DNA replication

One of the basic features of life is the ability to produce more of itself. On the level of organism, this means growth and reproduction; on cellular level it is cell division; and on molecular level it is DNA replication.

Replication is the copying of DNA by end-to-end template synthesis. It is based on complementary recognition of nucleotides.

Template synthesis, i.e. copying the primary structure from a preexisting macromolecule, is the only possible way to synthesize information-containing biopolymers (nucleic acids and proteins).

Replication was figured out early

In 1953, describing for the first time the double-helical structure of DNA, Watson and Crick stated, "*The specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material*."

Photo: Watson (left) & Crick with DNA model

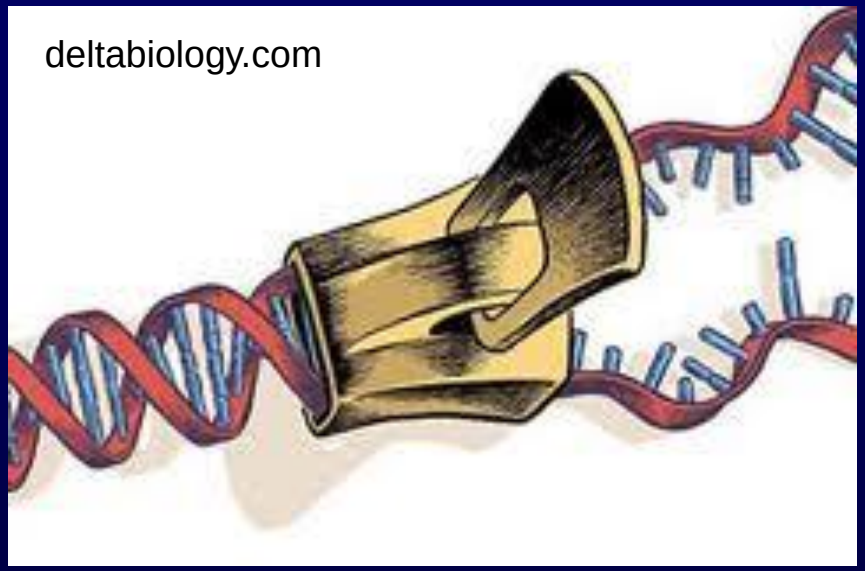
For replication, the two DNA strands first separate. This allows single complementary nucleotides to join by forming hydrogen bonds with the exposed DNA bases. Then, an enzyme forms covalent bonds between the newly joined nucleotides, connecting them in a new DNA strand.

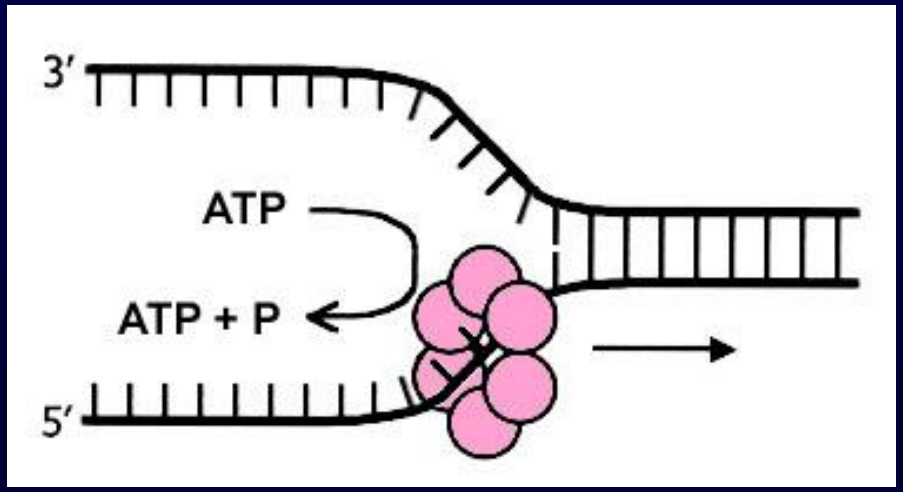
This way, the initial DNA molecule is replaced by two identical double helices. Because each of them is composed of one old and one new strand, the mechanism of DNA replication is called semi-conservative.

Helicase

The hydrogen bonds in the DNA double helix are weak but numerous. Therefore, strand separation requires energy and a special protein called helicase.

Its action resembles unzipping.





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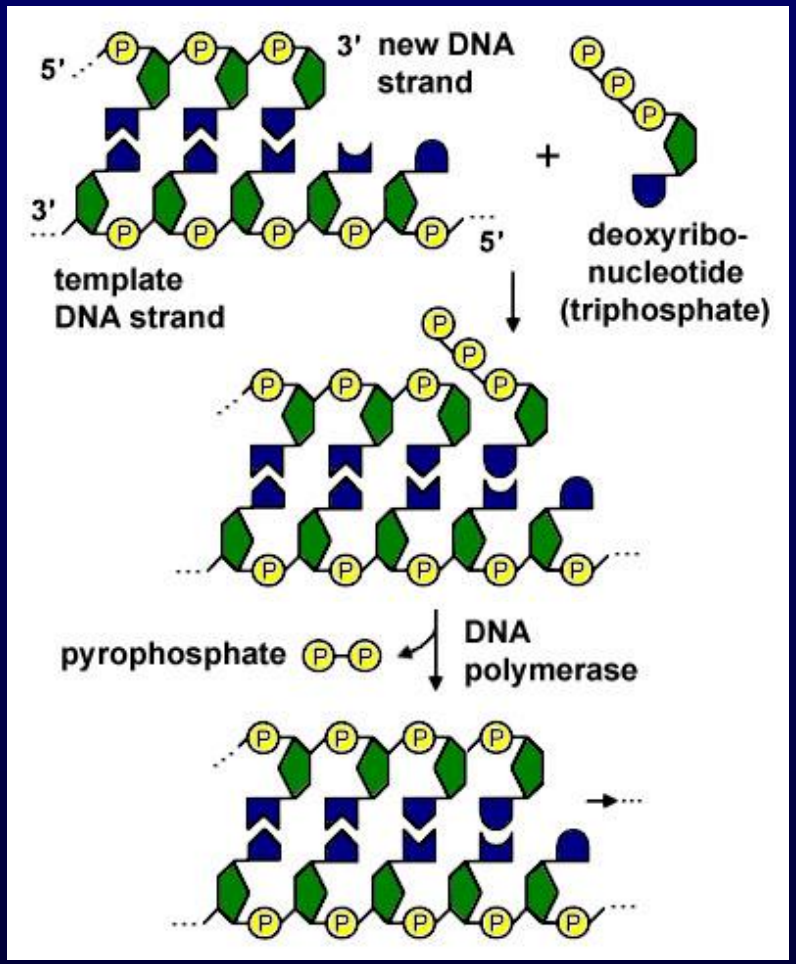
How the new DNA strand grows

DNA synthesis always proceeds in 5’ – 3’ direction. Of course, the template strand is read in the opposite, 3’ – 5’ direction.

Nucleotides are used in the form of triphosphates.

First, the nucleotide to join is selected by complementary binding. Its base forms hydrogen bonds with the exposed base on template DNA. This is spontaneous, requires no enzyme and no energy.

Then, an enzyme called DNA polymerase connects the nucleotide to the growing DNA strand, forming a covalent phosphodiester bond.



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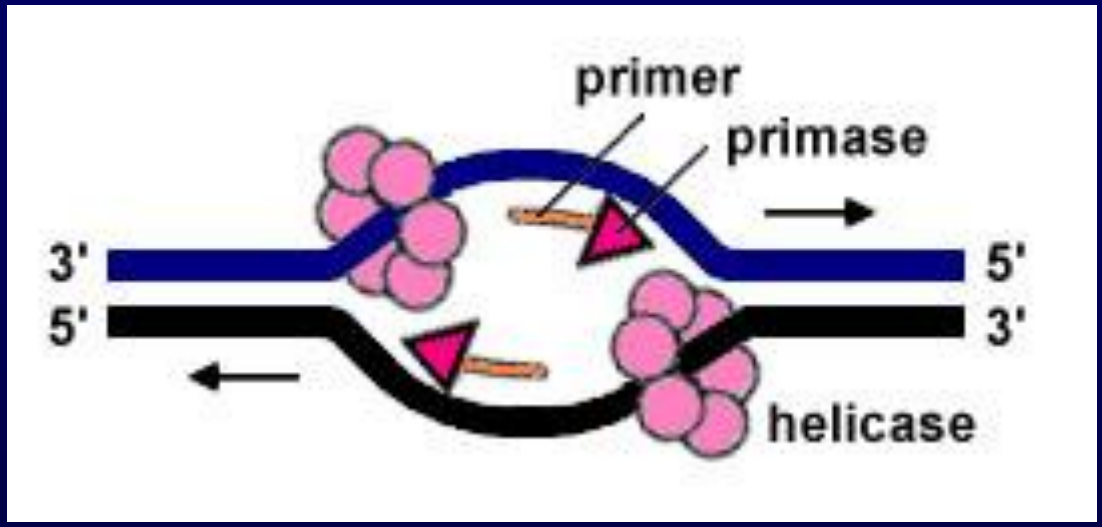
This is done by removing two of the three phosphates and binding the last phosphate to the 3’ OH group of the previous nucleotide.

How replication starts



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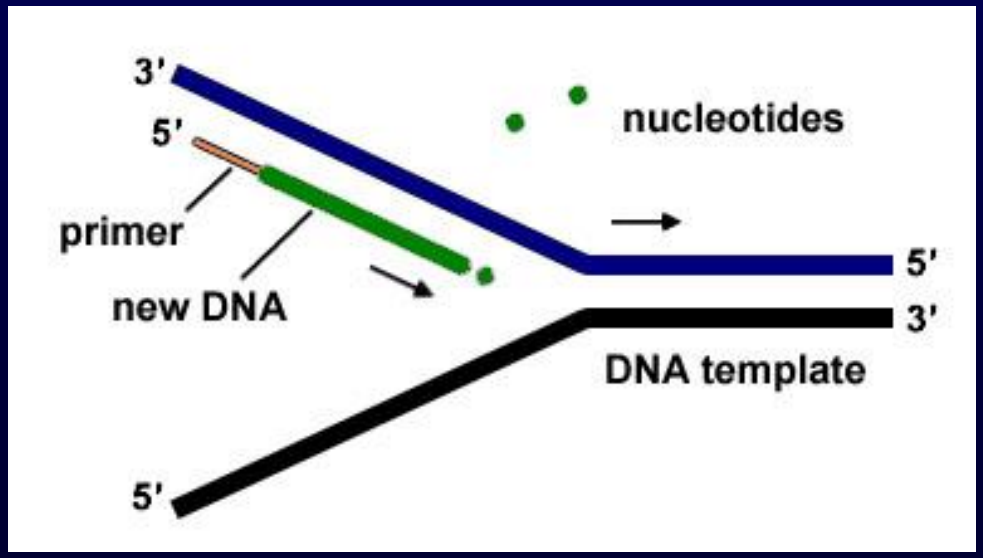
The primase is needed for replication because of its ability to initiate polynucleotide synthesis. It synthesizes a short RNA strands. After this, DNA replicase joins and continues synthesis.

The structure where DNA is being synthesized is fork-shaped and is called replication fork. It is gradually moving during elongation of DNA.

Because DNA synthesis can proceed only in 5’ – 3’ direction, it will conveniently follow the replication fork only for one of the two new DNA strands. It is called leading strand and progresses continuously by addition of nucleotides.

The other new strand, called lagging, is synthetized in a more complex way.

In this drawing, the lagging strand and the participating proteins are not shown.



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The lagging strand: Okazaki fragments

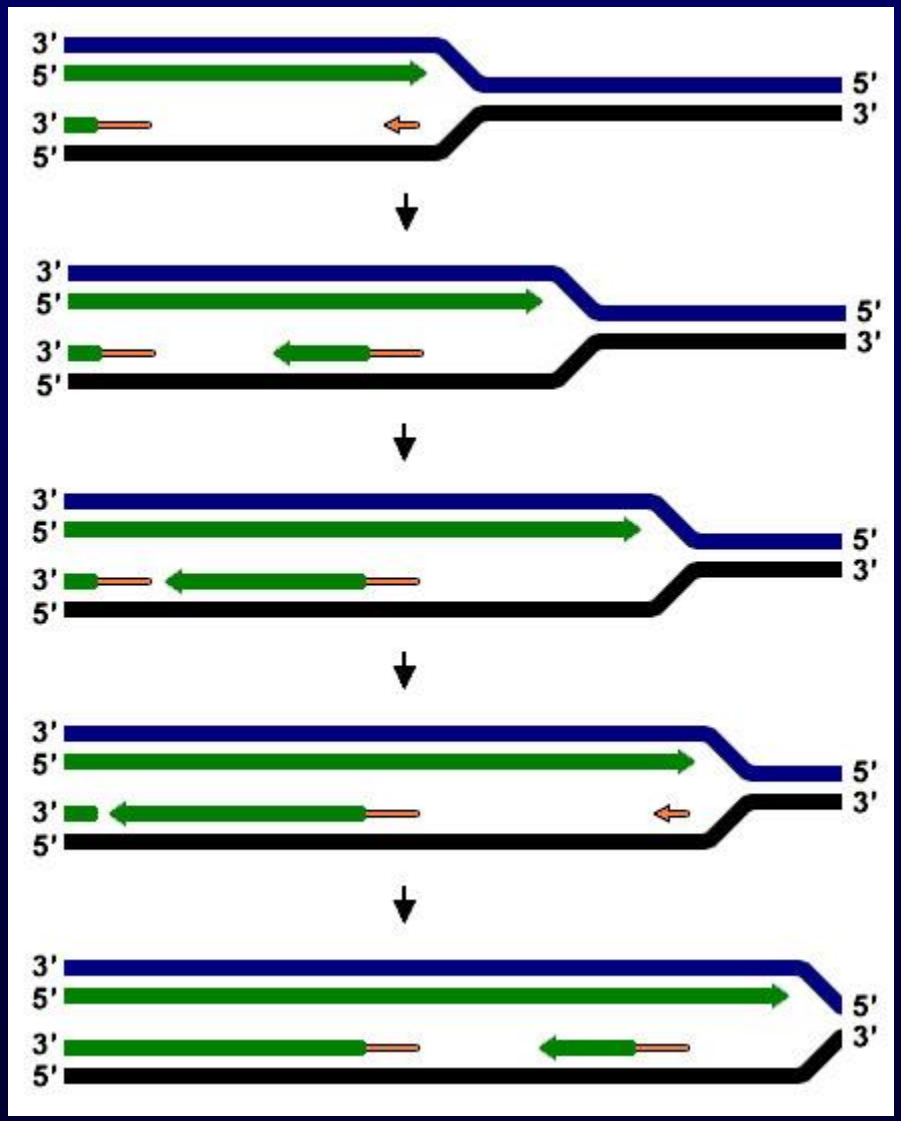
The lagging strand is produced discontinuously as short fragments.

They are called Okazaki fragments after their discoverer.

The synthesis of a fragment begins at the replication fork and proceeds backwards until it reaches the previous primer. Then, a nuclease digests the primer and the DNA polymerase fills its space.

Tsuneko Okazaki

When ready, the two fragments are joined together by another enzyme called DNA ligase.



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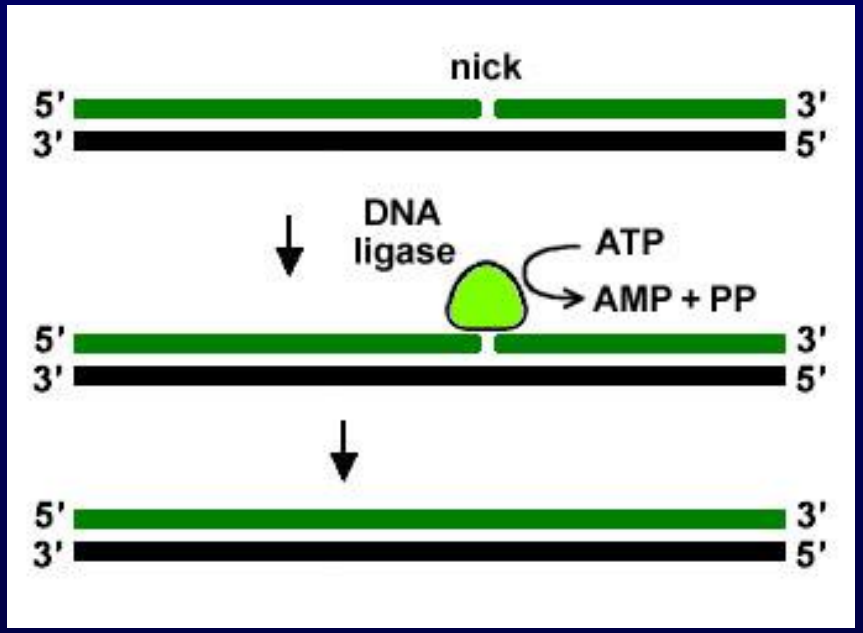
DNA ligase



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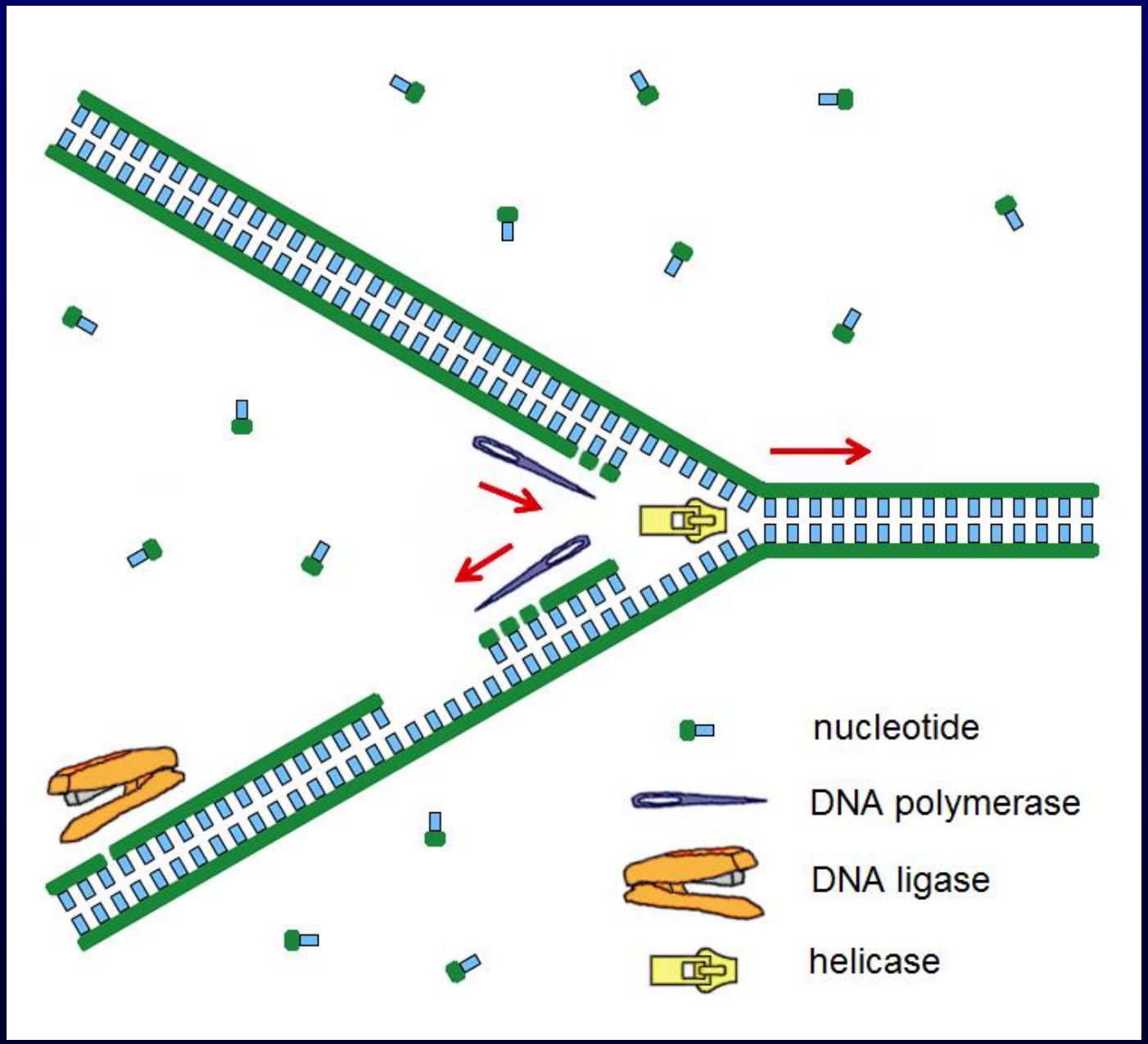
The DNA ligase stiches the fragments together. It needs energy from ATP for its work.

Such an enzyme is necessary because DNA polymerases can add to the polynucleotide chain only single nucleotides, not whole fragments.

The replication fork at a glance



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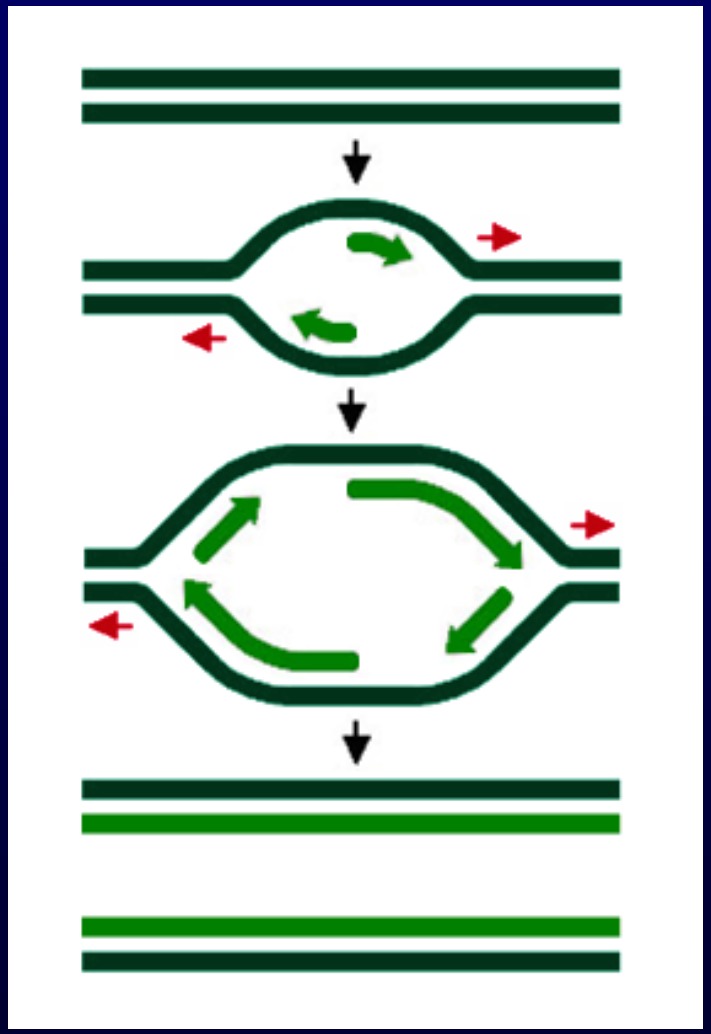
Three main stages of replication

Initiation

Elongation

Termination



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