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DNA function: replication as a molecular basis of heredity

Modul no. 1: Animal Genetics

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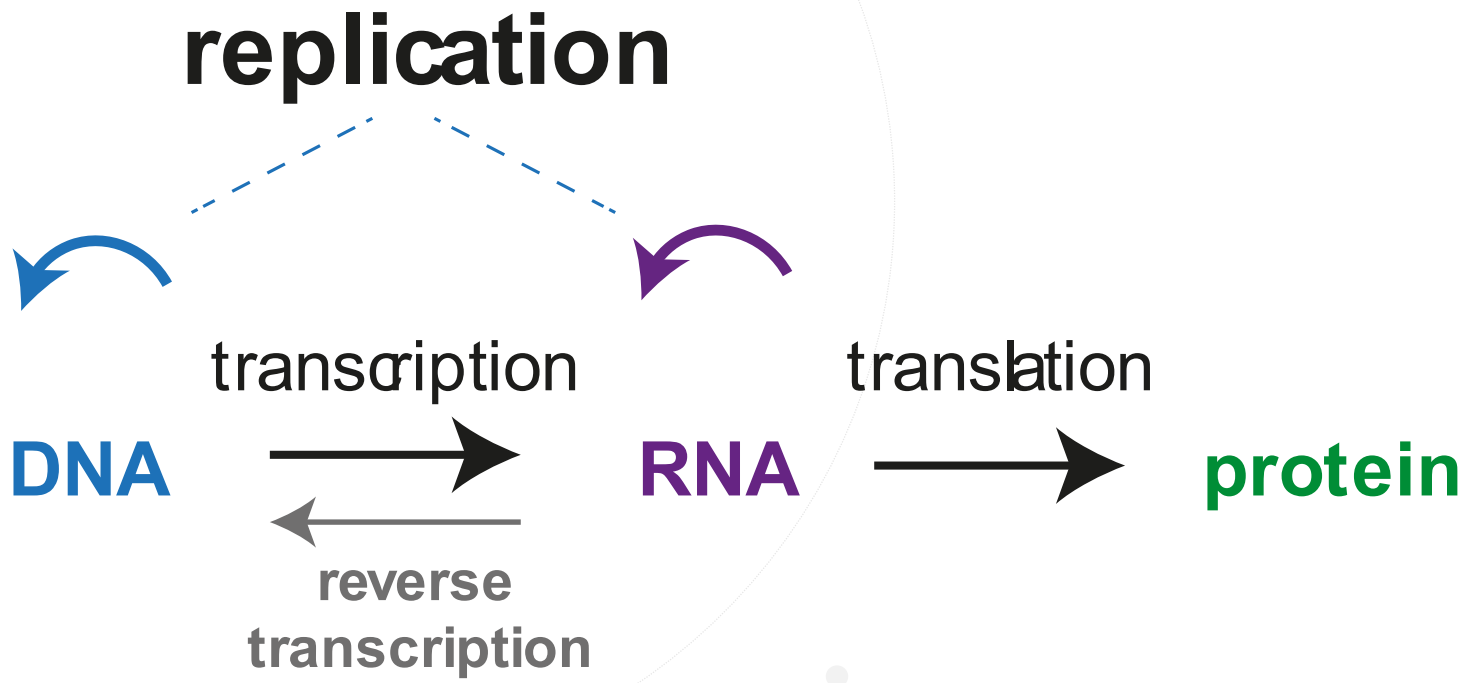
Function of DNA – Dogma of molecular biology

- The flow of genetic information in the cell ~ a central dogma of molecular biology
- **Replication (1 DNA -> 2 DNA)** is a process that occurs before cell division (mitosis or meiosis)



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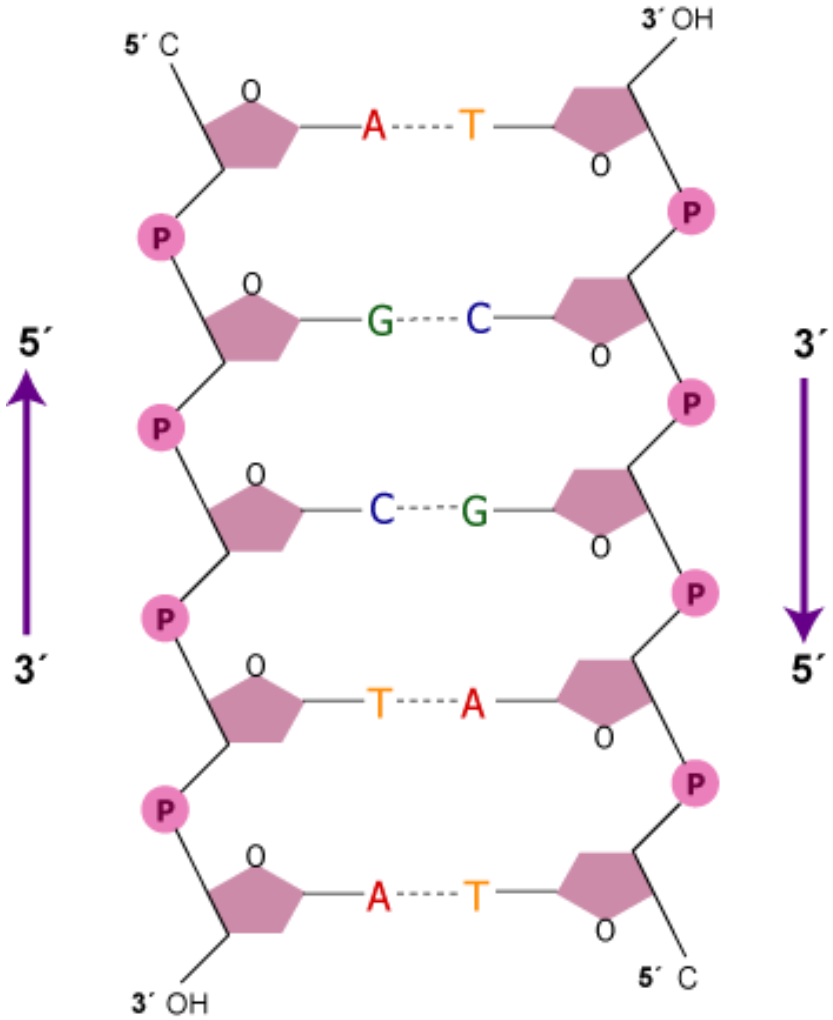
DNA as double helix



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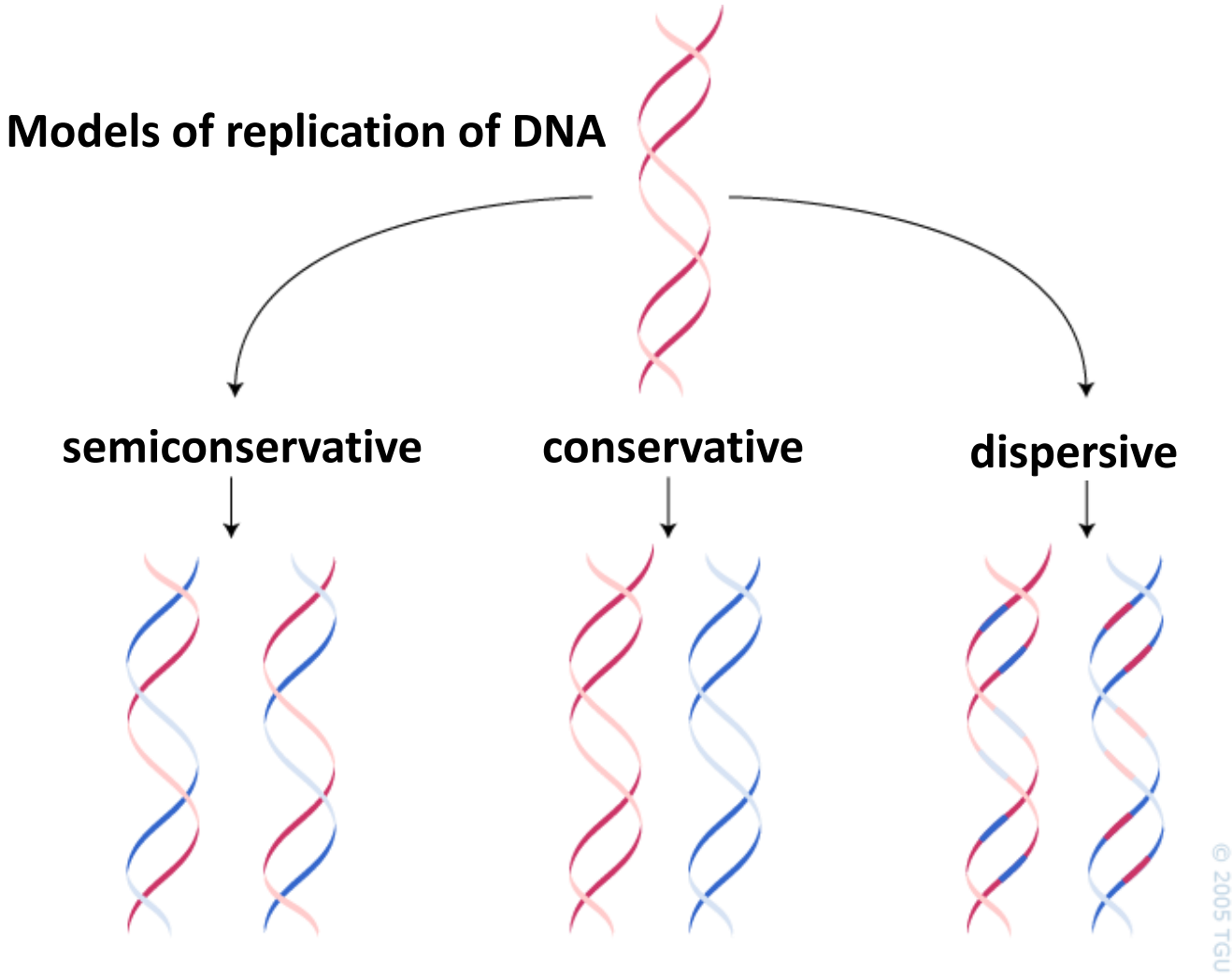
Theoretical models of replication of DNA



The newly synthesised fibres are blue

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Enzymes catalysing replication

- **DNA polymerases** - catalyse the synthesis of complementary DNA chains from deoxyribonucleotides on the DNA matrix (DNA-dependent DNA polymerases). Polymerization proceeds in the 5´>3´ direction. For their activity they require a short oligonucleotide (**primer**) from the 3´ end of which synthesis starts.
- **DNA polymerase I** - has polymerization function, 5´- 3´ and 3´- 5´ exonuclease activity.
- **DNA polymerase II** - It is involved in the termination of polymerization (5´- 3´ and 3´- 5´ exonuclease activity).
- **DNA polymerase III** - holoenzyme, has 3 subunits with multiple functions, which are combined into a dimer (2 x 3 subunits) for greater efficiency (processivity) and with other proteins recognizes the RNA primer complex with the DNA matrix chain. Polymerizes 30 thousand nucleotides per minute.
  - subunit catalyzing polymerization,
  - subunit with 5'- 3' exonuclease activity,
  - polymerase assembly subunit.
- **DNA ligase** - catalyzes the joining of polynucleotides, is involved in the joining of Okazaki fragments into a continuous chain.
- **Primase** - catalyzes the synthesis of an RNA primer (oligoribonucleotide) from whose 3' end a short polydeoxyribonucleotide is synthesized. This complex is called the Okazaki fragment.
- **DNA helicases** - catalyze the unwinding of DNA helix chains by disrupting hydrogen bonds.

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Scheme of semiconservative replication

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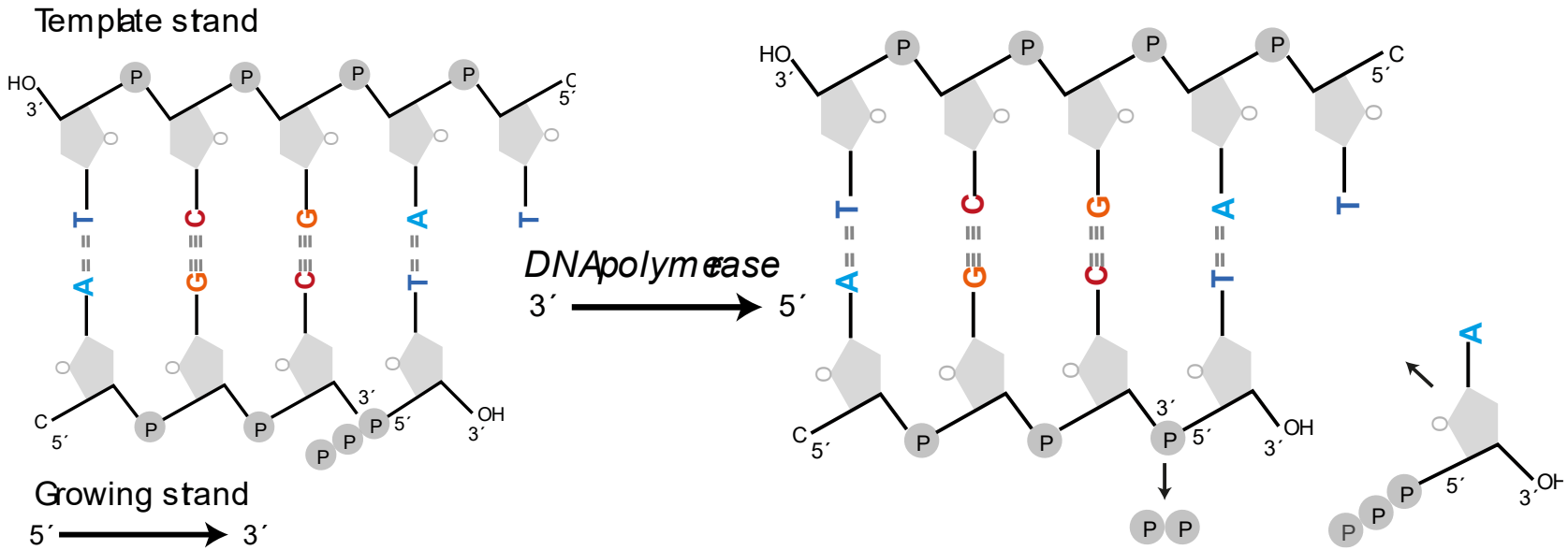
- Both original strands serve as templates for the synthesis of new strands.
- **DNA polymerase moves along the template chain in the direction 3´→ 5´**
- New strands are produced in the direction 5´ → 3´
- **The new DNA is made up of one original and one new strand.**



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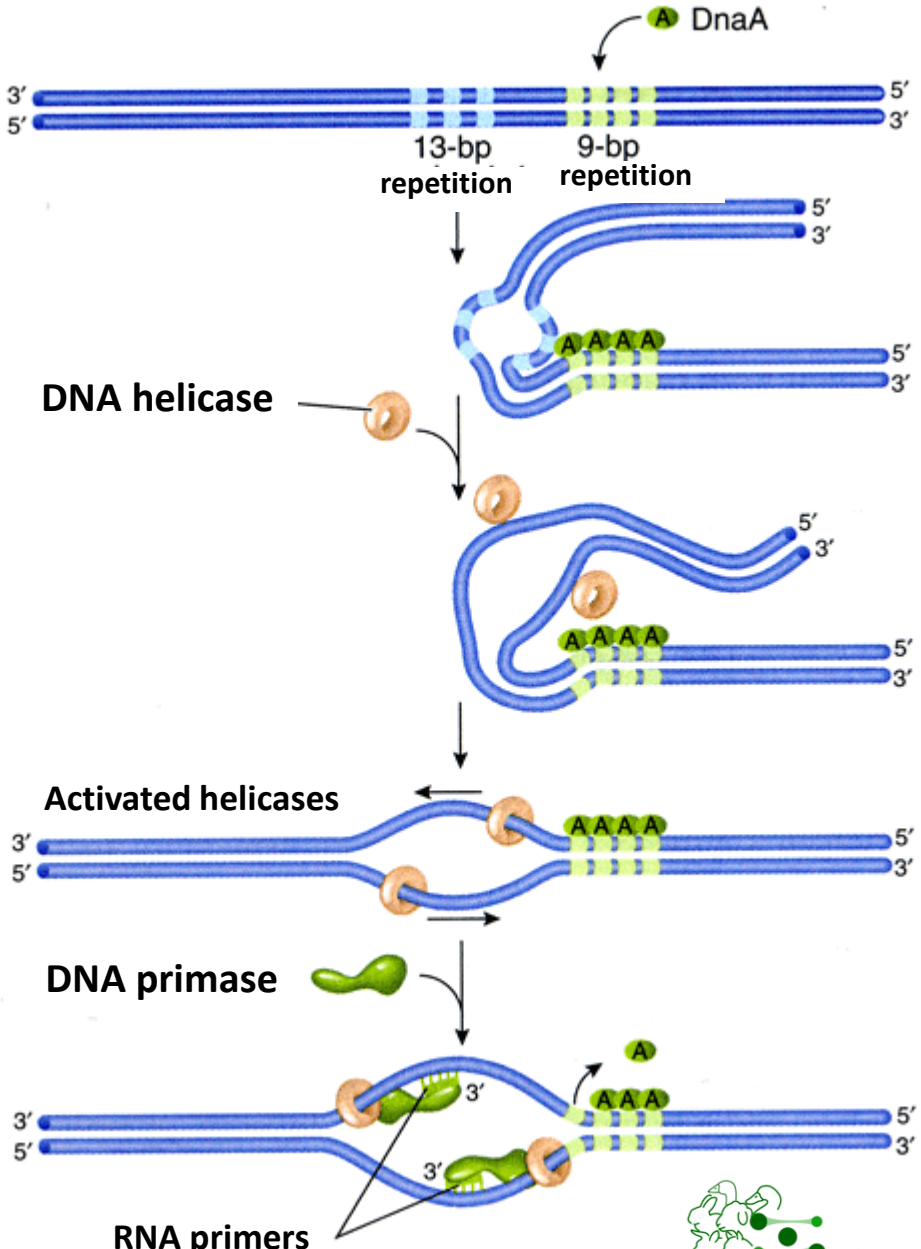
Initiation of replication

- **Denaturation** of dsDNA at *ori* (origin of replication) sites catalyzed by DNA helicase
- DnaA **initiation proteins** - bind to *ori* and stimulate DNA denaturation
- **DNA helicase** - binds to DNA strands and starts to unwind the double strand to **form a replication fork**
- **DNA primase** binds to helicase and denatures DNA and synthesizes RNA primer
- **The RNA primer** is extended by **DNA polymerase** as a new DNA strand
  - the RNA primer is later removed



Russell (2006)

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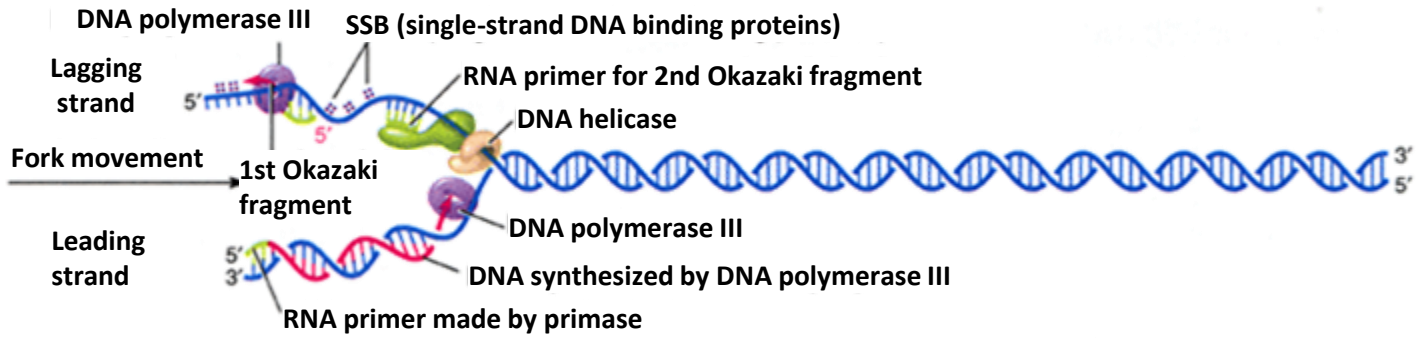
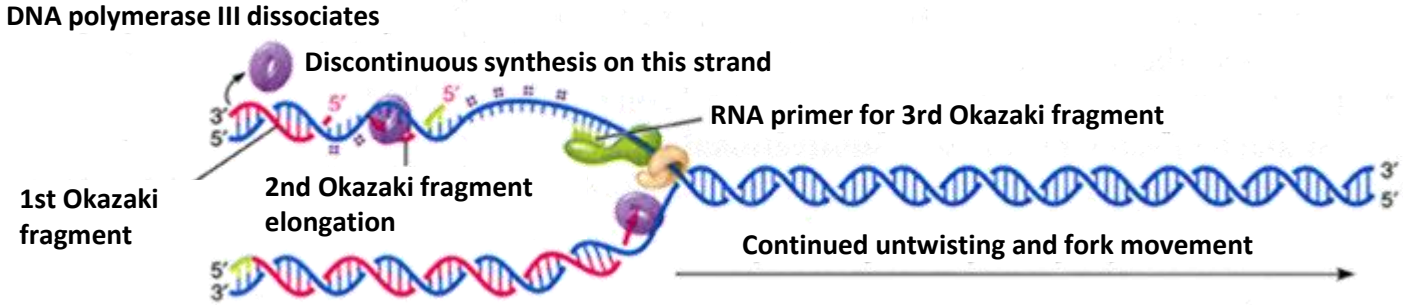
Events on the replication fork

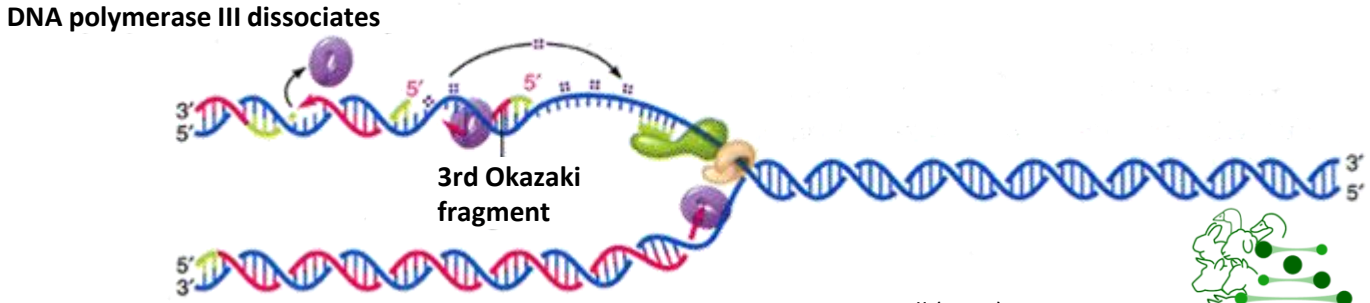
a) Initiation: RNA primer made by DNA primase starts replication of lagging strand (1st Okazaki fragment)



b) Further untwisting and **elongation** of new DNA strands**;** 2nd Okazaki fragment elongated



c) Process continues; 2nd Okazaki fragment finished; 3rd being synthesized; DNA primase beginning 4th fragment



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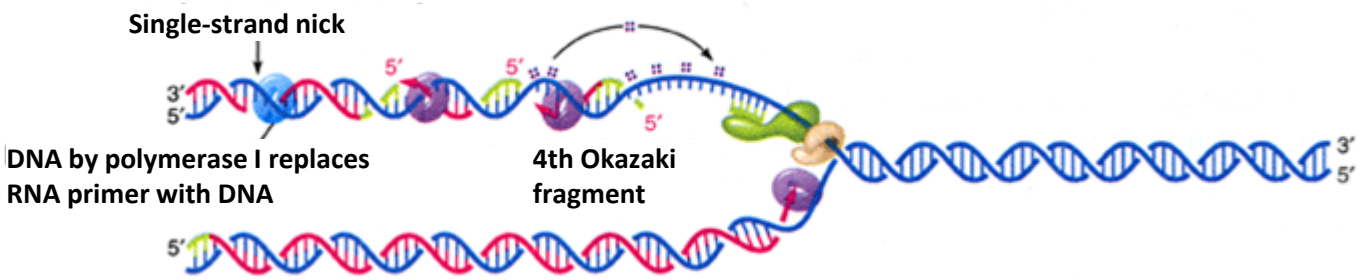
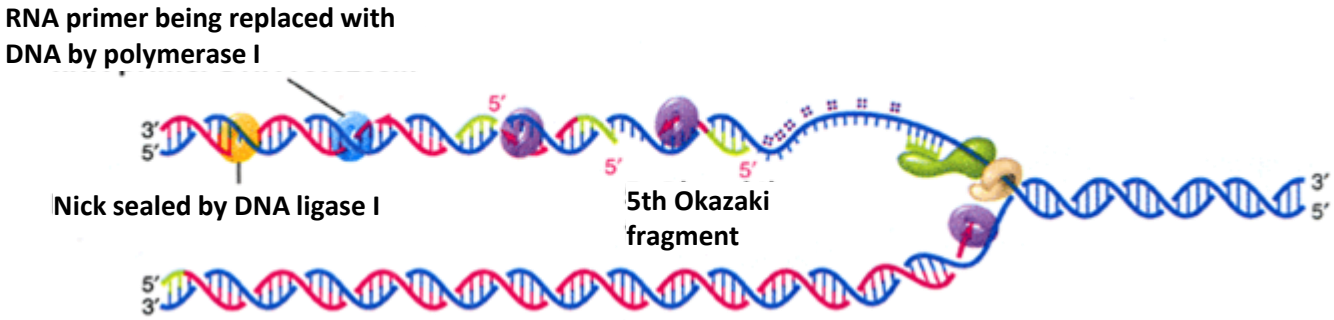
Events on the replication fork

d) Primer removed by DNA polymerase I



e) Joining of adjacent DNA fragments by DNA ligase



Russell (2006)

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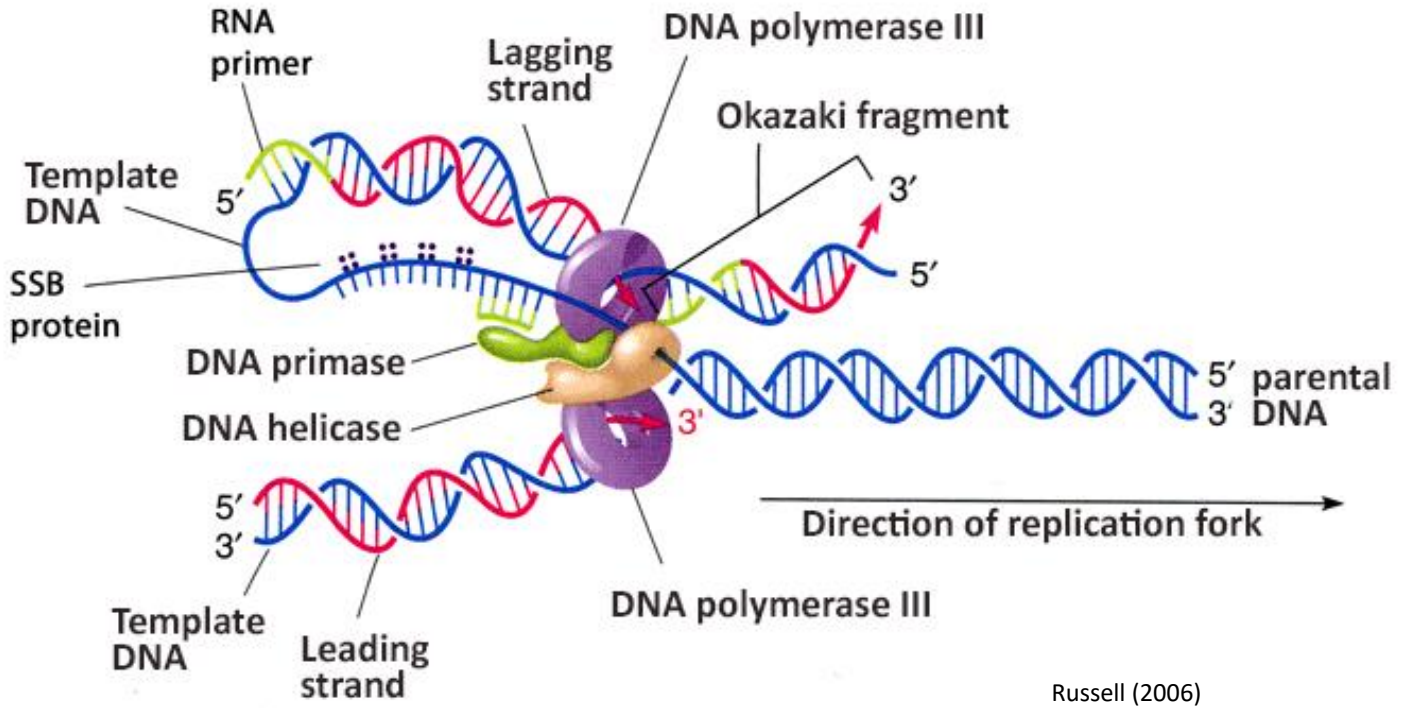
Model of the replisome



Russell (2006)

- Complex of key replication proteins with DNA replication fork
- DNA polymerase III on the lagging template strand terminates synthesis of the Okazaki fragment

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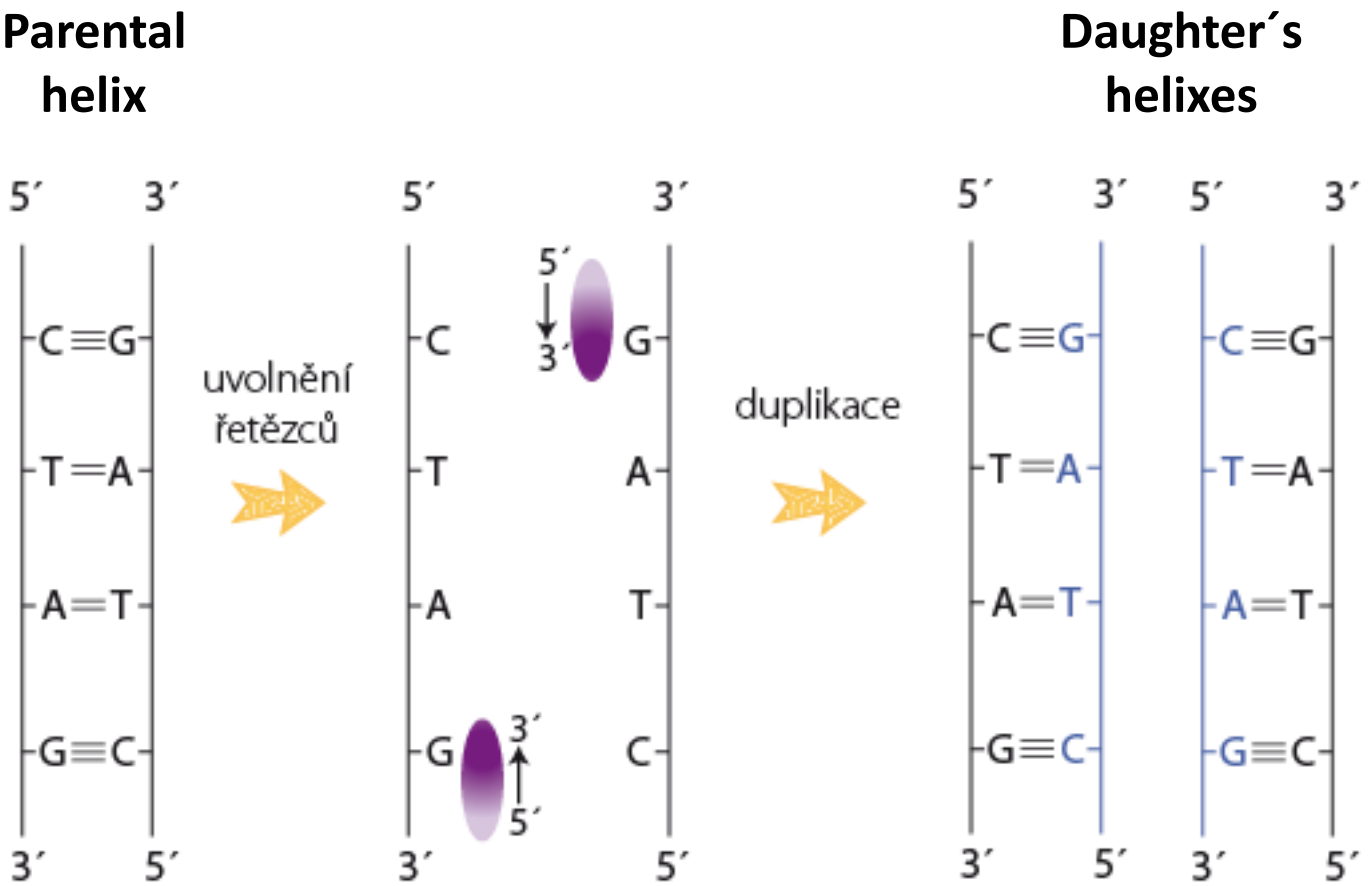
Complementary base pairing - a necessity in DNA double helix duplication



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Conclusion of replication

- DNA replication occurs by a semiconservative mechanism, with each strand serving as a template
- Enzymatic process - DNA polymerases; deoxyribonucleoside 5'-triphosphates
- Polymerization in the direction: 5´-> 3´
- DNA polymerase cannot initiate synthesis of new strand > DNA primase synthesizes short RNA primer
- Synthesis of the new chain is continuous (leading strand) on one template strand and discontinuous (lagging strand) on the other template strand.
- In eukaryotes - replication occurs in S phase, starting at many sites
- A fundamental property of genetic material is the ability to reproduce very precisely and to divide into new cells when dividing - heredity

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Thank you for your attention!

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