Chapter 16

The Molecular Basis of Inheritance

PowerPoint Lectures for

Biology, Seventh Edition

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Lectures by Chris Romero

- Overview: Life's Operating Instructions
- In 1953, James Watson and Francis Crick shook the world
  - With an elegant double-helical model for the structure of deoxyribonucleic acid, or DNA

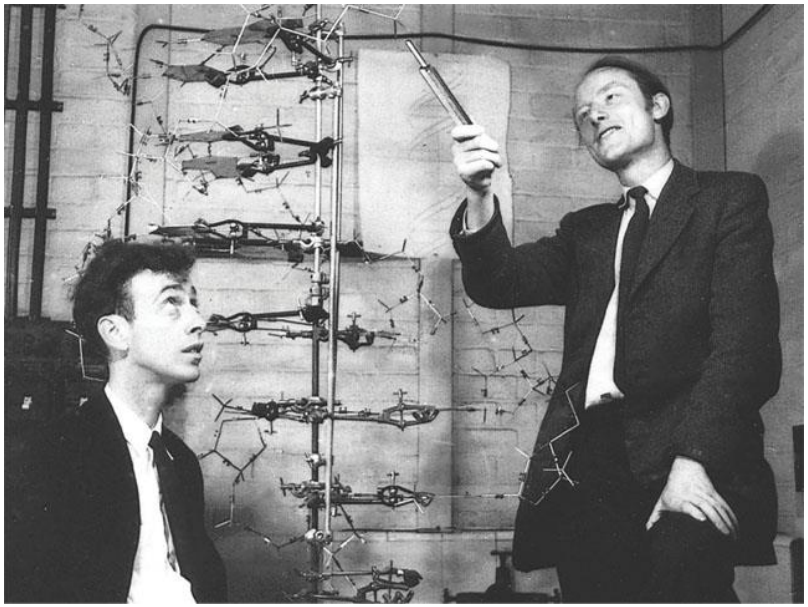


Figure 16.1

- DNA, the substance of inheritance
  - Is the most celebrated molecule of our time
- Hereditary information
  - Is encoded in the chemical language of DNA and reproduced in all the cells of your body
- It is the DNA program
  - That directs the development of many different types of traits

- Concept 16.1: DNA is the genetic material
- Early in the 20th century
  - The identification of the molecules of inheritance loomed as a major challenge to biologists

The Search for the Genetic Material: *Scientific Inquiry*

- The role of DNA in heredity
  - Was first worked out by studying bacteria and the viruses that infect them

Evidence That DNA Can Transform Bacteria

- Frederick Griffith was studying *Streptococcus pneumoniae*
  - A bacterium that causes pneumonia in mammals
- He worked with two strains of the bacterium
  - A pathogenic strain and a nonpathogenic strain

- Griffith found that when he mixed heat-killed remains of the pathogenic strain
  - With living cells of the nonpathogenic strain, some of these living cells became pathogenic

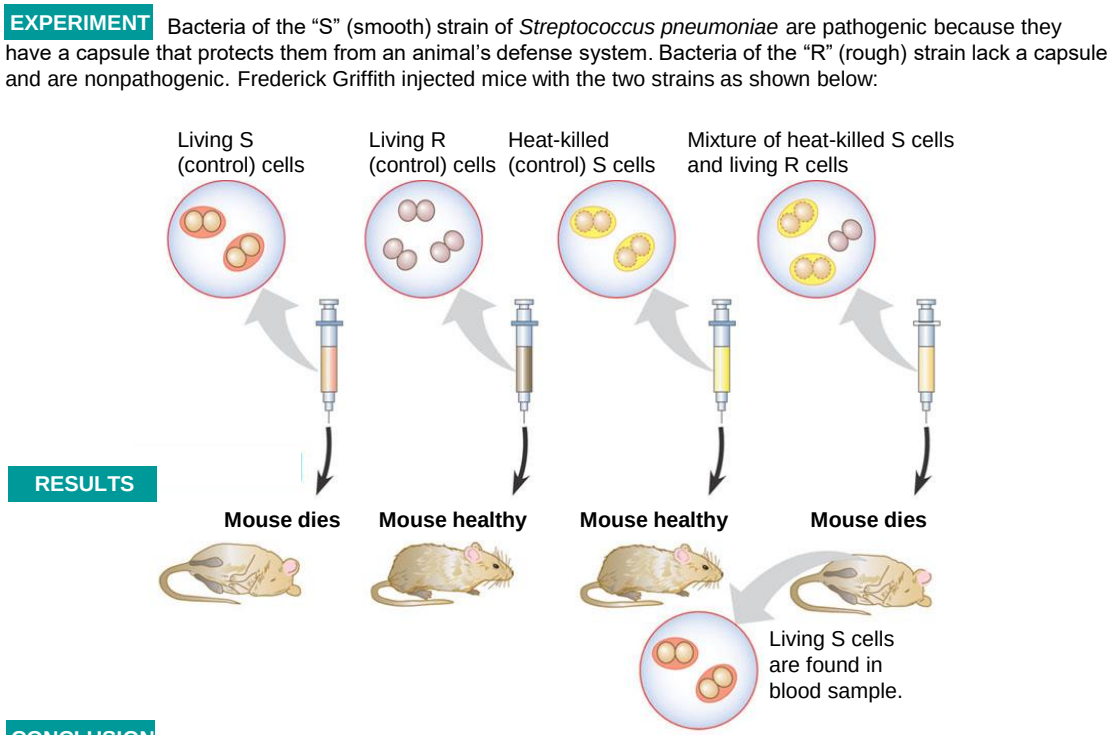


Figure 16.2

- Griffith called the phenomenon transformation
  - Now defined as a change in genotype and phenotype due to the assimilation of external DNA by a cell

Evidence That Viral DNA Can Program Cells

- Additional evidence for DNA as the genetic material
  - Came from studies of a virus that infects bacteria

- Viruses that infect bacteria, bacteriophages
  - Are widely used as tools by researchers in molecular genetics

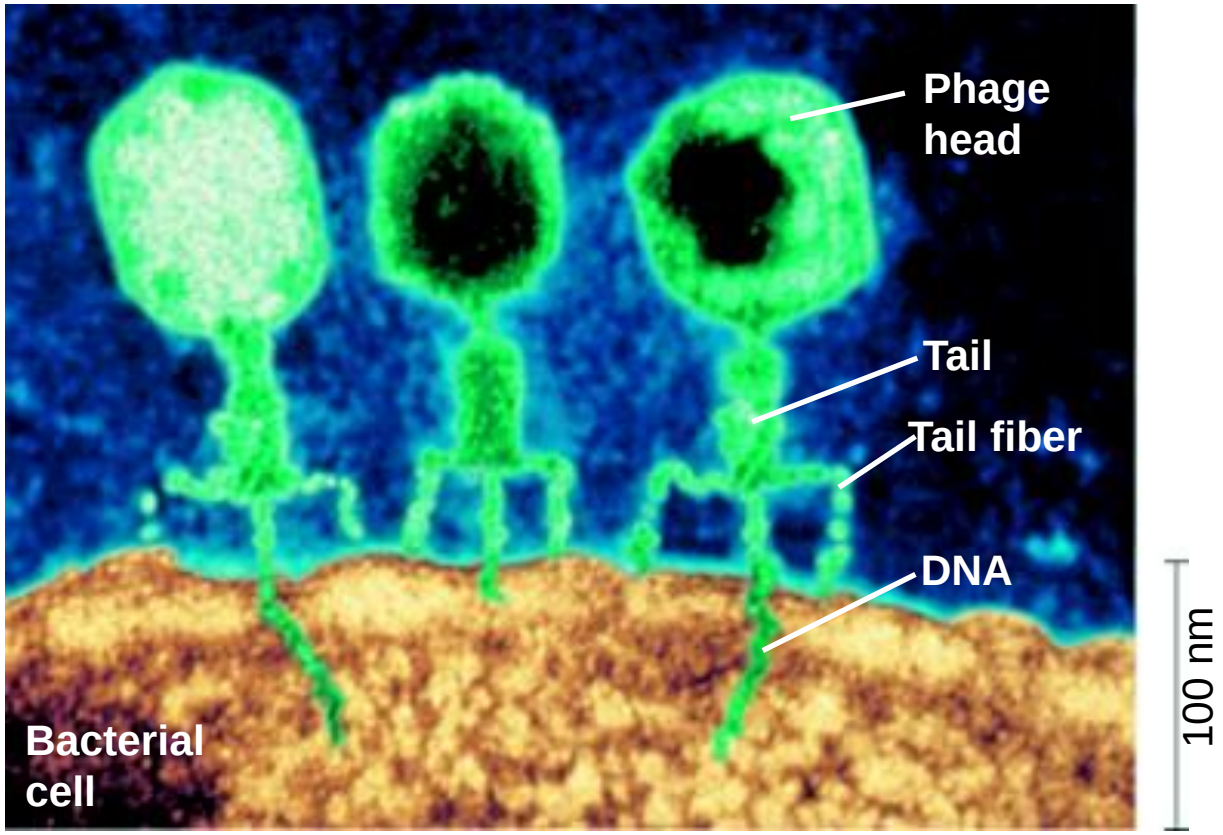
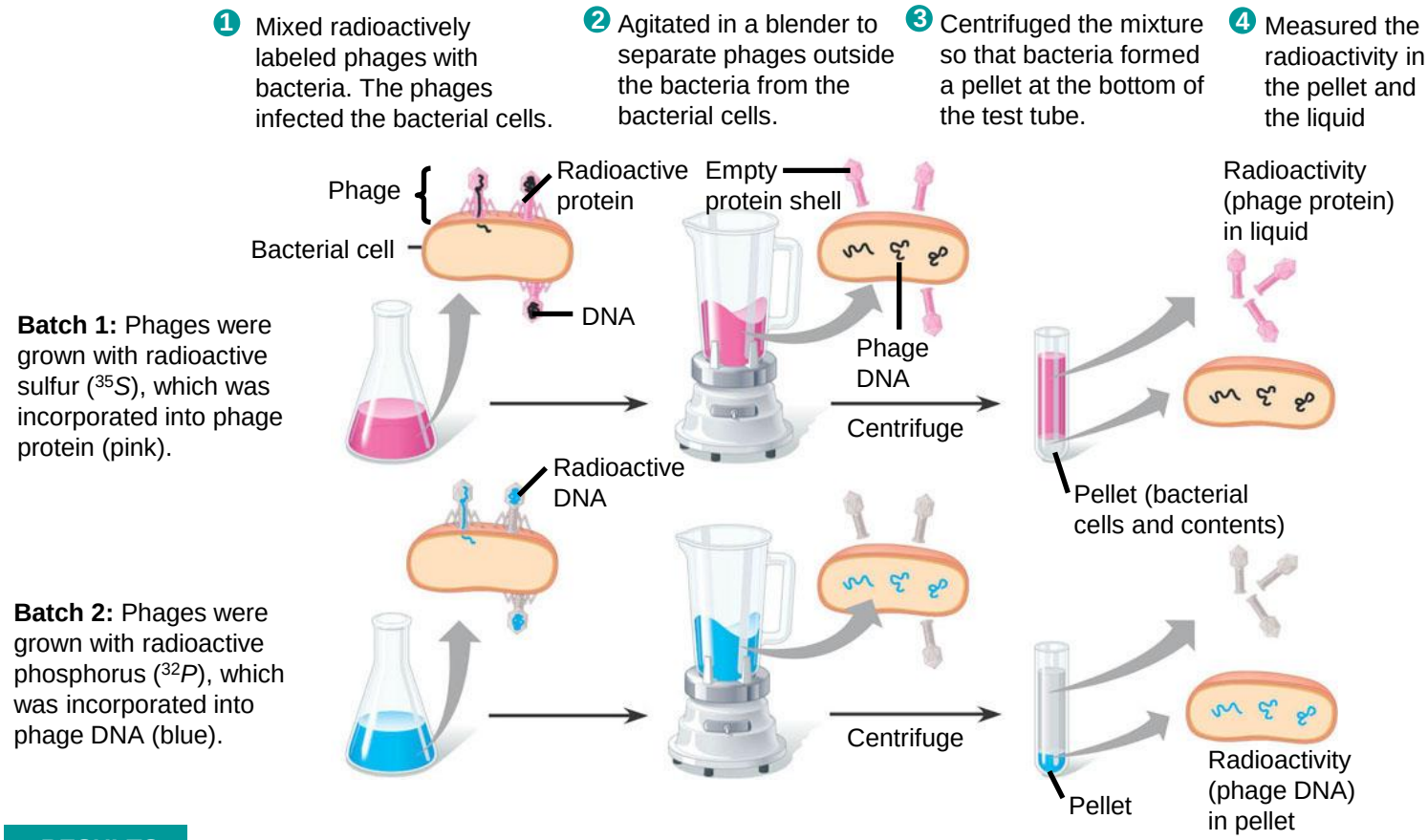


Figure 16.3

- Alfred Hershey and Martha Chase
  - Performed experiments showing that DNA is the genetic material of a phage known as T2

- # The Hershey and Chase experiment

EXPERIMENT In their famous 1952 experiment, Alfred Hershey and Martha Chase used radioactive sulfur and phosphorus to trace the fates of the protein and DNA, respectively, of T2 phages that infected bacterial cells.



RESULTS Phage proteins remained outside the bacterial cells during infection, while phage DNA entered the cells. When cultured, bacterial cells with radioactive phage DNA released new phages with some radioactive phosphorus.

CONCLUSION Hershey and Chase concluded that DNA, not protein, functions as the T2 phage's genetic material.

Figure 16.4

Additional Evidence That DNA Is the Genetic Materia

- Prior to the 1950s, it was already known that DNA
  - Is a polymer of nucleotides, each consisting of three components: a nitrogenous base, a sugar, and a phosphate group

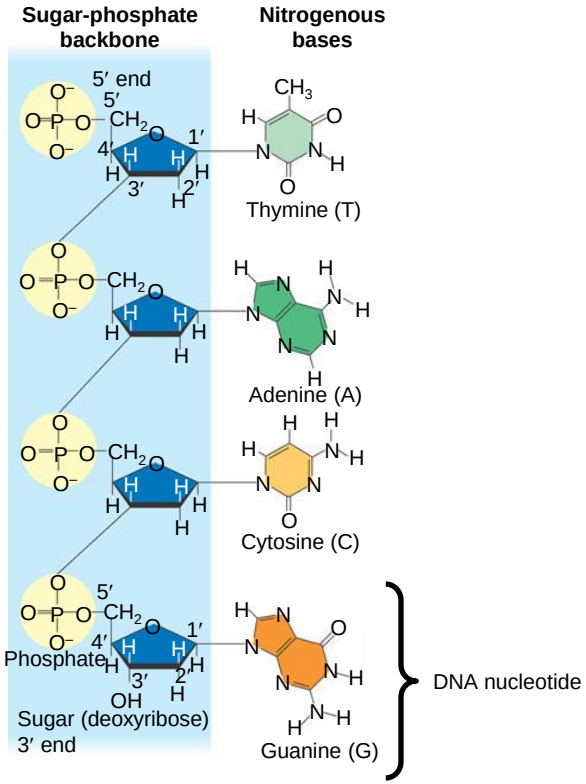


Figure 16.5

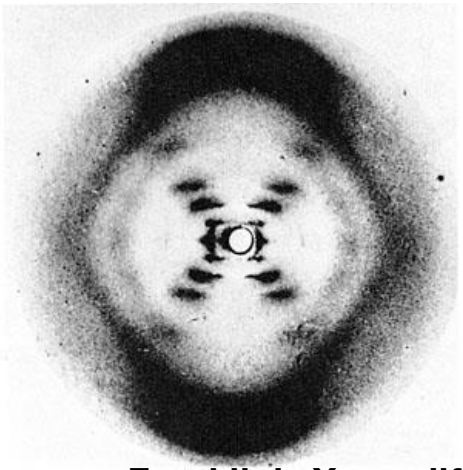
- Erwin Chargaff analyzed the base composition of DNA
  - From a number of different organisms
- In 1947, Chargaff reported
  - That DNA composition varies from one species to the next
- This evidence of molecular diversity among species
  - Made DNA a more credible candidate for the genetic material

Building a Structural Model of DNA: *Scientific Inquiry*

- Once most biologists were convinced that DNA was the genetic material
  - The challenge was to determine how the structure of DNA could account for its role in inheritance

- Maurice Wilkins and Rosalind Franklin
  - Were using a technique called X-ray crystallography to study molecular structure
- Rosalind Franklin
  - Produced a picture of the DNA molecule using this technique

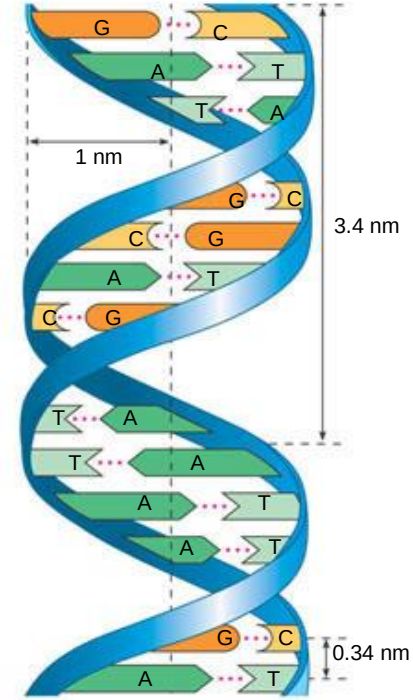
(a) Rosalind Franklin



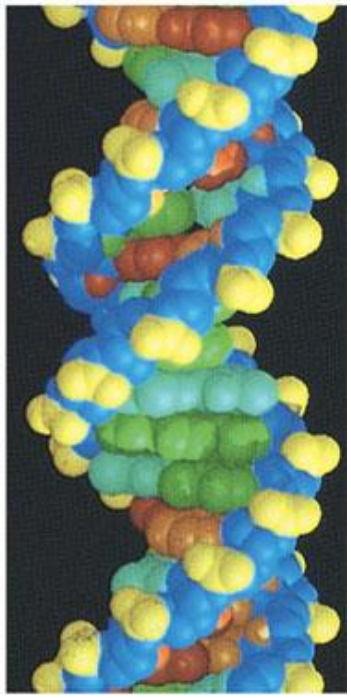
(b) Franklin's X-ray diffraction Photograph of DNA

Figure 16.6 a, b

- Watson and Crick deduced that DNA was a double helix
  - Through observations of the X-ray crystallographic images of DNA



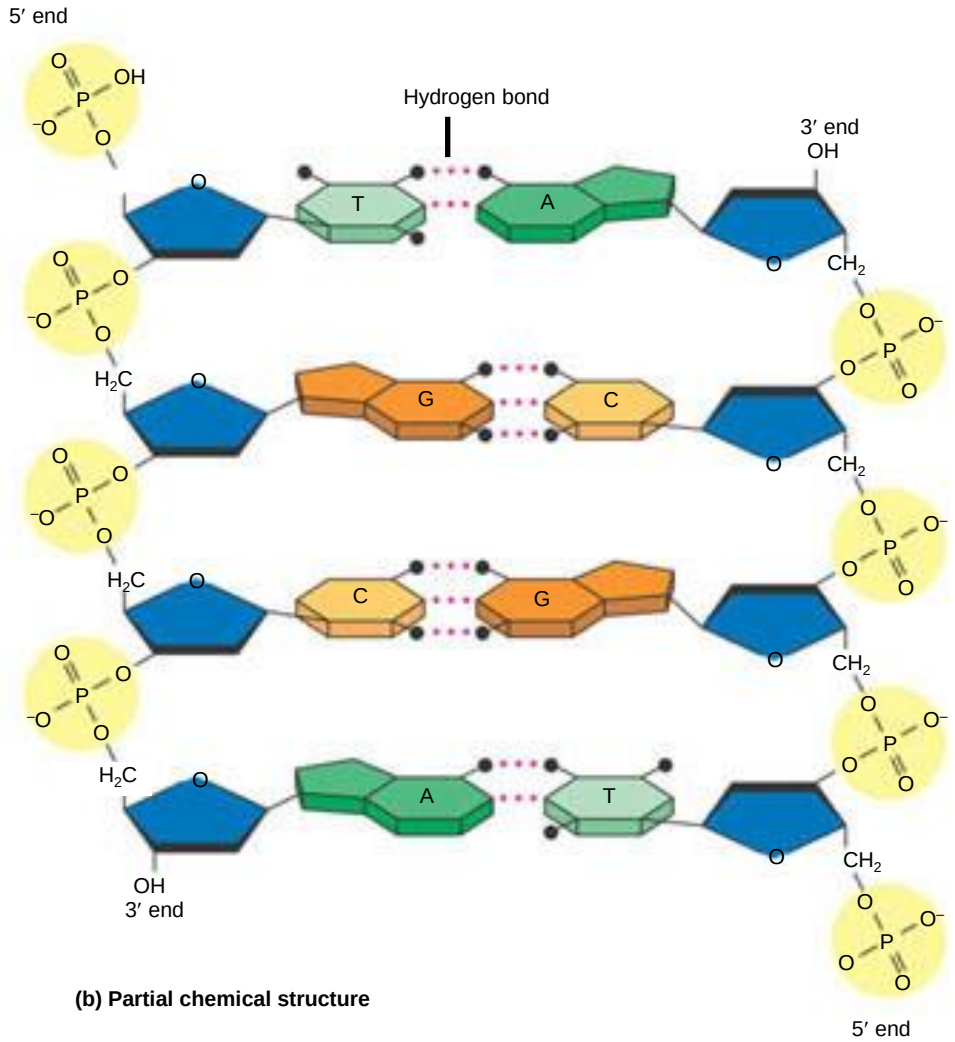
(a) Key features of DNA structure



(c) Space-filling model

Figure 16.7a, c

- Franklin had concluded that DNA
  - Was composed of two antiparallel sugar-phosphate backbones, with the nitrogenous bases paired in the molecule's interior
- The nitrogenous bases
  - Are paired in specific combinations: adenine with thymine, and cytosine with guanine



(b) Partial chemical structure

Figure 16.7b

- Watson and Crick reasoned that there must be additional specificity of pairing
  - Dictated by the structure of the bases
- Each base pair forms a different number of hydrogen bonds
  - Adenine and thymine form two bonds, cytosine and guanine form three bonds

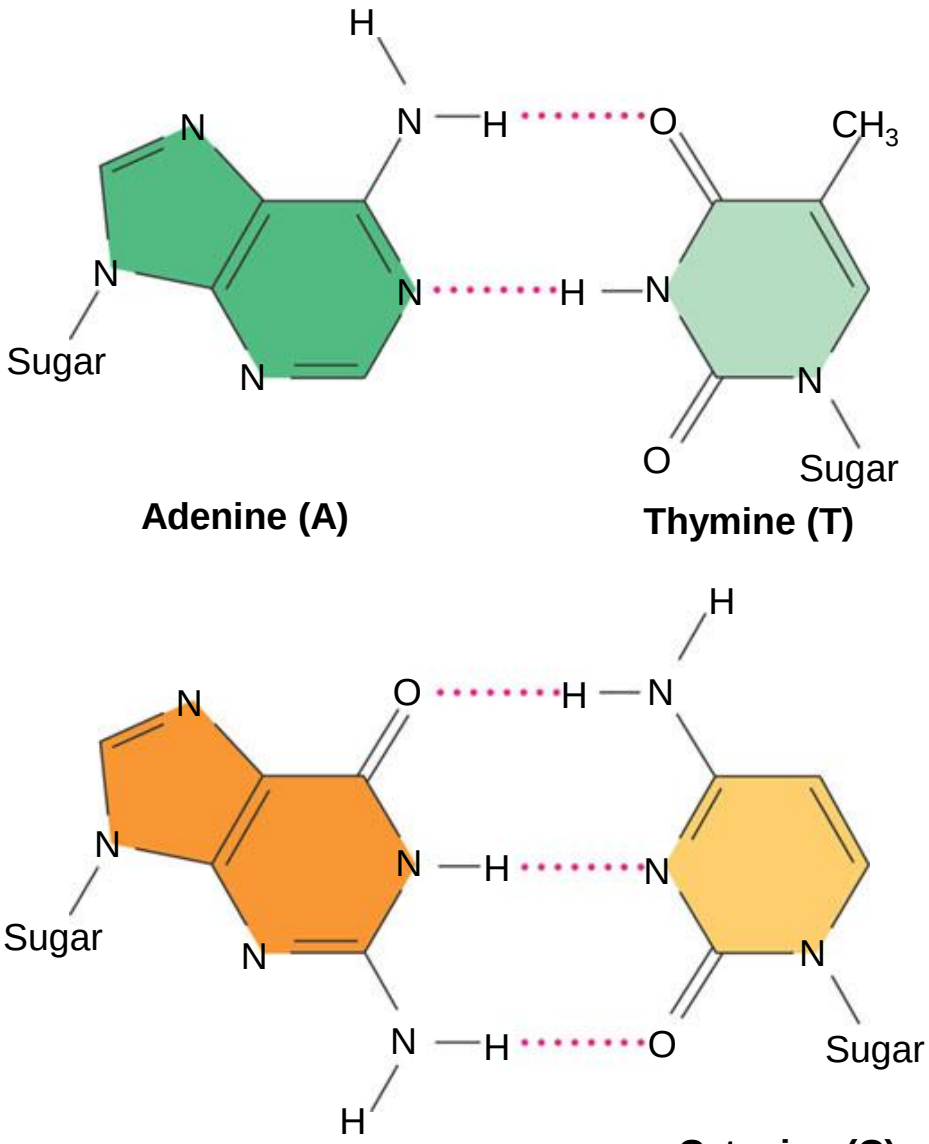


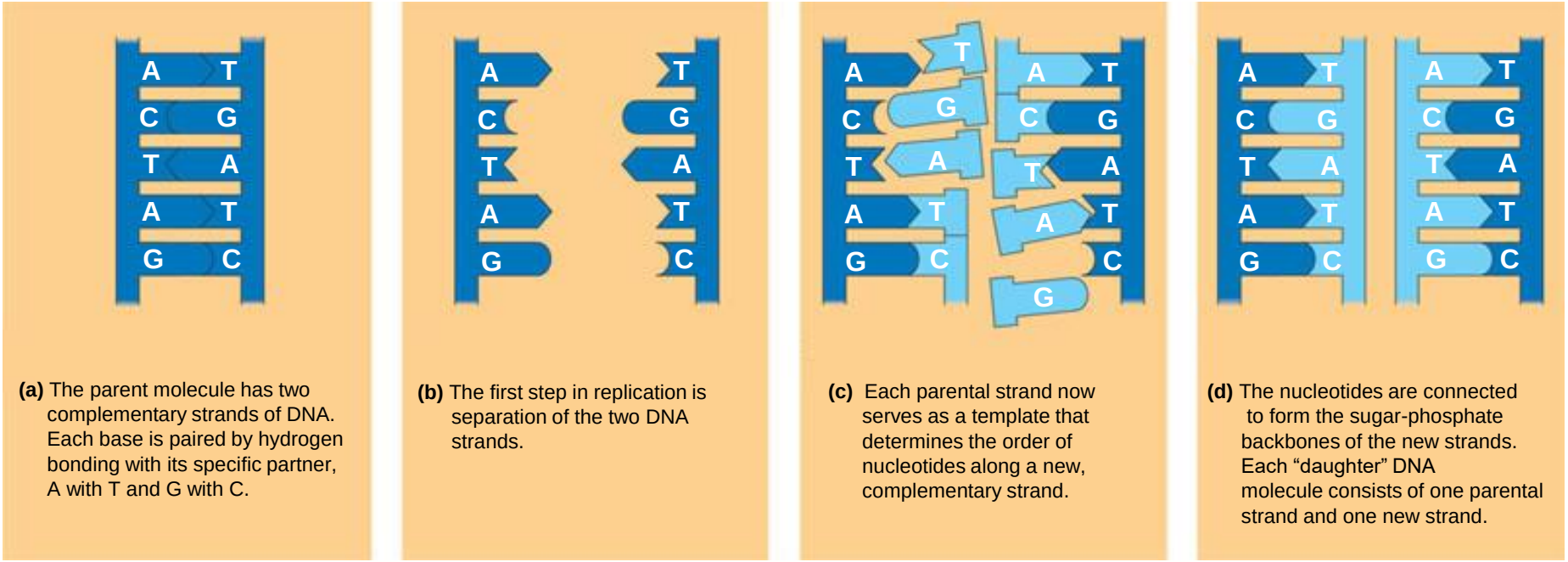
Figure 16.8

- Concept 16.2: Many proteins work together in DNA replication and repair
- The relationship between structure and function
  - Is manifest in the double helix

The Basic Principle: Base Pairing to a Template Strand

- Since the two strands of DNA are complementary
  - Each strand acts as a template for building a new strand in replication

- In DNA replication
  - The parent molecule unwinds, and two new daughter strands are built based on base-pairing rules



(a) The parent molecule has two complementary strands of DNA. Each base is paired by hydrogen bonding with its specific partner, A with T and G with C.

(b) The first step in replication is separation of the two DNA strands.

(c) Each parental strand now serves as a template that determines the order of nucleotides along a new, complementary strand.

(d) The nucleotides are connected to form the sugar-phosphate backbones of the new strands. Each "daughter" DNA molecule consists of one parental strand and one new strand.

Figure 16.9 a–d

- DNA replication is semiconservative
  - Each of the two new daughter molecules will have one old strand, derived from the parent molecule, and one newly made strand

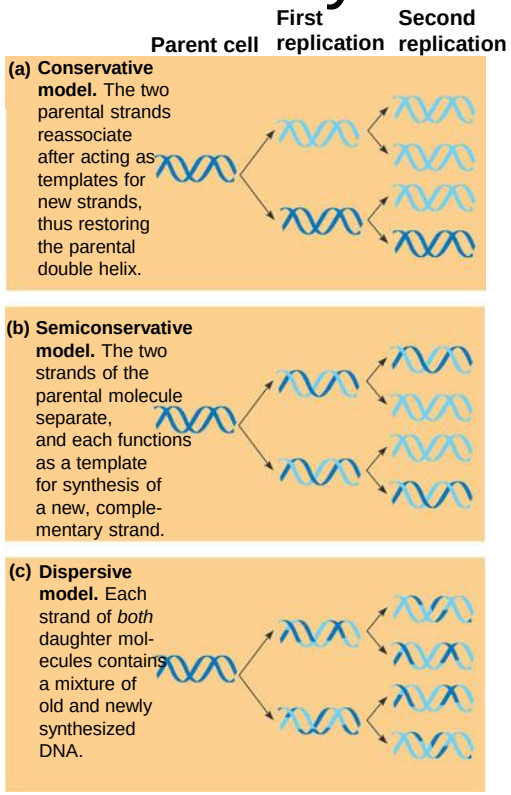


Figure 16.10 a–c

- Experiments performed by Meselson and Stahl
  - Supported the semiconservative model of DNA replication

EXPERIMENT Matthew Meselson and Franklin Stahl cultured *E. coli* bacteria for several generations on a medium containing nucleotide precursors labeled with a heavy isotope of nitrogen, ^{15}N. The bacteria incorporated the heavy nitrogen into their DNA. The scientists then transferred the bacteria to a medium with only ^{14}N, the lighter, more common isotope of nitrogen. Any new DNA that the bacteria synthesized would be lighter than the parental DNA made in the ^{15}N medium. Meselson and Stahl could distinguish DNA of different densities by centrifuging DNA extracted from the bacteria.

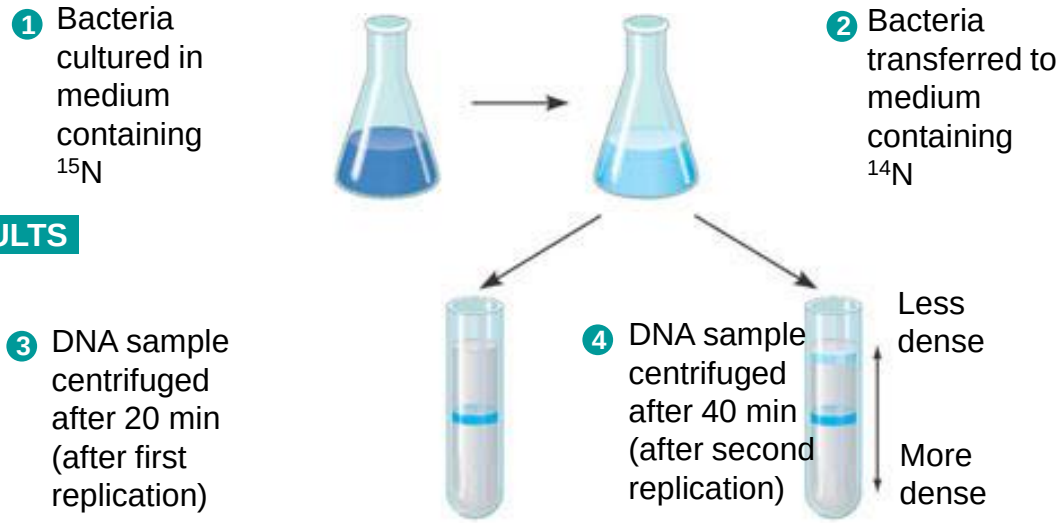
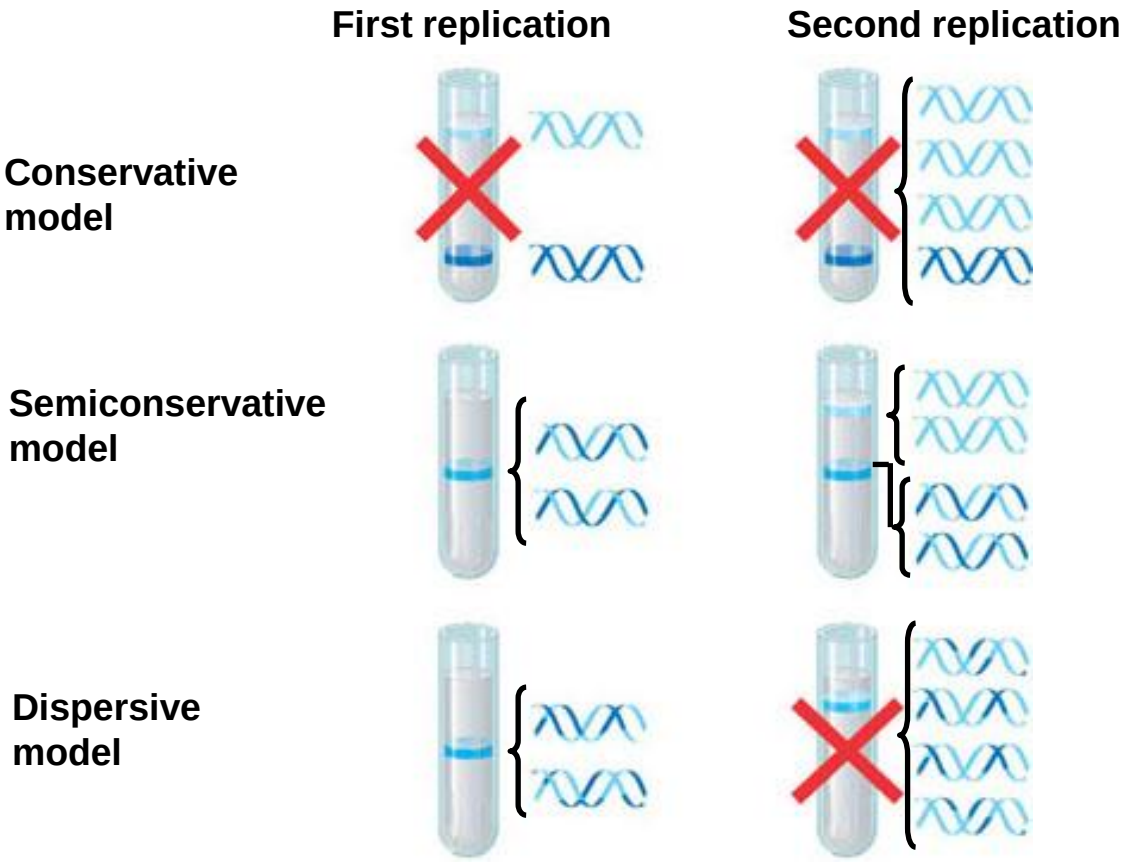


Figure 16.11 The bands in these two centrifuge tubes represent the results of centrifuging two DNA samples from the flask in step 2, one sample taken after 20 minutes and one after 40 minutes.

CONCLUSION Meselson and Stahl concluded that DNA replication follows the semiconservative model by comparing their result to the results predicted by each of the three models in Figure 16.10. The first replication in the ^{14}N medium produced a band of hybrid (^{15}N–^{14}N) DNA. This result eliminated the conservative model. A second replication produced both light and hybrid DNA, a result that eliminated the dispersive model and supported the semiconservative model.



DNA Replication: *A Closer Look*

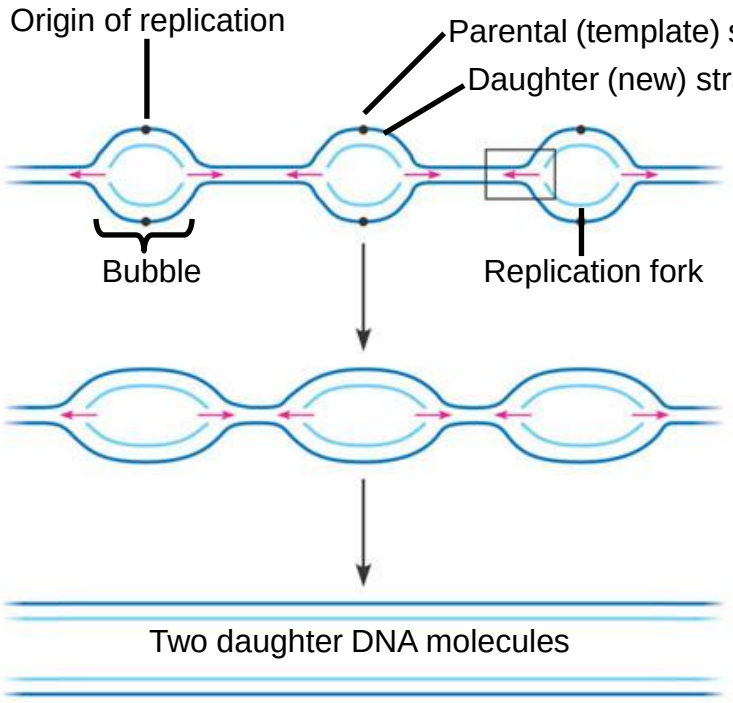
- The copying of DNA
  - Is remarkable in its speed and accuracy
- More than a dozen enzymes and other proteins
  - Participate in DNA replication

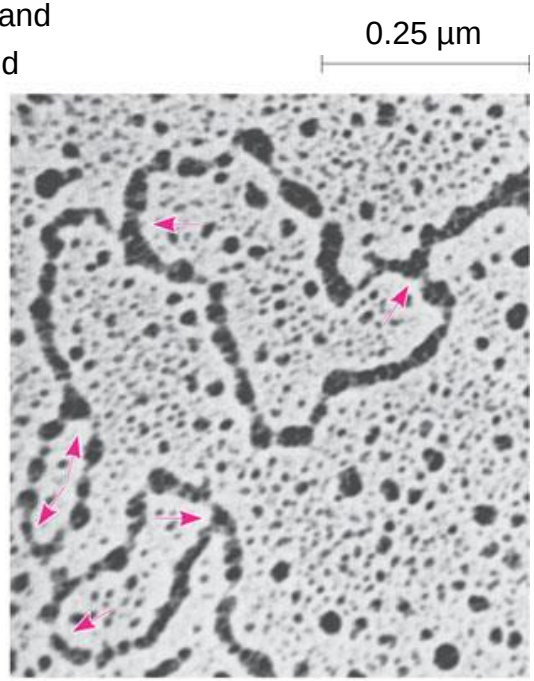
Getting Started: Origins of Replication

- The replication of a DNA molecule
  - Begins at special sites called origins of replication, where the two strands are separated

- A eukaryotic chromosome
  - May have hundreds or even thousands of replication origins

1. Replication begins at specific sites where the two parental strands separate and form replication bubbles.
2. The bubbles expand laterally, as DNA replication proceeds in both directions.
3. Eventually, the replication bubbles fuse, and synthesis of the daughter strands is complete.





(a) In eukaryotes, DNA replication begins at many sites along the giant DNA molecule of each chromosome.

(b) In this micrograph, three replication bubbles are visible along the DNA of a cultured Chinese hamster cell (TEM).

Figure 16.12 a, b

Elongating a New DNA Strand

- Elongation of new DNA at a replication fork
  - Is catalyzed by enzymes called DNA polymerases, which add nucleotides to the 3′ end of a growing strand

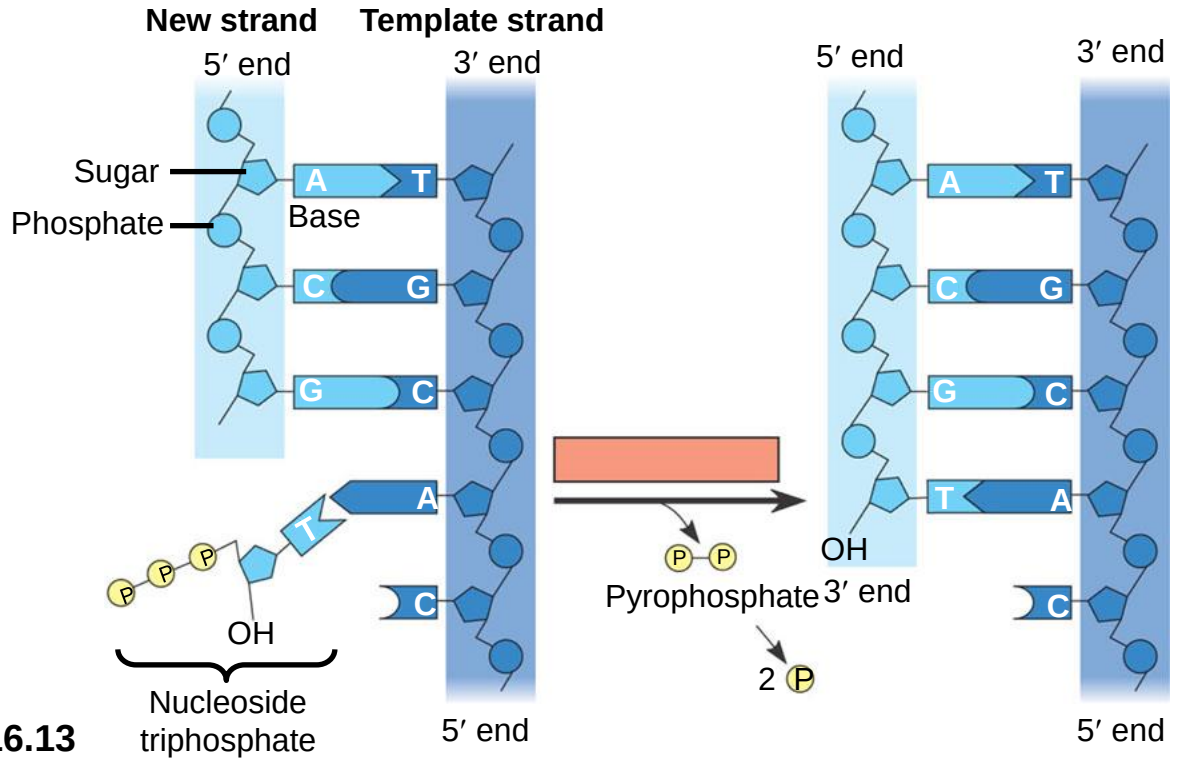


Figure 16.13

Antiparallel Elongation

- How does the antiparallel structure of the double helix affect replication?

- DNA polymerases add nucleotides
  - Only to the free 3′ end of a growing strand
- Along one template strand of DNA, the leading strand
  - DNA polymerase III can synthesize a complementary strand continuously, moving toward the replication fork

- To elongate the other new strand of DNA, the lagging strand
  - DNA polymerase III must work in the direction away from the replication fork
- The lagging strand
  - Is synthesized as a series of segments called Okazaki fragments, which are then joined together by DNA ligase

- Synthesis of leading and lagging strands during DNA replication

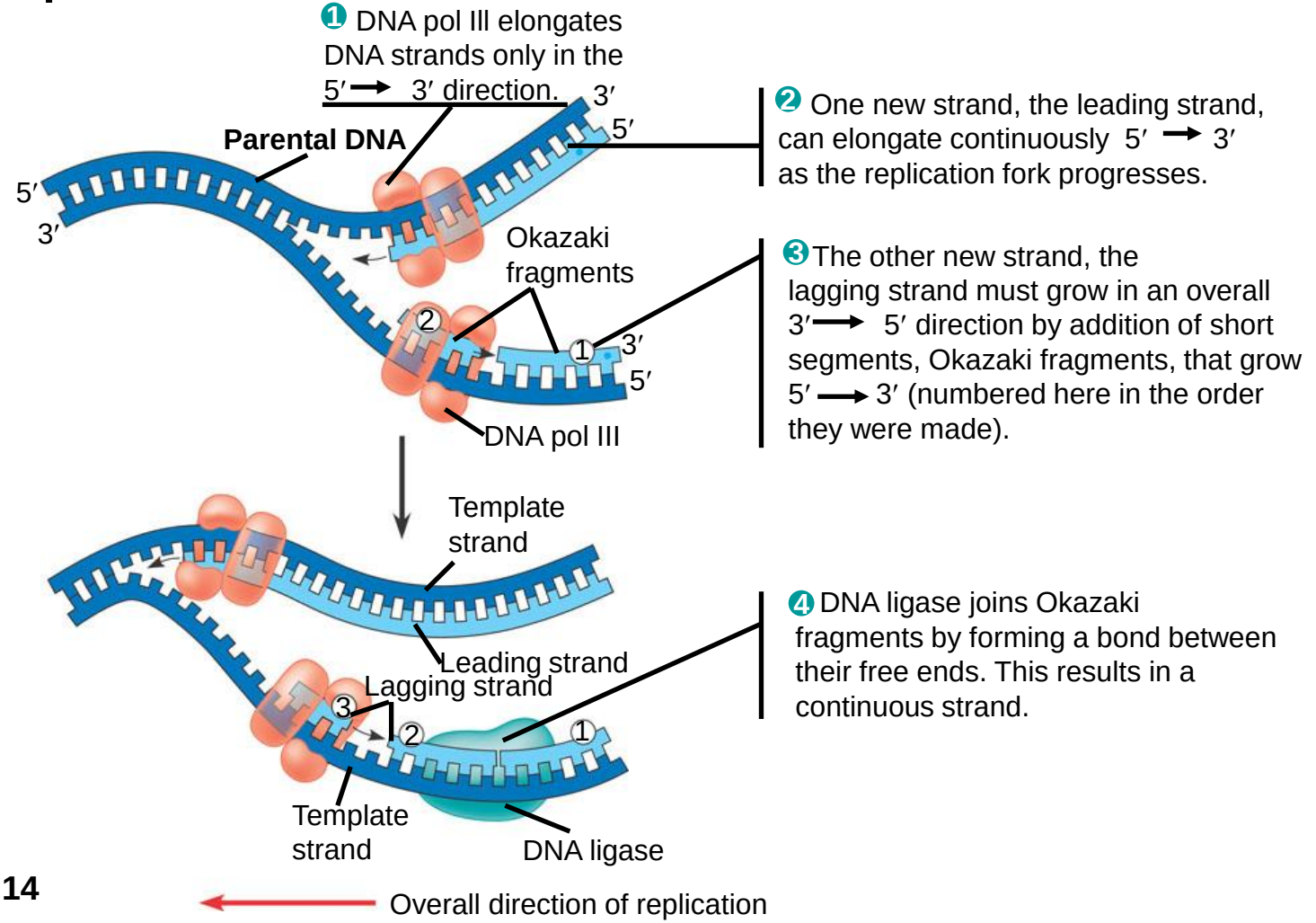


Figure 16.14

Priming DNA Synthesis

- DNA polymerases cannot initiate the synthesis of a polynucleotide
  - They can only add nucleotides to the 3′ end
- The initial nucleotide strand
  - Is an RNA or DNA primer

- Only one primer is needed for synthesis of the leading strand
  - But for synthesis of the lagging strand, each Okazaki fragment must be primed separately

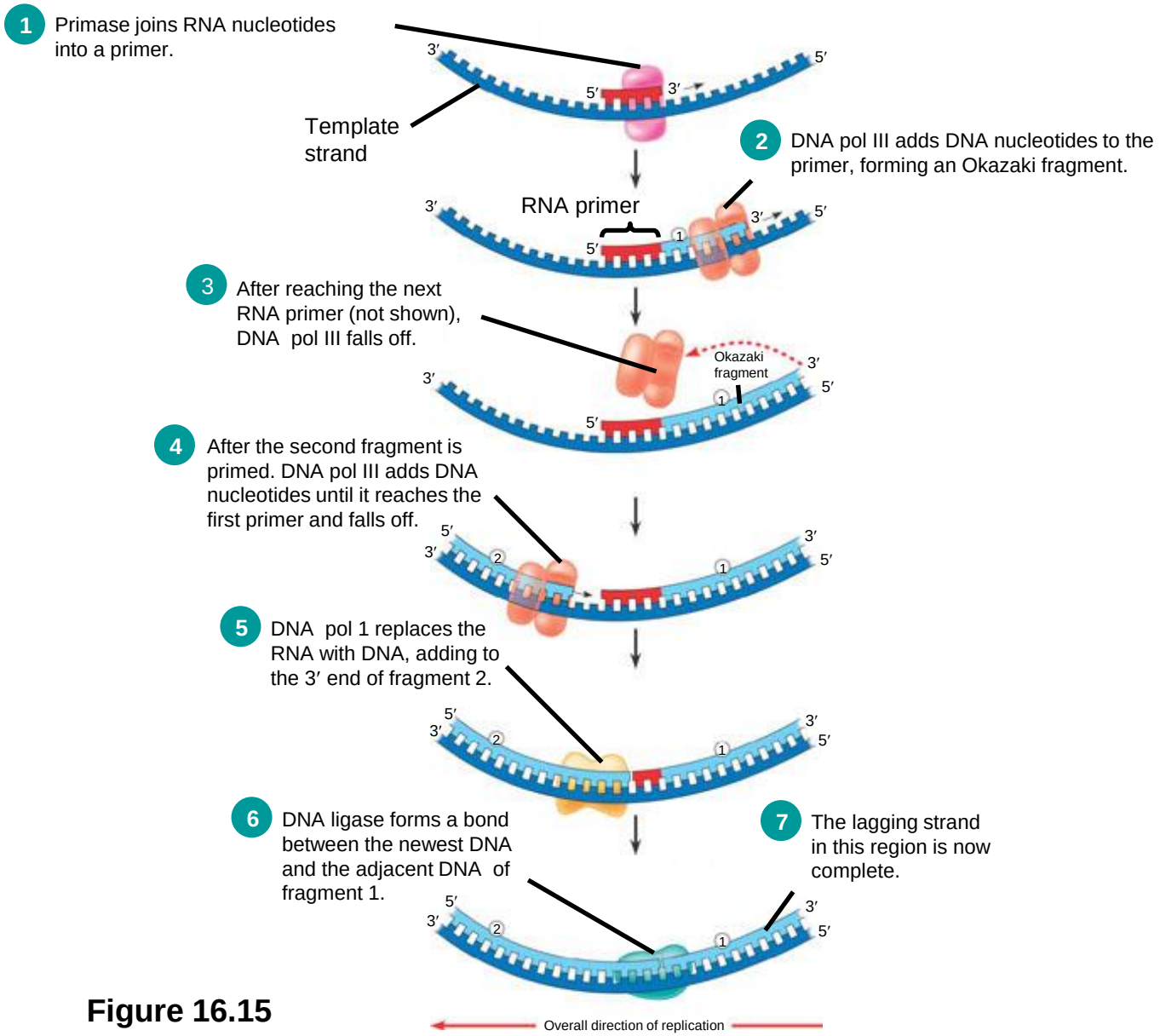


Figure 16.15

Other Proteins That Assist DNA Replication

- Helicase, topoisomerase, single-strand binding protein
  - Are all proteins that assist DNA replication

Table 16.1 Bacterial DNA replication proteins and their functions

Protein	Function for Leading and Lagging Strands
Helicase	Unwinds parental double helix at replication forks
Single-strand binding protein	Binds to and stabilizes single-stranded DNA until it can be used as a template
Topoisomerase	Corrects "overwinding" ahead of replication forks by breaking, swiveling, and rejoining DNA strands

	Function for Leading Strand	Function for Lagging Strand
Primase	Synthesizes a single RNA primer at the 5′ end of the leading strand	Synthesizes an RNA primer at the 5′ end of each Okazaki fragment
DNA pol III	Continuously synthesizes the leading strand, adding on to the primer	Elongates each Okazaki fragment, adding on to its primer
DNA pol I	Removes primer from the 5′ end of leading strand and replaces it with DNA, adding on to the adjacent 3′ end	Removes the primer from the 5′ end of each fragment and replaces it with DNA, adding on to the 3′ end of the adjacent fragment
DNA Ligase	Joins the 3′ end of the DNA that replaces the primer to the rest of the leading strand	Joins the Okazaki fragments

Table 16.1

- # A summary of DNA replication

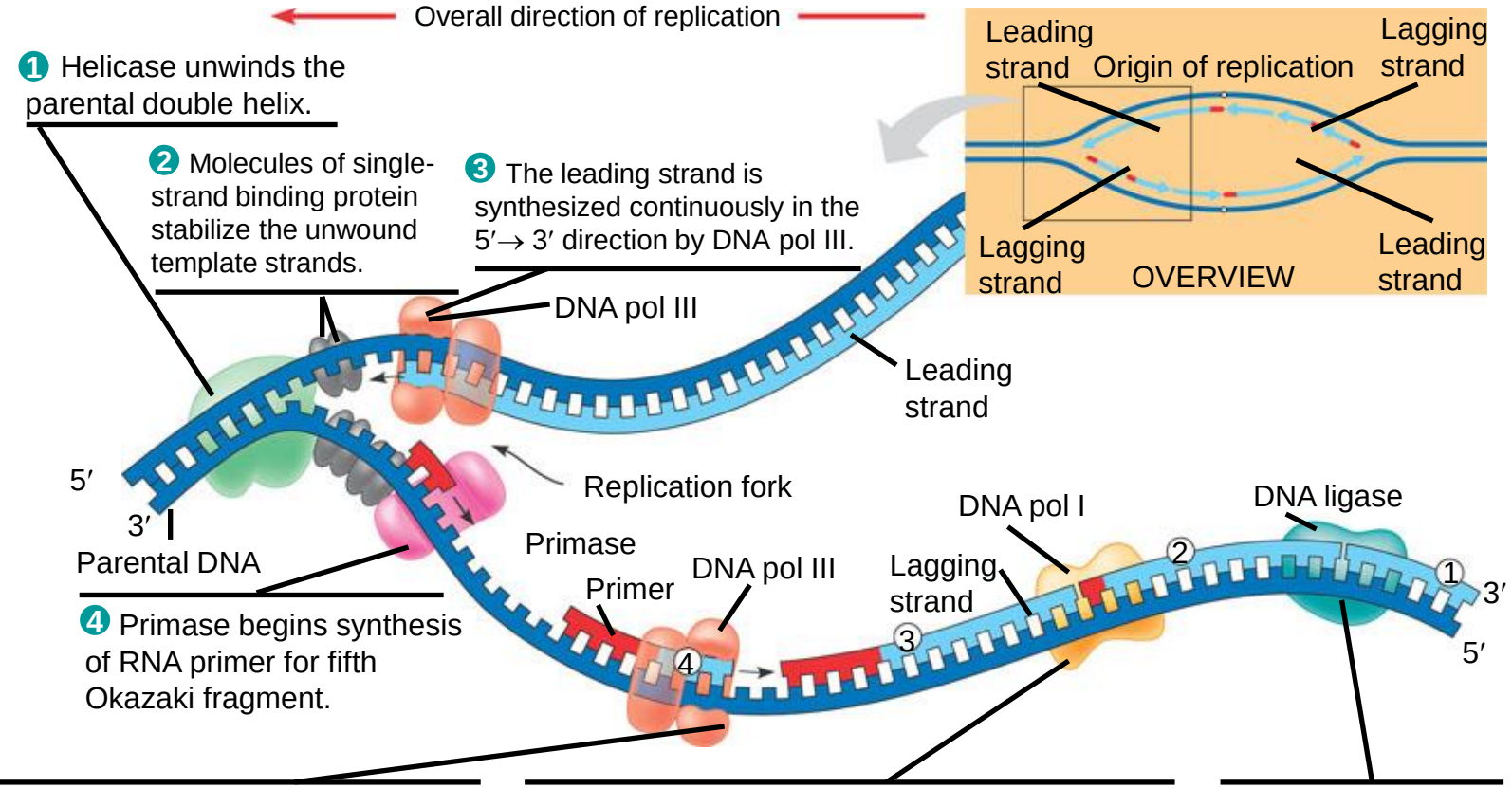


Figure 16.16

The DNA Replication Machine as a Stationary Complex

- The various proteins that participate in DNA replication
  - Form a single large complex, a DNA replication "machine"
- The DNA replication machine
  - Is probably stationary during the replication process

Proofreading and Repairing DNA

- DNA polymerases proofread newly made DNA
  - Replacing any incorrect nucleotides
- In mismatch repair of DNA
  - Repair enzymes correct errors in base pairing

- In nucleotide excision repair
  - Enzymes cut out and replace damaged stretches of DNA

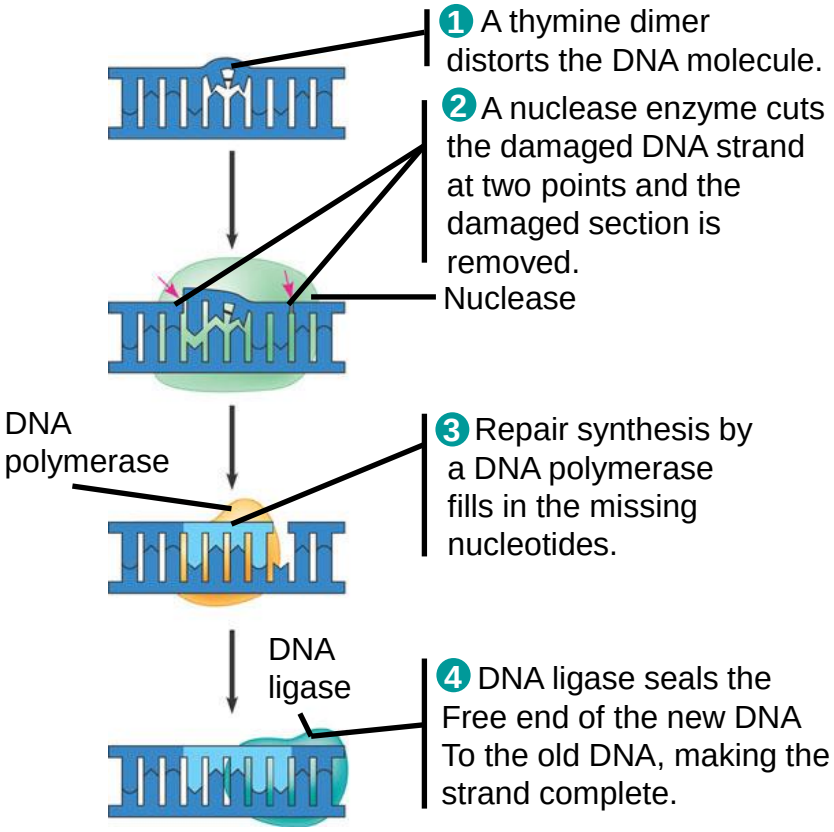


Figure 16.17

Replicating the Ends of DNA Molecules

- The ends of eukaryotic chromosomal DNA
  - Get shorter with each round of replication

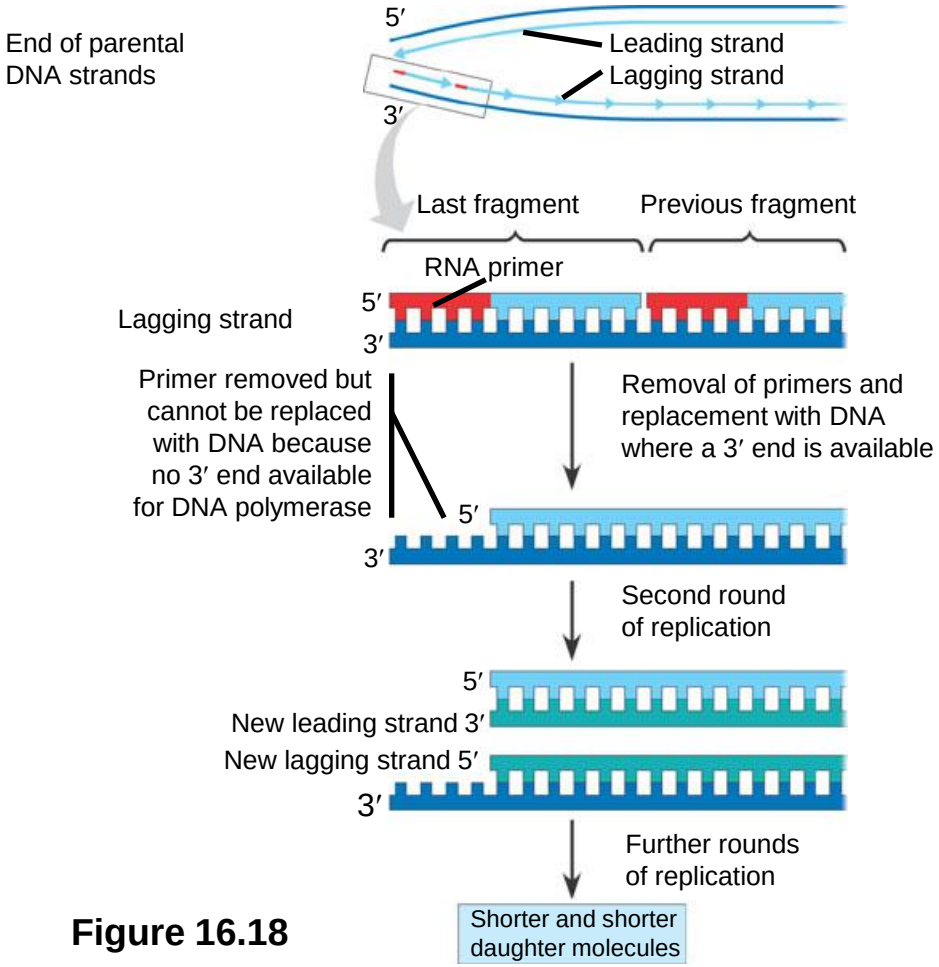


Figure 16.18

- Eukaryotic chromosomal DNA molecules
  - Have at their ends nucleotide sequences, called telomeres, that postpone the erosion of genes near the ends of DNA molecules

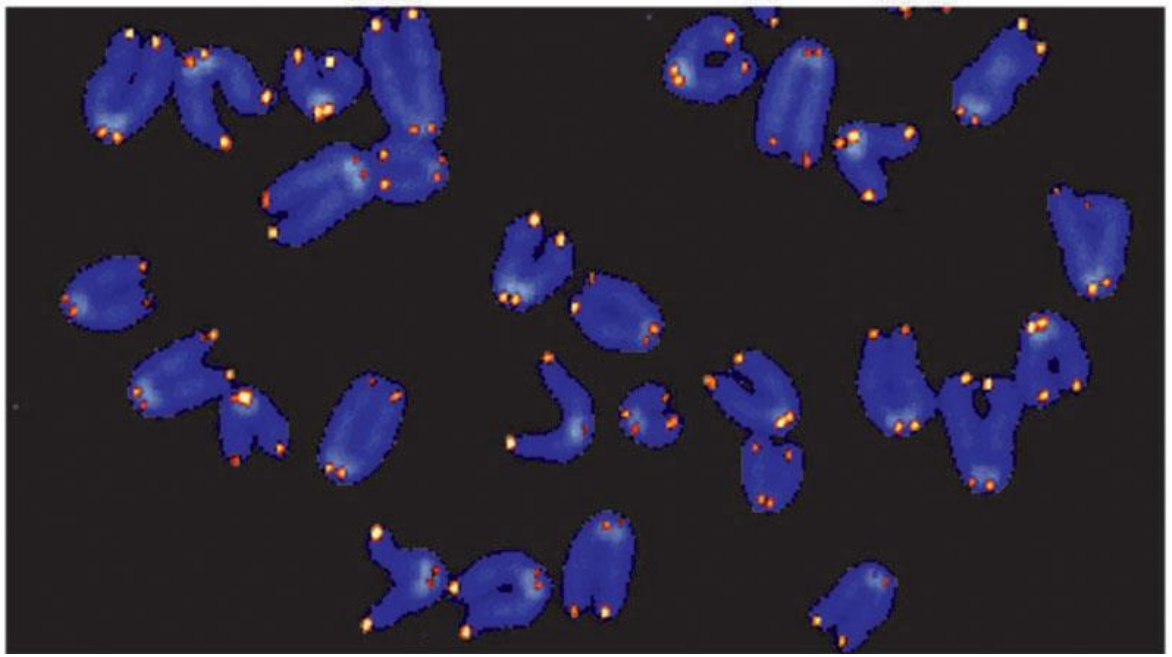


Figure 16.19

- If the chromosomes of germ cells became shorter in every cell cycle
  - Essential genes would eventually be missing from the gametes they produce
- An enzyme called telomerase
  - Catalyzes the lengthening of telomeres in germ cells