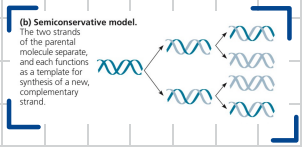
chapter 16: nucleic acids & inheritance

- **Chargaff's rule:** DNA base composition varies between species, and for each species, the % of A & T are approx. equal, as are those of C & G.

→ DNA is:

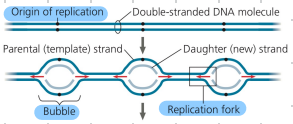
- **a double helix:** has 2 strands
- **antiparallel:** subunits run in opposite directions
- is formed of the nucleotides: purine adenine (A), purine guanine (G), pyrimidine cytosine (C), pyrimidine thymine (T). 2 H-bonds A=T ; 3 H-bonds C≡G
- **complementary:** nucleotides in one strand, have their base-pair in the other strand ex. AGCCTATGGA ⓑ / TCGGATACCT ⓠ

- **DNA replication:** copying of DNA
- When a cell copies a DNA molecule, each strand serves as template for ordering nucleotides into a new, complementary strand (according to base-pair rules)
- **semiconservative model:** when DNA is replicated, a strand of the parent DNA is preserved

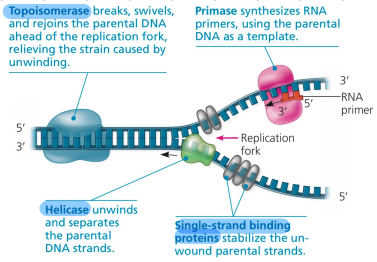


DNA Replication:

- **origin of replication:** short stretches of DNA that have a specific sequence of nucleotides, where DNA replication starts off
- proteins that initiate DNA replication recognize this sequence & attach to DNA, separating the two strands & opening up a replication bubble, replication then continues in both directions until the entire molecule is copied
- In eukaryotic cells, multiple replication bubbles form & eventually fuse
- **replication fork:** Y-shaped region where parental strands of DNA are being unwound, and they are found at the end of replication bubbles



- **helicase:** enzyme that untwists the double helix at replication forks, making parental strands separate & available as template strands (helix → enzyme that ends in -ase)
- **Single-strand binding proteins:** bind to separated DNA strands, keeping them from repairing
- **Topoisomerase:** enzyme that relieves strain of untwisting of the double helix by breaking, swiveling, & rejoining DNA strands



- the enzymes that synthesize DNA cannot initiate its replication, they can only add nucleotides to an existing chain that is base-paired with the template strand
- **primer:** RNA chain that is produced during DNA synthesis and can be used as a pre-existing chain
- **primase:** enzyme that synthesizes primer.
- primase starts a complementary RNA chain with a single RNA nucleotide & adds RNA nucleotides one at at atime, using the parental DNA strand as a template
- The completed primer is thus base-paired to the template strand
- The new DNA strand will start from the 3' end of the RNA primer
- **DNA polymerase:** enzymes that catalyze the synthesis of new DNA nucleotides to the 3' end of a pre-existing chain

- each nucleotide to be added to a growing DNA strand consists of a sugar attached to a base & to 3 phosphate groups → similar to ATP
- difference between ATP & dATP, adenine nucleotide used to make DNA, is the sugar component, which is deoxyribose in DNA & ribose in RNA
- nucleotides used for DNA synthesis are chemically reactive, partly because their triphosphate tails have an unstable cluster of (-) charge
- DNA polymerase catalyzes the addition of each monomer to the growing end of a DNA strand by a **condensation reaction** → 2 phosphate groups are lost as a molecule of pyrophosphate

→ Antiparallel Elongation:

- The 2 new strands formed during DNA replication must also be Antiparallel to their template strands
- Since DNA polymerase can only add nucleotides to the 3' end, the new DNA strand can elongate only in the 5'→3' direction
- DNA polymerase III is the DNA polymerase that synthesizes a complementary strand
- **leading strand:** DNA strand that is made by DNA pol III continuously adding nucleotides (elongating) in the 5'→3' direction. Only 1 primer is required for DNA pol III to synthesize the entire leading strand
- **lagging strand:** DNA strand that is synthesized in the opp 5'→3' direction. It is elongated discontinuously
- **okazaki fragments:** segments of the lagging strand

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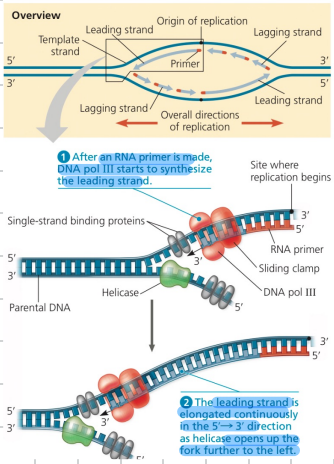
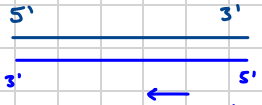
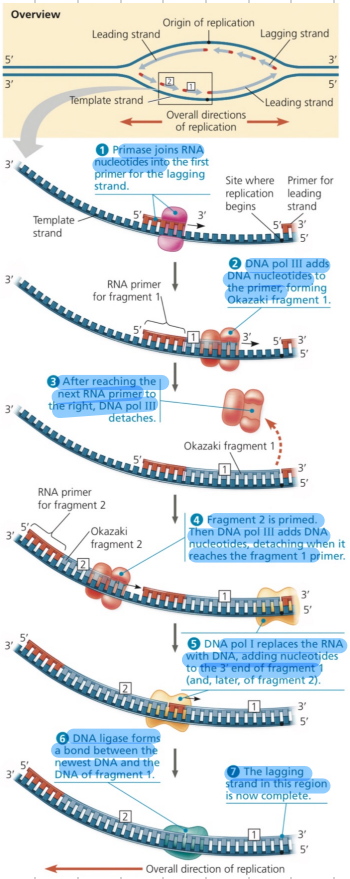




→ **the leading strand:**

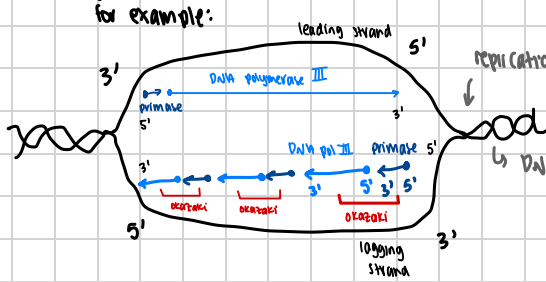
- synthesized in the 5'→3' direction
- synthesized continuously
- RNA primer → DNA pol III
- moves in the same direction as the replication fork



→ **lagging strand:**

- synthesized discontinuously
- moves in the opposite direction of the replication fork
- each Okazaki fragment must be primed separately
- primase begins synthesis of the RNA primer
- DNA pol III continues synthesis in the 5'→3' direction
  - ↳ BUT, since the strand is being synthesized in the opposite direction of the replication fork, RNA primase has to keep starting off synthesis

↓ for example:



- DNA pol III detaches from fragment once it reaches another primer
- DNA pol I replaces the RNA nucleotides with DNA, adding to the 3' end which leaves gaps in the strand
- DNA ligase forms bonds between DNA (from pol I) and DNA (from pol III)
- primase, RNA primer, DNA pol III, DNA pol I, DNA ligase

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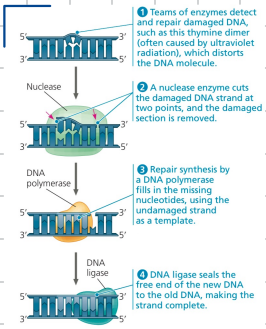
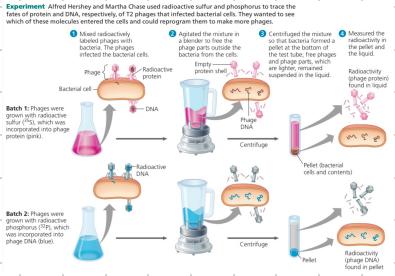
- **proofreading and repairing DNA:**
  - base-pair errors occur at a rate of $1:10^5$ nucleotides
  - errors in the completed DNA occur every $1:10^{10}$ nucleotides
    - ↳ why? because during DNA replication, many DNA polymerases proofread each nucleotide against its template
      - when an incorrectly paired nucleotide is found, polymerase removes it and continues synthesis
  - **mismatch repair:** other enzymes remove & replace incorrectly paired nucleotides
  - DNA can be damaged by exposure to harmful chemical / physical agents → why tanning & excessive exposure to sun can cause skin cancer
  - **nuclease:** DNA cutting enzyme that cuts out damaged segments of DNA, resulting gap is filled in with nucleotides using the undamaged strand as a template
    - ↳ DNA pol and ligase fill in the gaps
  - **nucleotide excision repair:** nuclease cuts out and replaces damaged stretches of DNA



experiments

1. Hershey & Chase:

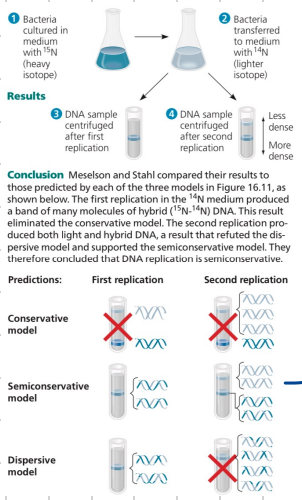


Batch 1: radioactive sulfur
↓
found in proteins

Batch 2: radioactive phosphorus
↓
found in DNA

Conclusion: DNA is the genetic material, not proteins

2. Meselson & Stahl:



→ DNA is semiconservative:
one strand from parent DNA
the other is newly synthesized

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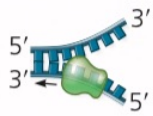
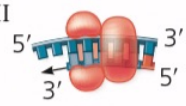
Enzymes used in DNA replication:

Table 16.1 Bacterial DNA Replication Proteins and Their Functions

Protein	Function
Helicase 	Unwinds parental double helix at replication forks
Single-strand binding protein 	Binds to and stabilizes single-stranded DNA until it is used as a template
Topoisomerase 	Relieves overwinding strain ahead of replication forks by breaking, swiveling, and rejoining DNA strands
Primase 	Synthesizes an RNA primer at 5′ end of leading strand and at 5′ end of each Okazaki fragment of lagging strand
DNA pol III 	Using parental DNA as a template, synthesizes new DNA strand by adding nucleotides to an RNA primer or a pre-existing DNA strand
DNA pol I 	Removes RNA nucleotides of primer from 5′ end and replaces them with DNA nucleotides added to 3′ end of adjacent fragment
DNA ligase 	Joins Okazaki fragments of lagging strand; on leading strand, joins 3′ end of DNA that replaces primer to rest of leading strand DNA