

During DNA replication, base pairing enables existing DNA strands to serve as templates for new complimentary strands

- In a second paper Watson and Crick published their hypothesis for how DNA replicates.
 - Because each strand is complementary to each other, each can form a template when separated.
 - The order of bases on one strand can be used to add in complementary bases and therefore duplicate the pairs of bases exactly.
- When a cell copies a DNA molecule (*during S phase of interphase*), each strand serves as a template for ordering nucleotides into a new complimentary strand.
 - One at a time, nucleotides line up along the template strand according to the base-pairing rules.
 - The nucleotides are linked to form new strands.
- Watson and Crick's model, **semiconservative replication**, predicts that when a double helix replicates each of the daughter molecules will have one old strand and one newly made strand.

A large team of enzymes and other proteins carries out DNA replication

- The replication of a DNA molecule begins at special sites, **origins of replication**.
- In eukaryotes, there may be hundreds or thousands of origin sites per chromosome.
 1. Replication begins at specific sites, called origin sites, where the two parental strands separate to form replication bubbles. There are replication forks at each end of the bubble.
 2. The bubbles expand laterally (elongate), as DNA replication proceeds in both directions.
 3. Eventually, the replication bubbles fuse, and synthesis of the daughter strands is complete.
- **DNA polymerases** (proteins) catalyze the elongation of new DNA at a replication fork.
- As nucleotides align with complementary bases along the template strand, they are added to the growing end of the new strand by the polymerases.
- The raw nucleotides are nucleoside triphosphates.
 - Each has a nitrogen base, deoxyribose, and a triphosphate tail.
- As each nucleotide is added, the last two phosphate groups are hydrolyzed to form pyrophosphate.
 - The exergonic hydrolysis of pyrophosphate to two inorganic phosphate molecules drives the polymerization of the nucleotide to the new strand.

- The strands in the double helix are *antiparallel*.
- The sugar-phosphate backbones run in opposite directions.
 - Each DNA strand has a 3' end with a free hydroxyl group attached to deoxyribose and a 5' end with a free phosphate group attached to deoxyribose.
 - The 5' → 3' direction of one strand runs counter to the 3' → 5' direction of the other strand.
- DNA polymerases can only add nucleotides to the free 3' end of a growing DNA strand.
- A new DNA strand can only elongate in the 5' → 3' direction.
- This creates a problem at the replication fork because one parental strand is oriented 3' → 5' into the fork, while the other antiparallel parental strand is oriented 5' → 3' into the fork.
- At the replication fork, one parental strand (3' → 5' into the fork), the **leading strand**, can be used by polymerases as a template for a continuous complimentary strand.
- The other parental strand (5' → 3' into the fork), the **lagging strand**, is copied away from the fork in short segments (Okazaki fragments).
- Okazaki fragments, each about 100-200 nucleotides, are joined by **DNA ligase** to form the sugar-phosphate backbone of a single DNA strand.
- DNA polymerases cannot *initiate* synthesis of a polynucleotide because they can only add nucleotides to the end of an existing chain that is base-paired with the template strand.
- To start a new chain requires a **primer**, a short segment of RNA (about 10 nucleotides long in eukaryotes).
- **Primase**, an RNA polymerase, links ribonucleotides that are complementary to the DNA template into the primer.
- After formation of the primer, DNA polymerases can add deoxyribonucleotides to the 3' end of the ribonucleotide chain.
- Another DNA polymerase later replaces the primer ribonucleotides with deoxyribonucleotides complimentary to the template.

- In addition to primase, DNA polymerases, and DNA ligases, several other proteins have prominent roles in DNA synthesis.
- A **helicase** untwists and separates the template DNA strands at the replication fork.
- **Single-strand binding proteins** keep the unpaired template strands apart during replication.
- To summarize, at the replication fork, the leading strand is copied continuously into the fork from a single primer.
- The lagging strand is copied away from the fork in short segments, each requiring a new primer.