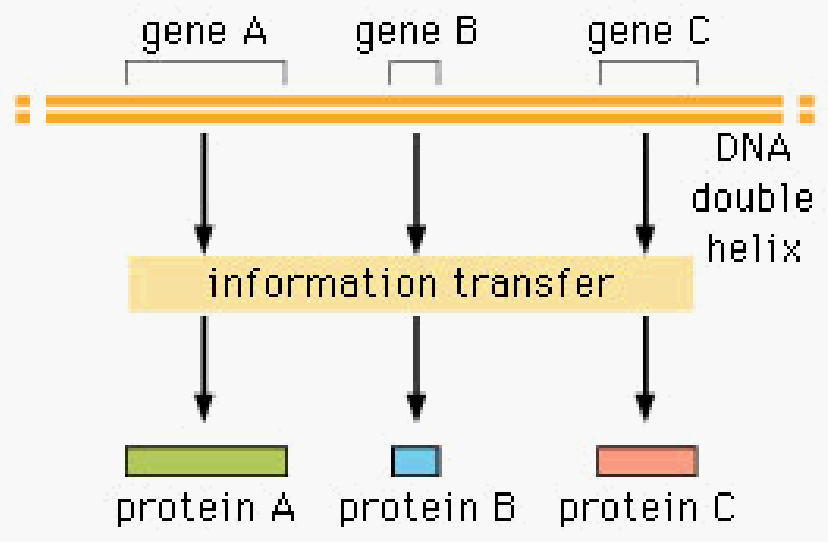
DNA Replication

Genes as Information Transfer



- A gene is the sequence of nucleotides within a portion of DNA that codes for a peptide or a functional RNA
- Sum of all genes = genome

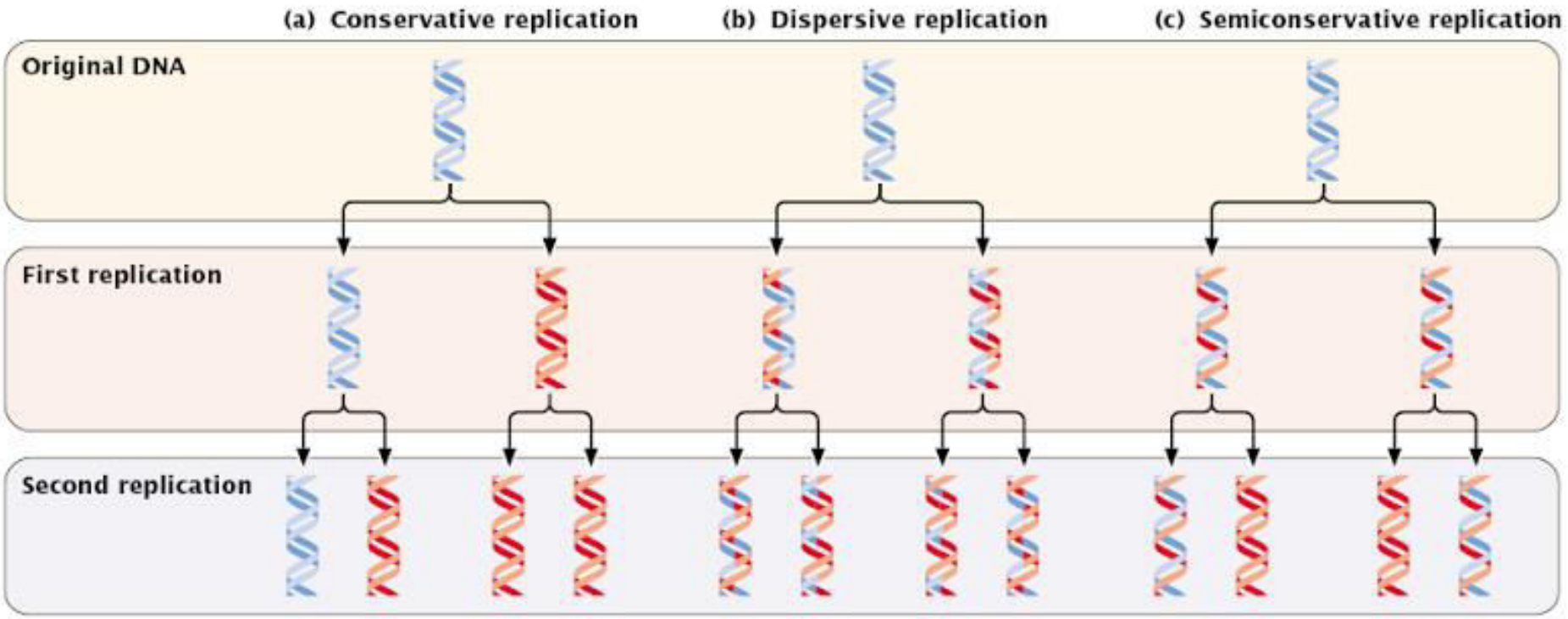
A, G, C and T as part of a special language –
translated to the language of amino acids in proteins

Semi conservative replication

- **Semi conservative replication** would produce two copies that each contained one of the original strands and one new strand.

- Conservative **replication** would leave the two original template **DNA** strands together in a double helix and would produce a copy composed of two new strands containing all of the new **DNA** base pairs.

Conservative, Dispersive and semi conservative Replication

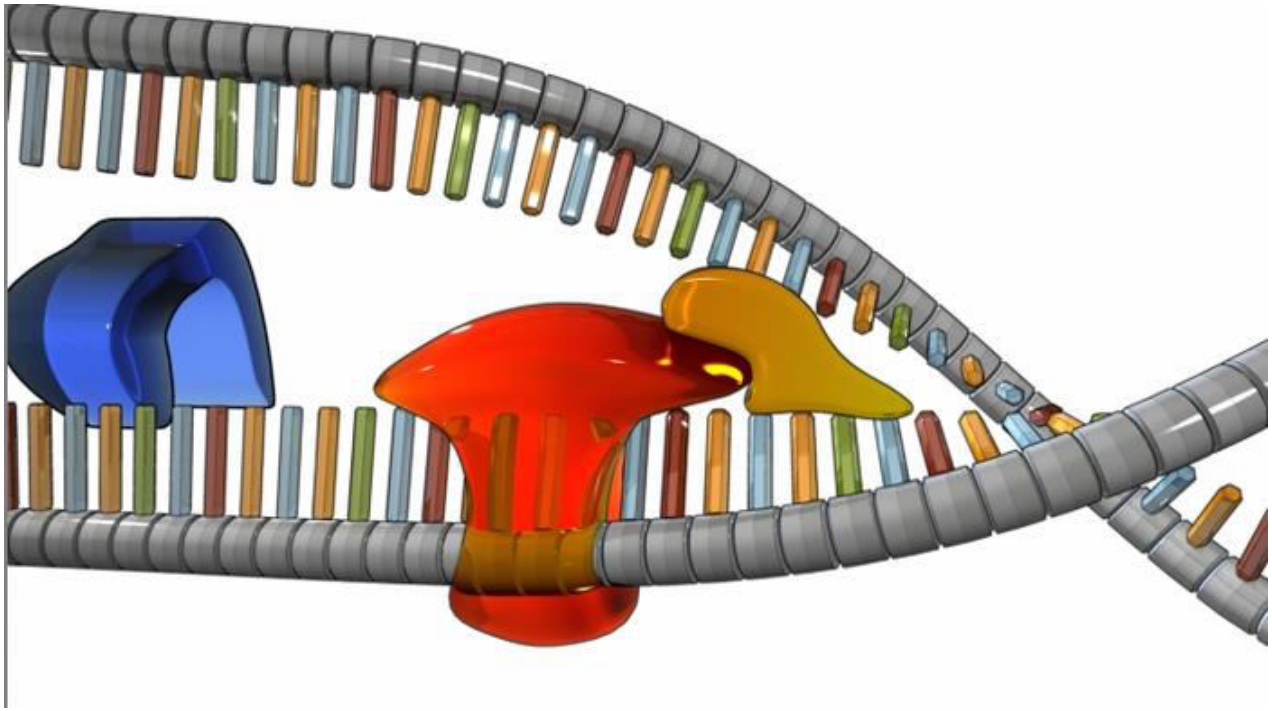


The mechanism of DNA replication

Arthur Kornberg, a Nobel prize winner and other biochemists deduced steps of replication

- Initiation
  - Proteins bind to DNA and open up double helix
  - Prepare DNA for complementary base pairing
- Elongation
  - Proteins connect the correct sequences of nucleotides into a continuous new strand of DNA
- Termination
  - Proteins release the replication complex

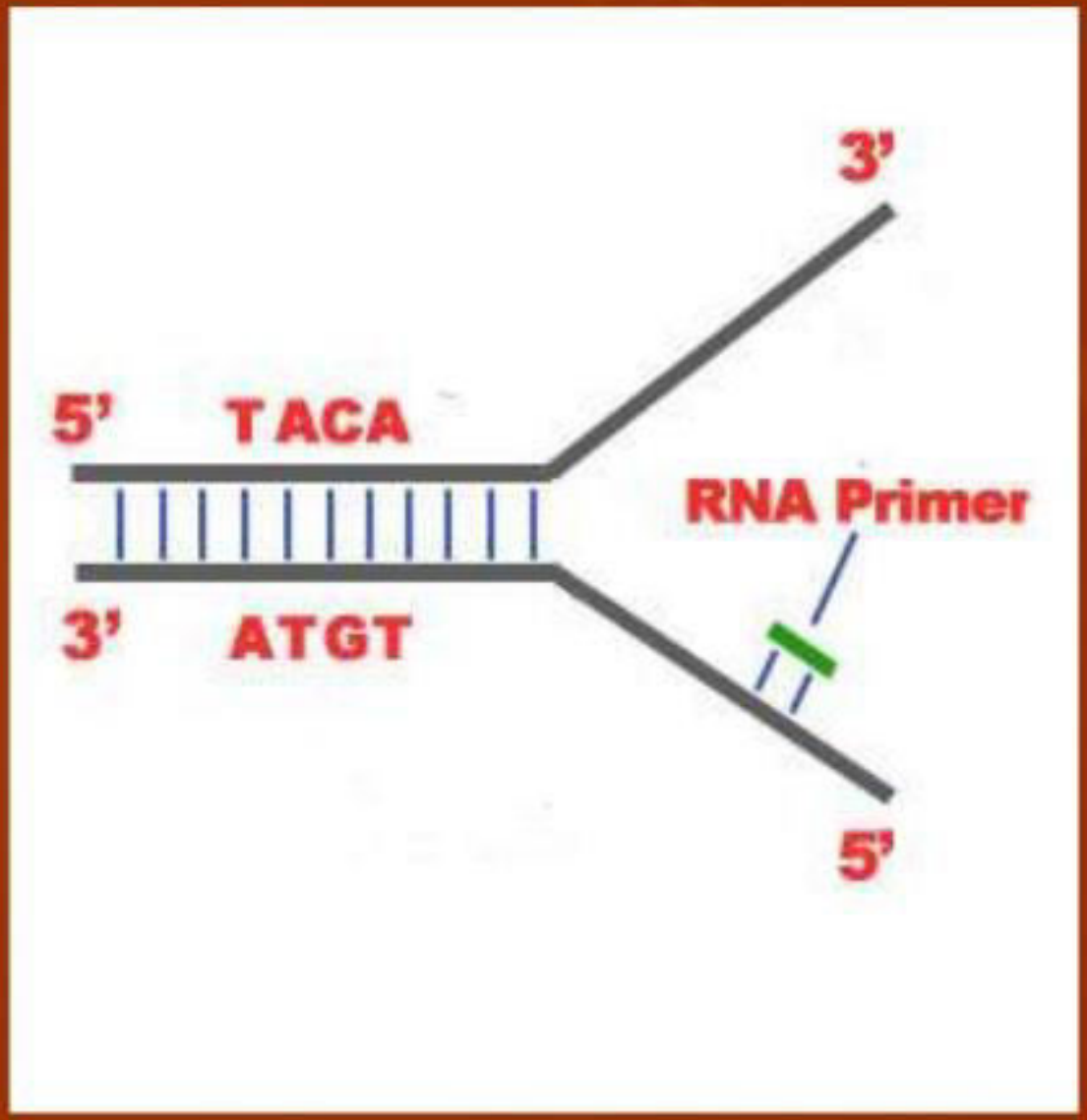
Replication initiation



helicase -(yellow) primase (red) DNA polymerase (blue)

RNA PRIMASE

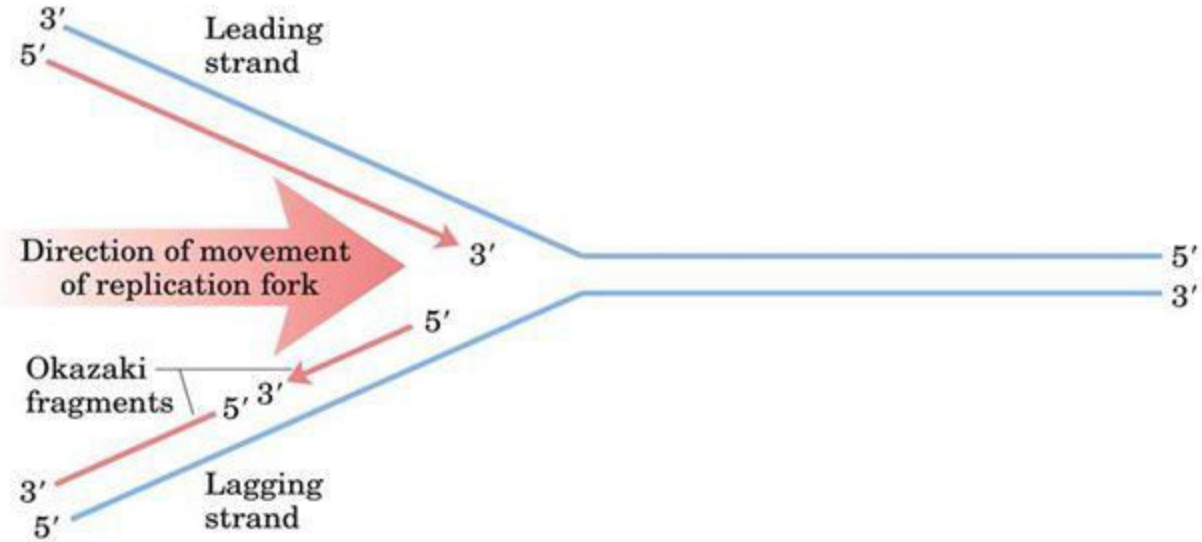
RNA Primase lays down the RNA primers so that the Polymerase III can get to work or can function.

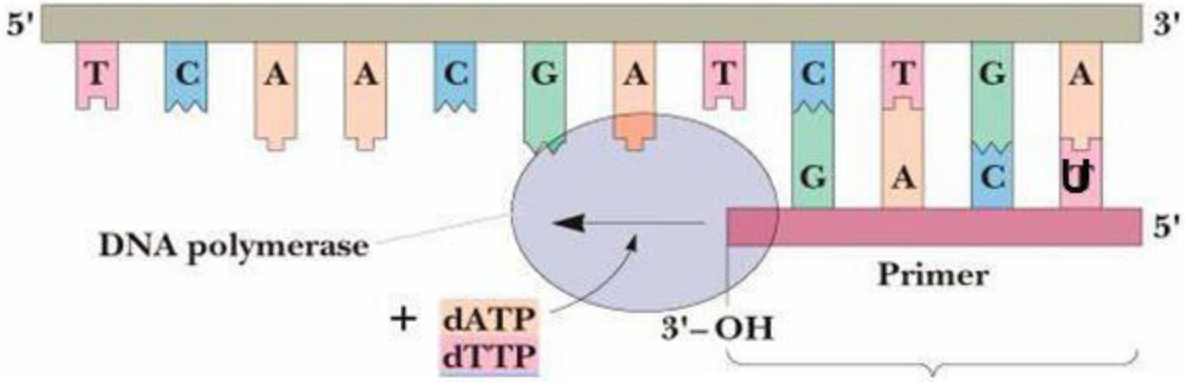


Elongation and replication

- Primase Complex Synthesizes short RNA primers.
- The class of enzymes which perform DNA synthesis are called the polymerase enzymes. The polymerases can only read DNA in a 3` →5` direction ➔ they synthesize DNA only in 5` to 3` direction.
- The DNA double helix has the following polarity:

Leading strand 3` → 5`
lagging strand is 5` → 3`
DNA polymerase uses the parent strands as template and synthesizes a new 5` → 3` strand





Termination

- The last step of DNA Replication is the Termination.
- This process happens when the DNA Polymerase reaches to an end of the strands.

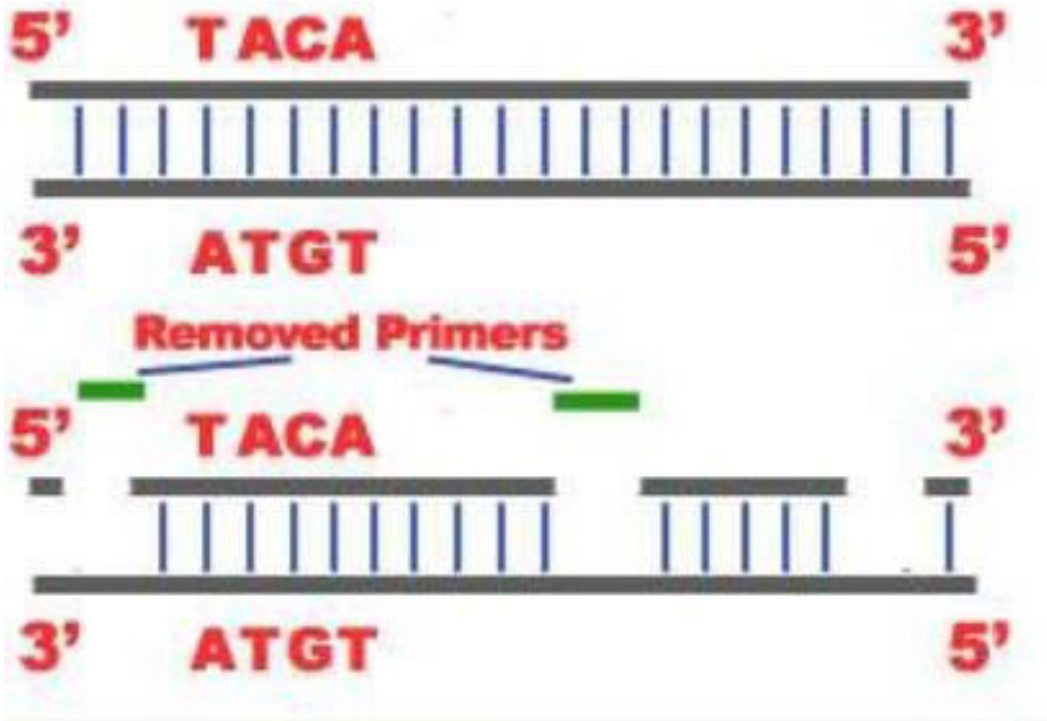
- We can easily understand that in the last section of the lagging strand, when the RNAprimer is removed, it is not possible for the DNAPolymerase to seal the gap (because there is no primer).

- So, the end of the parental strand where the last primer binds isnt replicated.

- These ends of linear (chromosomal) DNA consists of noncoding DNA that contains repeat sequences and are called telomeres.

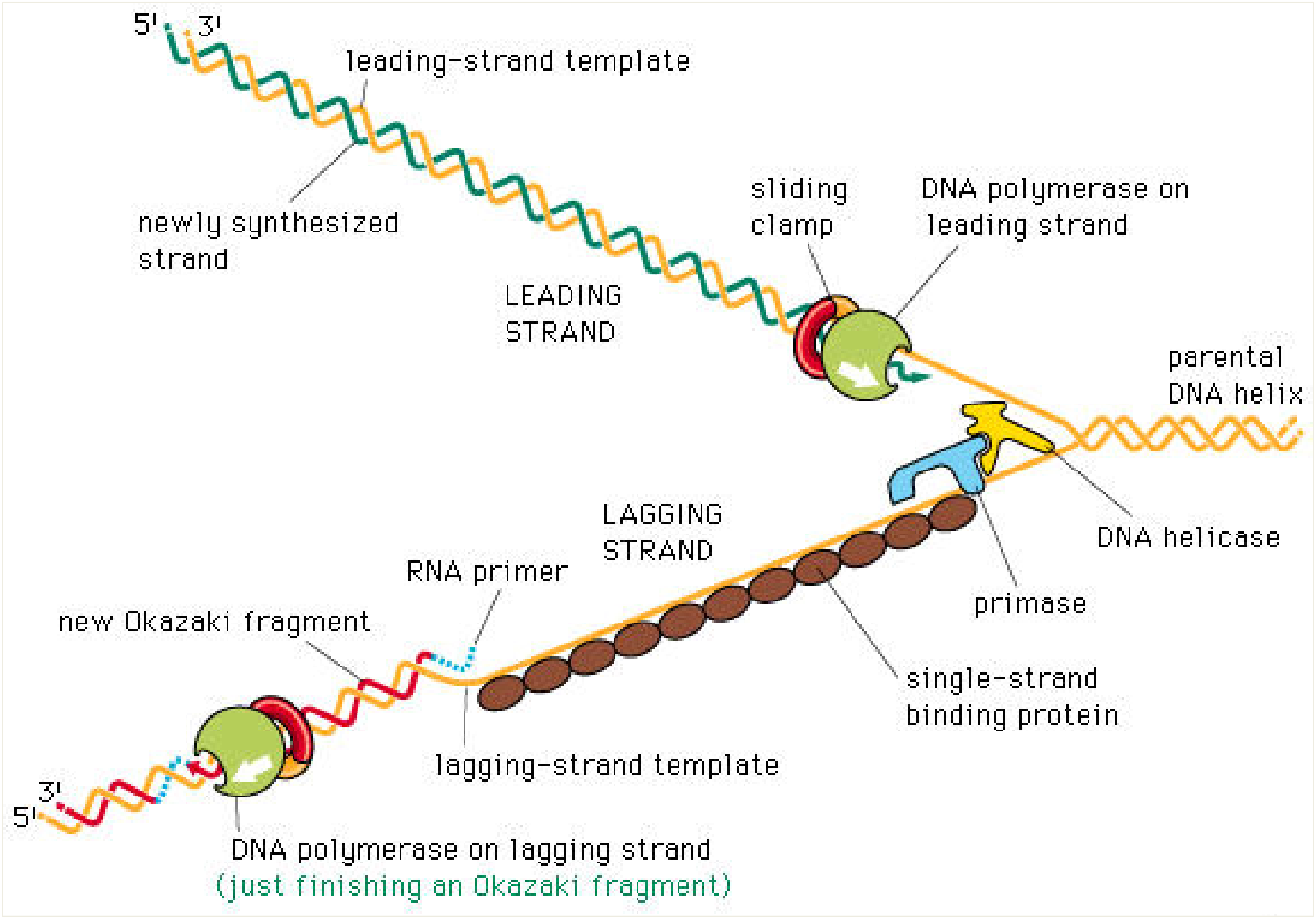
- As a result, a part of the telomere is removed in every cycle of DNA Replication

Major Mechanisms



- The total mechanism requires a cycle of repeating steps that include:
- 1) Creation of RNA Primers (Primase)
- 2) Synthesizing a short segment of DNA between the primers (Polymerase III)
- 3) Replacing the RNA primer with DNA (Polymerase I)
- 4) The binding of these pieces (Ligase)

Components of DNA replication

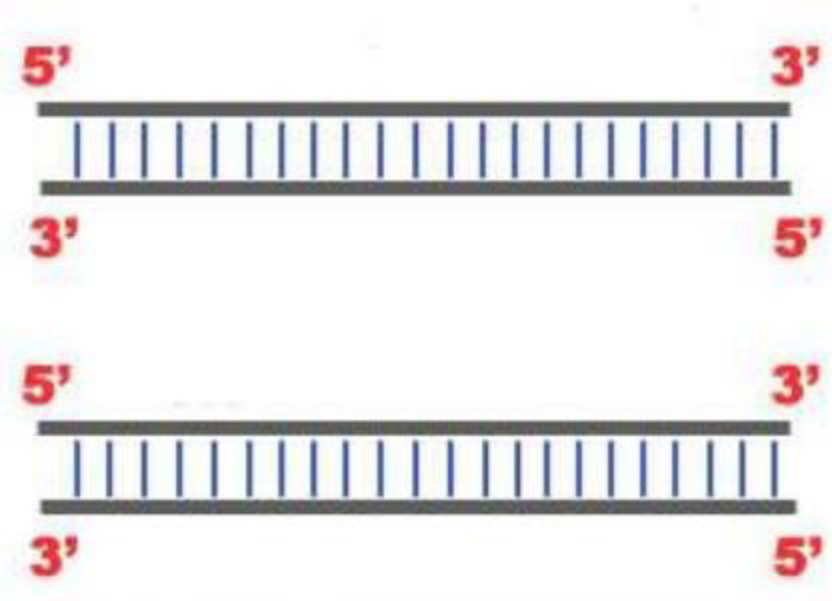


Single-Strand Binding Proteins

- Single-Strand DNA Binding Proteins, SSB for short, work to bind individuals strands in a DNA double stranded helix and aid the helicases in opening it up into single strands.

- They are particularly useful in stabilizing the unwound single-stranded formation.

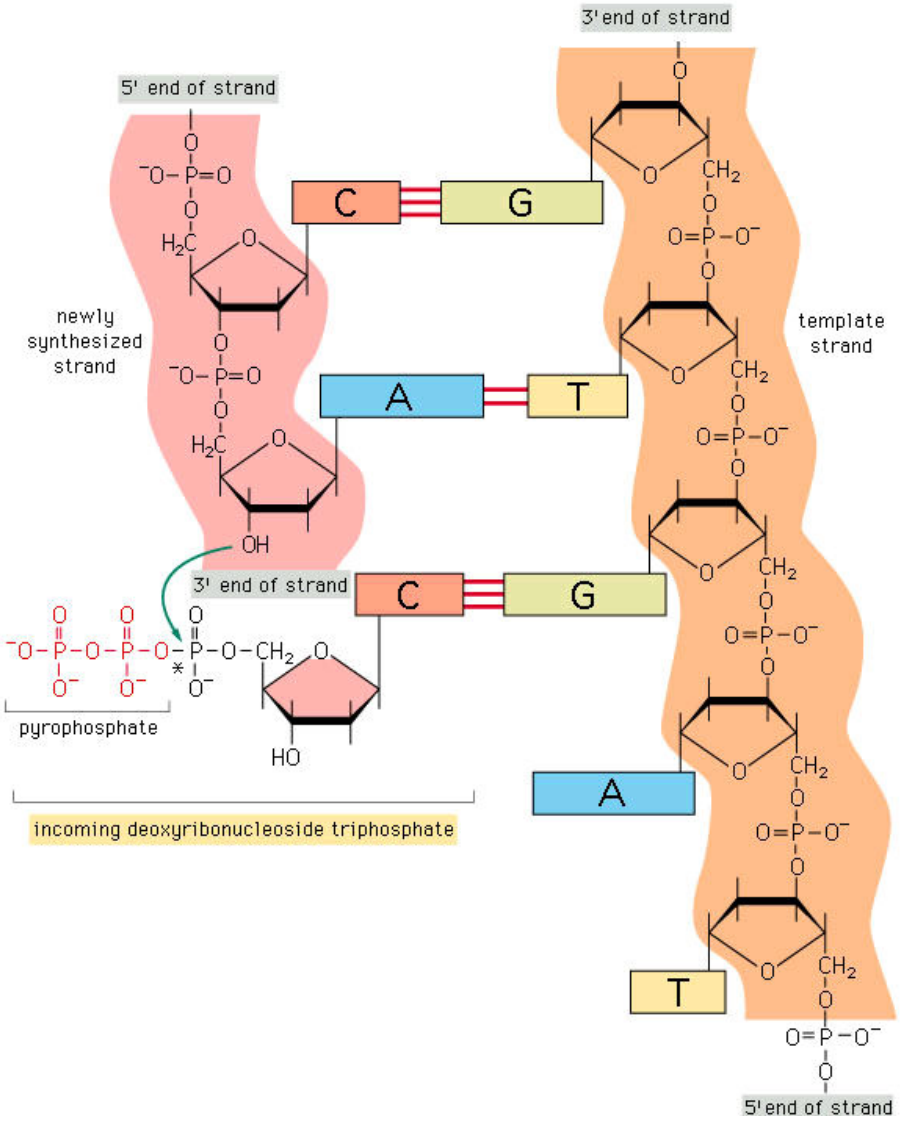
Proof readings



- The DNA Replication is not completed before a mechanism of repair fixes possible errors caused during the replication.
- Enzymes like nucleases remove the wrong nucleotides and the DNA Polymerase fills the gaps

DNA Polymerase

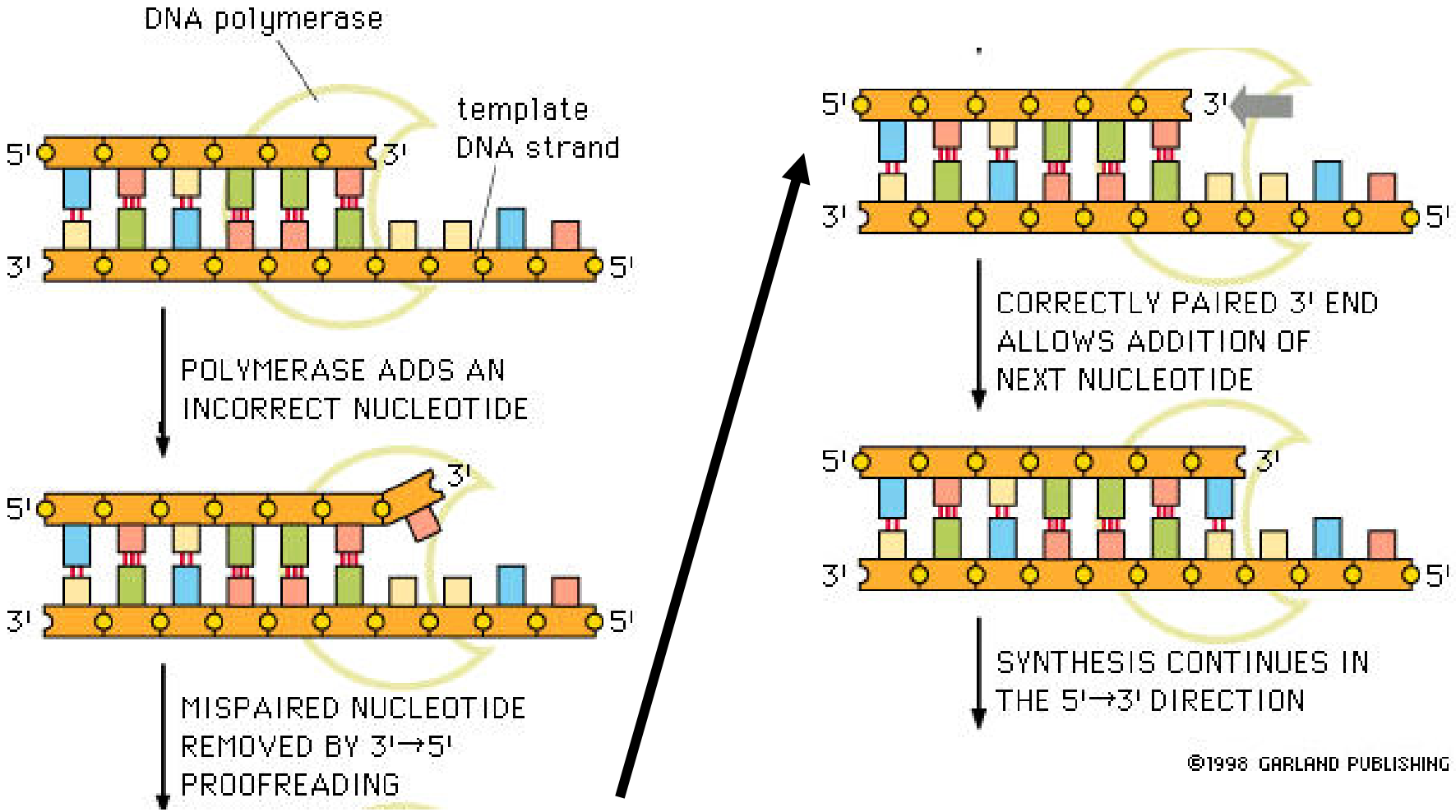
- An enzyme that catalyzes the addition of a nucleotide to the growing DNA chain
- Nucleotide enters as a nucleotide tri-PO_4
- 3'–OH of sugar attacks first phosphate of tri-PO_4 bond on the 5' C of the new nucleotide
  - releasing pyrophosphate (PP_i) + energy



DNA Polymerase

- Bidirectional synthesis of the DNA double helix
- Corrects mistaken base pairings
- Requires an established polymer (small RNA primer) before addition of more nucleotides
- Other proteins and enzymes necessary

Proofreading



Enzymes in replications

Helicase	Uses the hydrolysis of ATP to "unzip" or unwind the DNA helix at the replication fork to allow the resulting single strands to be copied.
Primase	Polymerises nucleotide triphosphates in a 5' to 3' direction. The enzyme synthesises RNA primers to act as a template for future Okazaki fragments to build on to.
DNA Polymerase III	In charge of synthesizing nucleotides onto the leading end in the classic 5' to 3' direction.
DNA Polymerase I	In charge of synthesizing nucleotides onto primers on the lagging strand, forming Okazaki fragments. However, this enzyme cannot completely synthesize all of the nucleotides.
Ligase	This enzyme is in charge of "gluing" together Okazaki fragments, an area that DNA Pol I is unable to synthesize.

Telomerase	Catalyzes the lengthening of telomeres; the enzyme includes a molecule of RNA that serves as a template for new telomere segments.
Nuclease	This enzyme is in charge of excising, or cutting out, unwanted or defective segments of nucleotides in a DNA sequence.
Topoisomerase	This enzyme introduces a single-strand nick in the DNA, enabling it to swivel and thereby relieve the accumulated winding strain generated during unwinding of the double helix.
Single Strand Binding Proteins	Responsible for holding the replication fork of DNA open while polymerases read the templates and prepare for synthesis.