The replication of DNA

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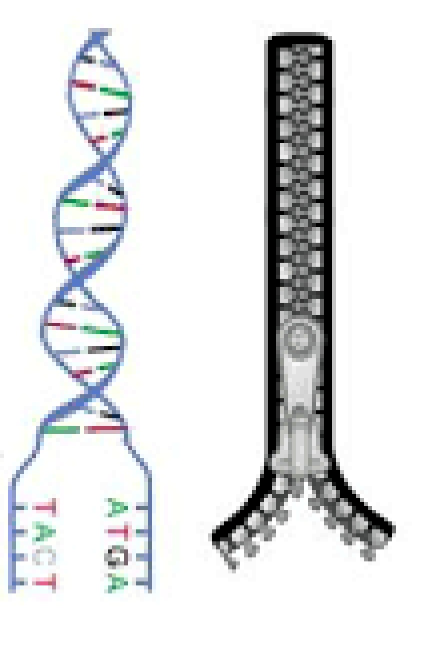
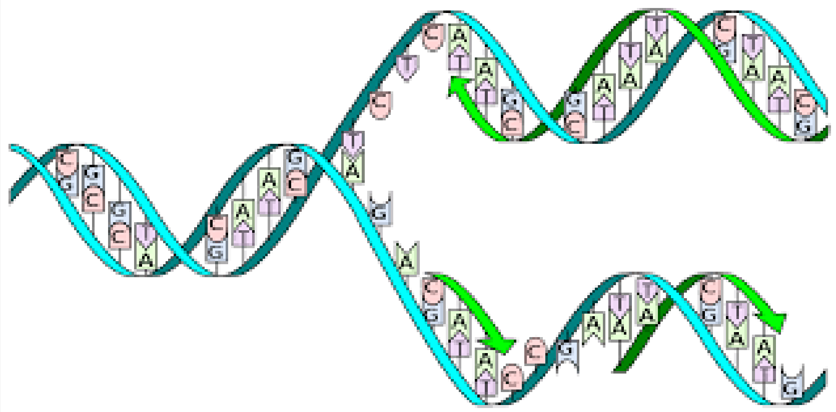
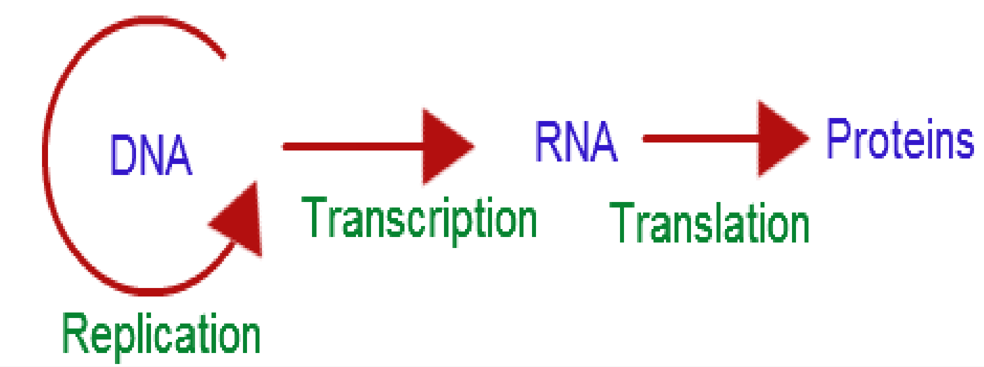
Lecture questions

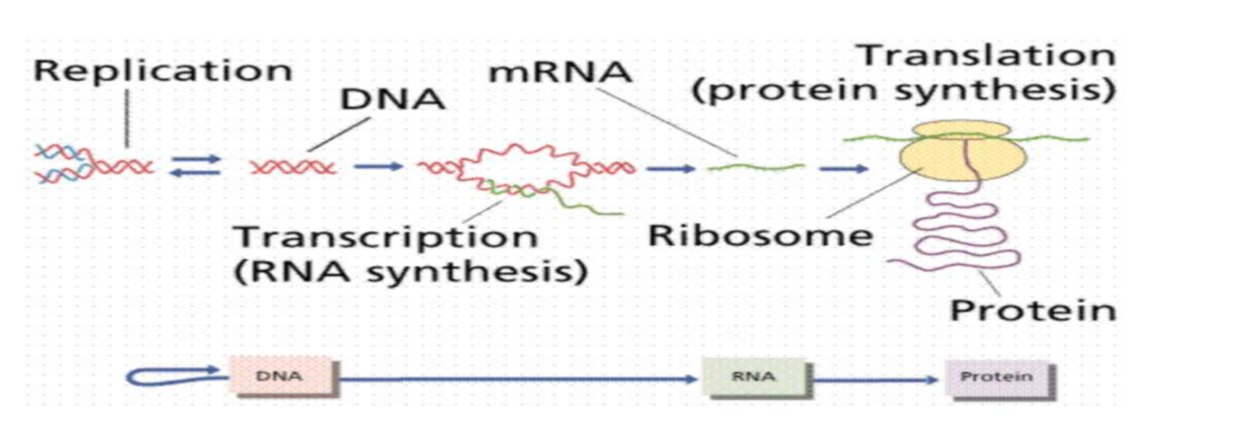


- What is the **Central dogma**
- Learn about the process of **DNA replication**
- Clarify the steps of DNA replication



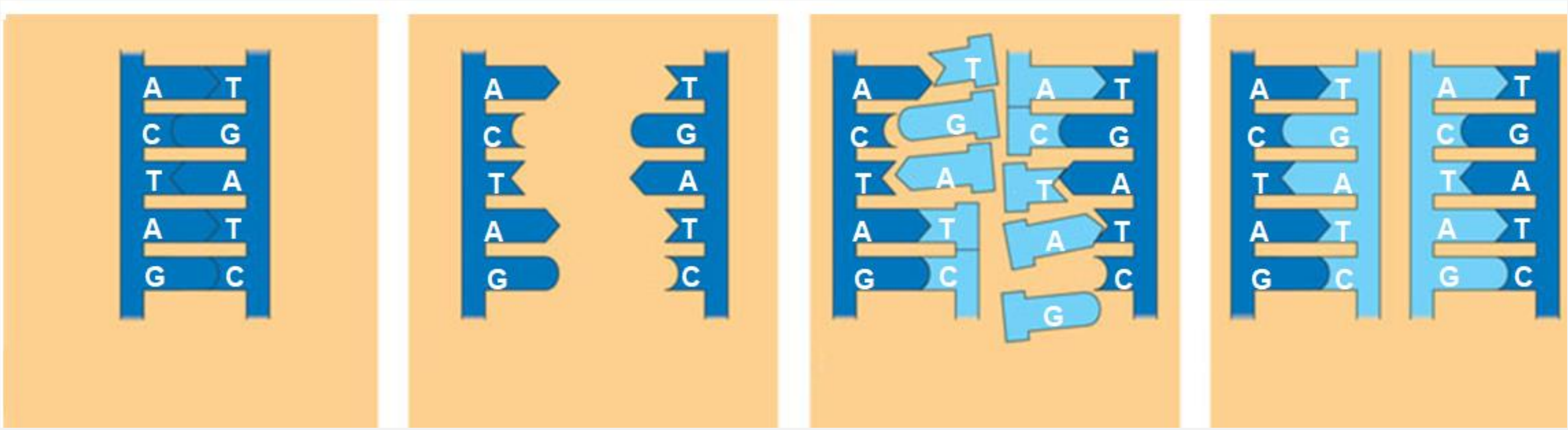
Central Dogma of Molecular Biology





In DNA replication

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

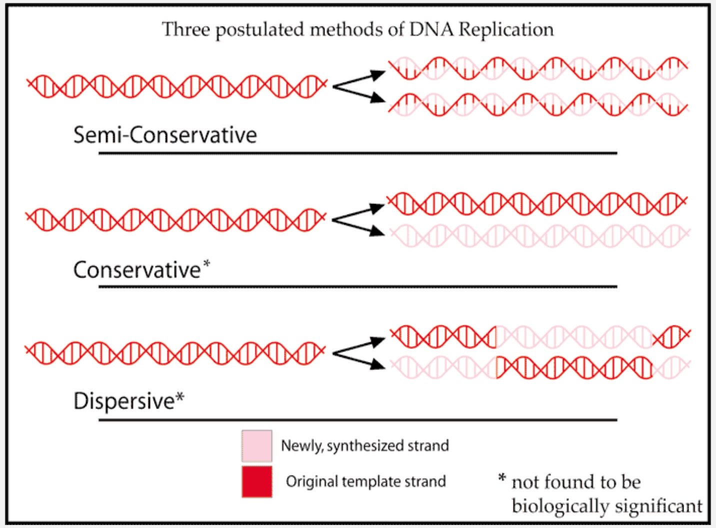


Three Possible Types of DNA Replication

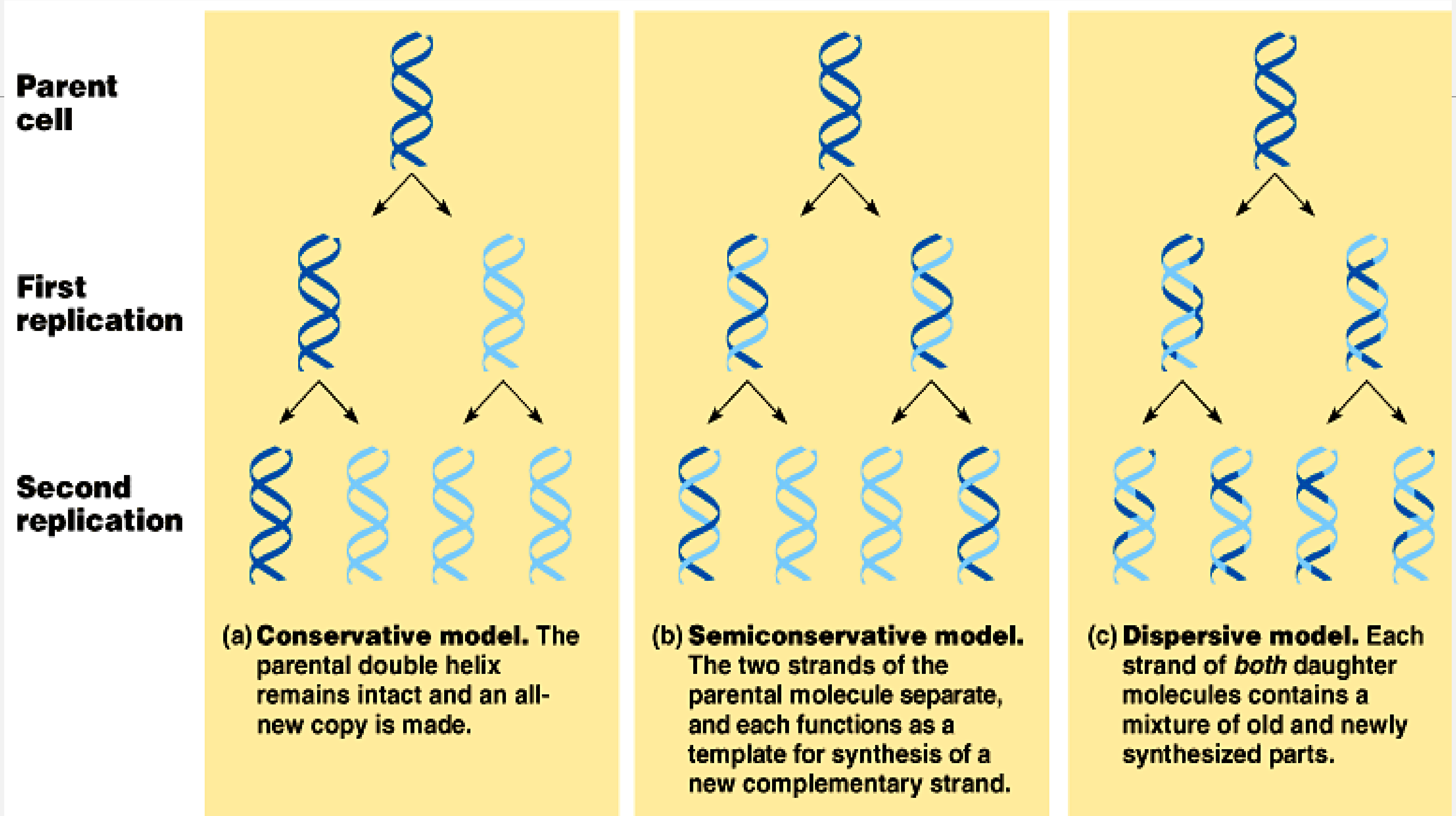
1. Conservative: The two parental strands associate after acting as templates for new strands, thus restoring the parental double helix.

2. Semiconservative: The two strands of the parental molecule separate, and each functions as a template for synthesis of a new, complementary strand.

3. Dispersive: Each strand of both daughter molecules contains a mixture of old and newly synthesized DNA.



Possible Scenarios for DNA Replication

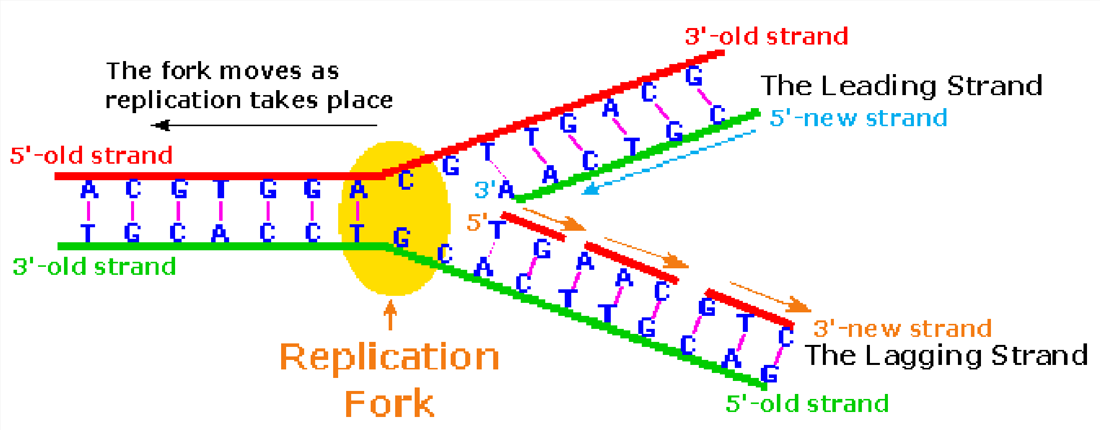


DNA Replication

- DNA replication is a process in which the DNA divides into two same copies during cell division, the genetic information is duplicated to produce two identical copies of the genome of an individual.
- It is occurs during the Synthesis Phase, or S phase of the cycle of a cell, before the process of mitosis or meiosis.
- Each of the two new daughter molecules will have one old strand, derived from the parent molecule, and one newly made strand.
- More than a dozen enzymes and other proteins participate in DNA replication.

General feature of DNA replication

- **In nature DNA replication is semiconservative.**
- It is bidirectional process.
- It proceed from a specific point called origin.
- It proceed in 5’-3’ direction.
- It is a multi-enzymatic process.



DNA replication steps

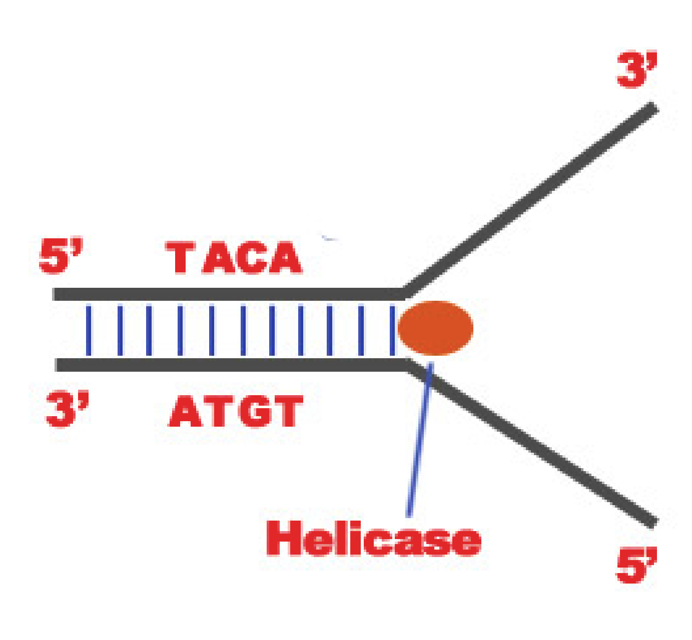
1. Initiation and Unwinding
2. Primer Synthesis
3. Elongation

Initiation and Unwinding

Step One

The point at which the replication begins is known as the Origin of Replication (oriC). An enzyme called **Helicase** breaks the hydrogen bonds between the bases of the two antiparallel strands. The strands are initially split apart in areas that are rich in A-T base paris (weak hydrogen bonds that have only two bonds between Adenine and Thymine) , forming a **replication fork**.

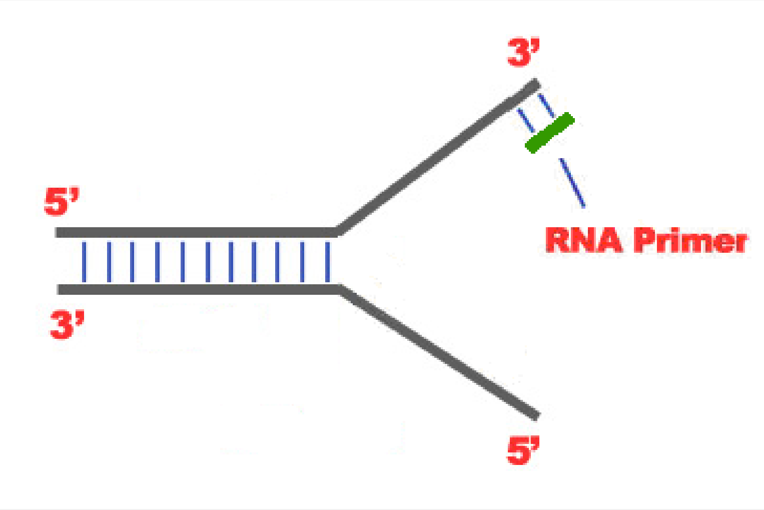
DNA Gyrase (also called Topoisomerase) relieves tension that builds up as a result of unwinding. Single strand binding proteins (SSBs) help to stabilise the single stranded DNA



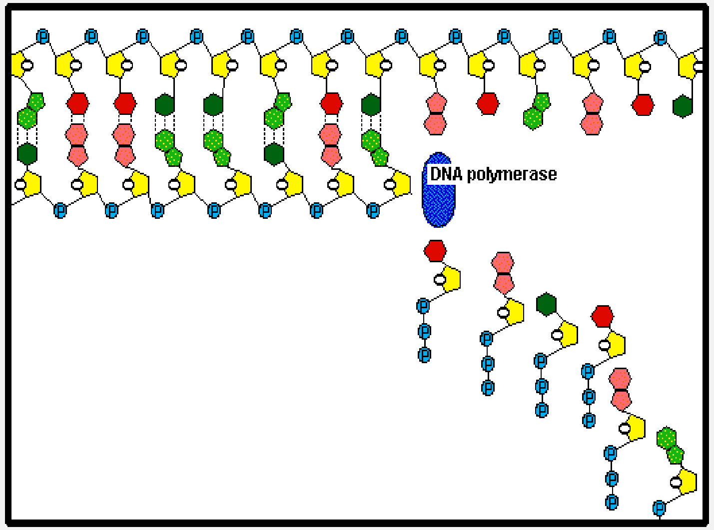
Primer Synthesis

Step Two

RNA polymerase (also known as **RNA Primase**) synthesizes short RNA nucleotides sequences that act as primers (starters). These essentially provide a starting point for DNA replication.



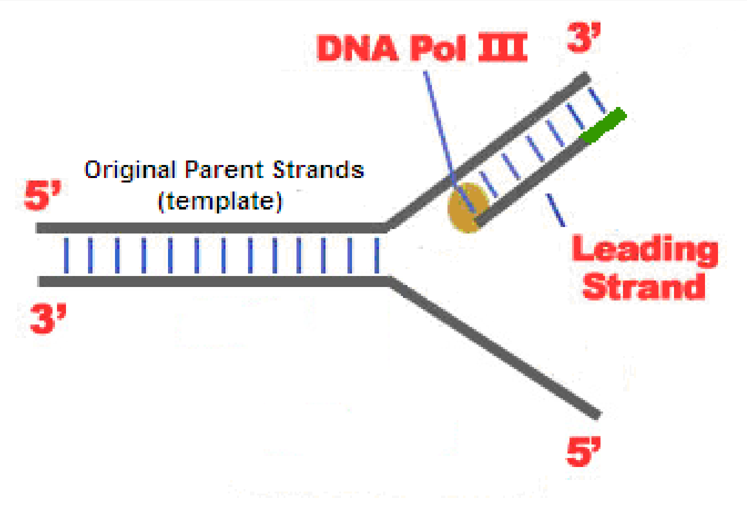
- Primase are required because DNA polymerases III, that makes the new strand by reading the nucleotides on the template strand and specifically adding one nucleotide after the other. If it reads an Adenine (A) on the template, it will only add a Thymine (T).
- the enzymes responsible for the actual addition of new nucleotides to the new DNA strand,.
- DNA replication can proceed only in the 5'-to-3' direction



Elongation

Step Three

DNA Polymerase III can now start synthesising the new DNA strand using free DNA nucleotides. However, DNA polymerase can only read the original template (parent strand) in the 3’ → 5’ direction (making DNA 5’ → 3’). This is not a problem on the leading strand, because the DNA polymerase can simply continue to read along as the two parent stands continue to unzip.

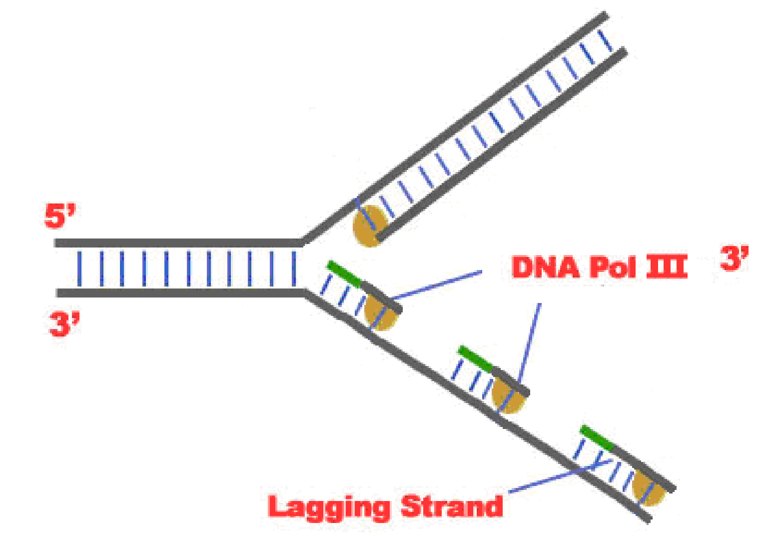


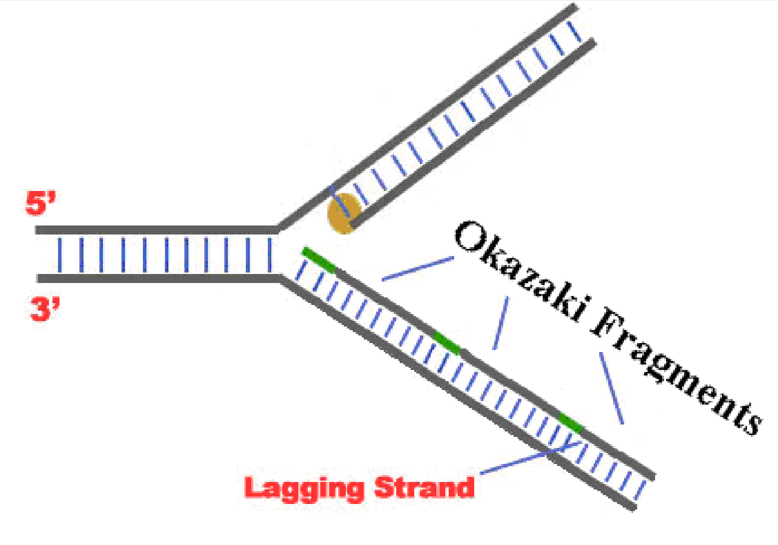
DNA is always synthesized in the 5'-to-3' direction, meaning that nucleotides are added only to the 3' end of the growing strand.

Step Four

On the lagging strand DNA polymerase moves away from the replication fork. As the strands continue to unzip more DNA is exposed and new RNA primers must be added. As a result the lagging strand is synthesised in short bursts as DNA polymerase synthesizes DNA in-between each of the RNA primers.

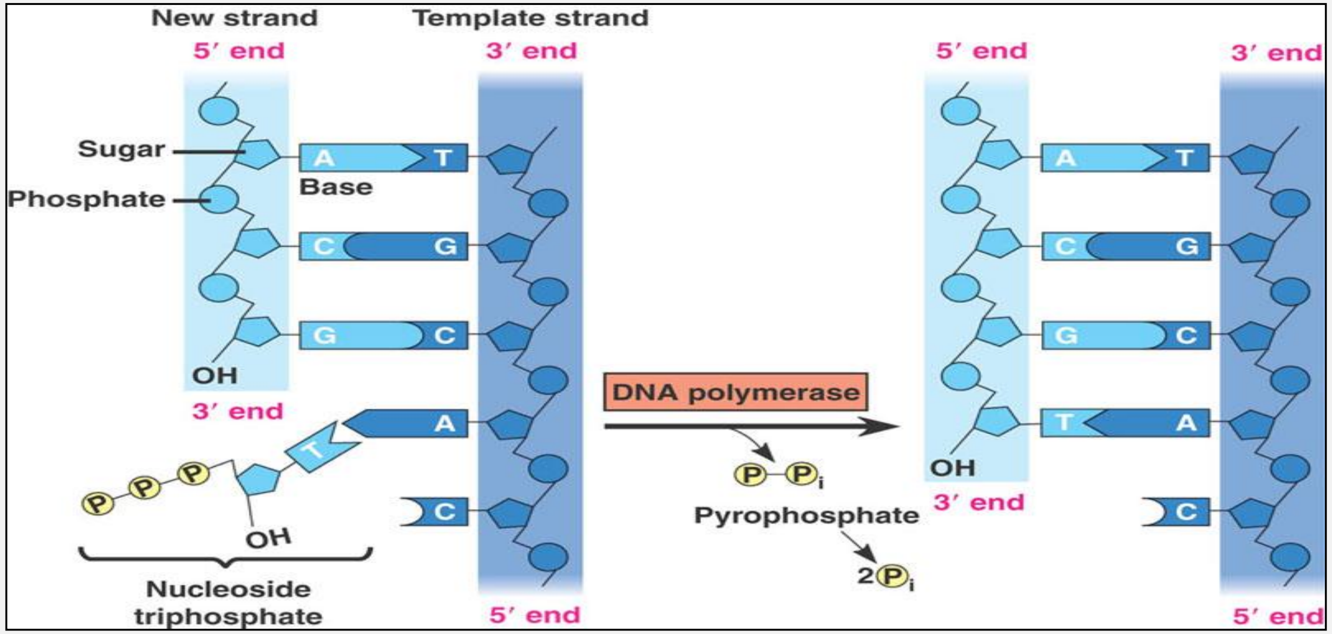
The newly synthesised lagging strand now consists of both RNA and DNA fragments. The DNA fragments are known as Okazaki fragments, after a Japanese scientist who noticed that heating DNA during replication, which separates the strands, gave many small fragments of DNA. From this he concluded that one stand must be synthesized in short bursts of DNA.





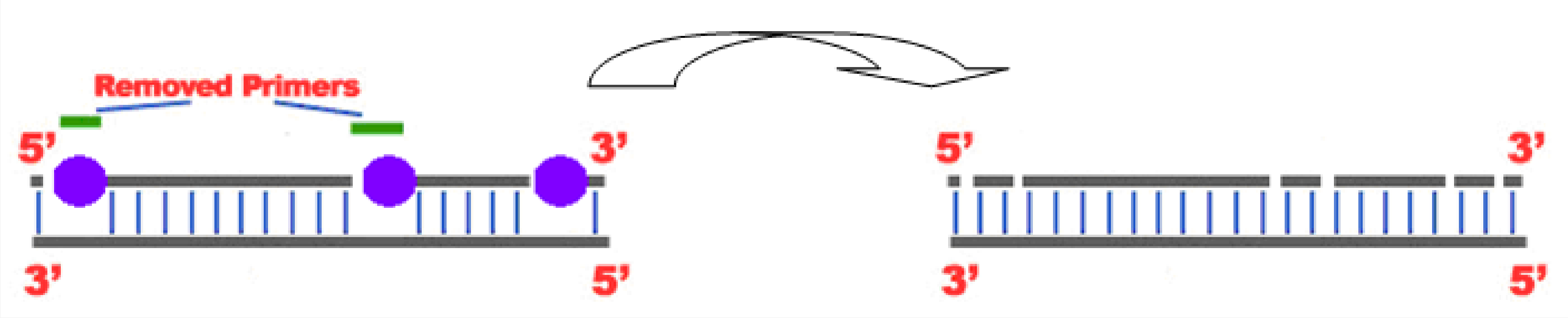
As shown in Figure, the 5'-phosphate group of the new nucleotide binds to the 3'-OH group of the last nucleotide of the growing strand.

Consequently, synthesis proceeds immediately only along the so-called **leading strand**. This immediate replication is known as **continuous replication.**



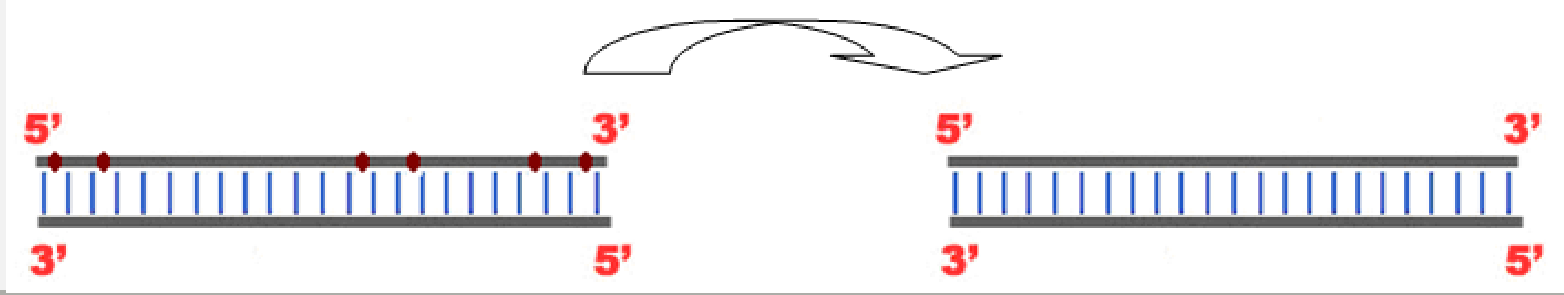
Step Six

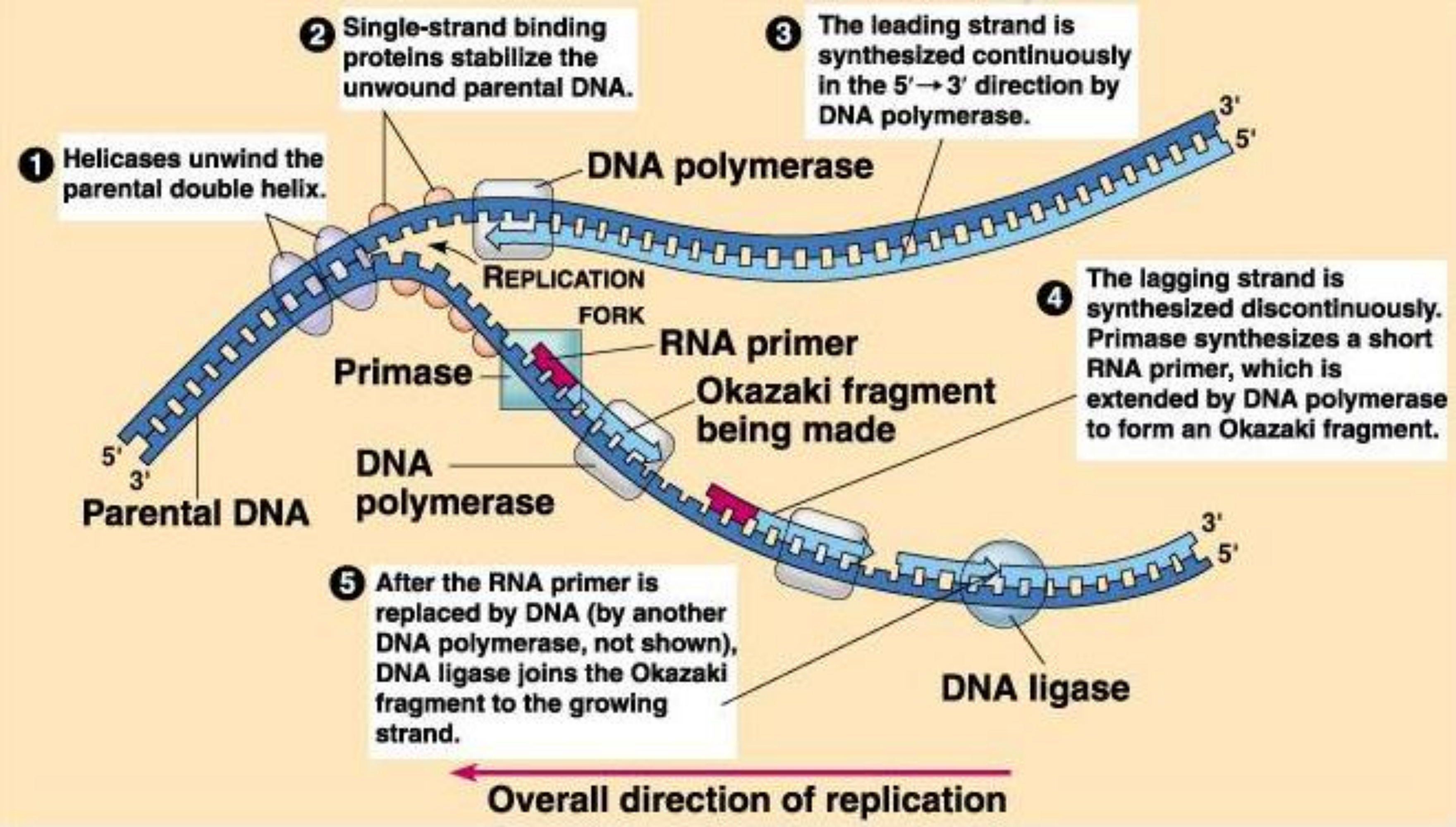
DNA Polymerase I now removes the RNA primers and replaces them with DNA



Step Seven

DNA Ligase joins the DNA fragments of the lagging strand together to form one continuous length of DNA.





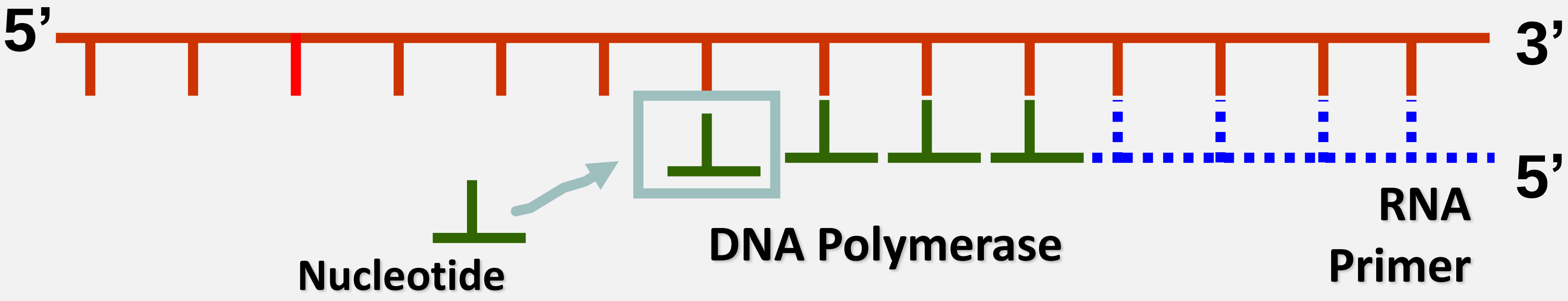
1 Helicases unwind the parental double helix.
2 Single-strand binding proteins stabilize the unwound parental DNA.
3 The leading strand is synthesized continuously in the 5′ → 3′ direction by DNA polymerase.
4 The lagging strand is synthesized discontinuously. Primase synthesizes a short RNA primer, which is extended by DNA polymerase to form an Okazaki fragment.
5 After the RNA primer is replaced by DNA (by another DNA polymerase, not shown), DNA ligase joins the Okazaki fragment to the growing strand.
DNA polymerase
REPLICATION FORK
RNA primer
Primase
Okazaki fragment being made
DNA polymerase
Parental DNA
DNA ligase
3'
5'
Overall direction of replication

Accuracy and Repair

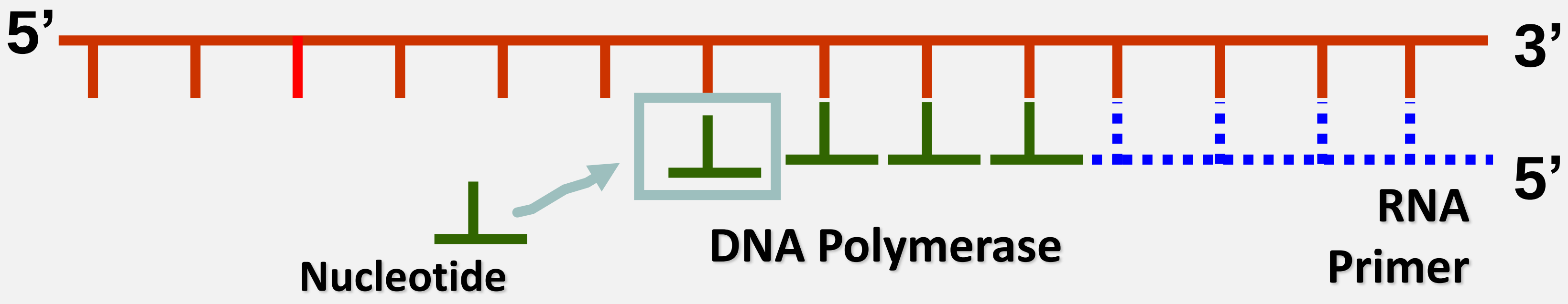
- DNA replication occurs at a surprisingly fast rate. Despite this, errors are very rare.
- DNA replication is very accurate – about 1 error in every 10,000 paired nucleotides.
- DNA has the ability to proofread and repair mistakes.
- An error in replication is known as a MUTATION.
- DNA may also be damaged by a variety of agents which include chemicals and ultraviolet light.

Definitions

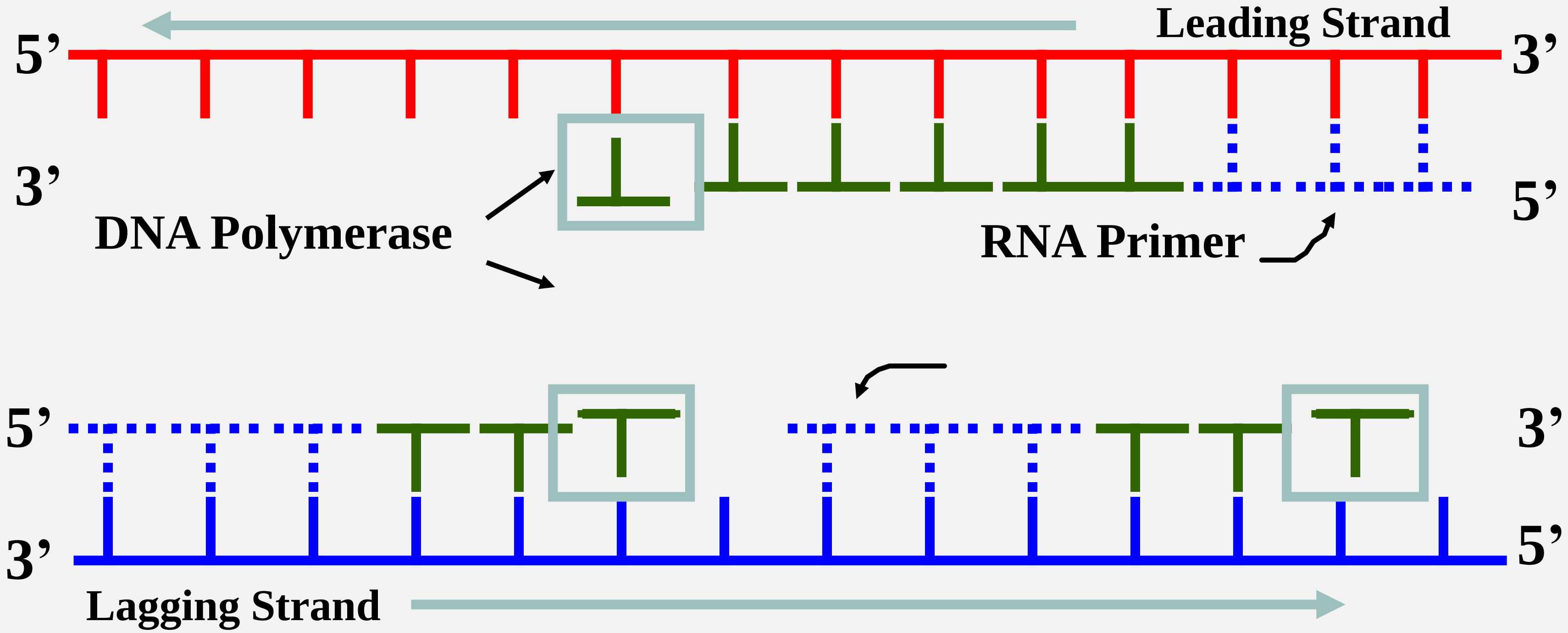
1. DNA Polymerase III: with a RNA primer in place, DNA Polymerase (enzyme) catalyze the synthesis of a new DNA strand in the 5' to 3' direction.



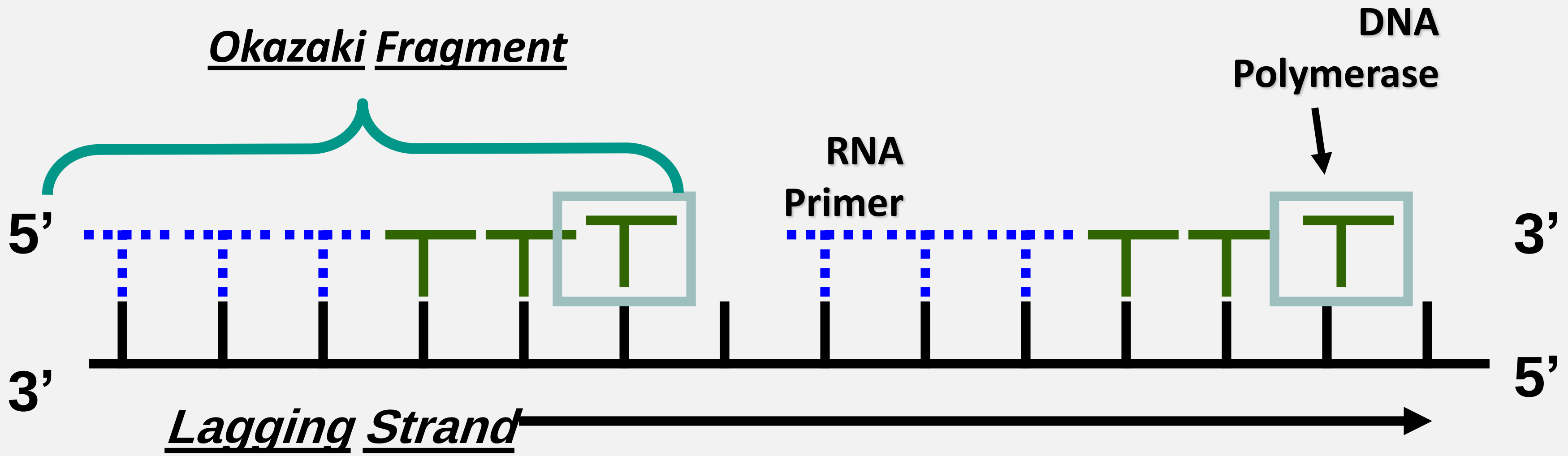
2. Leading Strand: synthesized as a single polymer in the 5' to 3' direction



3. Lagging Strand: also synthesized in the 5’ to 3’ direction, but discontinuously against overall direction of replication.

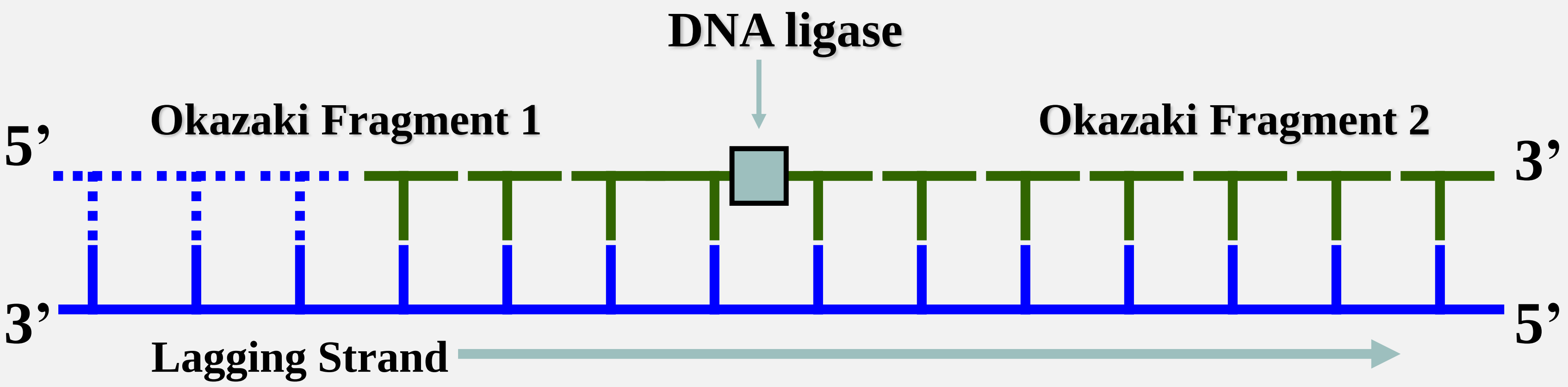


4. **Okazaki Fragments**: series of short segments on the lagging strand



5. **DNA ligase**: a linking enzyme that catalyzes the formation of a covalent bond from the 3’ to 5’ end of joining stands.

Example: joining two Okazaki fragments together.



https://www.youtube.com/watch?v=Qqe٤thU-os٨

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