DNA REPLICATION
Semi Conservative Model

Central dogma

replication transcription translation

NA → RNA → protein

reverse transcription

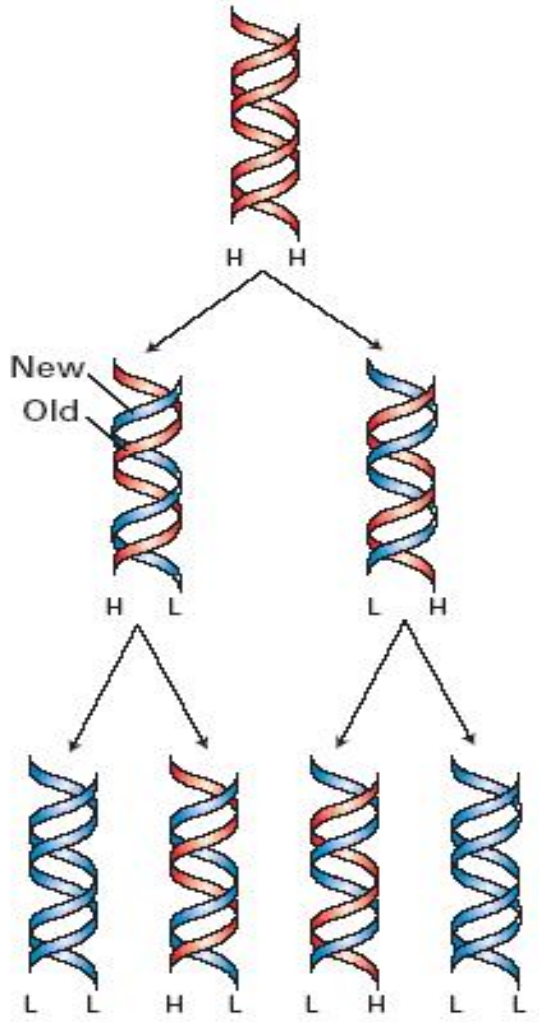
Replication: synthesis of daughter DNA from parental DNA

Transcription: synthesis of RNA using DNA as the template

Translation: protein synthesis using mRNA molecules as the template

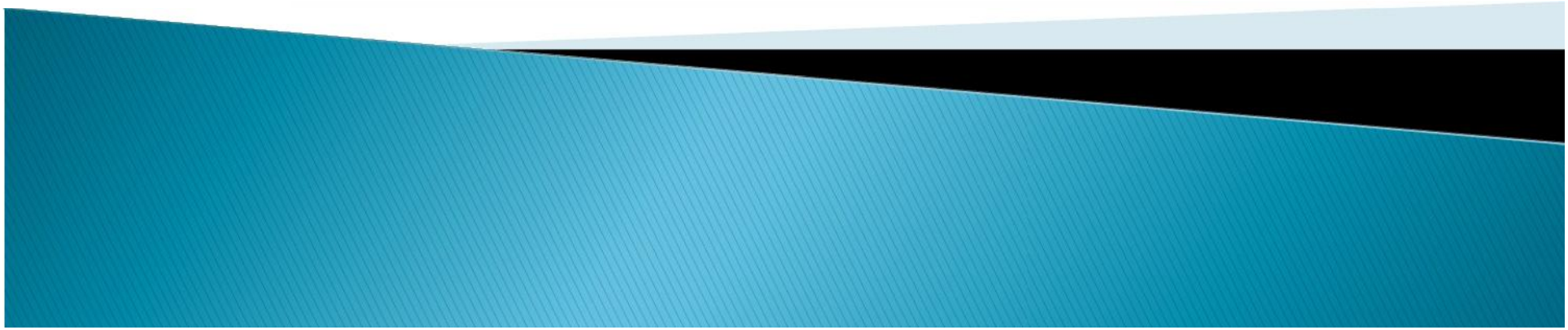
Reverse transcription: synthesis of DNA using RNA as the template

DNA Replication



Section 1

General Concepts of DNA Replication



DNA replication

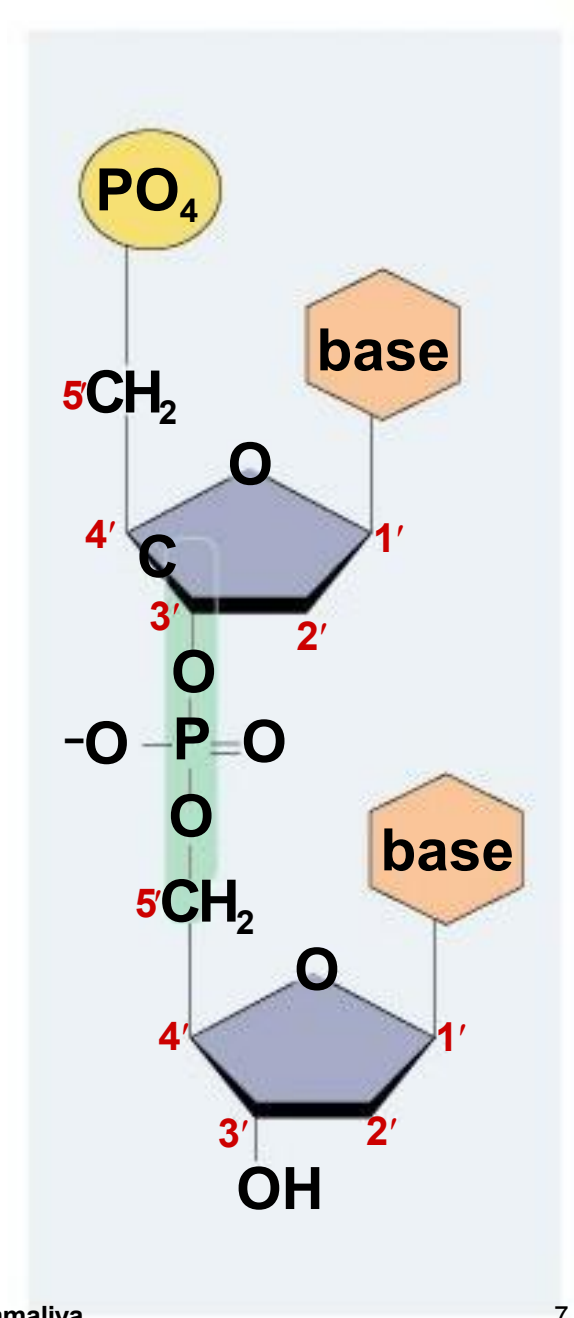
A reaction in which daughter DNAs are synthesized using the parental DNAs as the template.

Transferring the genetic information to the descendant generation.

The DNA backbone

Putting the DNA backbone together

- refer to the 3′and 5′ends of the DNA



DNA replication system

Template: double stranded DNA

Substrate: dNTP

Primer: short RNA fragment with a free 3´-OH end

Enzyme: DNA-dependent DNA polymerase (DDDP),
other enzymes,
protein factor

Characteristics of replication

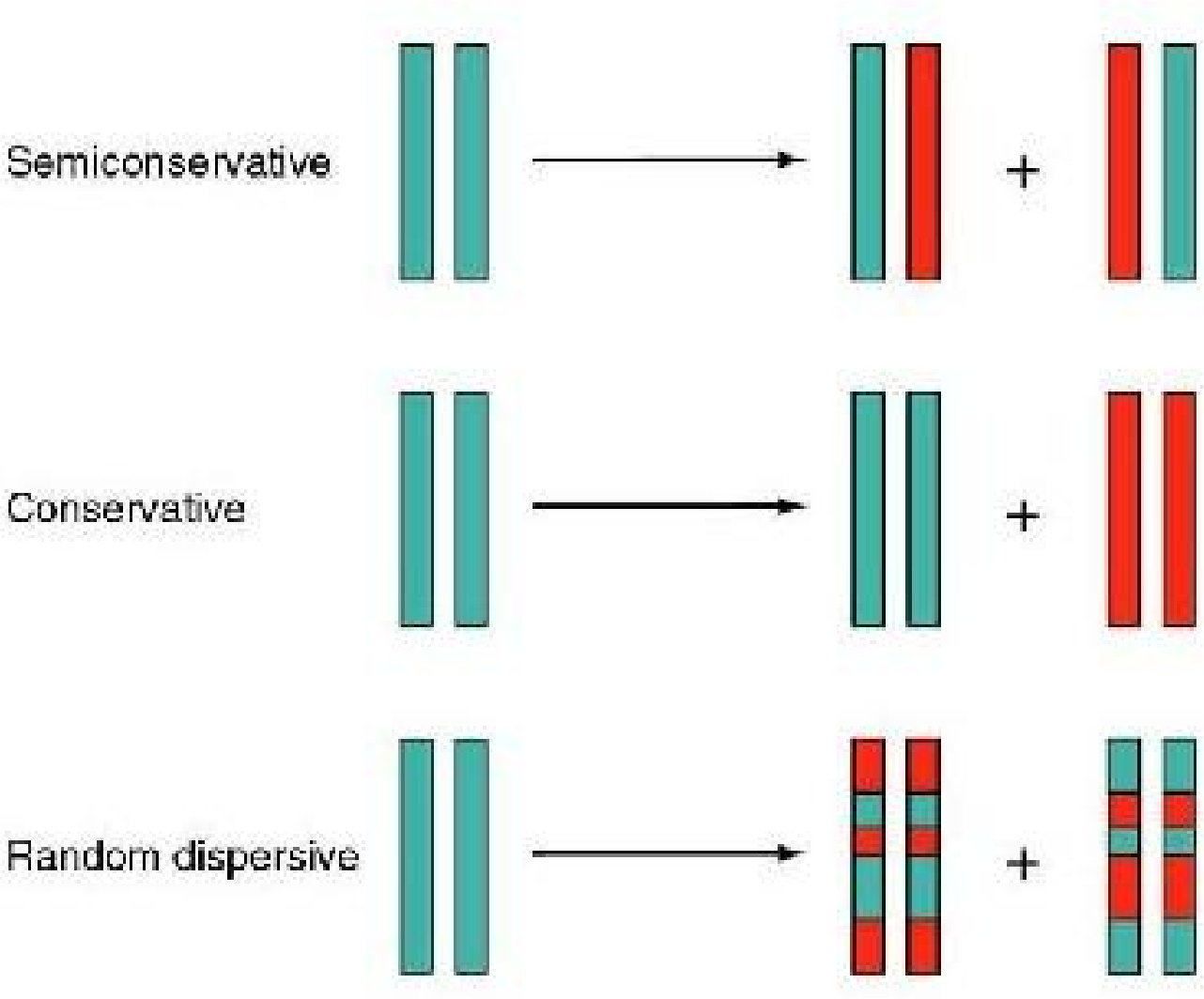
Semi-conservative replication

Bidirectional replication

Semi-continuous replication

High fidelity

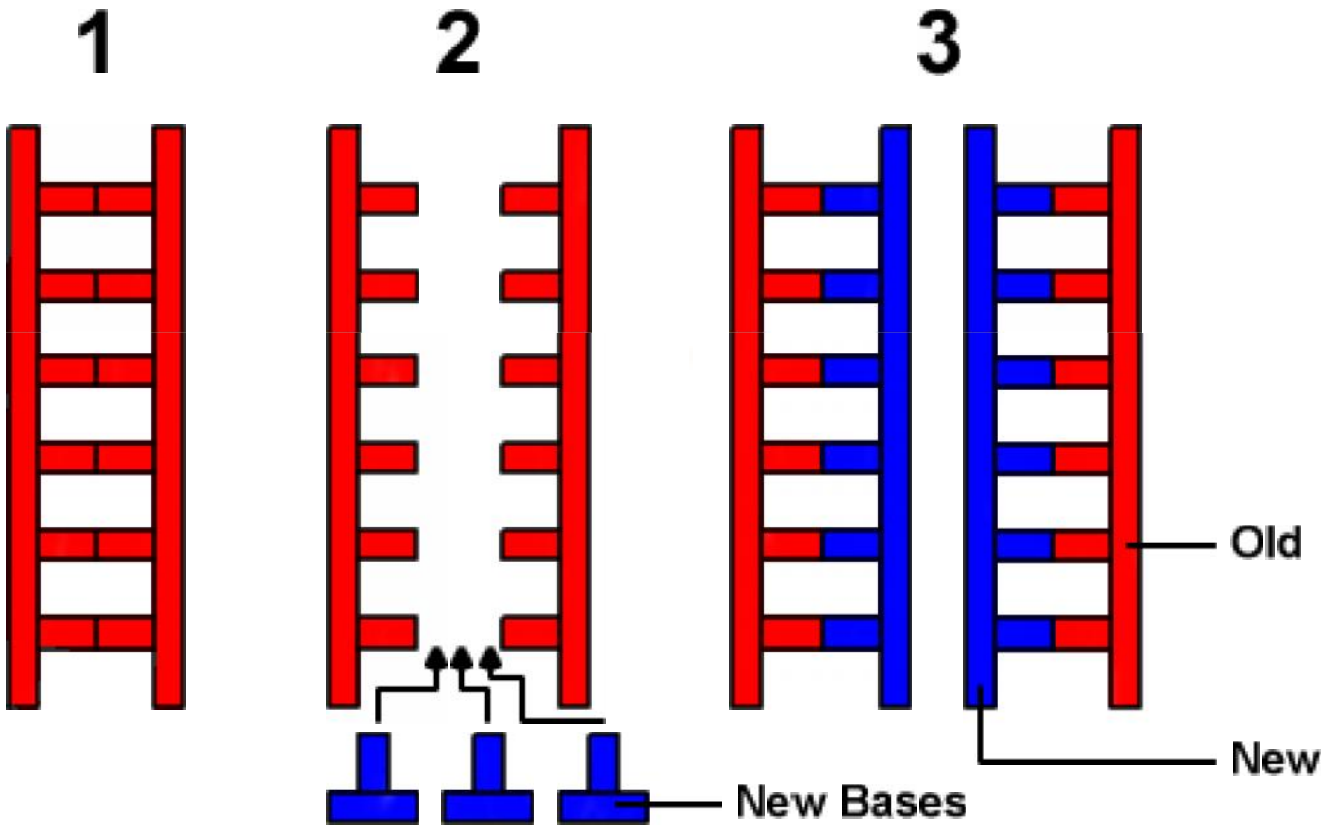
Semi-Conservative Replication



Semiconservative replication

Half of the parental DNA molecule is conserved in each new double helix, paired with a newly synthesized complementary strand. This is called semiconservative replication

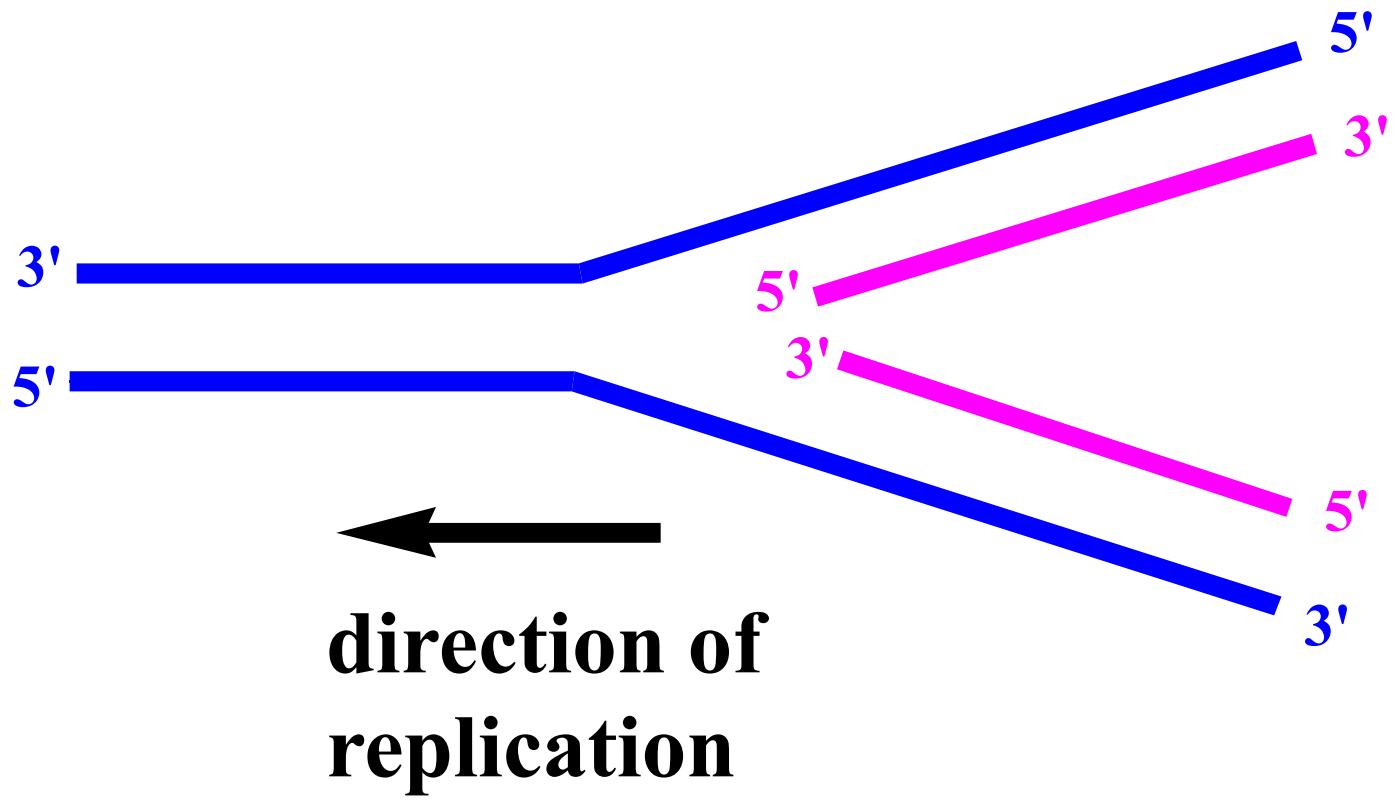
Semiconservative replication



Bidirectional Replication

- **Replication starts from unwinding the dsDNA at a particular point (called origin), followed by the synthesis on each strand.**
- **The parental dsDNA and two newly formed dsDNA form a Y-shape structure called replication fork.**

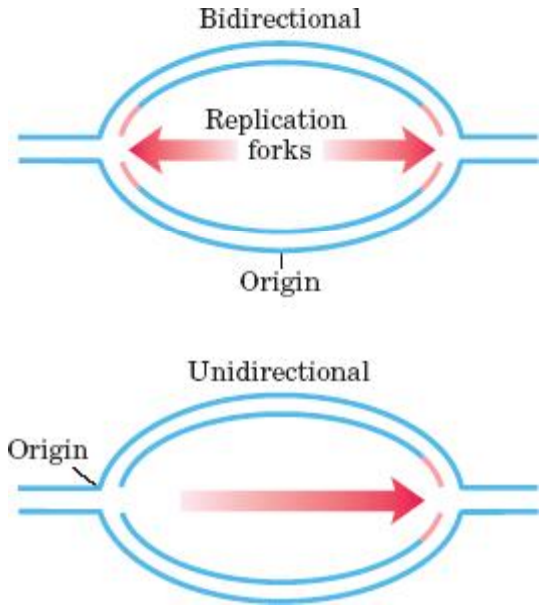
Replication fork



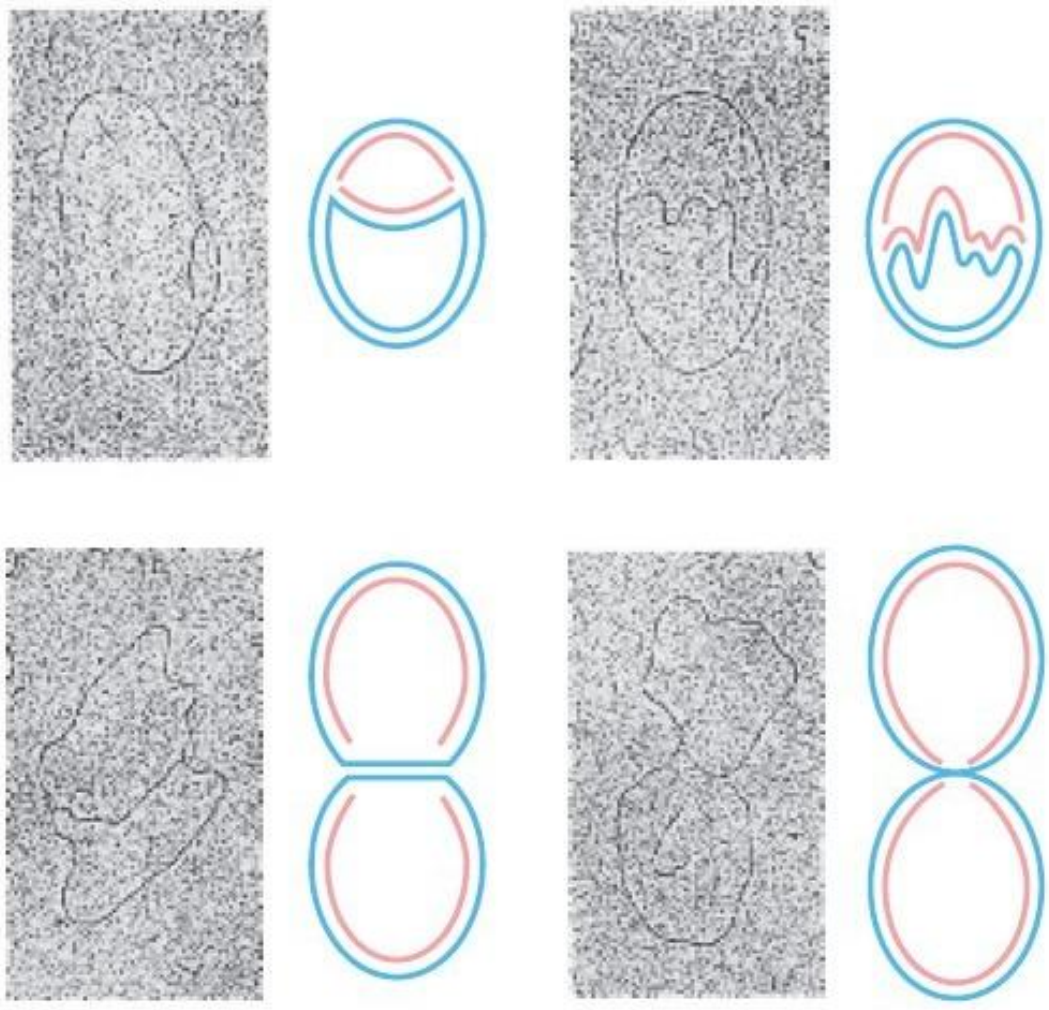
Bidirectional replication

- Once the DNA is opened at the origin, two replication forks are formed spontaneously.
- These two replication forks move in opposite directions as the syntheses continue.

Bidirectional replication



Replication of prokaryotes



The replication process starts from the origin, and proceeds in two opposite directions. It is named θ replication.

Replication of eukaryotes

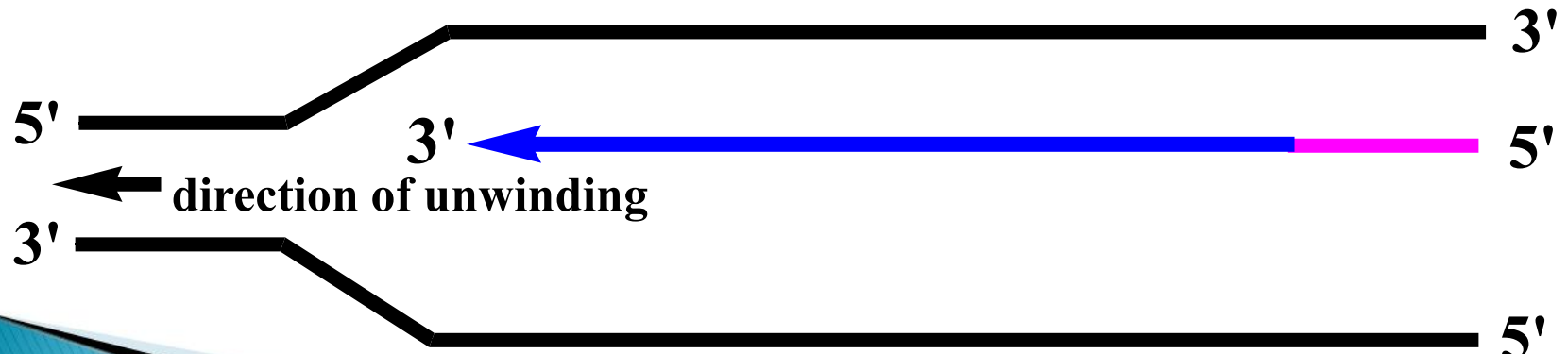
- **Chromosomes of eukaryotes have multiple origins.**
- **The space between two adjacent origins is called the replicon, a functional unit of replication.**

Semi-continuous Replication

The daughter strands on two template strands are synthesized differently since the replication process obeys the principle that DNA is synthesized from the 5´ end to the 3´end.

Leading strand

On the template having the 3´- end, the daughter strand is synthesized continuously in the 5'-3' direction. This strand is referred to as the leading strand.



Semi-continuous replication

Okazaki fragments

- **Many DNA fragments are synthesized sequentially on the DNA template strand having the 5´- end. These DNA fragments are called Okazaki fragments. They are 1000 – 2000nt (Nano Tesla) long for prokaryotes and 100-150 nt long for eukaryotes.**
- **The daughter strand consisting of Okazaki fragments is called the lagging strand.**

Semi-continuous replication

Continuous synthesis of the leading strand and discontinuous synthesis of the lagging strand represent a unique feature of DNA replication. It is referred to as the semi-continuous replication.

Primase

- Also called DnaG
- Primase is able to synthesize primers using free NTPs(Nucleoside triphosphate) as the substrate and the ssDNA as the template.
- Primers are short RNA fragments of a several decades of nucleotides long.

Helicase

- Also referred to as DnaB.
- It opens the double strand DNA with consuming ATP.
- The opening process with the assistance of DnaA and DnaC

Replication Fidelity

- Replication based on the principle of base pairing is crucial to the high accuracy of the genetic information transfer.
- Enzymes use two mechanisms to ensure the replication fidelity.
  - Proofreading and real-time correction
  - Base selection

Sequential actions

Initiation: recognize the starting point, separate dsDNA, primer synthesis, …

Elongation: add dNTPs to the existing strand, form phosphoester bonds, correct the mismatch bases, extending the DNA strand, …

Termination: stop the replication

Primer synthesis

Primase joins and forms a complex called primosome.

Primase starts the synthesis of primers on the ssDNA template using NTP as the substrates in the 5´- 3´ direction at the expense of ATP.

The short RNA fragments provide free 3´-OH groups for DNA elongation.

Releasing supercoil constraint

The supercoil constraints are generated ahead of the replication forks.

Topoisomerase binds to the dsDNA region just before the replication forks to release the supercoil constraint.

The negatively supercoiled DNA serves as a better template than the positively supercoiled DNA.

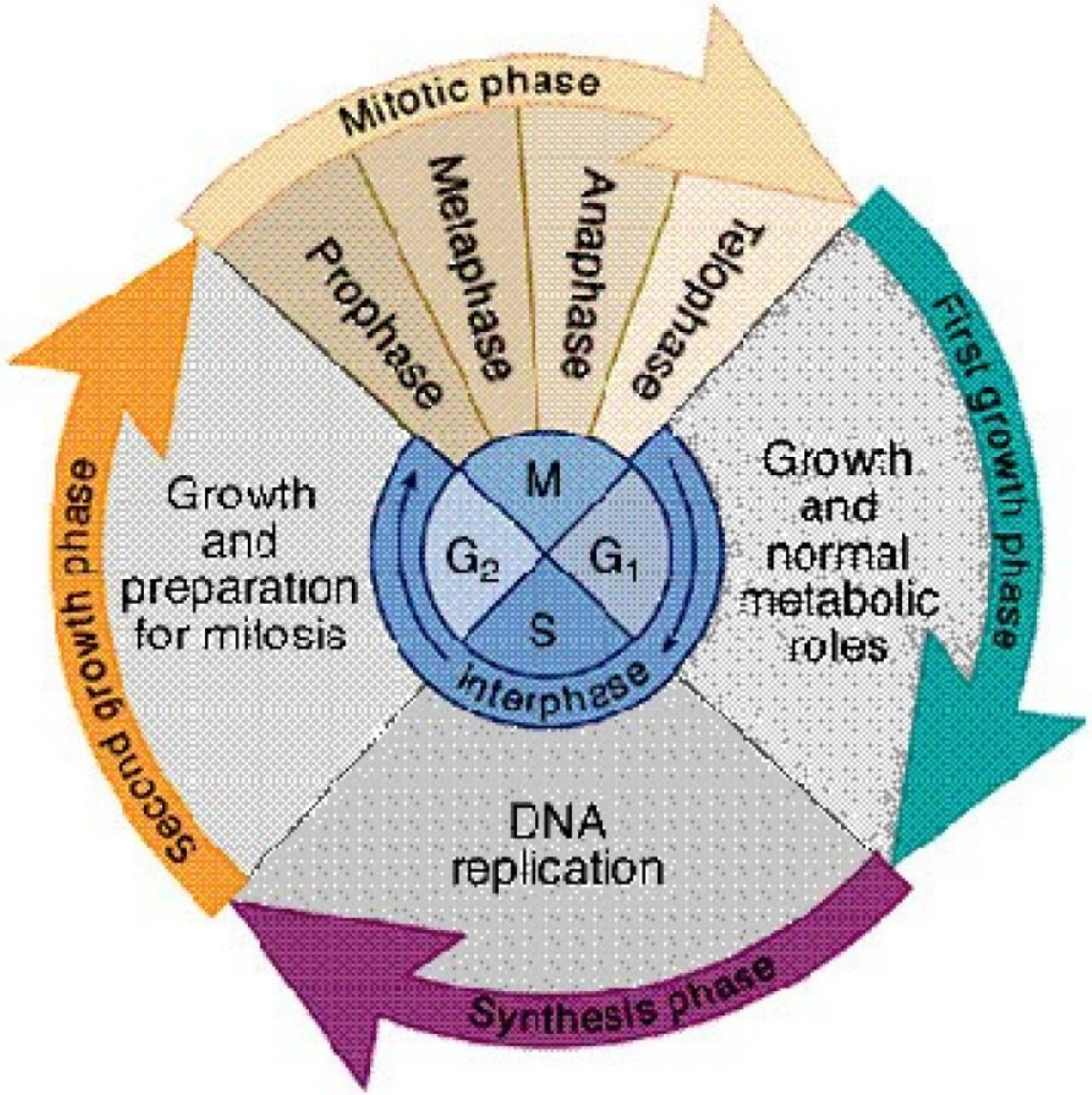
Lagging strand synthesis

Primers on Okazaki fragments are digested by RNase.

The gaps are filled by DNA-pol I in the 5′→3′direction.

The nick between the 5′end of one fragment and the 3′end of the next fragment is sealed by ligase.

Cell cycle


Mitotic phase
Prophase
Metaphase
Anaphase
Telophase
First growth phase
Growth and normal metabolic roles
DNA replication
Synthesis phase
Second growth phase
Growth and preparation for mitosis
M
G2
G1
S
Interphase