Chapter 16

The Molecular Basis of Inheritance

PowerPoint Lectures for
Biology, Seventh Edition
Neil Campbell and Jane Reece

Lectures by Chris Romero

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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

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DNA, the substance of inheritance

- Hereditary information
  - Is encoded in the chemical language of DNA and reproduced in all the cells of your body
- DNA
  - Codes for the development of and the traits of all organisms.
- What are some traits you inherited from your parents? Your grandparents?

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How did they figure it out?

- 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
- Who was the guy who worked out heredity?

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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

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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

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- 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

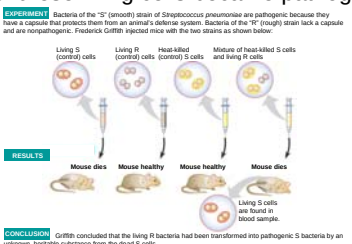

Figure 16.2 CONCLUSION Griffith concluded that the living R bacteria had been transformed into pathogenic S bacteria by an unknown, heritable substance from the dead S cells.

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

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Evidence That Viral DNA Can Program Cells

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

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

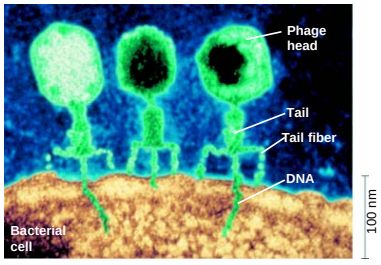

Figure 16.3

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

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- The Hershey and Chase experiment

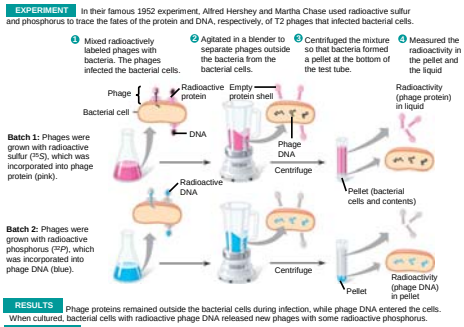

Figure 16.4

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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

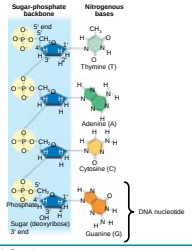

Figure 16.5

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- Erwin Chargaff analyzed the base composition of DNA
  - From a number of different organisms
  - He found that DNA composition varies from one species to the next
  - And that the four bases (A,T,C,G) had corresponding frequencies in every organism
    - e.g., Animal X
      Adenine-Thymine (30% to 30%),
      Guanine-Cytosine (20% to 20%)

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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
  - Of particular curiosity was the Y chromosome, which later was found to contain the following genes encoding for male traits

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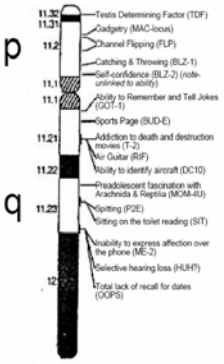
CHROMOSOME Y



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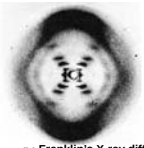
- Maurice Wilkins and Rosalind Franklin
  - Were using a technique called X-ray crystallography to study molecular structure
- Rosalind Franklin
  - Produced a picture of the DNA molecule using this technique

(a) Rosalind Franklin



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

Figure 16.6 a, b

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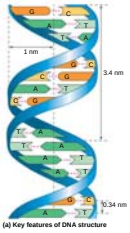
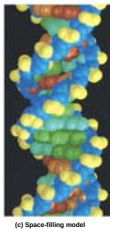
- Watson and Crick deduced that DNA was a double helix
  - Through observations of the X-ray crystallographic images of DNA





(c) Space-filling model

Figure 16.7a, c

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- 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

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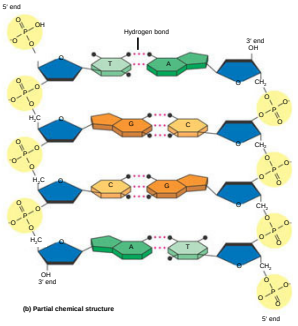

Figure 16.7b

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- 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

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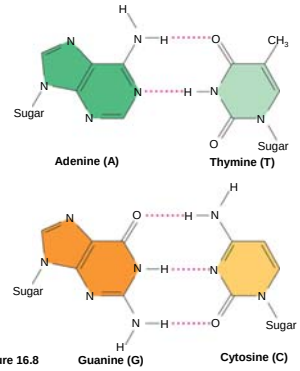

Figure 16.8

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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
  - Play the DNA helix game:
  - http://nobelprize.org/educational_games/medicine/dna_double_helix/

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

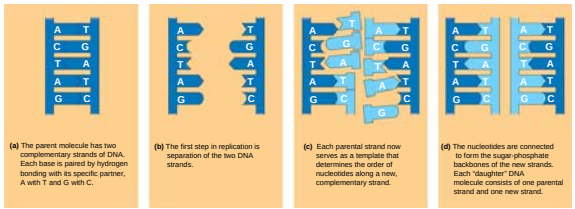

Figure 16.9 a–d

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- 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

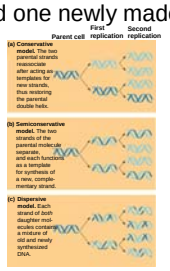

Figure 16.10 a–c

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- 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.

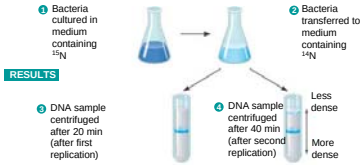

Figure 16.11 The bands in these two centrifuge tubes represent the results of centrifuging two DNA samples from the flask in step 2, one sample taken after 20 minutes and one after 40 minutes.

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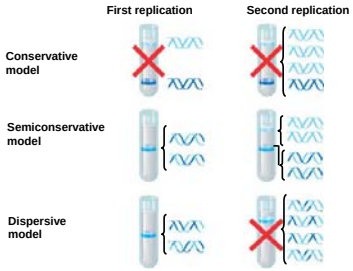
CONCLUSION Meselson and Stahl concluded that DNA replication follows the semiconservative model by comparing their result to the results predicted by each of the three models in Figure 16.10. The first replication in the ^{14}N medium produced a band of hybrid (^{15}N–^{14}N) DNA. This result eliminated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



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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
  - http://bioteach.ubc.ca/TeachingResources/MolecularBiology/DNAReplication.swf

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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

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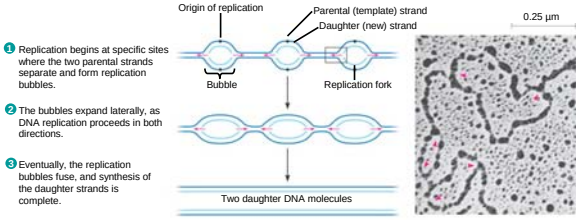
- A eukaryotic chromosome
  - May have hundreds or even thousands of replication origins



(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

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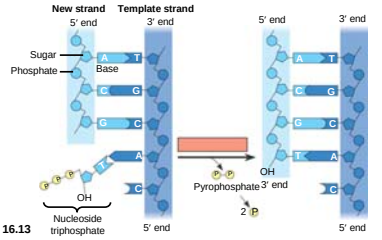
Elongating a New DNA Strand

- 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



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Antiparallel Elongation

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

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- 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

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- 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

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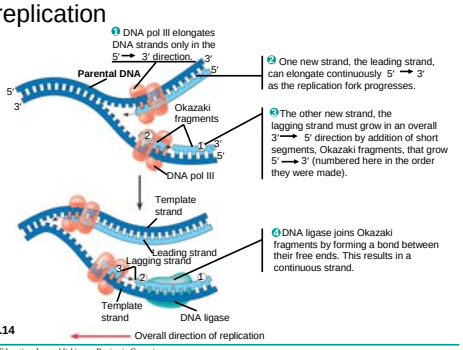
- Synthesis of leading and lagging strands during DNA replication



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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

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- 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

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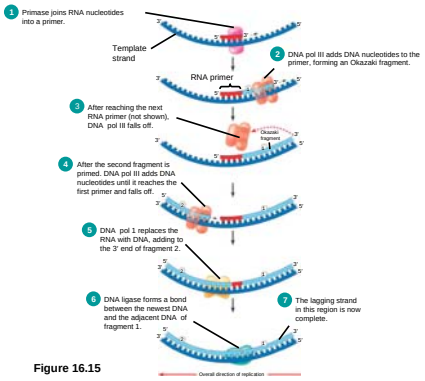

Figure 16.15

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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

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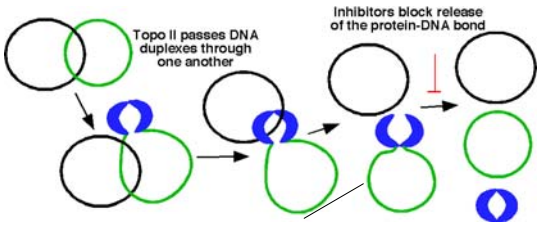
Type II Topoisomerases Pass DNA Strands Through One Another



Stabilization of the "cleavage complex for (topo I or) topo II causes DNA damage that is difficult to repair due to the large protein molecule attached to the broken DNA.

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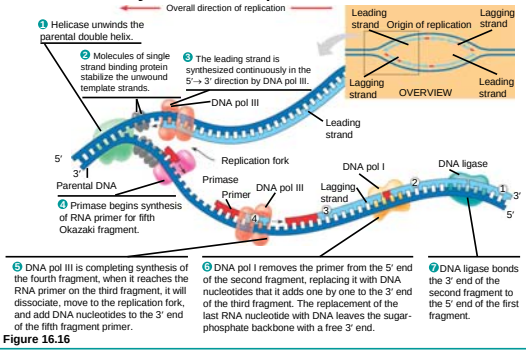
- A summary of DNA replication



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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

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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

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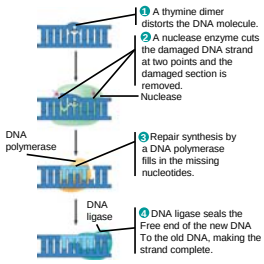
- In nucleotide excision repair
  - Enzymes cut out and replace damaged stretches of DNA



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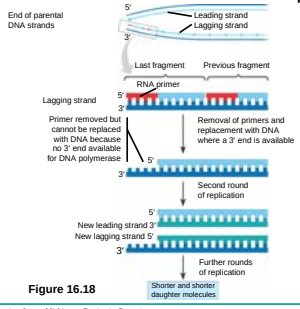
Replicating the Ends of DNA Molecules

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



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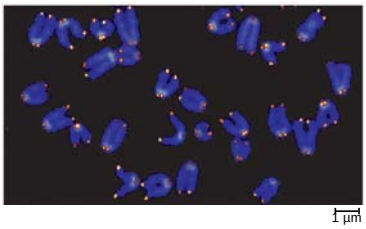
- Eukaryotic chromosomal DNA molecules
  - Have at their ends nucleotide sequences, called telomeres, that postpone the erosion of genes near the ends of DNA molecules



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- 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

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