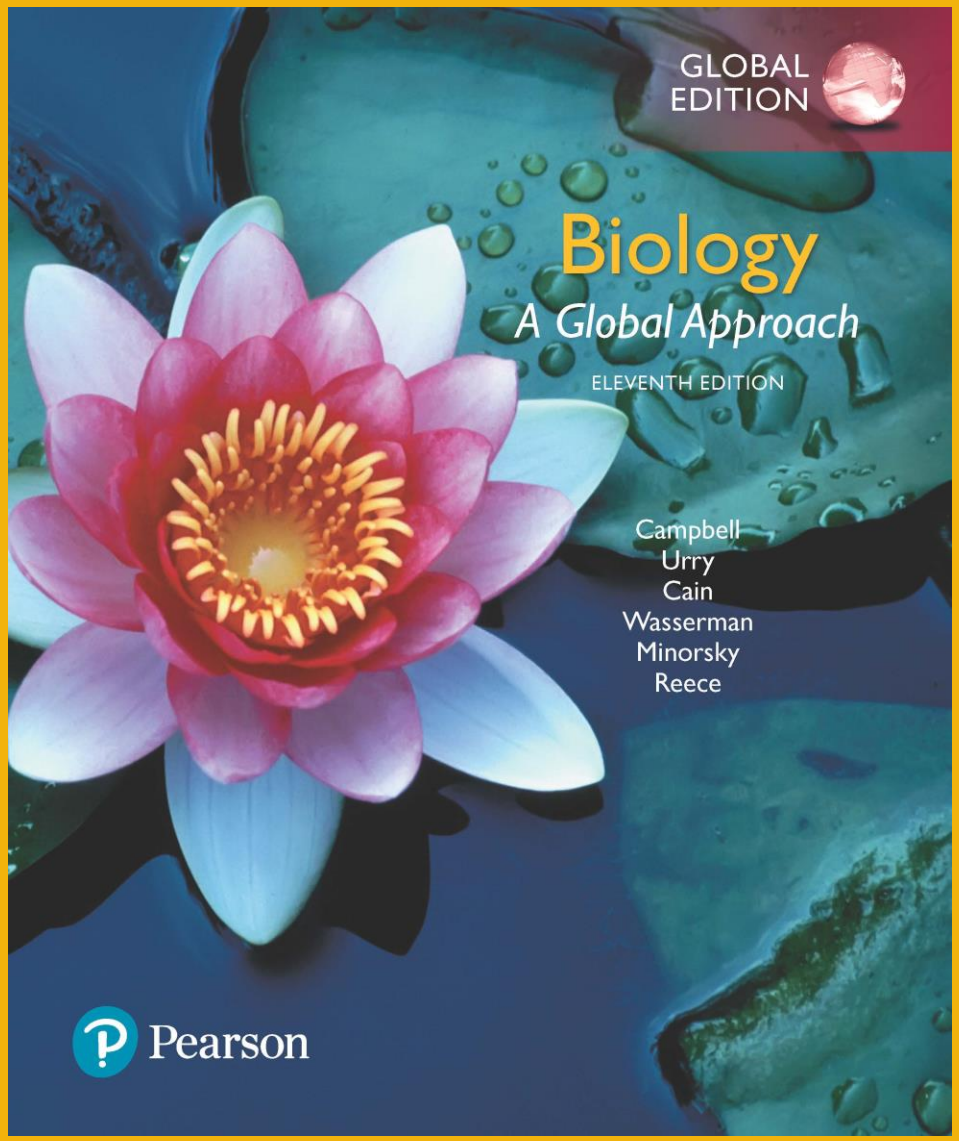



# Chapter 16

# Nucleic Acids and Inheritance

Lecture Presentations by
Nicole Tunbridge and
Kathleen Fitzpatrick

# Life’s Operating Instructions

- In 1953, James Watson and Francis Crick introduced an elegant double-helical model for the structure of deoxyribonucleic acid, or DNA
- Hereditary information is encoded in DNA and reproduced in all cells of the body
- This DNA program directs the development of biochemical, anatomical, physiological, and (to some extent) behavioral traits

Figure 16.1

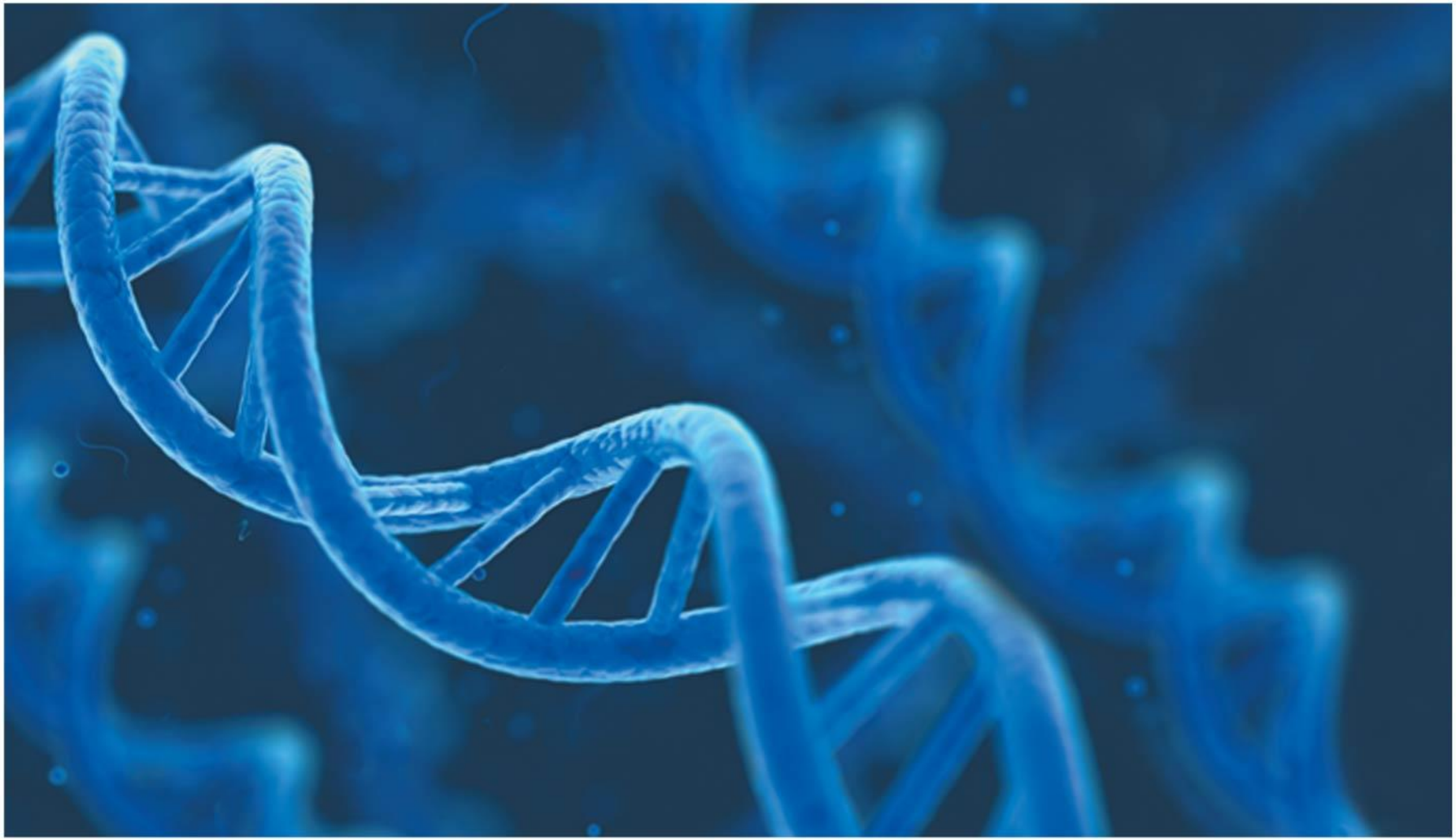
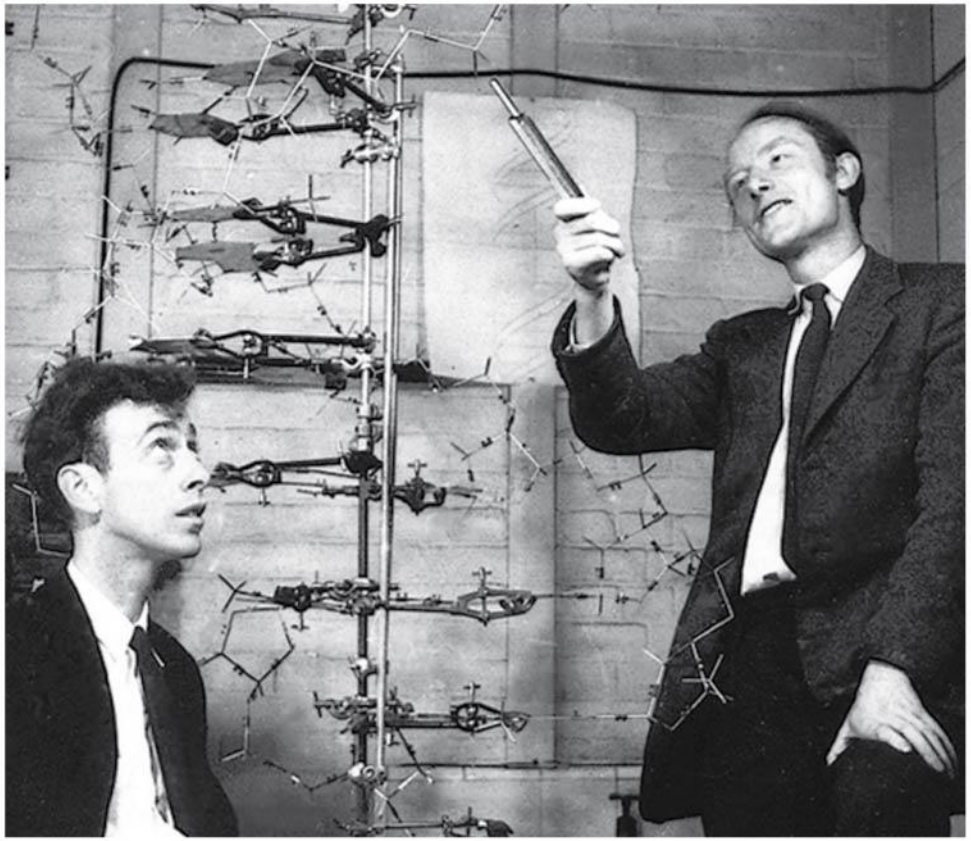


Figure 16.1a



- DNA is copied during **DNA replication**, and cells can repair their DNA

# 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*

- When T. H. Morgan's group showed that genes are located on chromosomes, the two components of chromosomes—DNA and protein—became candidates for the genetic material
- The role of DNA in heredity was first discovered by studying bacteria and the viruses that infect them

# *Evidence That DNA Can Transform Bacteria*

- The discovery of the genetic role of DNA began with research by Frederick Griffith in 1928
- Griffith worked with two strains of a bacterium, one pathogenic and one harmless

- When he mixed heat-killed remains of the pathogenic strain with living cells of the harmless strain, some living cells became pathogenic
- He called this phenomenon **transformation**, now defined as a change in genotype and phenotype due to assimilation of foreign DNA

Figure 16.2

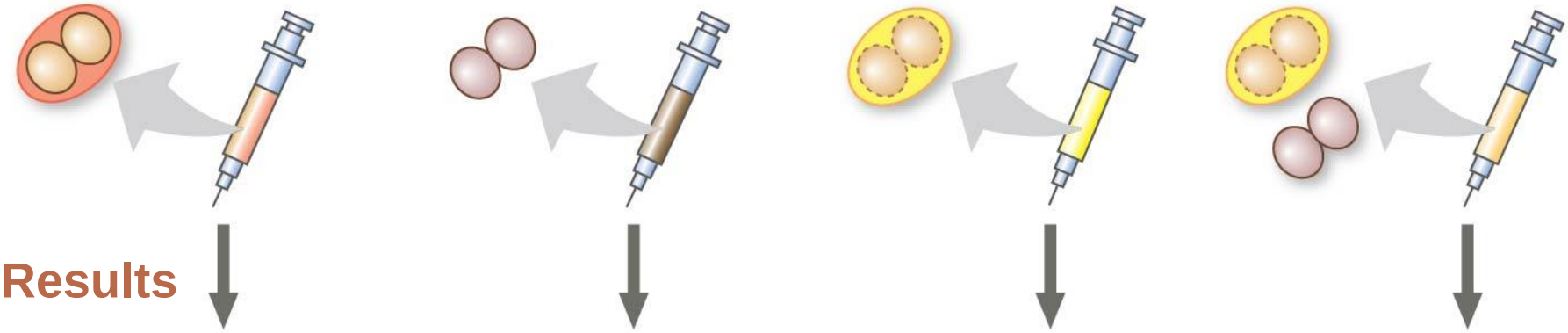
## Experiment

**Living S cells (pathogenic control)**

**Living R cells (nonpathogenic control)**

**Heat-killed S cells (nonpathogenic control)**

**Mixture of heat-killed S cells and living R cells**



## Results

**Mouse dies**

**Mouse healthy**

**Mouse healthy**

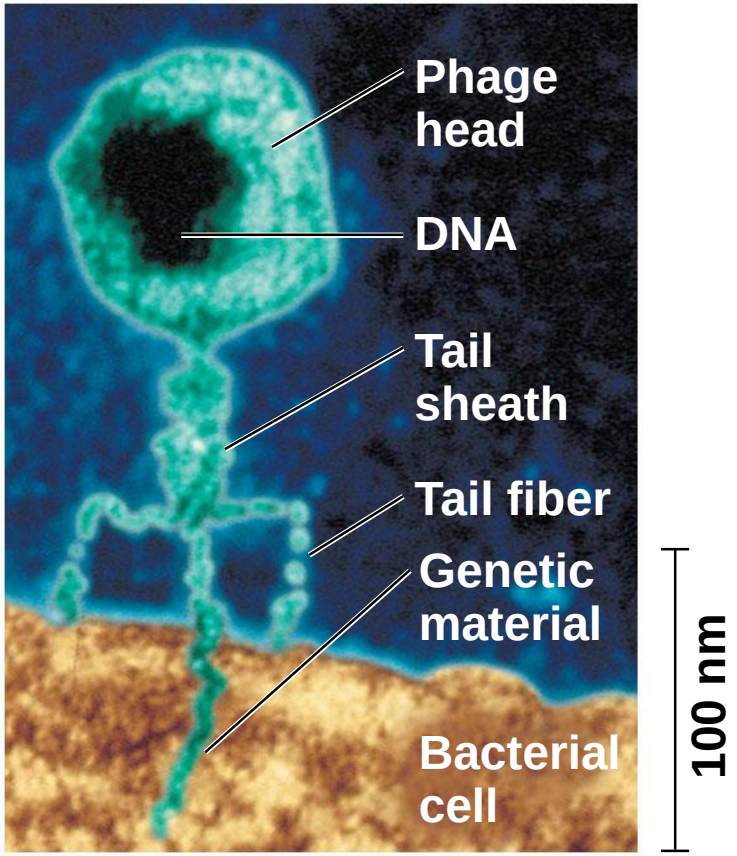
**Mouse dies**

- Later work by Oswald Avery, Maclyn McCarty, and Colin MacLeod identified the transforming substance as DNA
- Many biologists remained skeptical, mainly because little was known about DNA

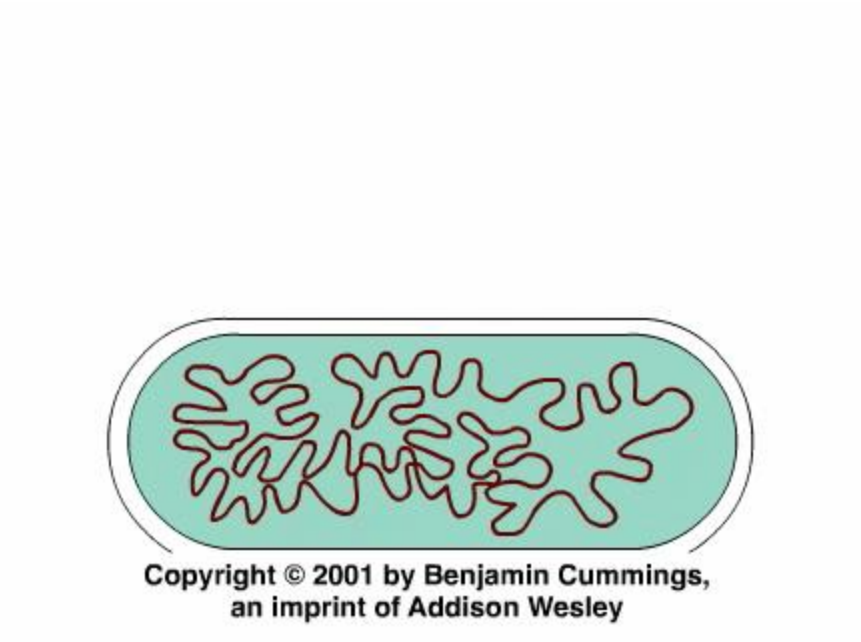
# *Evidence That Viral DNA Can Program Cells*

- More evidence for DNA as the genetic material came from studies of viruses that infect bacteria
- Such viruses, called **bacteriophages** (or **phages**), are widely used in molecular genetics research
- A **virus** is DNA (sometimes RNA) enclosed by a protective coat, often simply protein

Figure 16.3



# Animation: Phage T2 Reproductive Cycle



- In 1952, Alfred Hershey and Martha Chase showed that DNA is the genetic material of a phage known as T2
- They designed an experiment showing that only one of the two components of T2 (DNA or protein) enters an *E. coli* cell during infection
- They concluded that the injected DNA of the phage provides the genetic information

Figure 16.4

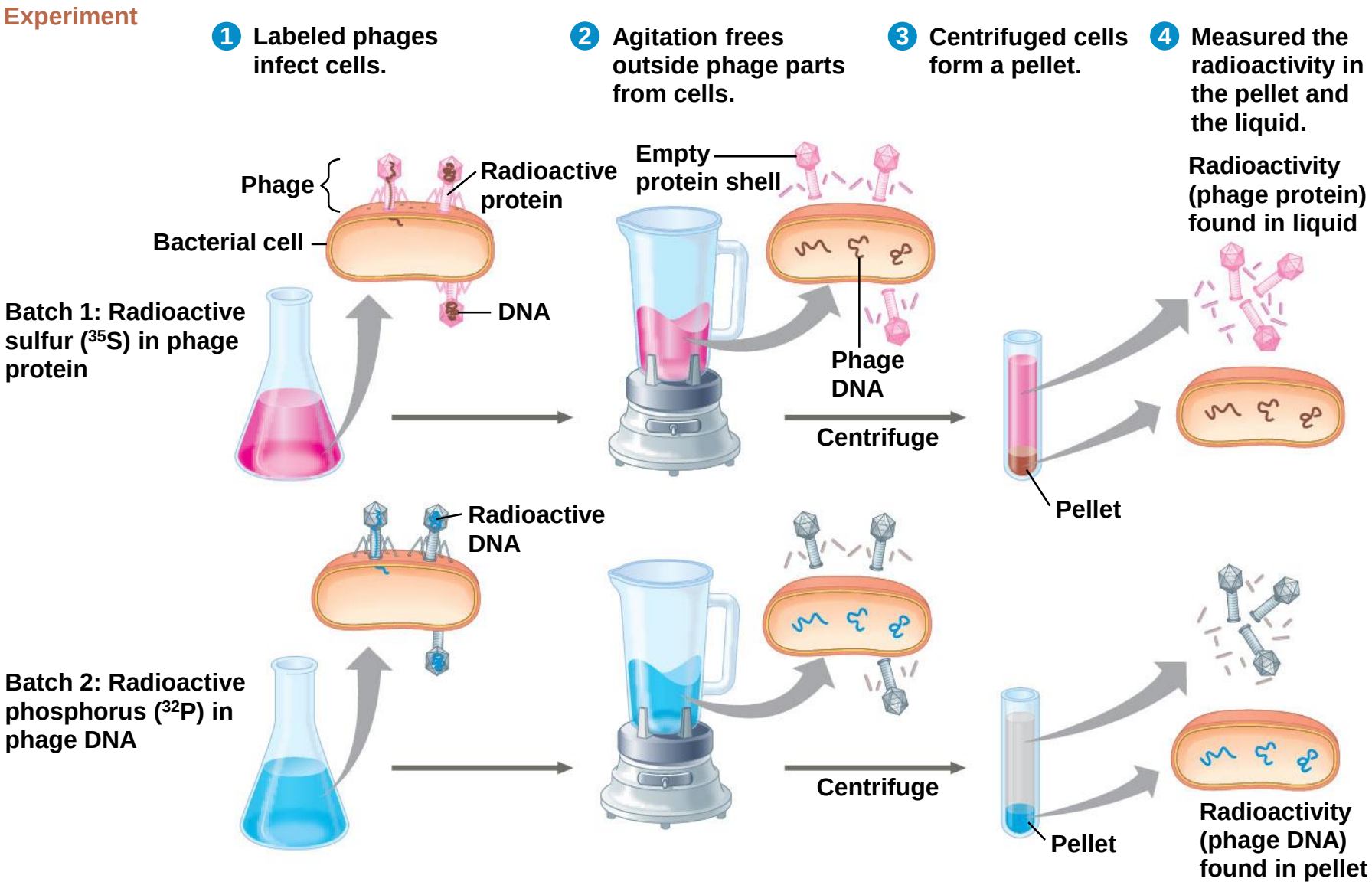


Figure 16.4a

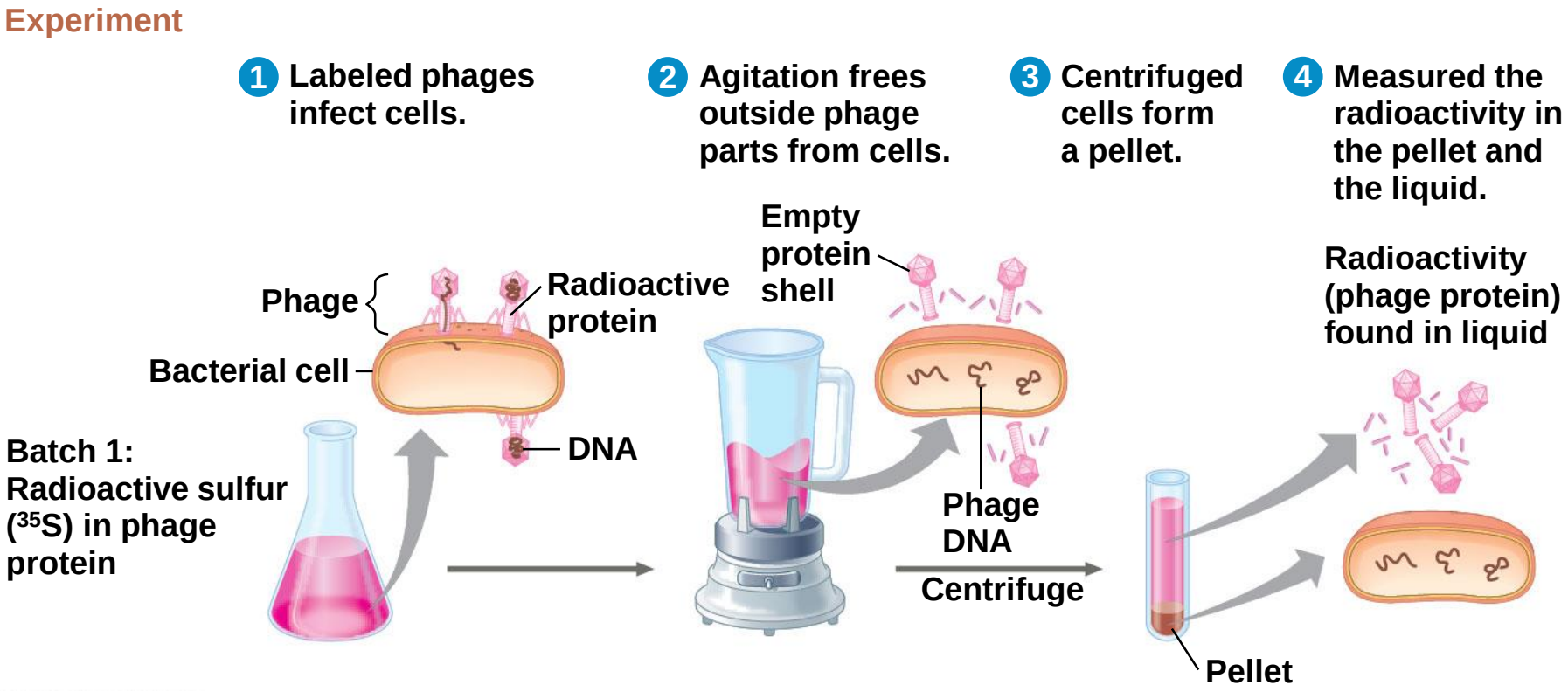
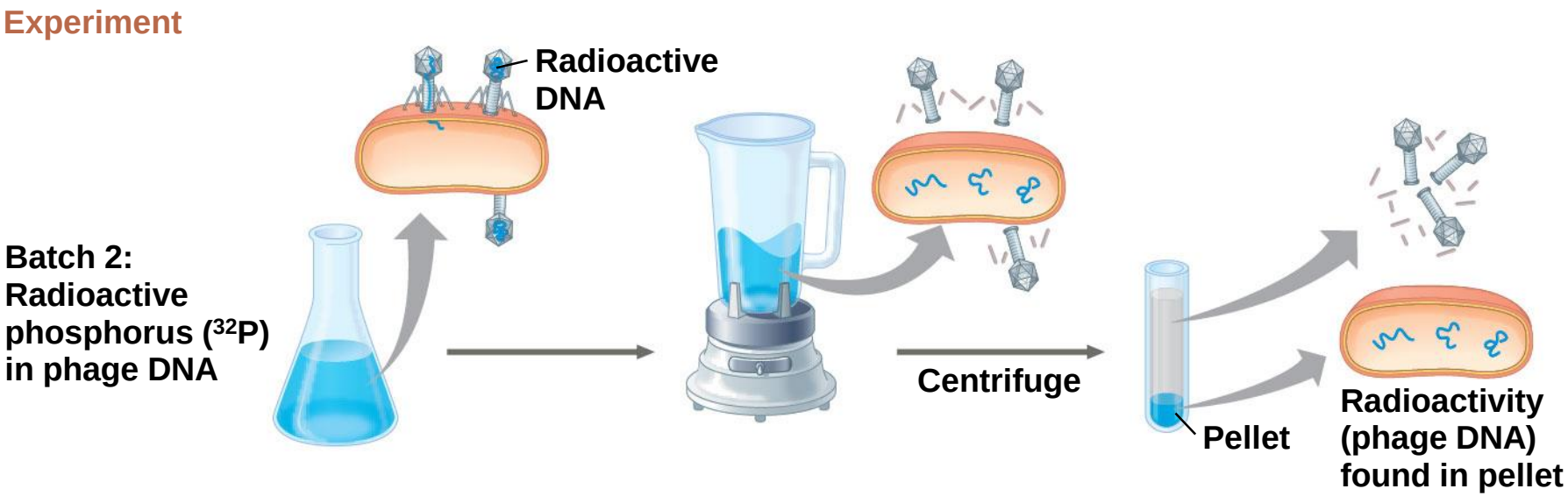


Figure 16.4b



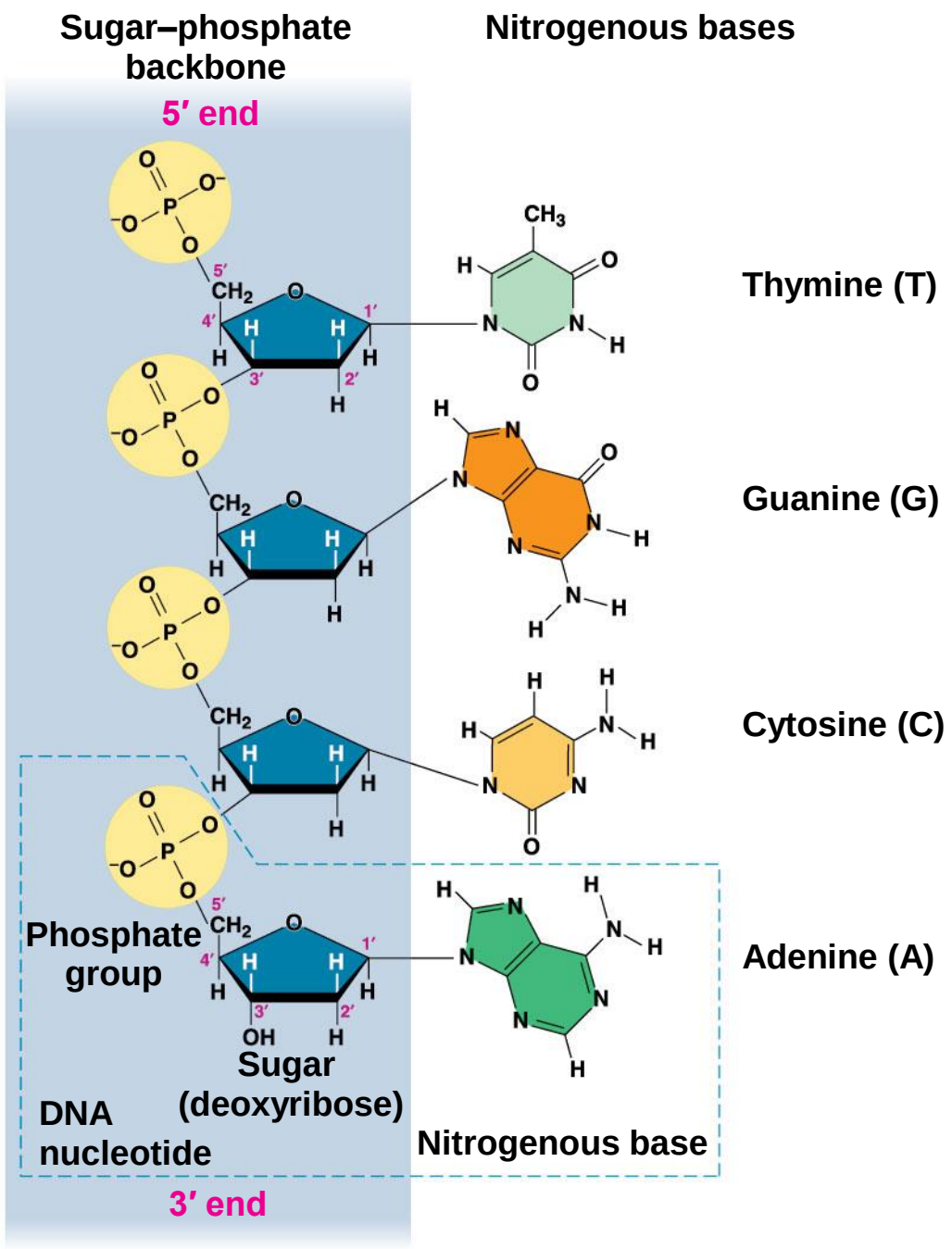
# Animation: Hershey-Chase Experiment

# *Additional Evidence That DNA Is the Genetic Material*

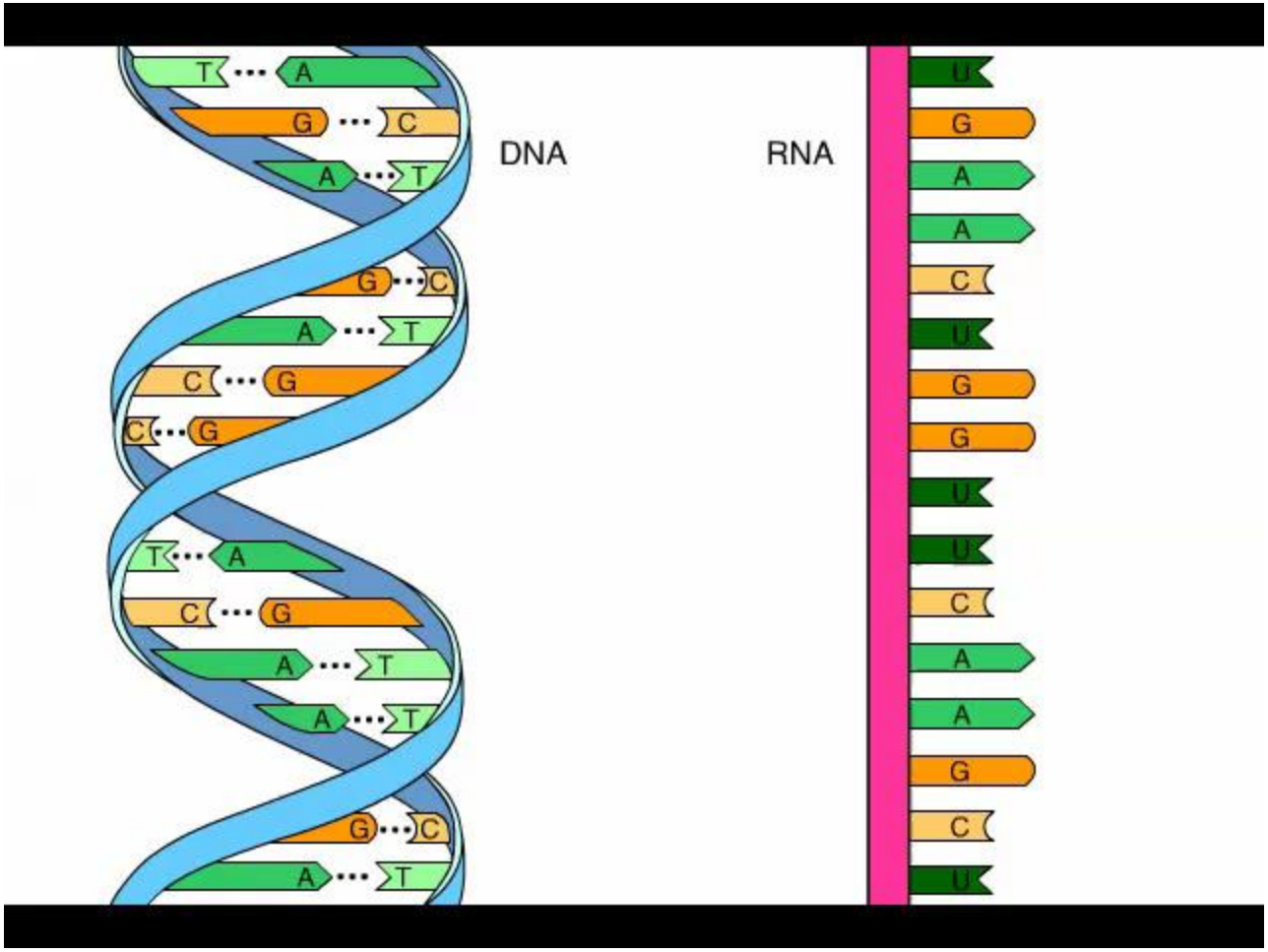
- DNA is a polymer of nucleotides, each consisting of a nitrogenous base, a sugar, and a phosphate group
- The nitrogenous bases can be adenine (A), thymine (T), guanine (G), or cytosine (C)
- In 1950, Erwin Chargaff reported that DNA composition varies from one species to the next
- This evidence of diversity made DNA a more credible candidate for the genetic material

- Two findings became known as Chargaff's rules
  - The base composition of DNA varies between species
  - In any species the number of A and T bases is equal and the number of G and C bases is equal
- The basis for these rules was not understood until the discovery of the double helix

Figure 16.5



# Animation: DNA and RNA Structure



# Building a Structural Model of DNA: *Scientific Inquiry*

- After DNA was accepted as the genetic material, the challenge was to determine how its structure accounts for its role in heredity
- Maurice Wilkins and Rosalind Franklin were using a technique called X-ray crystallography to study molecular structure
- Franklin produced a picture of the DNA molecule using this technique

Figure 16.6

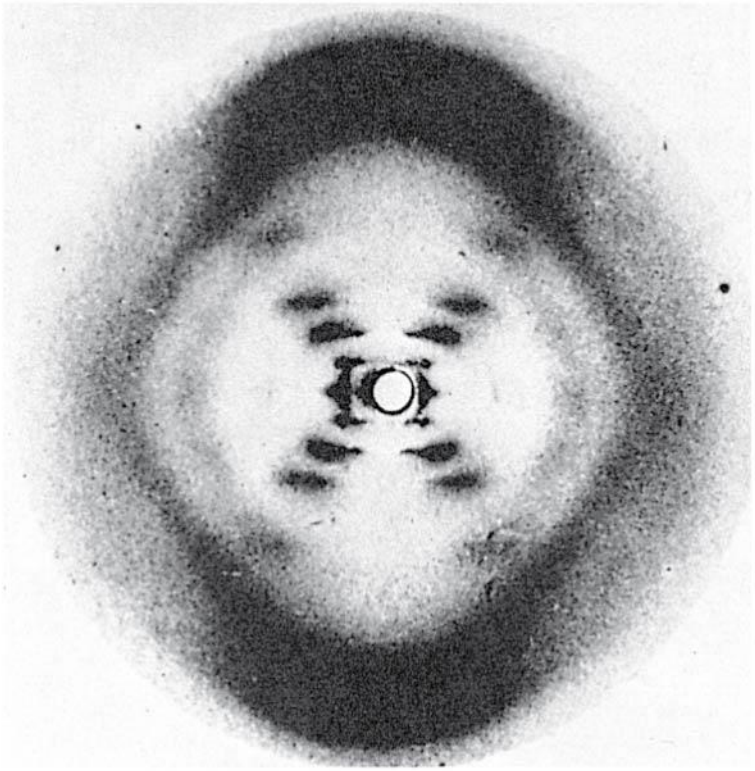
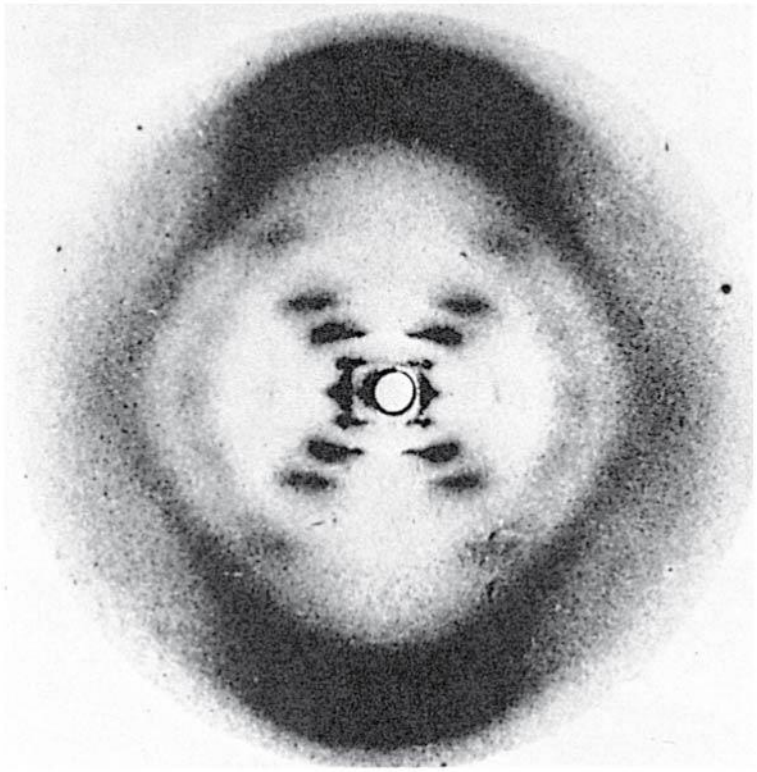


Figure 16.6a

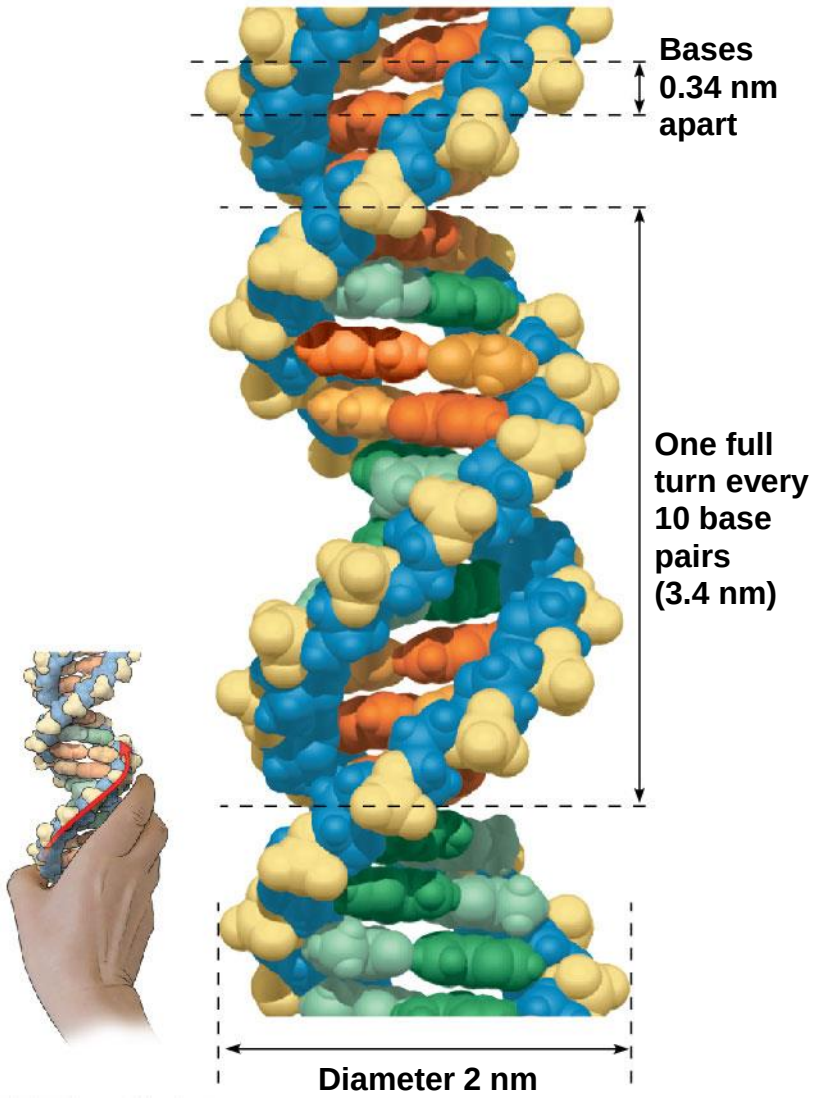
Figure 16.6b



- Franklin's X-ray crystallographic images of DNA enabled Watson to deduce that DNA was helical
- The X-ray images also enabled Watson to deduce the width of the helix and the spacing of the nitrogenous bases
- The pattern in the photo suggested that the DNA molecule was made up of two strands, forming a **double helix**

Figure 16.7a

## Structural Images



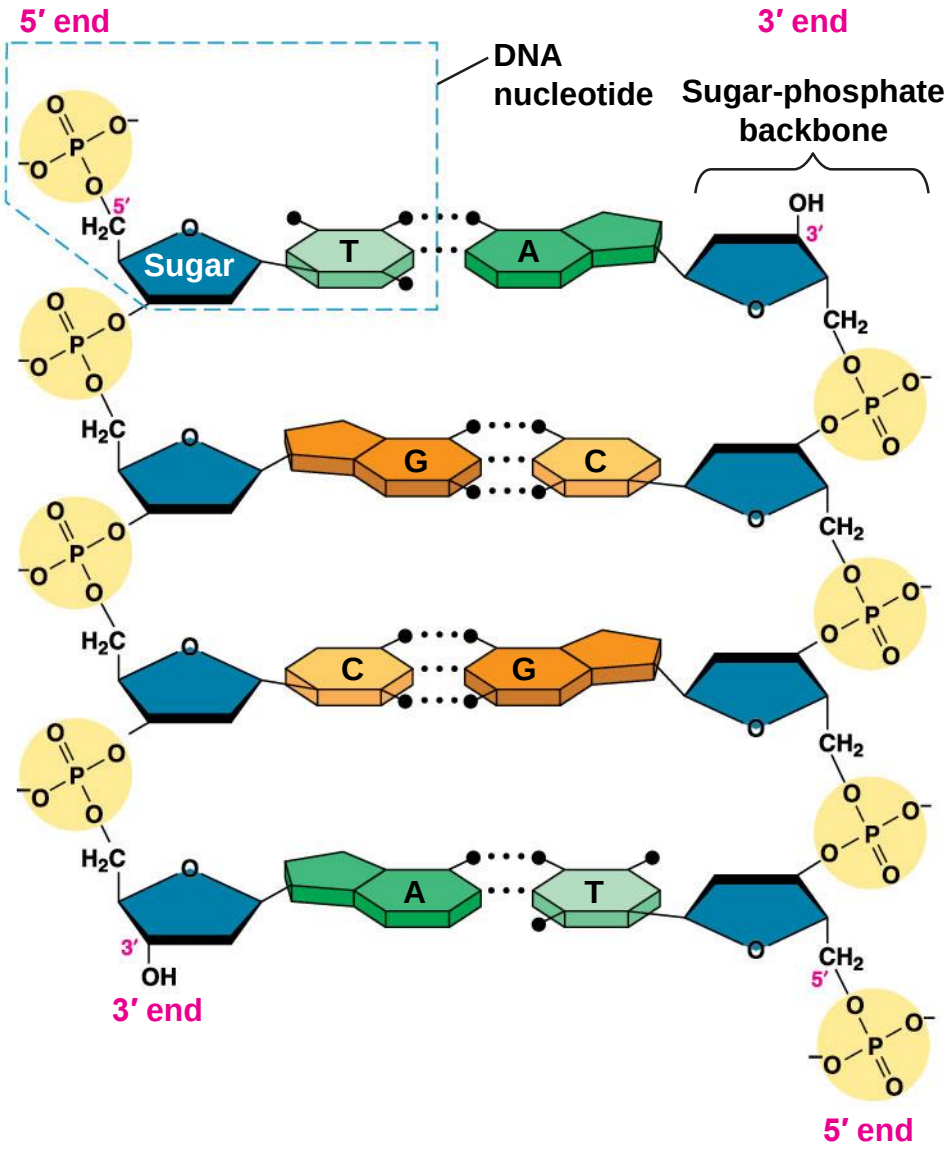



Figure 16.7aa

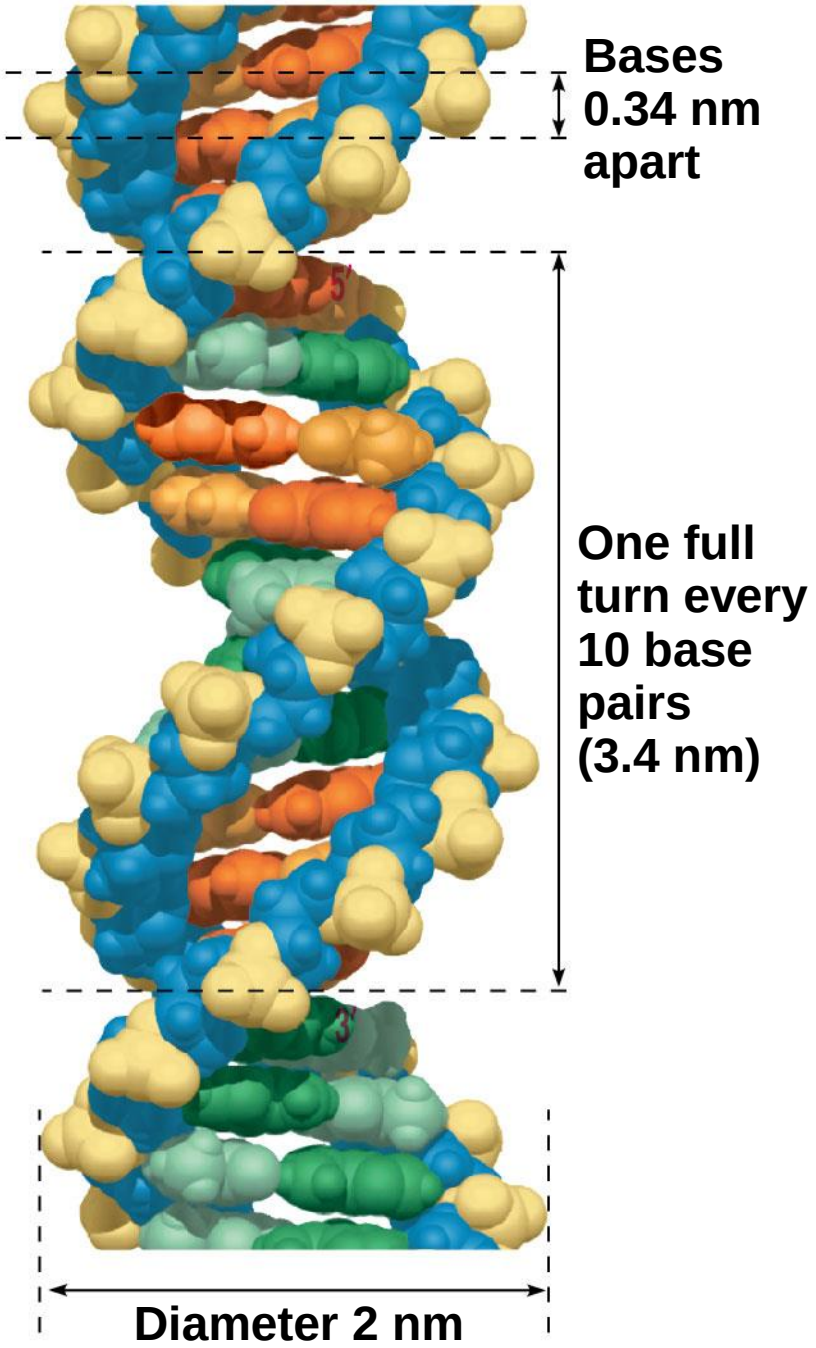


Figure 16.7ab

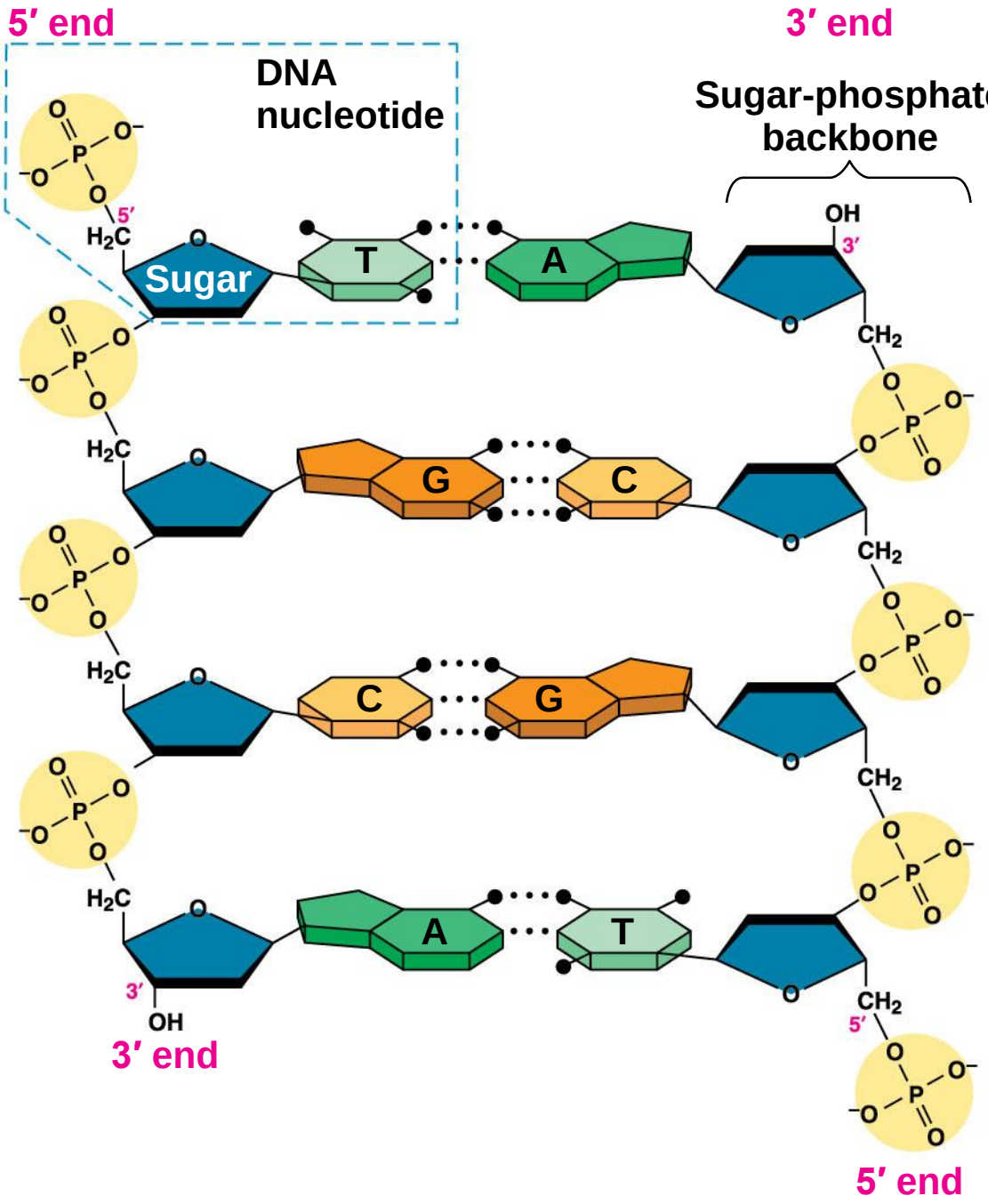


Figure 16.7b

## Simplified Images

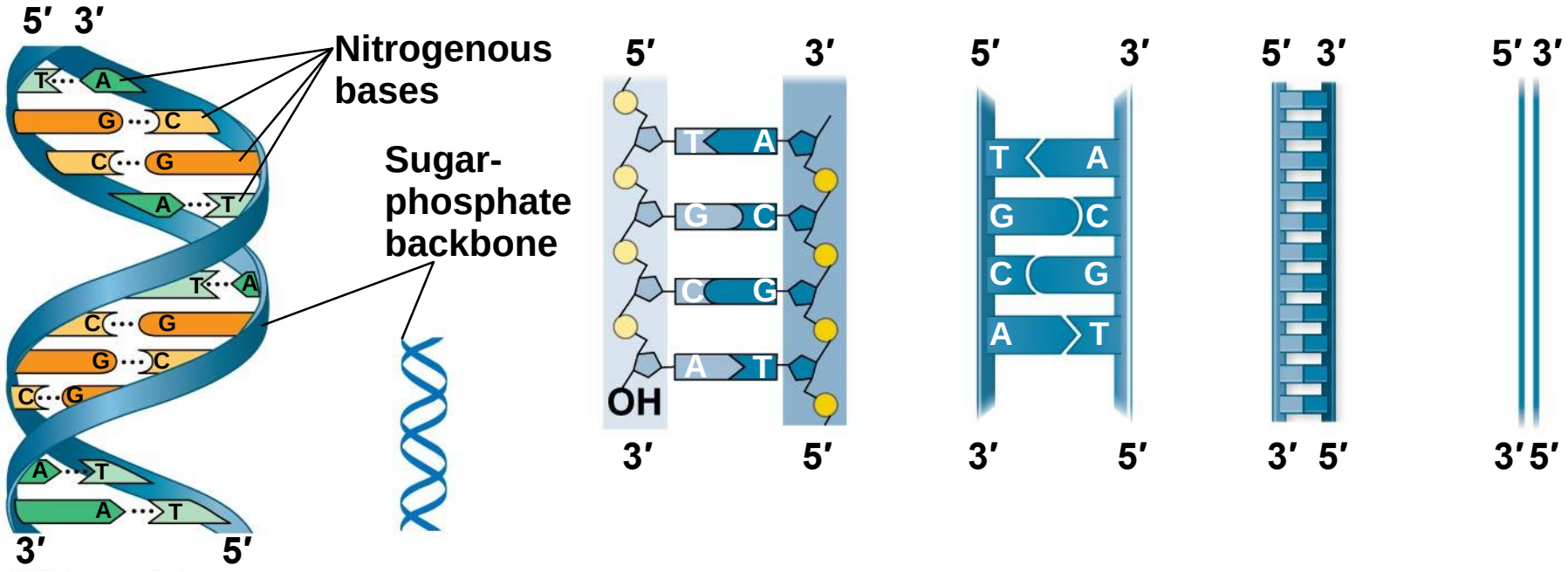


Figure 16.7ba

# Simplified Images

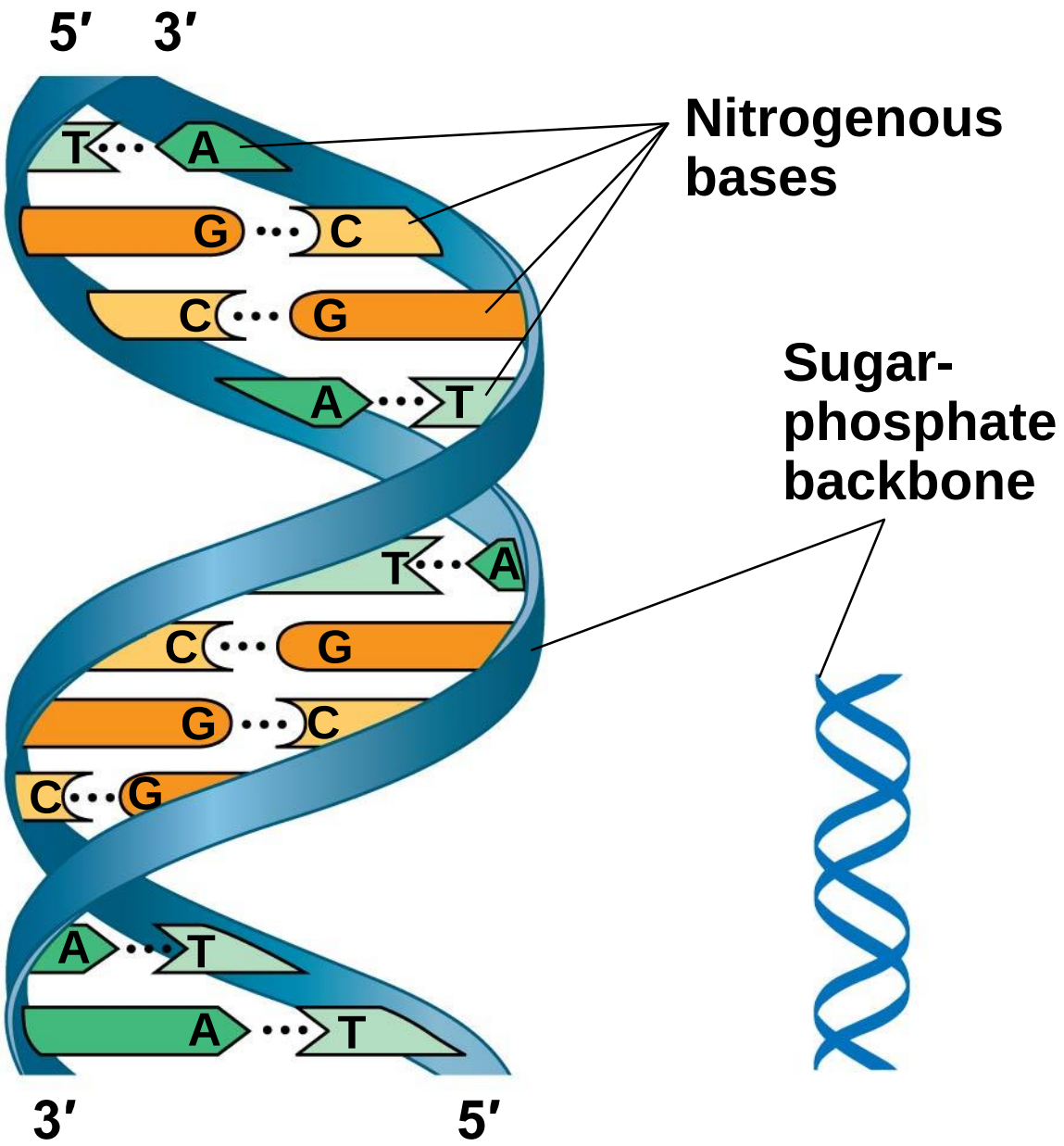
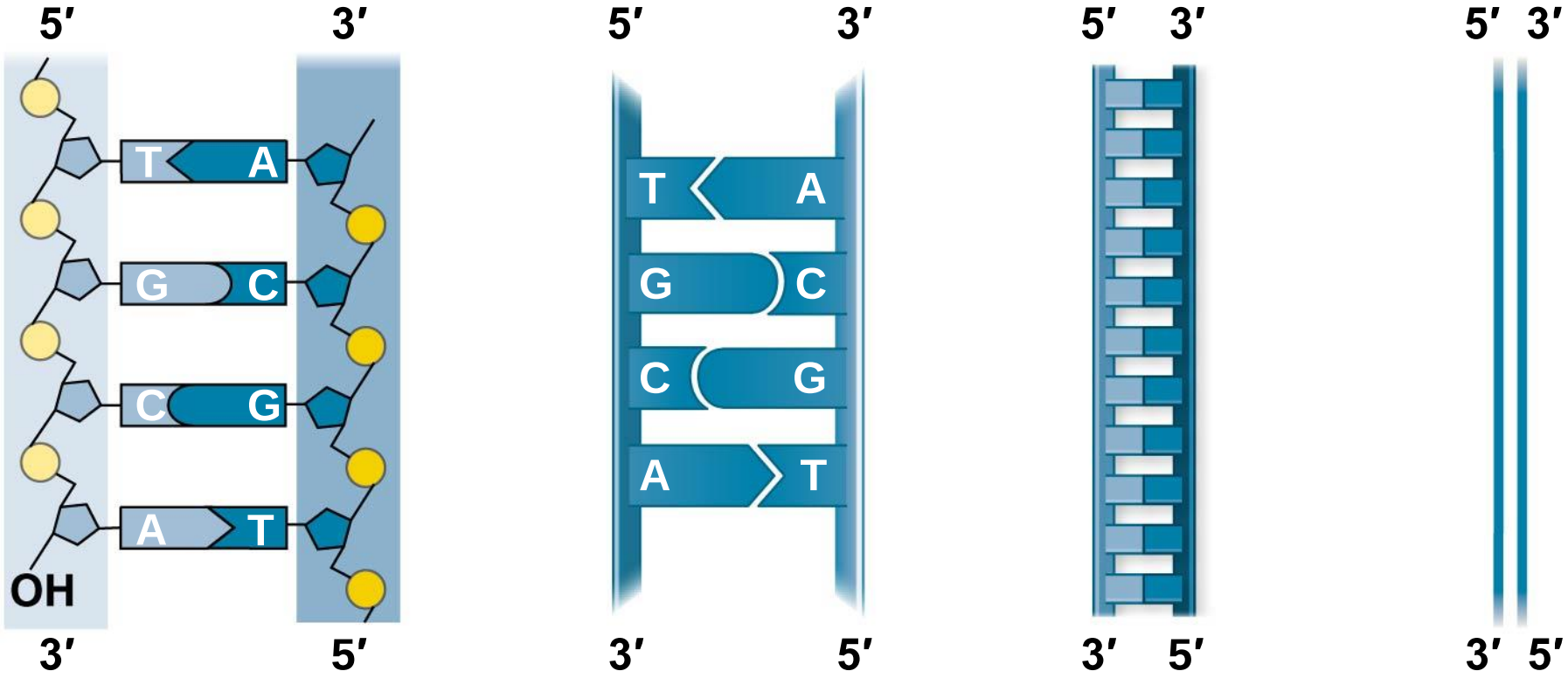
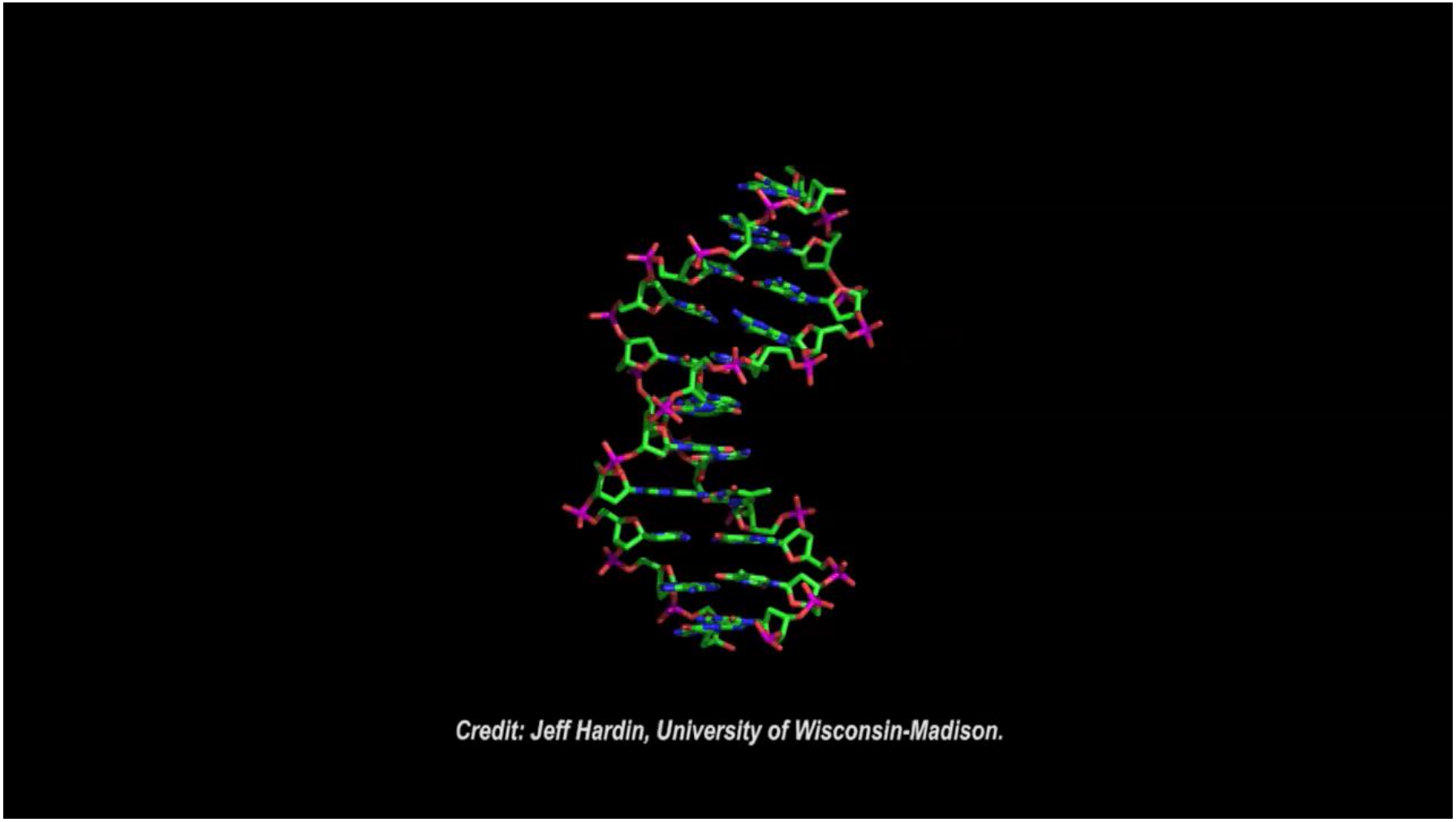


Figure 16.7bb

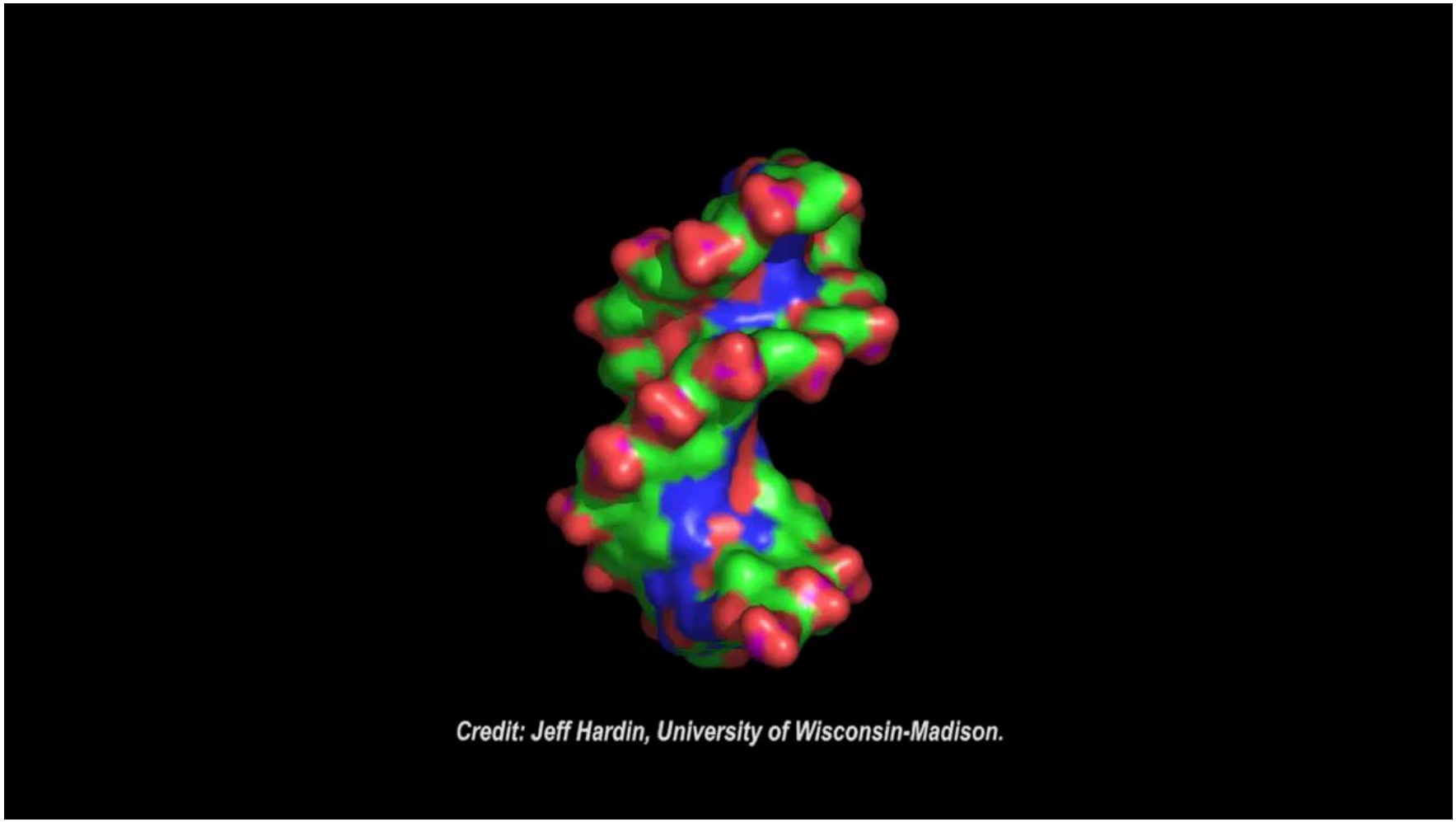


# Animation: DNA Double Helix

# Video: Stick Model of DNA (Deoxyribonucleic Acid)



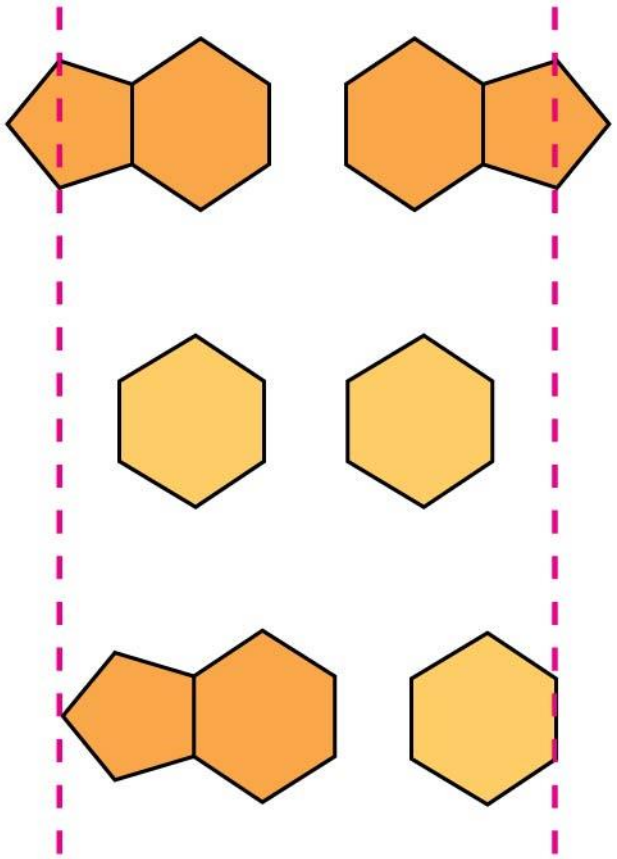
# Video: Surface Model of DNA (Deoxyribonucleic Acid)



- Watson and Crick built models of a double helix to conform to the X-rays and chemistry of DNA
- Franklin had concluded that there were two outer sugar-phosphate backbones, with the nitrogenous bases paired in the molecule's interior
- Watson built a model in which the backbones were **antiparallel** (their subunits run in opposite directions)

- At first, Watson and Crick thought the bases paired like with like (A with A, and so on), but such pairings did not result in a uniform width
- Instead, pairing a purine (A or G) with a pyrimidine (C or T) resulted in a uniform width consistent with the X-ray data

Figure 16.UN02



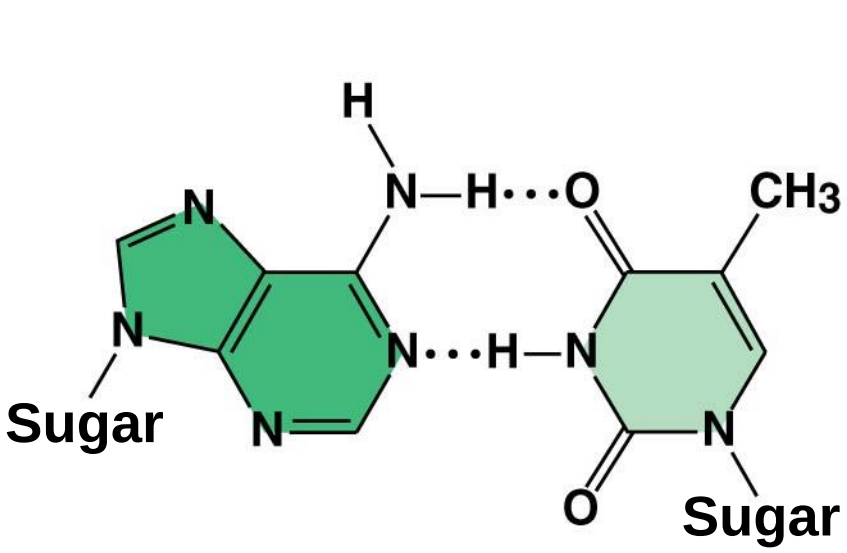
**Purine + purine: too wide**

**Pyrimidine + pyrimidine: too narrow**

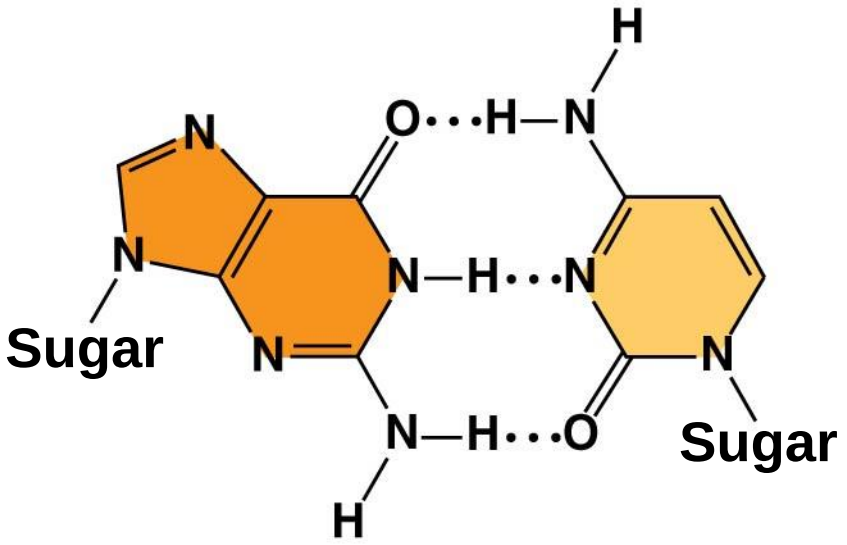
**Purine + pyrimidine: width consistent with X-ray data**

- Watson and Crick reasoned that the pairing was more specific, dictated by the base structures
- They determined that adenine (A) paired only with thymine (T), and guanine (G) paired only with cytosine (C)
- The Watson-Crick model explains Chargaff's rules: in any organism the amount of A = T, and the amount of G = C

Figure 16.8




Adenine (A) Thymine (T)




Guanine (G) Cytosine (C)

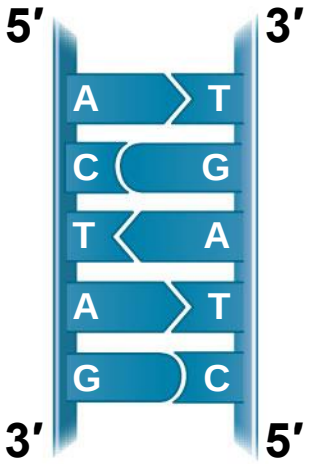
# Concept 16.2: Many proteins work together in DNA replication and repair

- The relationship between structure and function is manifest in the double helix
- Watson and Crick noted that the specific base pairing suggested a possible copying mechanism for genetic material

# The Basic Principle: Base Pairing to a Template Strand

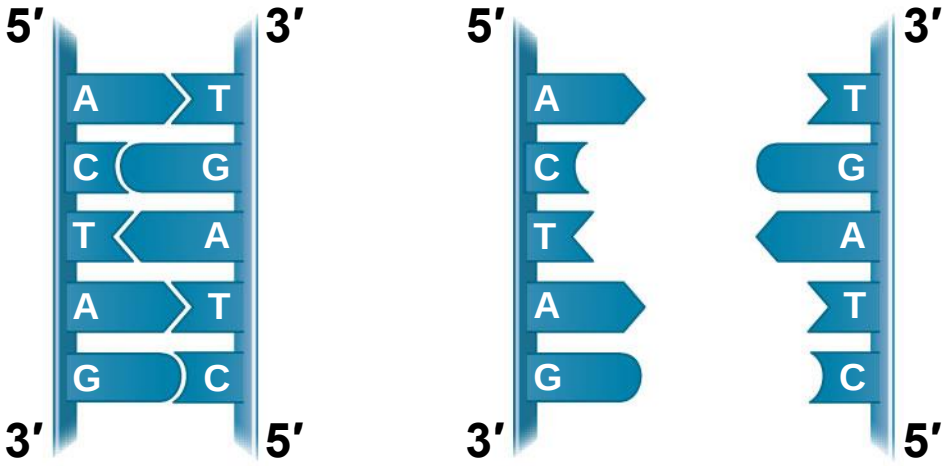
- Since the two strands of DNA are complementary, each strand acts as a template for building a new strand in replication
- In DNA replication, the parent molecule unwinds, and two new daughter strands are built based on base-pairing rules

Figure 16.9_1




**(a) Parental molecule**

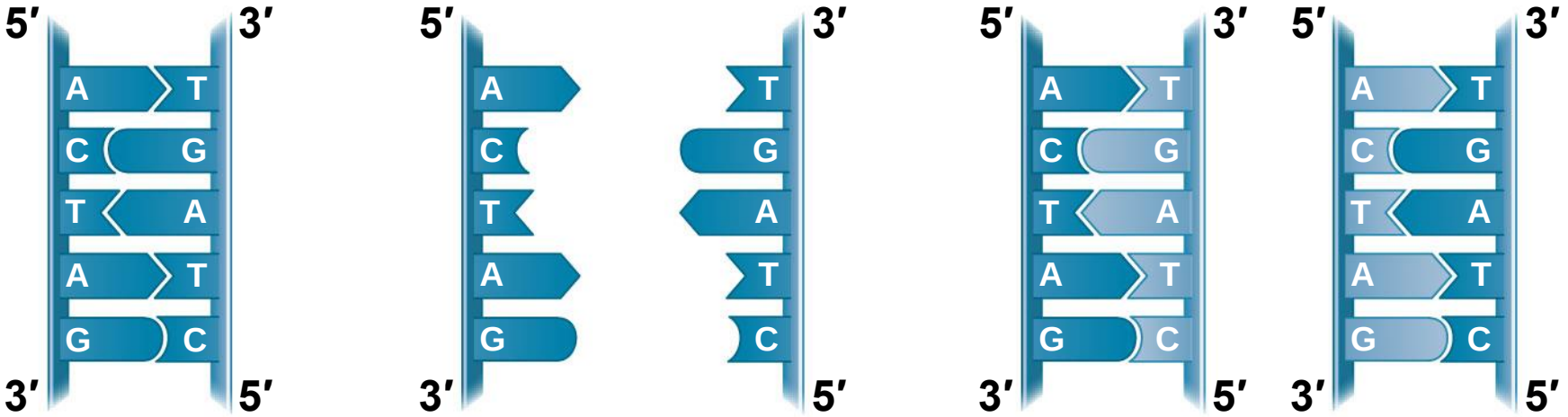
Figure 16.9_2




(a) Parental molecule

(b) Separation of parental strands into templates

Figure 16.9_3



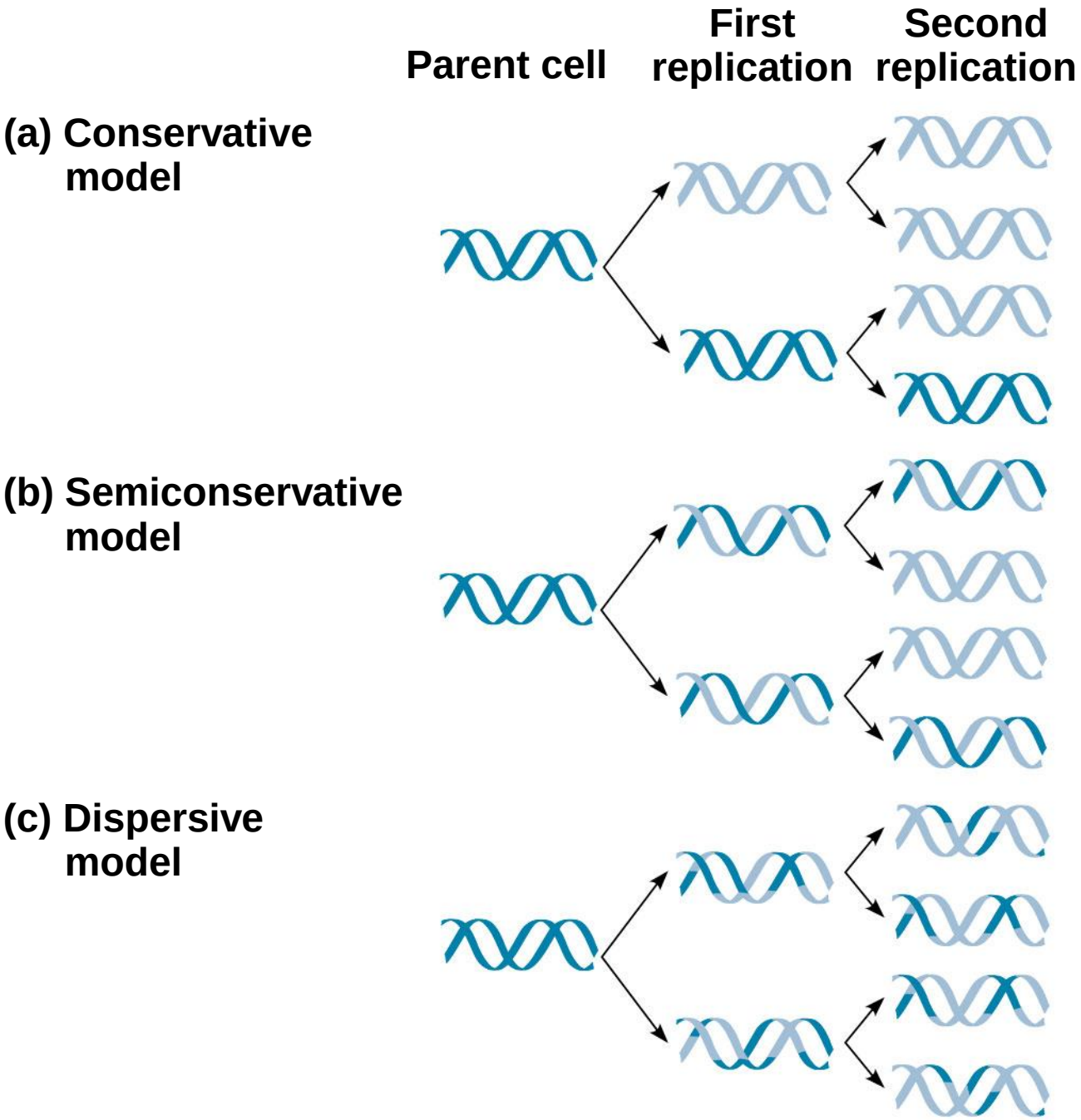

**(a) Parental molecule**

**(b) Separation of parental strands into templates**

**(c) Formation of new strands complementary to template strands**

- Watson and Crick's **semiconservative model** of replication predicts that when a double helix replicates, each daughter molecule will have one old strand (derived or "conserved" from the parent molecule) and one newly made strand
- Competing models were the conservative model (the two parent strands rejoin) and the dispersive model (each strand is a mix of old and new)

Figure 16.10



- Experiments by Matthew Meselson and Franklin Stahl supported the semiconservative model

Figure 16.11

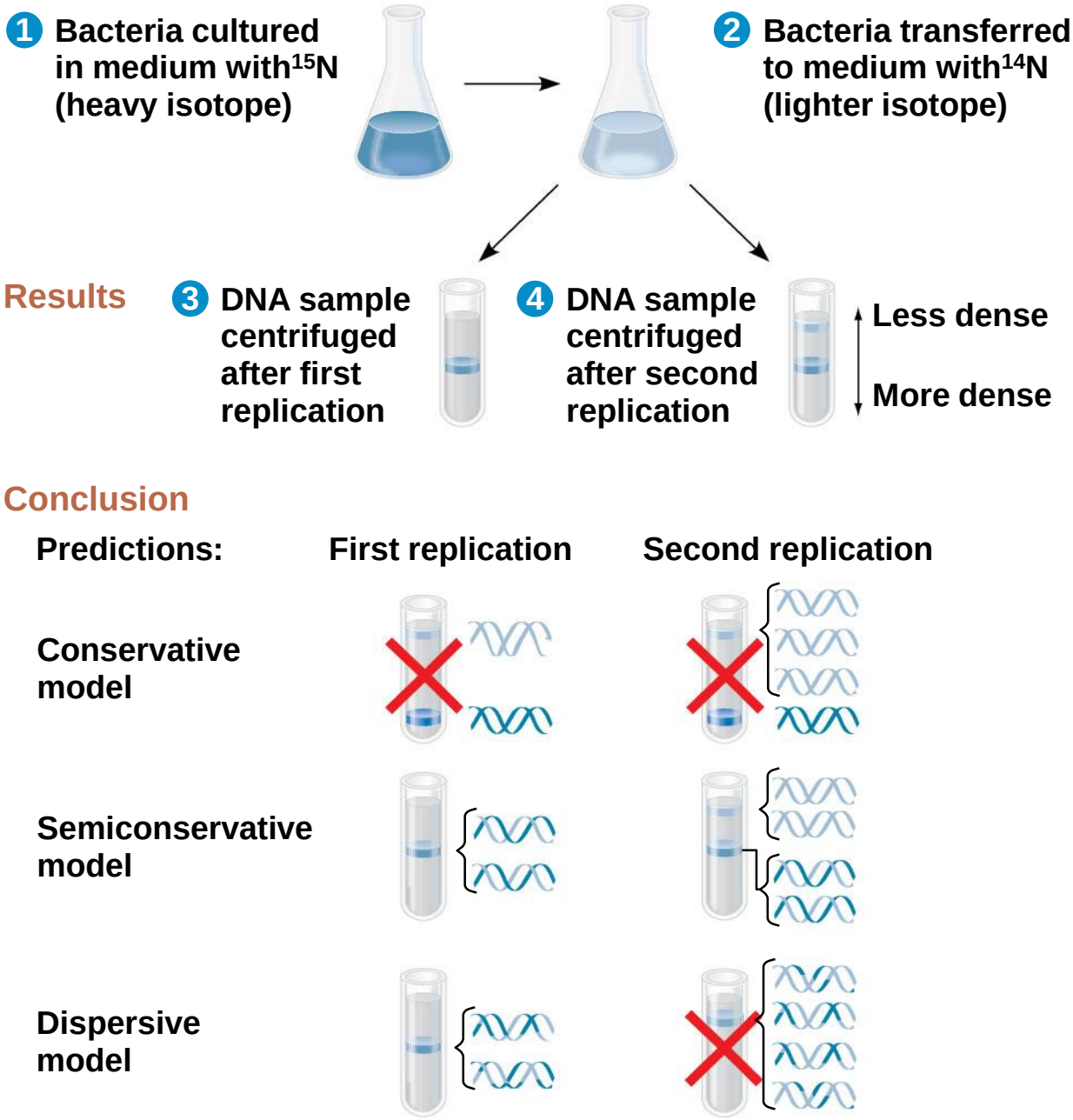


Figure 16.11a

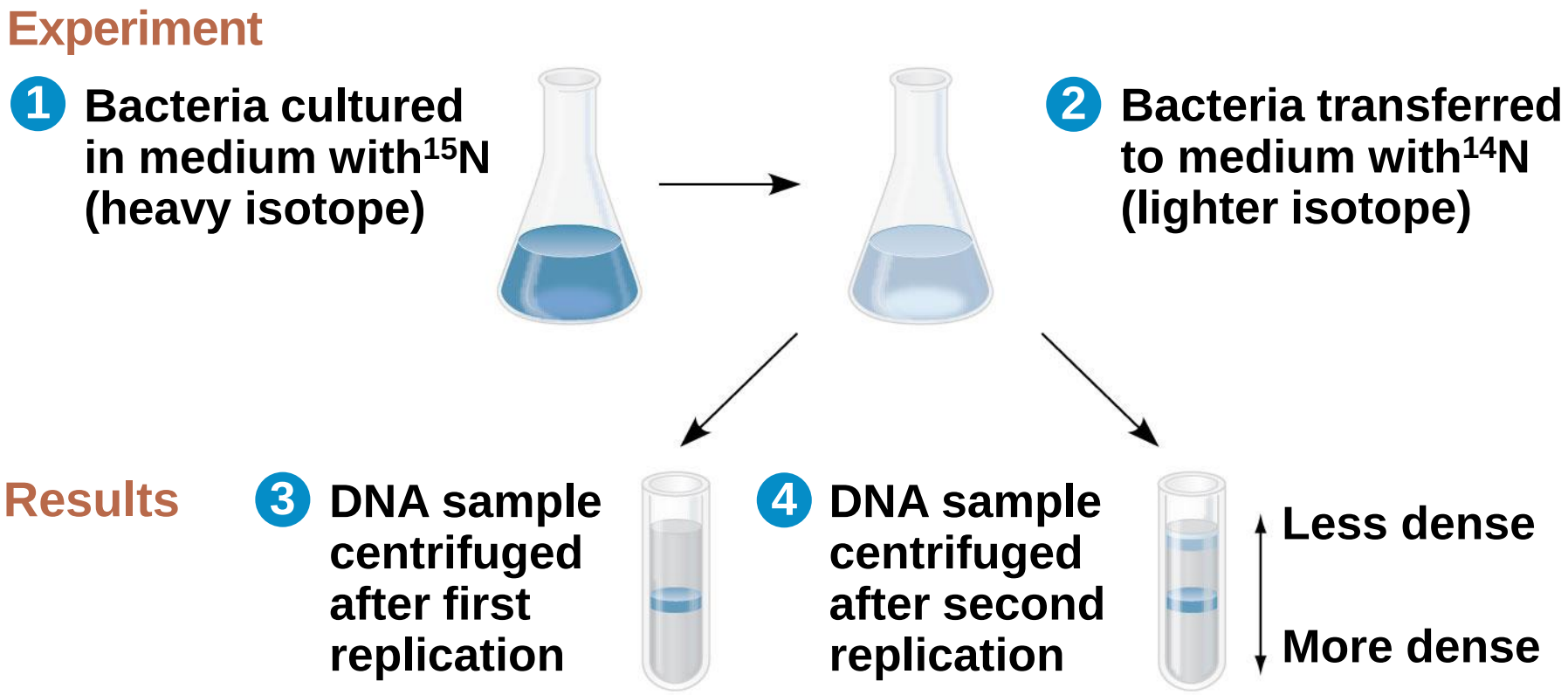
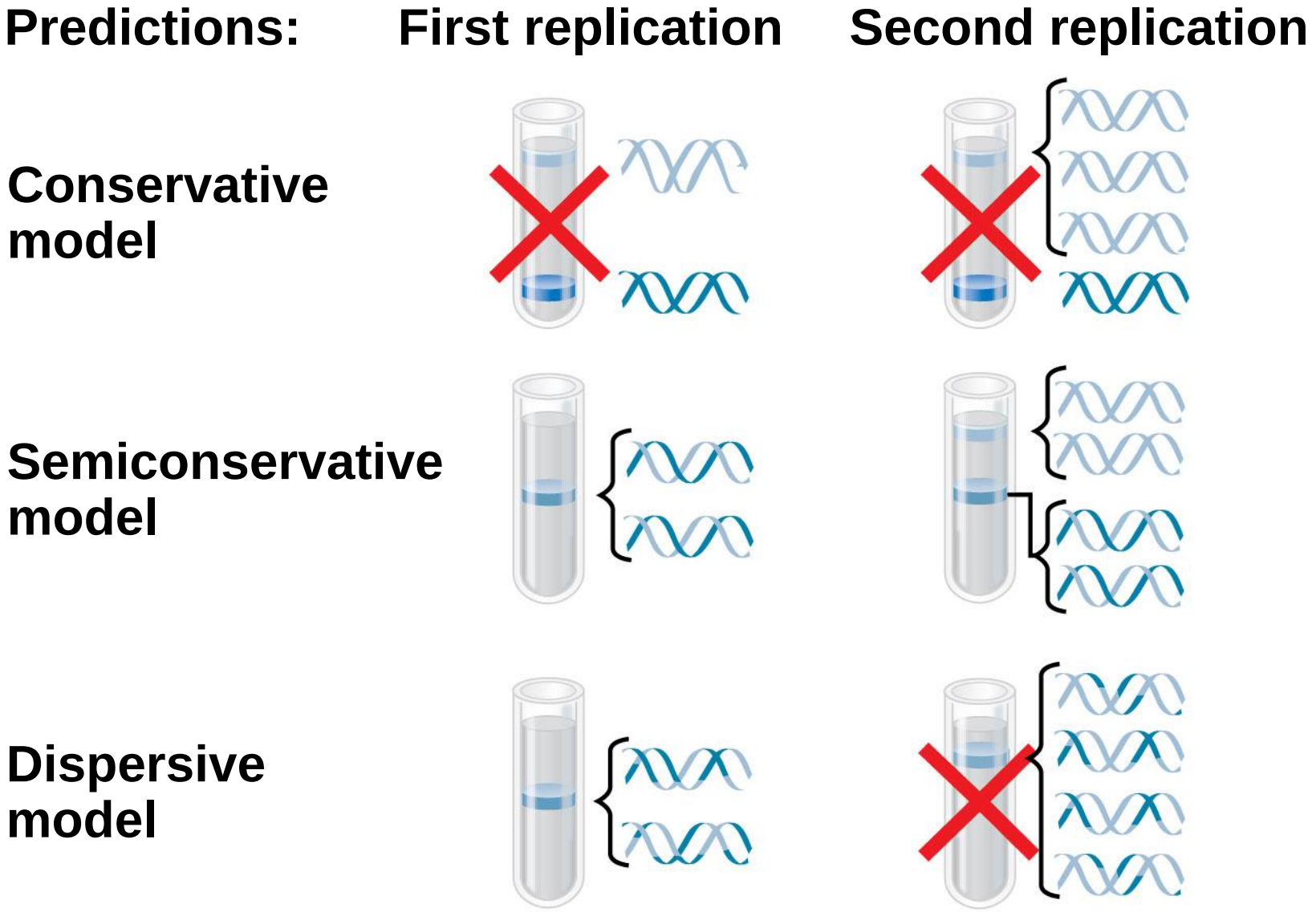


Figure 16.11b

## Conclusion



# 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*

- Replication begins at particular sites called **origins of replication**, where the two DNA strands are separated, opening up a replication "bubble"
- A eukaryotic chromosome may have hundreds or even thousands of origins of replication
- Replication proceeds in both directions from each origin, until the entire molecule is copied

Figure 16.12

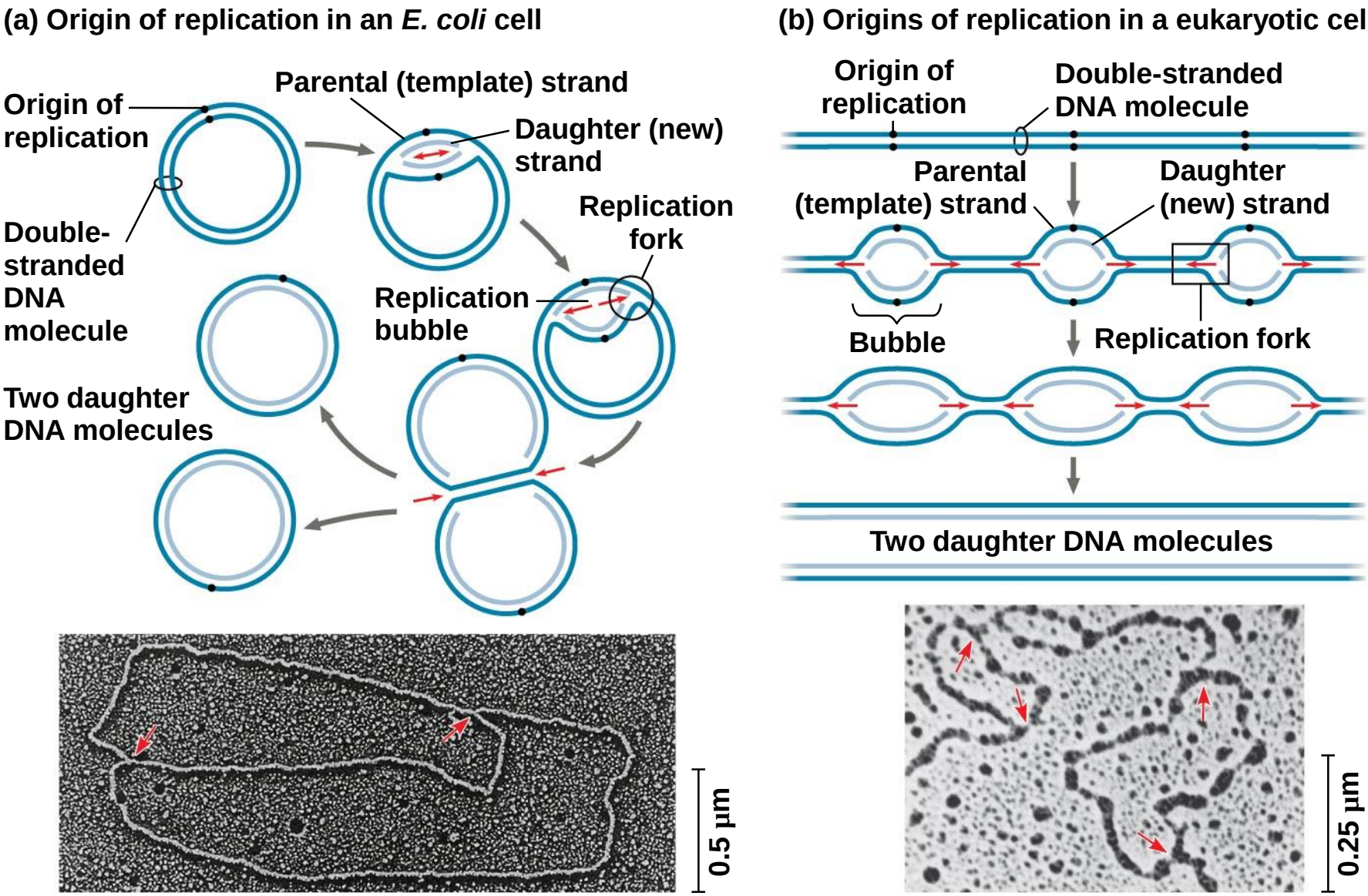
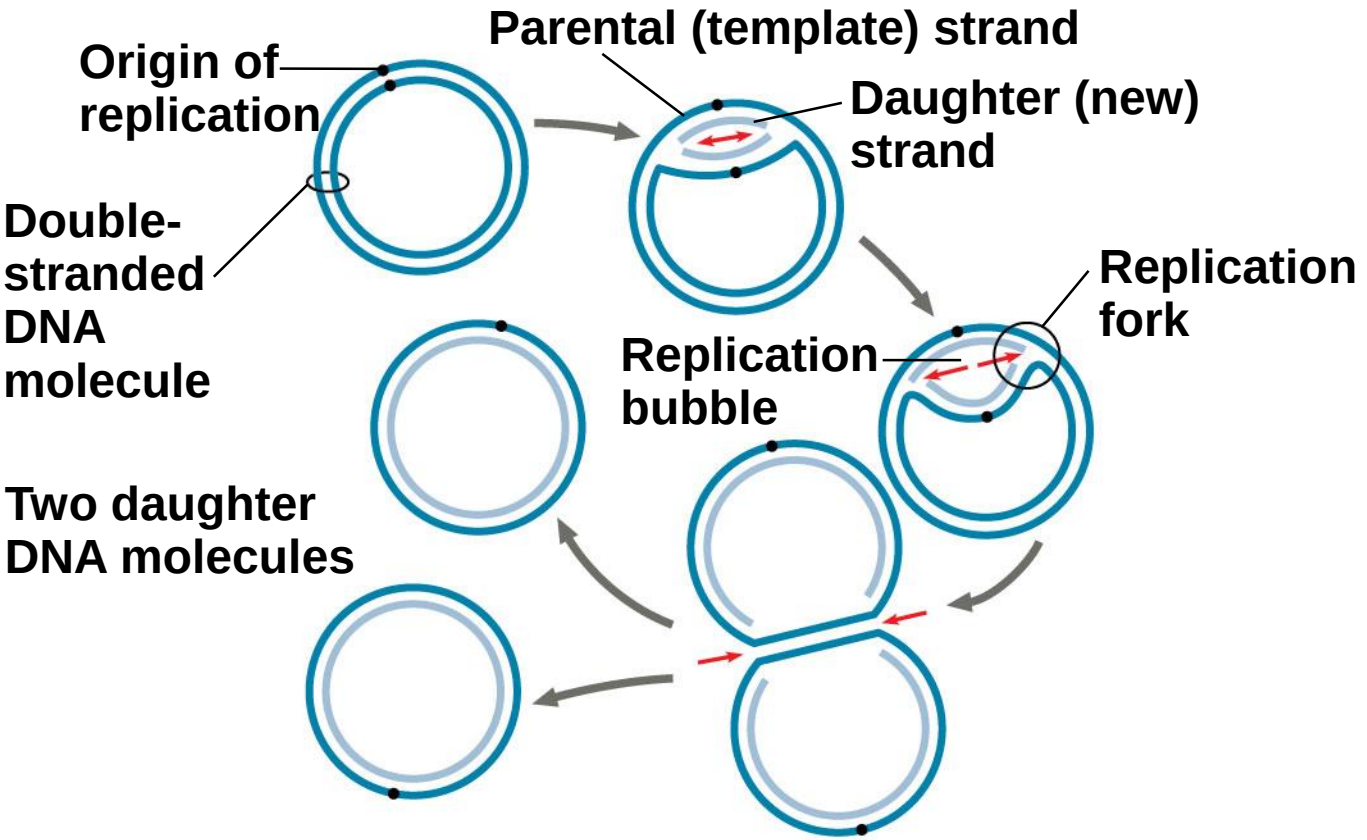


Figure 16.12a

## (a) Origin of replication in an *E. coli* cell



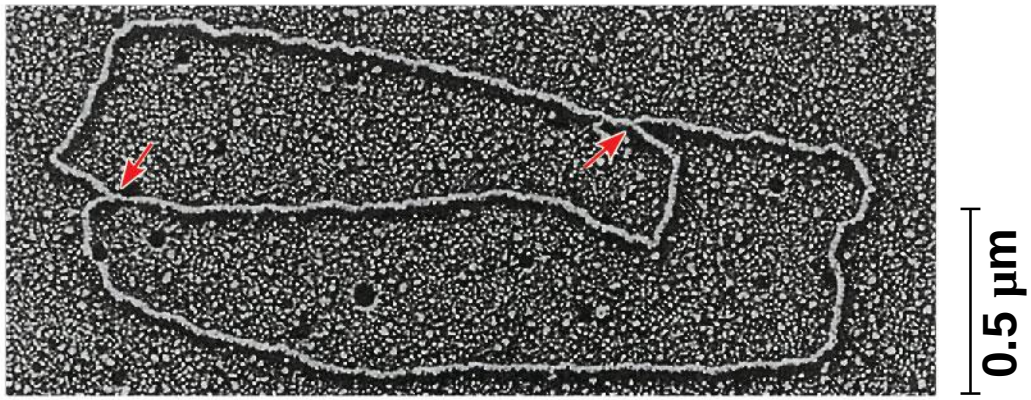



Figure 16.12aa

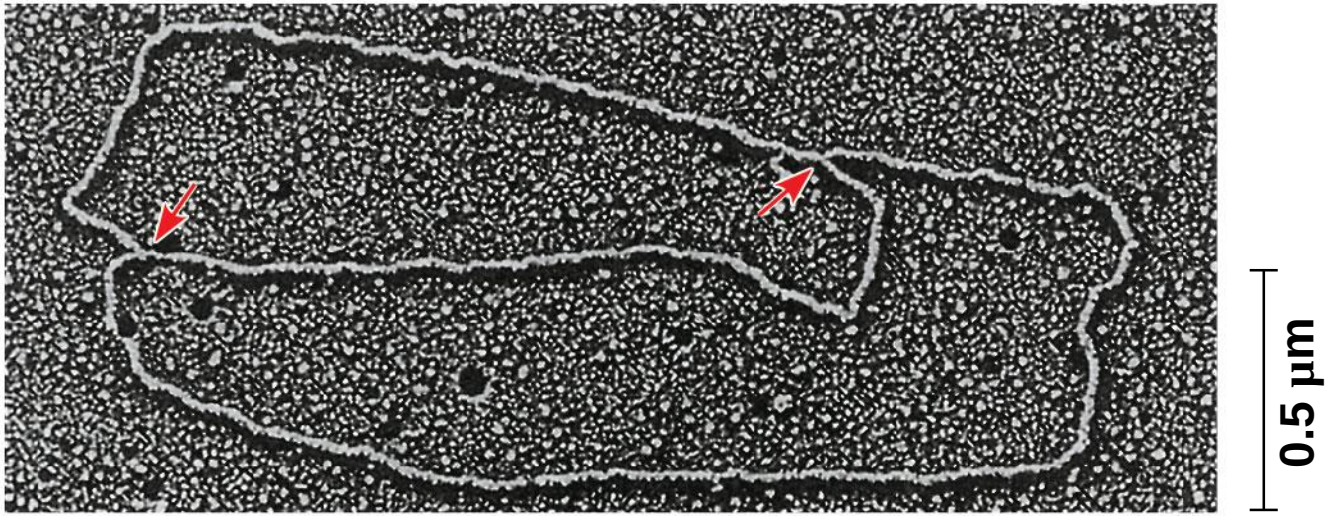


Figure 16.12b

## (b) Origins of replication in a eukaryotic cell

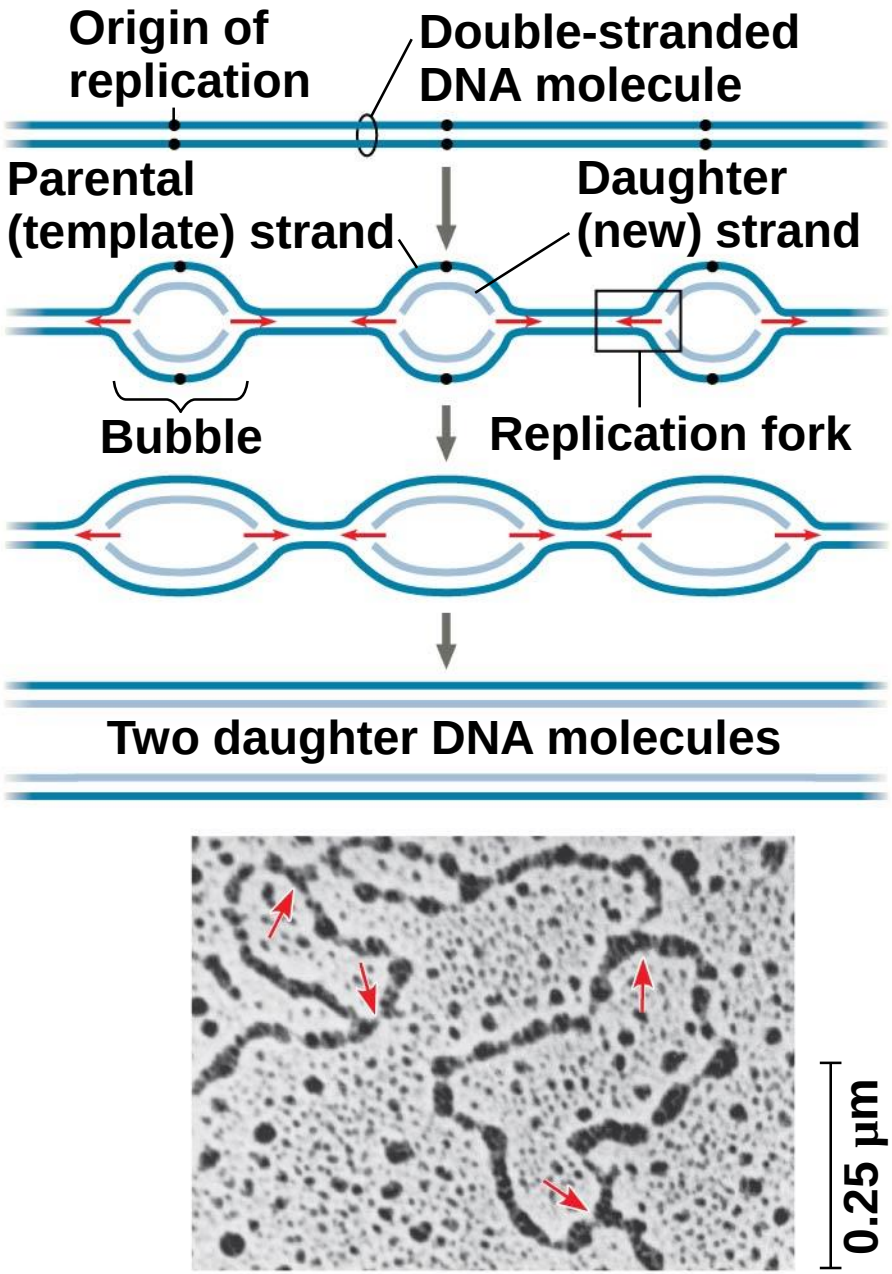
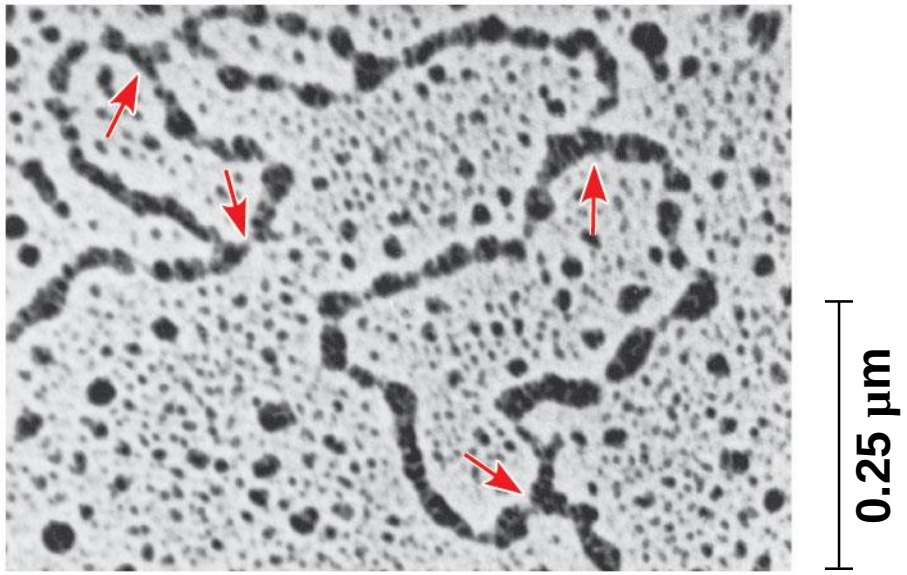
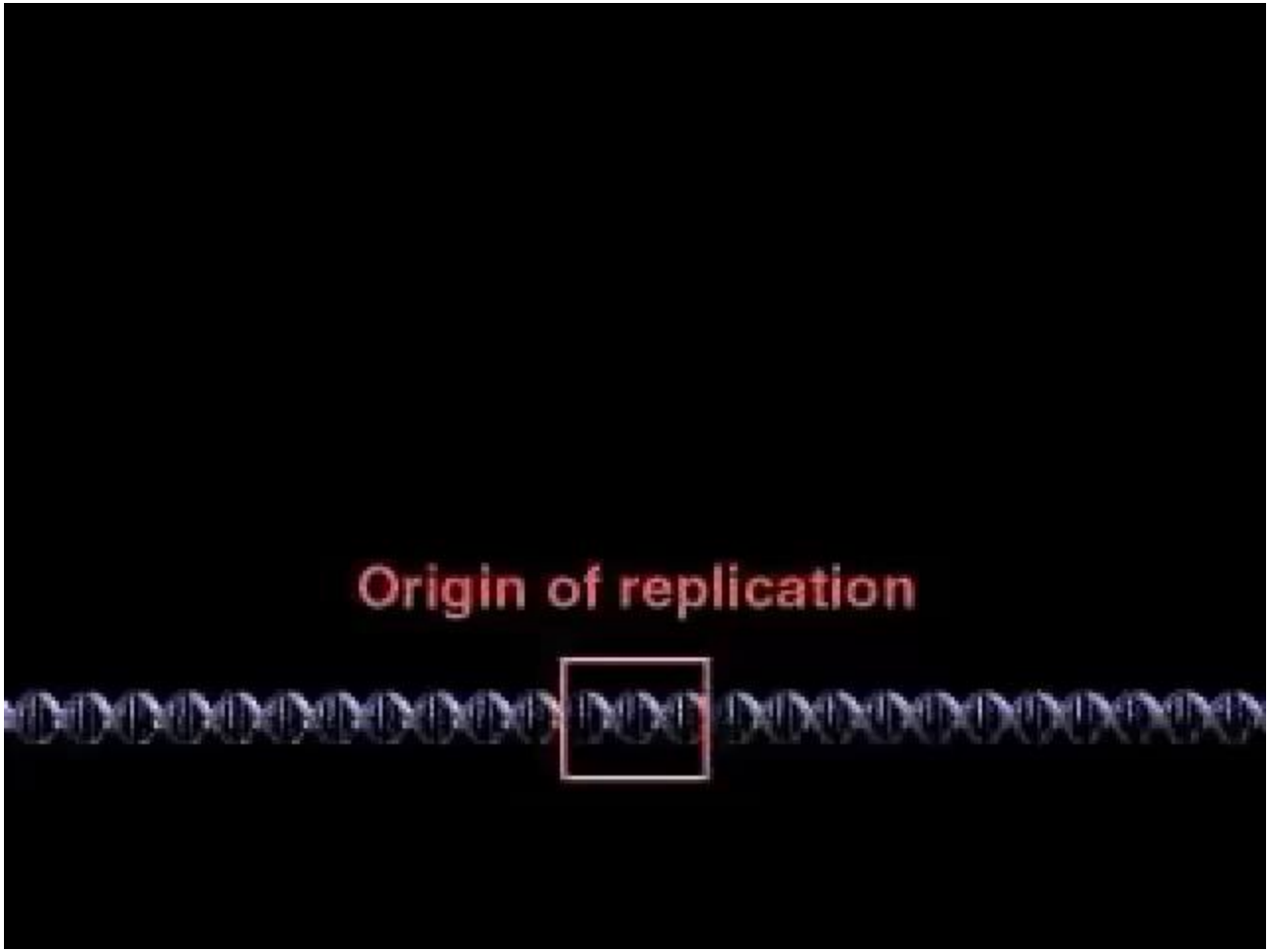


Figure 16.12ba

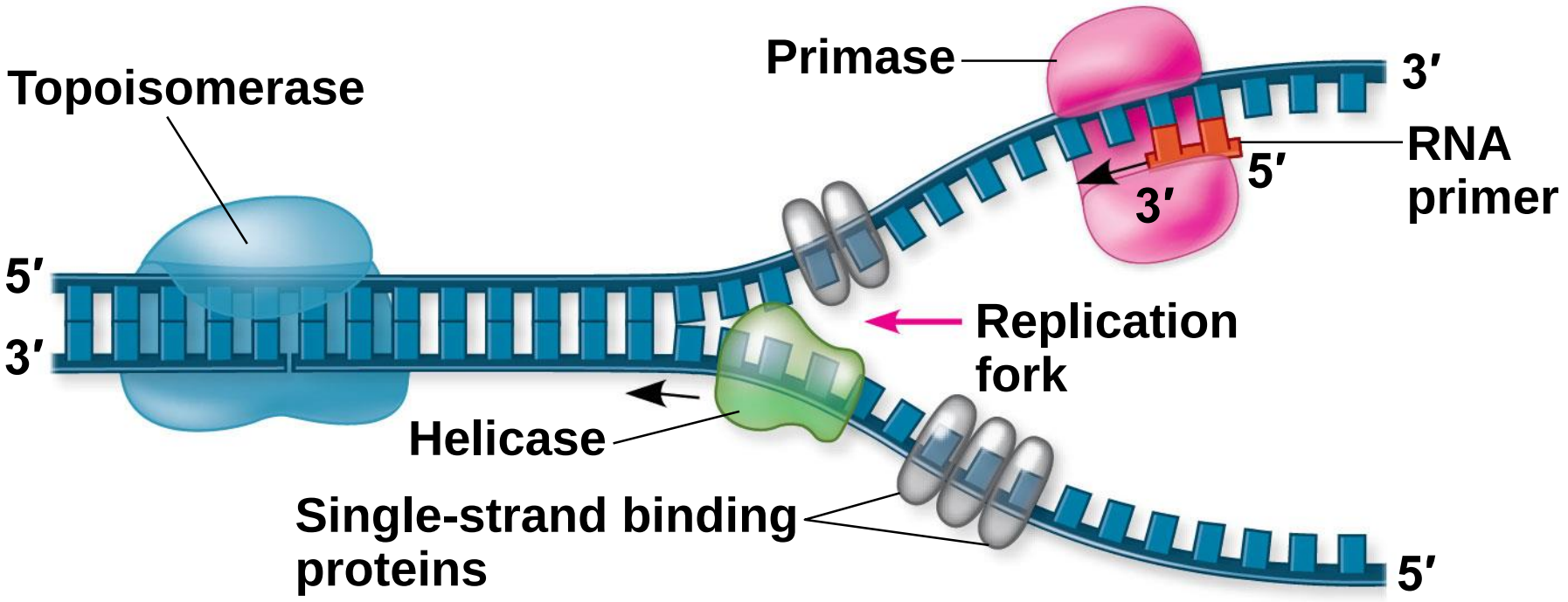


# Animation: Origins of Replication



- At the end of each replication bubble is a **replication fork**, a Y-shaped region where new DNA strands are elongating
- **Helicases** are enzymes that untwist the double helix at the replication forks
- **Single-strand binding proteins** bind to and stabilize single-stranded DNA
- **Topoisomerase** relieves the strain of twisting of the double helix by breaking, swiveling, and rejoining DNA strands

Figure 16.13



# *Synthesizing a New DNA Strand*

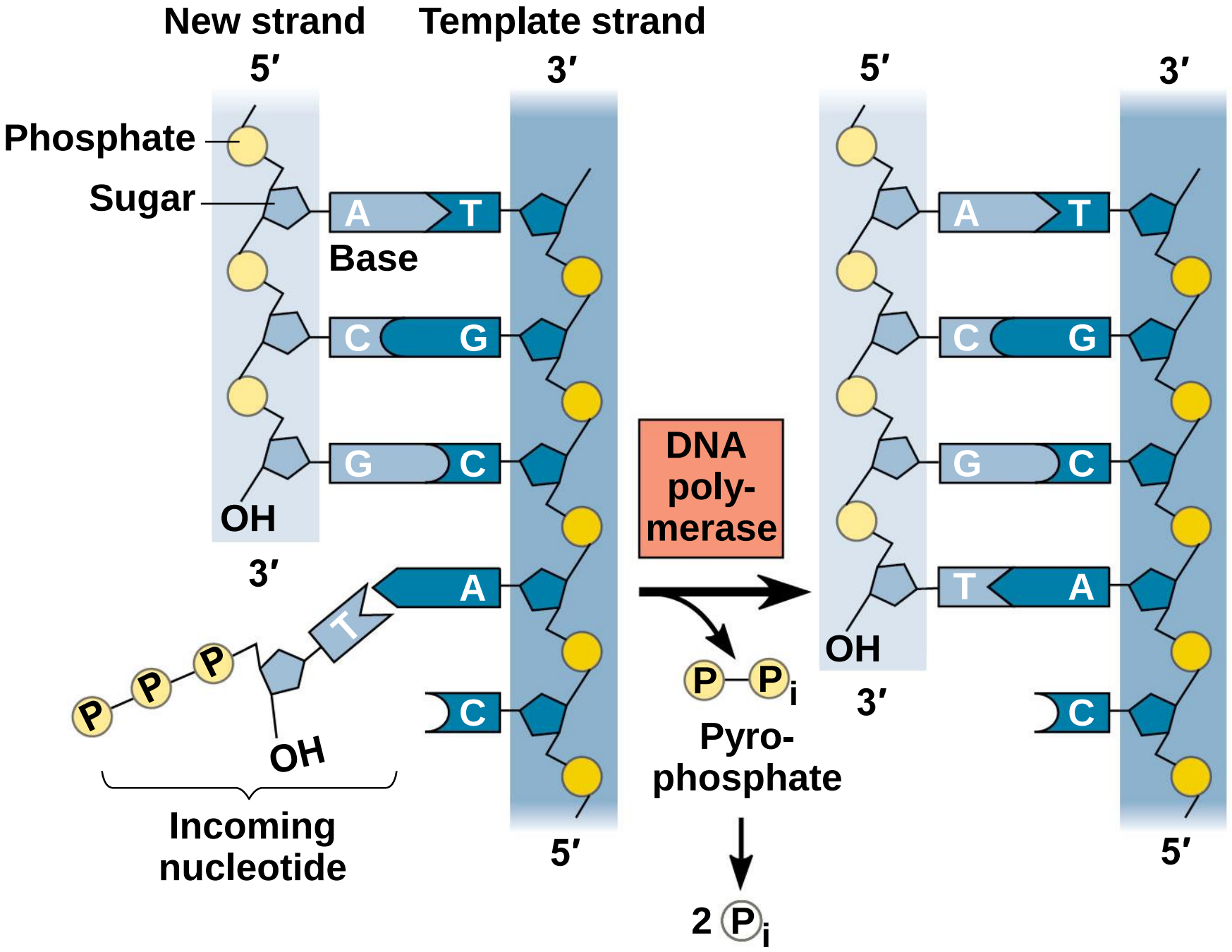
- DNA polymerases require a primer to which they can add nucleotides
- The initial nucleotide strand is a short RNA **primer**
- This is synthesized by the enzyme **primase**

- Primase can start an RNA chain from scratch and adds RNA nucleotides one at a time using the parental DNA as a template
- The primer is short (5–10 nucleotides long), and the 3′ end serves as the starting point for the new DNA strand

- Enzymes called **DNA polymerases** catalyze the synthesis of new DNA at a replication fork
- Most DNA polymerases require a primer and a DNA template strand
- The rate of elongation is about 500 nucleotides per second in bacteria and 50 per second in human cells

- Each nucleotide that is added to a growing DNA strand is a nucleoside triphosphate
- dATP supplies adenine to DNA and is similar to the ATP of energy metabolism
- The difference is in their sugars: dATP has deoxyribose while ATP has ribose
- As each monomer joins the DNA strand, via a dehydration reaction, it loses two phosphate groups as a molecule of pyrophosphate

Figure 16.14



# *Antiparallel Elongation*

- The antiparallel structure of the double helix affects replication
- DNA polymerases add nucleotides only to the free 3′ end of a growing strand; therefore, a new DNA strand can elongate only in the 5′ to 3′ direction

Figure 16.15

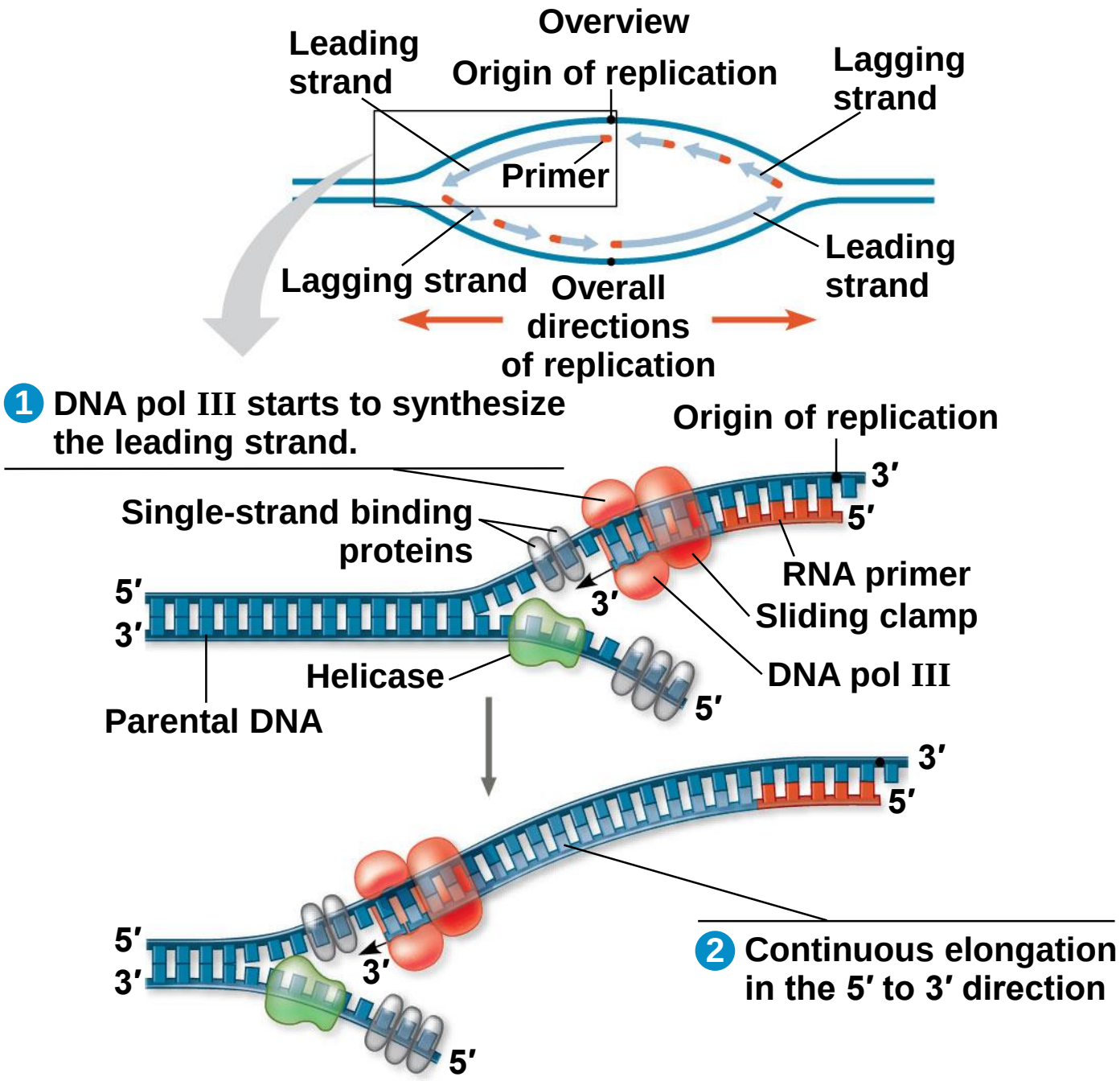


Figure 16.15a

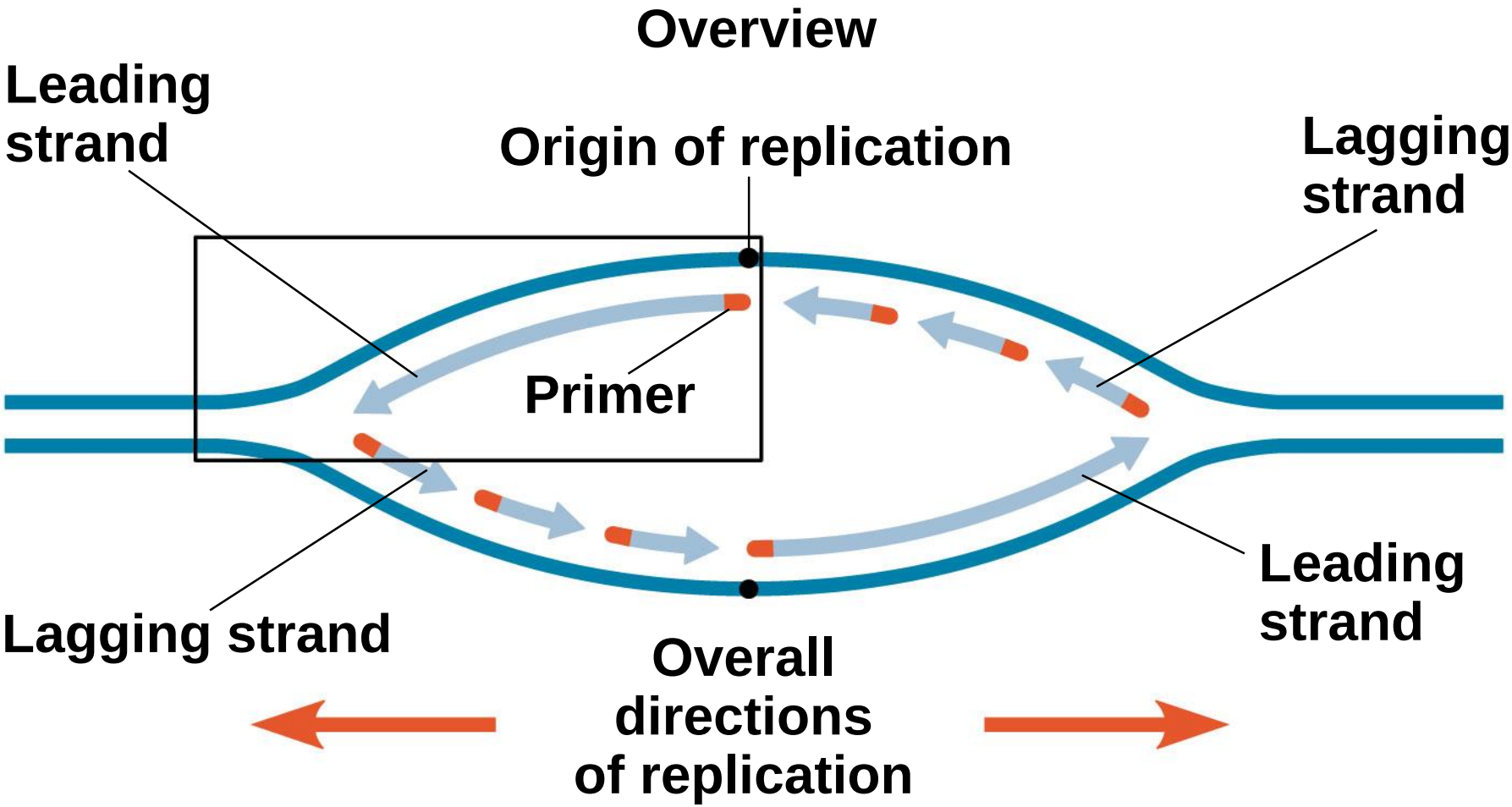
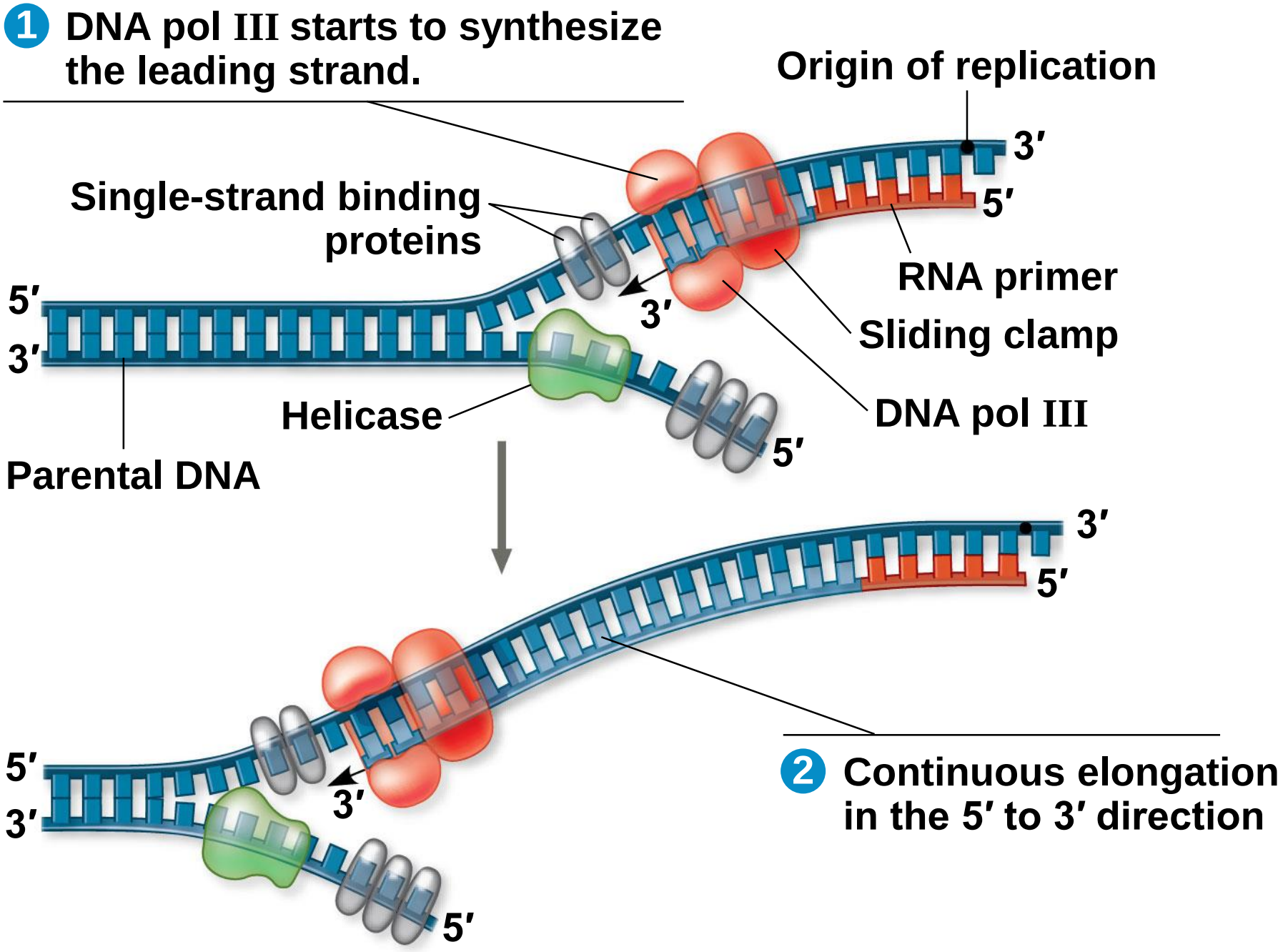
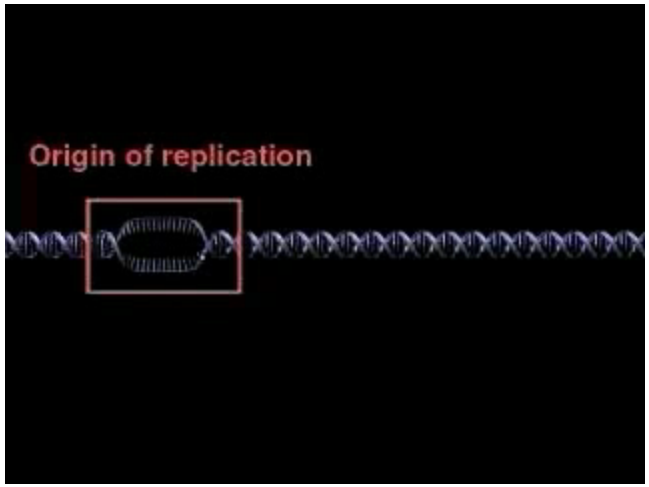


Figure 16.15b



- Along one template strand of DNA, the DNA polymerase synthesizes a **leading strand** continuously, moving toward the replication fork

# Animation: Leading Strand



- To elongate the other new strand, called the **lagging strand**, DNA polymerase 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 joined together by **DNA ligase**

Figure 16.16

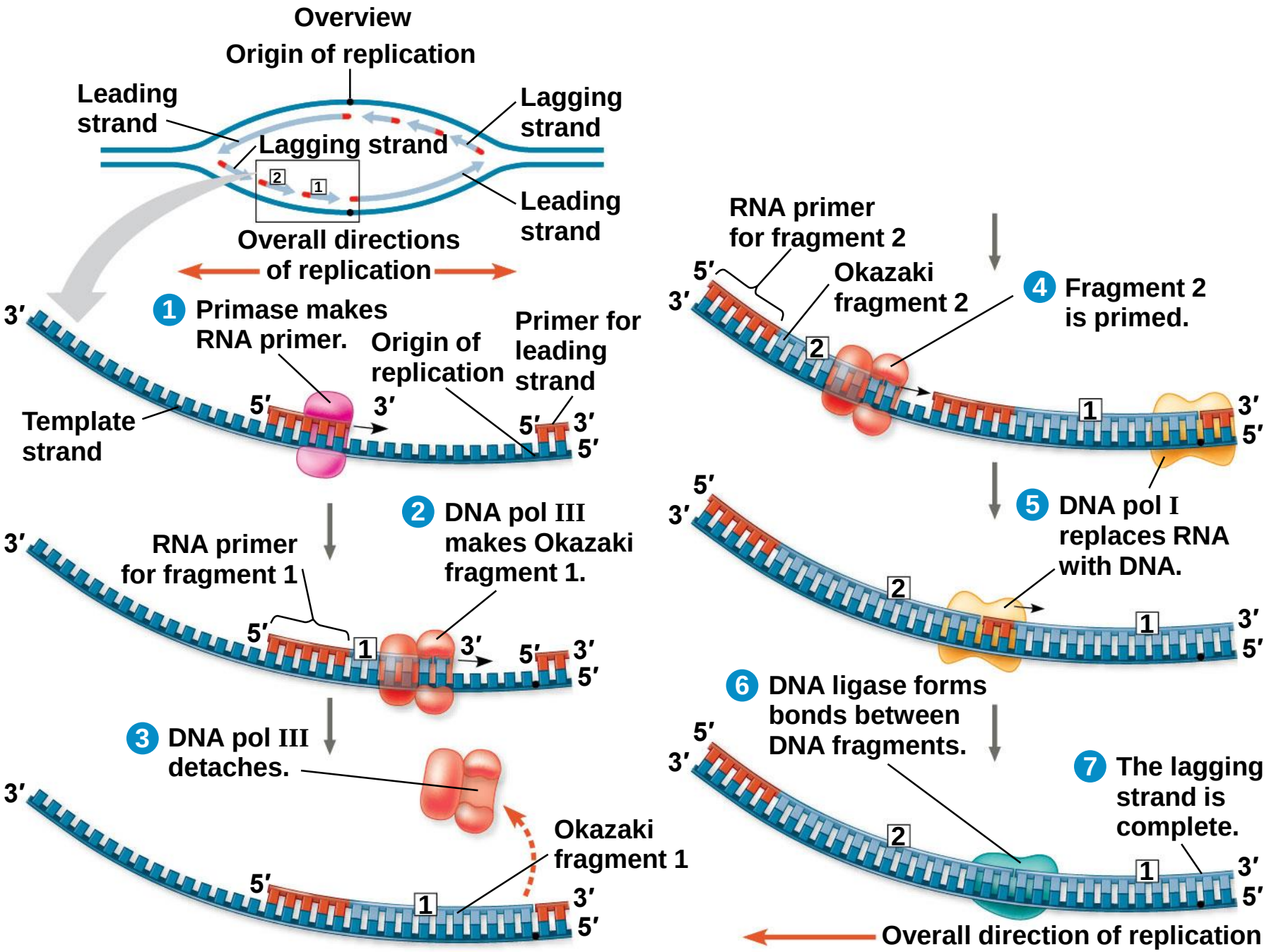


Figure 16.16a

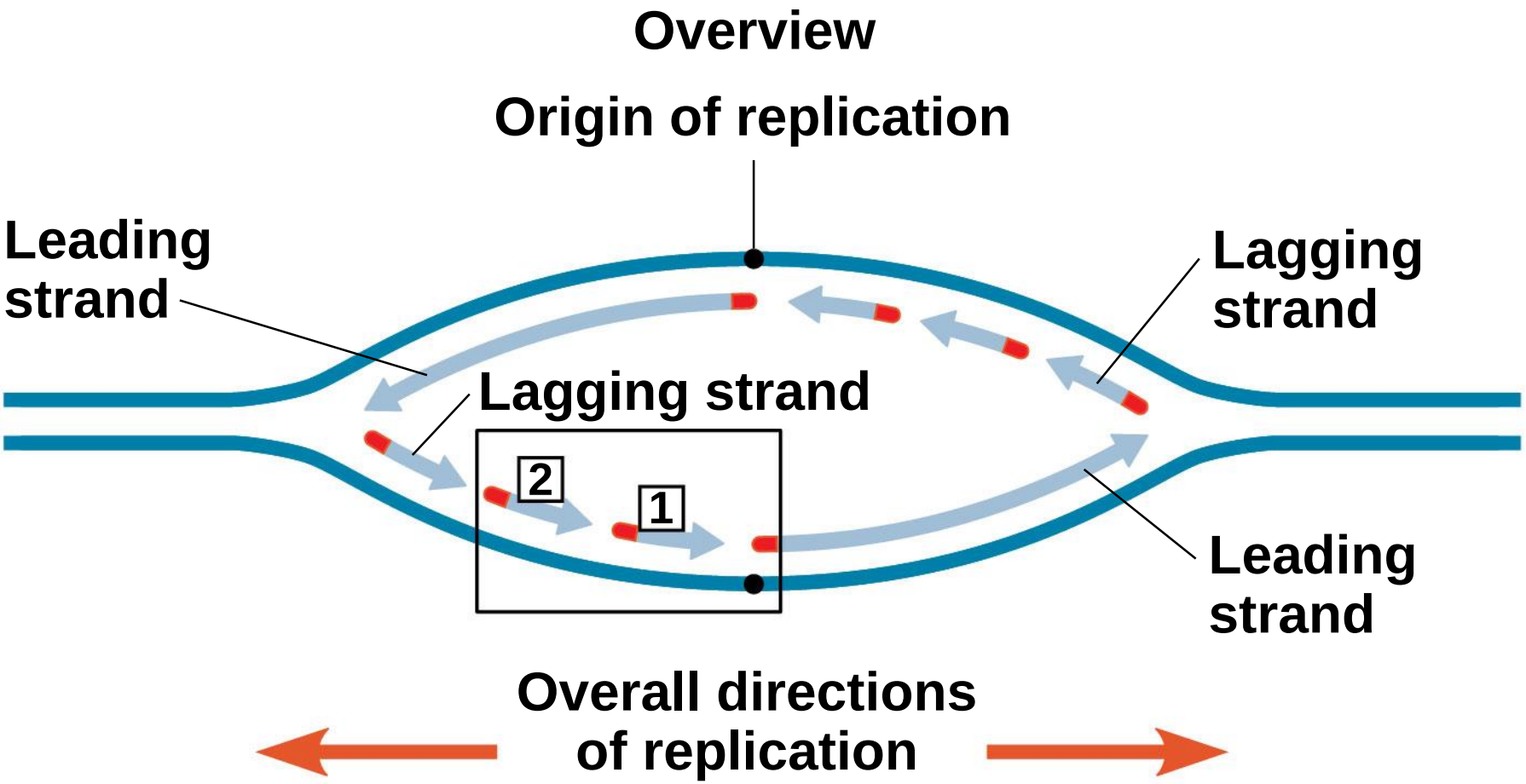


Figure 16.16b_1

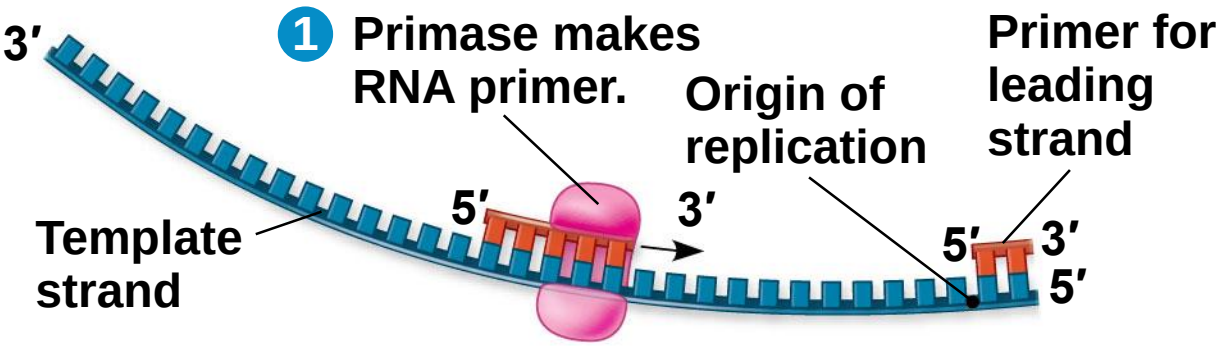


Figure 16.16b_2

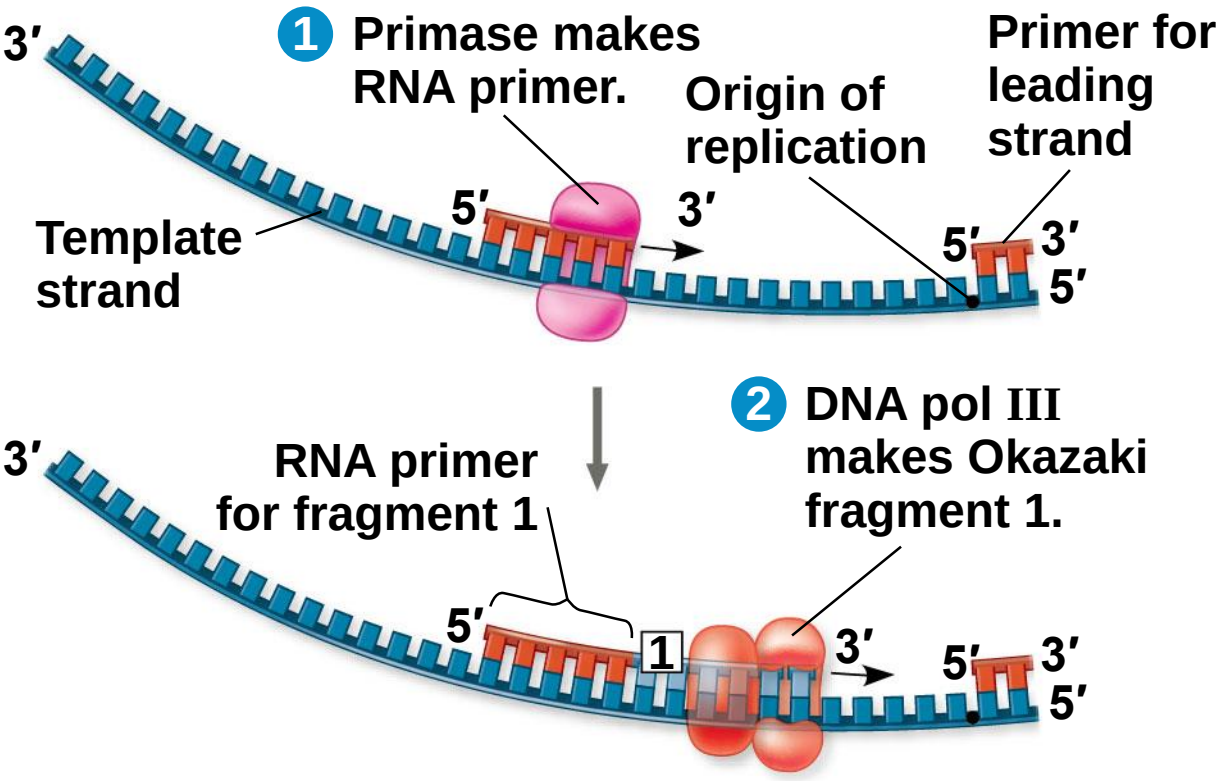


Figure 16.16b_3

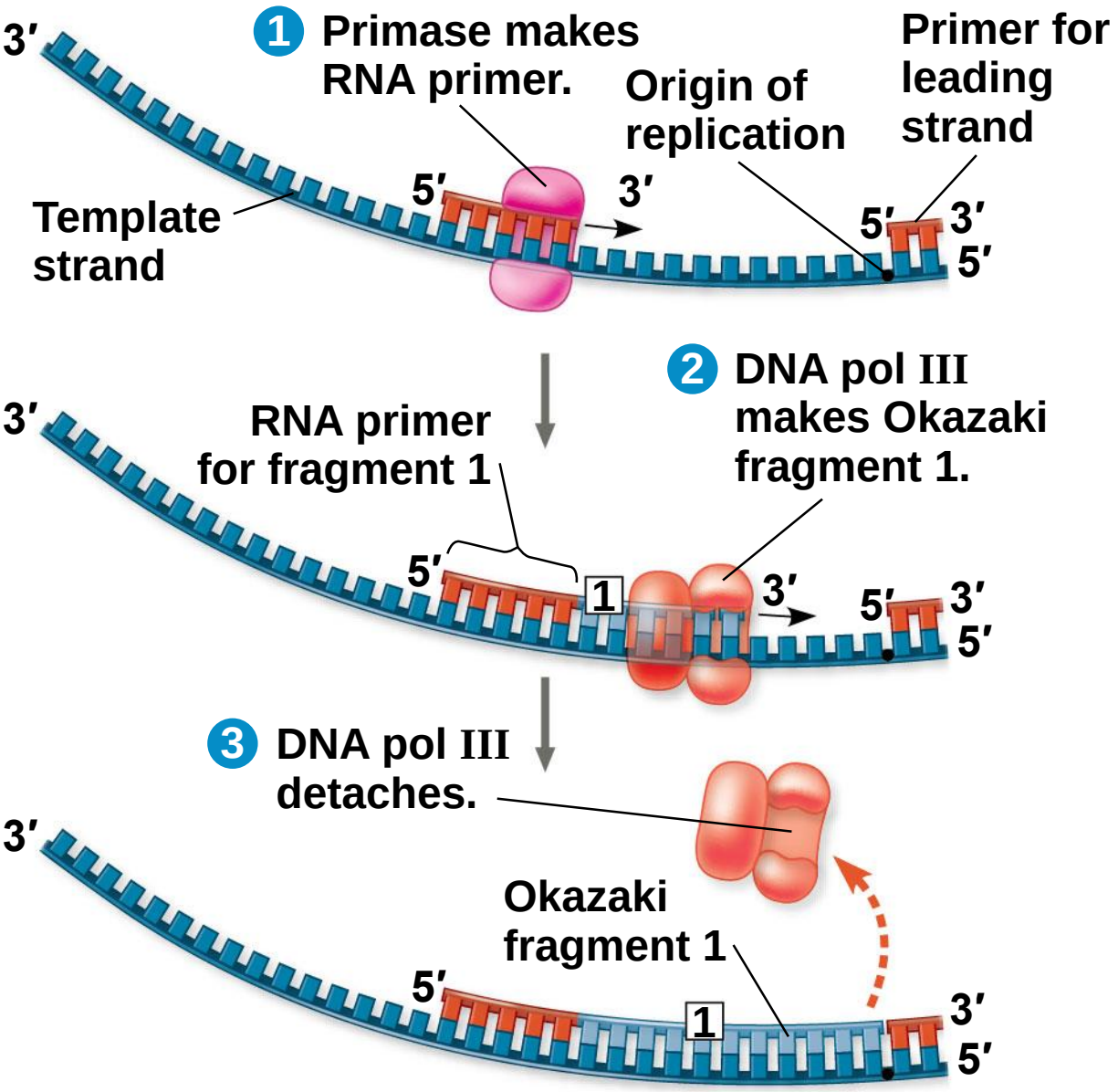


Figure 16.16c_1

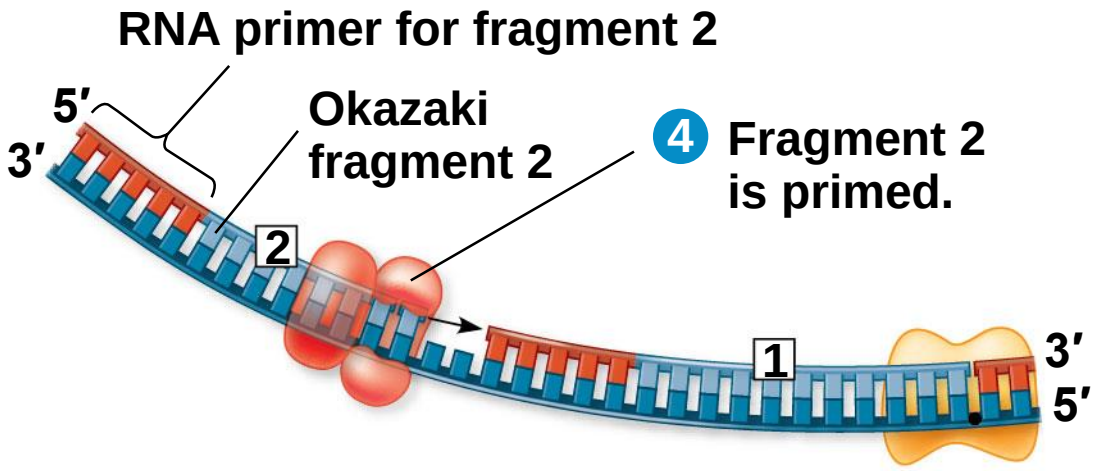


Figure 16.16c_2

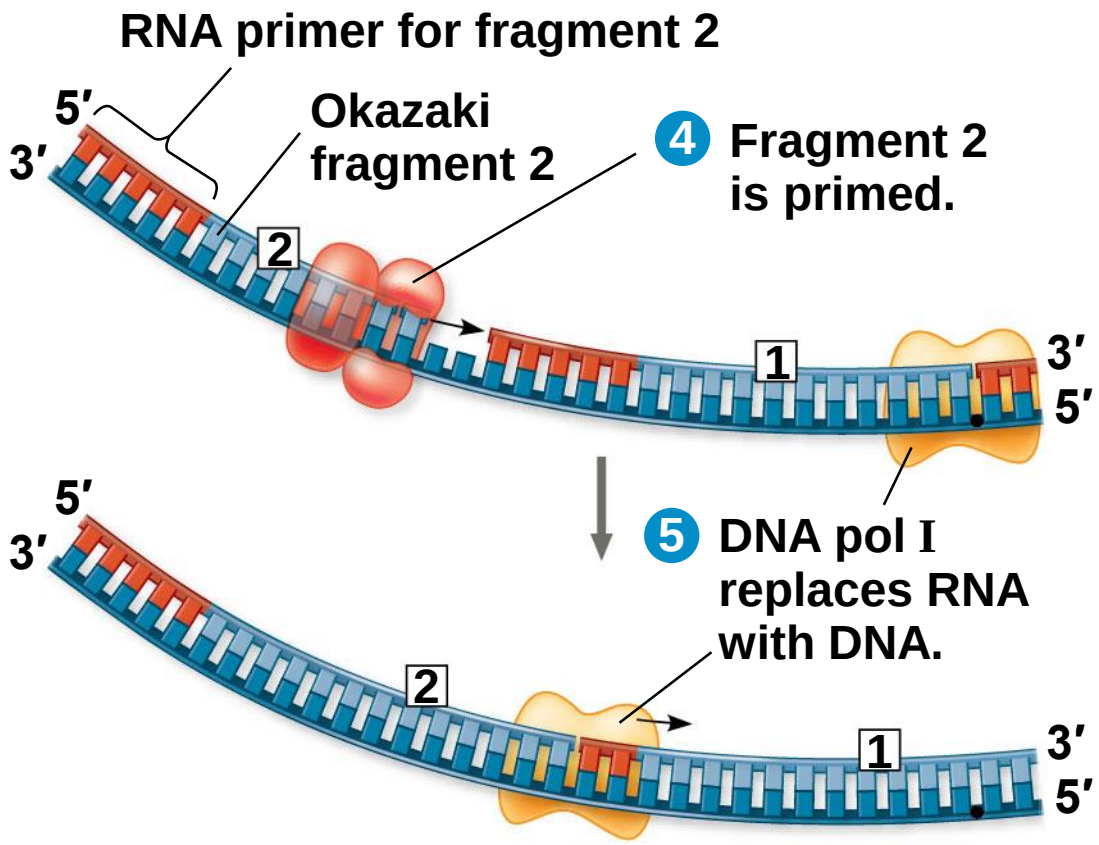
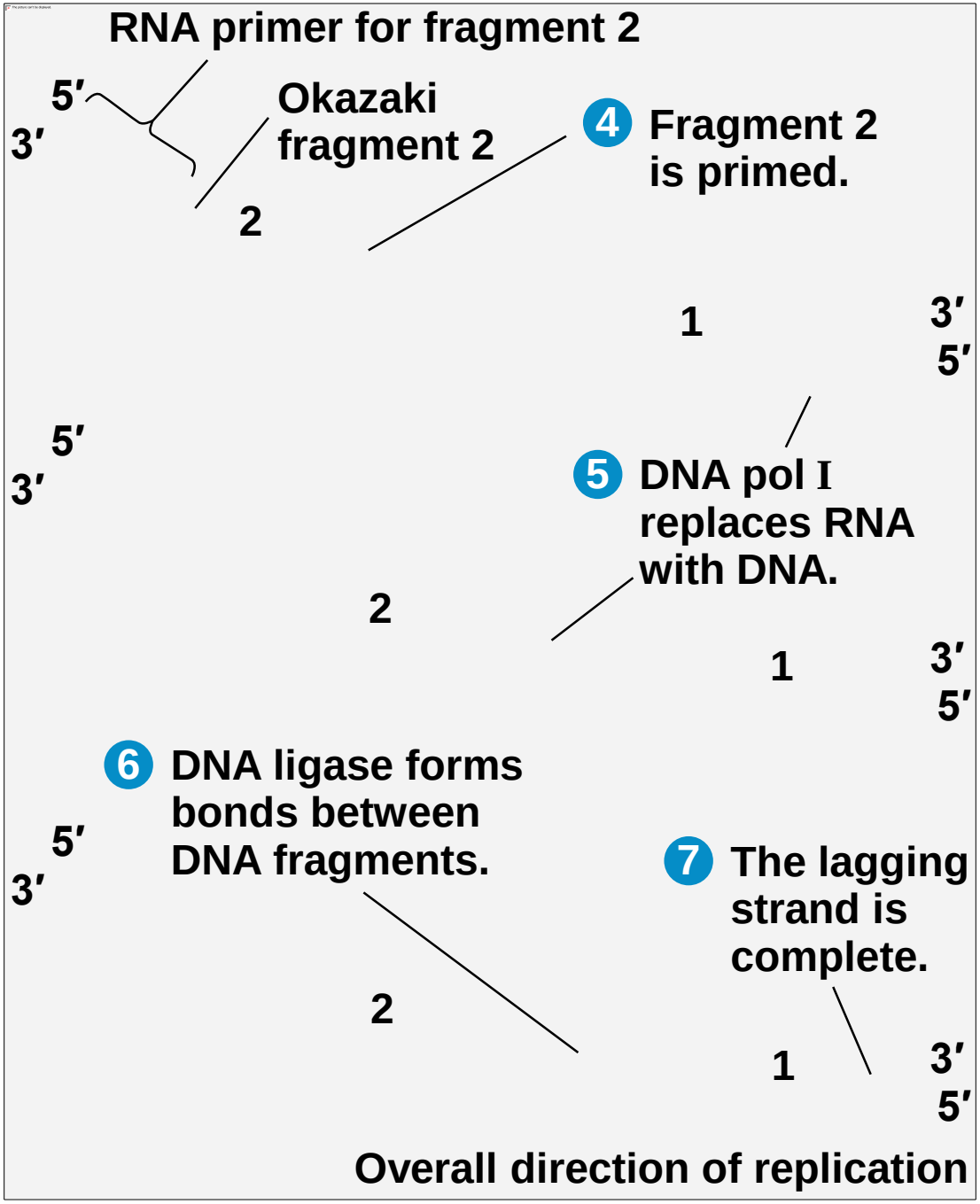
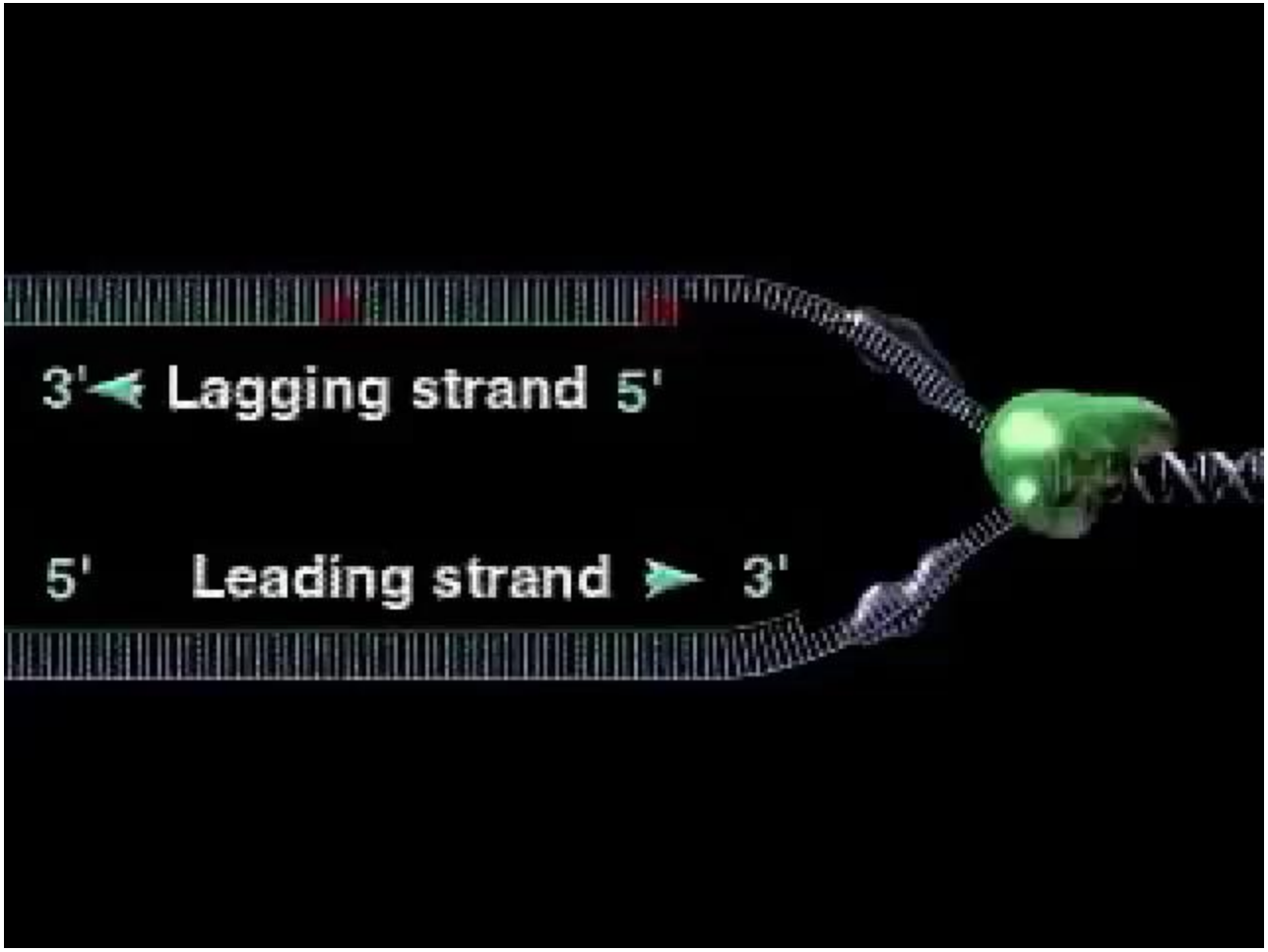


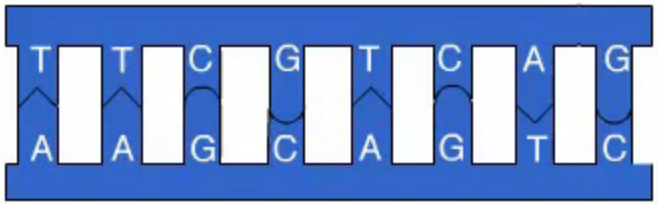
Figure 16.16c_3



# Animation: Lagging Strand



# Animation: DNA Replication Overview



# Animation: DNA Replication Review

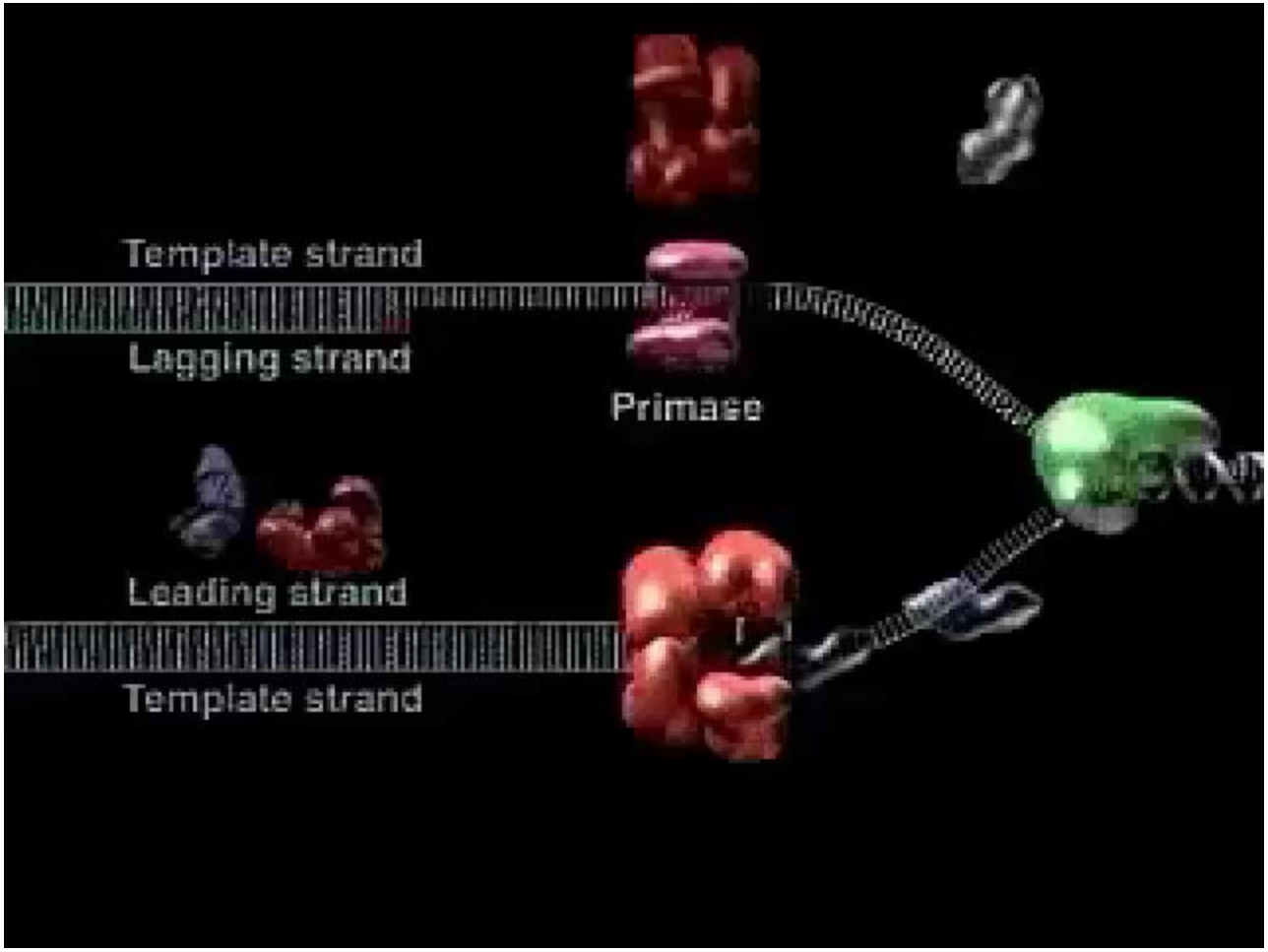


Figure 16.17

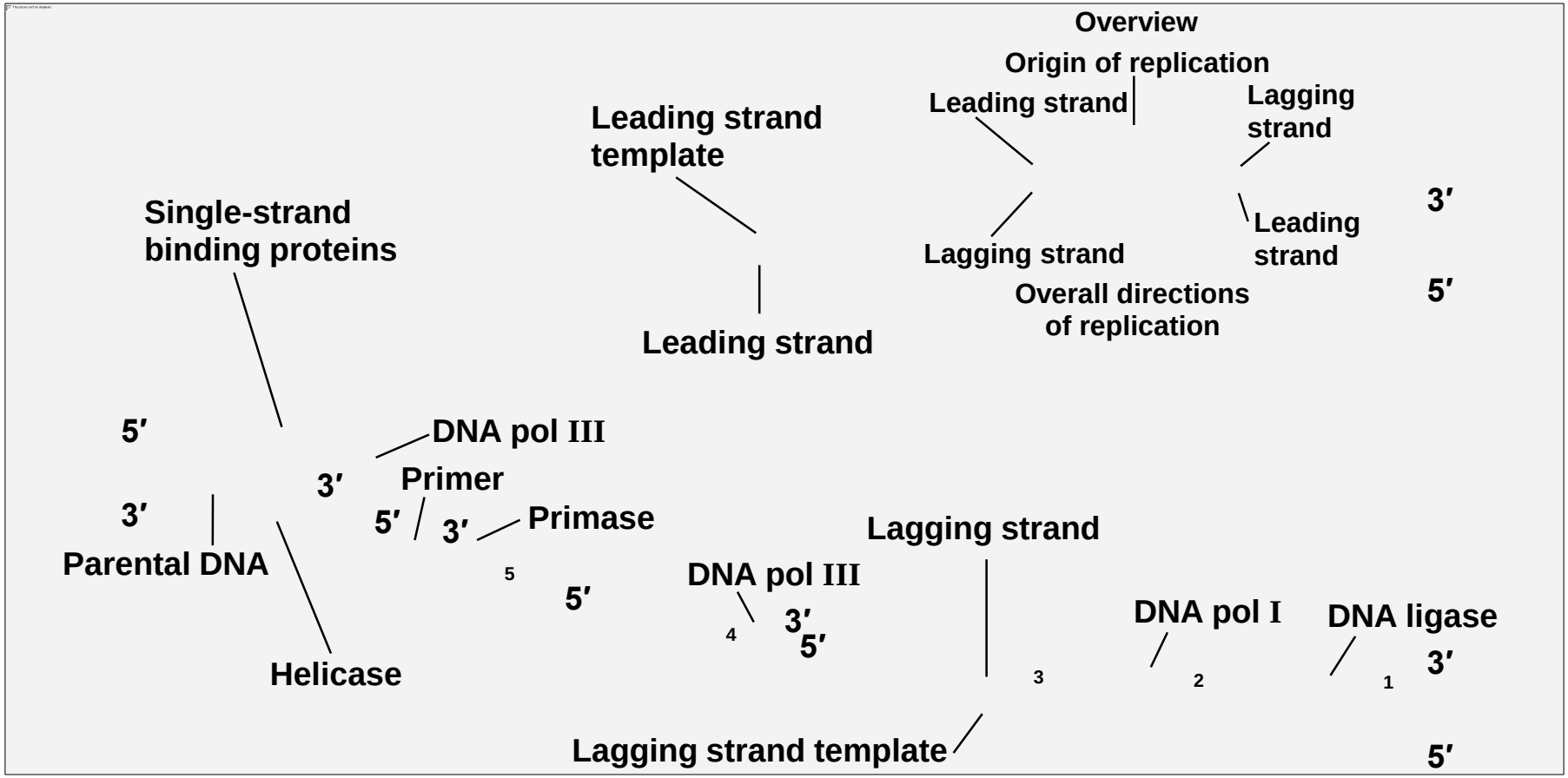


Figure 16.17a

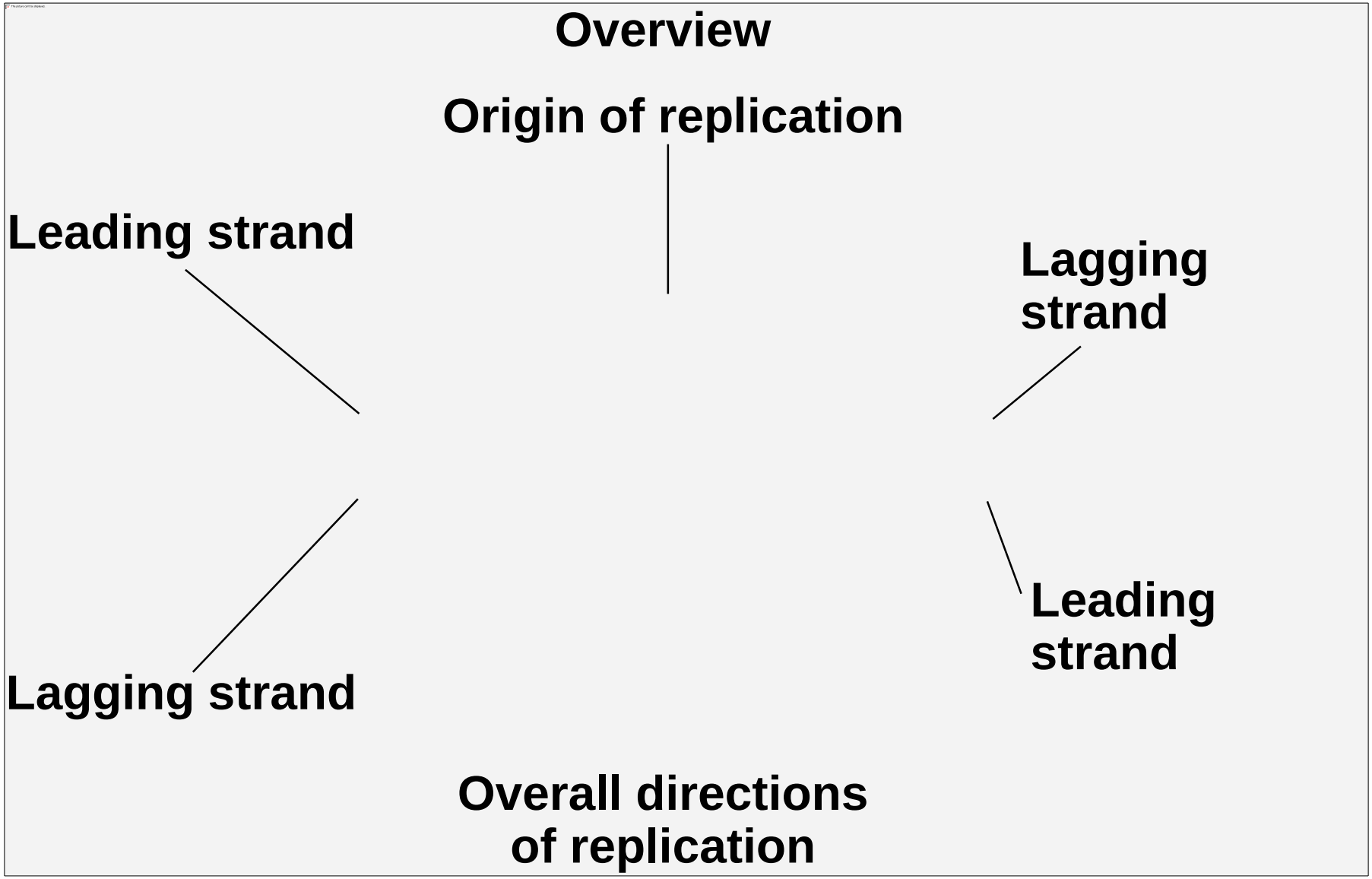


Figure 16.17b

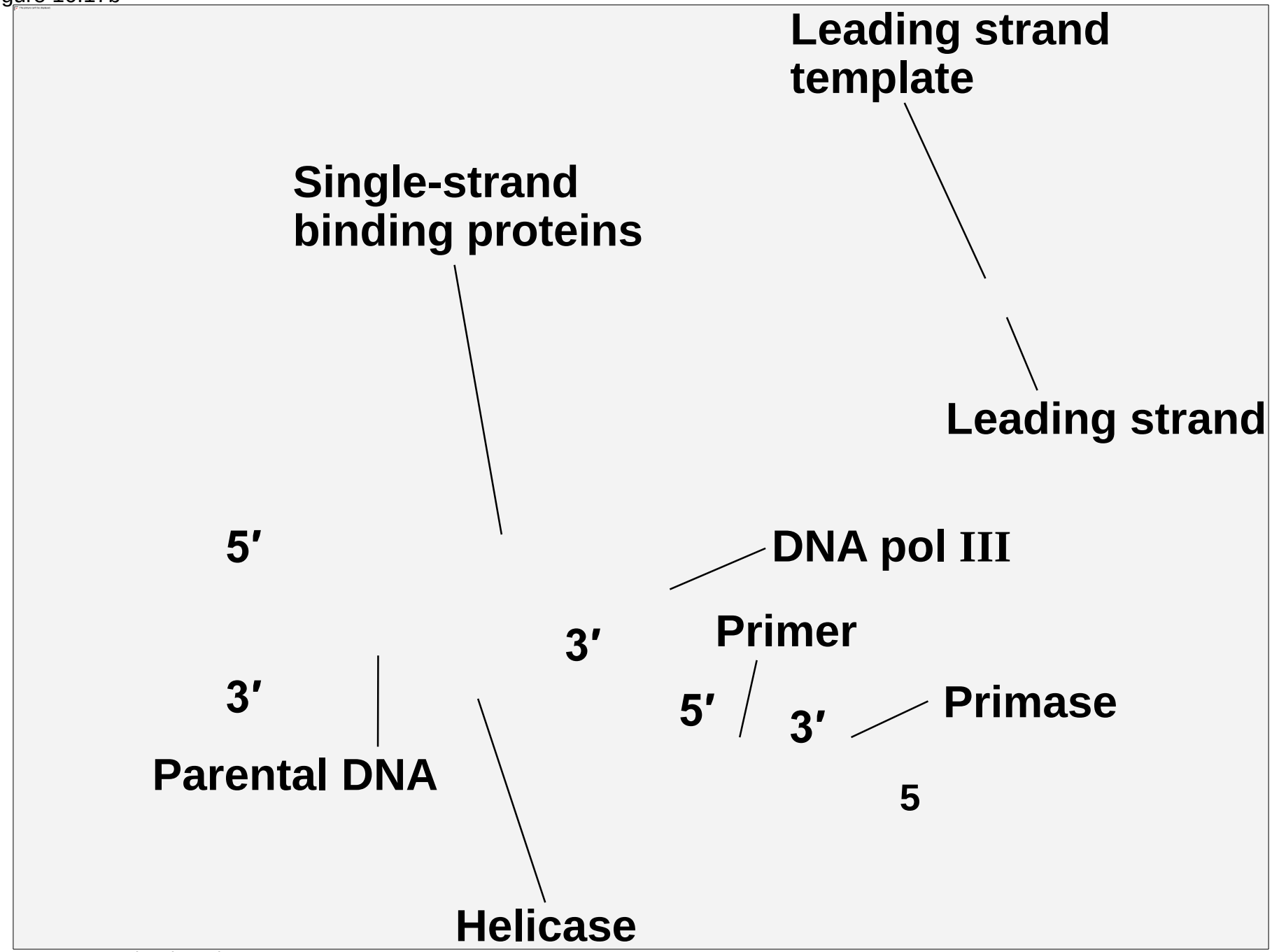
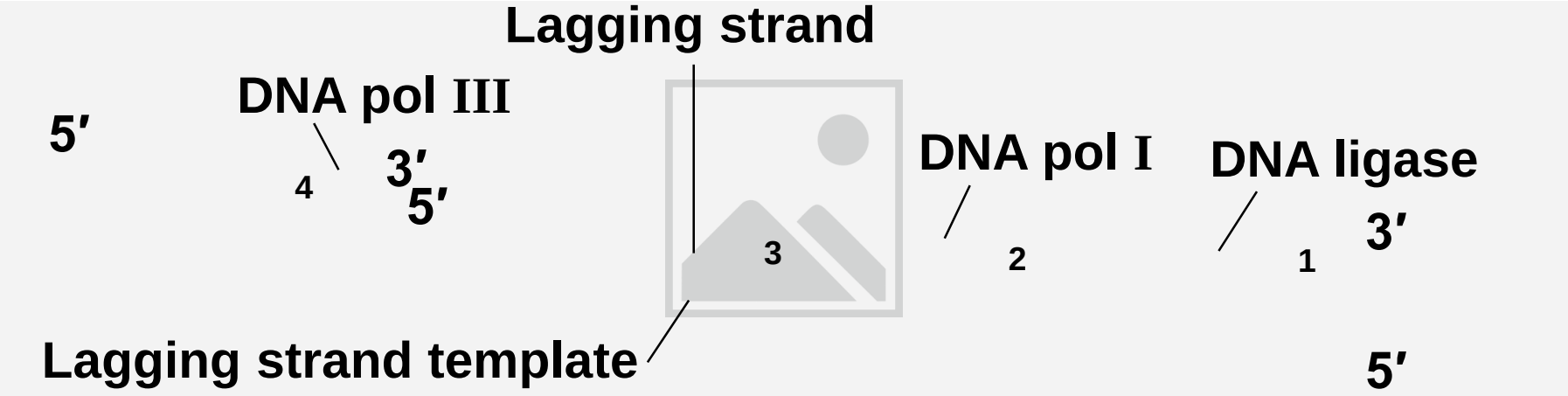


Figure 16.17c



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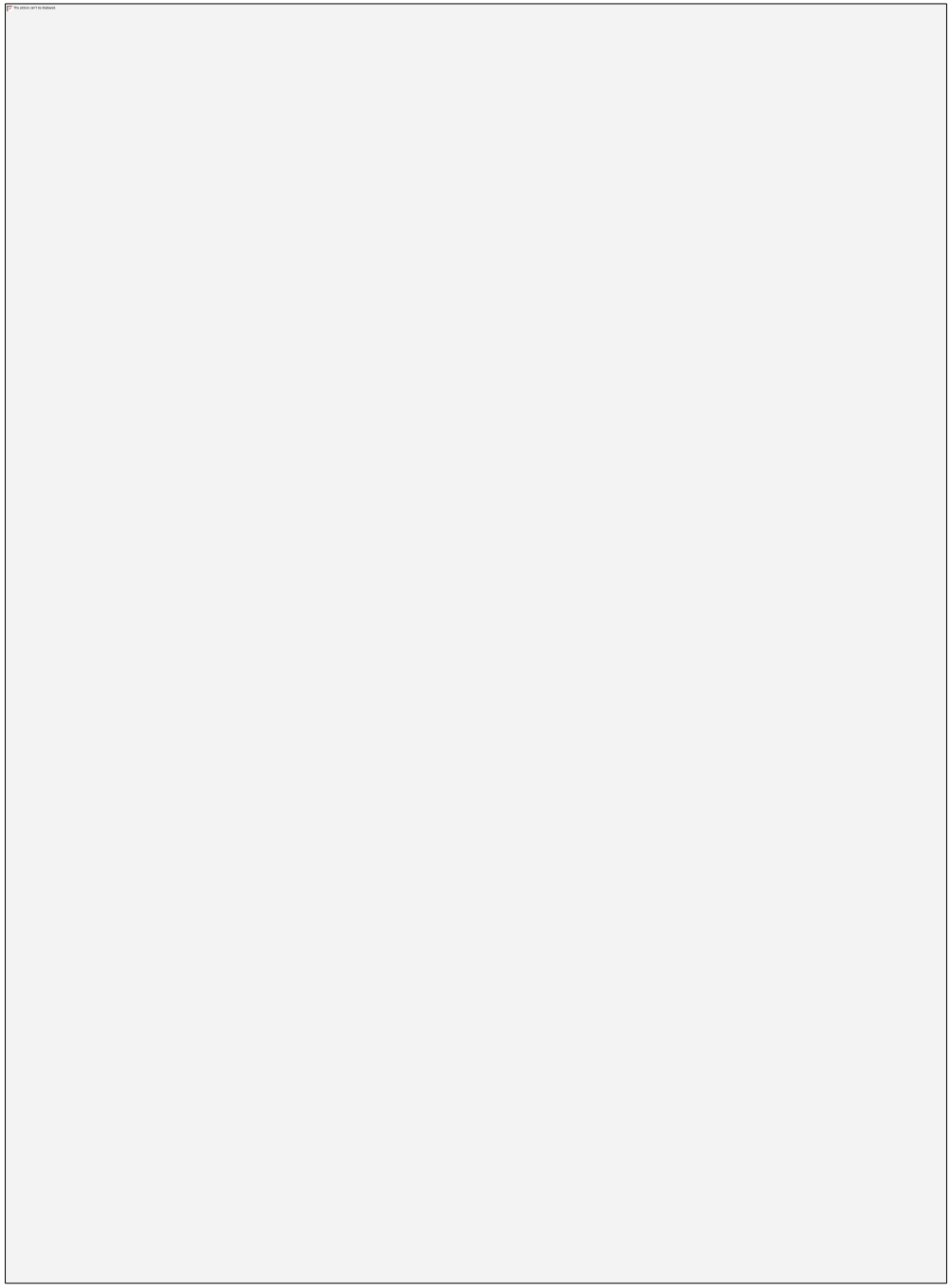
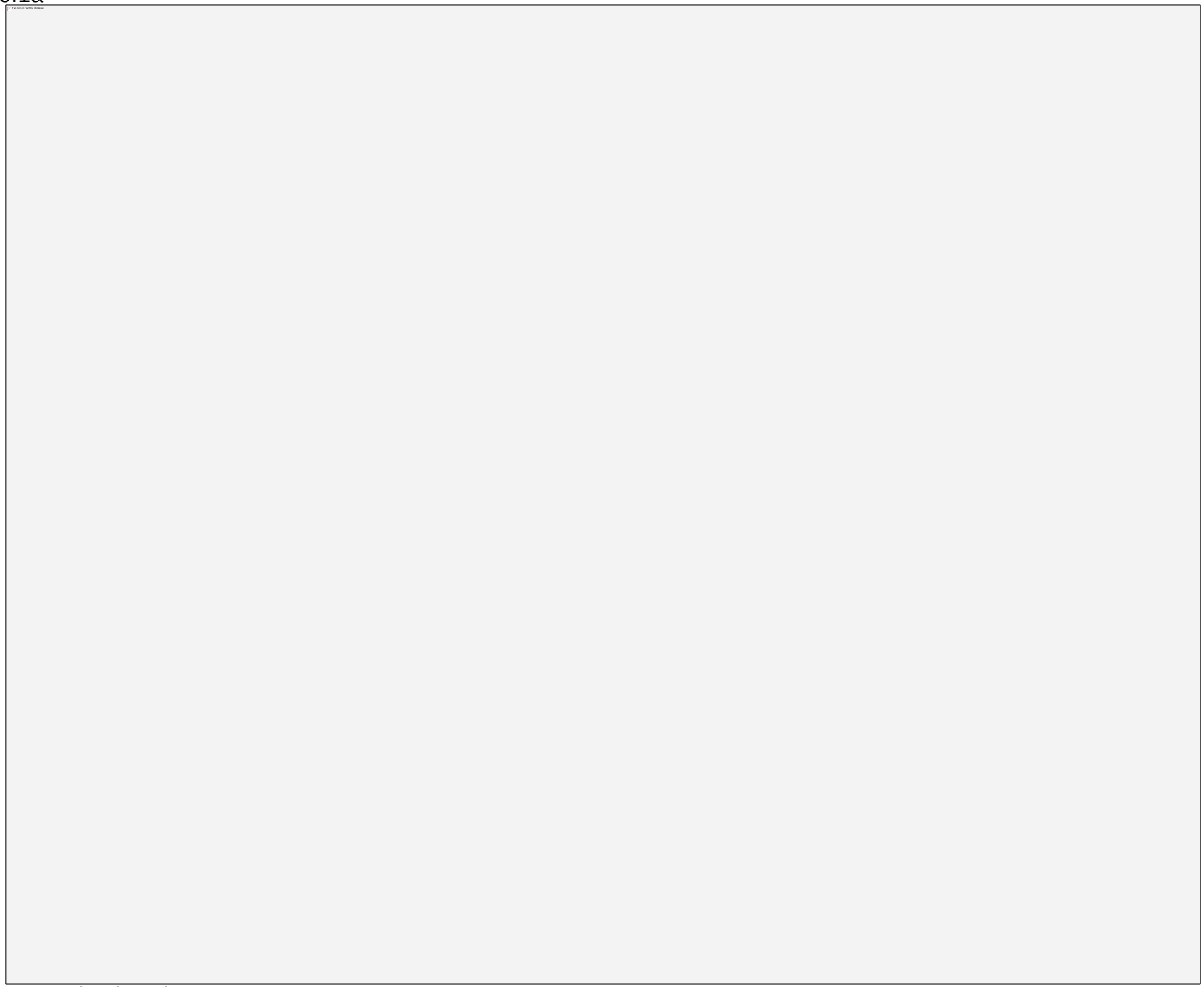


Table 16.1a



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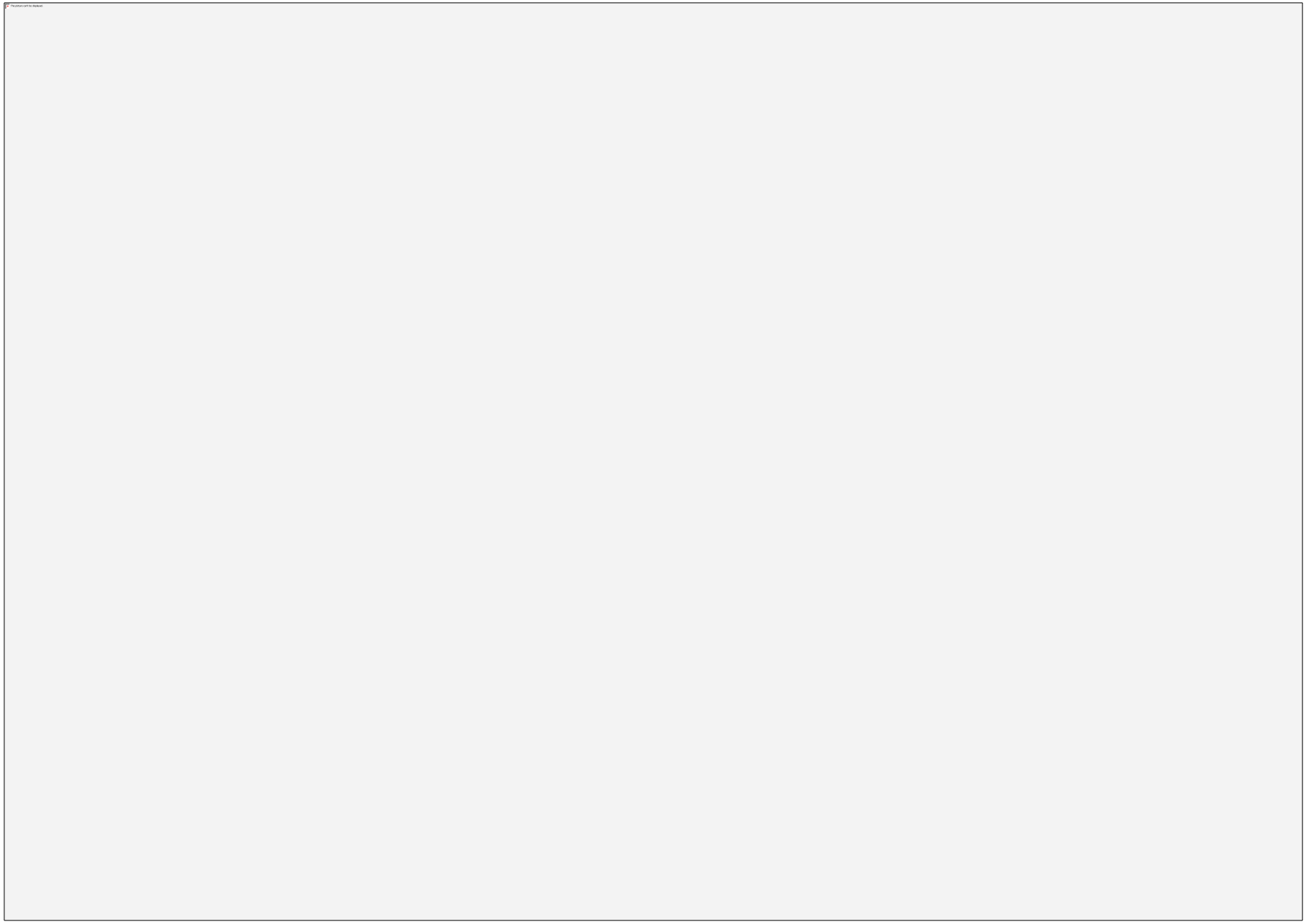
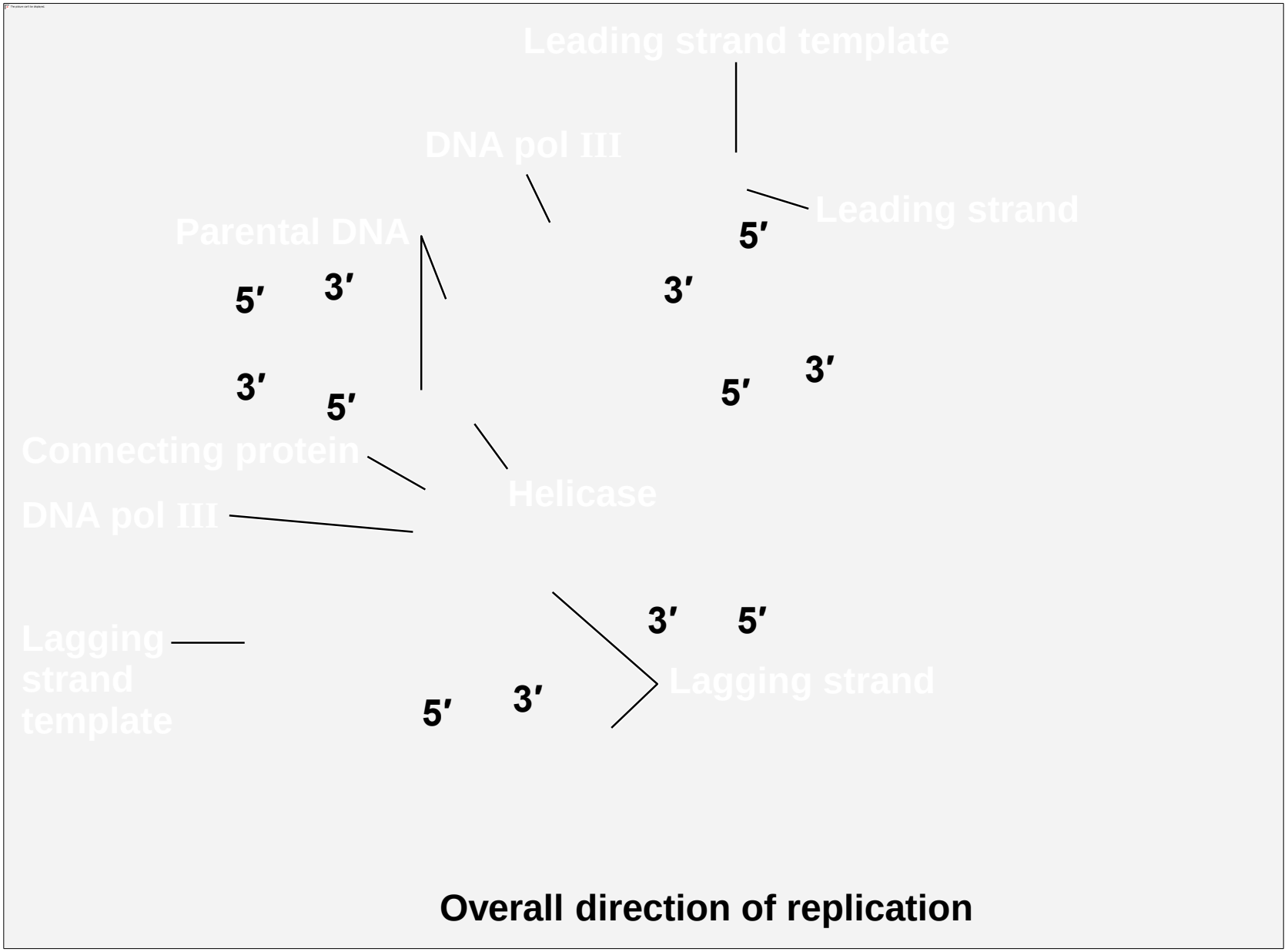


# *The DNA Replication Complex*

- The proteins that participate in DNA replication form a large complex, a “DNA replication machine”
- The DNA replication machine may be stationary during the replication process
- Recent studies support a model in which DNA polymerase molecules “reel in” parental DNA and extrude newly made daughter DNA molecules
- The exact mechanism is not yet resolved

Figure 16.18



# 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
- DNA can be damaged by exposure to harmful chemical or physical agents such as cigarette smoke and X-rays; it can also undergo spontaneous changes
- In **nucleotide excision repair**, a **nuclease** cuts out and replaces damaged stretches of DNA

Figure 16.19_1

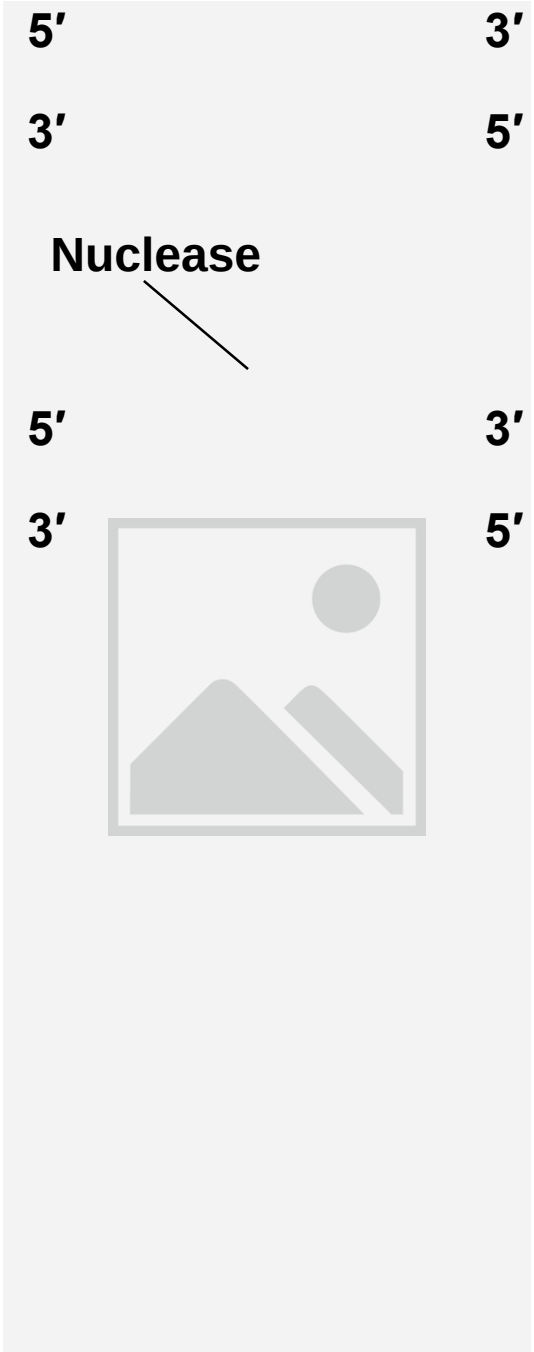


Figure 16.19_2

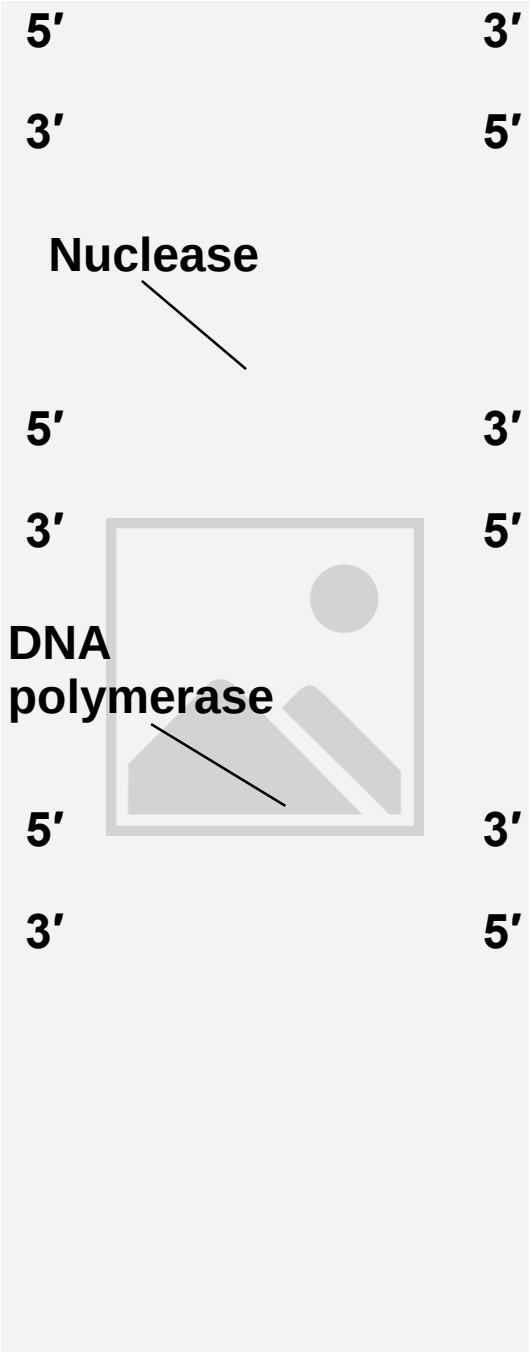
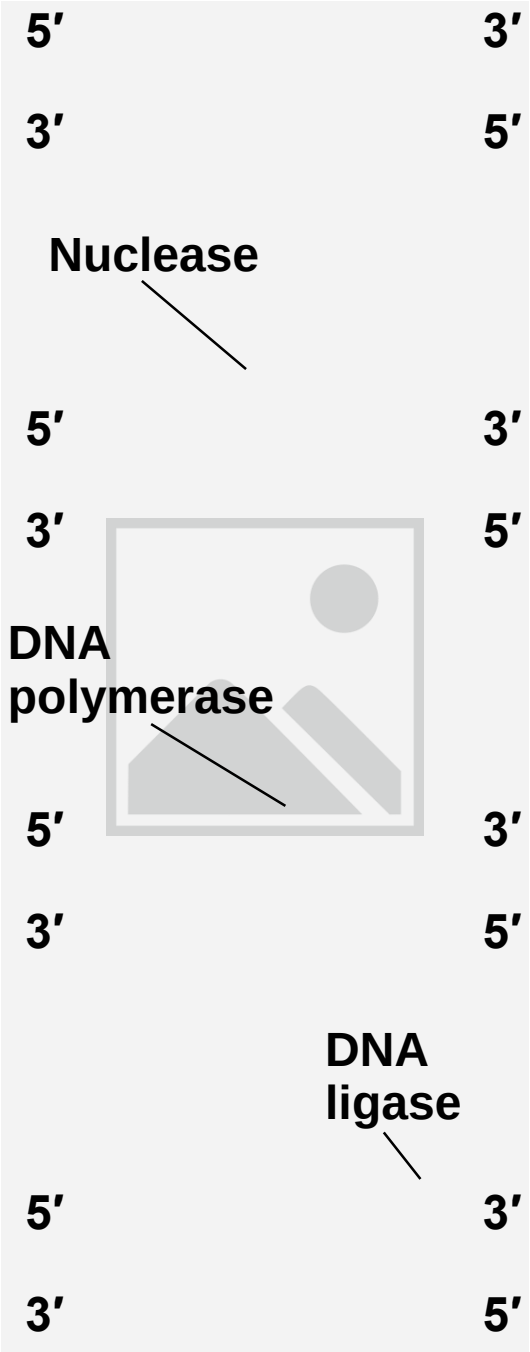


Figure 16.19_3



# Evolutionary Significance of Altered DNA Nucleotides

- The error rate after proofreading and repair is low but not zero
- Sequence changes may become permanent and can be passed on to the next generation
- These changes (mutations) are the source of the genetic variation upon which natural selection operates and are ultimately responsible for the appearance of new species

# Replicating the Ends of DNA Molecules

- Limitations of DNA polymerase create problems for the linear DNA of eukaryotic chromosomes
- The usual replication machinery provides no way to complete the 5′ ends, so repeated rounds of replication produce shorter DNA molecules with uneven ends
- This is not a problem for prokaryotes, most of which have circular chromosomes

Figure 16.20

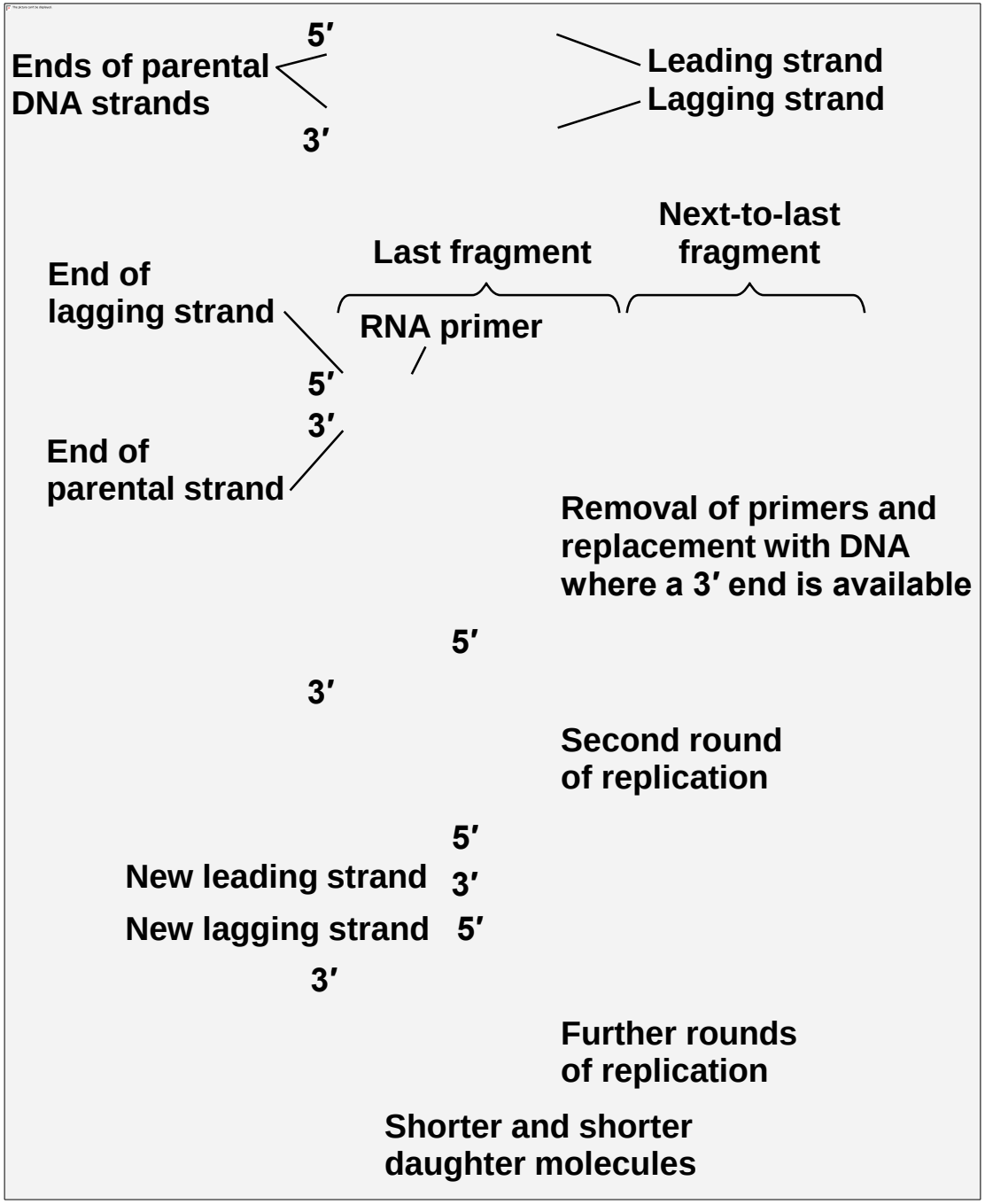


Figure 16.20a

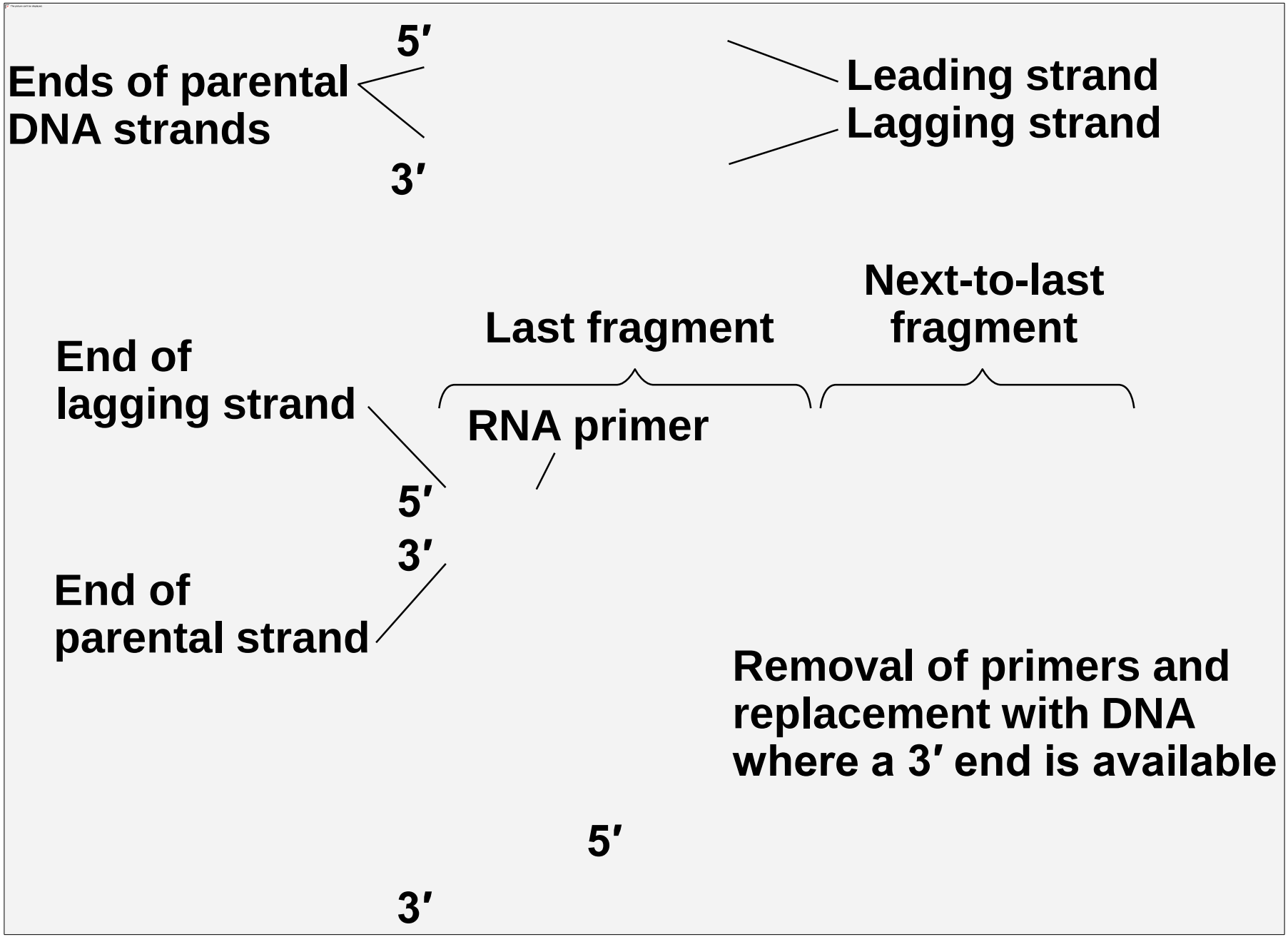
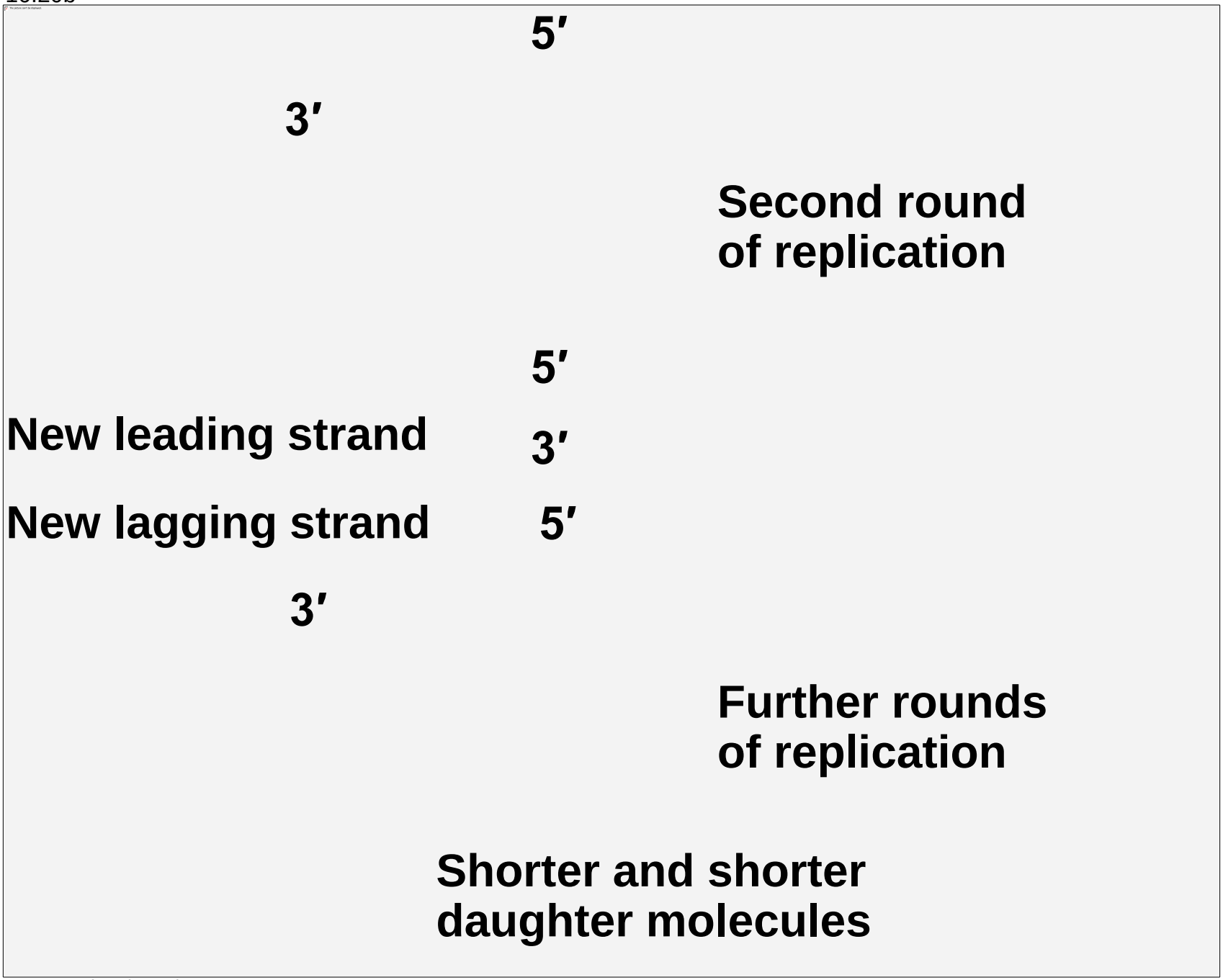
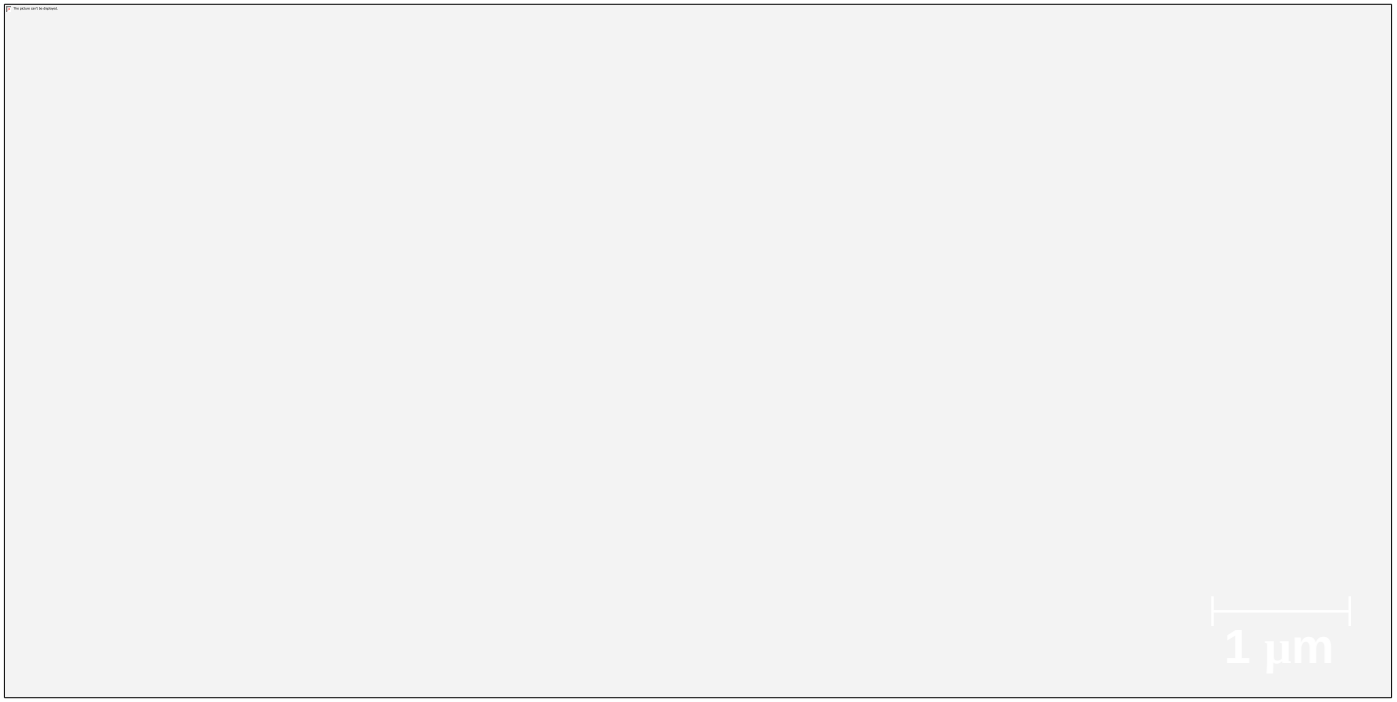


Figure 16.20b



- Eukaryotic chromosomal DNA molecules have special nucleotide sequences at their ends called **telomeres**
- Telomeres do not prevent the shortening of DNA molecules, but they do postpone the erosion of genes near the ends of DNA molecules
- It has been proposed that the shortening of telomeres is connected to aging

Figure 16.21



- If 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

- The shortening of telomeres might protect cells from cancerous growth by limiting the number of cell divisions
- There is evidence of telomerase activity in cancer cells, which may allow cancer cells to persist

# Concept 16.3: A chromosome consists of a DNA molecule packed together with proteins

- The bacterial chromosome is a double-stranded, circular DNA molecule associated with a small amount of protein
- Eukaryotic chromosomes have linear DNA molecules associated with a large amount of protein
- In a bacterium, the DNA is “supercoiled” and found in a region of the cell called the nucleoid

- In the eukaryotic cell, DNA is precisely combined with proteins in a complex called **chromatin**
- Chromosomes fit into the nucleus through an elaborate, multilevel system of packing
- Proteins called **histones** are responsible for the first level of packing in chromatin

- Unfolded chromatin resembles beads on a string, with each “bead” being a **nucleosome**, the basic unit of DNA packaging
- They are composed of two each of the four basic histone types, with DNA wrapped twice around the core of the eight histones
- The N-termini (“tails”) of the histones protrude from the nucleosome
- Nucleosomes, and especially their histone tails, are involved in the regulation of gene expression

Figure 16.22

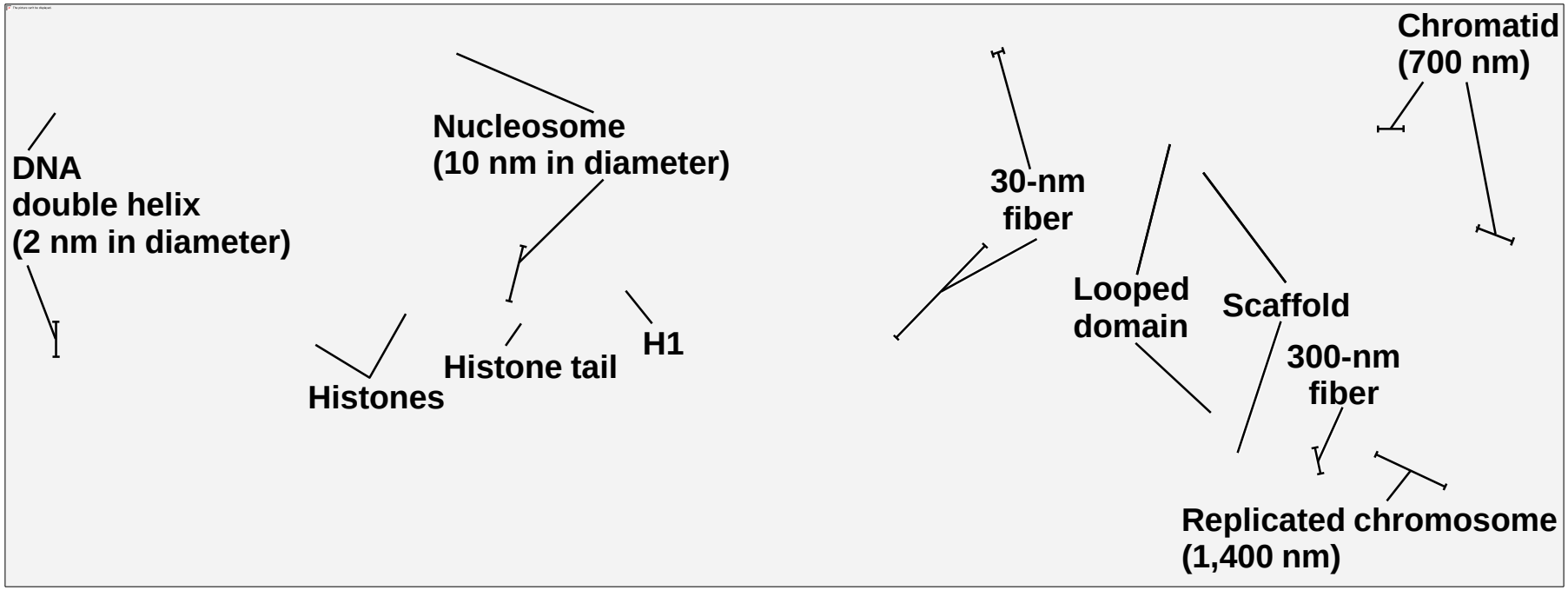


Figure 16.22a

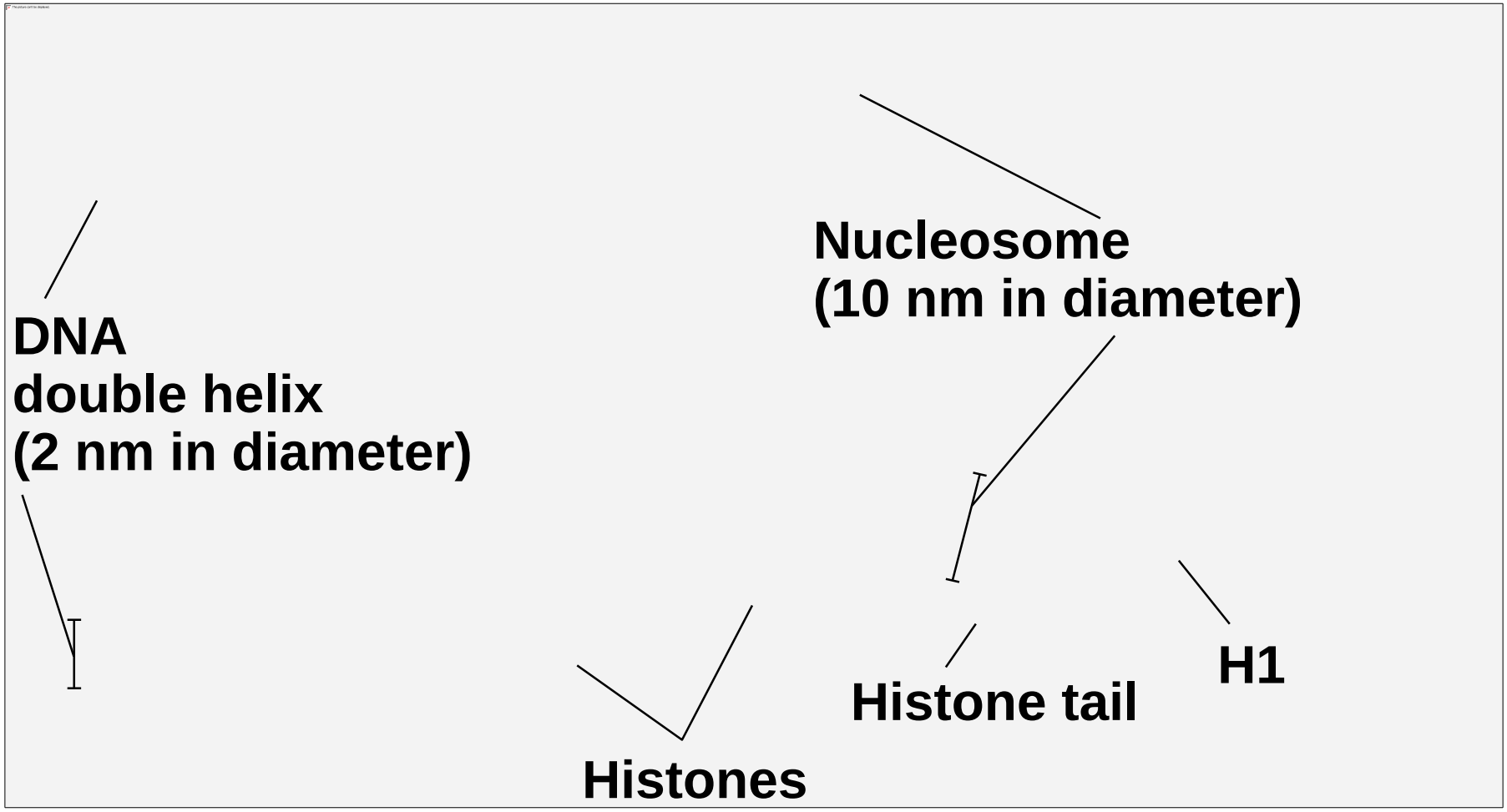


Figure 16.22aa

Figure 16.22ab

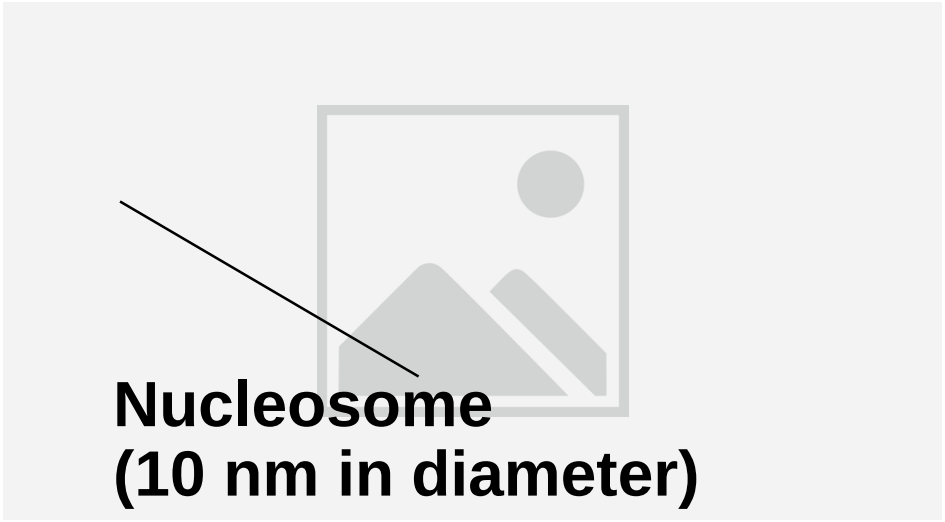


Figure 16.22b

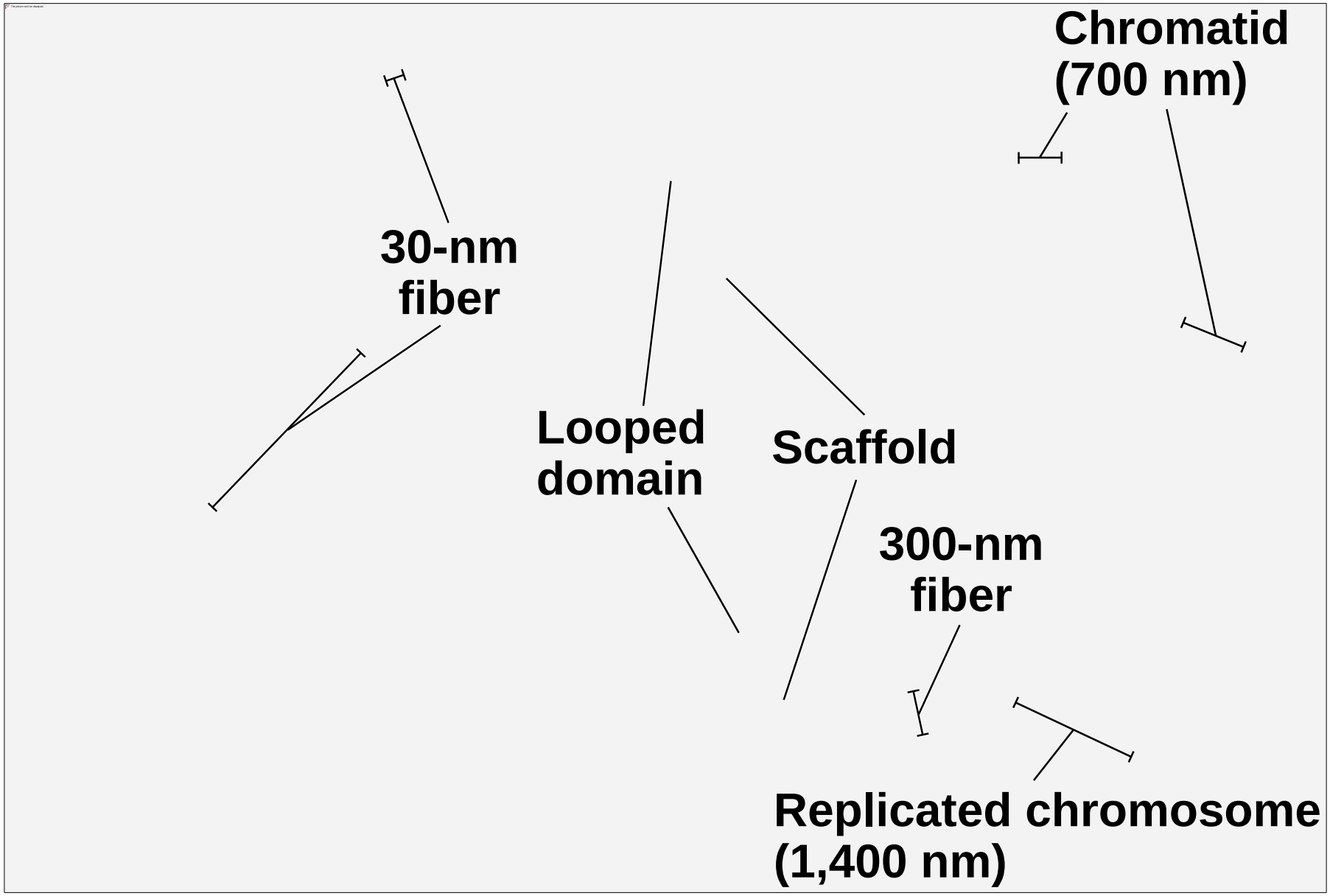
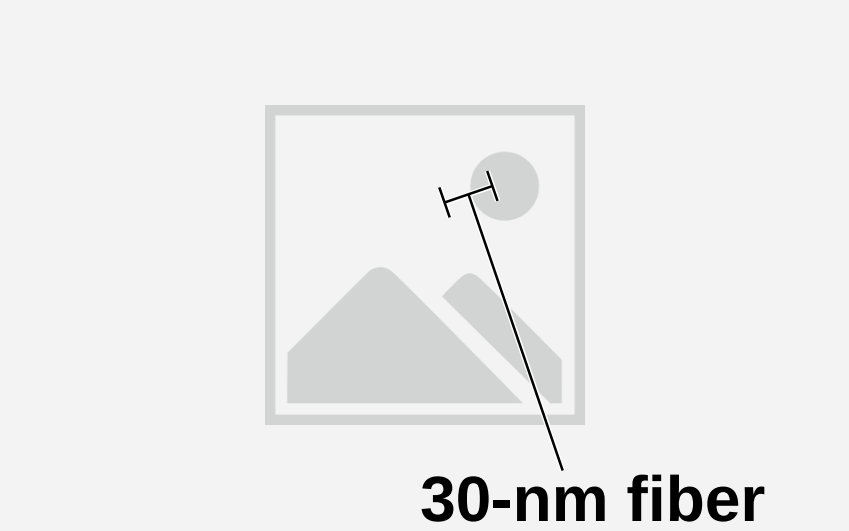


Figure 16.22ba



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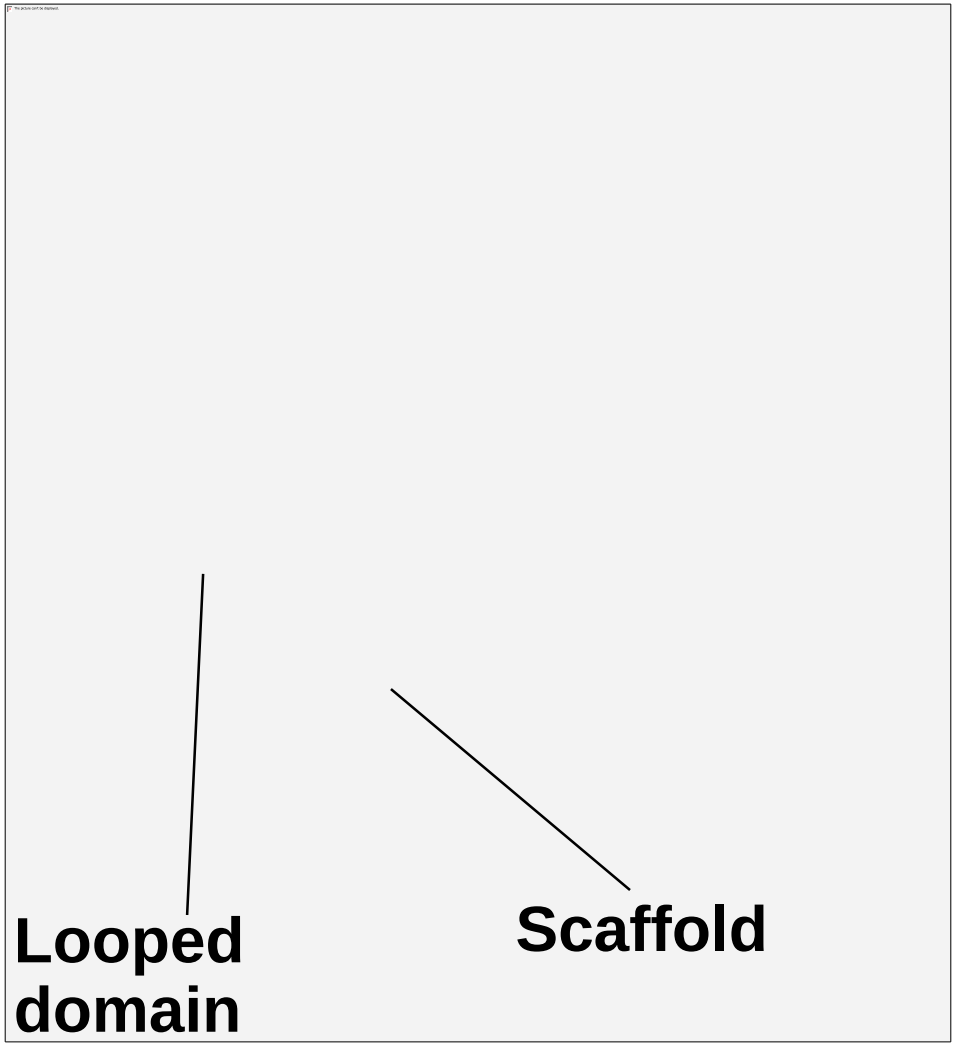
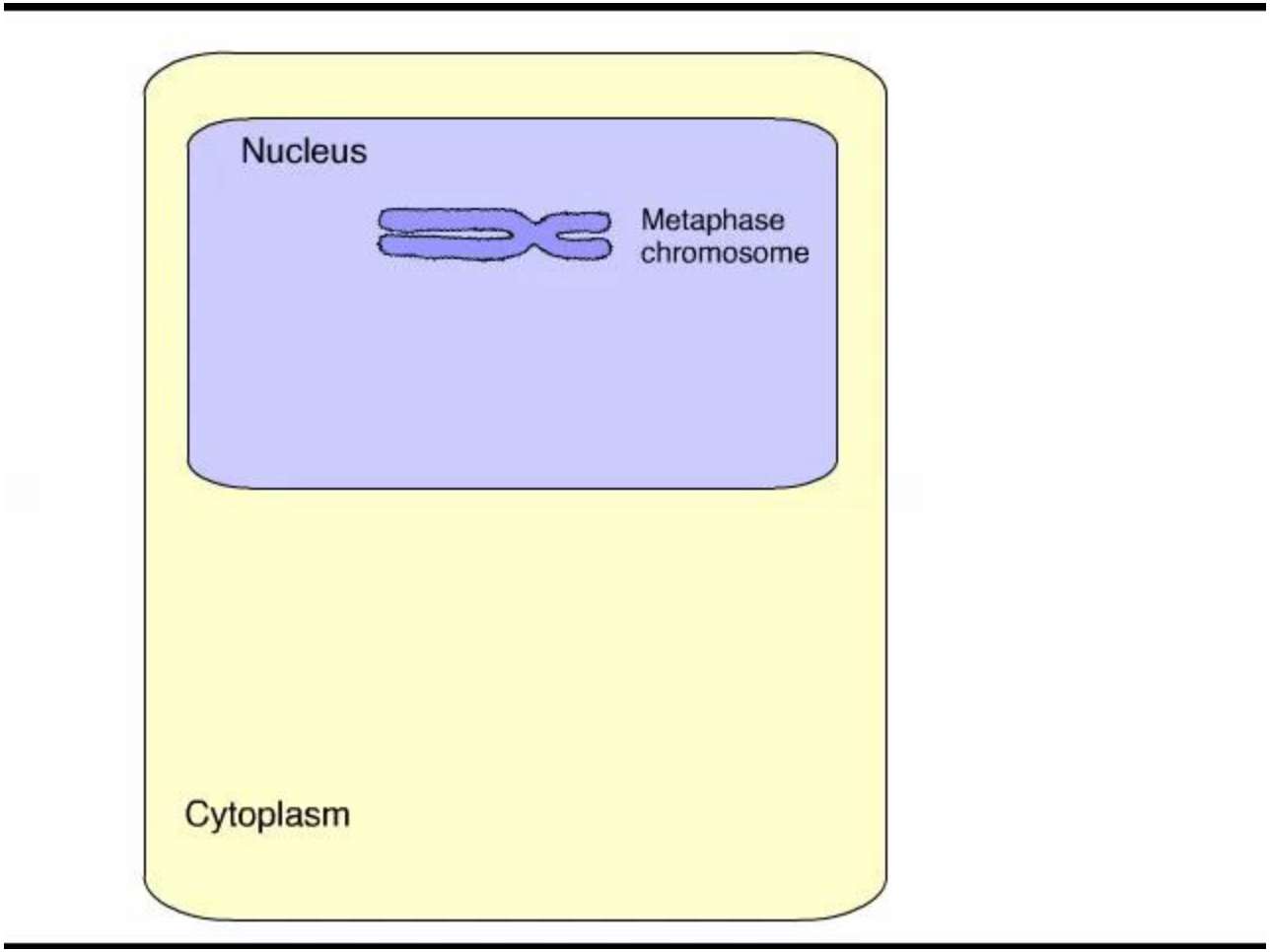
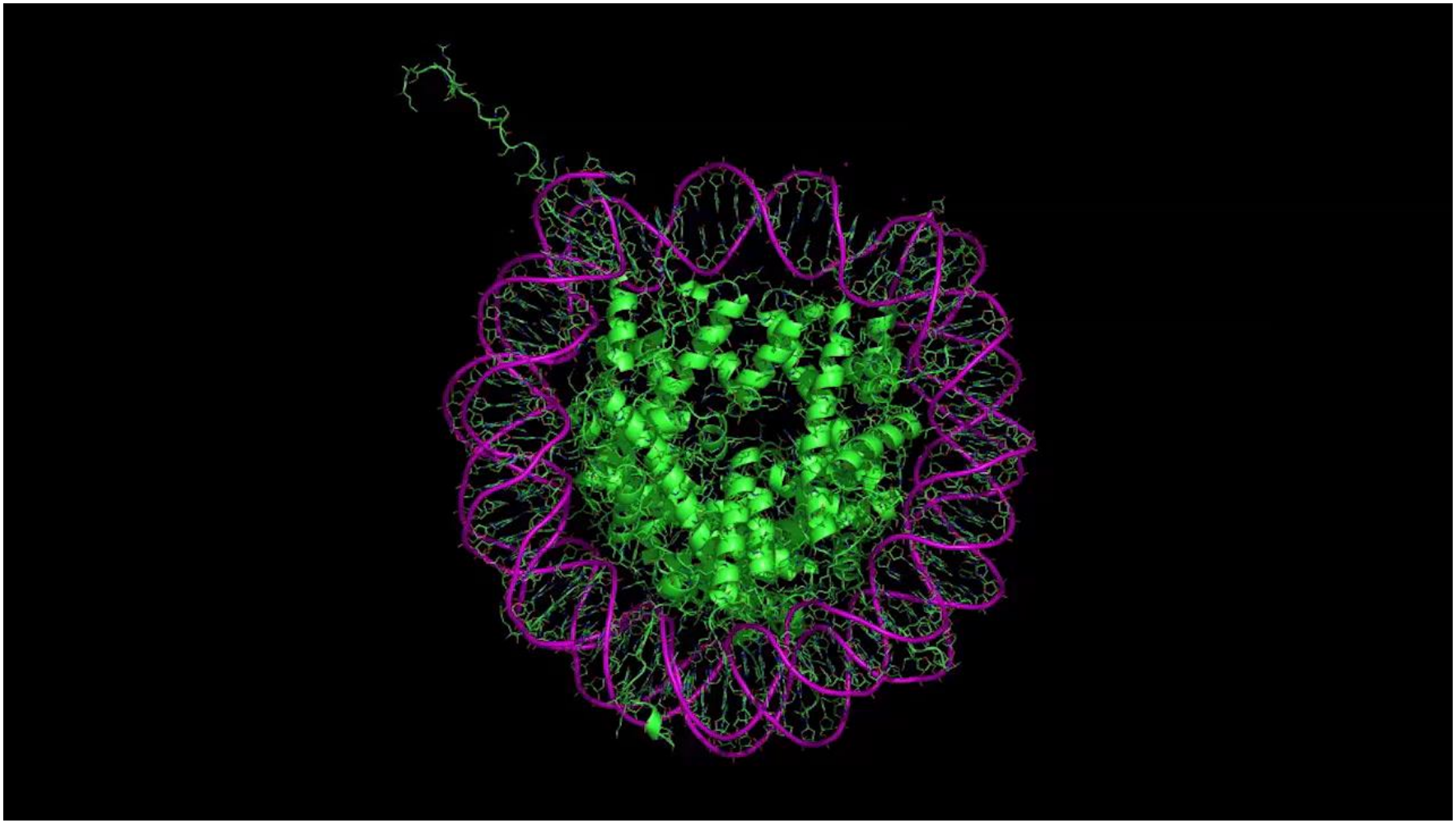


Figure 16.22bc

# Animation: DNA Packing



# Video: Cartoon and Stick Model of a Nucleosomal Particle



- Chromatin undergoes changes in packing during the cell cycle
- At interphase, some chromatin seems to be organized into a 10-nm fiber, but much is compacted into a 30-nm fiber, through folding and looping
- Interphase chromosomes occupy specific restricted regions in the nucleus, and the fibers of different chromosomes do not become entangled

Figure 16.23

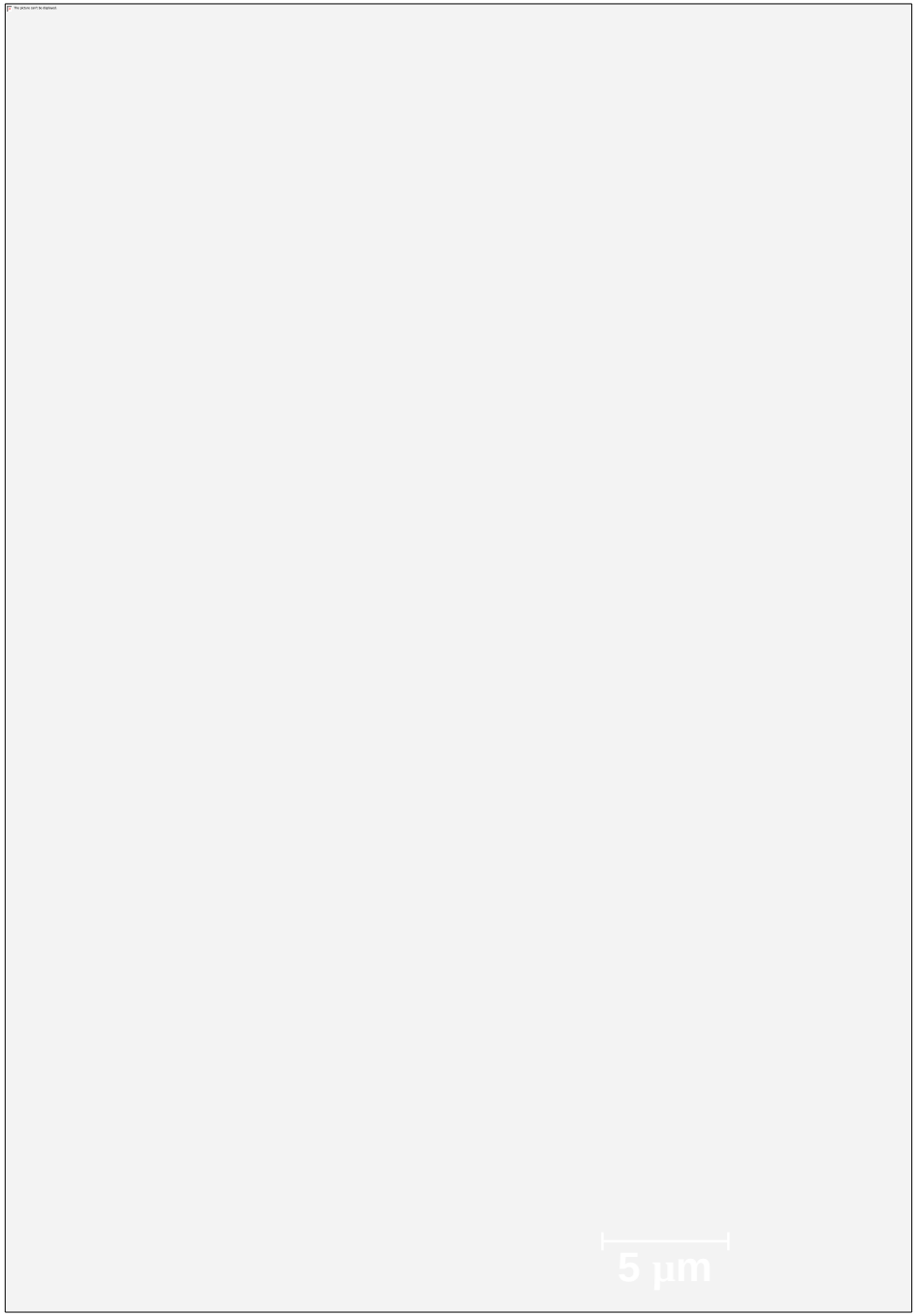


Figure 16.23a

Figure 16.23b

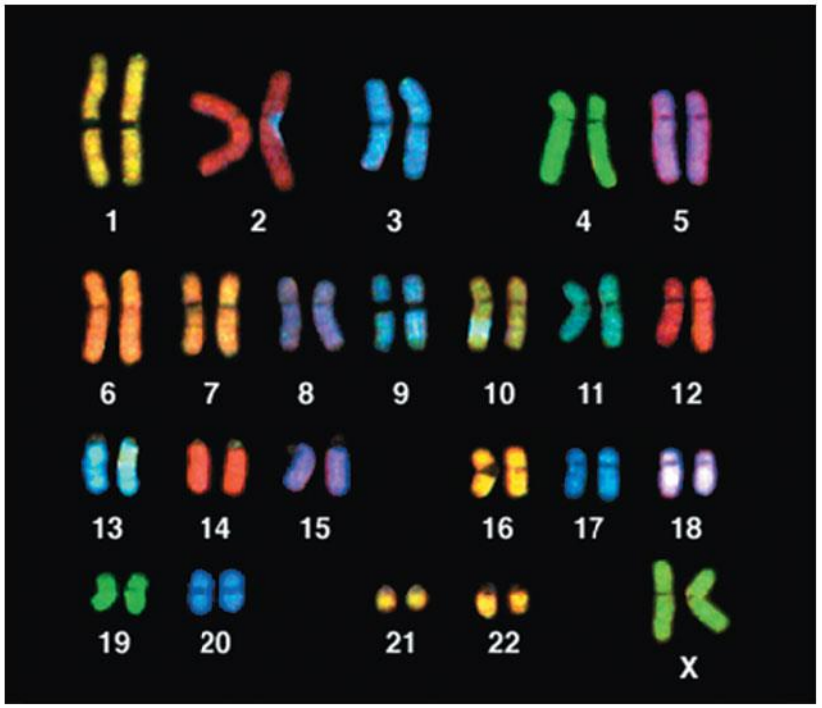
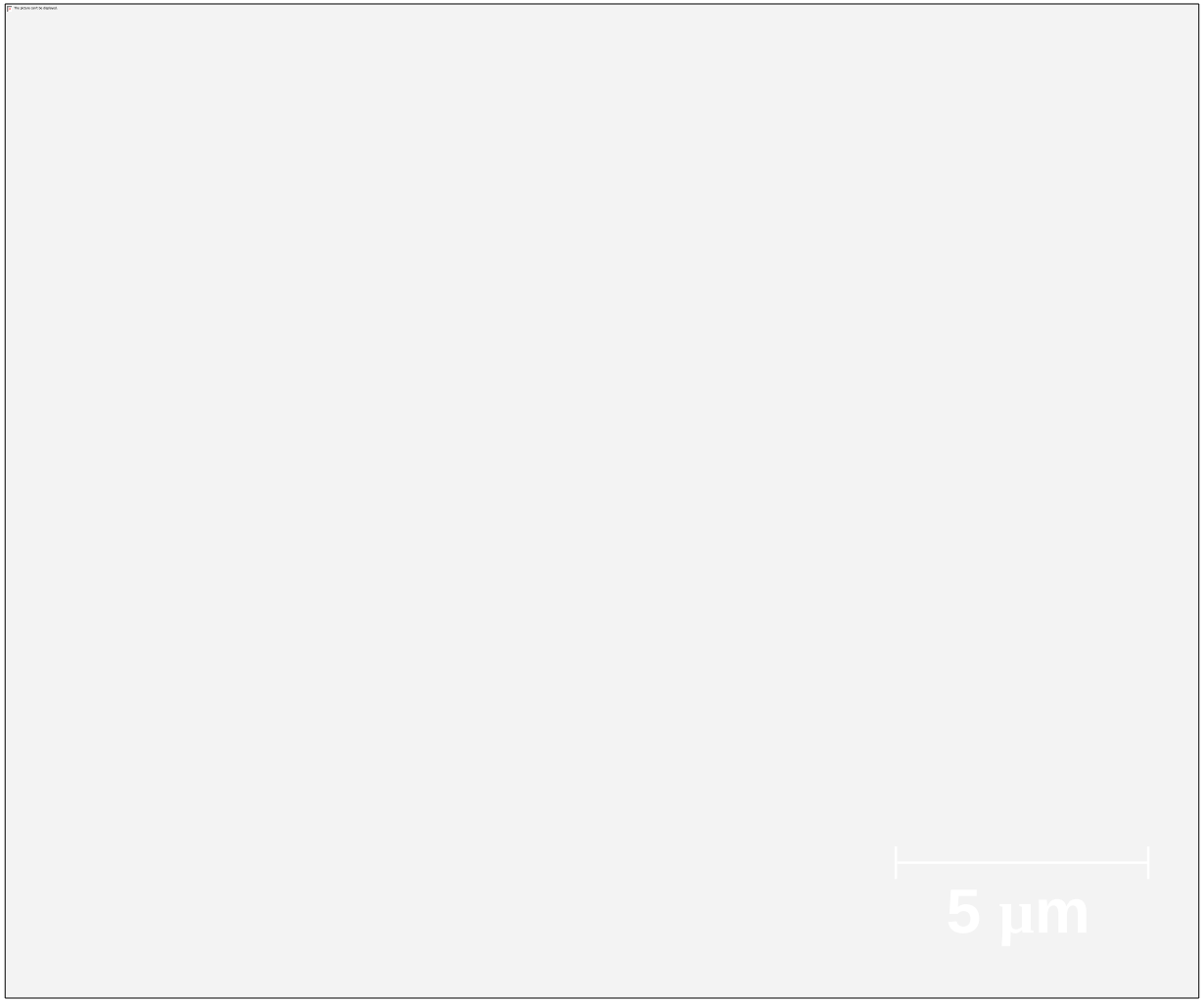


Figure 16.23c



- Most chromatin is loosely packed in the nucleus during interphase and condenses prior to mitosis
- Loosely packed chromatin is called **euchromatin**
- During interphase a few regions of chromatin (centromeres and telomeres) are highly condensed into **heterochromatin**
- Dense packing of the heterochromatin makes it difficult for the cell to express genetic information coded in these regions

- Histones can undergo chemical modifications that result in changes in chromatin condensation
- These changes can also have multiple effects on gene expression

Figure 16.UN01a

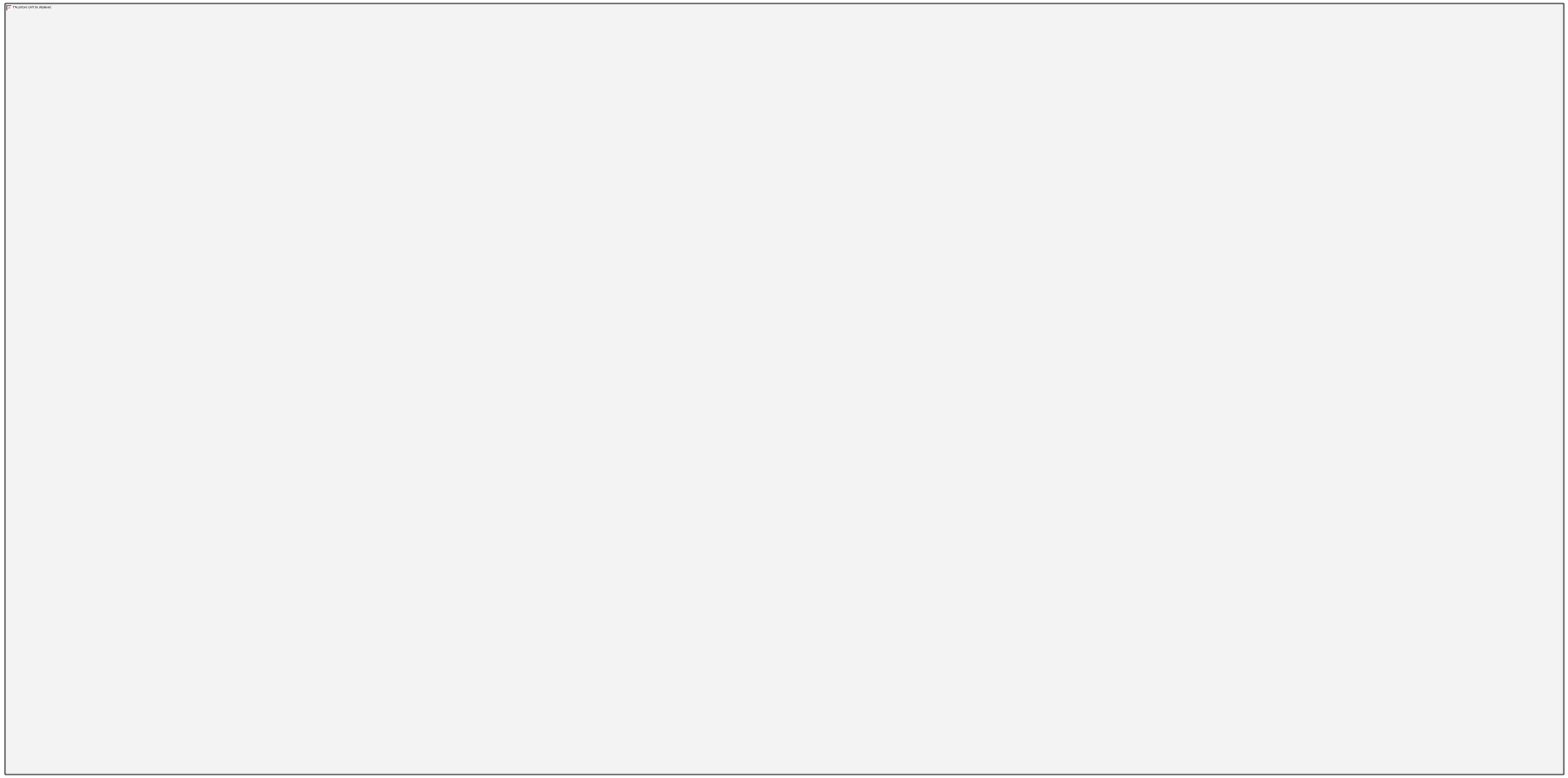


Figure 16.UN01b

Figure 16.UN03

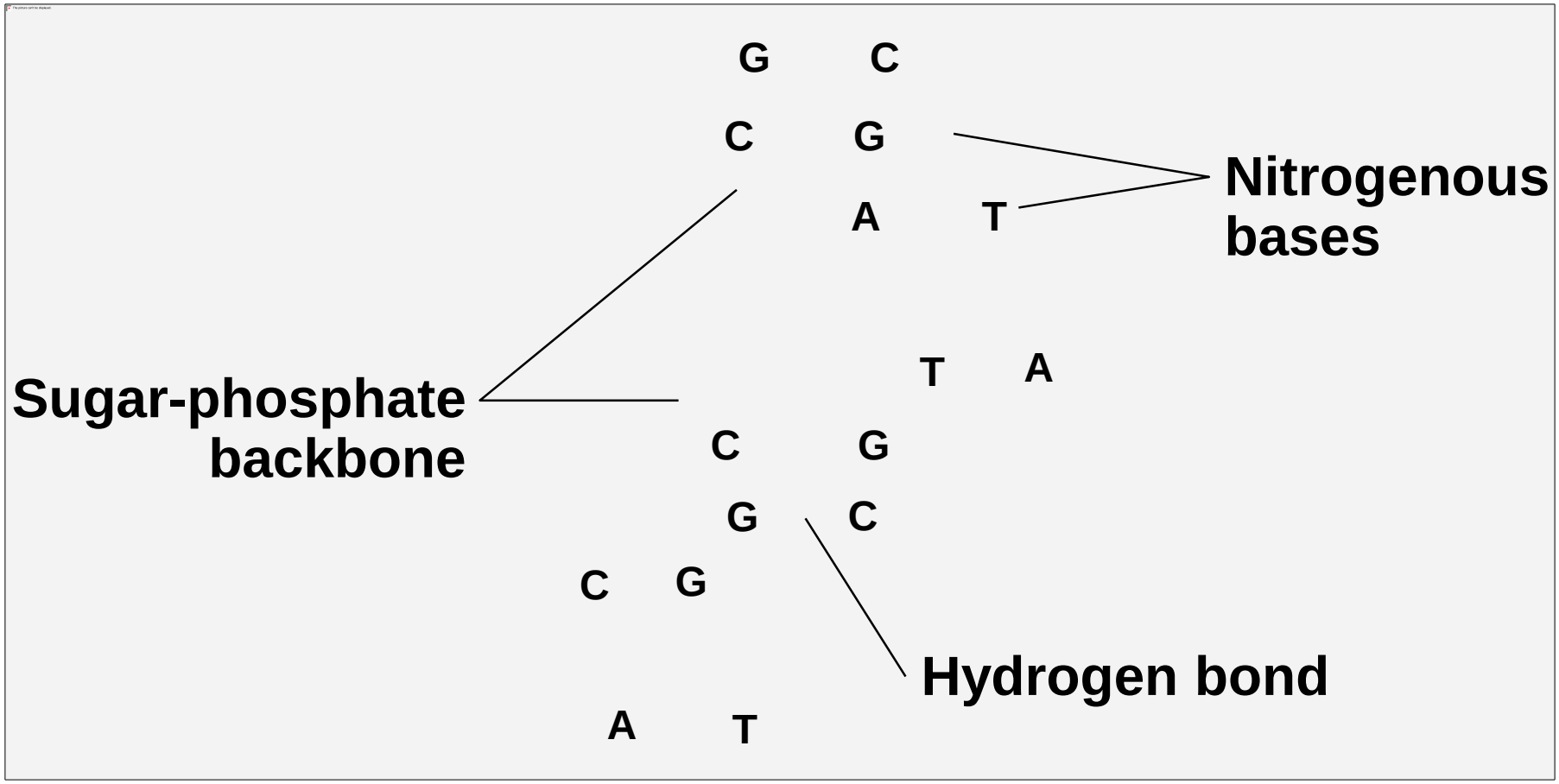


Figure 16.UN04

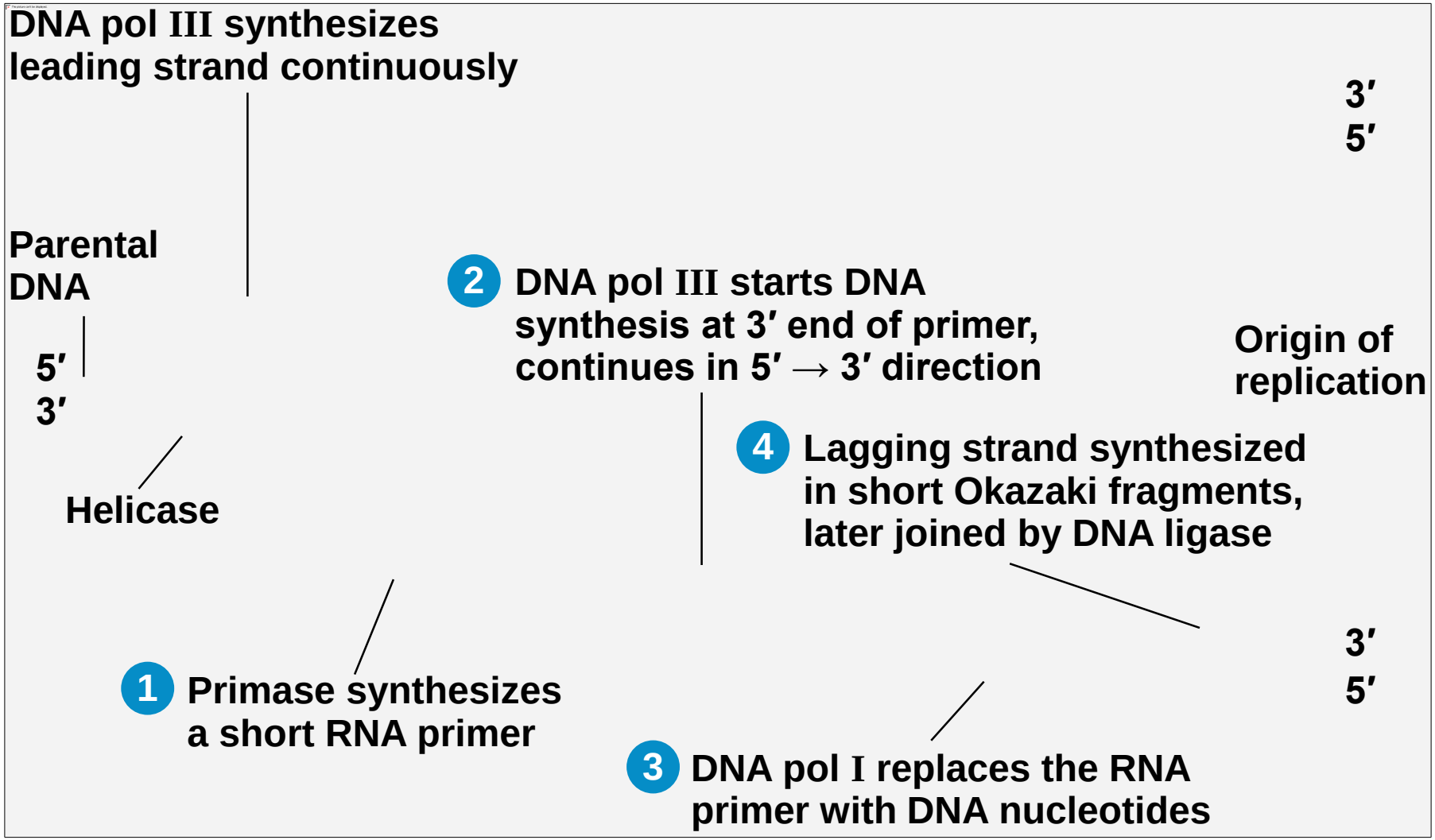


Figure 16.UN05

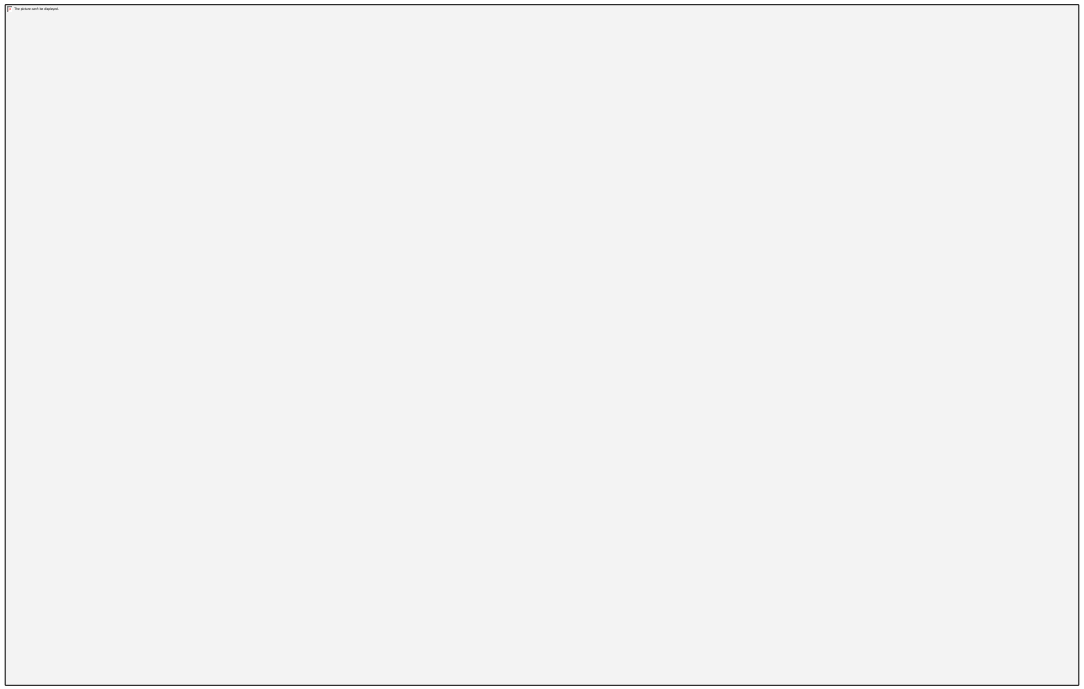


Figure 16.UN06