Ch. 13 Warm-Up

1. Draw and label a nucleotide.

2. Why is DNA a double helix?

3. What is the complementary DNA strand to:

   DNA strand: A T C C G T A T G A A C

Ch. 13 Warm-Up

1. What was the contribution made to science by these people:

a. Hershey and Chase

b. Avery et. al.

c. Franklin & Wilkins

d. Watson and Crick

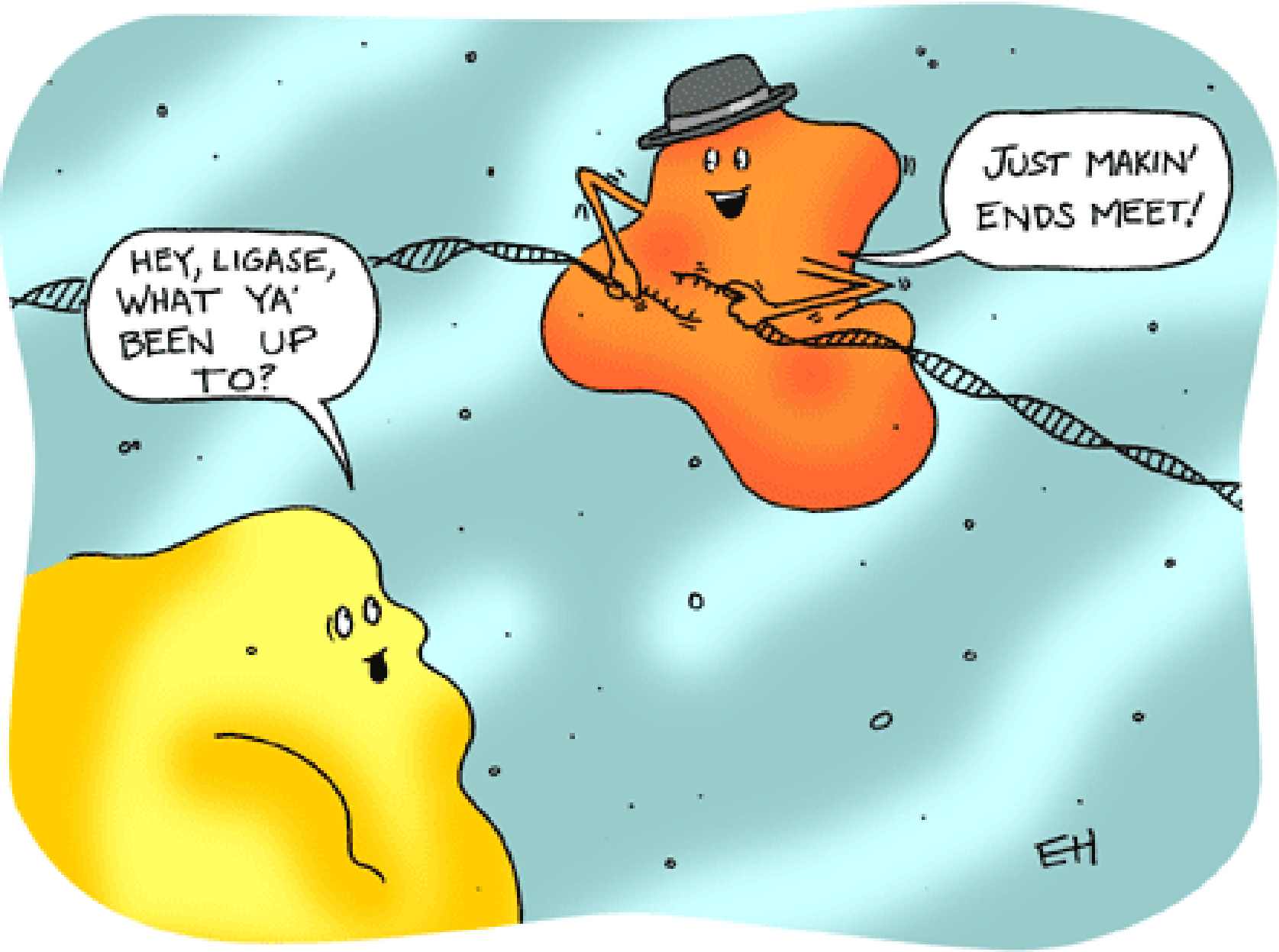
2. Chargaff's Rules: If cytosine makes up 22% of the nucleotides, then adenine would make up ___ % ?

3. Code the complementary DNA strand:

3' - T A G C T A A G C T A C - 5'

Ch. 13 Warm-Up

1. Explain the semiconservative model of DNA replication.
2. What is the function of the following:
   - ❑ Helicase
   - ❑ DNA Ligase
   - ❑ DNA Polymerase (I and III)
   - ❑ Primase
   - ❑ Nuclease
3. What is the difference between the leading and lagging strand of DNA?
4. What is the function of telomeres?


HEY, LIGASE, WHAT YA' BEEN UP TO?
JUST MAKIN' ENDS MEET!
EH

The Molecular Basis Of Inheritance

Chapter 13

What you must know

The structure of DNA.

The knowledge about DNA gained from the work of Griffith; Avery, MacLeod, and McCarty; Hershey and Chase; Wilkins and Franklin; and Watson and Crick.

That replication is semiconservative and occurs 5’ to 3’.

The roles of DNA polymerase, ligase, helicase, and topoisomerase in replication.

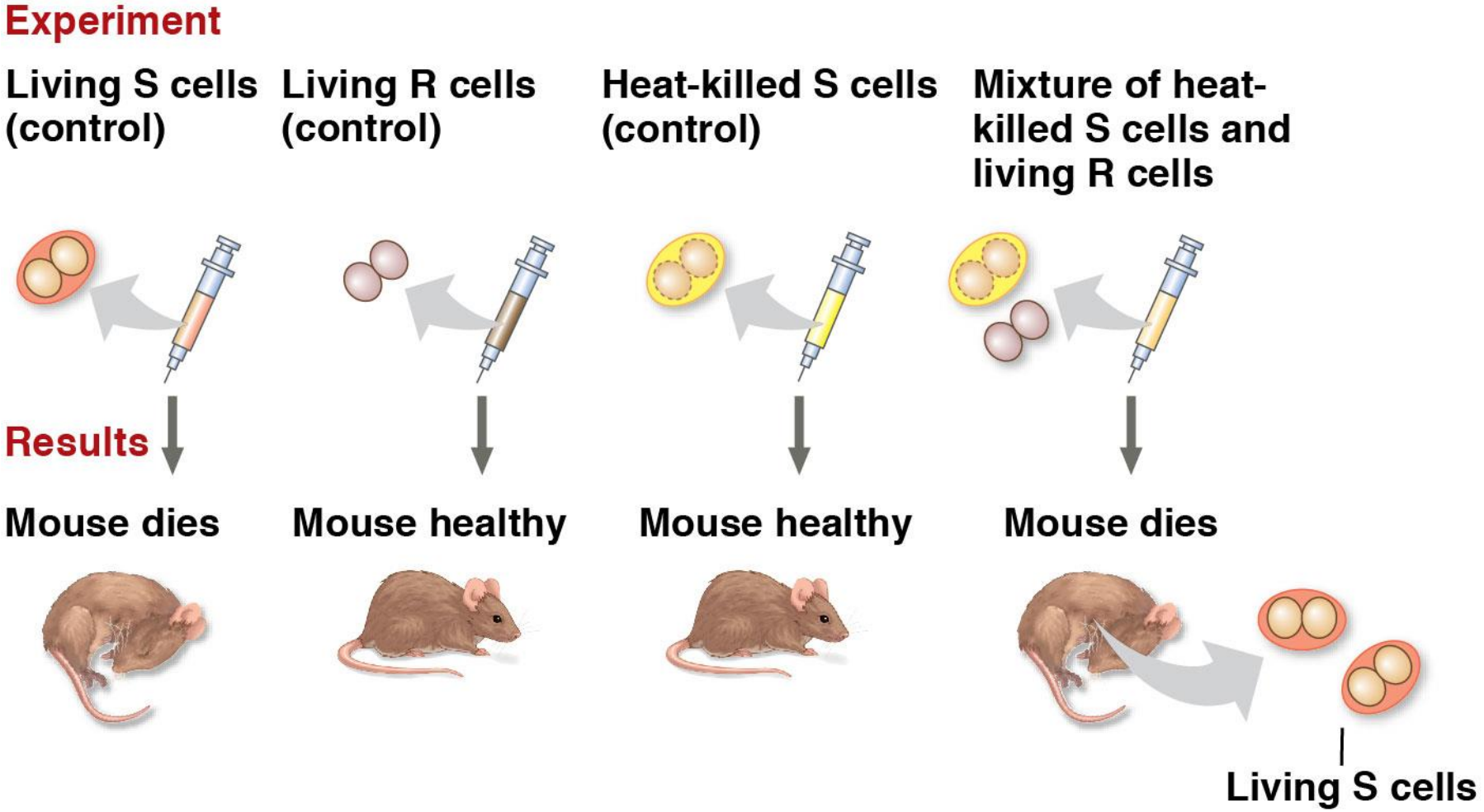
The general differences between bacterial chromosomes and eukaryotic chromosomes.

How DNA is packaged can affect gene expression.

Problem:

Is the genetic material of organisms made of DNA or proteins?

Frederick Griffith (1928)



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Frederick Griffith (1928)

Conclusion:

Living R bacteria transformed into deadly S bacteria by unknown, heritable substance

Avery, McCarty, MacLeod (1944)

Tested DNA, RNA, & proteins in heat-killed pathogenic bacteria

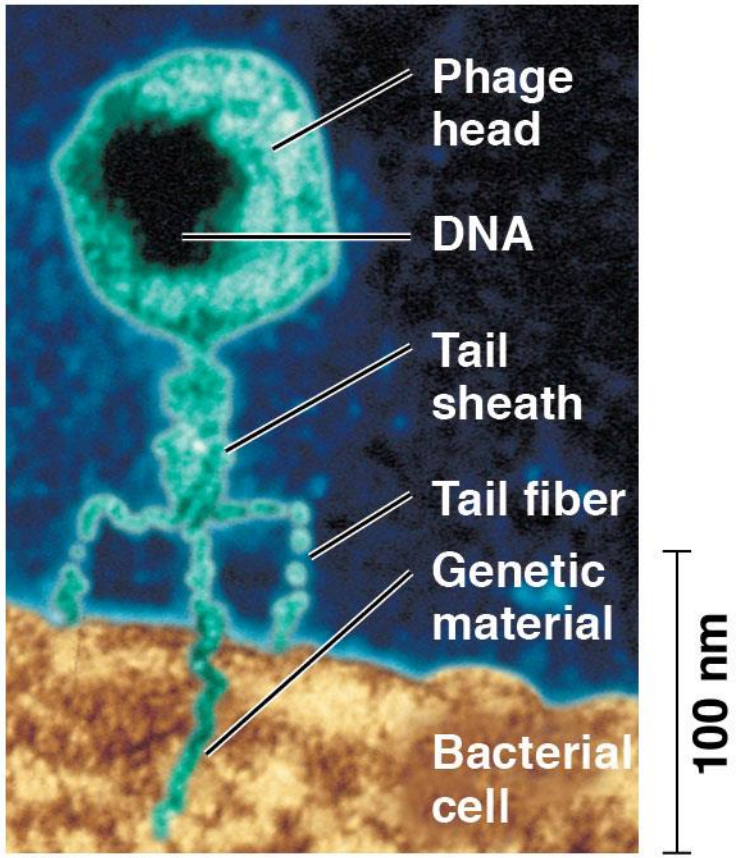
Discovered that the transforming agent was DNA

Hershey and Chase (1952)

Bacteriophages: virus that infects bacteria; composed of **DNA and protein**

Protein = radiolabel S

DNA = radiolabel P



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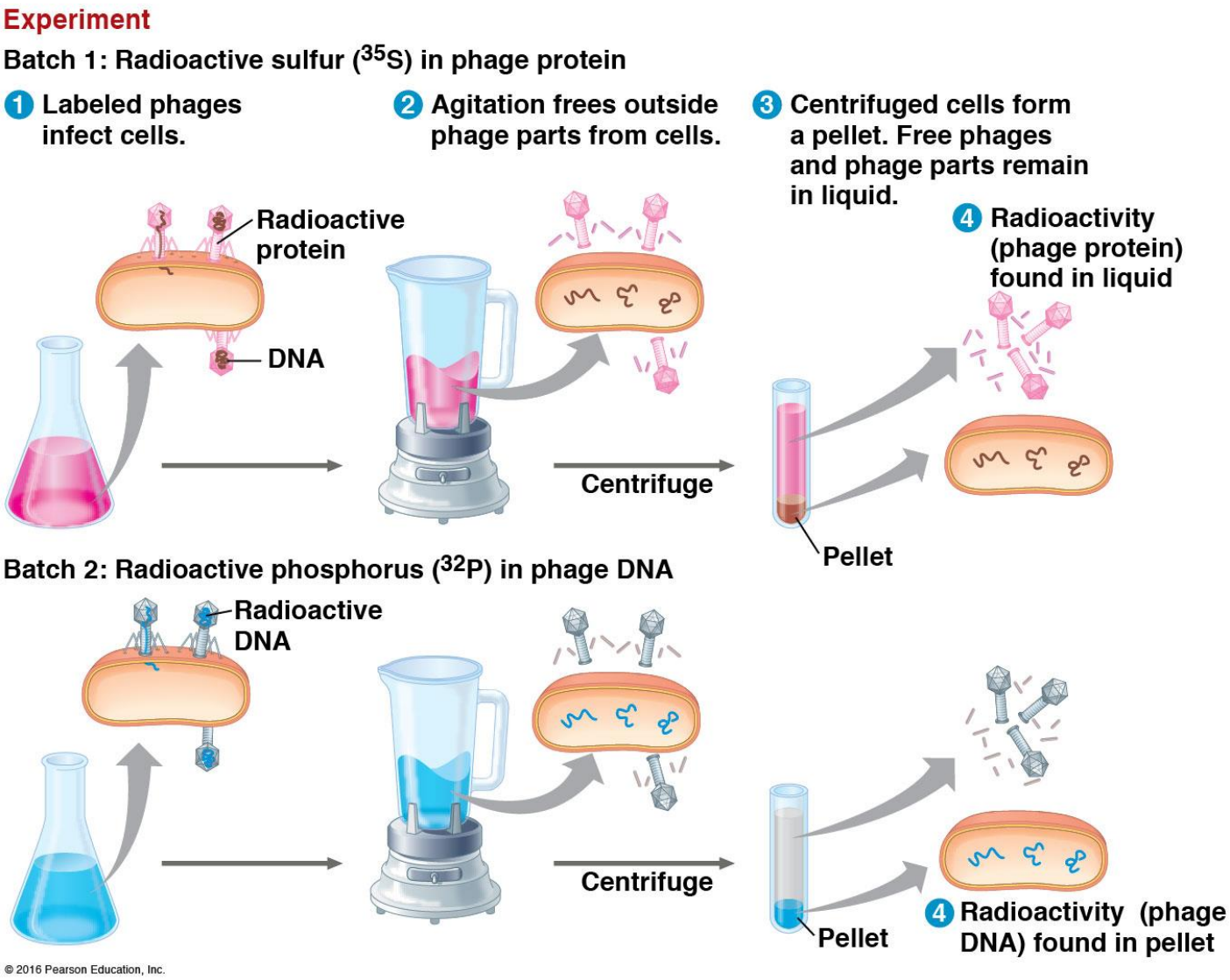


<u>Conclusion</u>: DNA entered infected bacteria → DNA must be the genetic material!

Problem:

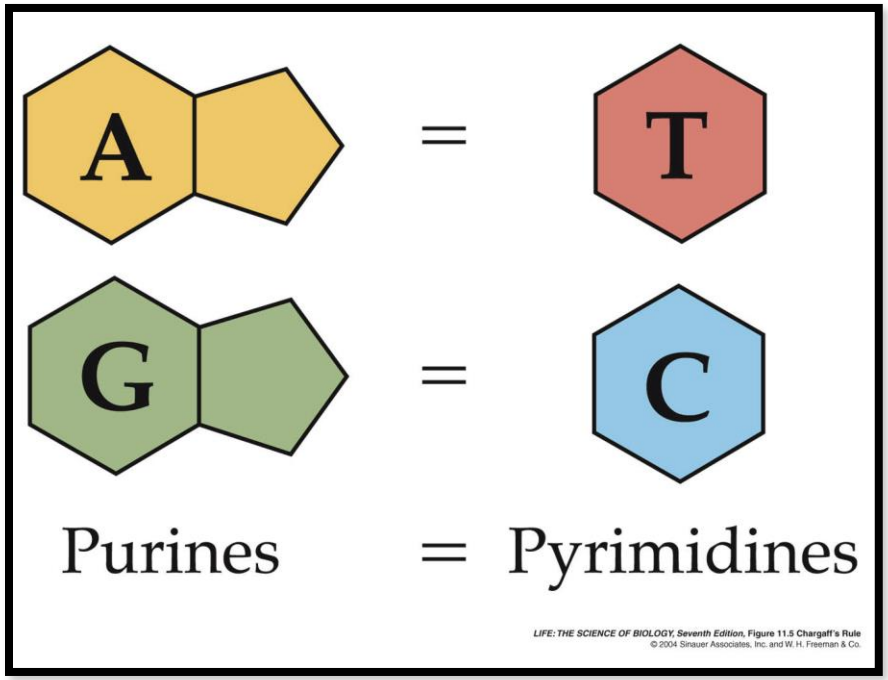
What is the structure of DNA?

Edwin Chargaff (1947)

Chargaff's Rules:

DNA composition varies between species

Ratios: %A = %T and %G = %C

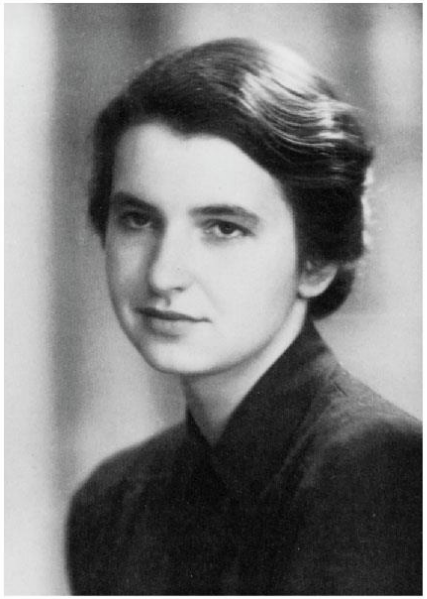


Rosalind Franklin (1950's)

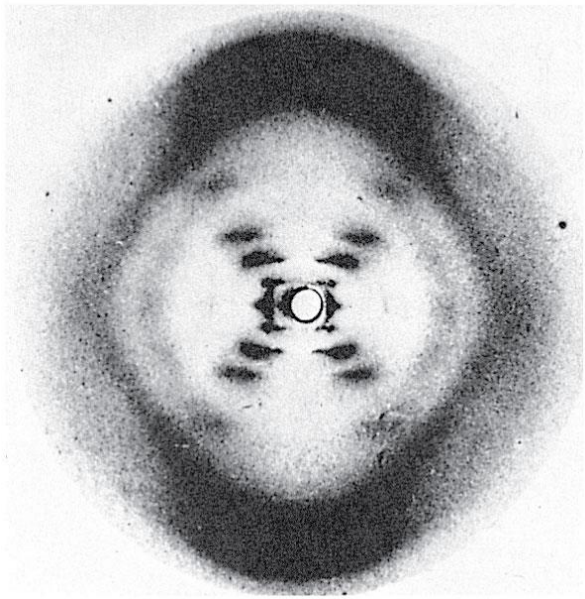
Worked with Maurice Wilkins

X-ray crystallography = images of DNA

Provided measurements on chemistry of DNA



(a) Rosalind Franklin



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

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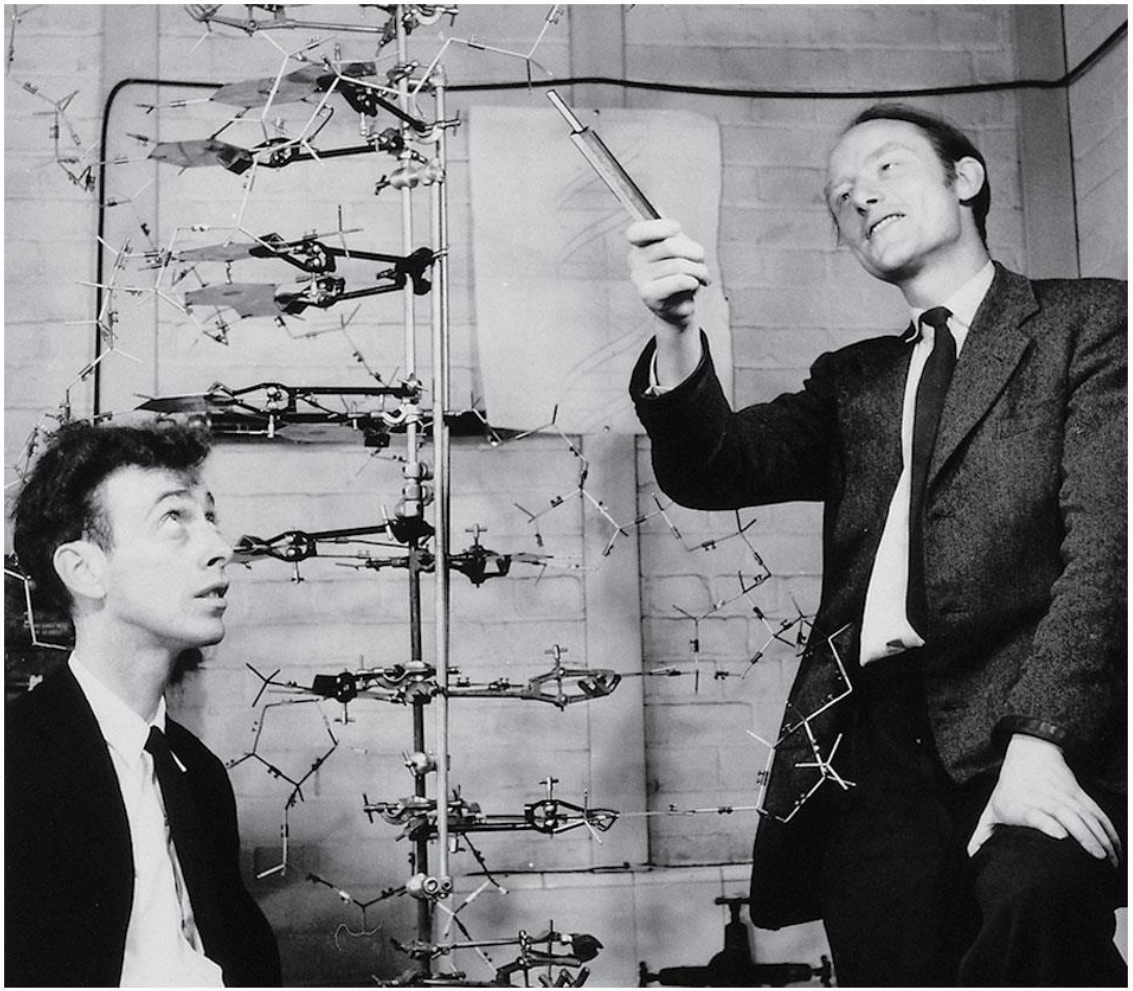
James Watson & Francis Crick (1953)

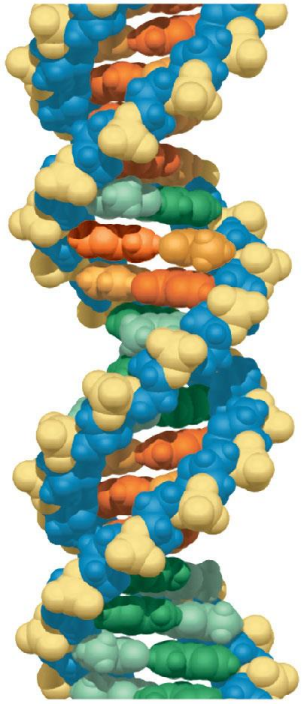
Discovered the double helix by building models to conform to Franklin's X-ray data and Chargaff's Rules.



DNA = Double Helix

"Backbone" = sugar + phosphate

"Rungs" = nitrogenous bases



(c) Space-filling model

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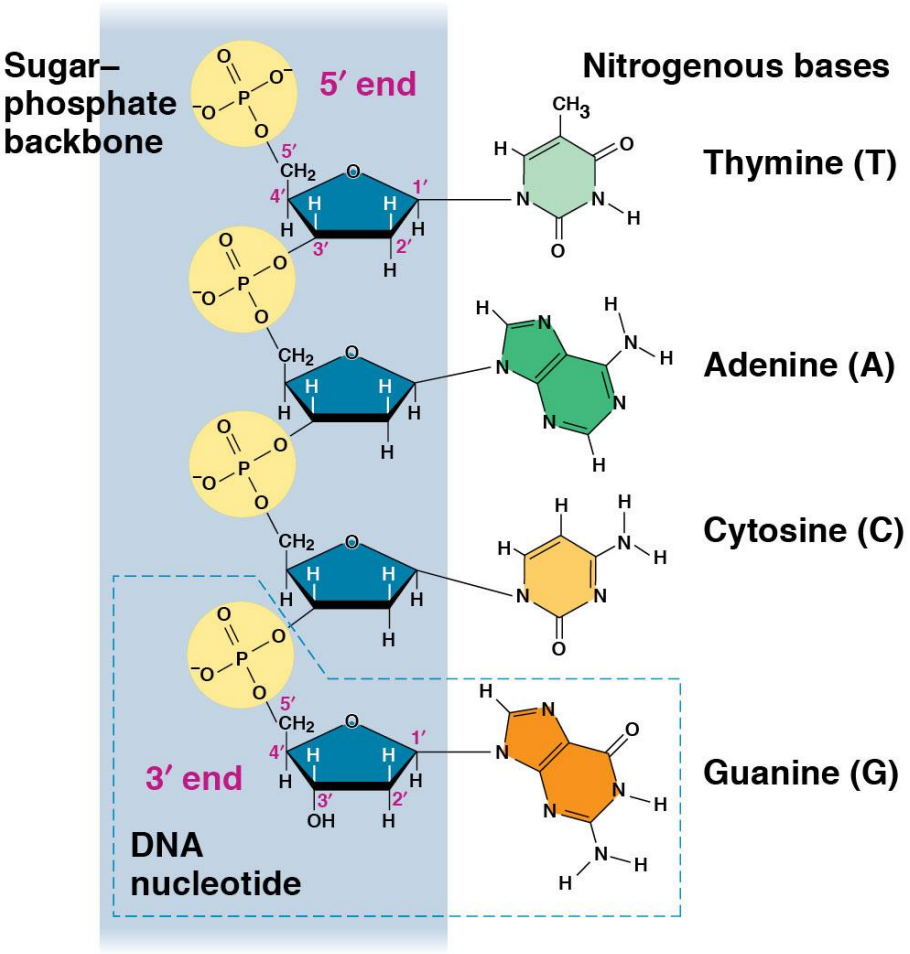

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Nitrogenous Bases

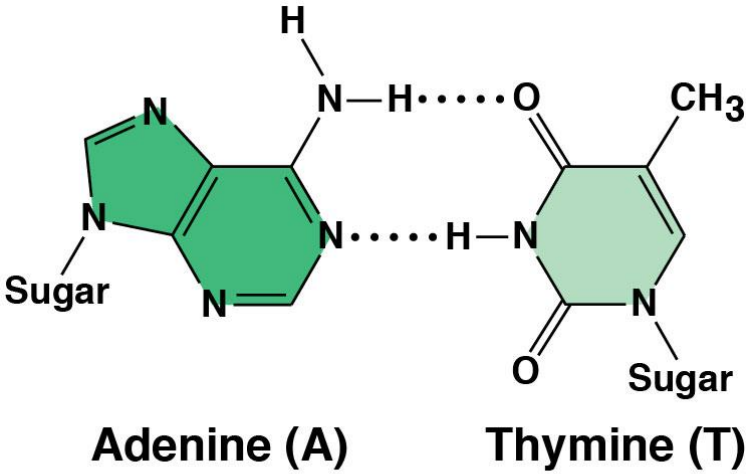
Adenine (A)
Guanine (G) — purine
Thymine (T)
Cytosine (C) — pyrimidine

Pairing:

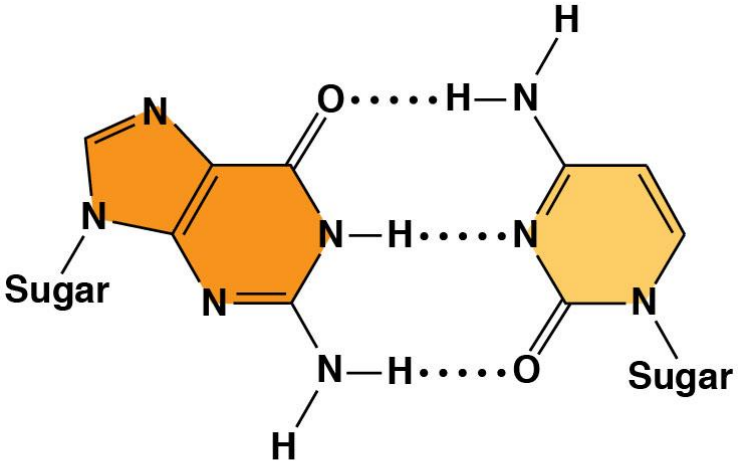
Purine + Pyrimidine

$A = T$

$G \equiv C$



Adenine (A) Thymine (T)



Guanine (G) Cytosine (C)

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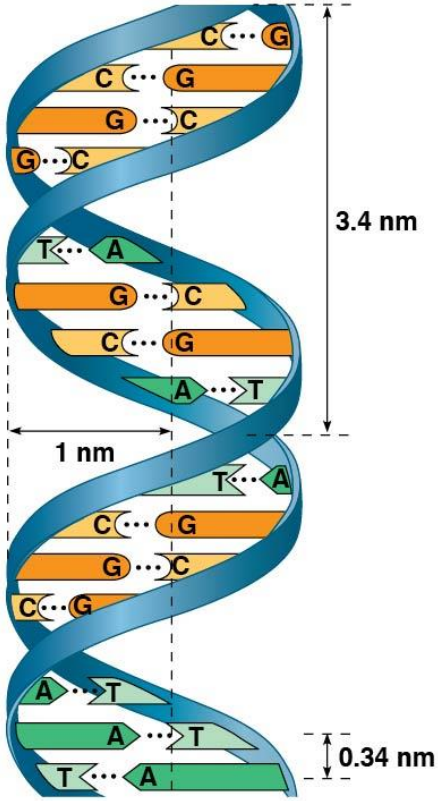
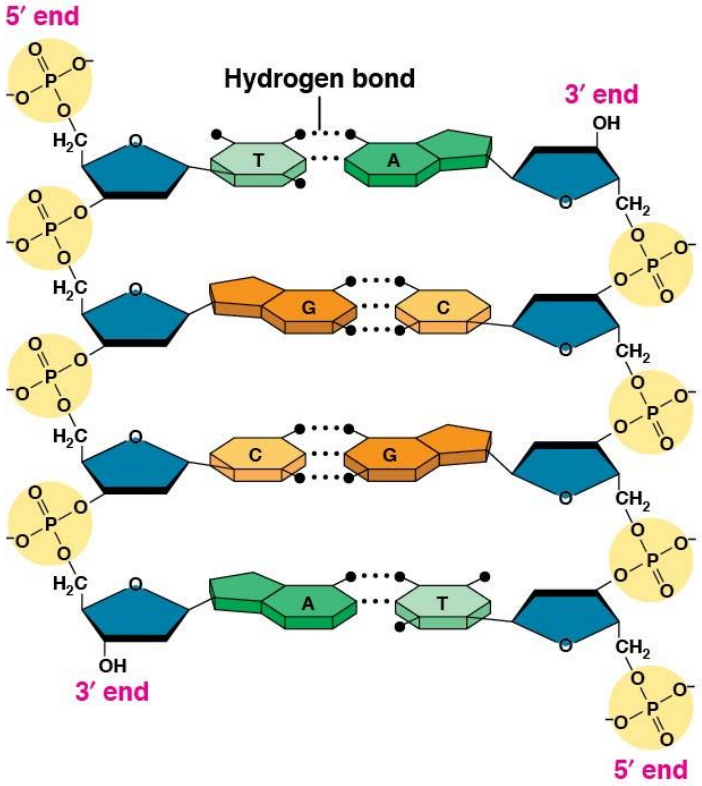
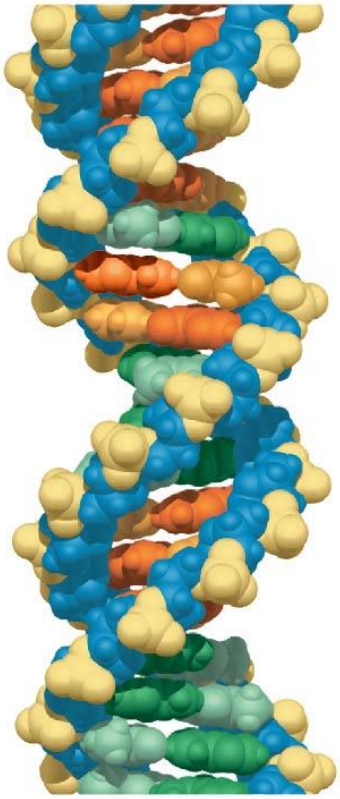
Hydrogen Bonds



(a) Key features of DNA structure



(b) Partial chemical structure



(c) Space-filling model

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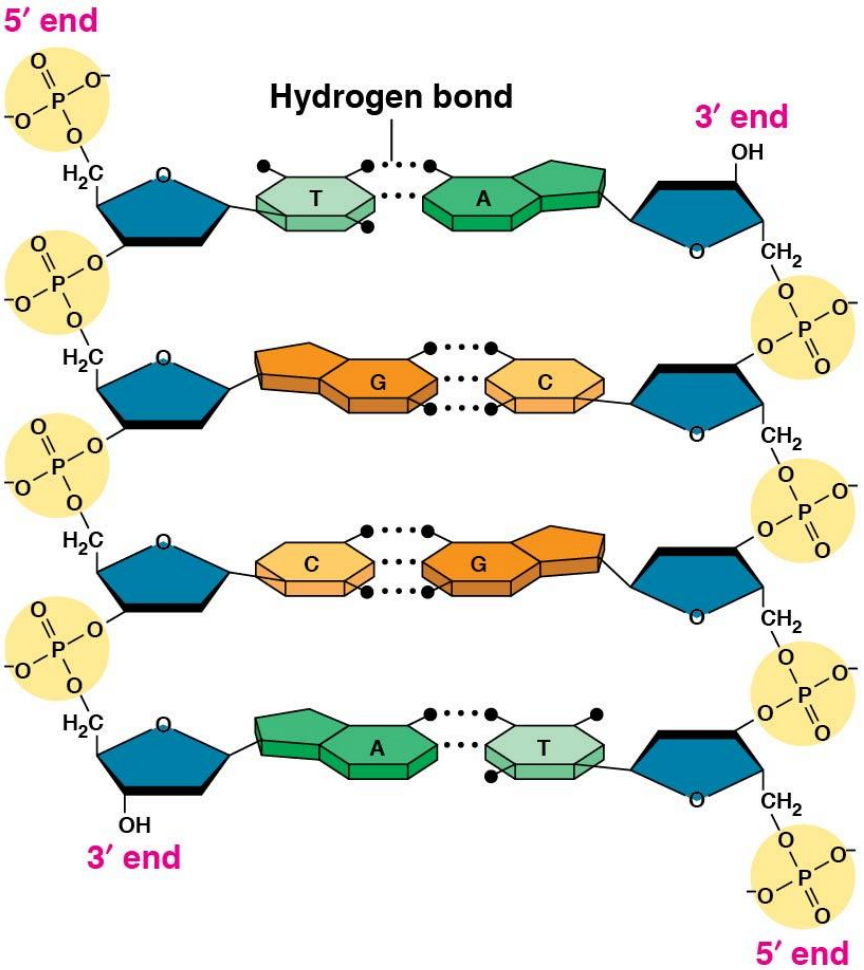
Hydrogen bonds between base pairs of the two strands hold the molecule together like a zipper.

DNA strands are **Antiparallel**

One strand (5’ → 3’) other strand runs in opposite, upside-down direction (3’ → 5’)



(b) Partial chemical structure

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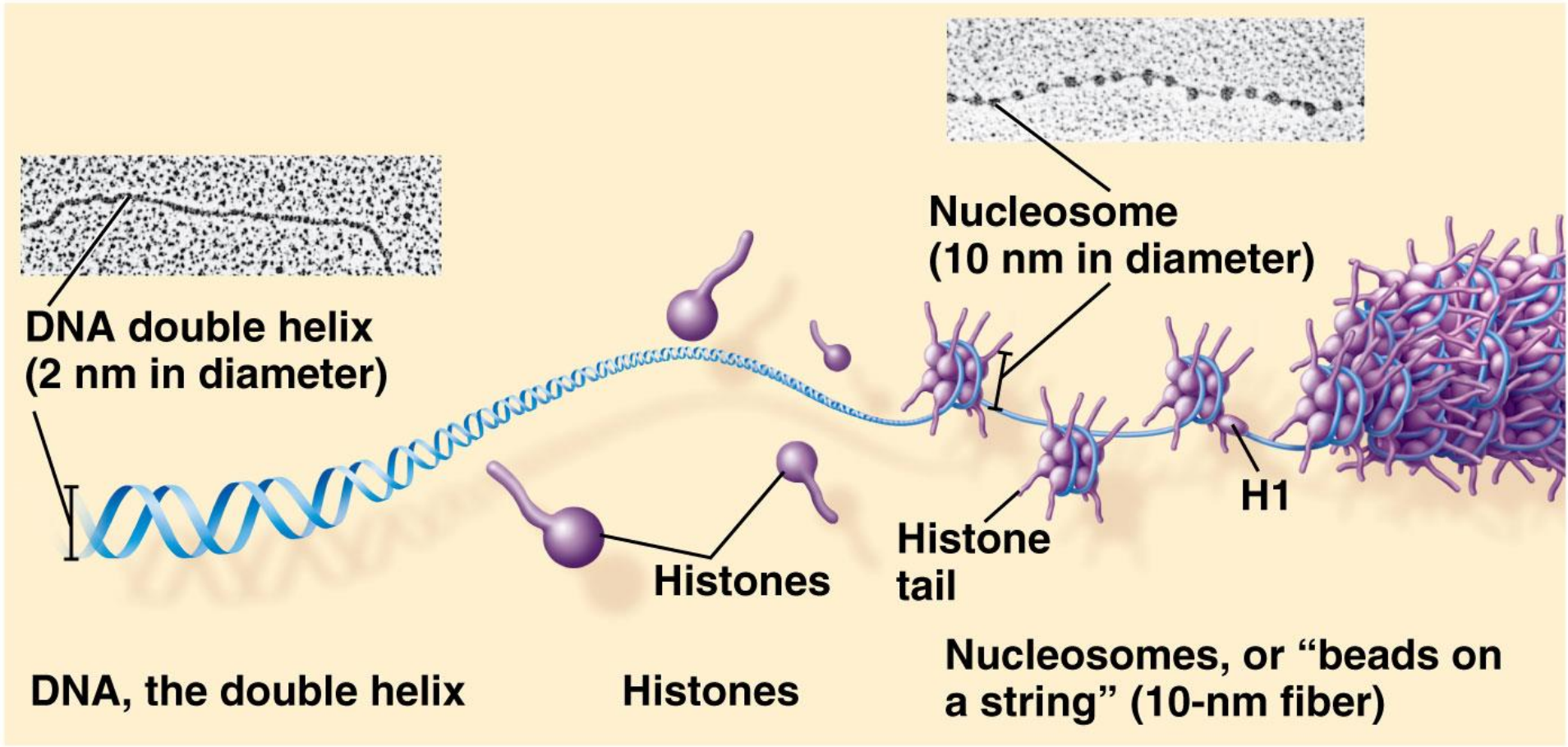
How DNA is packaged



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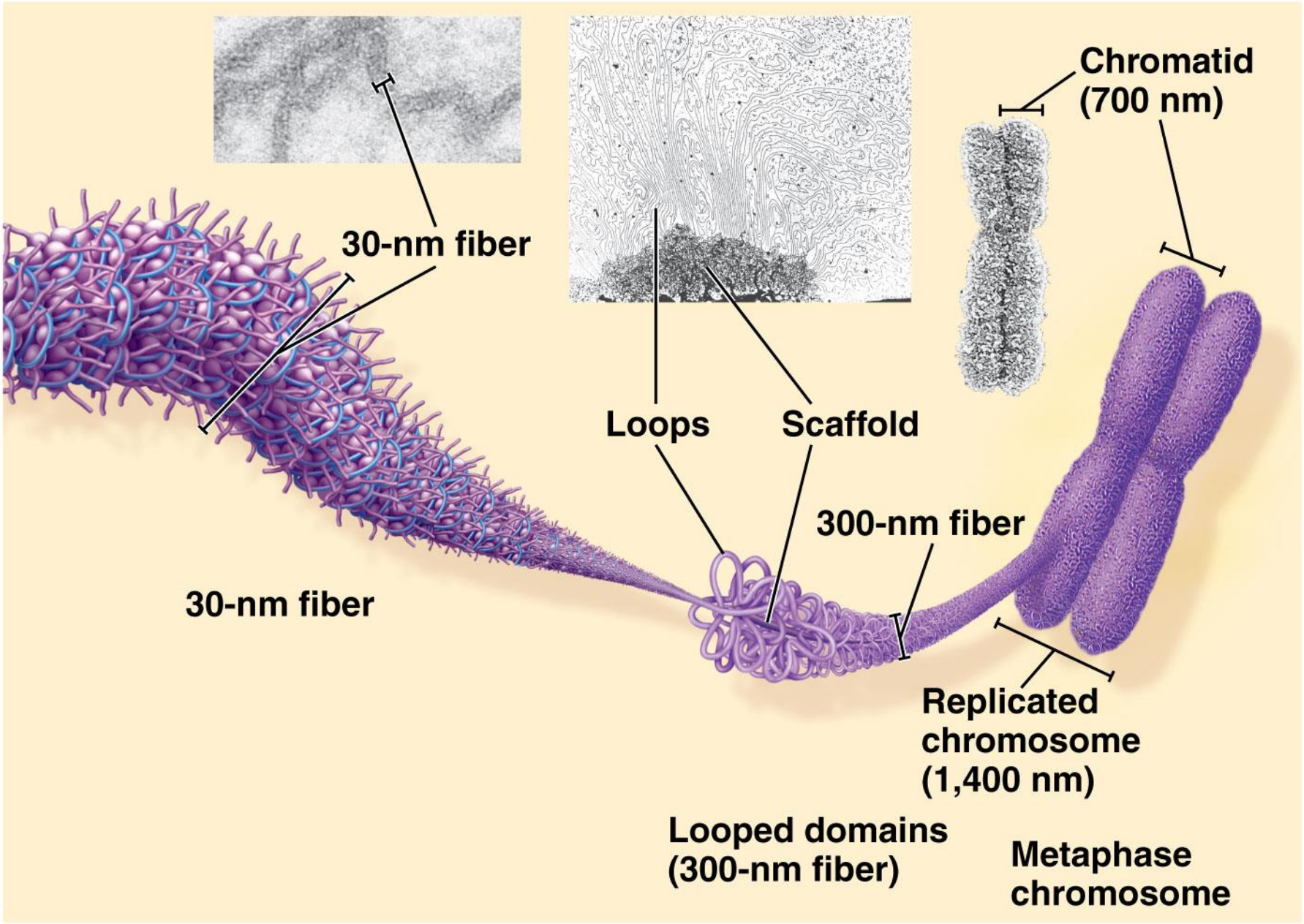

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DNA Comparison

PROKARYOTIC DNA

- Double-stranded
- Circular
- One chromosome
- In cytoplasm
- Supercoiled DNA (nucleoid)
- No histones

EUKARYOTIC DNA

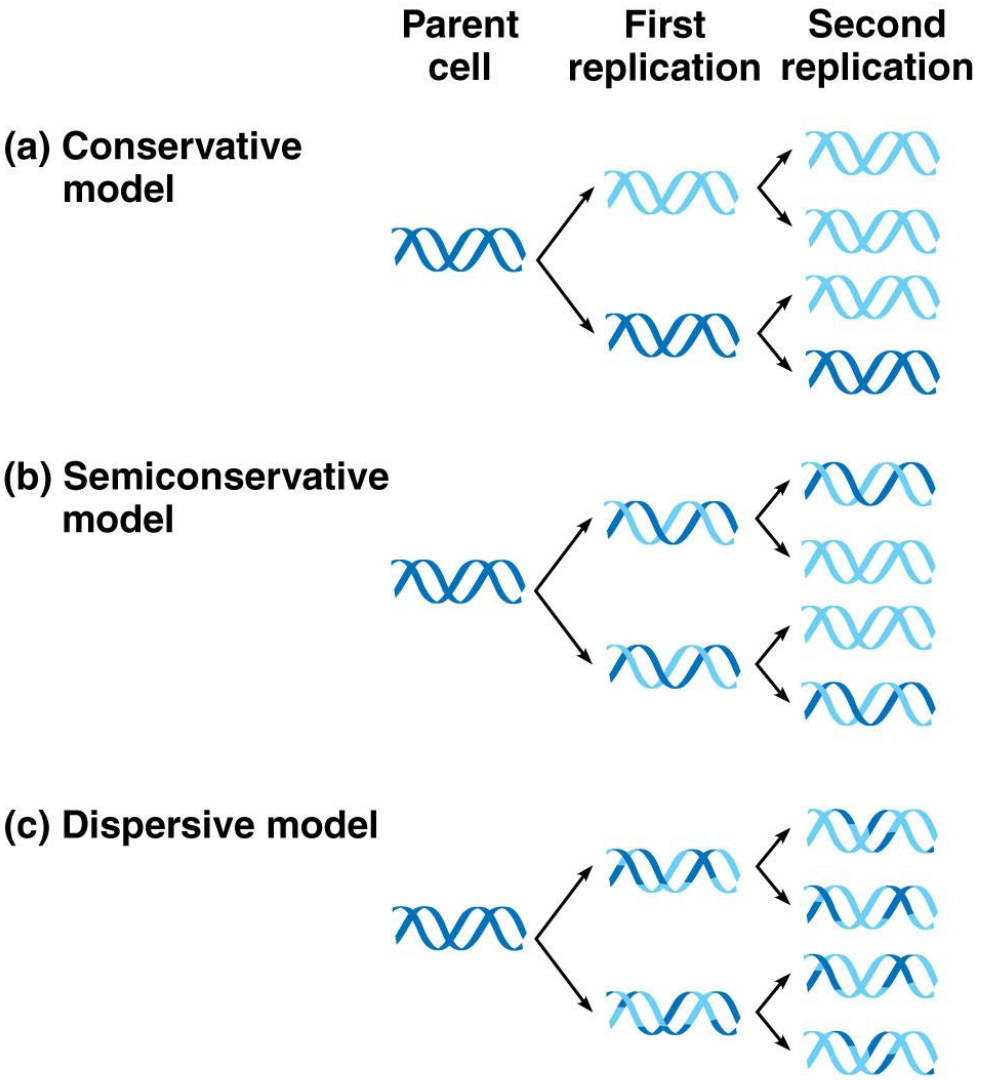
- Double-stranded
- Linear
- Usually 1+ chromosomes
- In nucleus
- Chromatin = DNA wrapped around histones (proteins)

Problem:

How does DNA replicate?

Replication: Making DNA from existing DNA

3 alternative models of DNA replication



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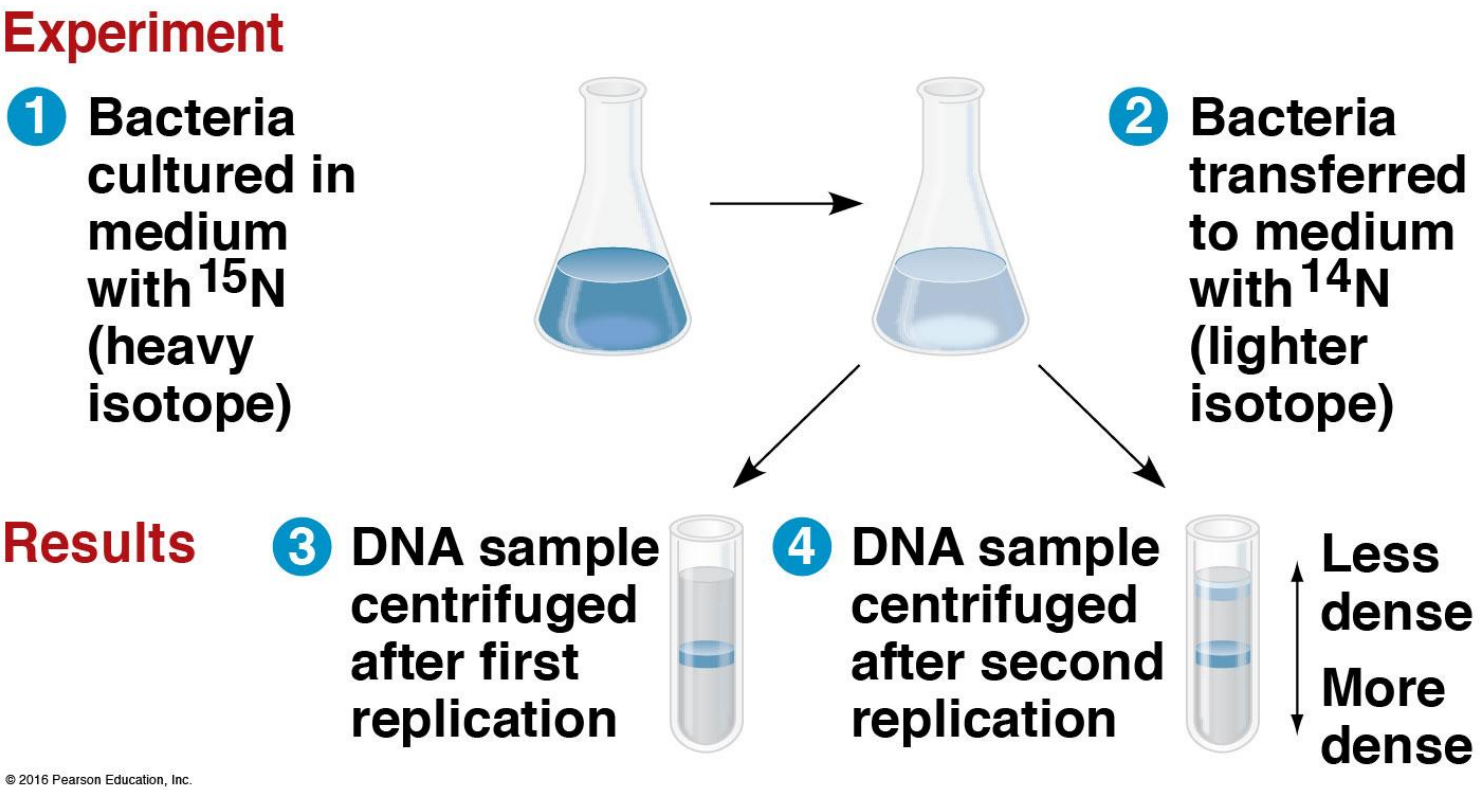
Meselson & Stahl



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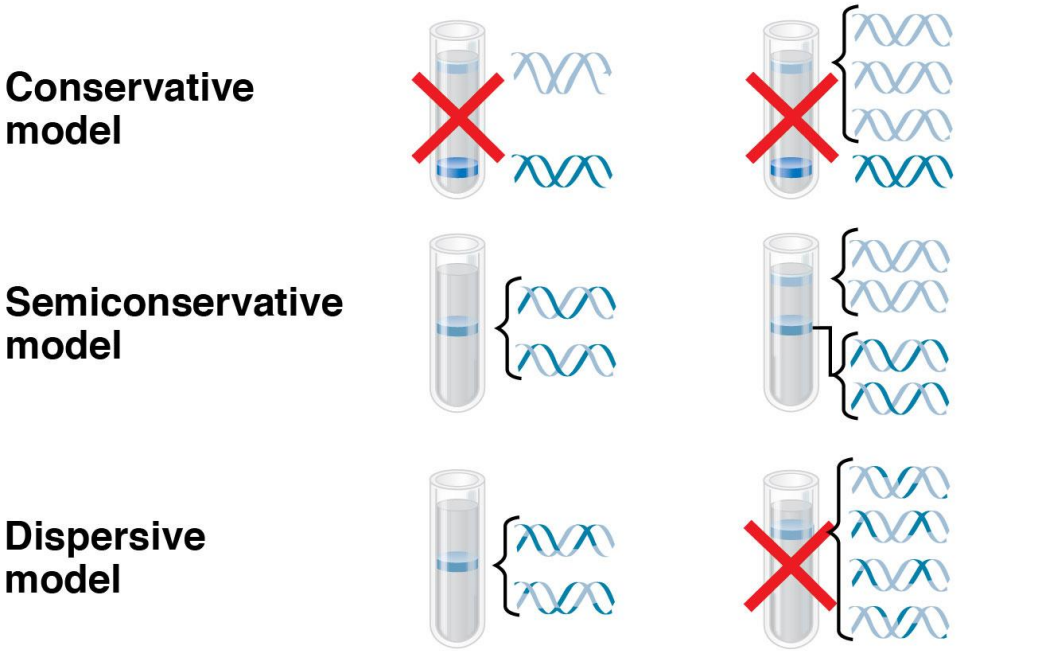
Meselson & Stahl

Conclusion



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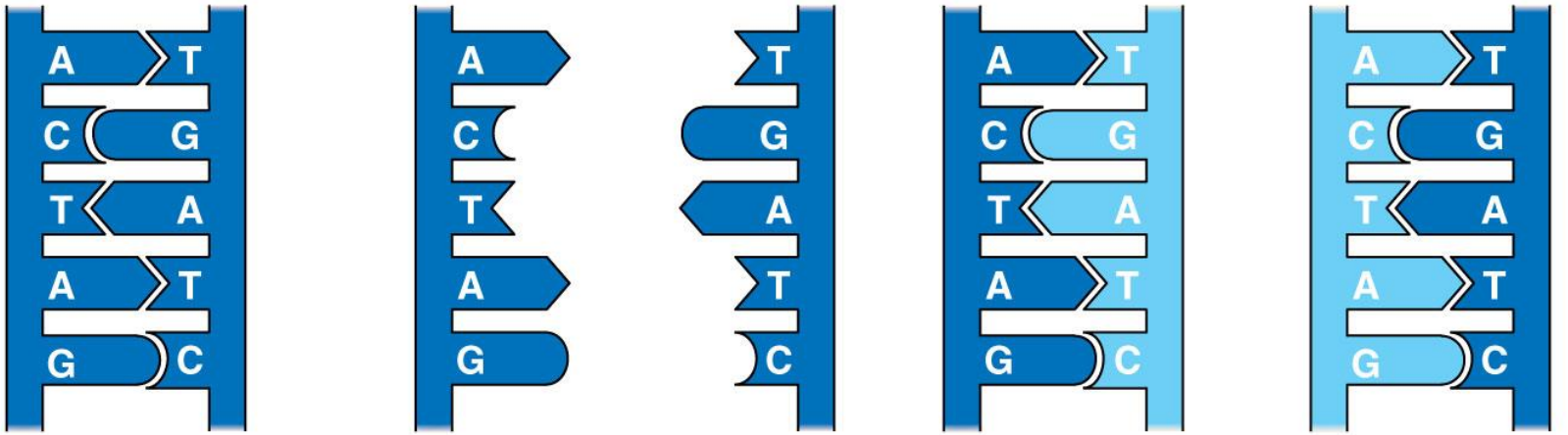
Replication is **semiconservative**



(a) Parent molecule

(b) Separation of strands

(c) "Daughter" DNA molecules, each consisting of one parental strand and one new strand

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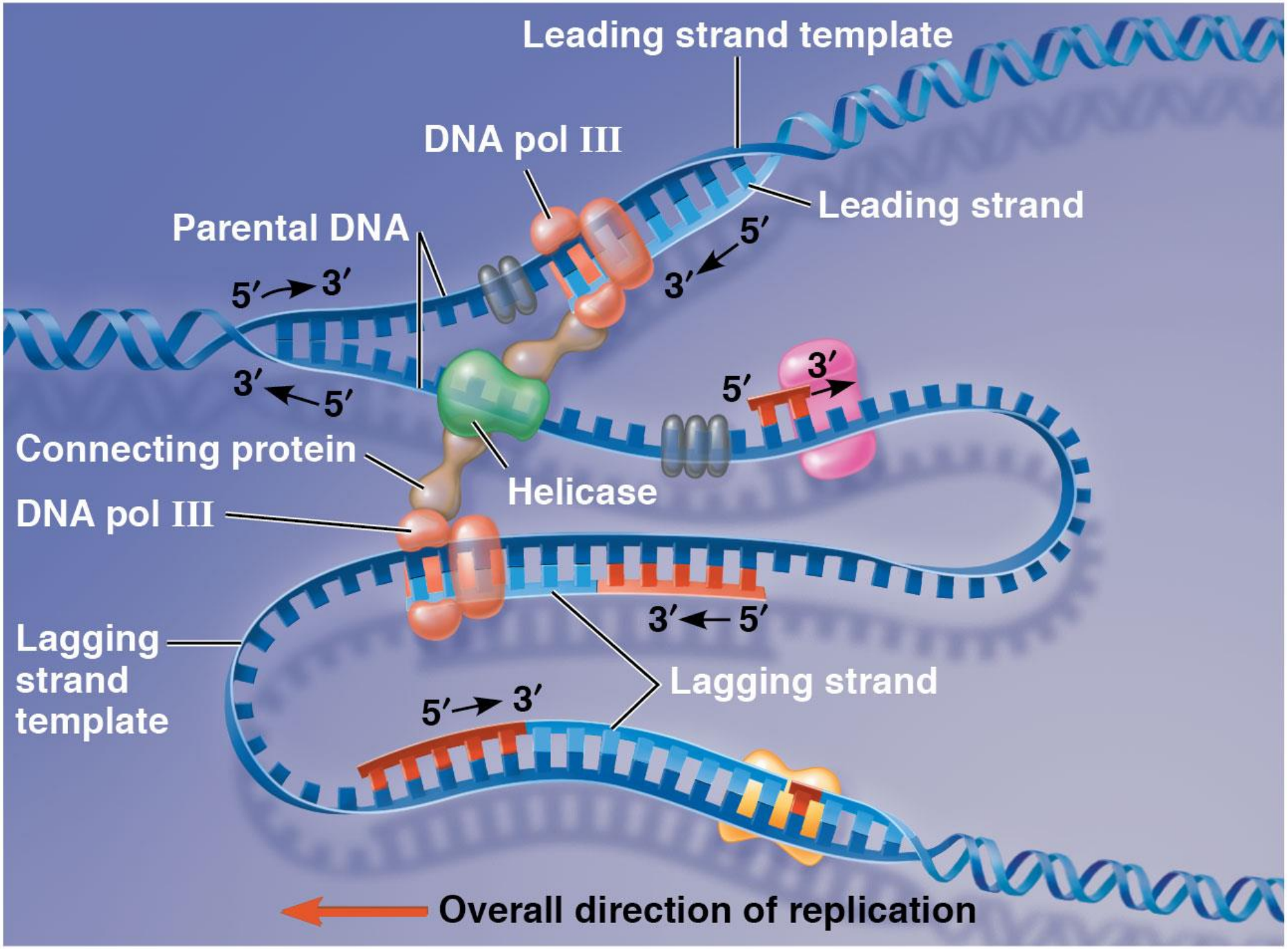
DNA Replication Video

http://www.youtube.com/watch?v=4jtmOZaIvS0&feature=related



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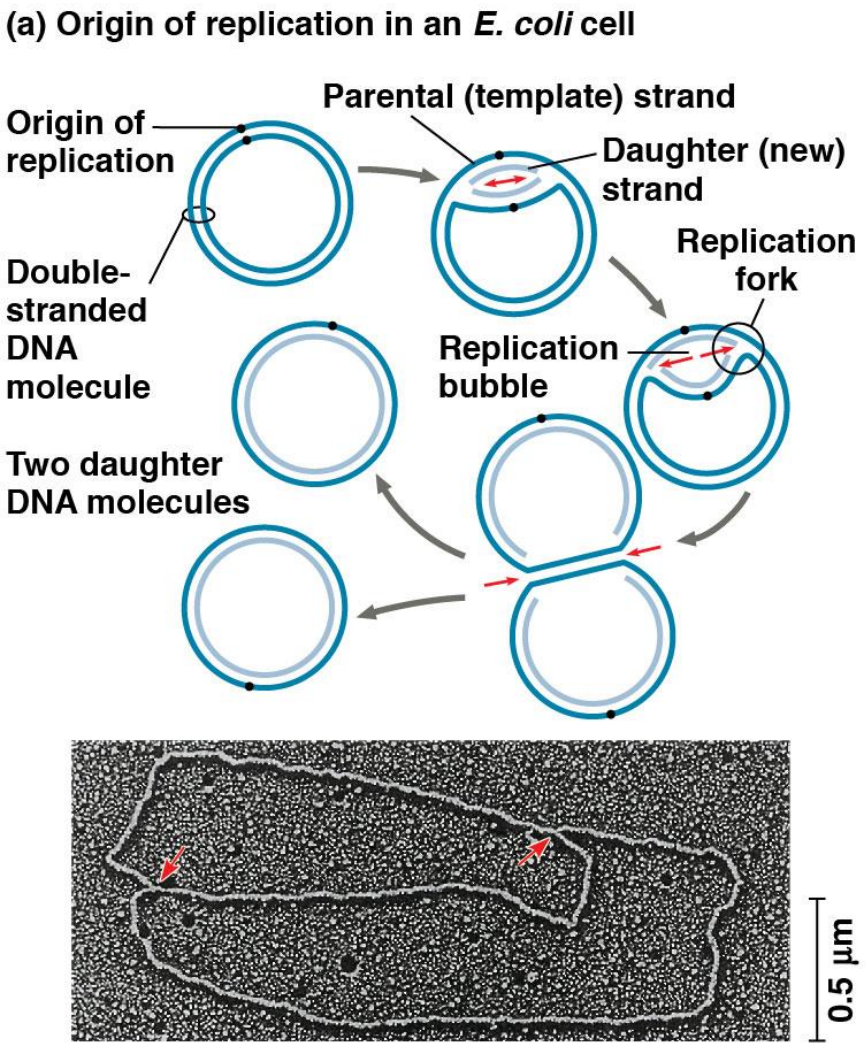
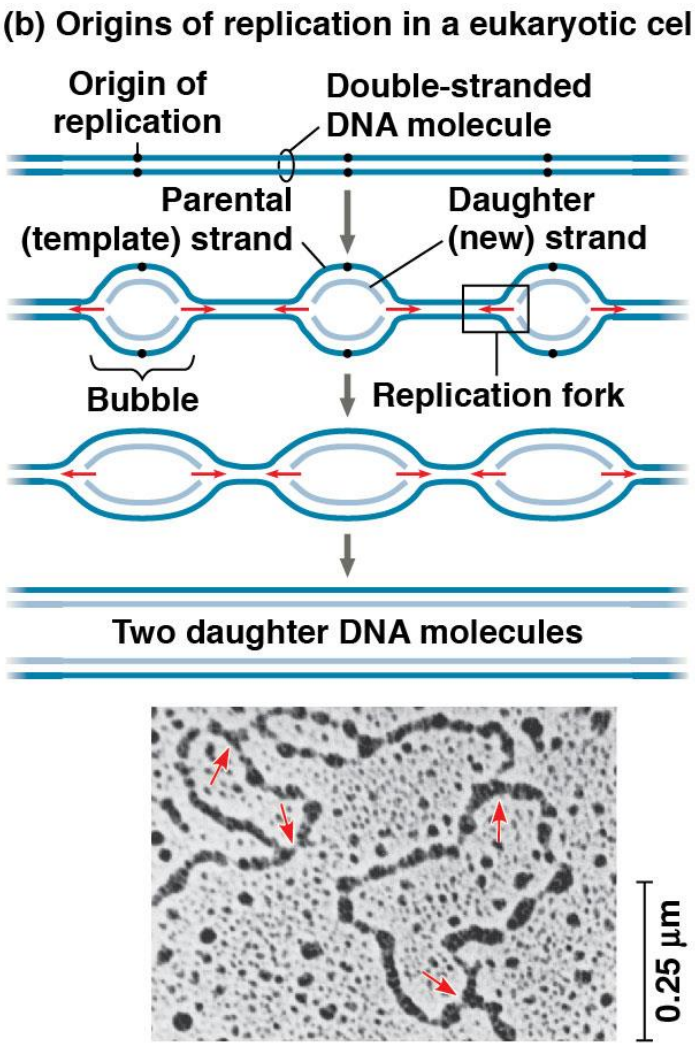
Major Steps of Replication:

1. Helicase: unwinds DNA at *origins of replication*
2. Initiation proteins separate 2 strands → forms *replication bubble*
3. Topoisomerase: relieves overwinding strain ahead of replication forks by breaking, swiveling, rejoining DNA strands
4. Primase: puts down RNA primer to start replication
5. DNA polymerase III: adds complimentary bases to *leading strand* (new DNA is made 5' → 3')
6. *Lagging strand* grows in 3'→5' direction by the addition of *Okazaki fragments*
7. DNA polymerase I: replaces RNA primers with DNA
8. DNA ligase: seals fragments together

1. Helicase unwinds DNA at origins of replication and creates replication forks





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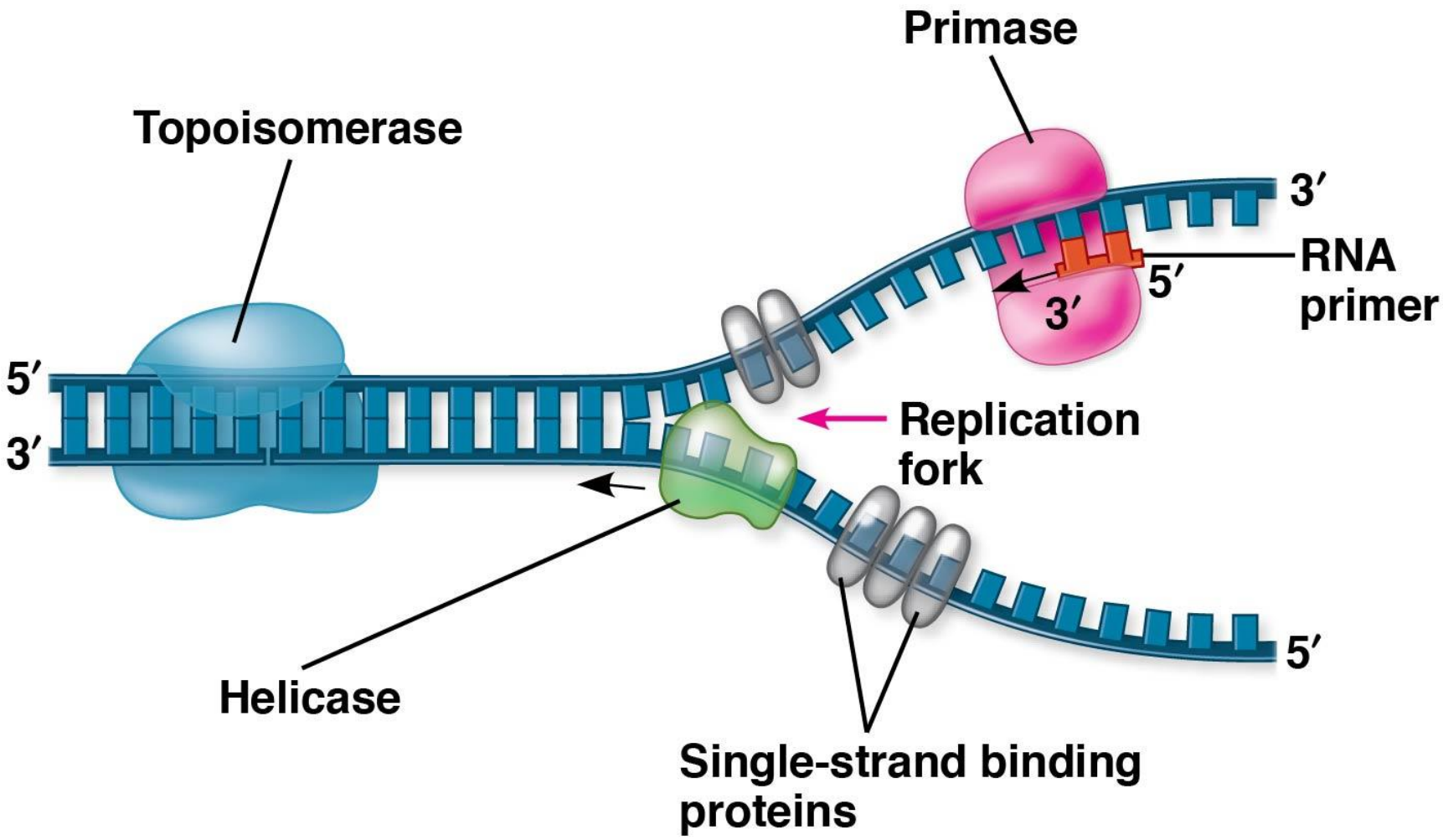
4. Primase adds RNA primer



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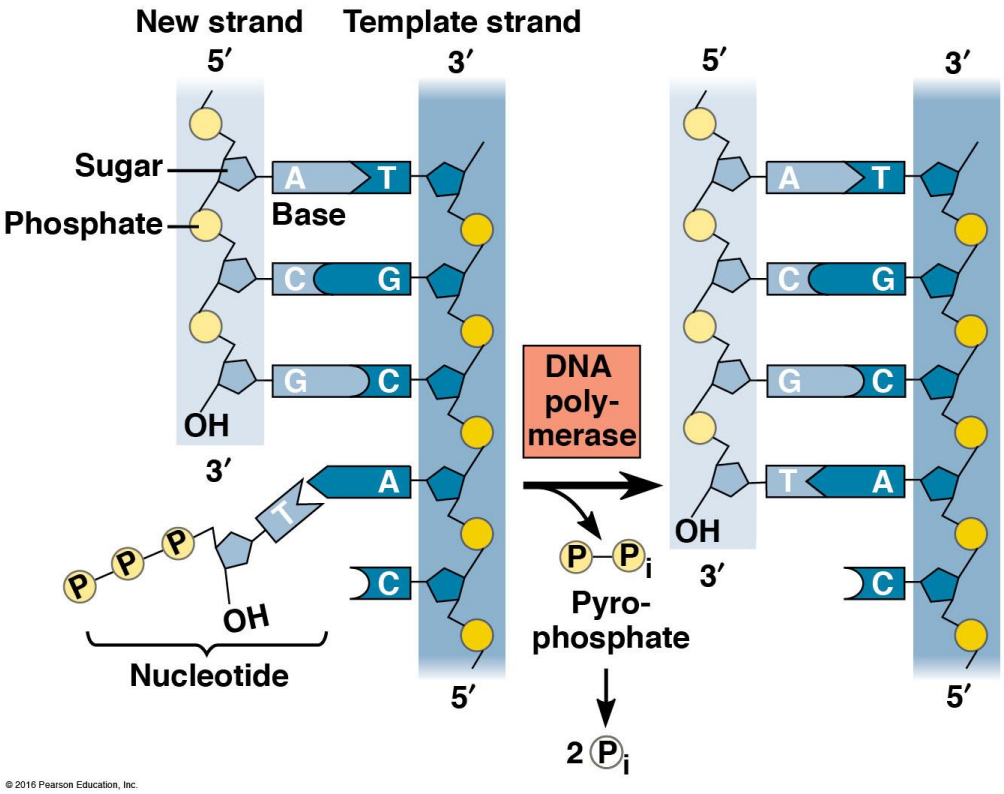
5. DNA polymerase III adds nucleotides in 5' → 3' direction on leading strand



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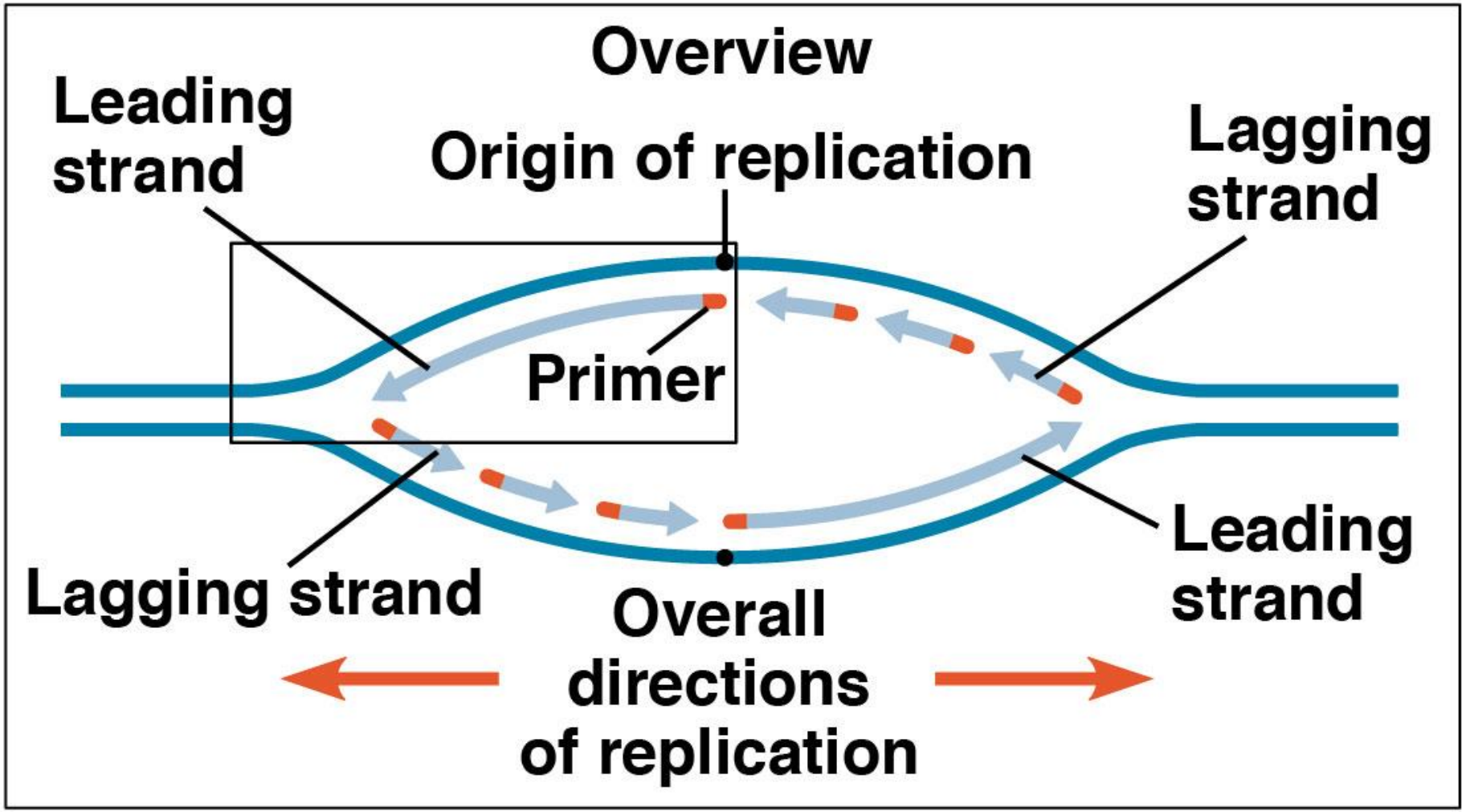
Leading strand vs. Lagging strand



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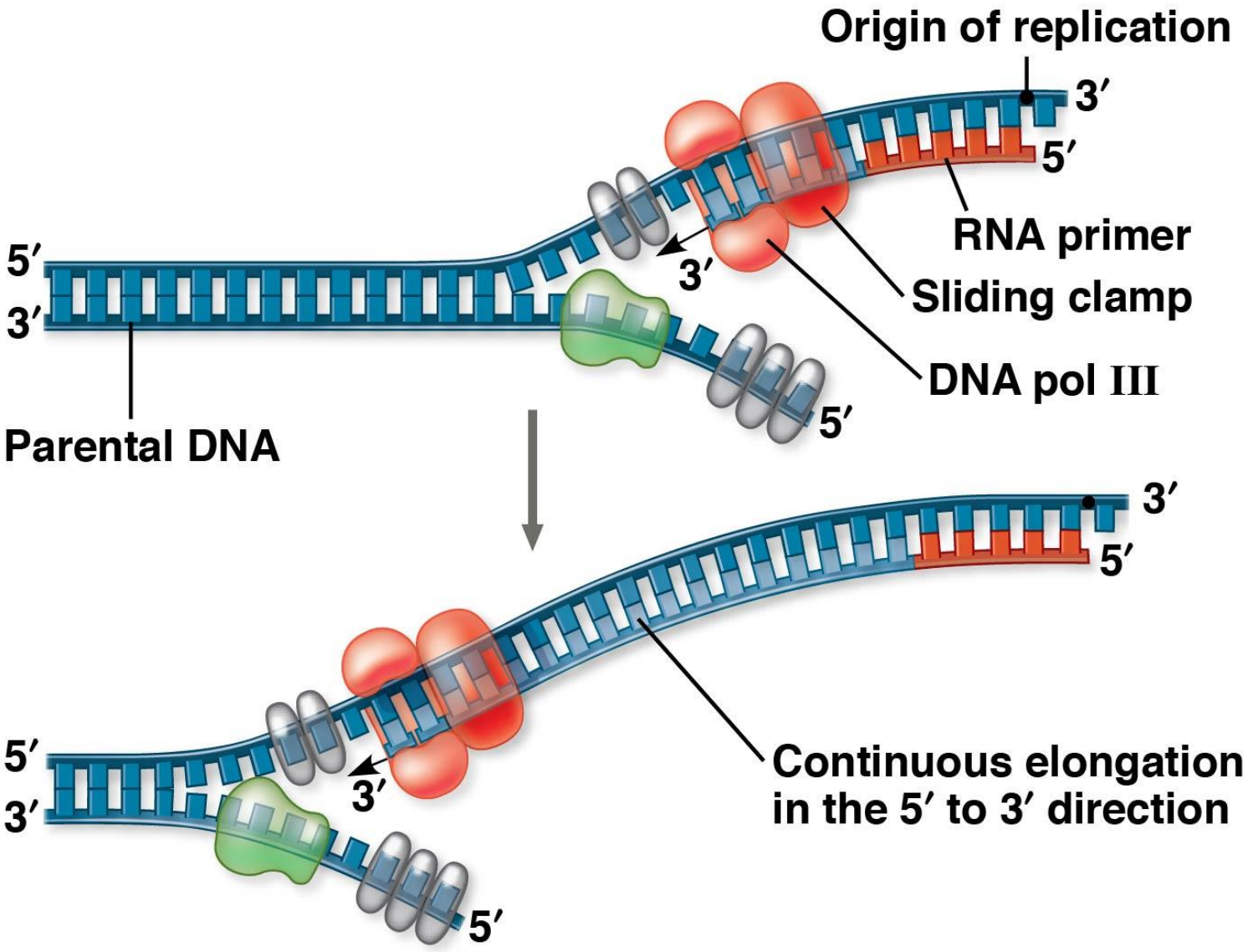
Replication on leading strand



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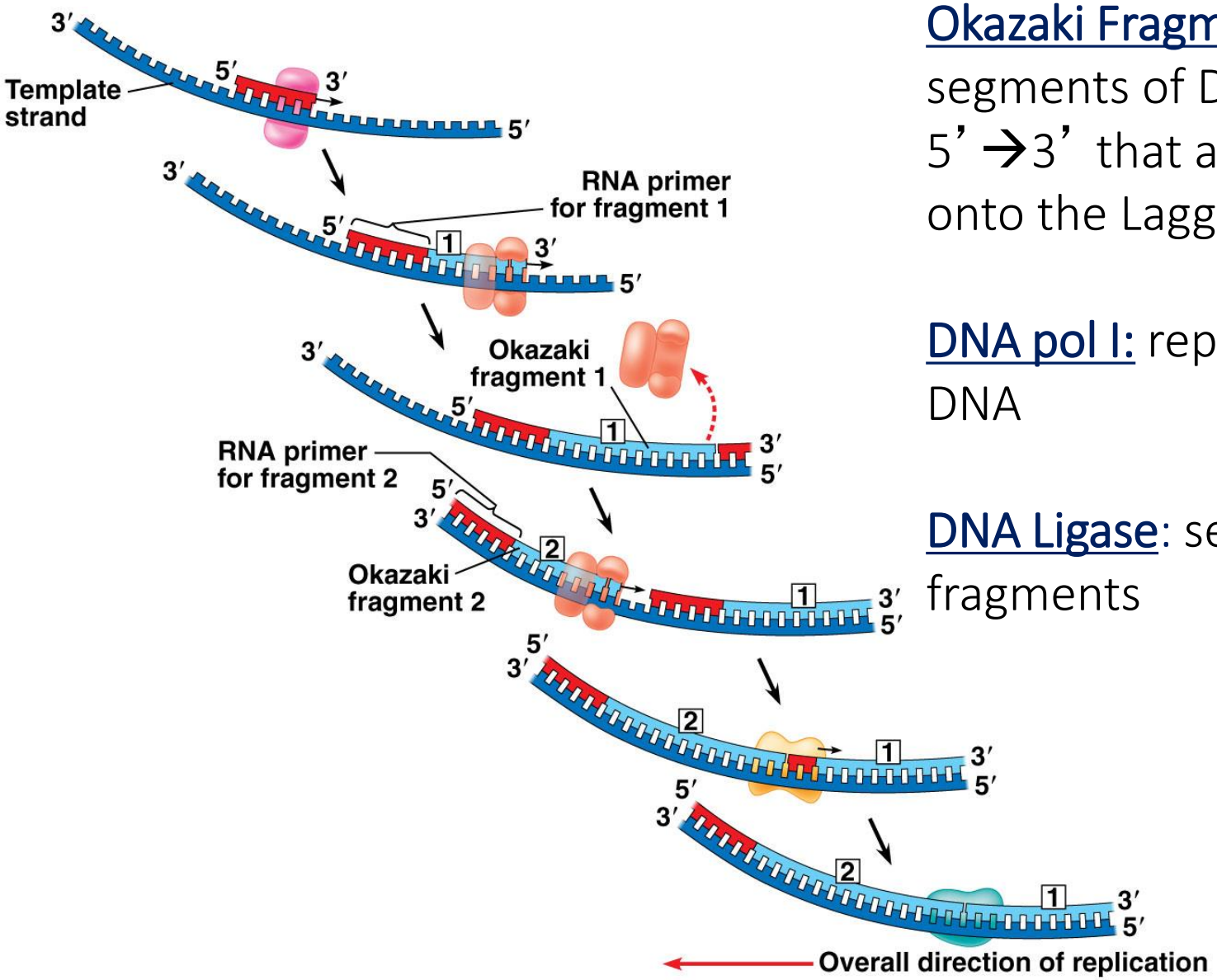
Replication on lagging strand



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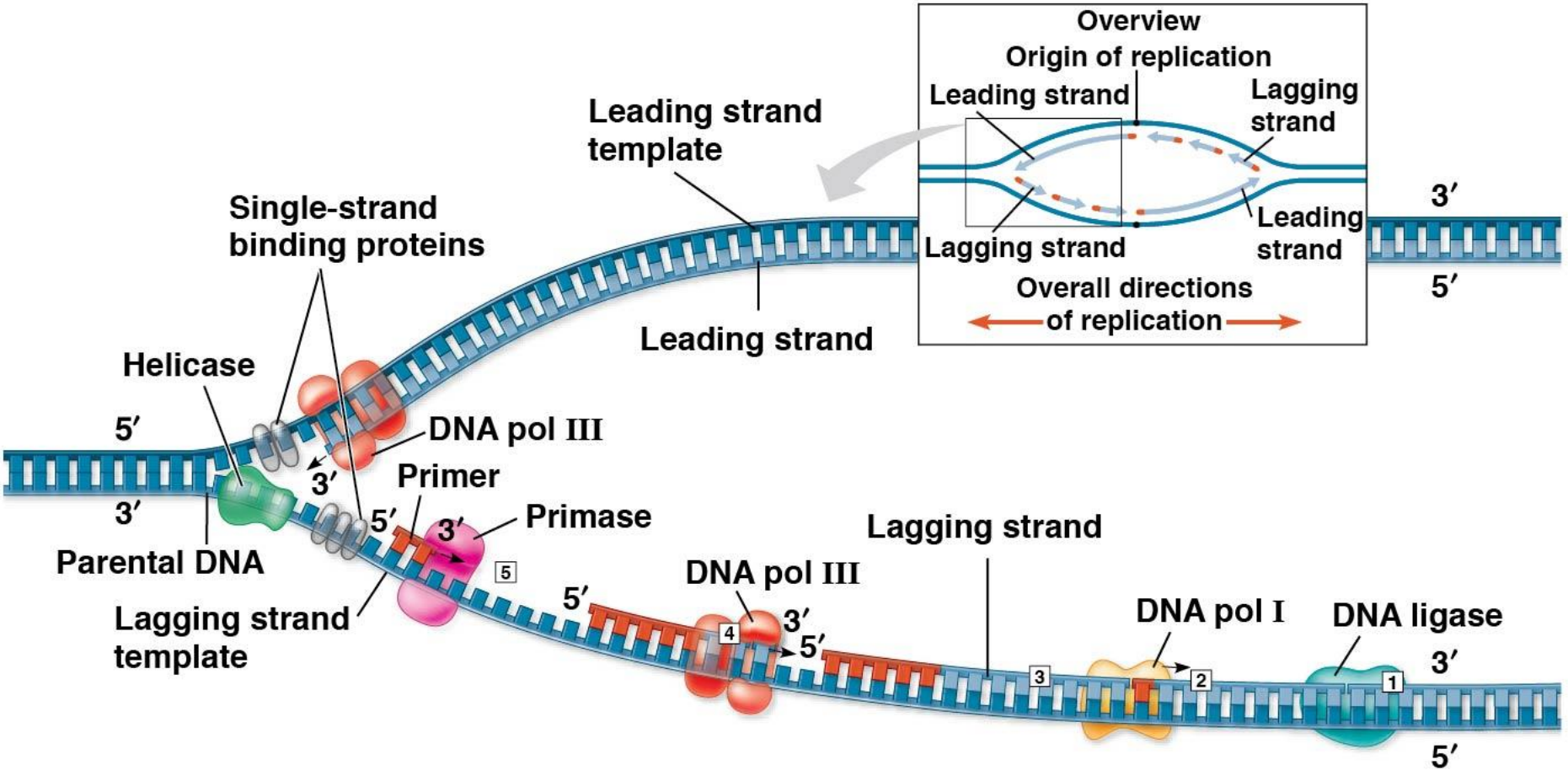
Okazaki Fragments: Short segments of DNA that grow 5'→3' that are added onto the Lagging Strand

DNA pol I: replace RNA with DNA

DNA Ligase: seals together fragments

Summary of DNA Replication



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Proofreading and Repair

DNA polymerases proofread as bases added

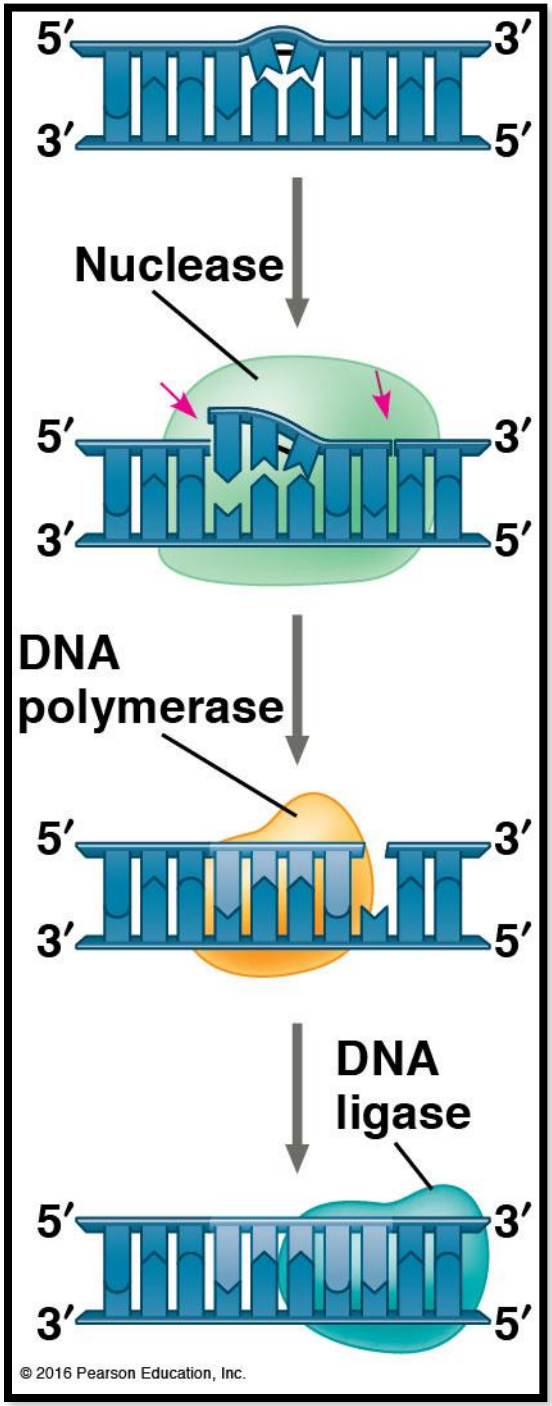
Errors:

- Pairing errors: 1 in 100,000 nucleotides
- Complete DNA: 1 in 10 billion nucleotides

Mismatch repair: special enzymes fix incorrect pairings

Nucleotide Excision Repair

- Nucleases cut damaged DNA
- DNA polymerase and ligase fill in gaps

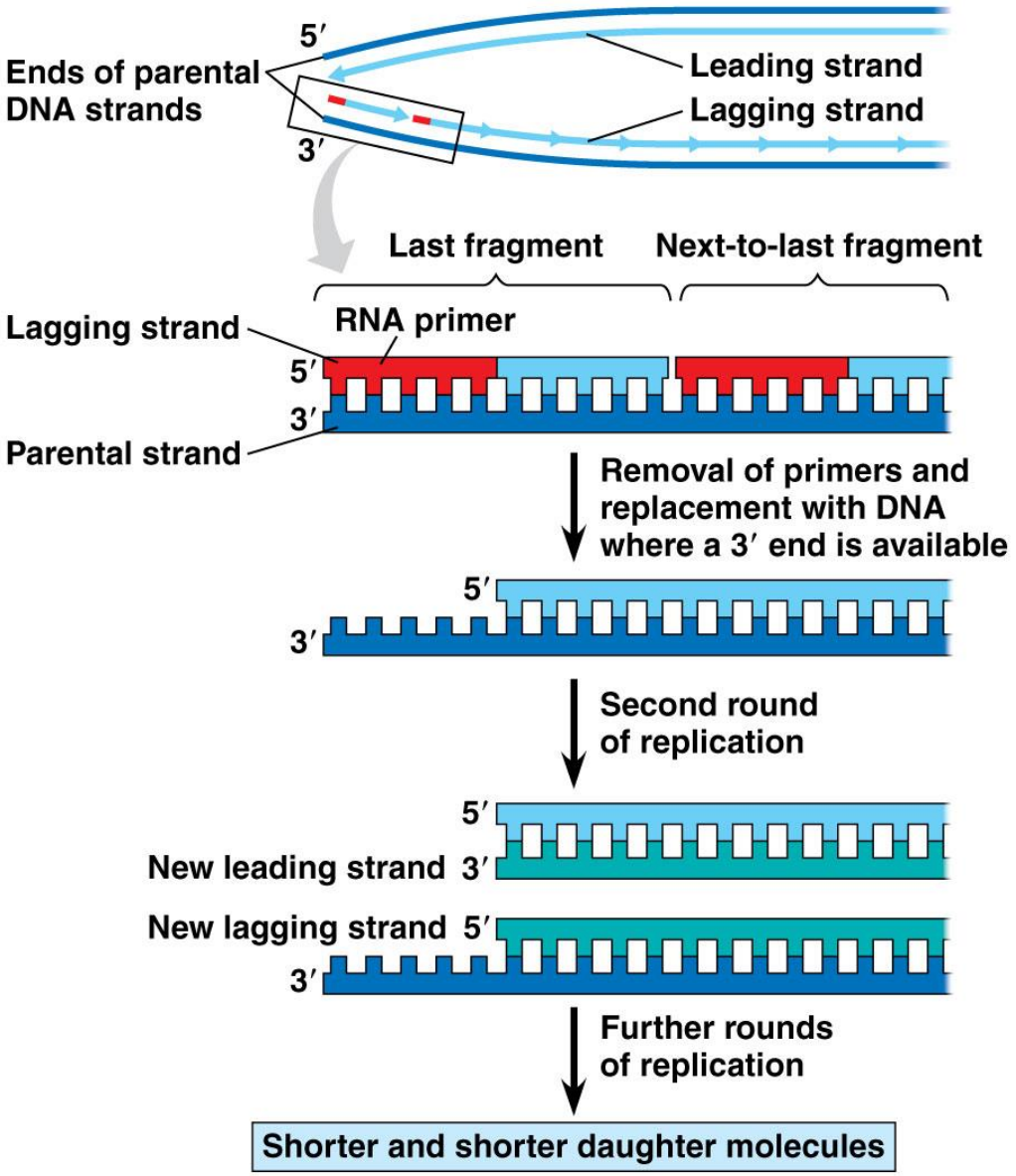


Problem at the 5’ End

DNA poly only adds nucleotides to 3’ end

No way to complete 5’ ends of daughter strands

Over many replications, DNA strands will grow shorter and shorter



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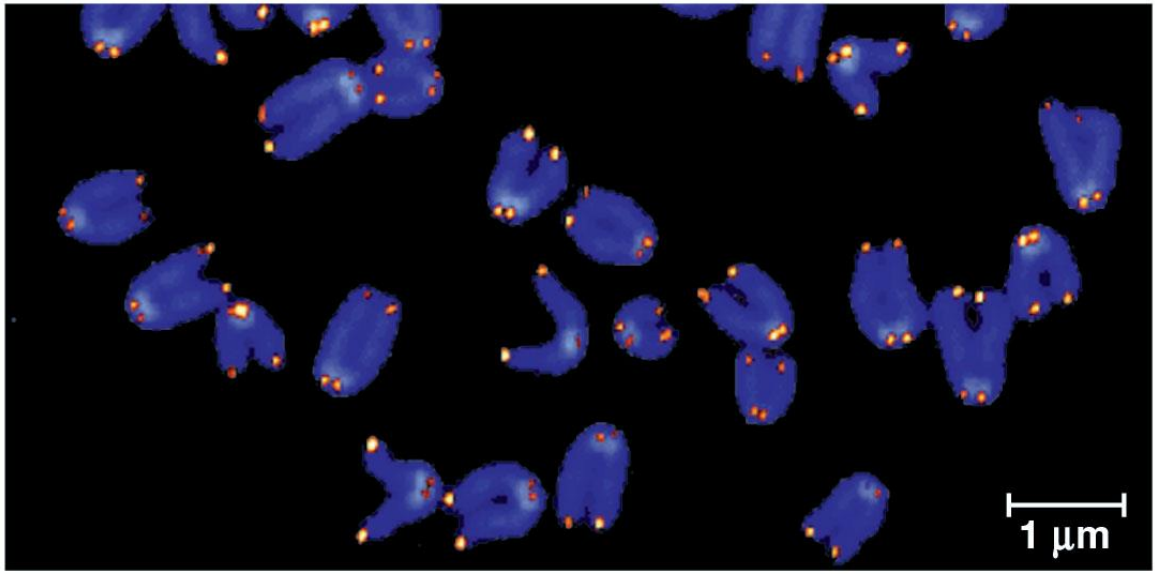
Telomeres: repeated units of short nucleotide sequences (TTAGGG) at ends of DNA

Telomeres "cap" ends of DNA to postpone erosion of genes at ends (TTAGGG)

Telomerase: enzyme that adds to telomeres

- Eukaryotic germ cells, cancer cells



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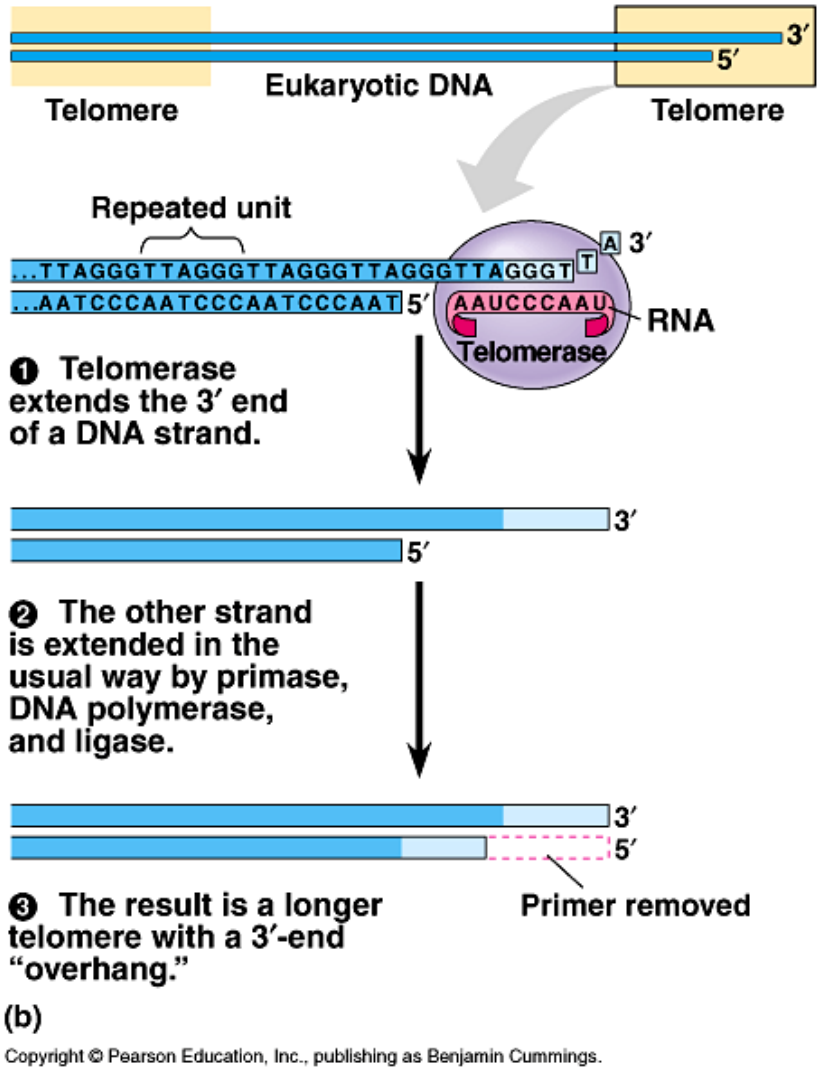
Telomeres stained orange at the ends of mouse chromosomes

Telomeres & Telomerase



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BioFlix: DNA Replication

http://media.pearsoncmg.com/bc/bc_0media_bio/bioflix/bioflix.htm?8apdnarep