Molecular and Cellular Biology (MCB)
BB 101

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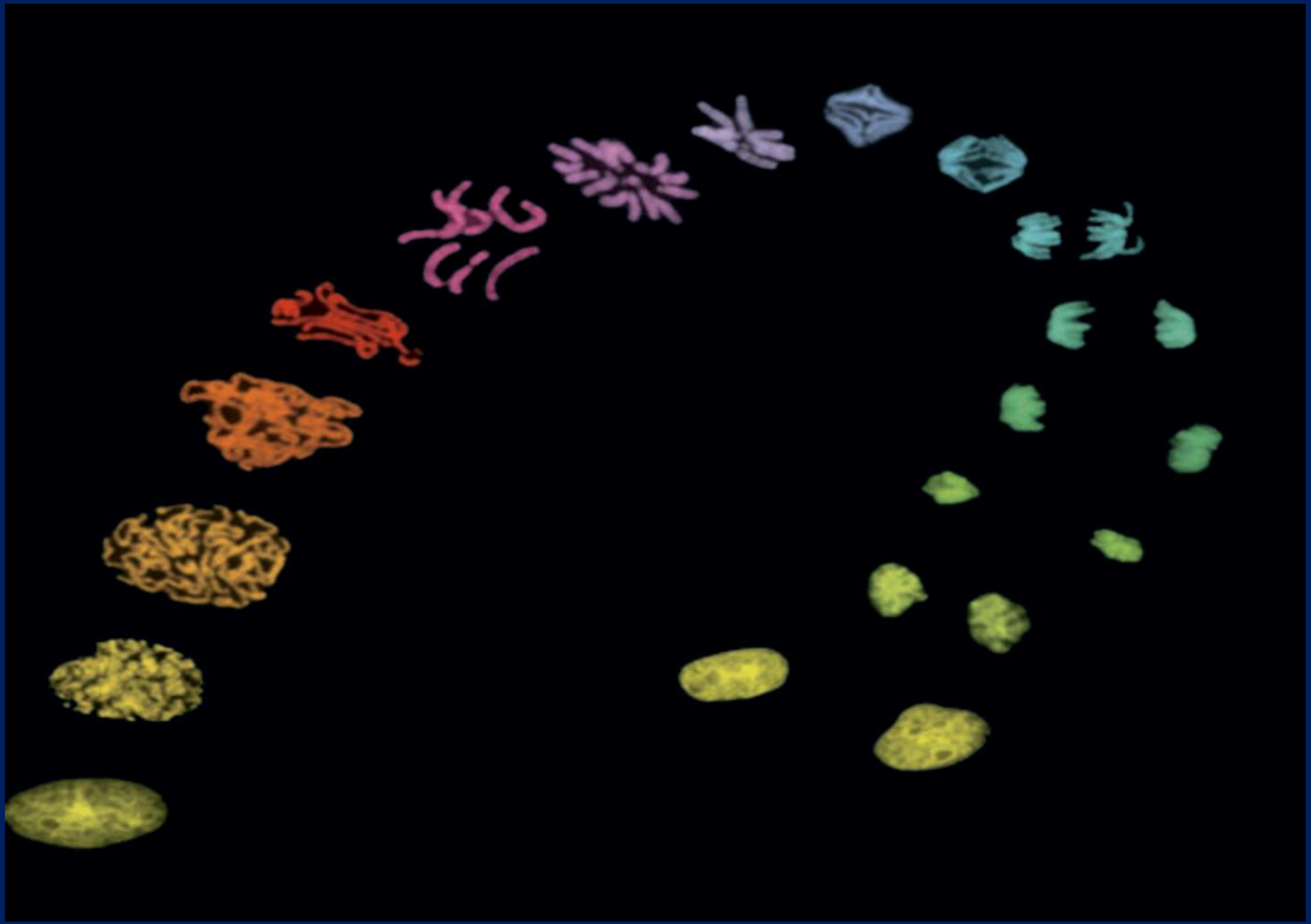
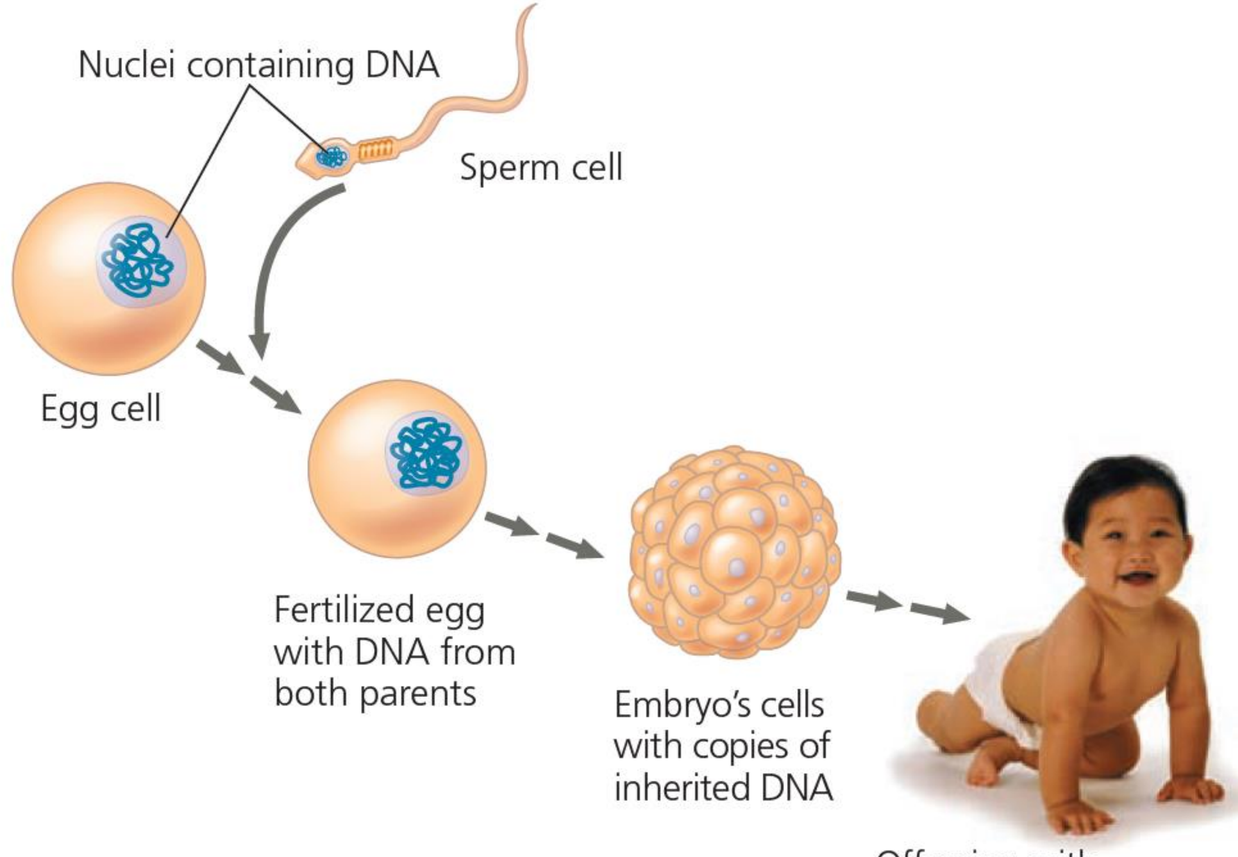
Class 5: Learning Objectives

- Cell Cycle
  - Mitosis
  - Meiosis
  - Checkpoints
- Structure of DNA
  - Chargaff's observations
  - Rosalind Franklin's x-ray diffraction patterns of DNA fibers
  - Watson-Crick's model
  - Meselson-Stahl's proof of replication model

Cell Cycle



Role of Cell Division

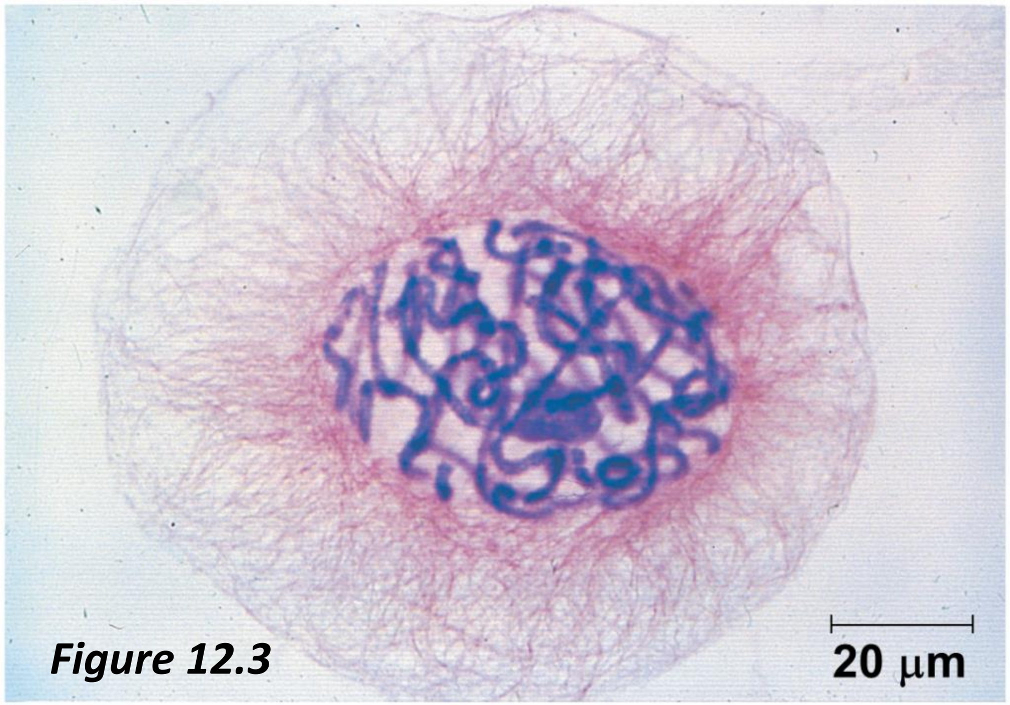


▲ **Figure 1.6 Inherited DNA directs development of an organism.**

- Cell division distributes DNA (chromosomes) of a mother cell equally between two daughter cells thereby allowing a cell to proliferate
- Cell proliferation is essential for growth, repair & reproduction

Cellular Organization of the Genetic Material

- A genome consist of a number of DNA molecules (eukaryotic cells) or a single DNA molecule (prokaryotic cells)
- **Somatic cells:** Non-reproductive cells - two sets of chromosomes
- **Gametes:** Reproductive cells: sperm & egg - have half as many chromosomes as somatic cells



The Cell cycle

Mitotic (M) phase alternates with interphase (growth period)

- **G1 phase** – first part of interphase
- **S phase** - chromosomes duplicate
- **G2 phase** - last part of interphase
- **M phase** - mitosis distributes chromosomes to daughter nuclei
- **Cytokinesis** - divides cytoplasm and produces two daughter cells

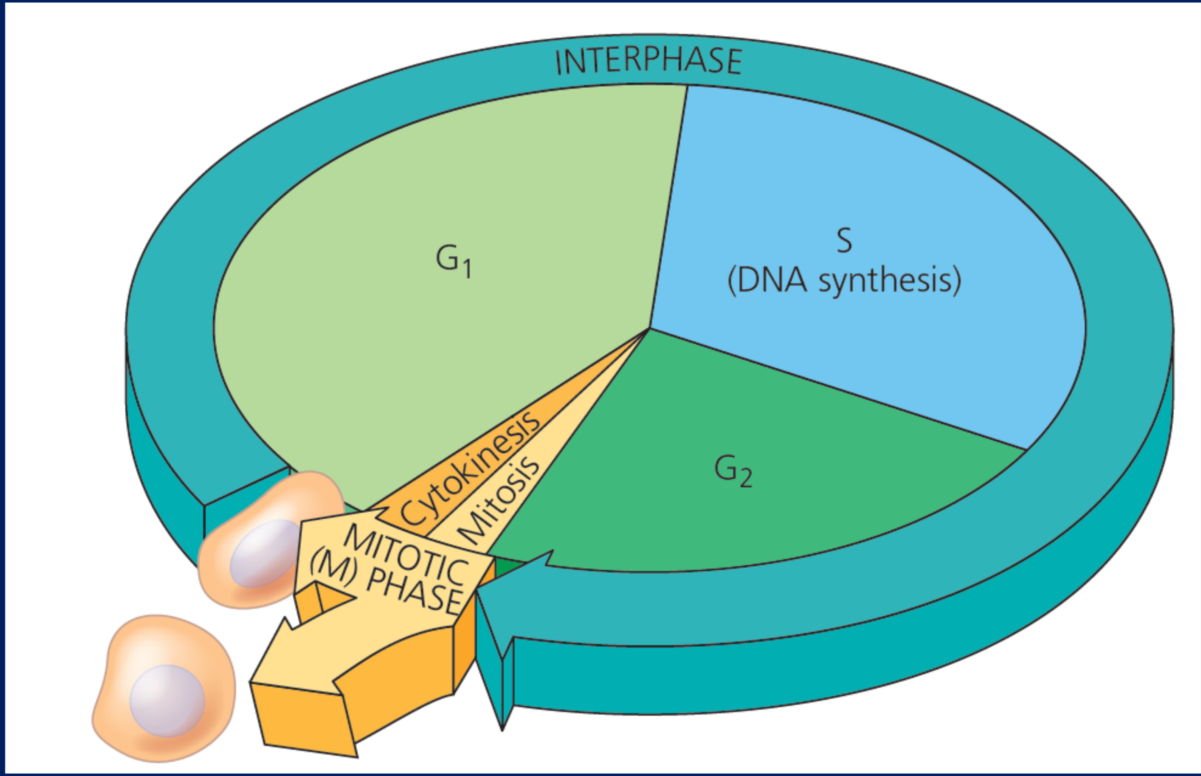
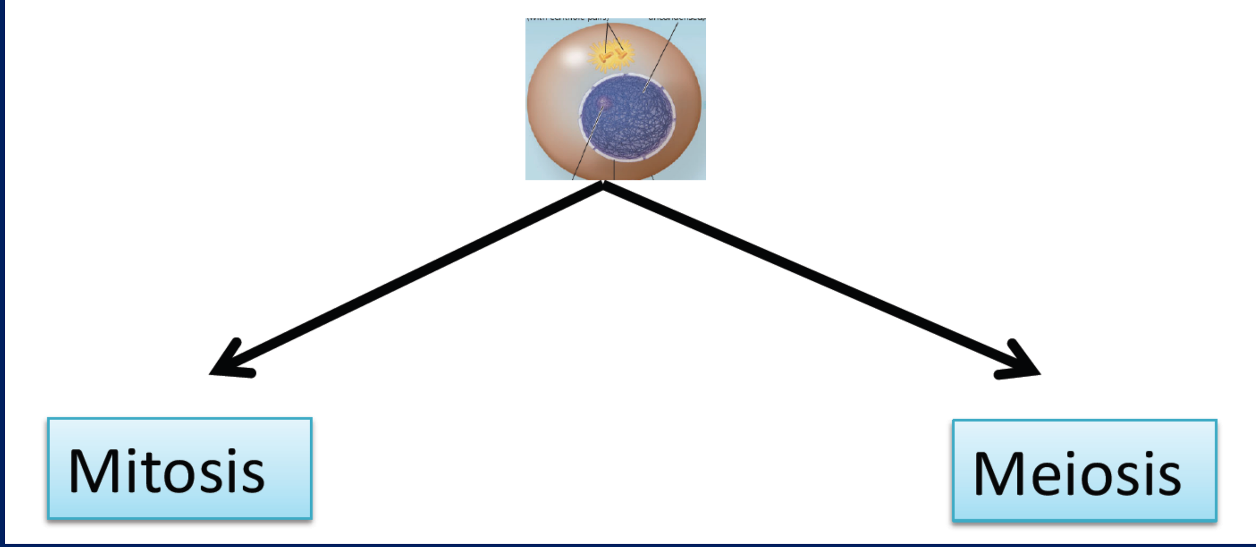


Figure 12.6

The Cell Cycle



- Division of somatic cells
- Two daughter cells are produced with *same amount of DNA* as mother cell

- Division of gamete cells (Sperm and ovum)
- Four daughter cells are produced with *half the amount of DNA* as mother cell

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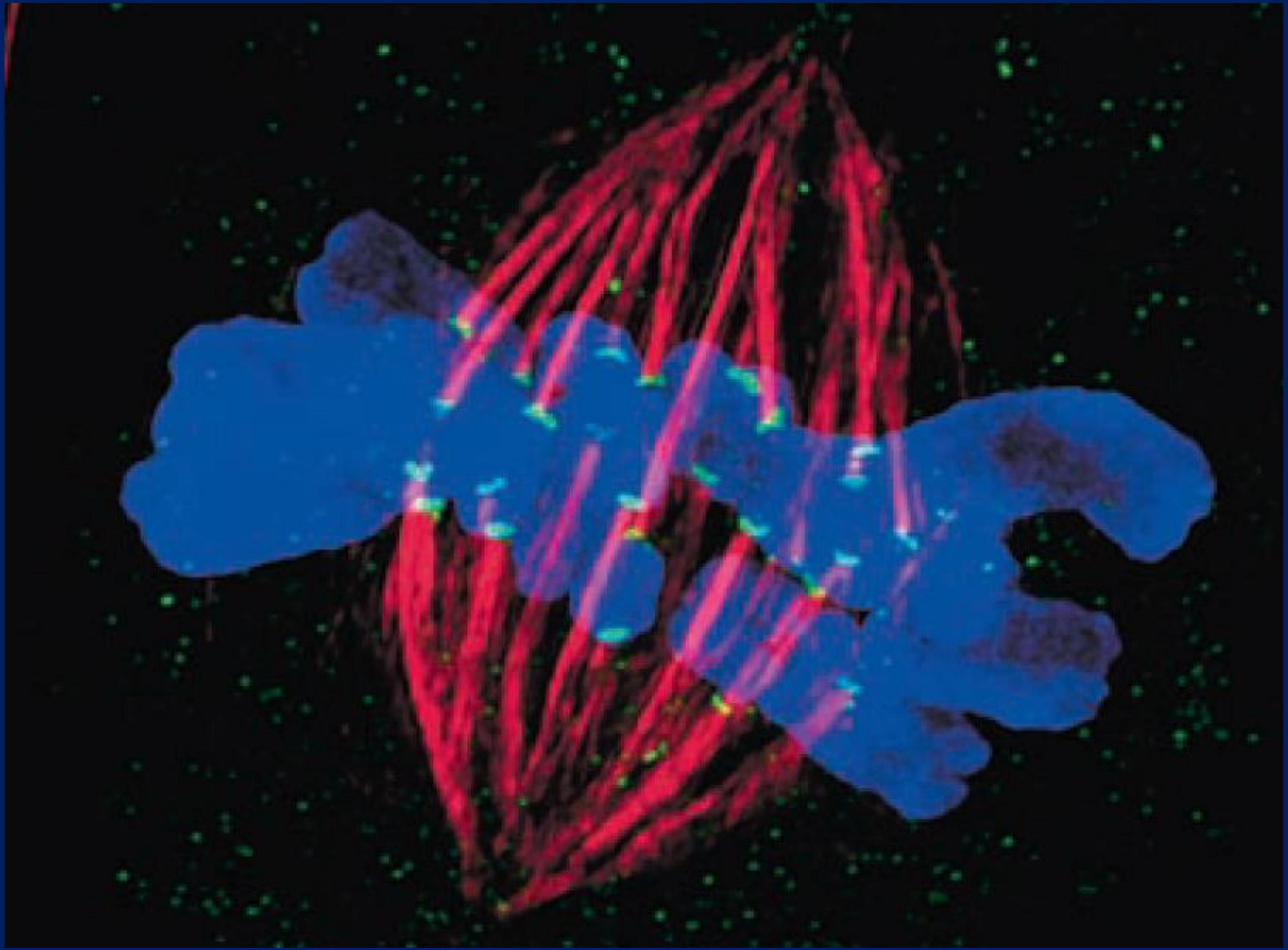


Mitosis produces new cells, and replaces cells that are old, lost or damaged.
In mitosis a cell divides to form two identical daughter cells.

Chromatids: Basics

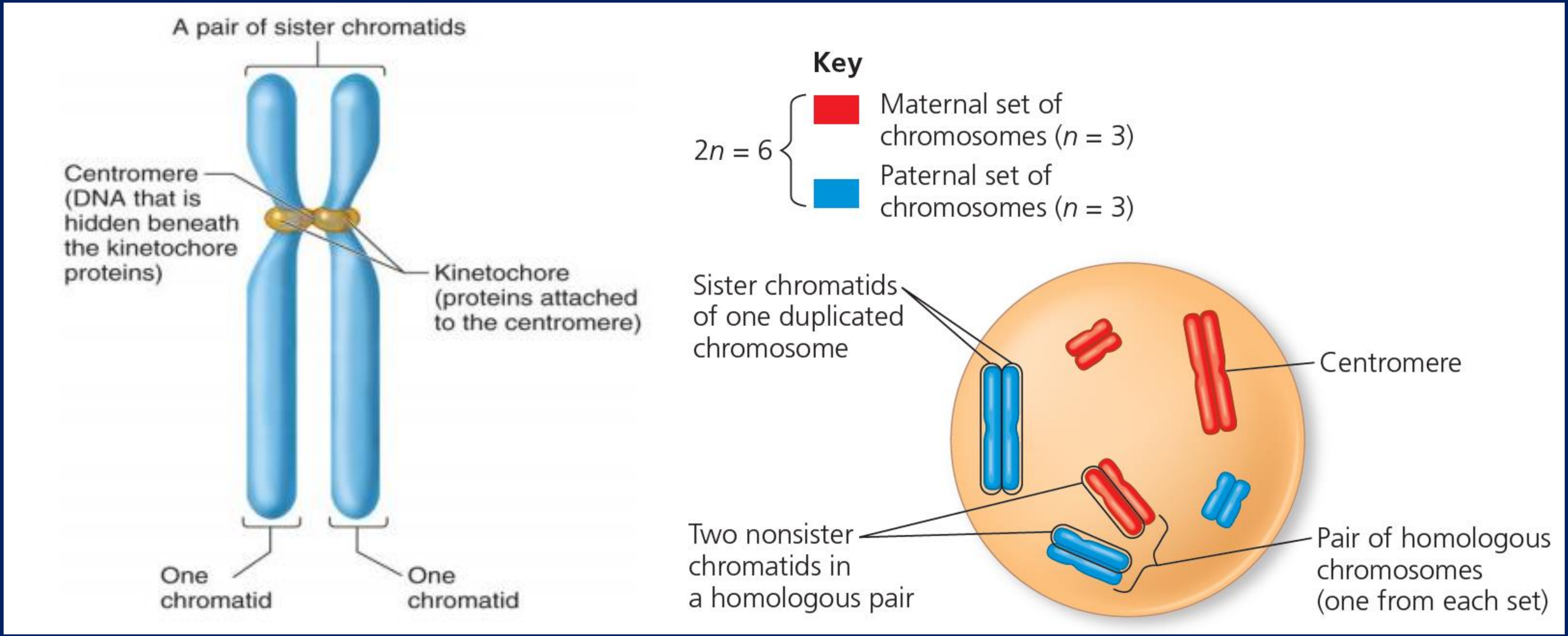


Figure 13.4

Human chromosomes

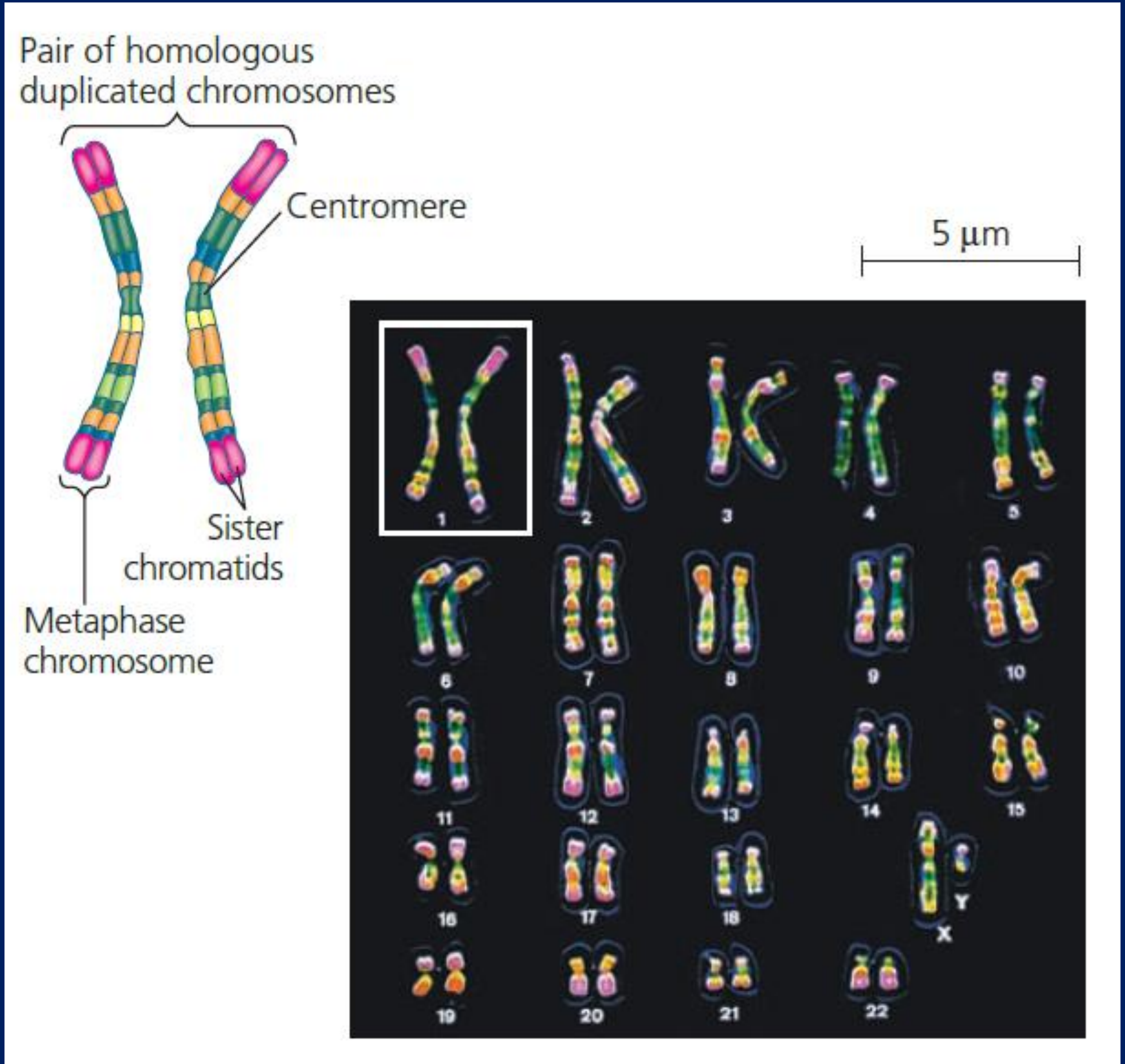


Figure 13.3

Mitosis

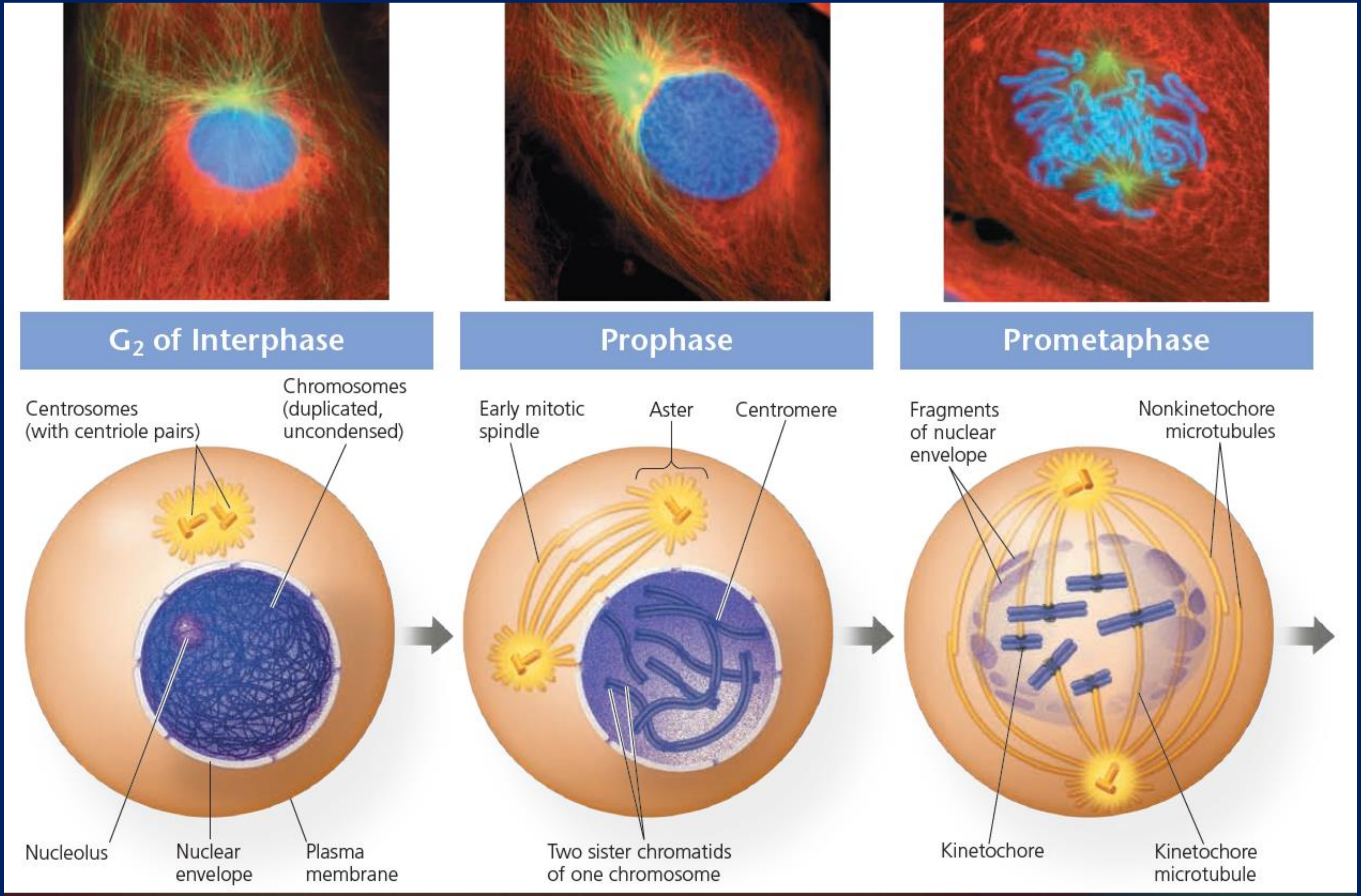


Figure 12.7

Mitosis

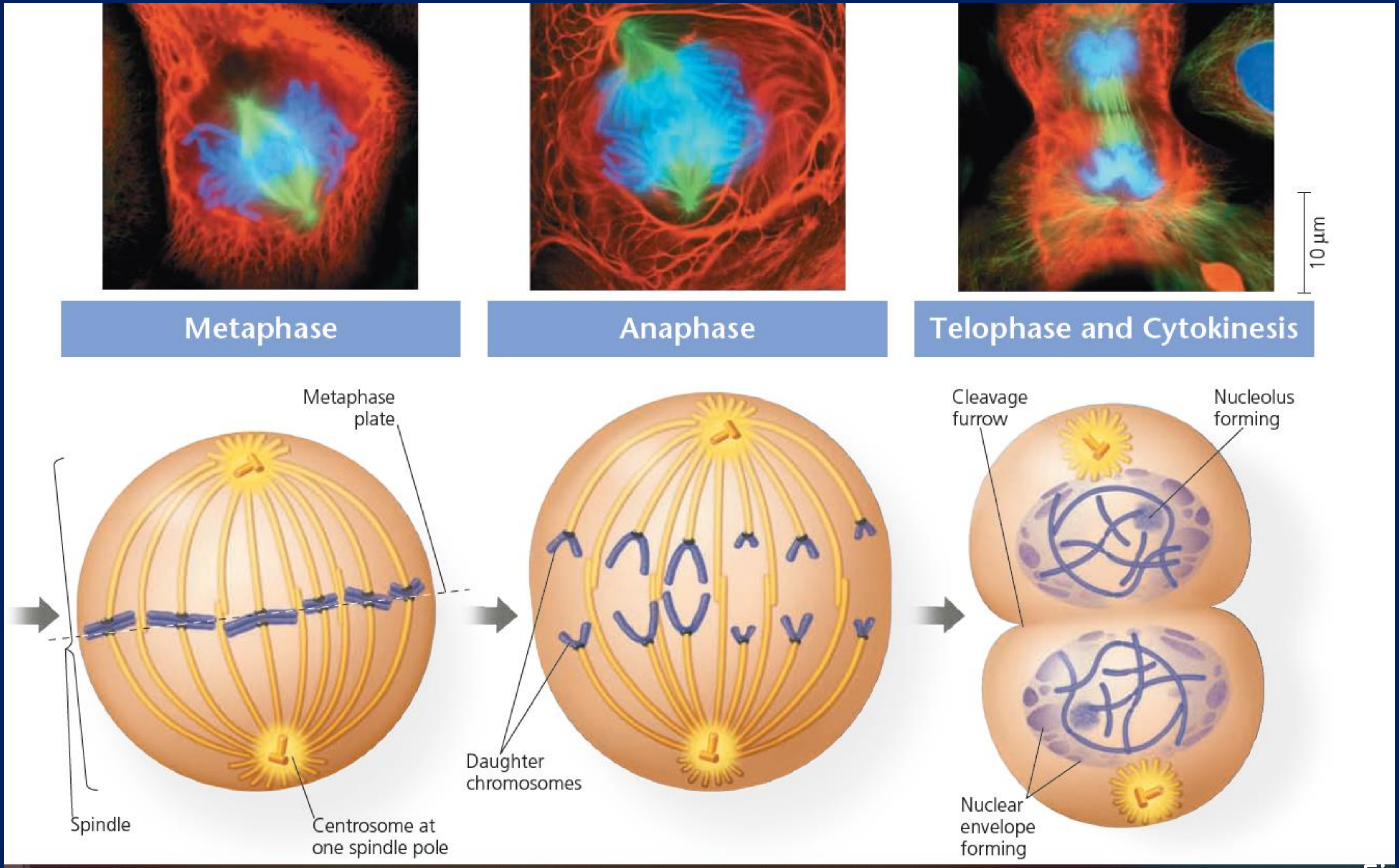
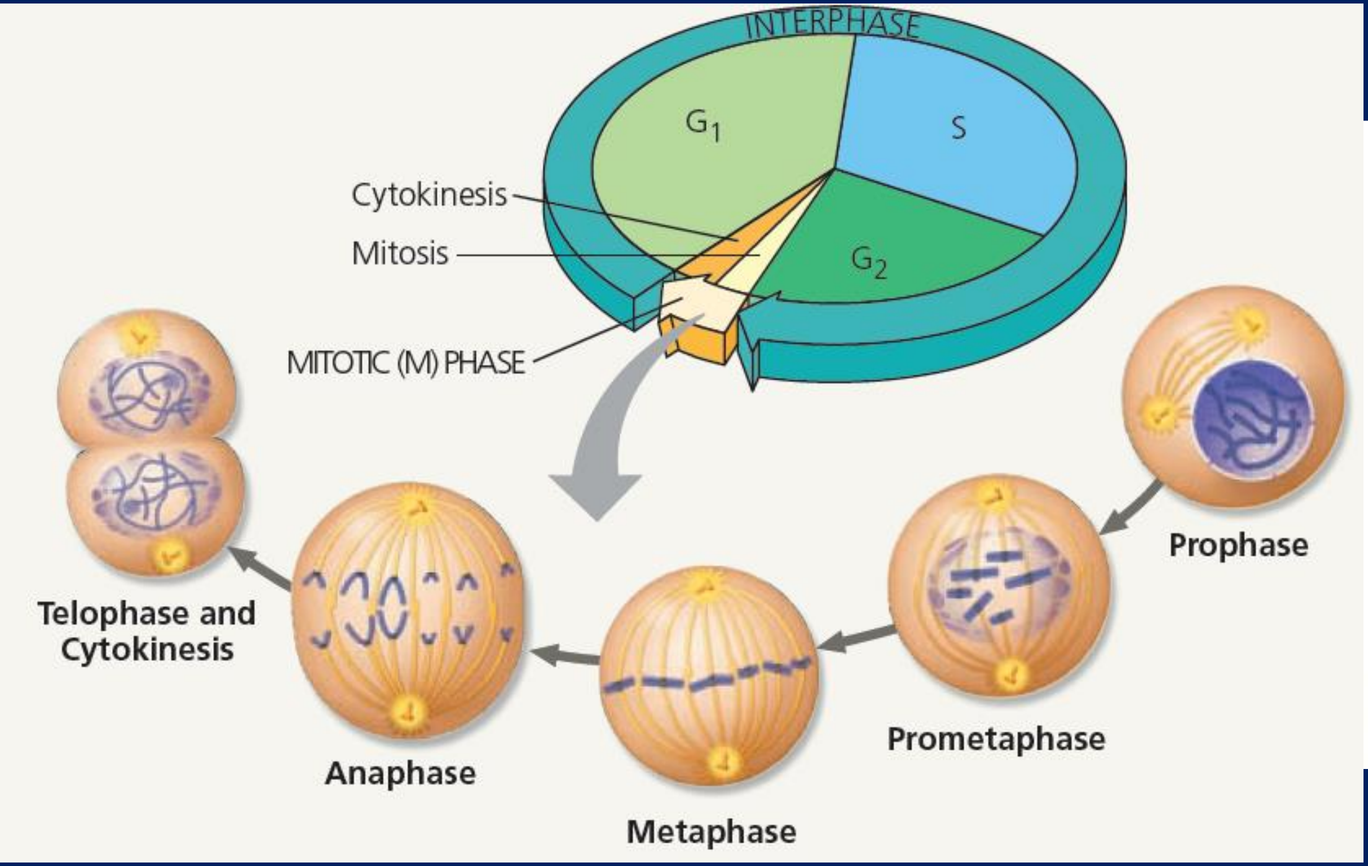


Figure 12.7

Cytokinesis



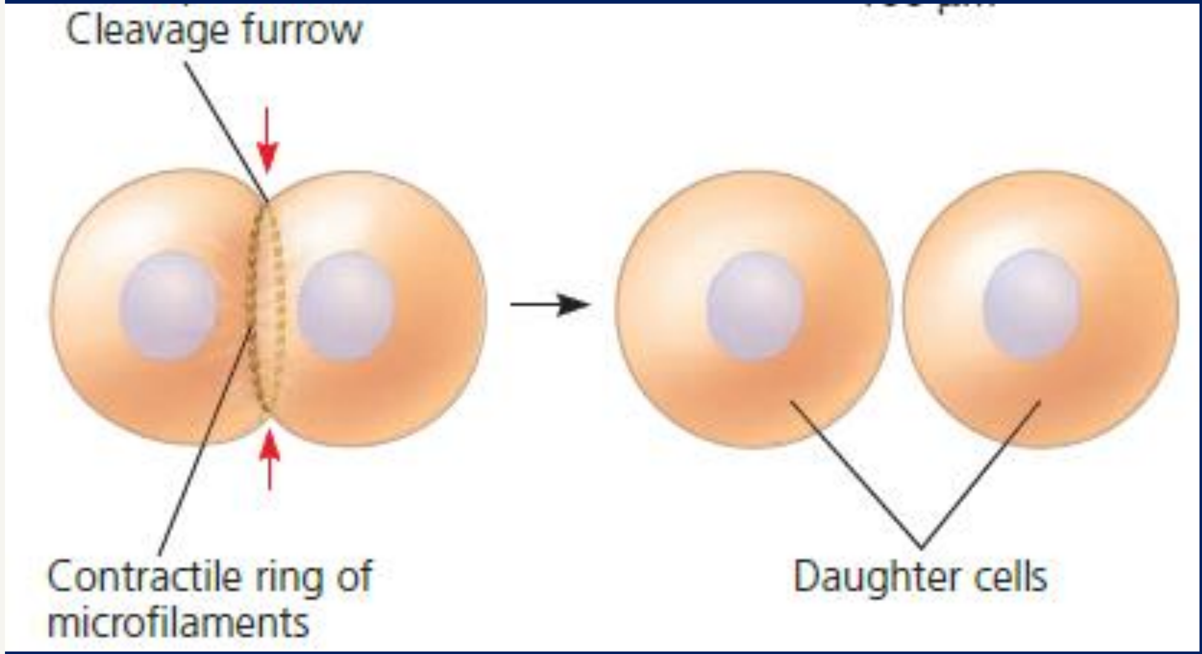


Figure 12.10

Mitosis

Real Microscopic Mitosis (MRC) - YouTube

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Meiosis

Why meiosis is important?

Able to generate genetic variation in offspring because the process of meiosis randomly shuffles genes across chromosomes

Meiosis : central to reproduction

- The resulting fertilized egg, or **zygote**, is diploid.
- Diploid cell contains two haploid sets of chromosomes bearing genes representing the maternal and paternal family.
- Both chromosome sets in the zygote and all the genes they carry are passed with precision to the somatic cells

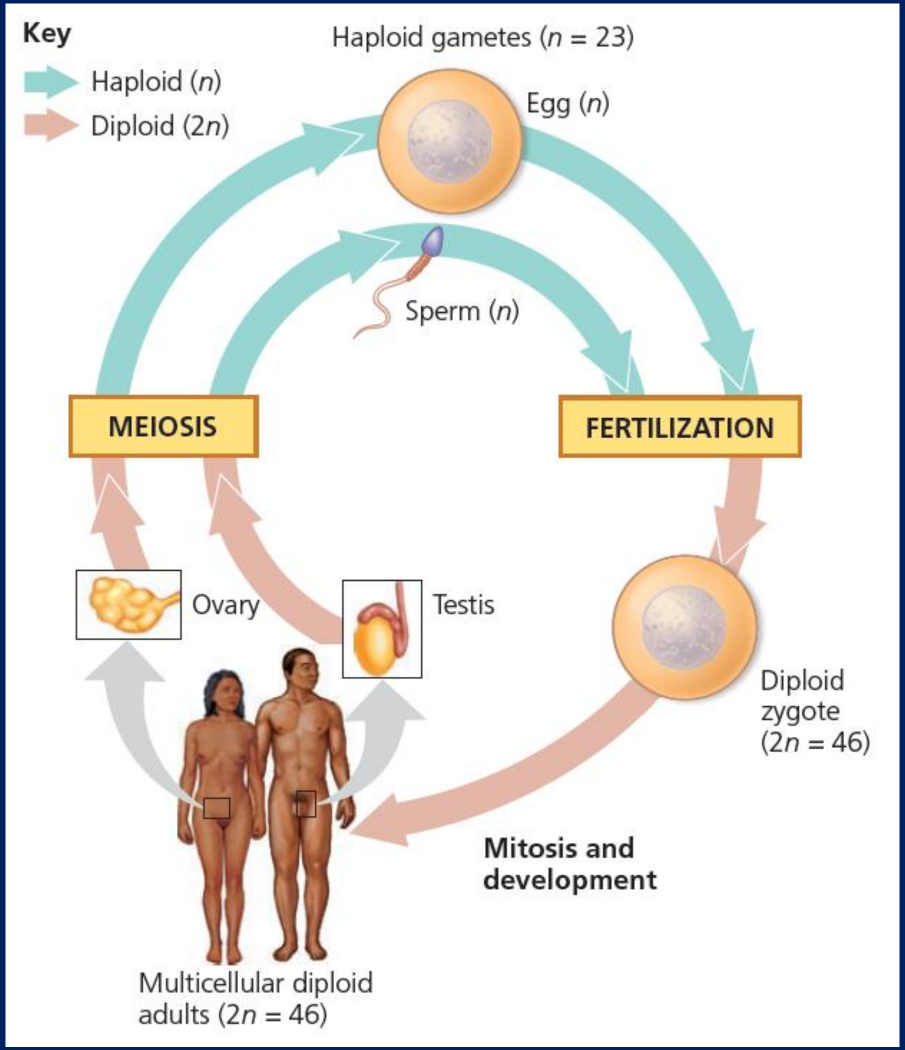

Figure 13.5

Meiosis-I

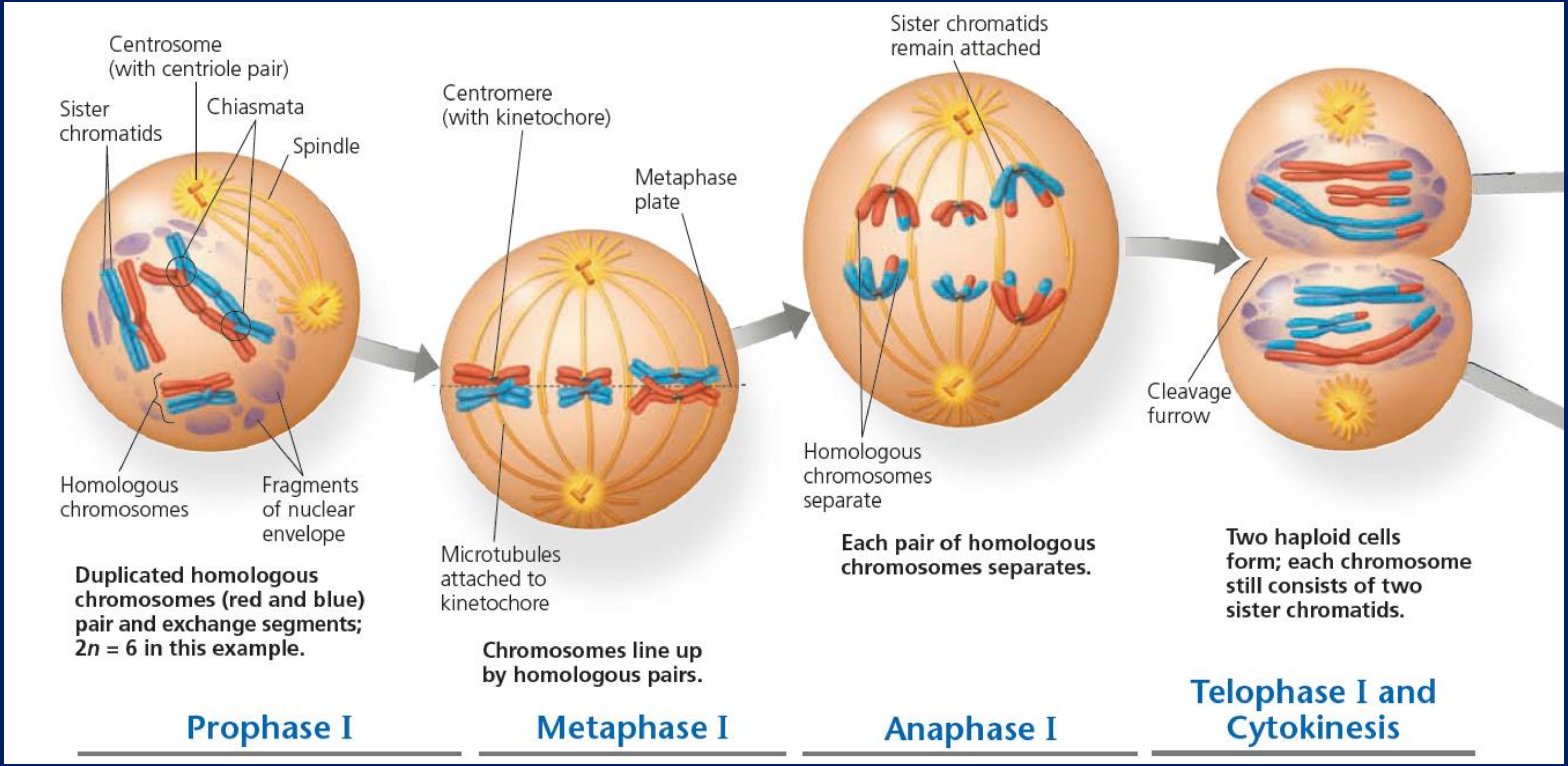

Figure 13.8

Meiosis-II

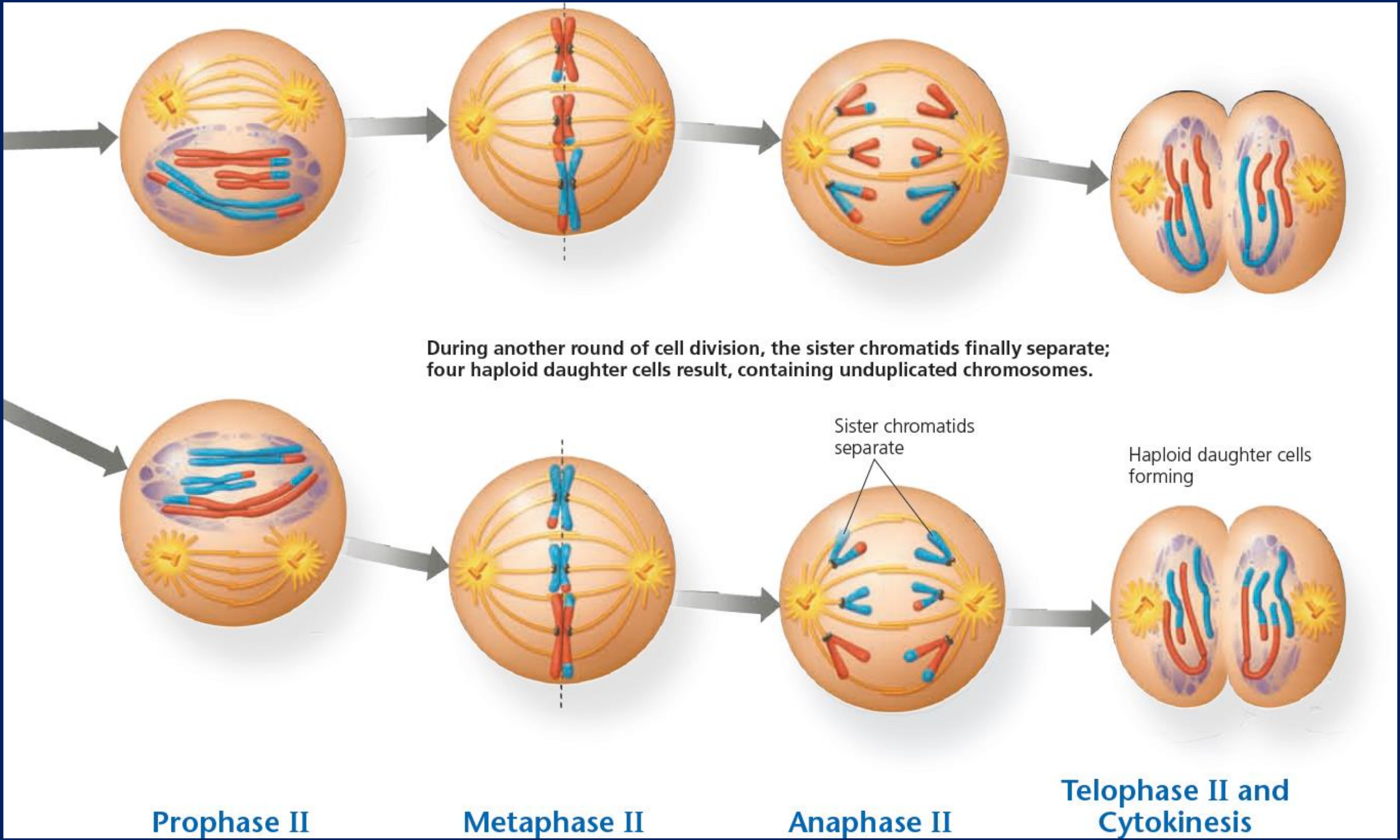

Figure 13.8

Meiosis

https://youtu.be/84jlwjvrJwY

Comparison: Mitosis and Meiosis

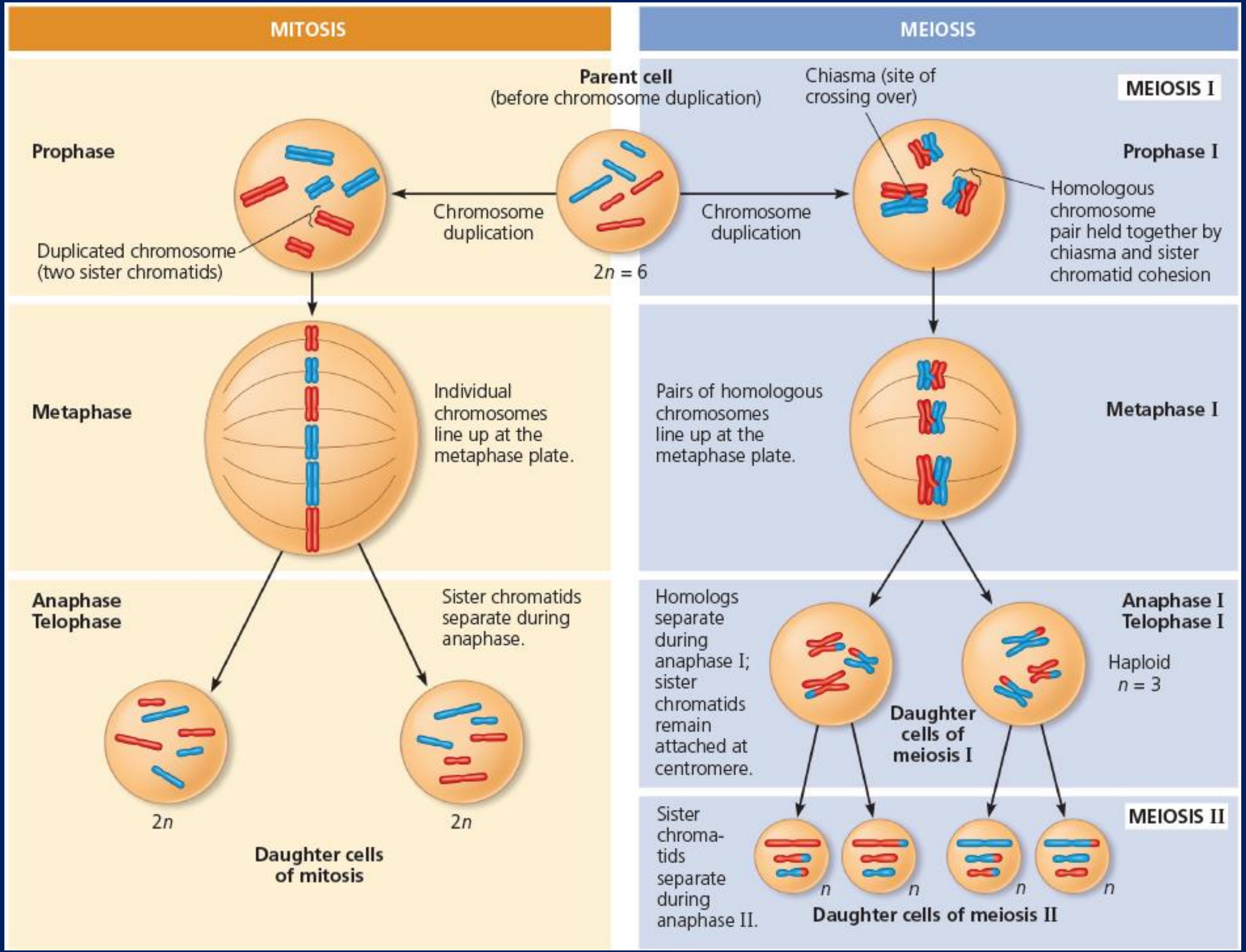

Figure 13.10

Comparison: Mitosis and Meiosis

Property	Mitosis	Meiosis
DNA Replication	Occurs during interphase before mitosis begins	Occurs during interphase before meiosis begins
Number of divisions	One	Two
Synapsis of homologous chromosomes	Does not occur	Occurs along with crossing over between non sister chromatids in prophase I
Number of daughter cells and genetic composition	Two diploid (2n) daughter cells that are genetically identical the parent cell	4 haploid (n) daughter cells, each containing half as many chromosomes as the parent cell. Daughter cells are generally different from the parent cell and each other
Role in animal body	Produces cells for growth and repair	Produces gametes and assures genetic diversity in sexual reproduction

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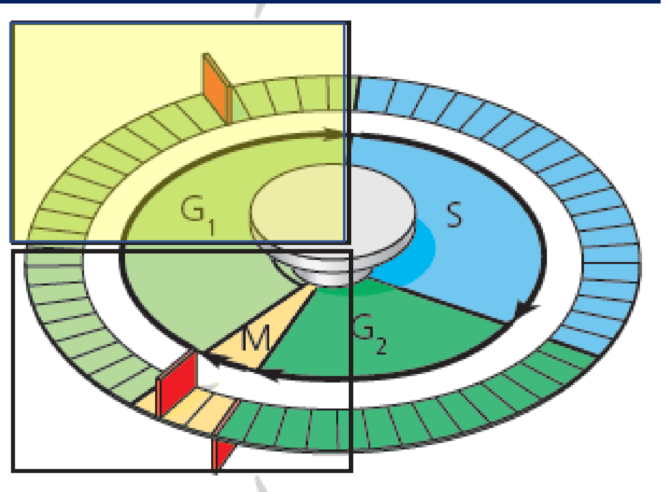
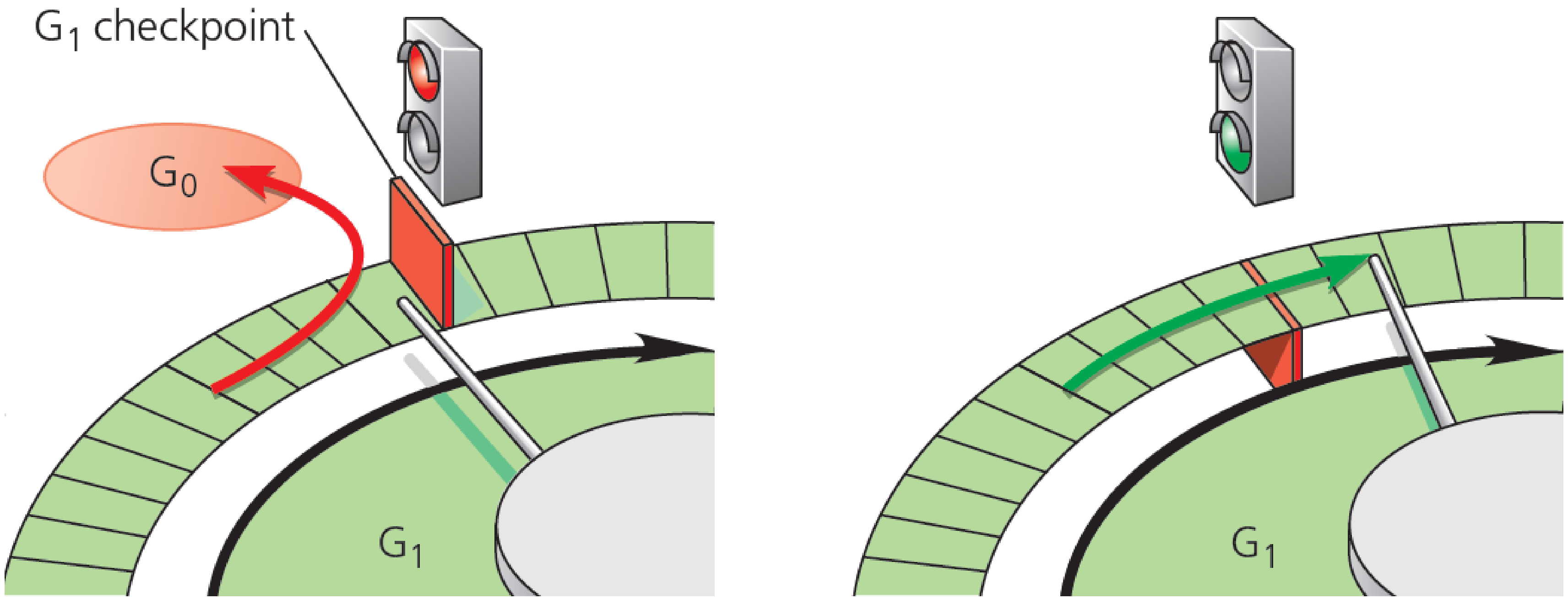
Checkpoints





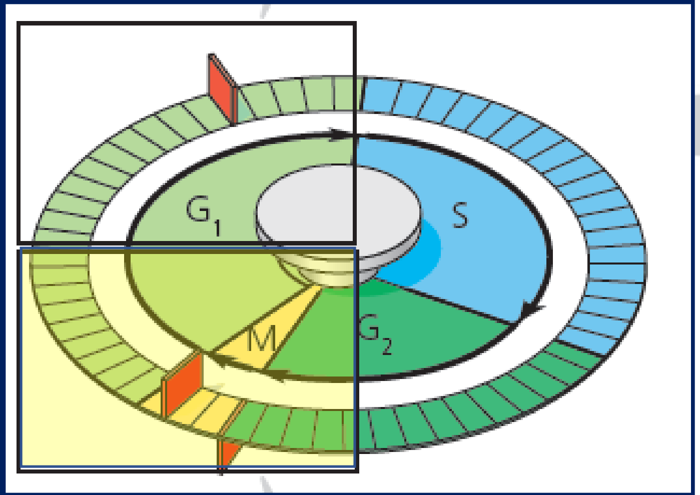
In the absence of a go-ahead signal, a cell exits the cell cycle and enters G_0, a nondividing state.

If a cell receives a go-ahead signal, the cell continues on in the cell cycle.

(a) G_1 checkpoint

Figure 12.17

Checkpoints



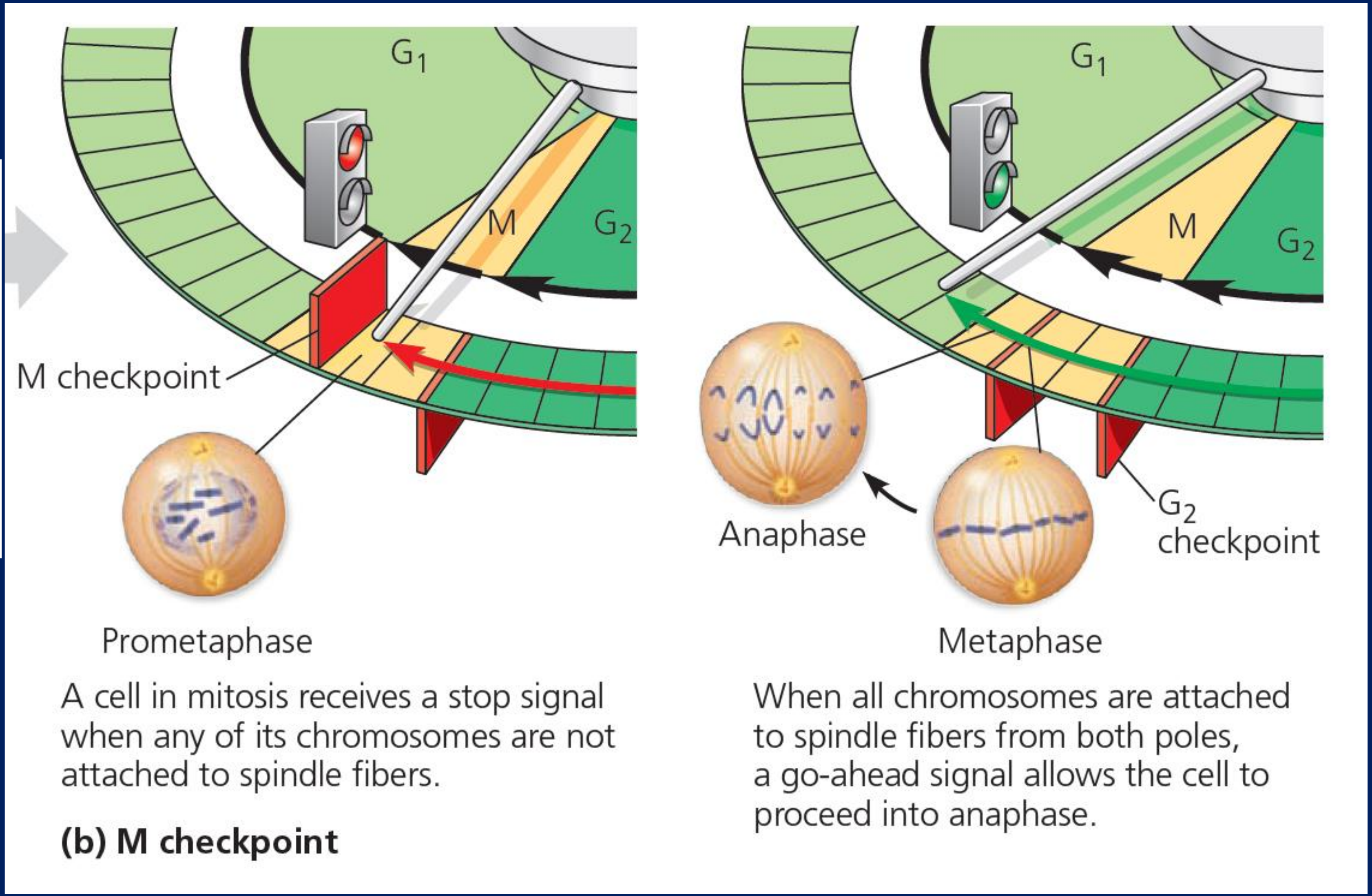


Figure 12.17

Regulation of Cell Cycle by External Signals

- In addition to the internal signals following external signals are also required for the progression of cell cycle
  - Nutrients
  - Growth factors
  - Space (Crowded cells stop dividing) also known as density dependent inhibition
  - Substratum for anchorage (anchorage dependence)

Cancer cells lose Dependence on Internal and External signals for Proliferation

- Cancer cells do not stop at cell cycle checkpoints
- Do not exhibit density dependent inhibition (form multiple layers of cells)
- Do not require anchorage with the substratum

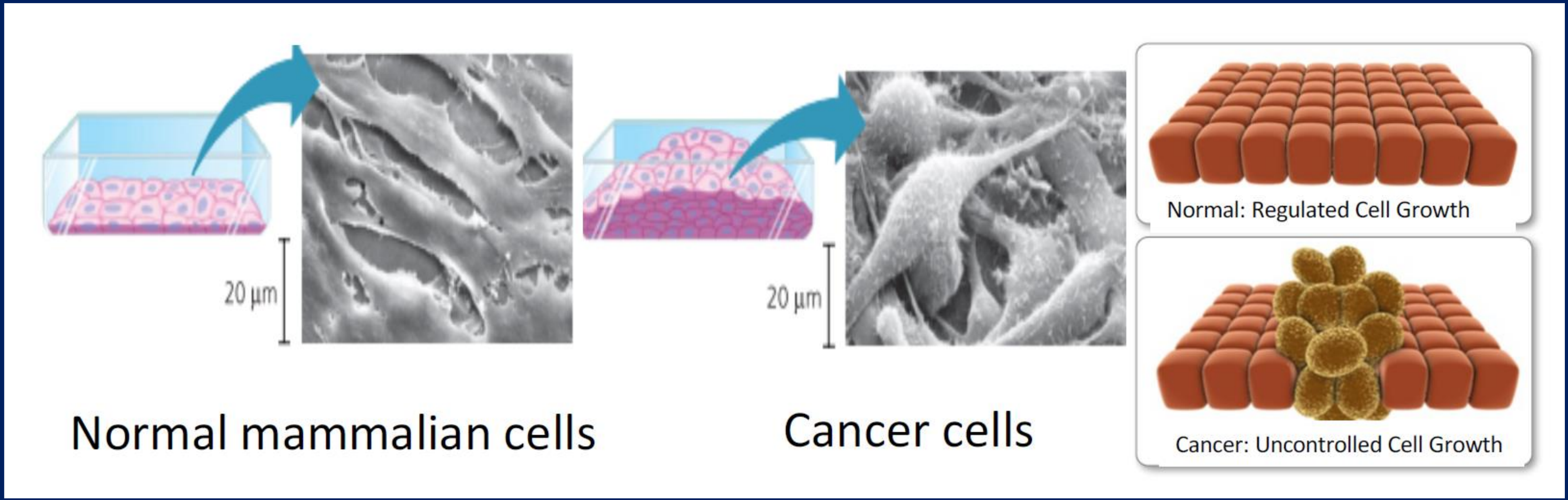


Figure 12.19

Class 3: learning objectives

- Cell Cycle
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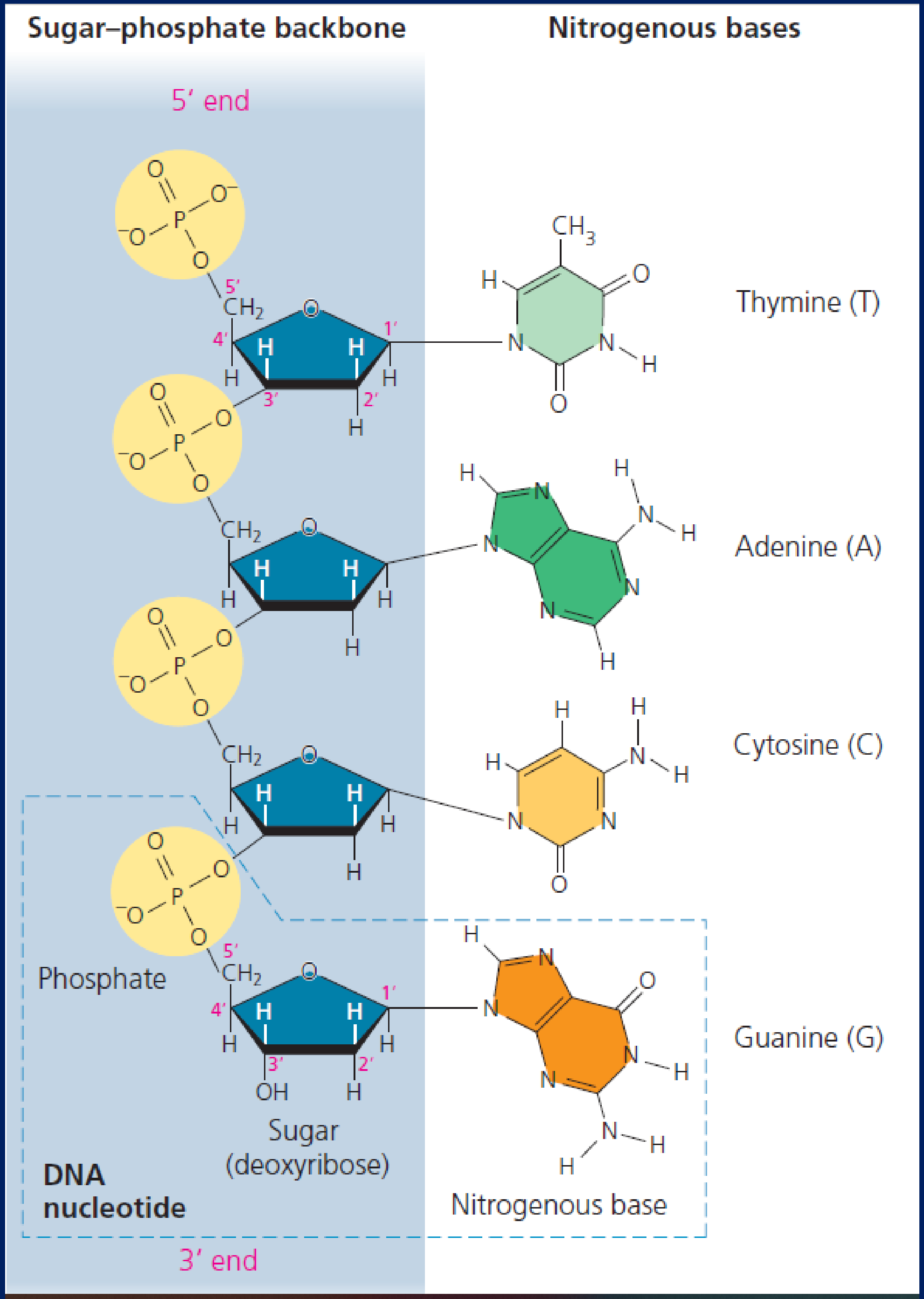

Sugar–phosphate backbone
Nitrogenous bases
5′ end
Thymine (T)
Adenine (A)
Cytosine (C)
Guanine (G)
Phosphate
Sugar
(deoxyribose)
Nitrogenous base
DNA
nucleotide
3′ end

Base composition of DNA

Source of DNA	Base percentage			
	Adenine	Guanine	Cytosine	Thymine
Sea urchin	32.8	17.7	17.3	32.1
Salmon	29.7	20.8	20.4	29.1
Wheat	28.1	21.8	22.7	27.4
E. coli	24.7	26.0	25.7	23.6
Human	30.4	19.6	19.9	30.1
Ox	29.0	21.2	21.2	28.7

From Concept 16.1

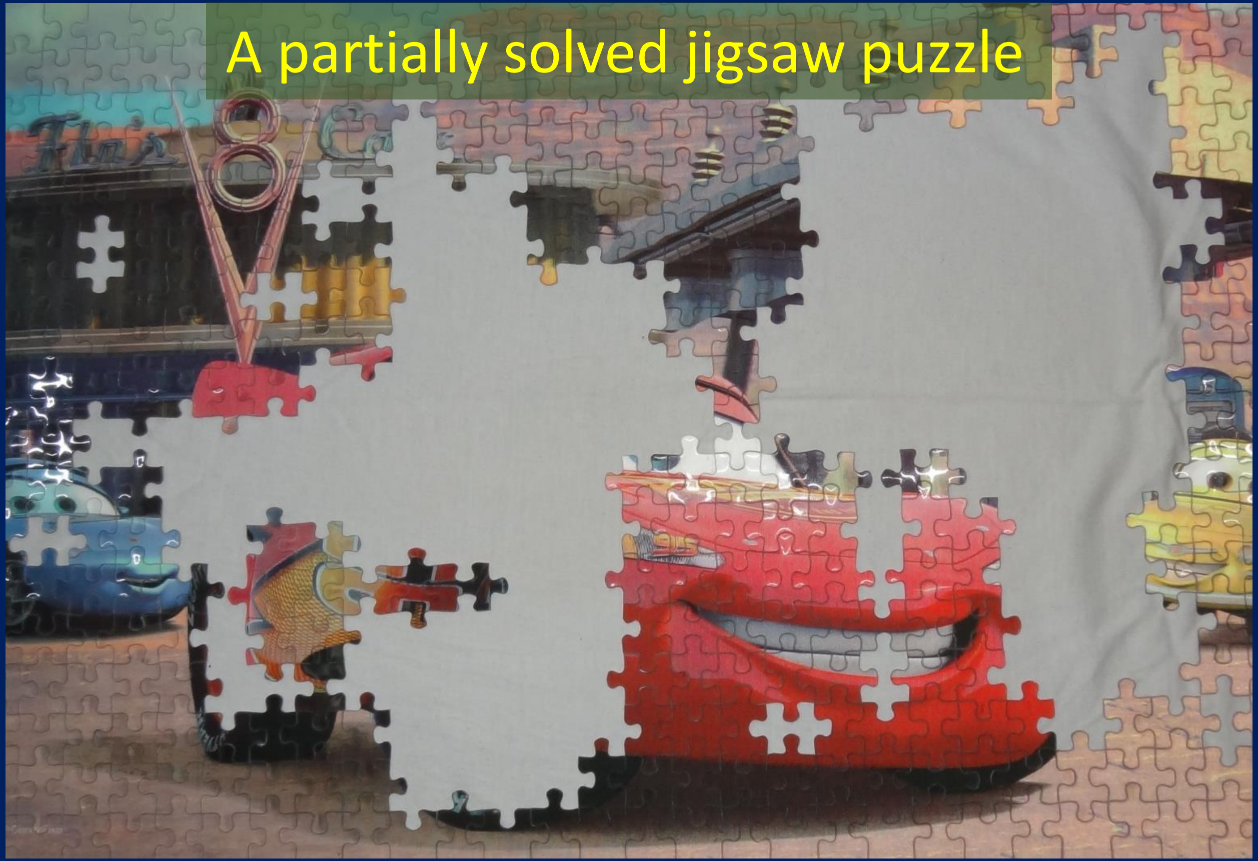
Erwin Chargaff's observations

What was already known: DNA is a polymer consisting of A, C, G and T (referred to as nucleotide bases)

- **Observation #1**: Base composition of one organism differs from that of another
  Example: Adenine base constitutes 30.4% of human DNA but only 24.7% of *E. coli* (*Escherichia coli*)
- **Observation #2**: No. of A $\simeq$ No. of T; No. of G $\simeq$ No. of C
  Example: human DNA: A = 30.4%, C = 19.9%, G = 19.6%, T = 30.1%
- **Implication**: DNA captures the molecular diversity among species

Is DNA THE genetic material?

Have we solved the problem “sufficiently enough” to arrive at the final answer?



Several experimental observations indicated that DNA is indeed the genetic material

But was the evidence conclusive?

Is there a definite end point to solving the problem?

What is the structure of DNA?

Key question

If DNA is indeed the genetic material…

What is its structure?
How does the structure account for it being the genetic material?

X-ray diffraction pattern of DNA fibers

Top quality diffraction pattern that no one else could produce!

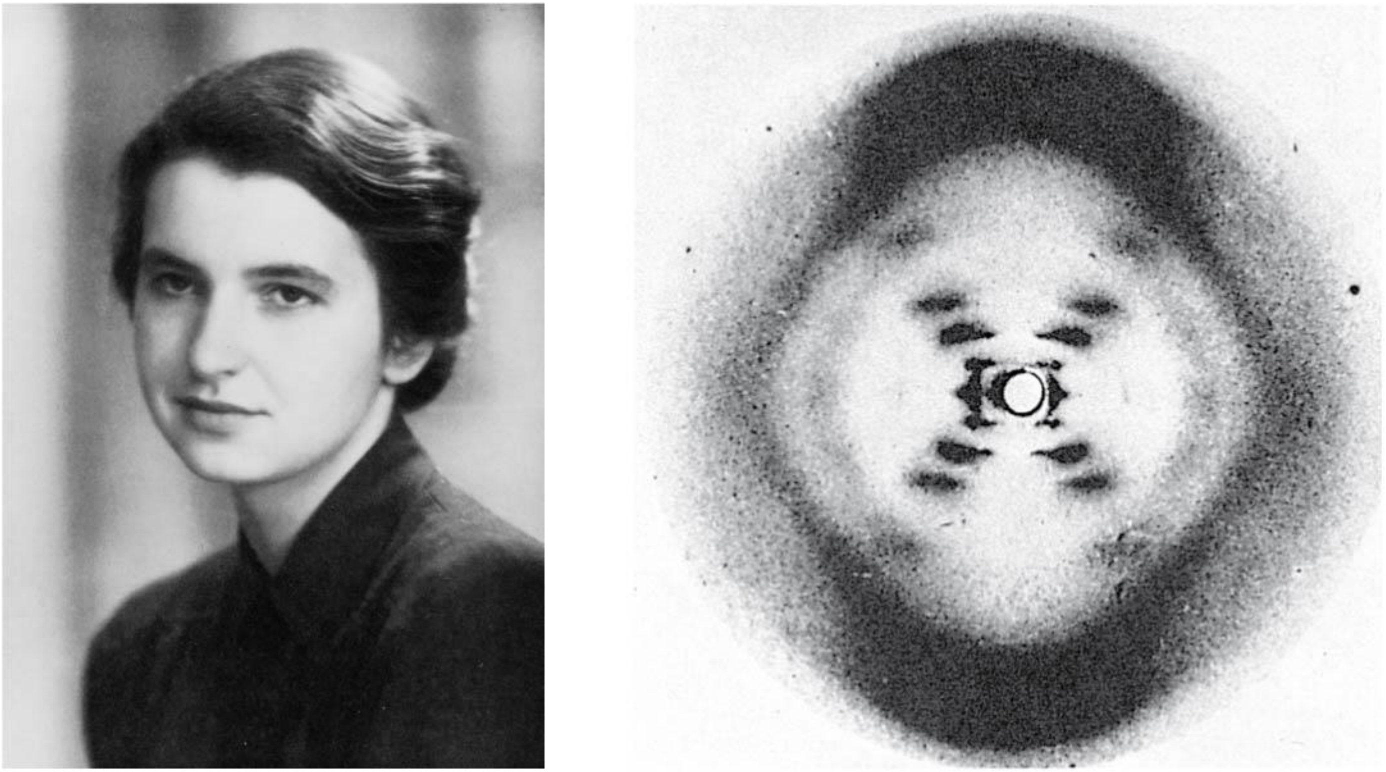


Figure 16.6

(a) Rosalind Franklin

(b) Franklin’s X-ray diffraction photograph of DNA

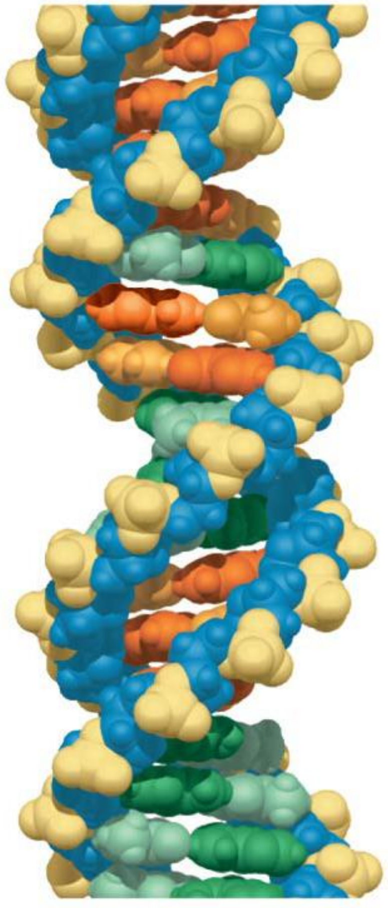
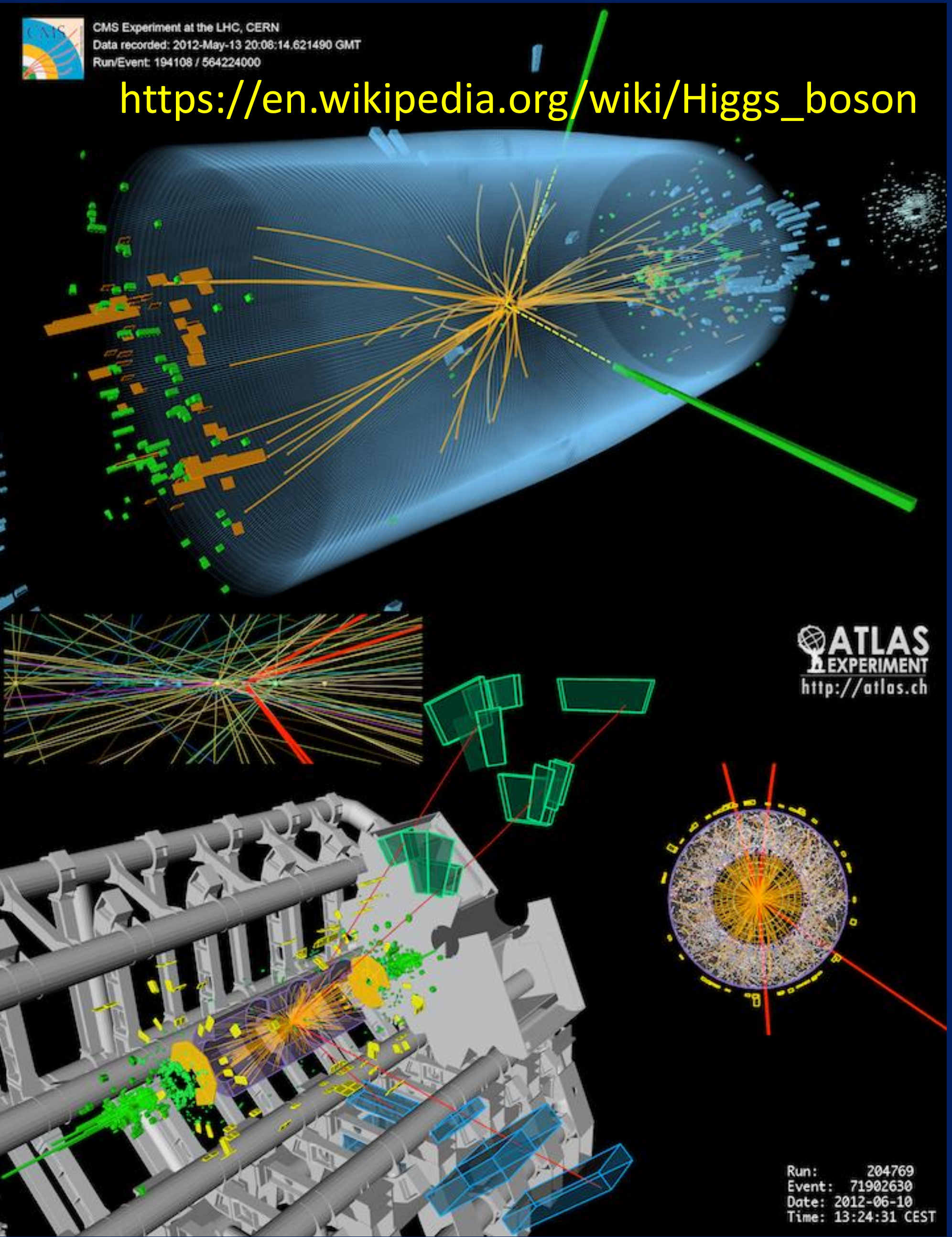


Figure 16.7

She could infer that sugar-phosphate are outside, but could not propose a model based on this data!

Higgs boson and particle physics



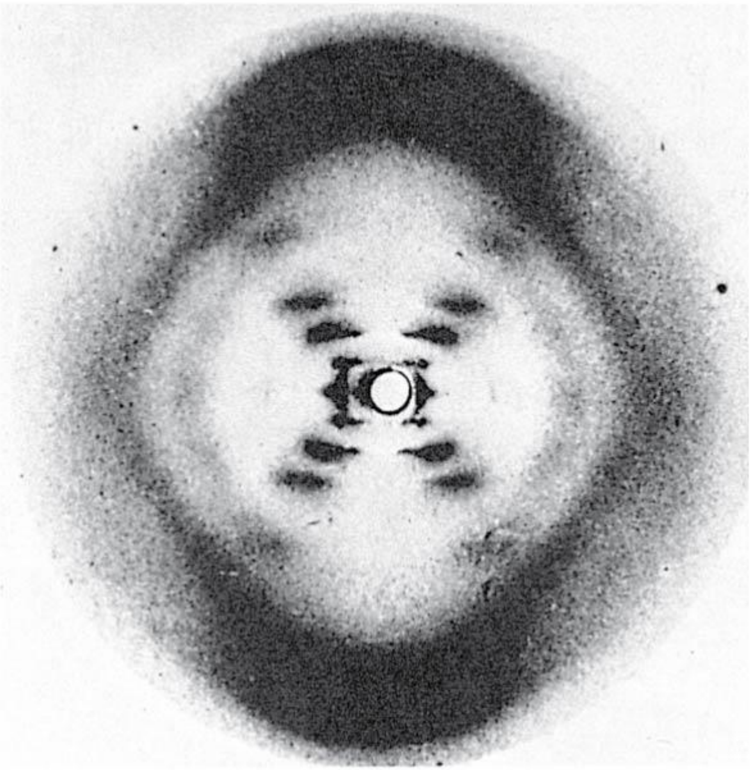
Make a hypothesis
Set up an experiment to verify

We don’t actually see a Higgs boson
But you see the “consequence” of its presence

Given the current level of our understanding, we ASSUME (INFER) that our prediction is correct

Same is true in other cases, e.g., an electron

Diffraction data to model…



(b) Franklin's X-ray diffraction photograph of DNA

Figure 16.6

Watson and Crick's inferences from this data

- DNA is helical
- Width of the helix is 2 nm
- Spacing between two bases is 0.34 nm
- There are 10 bases per turn of the helix
- DNA has two strands

The discovery that revolutionized Biology

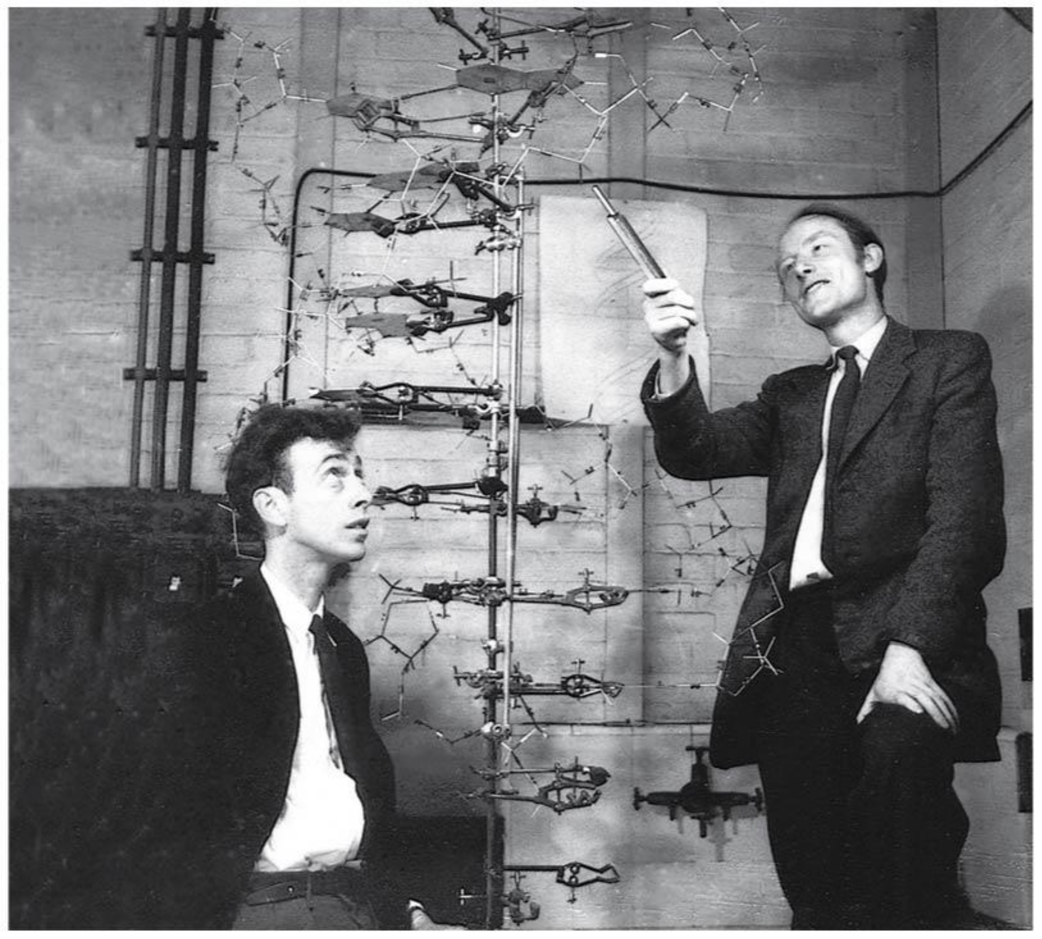


Figure 16.1

Francis Crick

James Watson

Double helix model

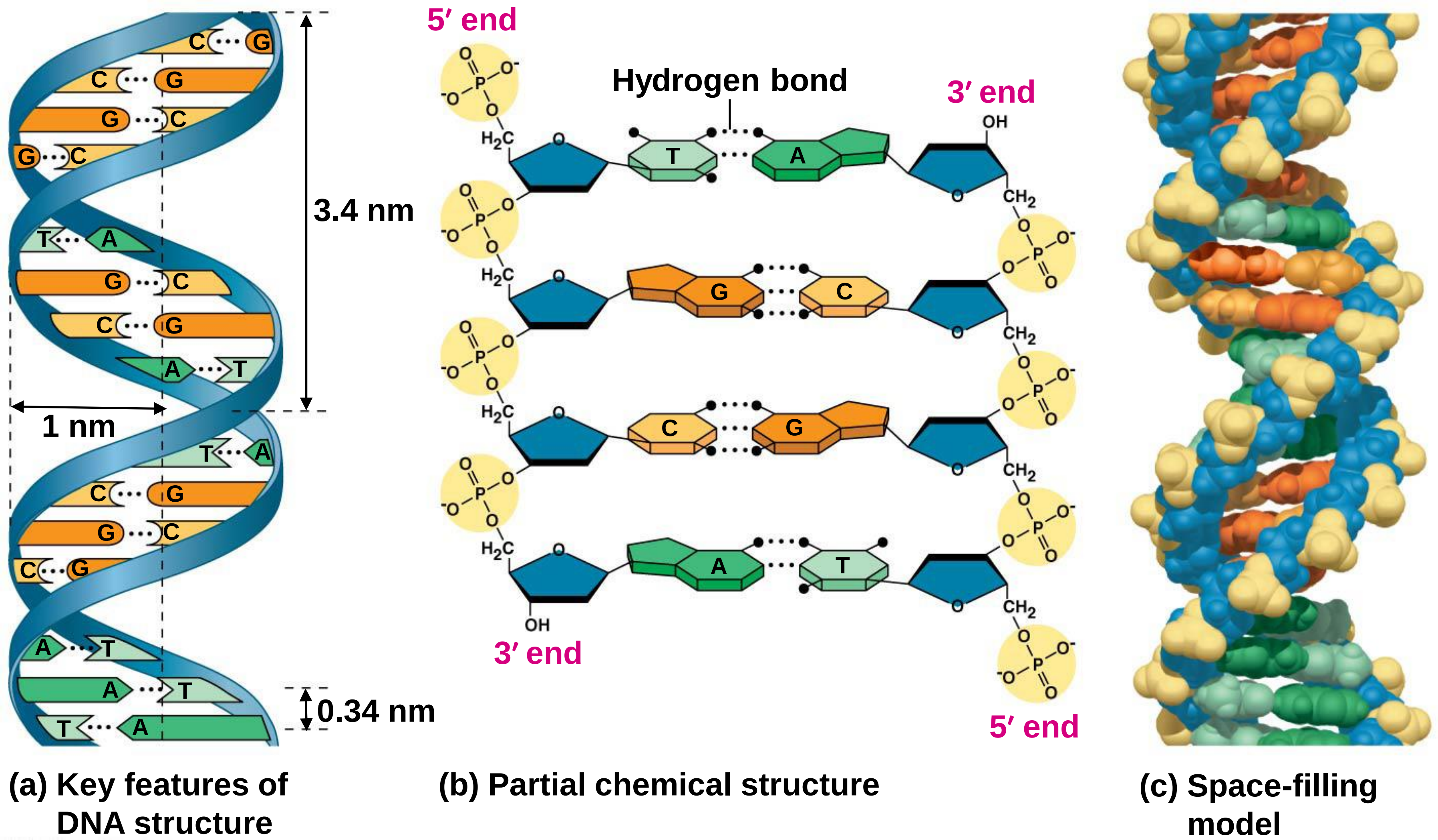
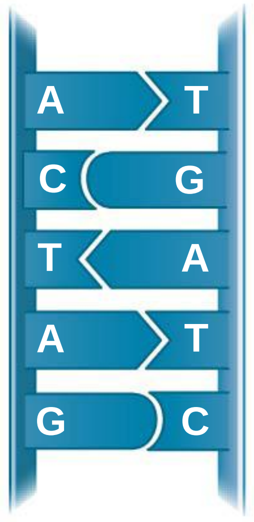


Figure 16.7

Accounts for Chargaff's observation also

Tying up: structure and being genetic material



(a) Parental molecule

Structure (form) and function (purpose)

Figure 16.9

If DNA is indeed the genetic material,
does the proposed structure offer
a “simple” mode of copying (replication)?

Tying up: structure and being genetic material

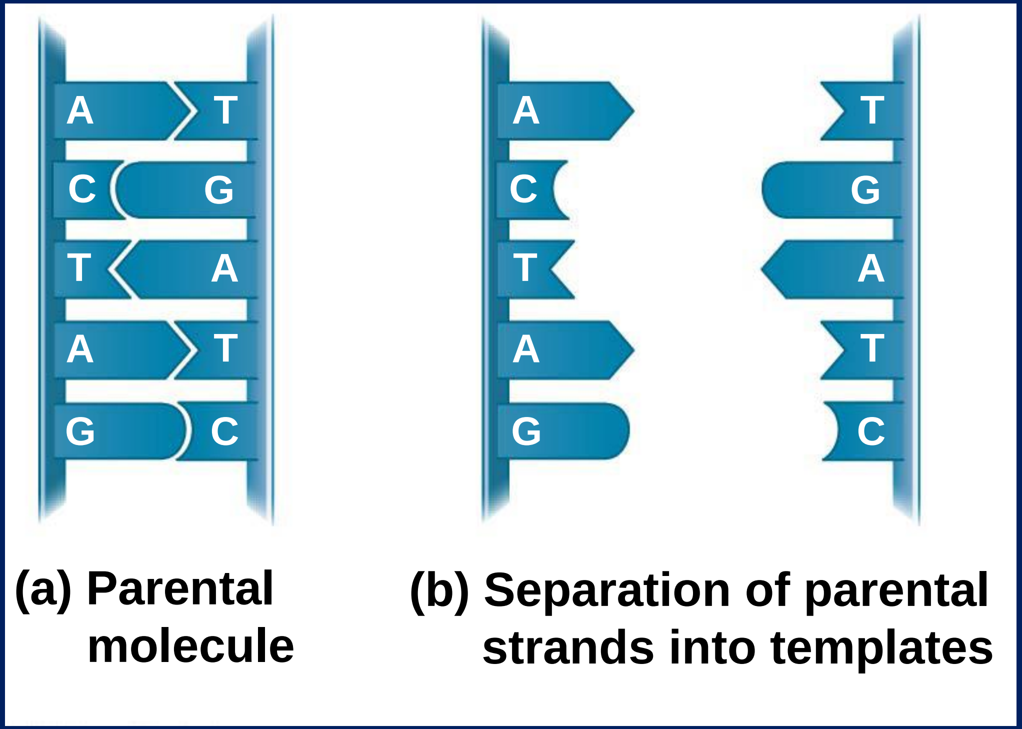


Figure 16.9

Replication model envisaged by Watson and Crick

Tying up: structure and being genetic material

Dark blue: parental strand
Light blue: daughter (new) strand

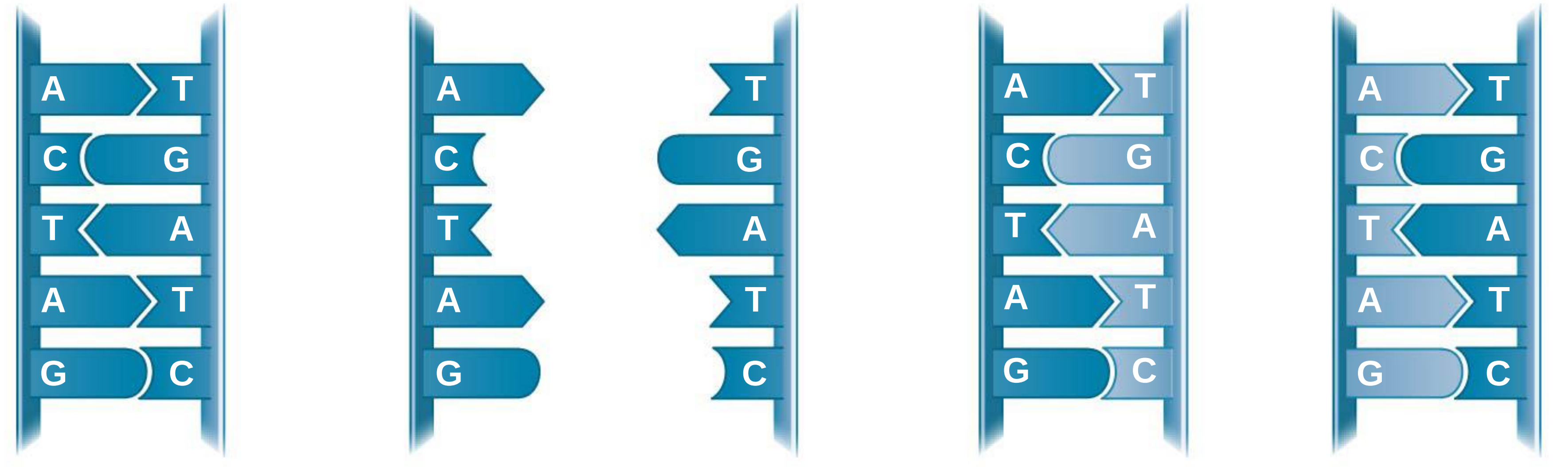


Figure 16.9

(a) Parental molecule **(b) Separation of parental strands into templates** **(c) Formation of new strands complementary to template strands**

Replication model envisaged by Watson and Crick
Semi-conservative replication model
Other proposals: conservative model, dispersive model

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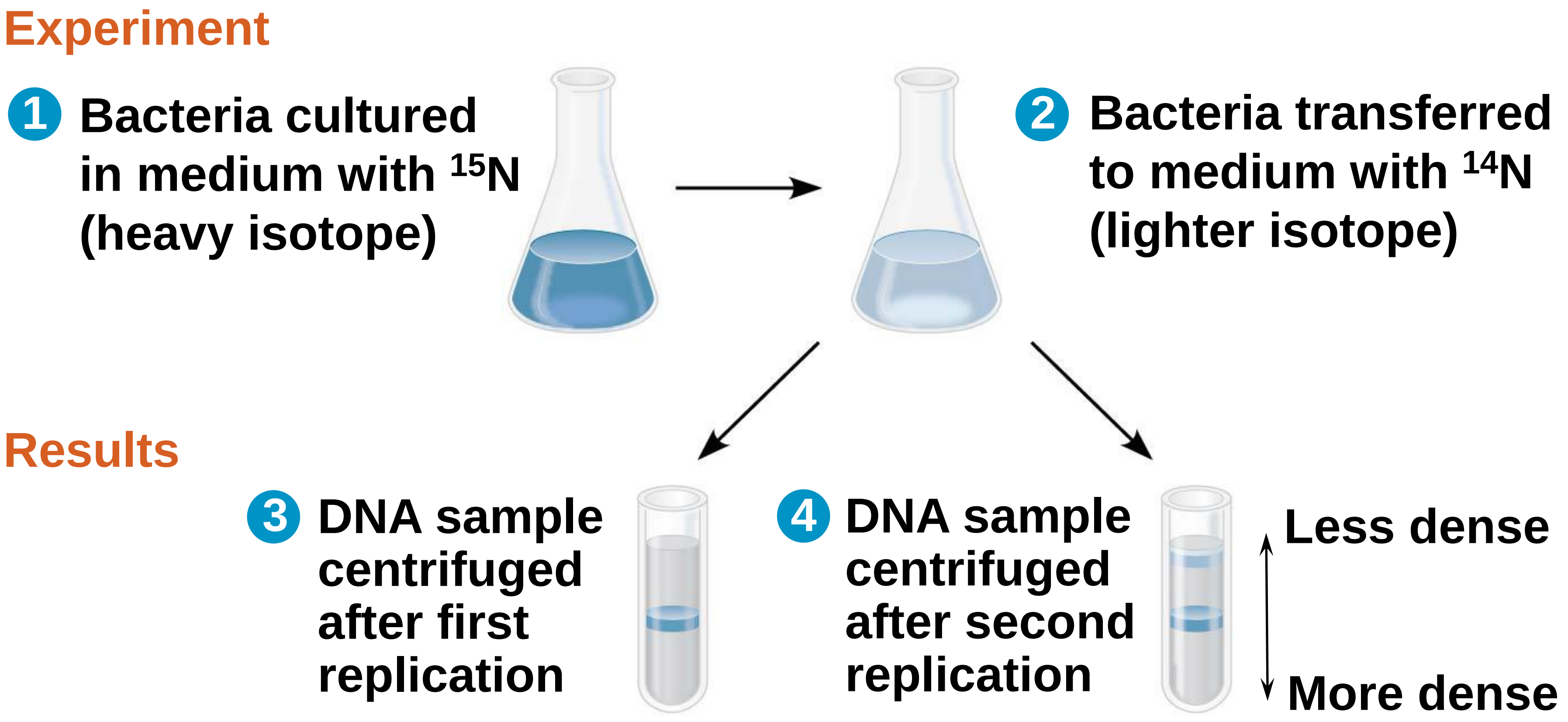
Experimental proof for the model of replication

- Matt Meselson and Frank Stahl designed **the most beautiful experiment in biology.**
- The experiment tests the DNA replication models.
- They used bacteria grown in a media of a heavy isotope of nitrogen .

http://www.slideshare.net/hhalhaddad/281-lec8-replicationexperiments

Meselson and Stahl experiment: design

Figure 16.11



Meselson and Stahl experiment: interpretation

Other possibilities:

Conservative model

Dispersive model

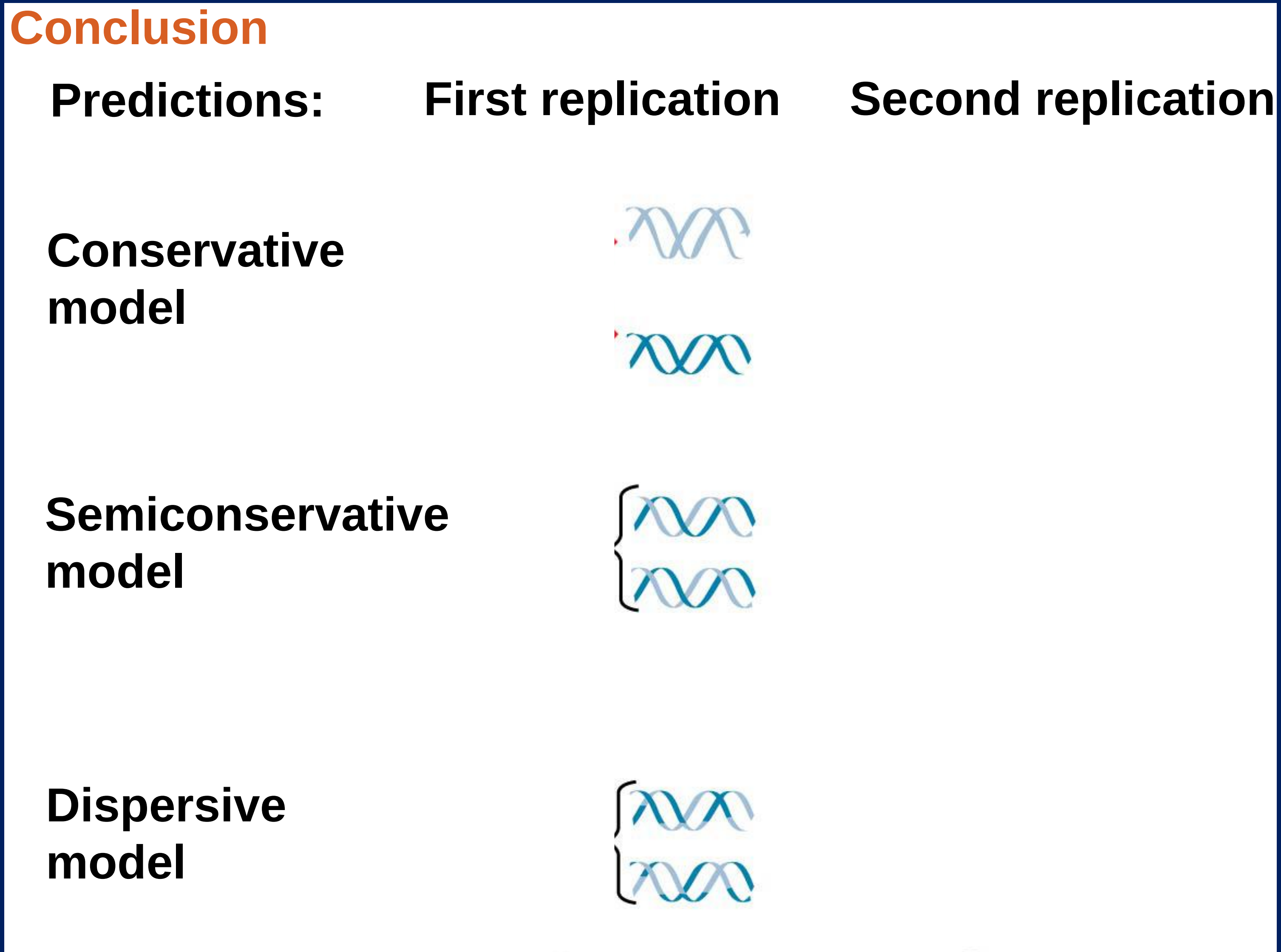


Figure 16.11

^{14}N-DNA

^{15}N-DNA

Meselson and Stahl experiment: interpretation

Other possibilities:

Conservative model

Dispersive model

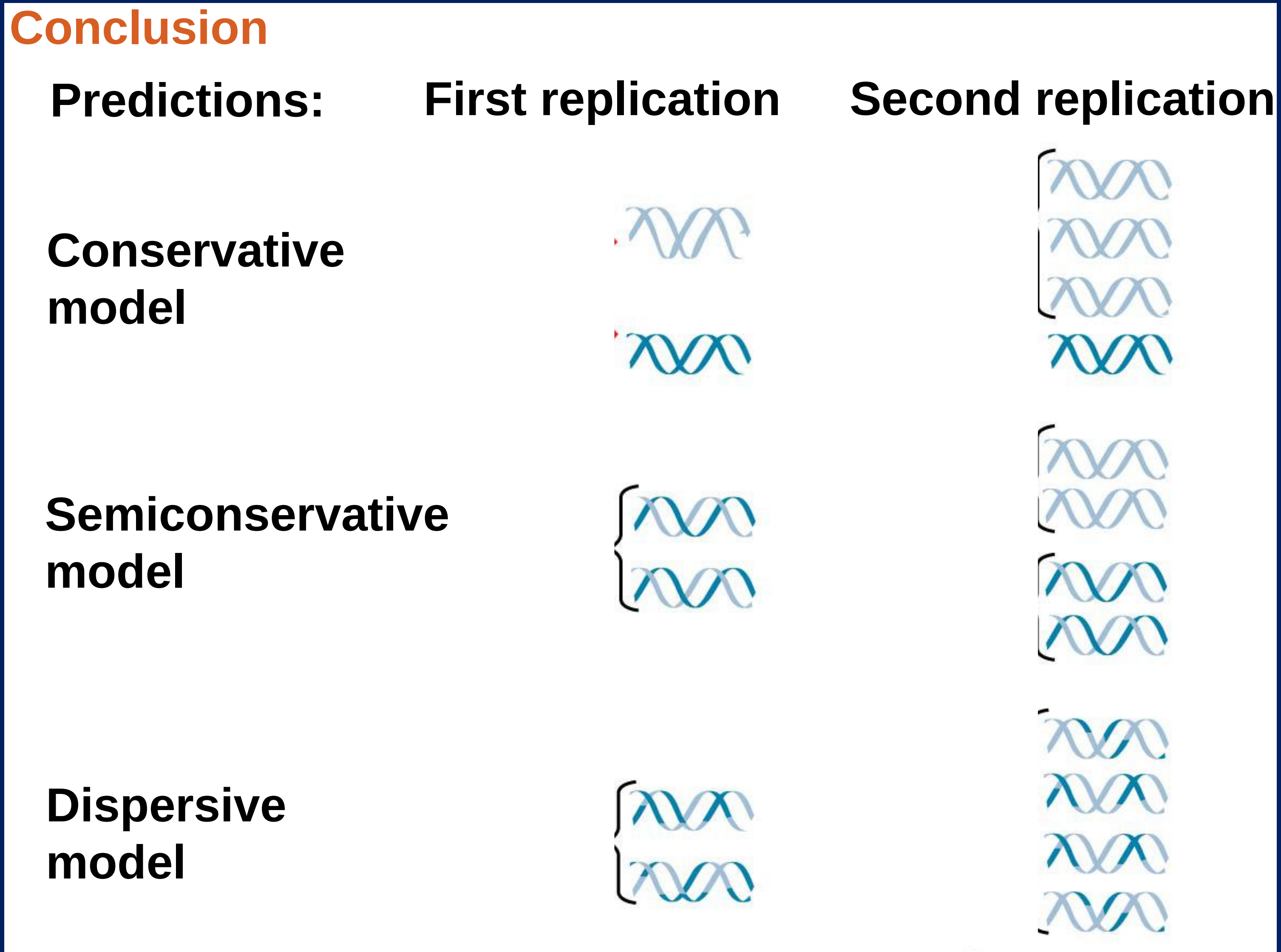
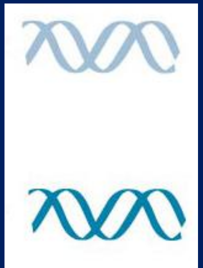


Figure 16.11

^{14}N-DNA



^{15}N-DNA

Possible models for DNA replication

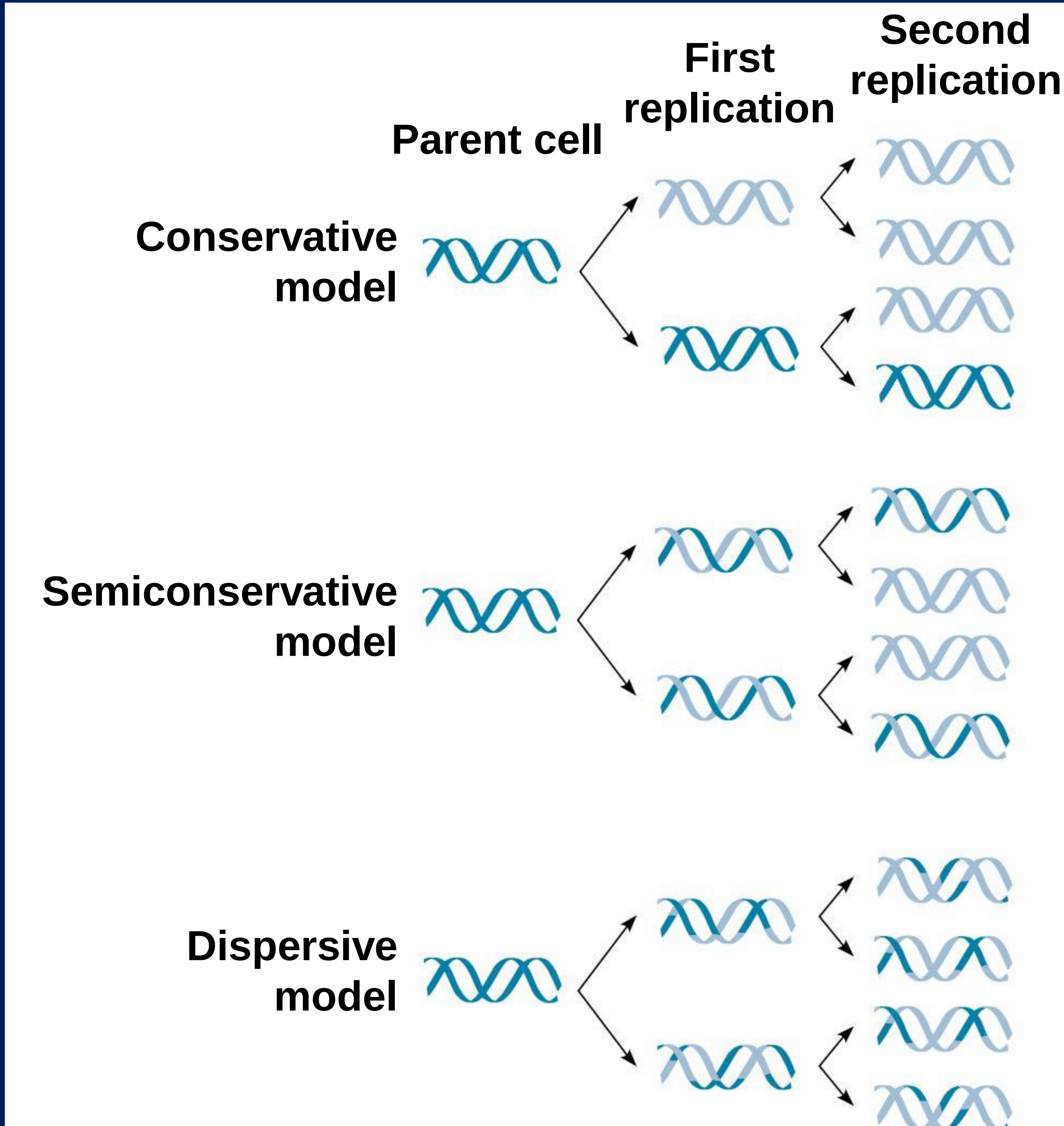
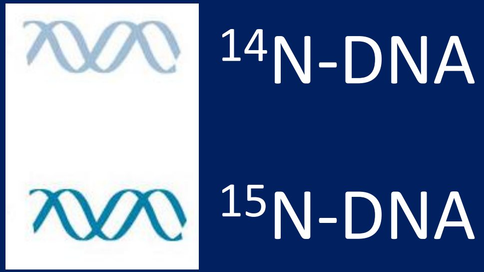


Figure 16.10



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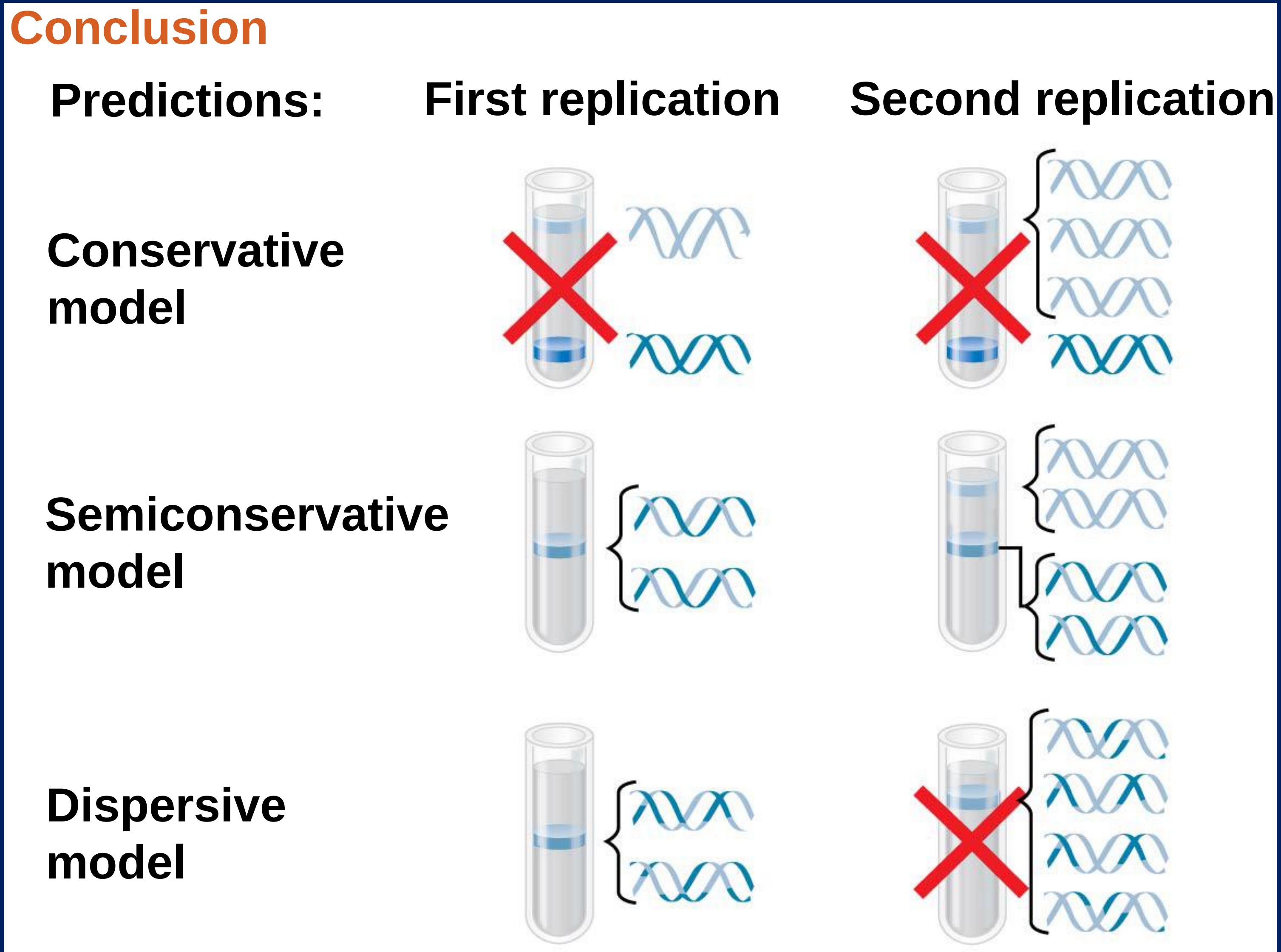

Figure 16.11