



# Initiating DNA Replication

Phuc Loi Luu, PhD

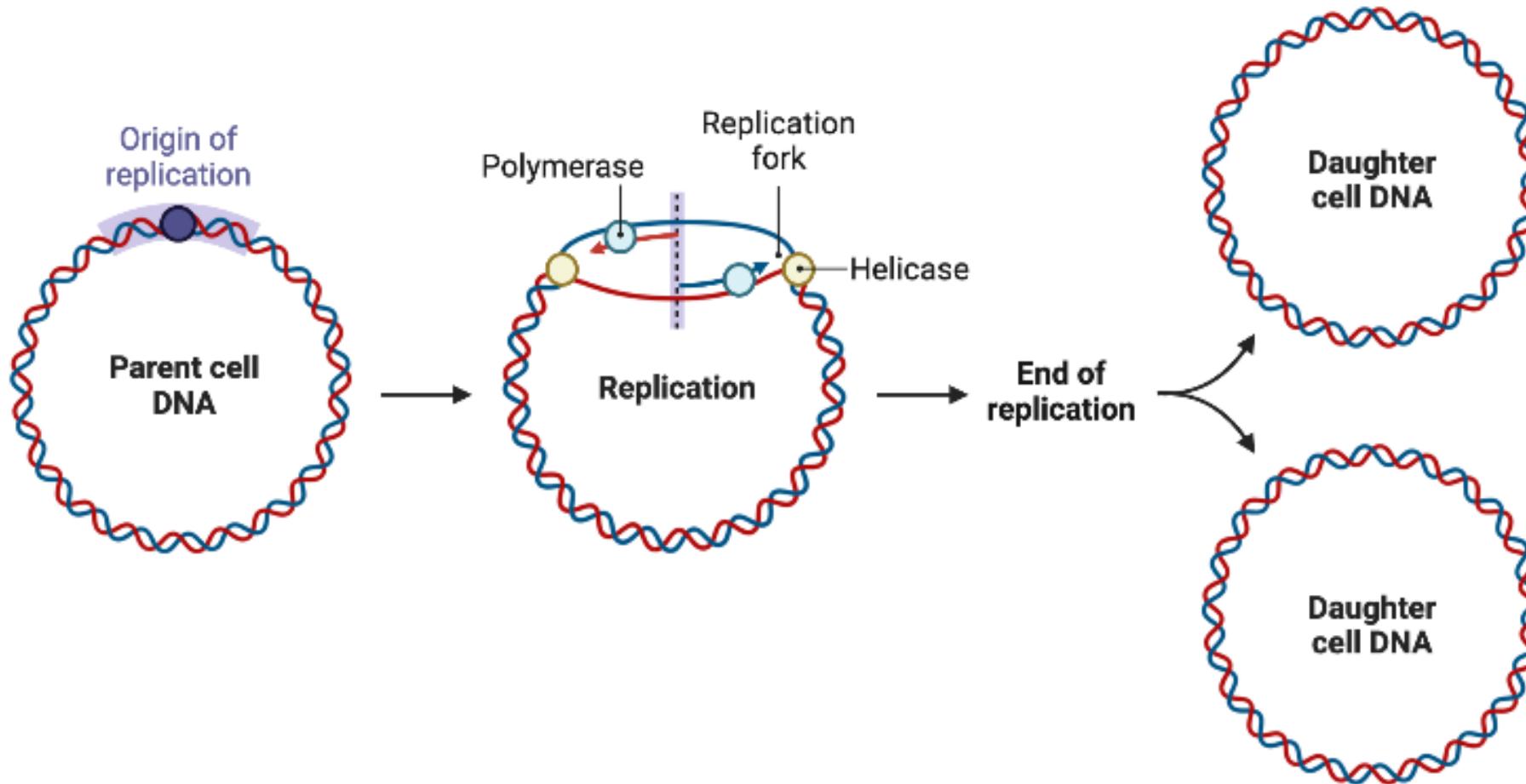
Email: Luu.p.loi@googlemail.com

Zalo: 0901802182

Feb 03 2026

# DNA Replication

## PROKARYOTIC DNA REPLICATION



# Three-stage process of DNA Replication

## 1. Initiation

**a) Origin Recognition:** Replication begins at specific locations called the "origin of replication". Initiator proteins identify these sites, and enzymes like helicase begin to unwind the double helix, forming a "replication fork".

**b) Unwinding and Stabilizing:** Helicase breaks the hydrogen bonds between base pairs, separating the two strands. Single-strand binding proteins coat the DNA around the fork to prevent it from rewinding, while Topoisomerase/Gyrase acts ahead of the fork to prevent excessive supercoiling.

**c) Priming:** DNA primase binds to the template strand and synthesizes a short RNA primer, providing the starting point (a 3' end) for DNA polymerase to begin building the new strand.

## 2. Elongation (Synthesis):

DNA polymerase adds nucleotides to the primer, moving in a 5' to 3' direction.

**a) Leading Strand:** Synthesized continuously toward the replication fork.

**b) Lagging Strand:** Synthesized discontinuously away from the fork in short, 5' to 3' segments called Okazaki fragments, which require multiple primers.

## 3. Termination and Proofreading:

Once the entire strand is copied, RNA primers are removed, and the gaps are filled by DNA polymerase I and sealed by DNA ligase, which joins Okazaki fragments. The newly synthesized DNA is then proofread for errors.

# Beyond the "Ends": Where Replication Begins

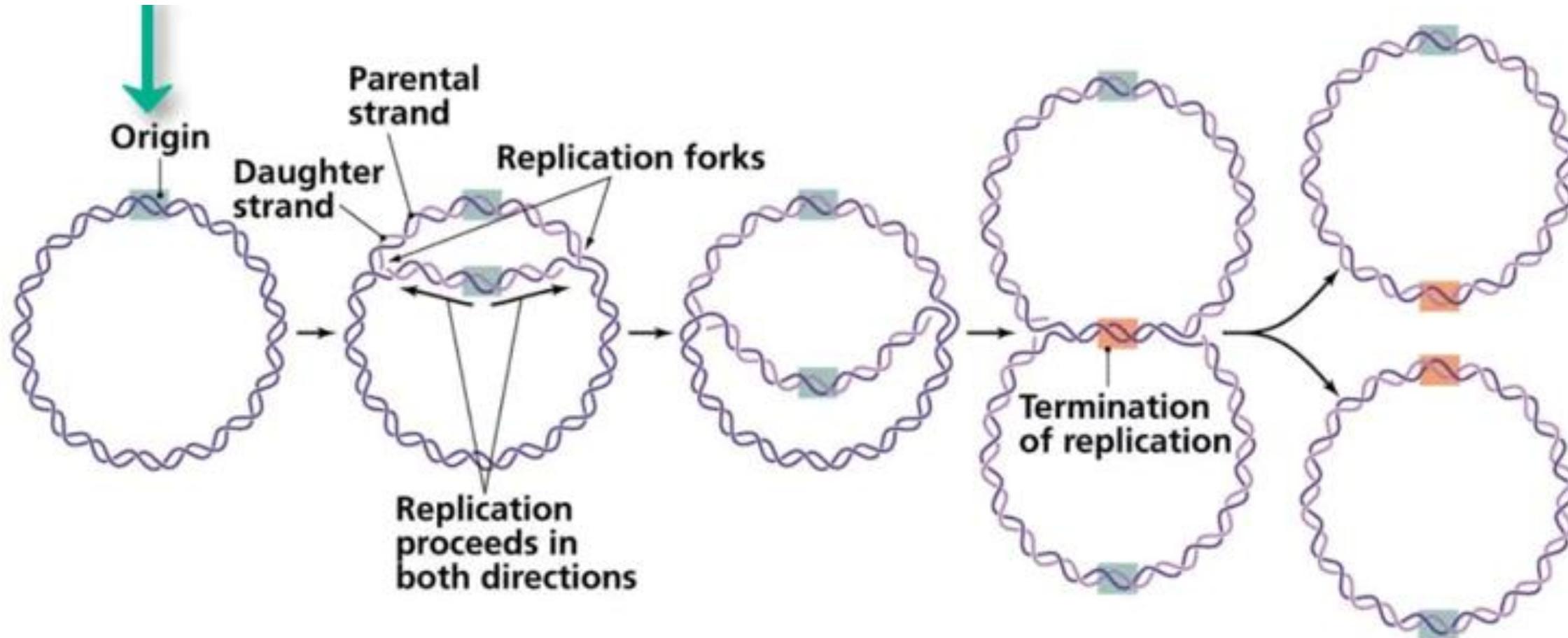
- Most organisms do not start replication at the end of a chromosome.
- Bacteria (*E. coli*): Chromosomes are circular; therefore, there is no "end" to start from.
- Eukaryotes: Though chromosomes are linear, replication still initiates internally rather than at the tips.
- Exceptions: Only a few specific viruses are known to initiate replication from the ends of the genome.

# Some Definitions

Term	Definition
Origin of Replication	The physical site where DNA is initially unwound and synthesis is initiated.
Efficiency	The percentage of cell divisions in which a specific origin initiates.
Replicon	The total region of DNA replicated by the forks derived from a single origin.

- **Origin Efficiency:** Bacterial origins usually initiate at or near 100%, while most eukaryotic origins are much less efficient.
- **Directionality:** Almost all known origins are bi-directional, generating two replication forks that move in opposite directions.

# DNA Replication



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# The Replicon Model

Proposed by Sydney Brenner and François Jacob, this model defines two functional components required for initiation:

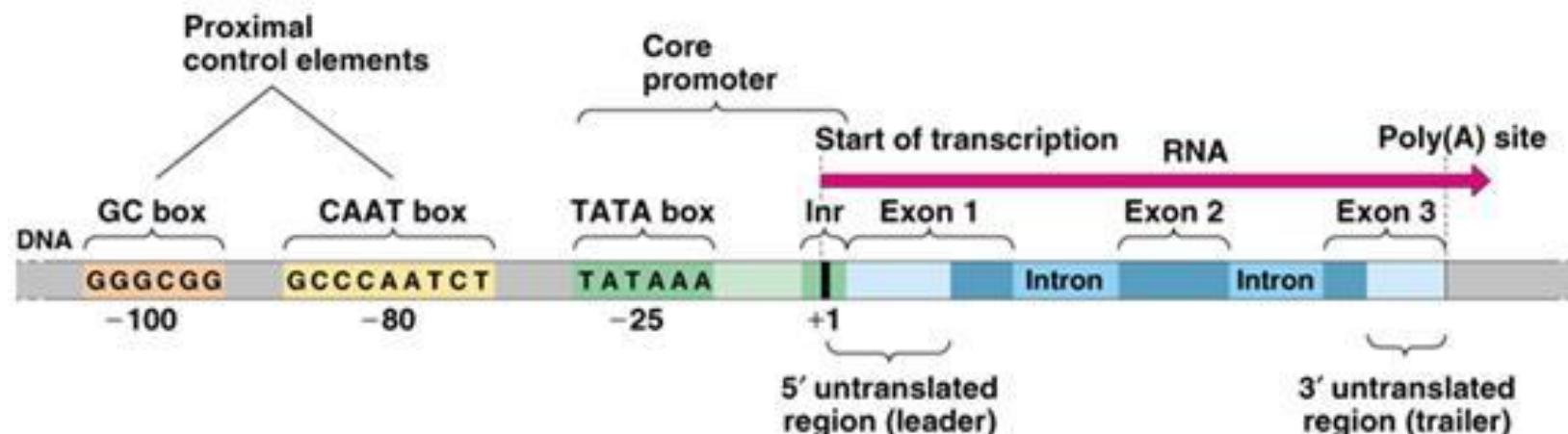
- **The Replicator (Genetic Entity):** The specific DNA sequence required to initiate replication. If essential parts of this sequence are removed, replication will not start.
- **The Initiator (Protein):** A protein that recognizes and binds to the replicator to activate the initiation process.

# Replicator vs. Origin: The Transcription Analogy

It is vital to distinguish between the genetic instructions and the physical action.

"The replicator is to the origin as a promoter is to a transcription start site."

- Overlap: Replicators and origins typically overlap, but they are not identical.
- Size Variance: The replicator is usually the same size or much larger than the origin.
- Extreme Cases: Some replicators exceed 50 Kb in size, while the physical origin may only be a 100 base pair region.



# Test your understanding of the lecture

**1. True or False? Most eukaryotic organisms initiate DNA replication at the very ends of their linear chromosomes.**

Answer: False. In all but a few viruses, replication does not start from the ends.

**2. Efficiency Check: If a specific origin of replication in a eukaryotic cell has an "efficiency" of 60%, what does that mean?**

Answer: It means the origin initiates replication in 60% of cell divisions. Unlike bacterial origins, eukaryotic origins are often much less than 100% efficient.

**3. The Genetic vs. Physical: Which term refers to the physical site where DNA is initially unwound?**

Answer: The Origin of Replication. The "Replicator" is the genetic DNA sequence required for that initiation to occur.

**4. The Initiator's Role: According to the Brenner and Jacob "Replicon Model," what is the function of the Initiator?**

Answer: It is a protein that recognizes and binds to the replicator sequence to activate the initiation of replication.