crofts.

- The chromosome theory of inheritance is based on a few fundamental principles
  - 1. Chromosomes contain the genetic material
  - 2. Chromosomes are replicated and passed along from parent to offspring
  - 3. The nuclei of most eukaryotic cells contain chromosomes that are found in homologous pairs
    - During meiosis, each homologue segregates into one of the two daughter nuclei
  - 4. During the formation of gametes, different types of (nonhomologous) chromosomes segregate independently
  - 5. Each parent contributes one set of chromosomes to its offspring
    - The sets are functionally equivalent
      - Each carries a full complement of genes

- The chromosome theory of inheritance allows us to see the relationship between Mendel's laws and chromosome transmission
  - Mendel's law of segregation can be explained by the homologous pairing and segregation of chromosomes during meiosis
    - Refer to Figure 3.16
  - Mendel's law of independent assortment can be explained by the relative behavior of different (nonhomologous chromosomes) during meiosis
    - Refer to Figure 3.17

Figure 3.16

Homologous chromosomes segregate from each other

This leads to the segregation of the alleles into separate gametes

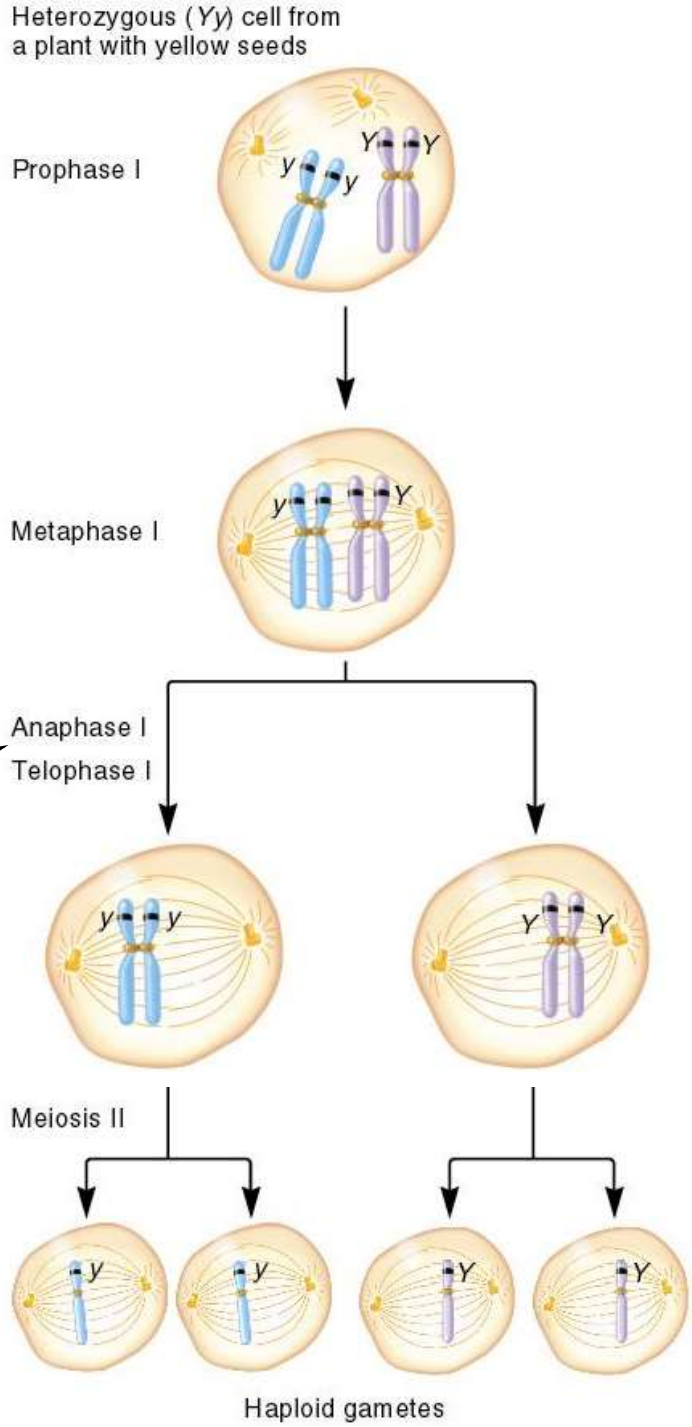
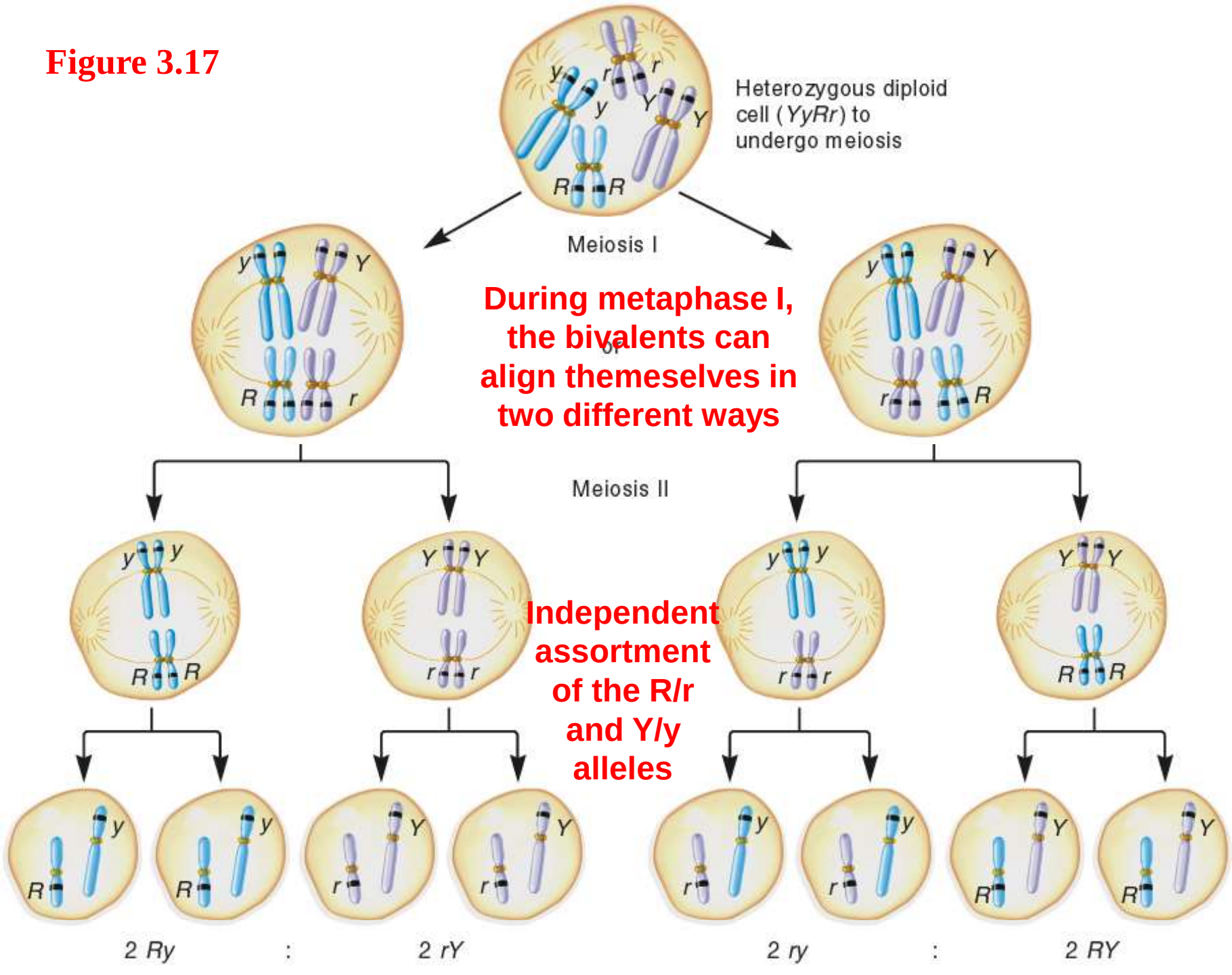


Figure 3.17

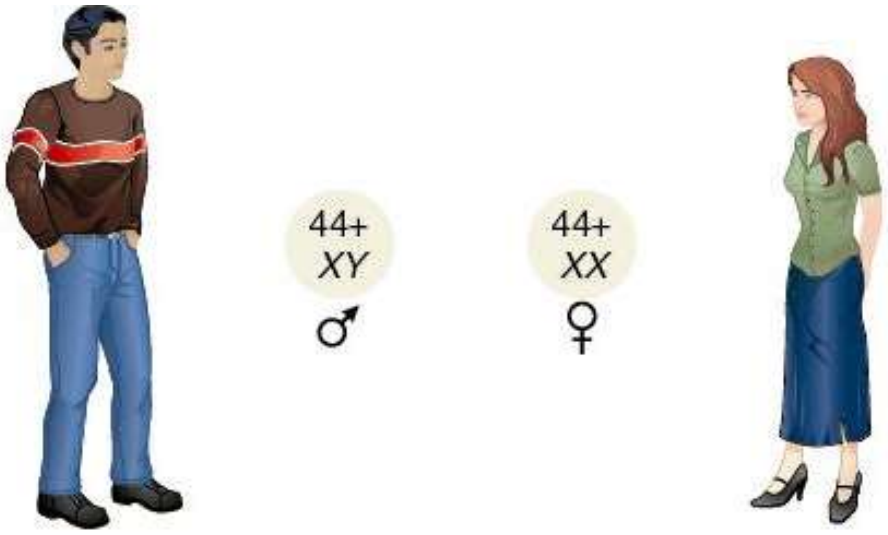

Heterozygous diploid cell (YyRr) to undergo meiosis
Meiosis I
Meiosis II
or
During metaphase I, the bivalents can align themeselves in two different ways
Independent assortment of the R/r and Y/y alleles
2 Ry : 2 rY
2 ry : 2 RY

Sex Determination

- In many animal species, chromosomes play a role in sex determination

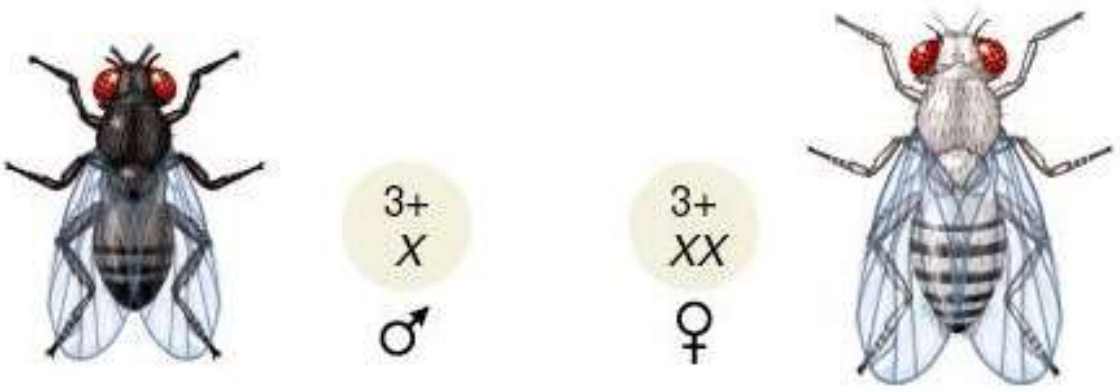
- Refer to Figure 3.18

- Humans have 46 chromosomes
  - 44 autosomes
  - 2 sex chromosomes
- Males contain one X and one Y chromosome
  - They are termed heterogametic
- Females have two X chromosomes
  - They are termed homogametic
- The Y chromosome determines maleness



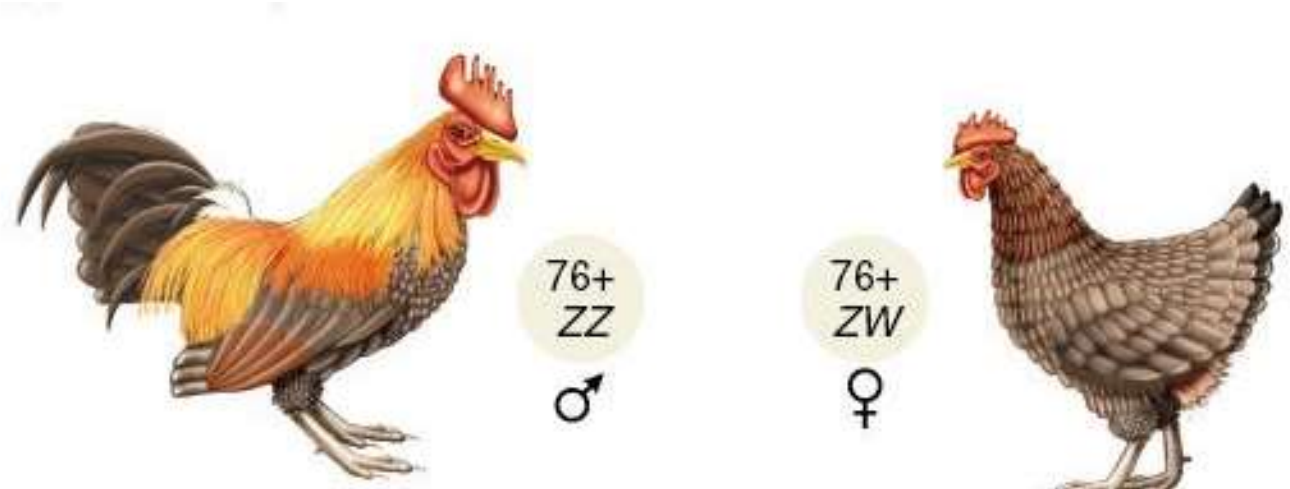
(a) *X-Y* system in mammals

- In some insects,
  - Males are XO and females are XX
- In other insects (fruit fly, for example)
  - Males are XY and females are XX
- The Y chromosome does not determines maleness
- Rather, it is the ratio between the X chromosomes and the number of sets of autosomes (X/A)
  - If X/A = 0.5, the fly becomes a male
  - If X/A = 1.0, the fly becomes a female



(b) The *X*-O system in certain insects

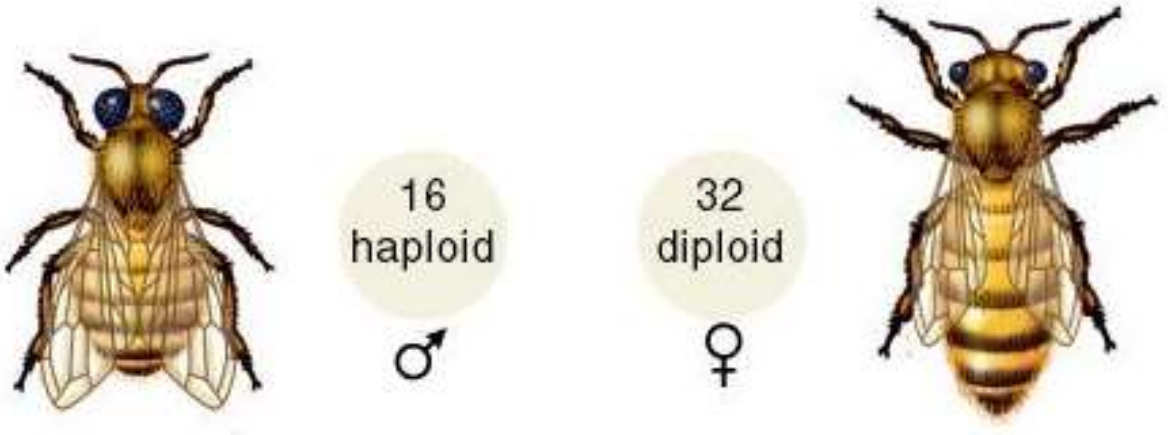
- The sex chromosomes are designated Z and W to distinguish them from the X and Y chromosomes of mammals
- Males contain two Z chromosomes
  - Hence, they are homogametic
- Females have one X and one Y chromosome
  - Hence, they are heterogametic



and some fish

(c) The *Z-W* system in birds

- Males are known as the drones
  - They are haploid
  - Produced from unfertilized eggs
- Females include the worker bees and queen bees
  - They are diploid
  - Produced from fertilized eggs



(d) The haplo-diploid system in bees

Transmission of Genes Located on Human Sex Chromosomes

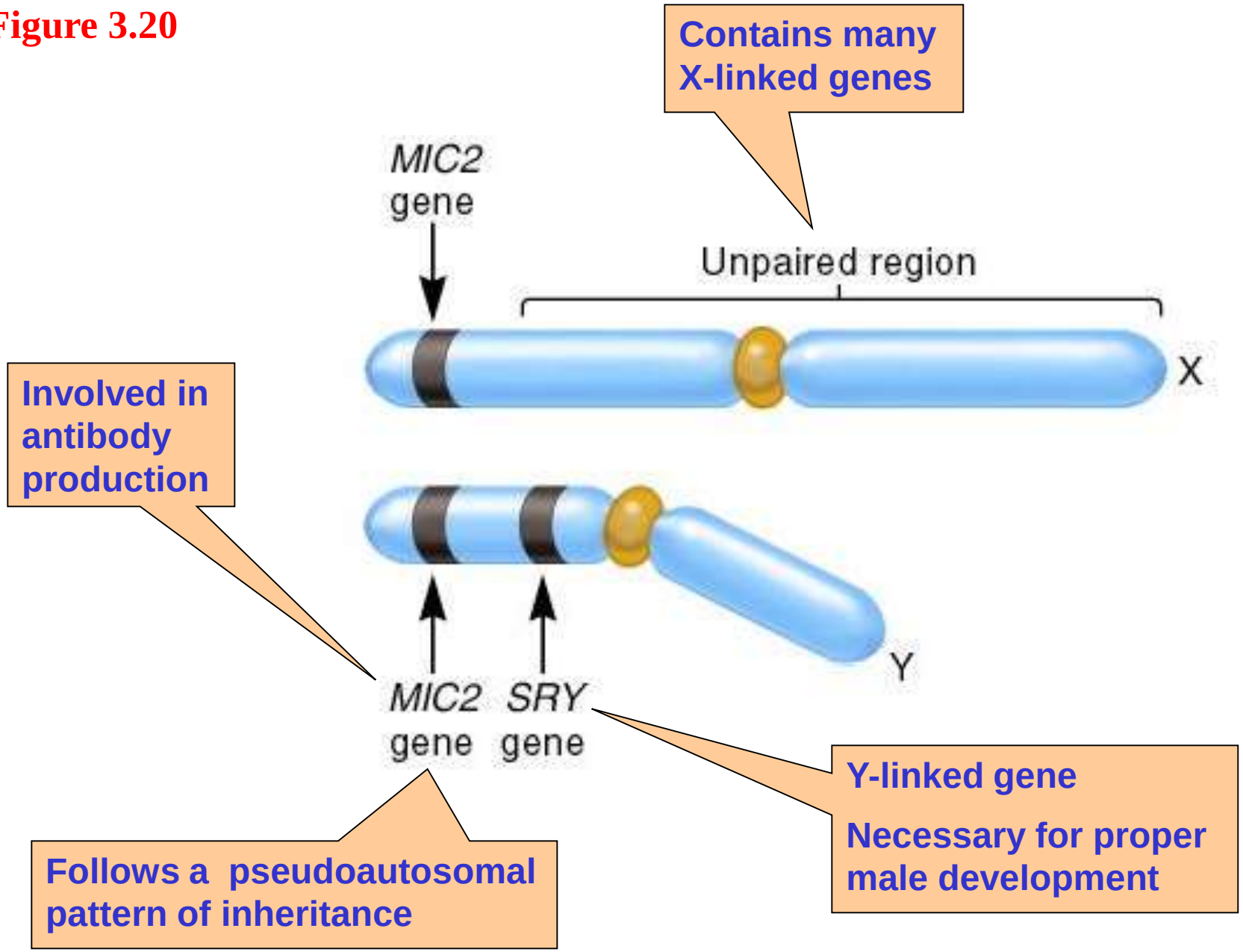
- Genes that are found on one of the two types of sex chromosomes but not on both are termed sex-linked
  - Indeed, sex-linked and X-linked tend to be used synonymously
- Males have only one copy of the X chromosome
  - They are said to be hemizygous for their X-linked genes

- Genes that are found on the Y chromosome are called holandric genes

- The X and Y chromosomes also contain short regions of homology at one end
  - These promote the necessary pairing of the two chromosomes in meiosis I of spermatogenesis

- The few genes found in this homologous region follow a pseudoautosomal pattern of inheritance
  - Their inheritance pattern is the same as that of a gene found on an autosome

Figure 3.20


Contains many X-linked genes
MIC2 gene
Unpaired region
X
Involved in antibody production
Y
MIC2 gene
SRY gene
Y-linked gene
Necessary for proper male development
Follows a pseudoautosomal pattern of inheritance