



Initiating DNA Replication

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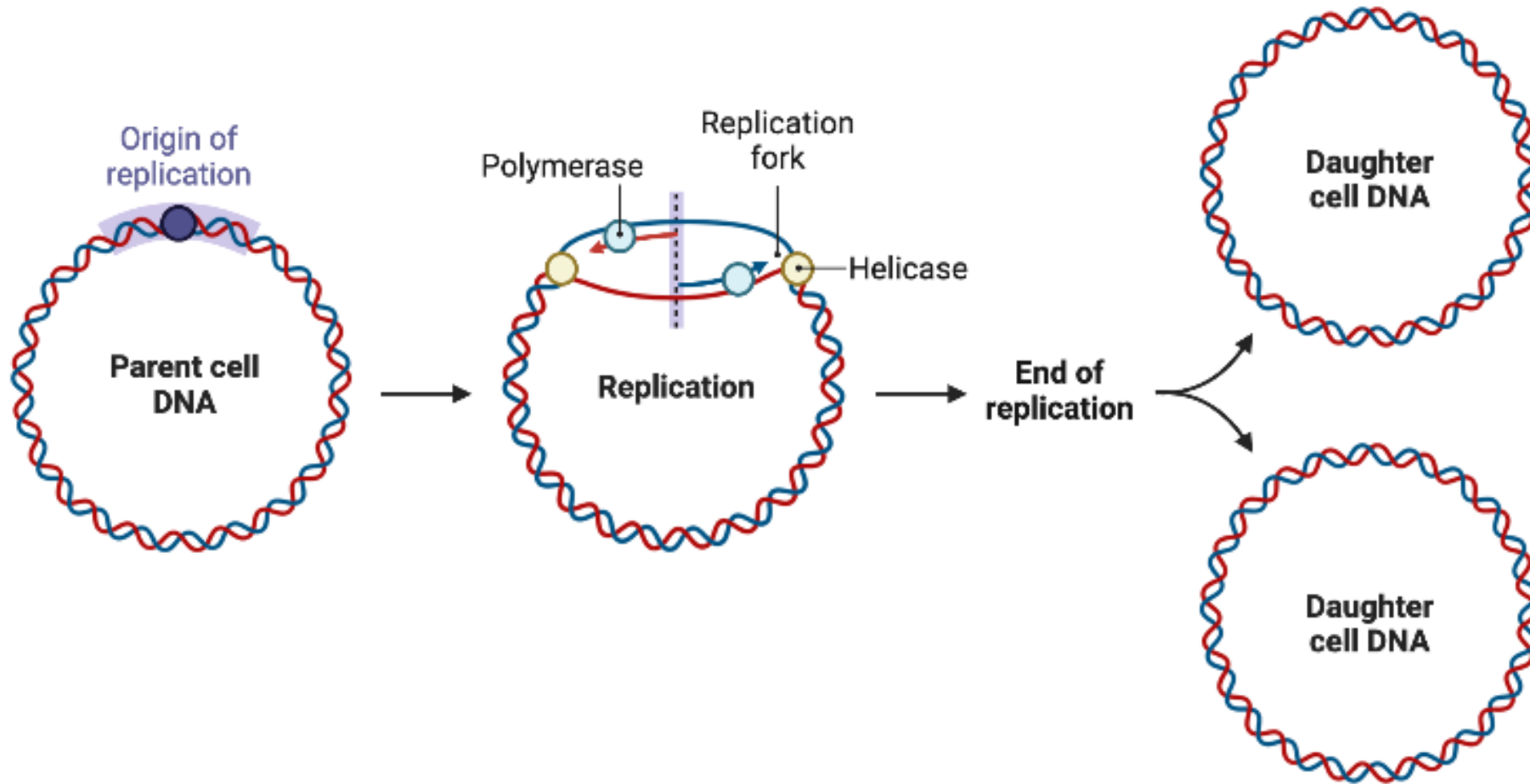
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Feb 03 2026

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

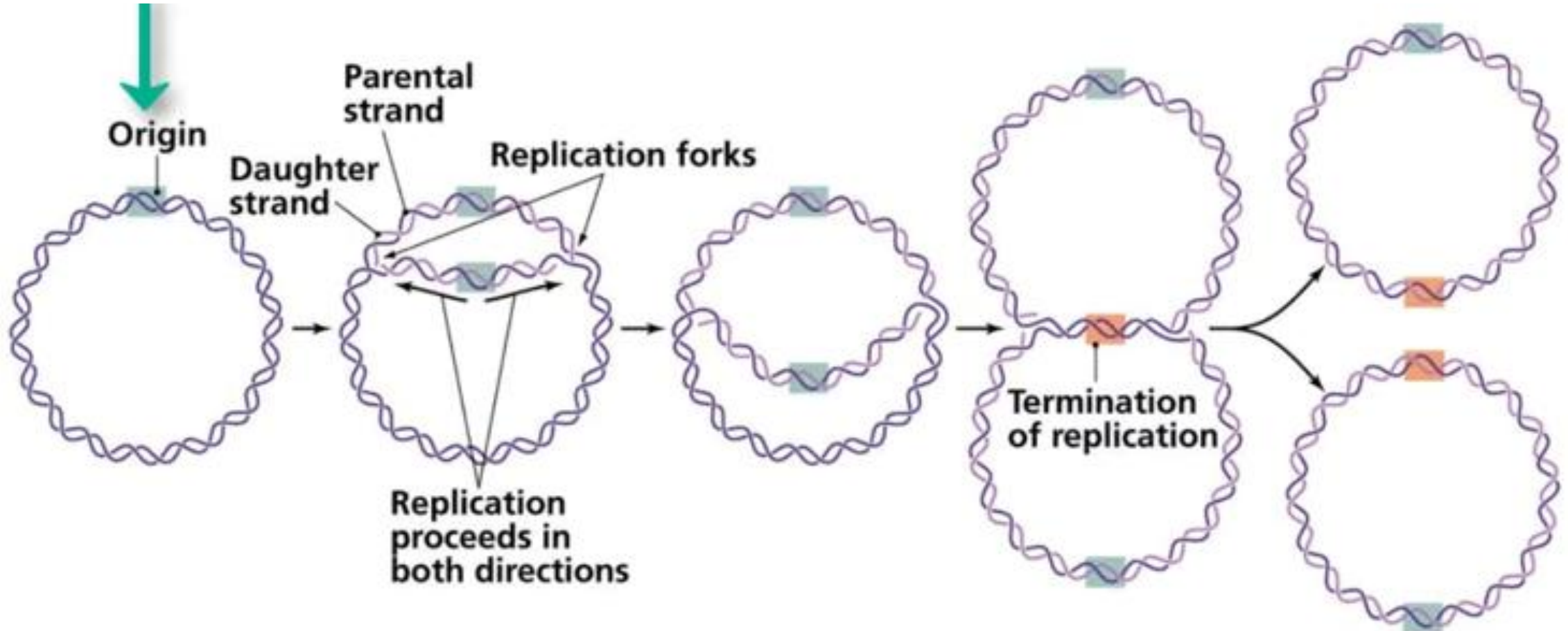
- Most organisms do not start replication at the end of a chromosome.
- Bacteria (E. coli): Chromosomes are circular; therefore, there is no "end" to start from.
- Eukaryotes: Though chromosomes are linear, replication still initiates internally rather than at the tips.
- Exceptions: Only a few specific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



The Replicon Model

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

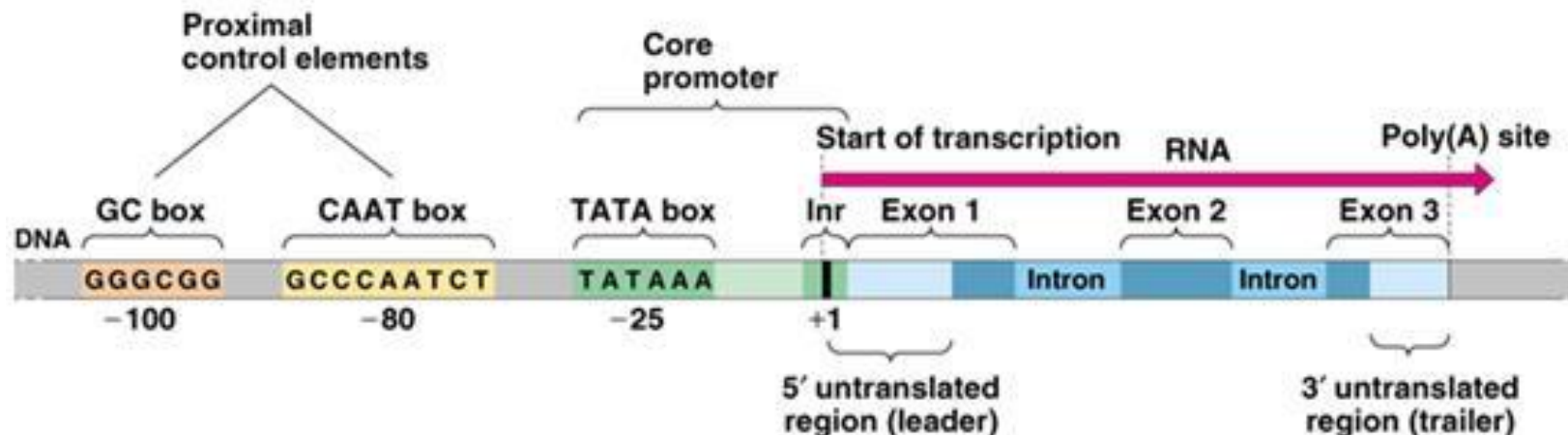
- **The Replicator (Genetic Entity):** The specific DNA sequence required to initiate replication. If essential parts of this sequence are removed, replication will not start.
- **The Initiator (Protein):** A protein that recognizes and binds to the replicator to activate the initiation process.

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.