DNA replication in cells

The Central Dogma of Molecular Biology

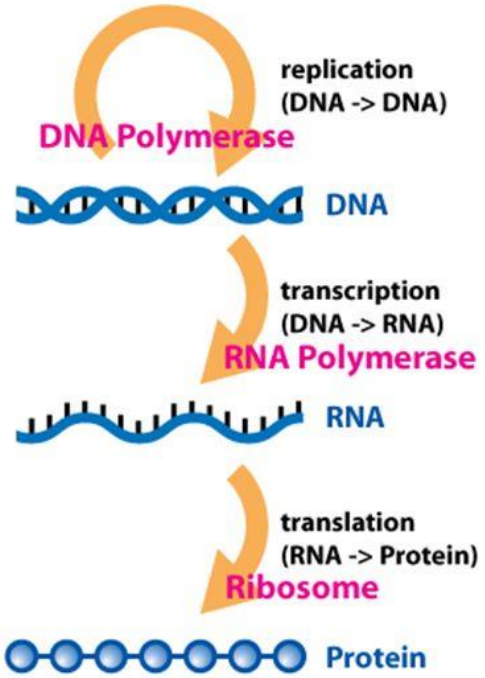
- Information is transferred from DNA to RNA to protein

  DNA -> RNA -> Protein

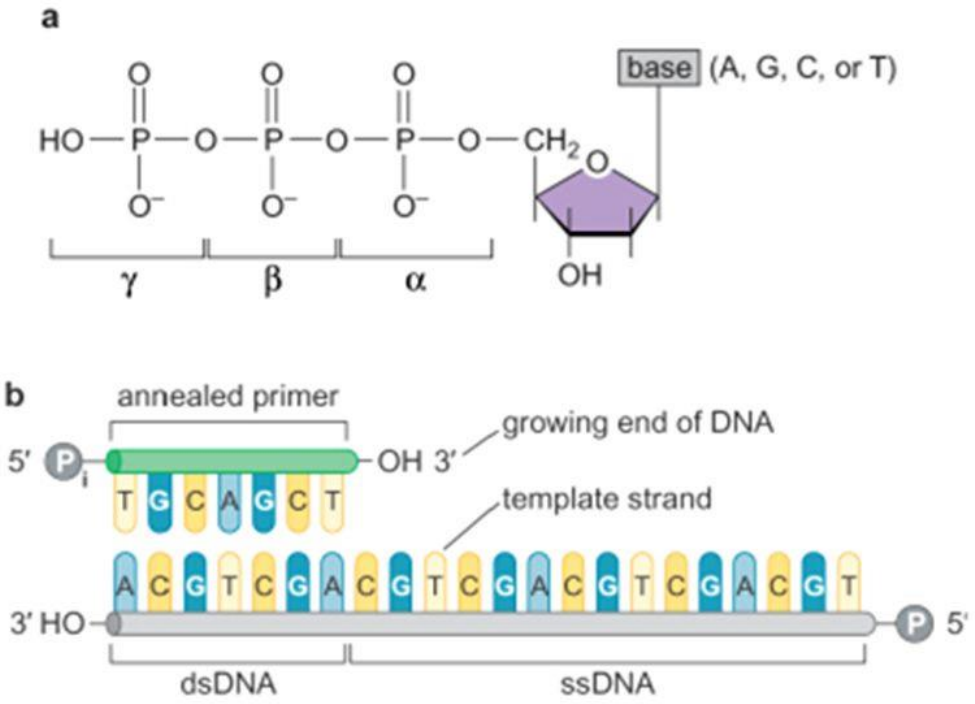
- Proteins create traits

- This is called **gene expression**

- This process is found in all organisms

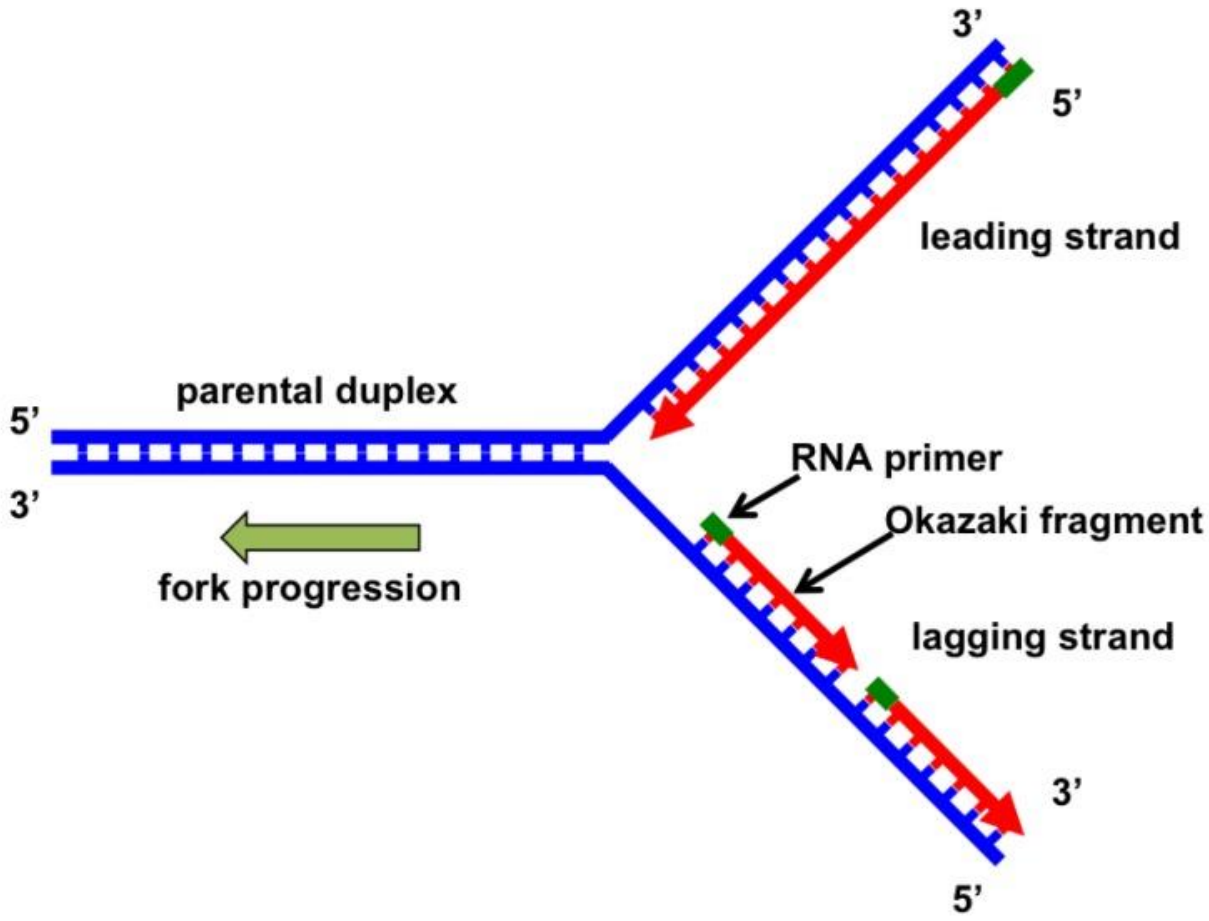


Substrates required for DNA synthesis

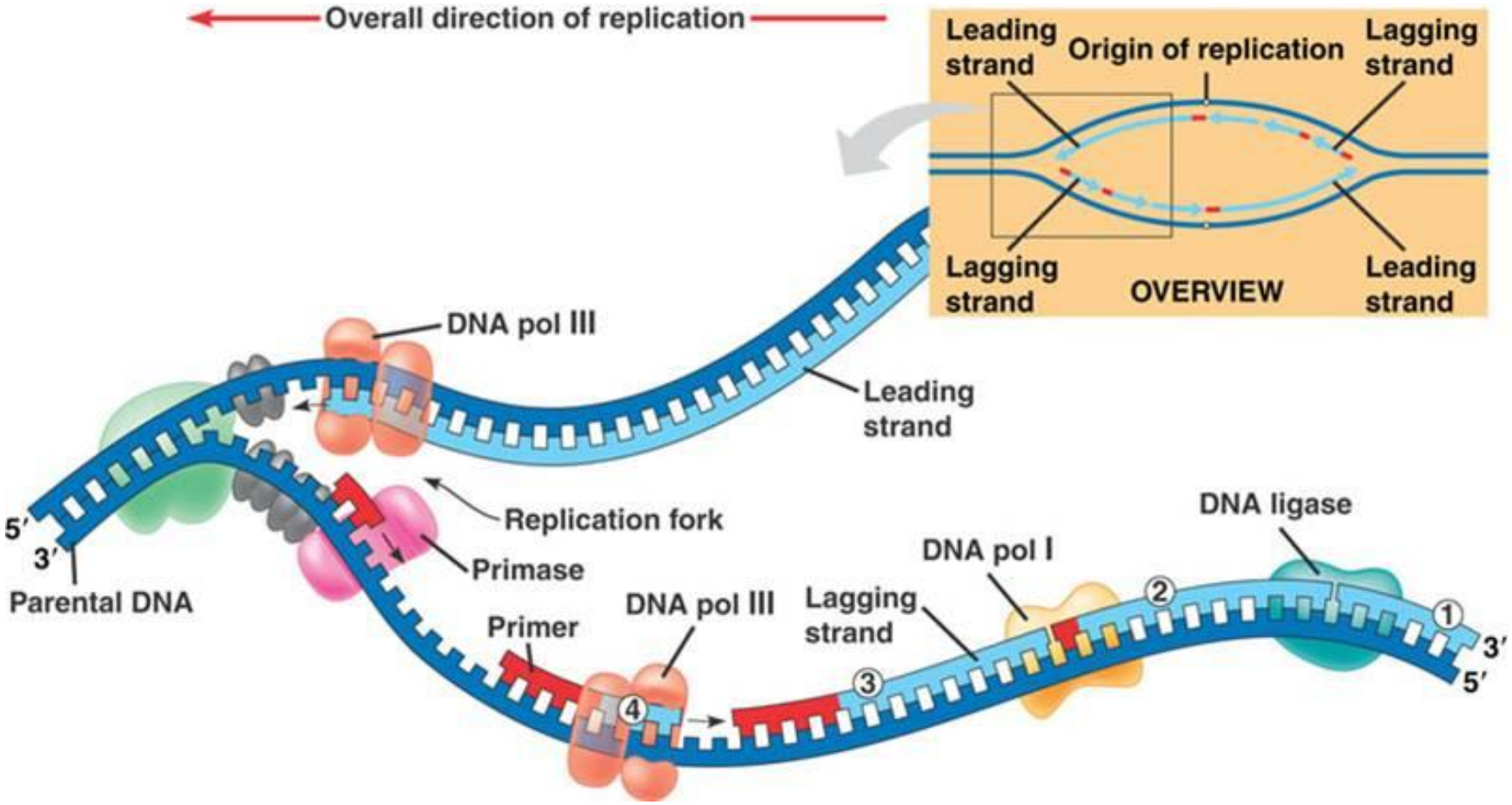


Newly synthesized NA strand grows from in the 5’ to 3’ direction

DNA replication



DNA replication

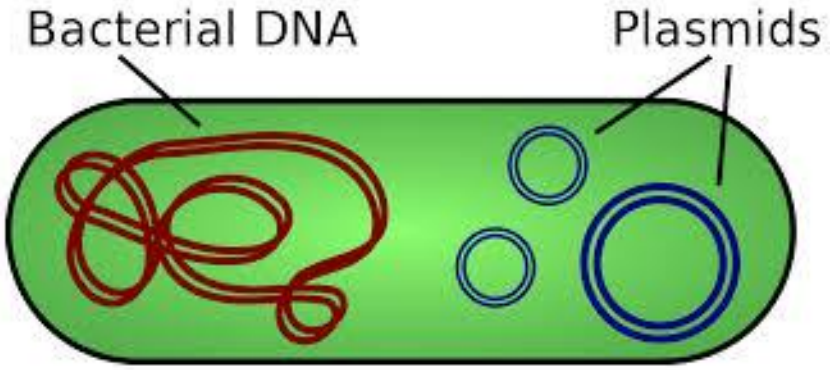


3 stages of a new nucleic acid strand synthesis

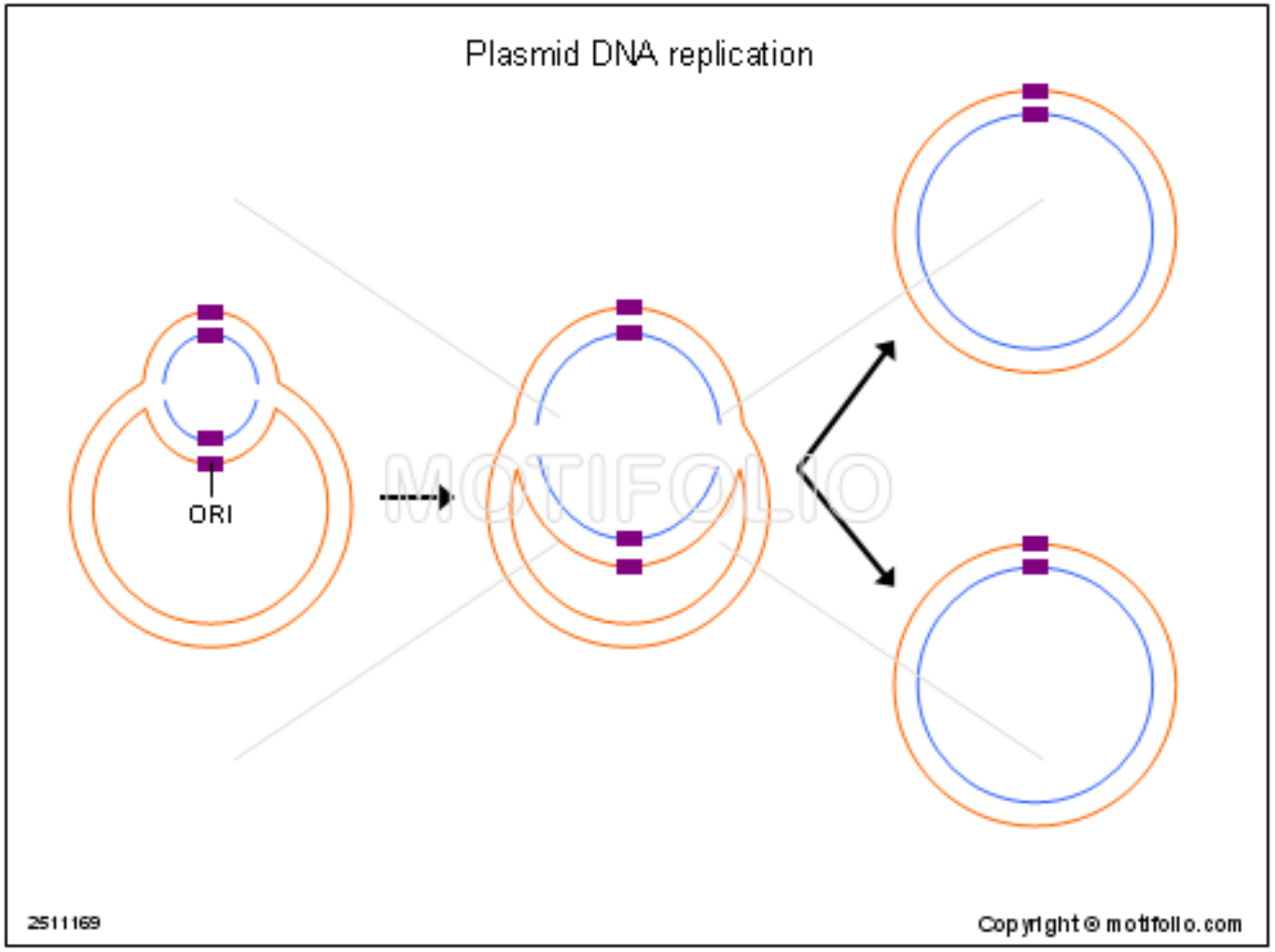
- Initiation
- Elongation
- Termination

Plasmids

A *plasmid* is a small, extrachromosomal DNA molecule within a cell that is physically separated from chromosomal DNA and can replicate independently. They are most commonly found as small circular, double-stranded DNA molecules in bacteria; however, plasmids are sometimes present in archaea and eukaryotic organisms. In nature, plasmids often carry genes that benefit the survival of the organism and confer selective advantage such as antibiotic resistance.



Plasmid DNA replication



Cell cycle

- The *cell cycle*, or cell-division cycle, is the series of events that take place in a cell leading to its division and duplication of its DNA (DNA replication) to produce two daughter cells.
- Cell cycle is a complexly regulated process.

Bacterial cell cycle

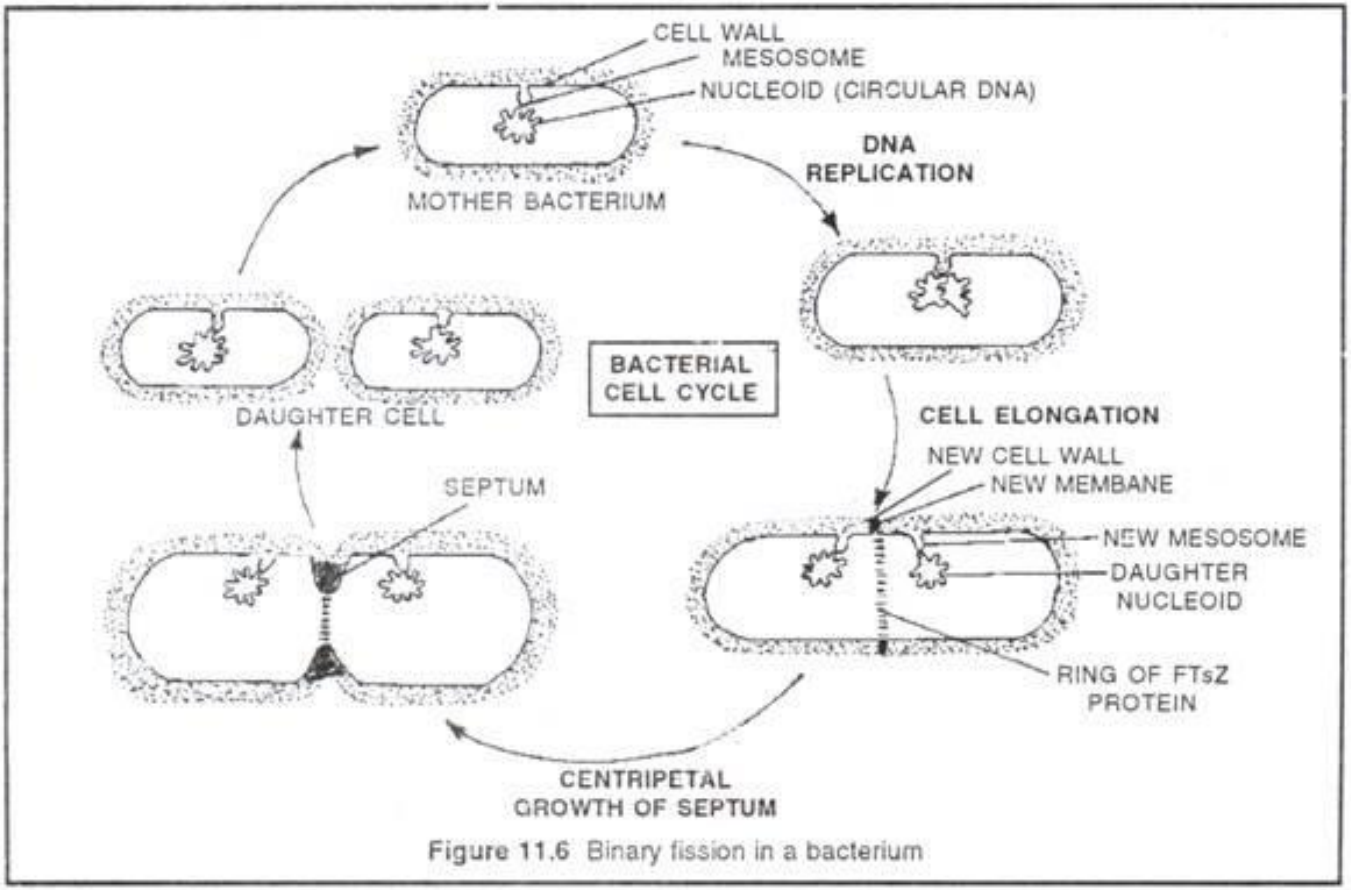
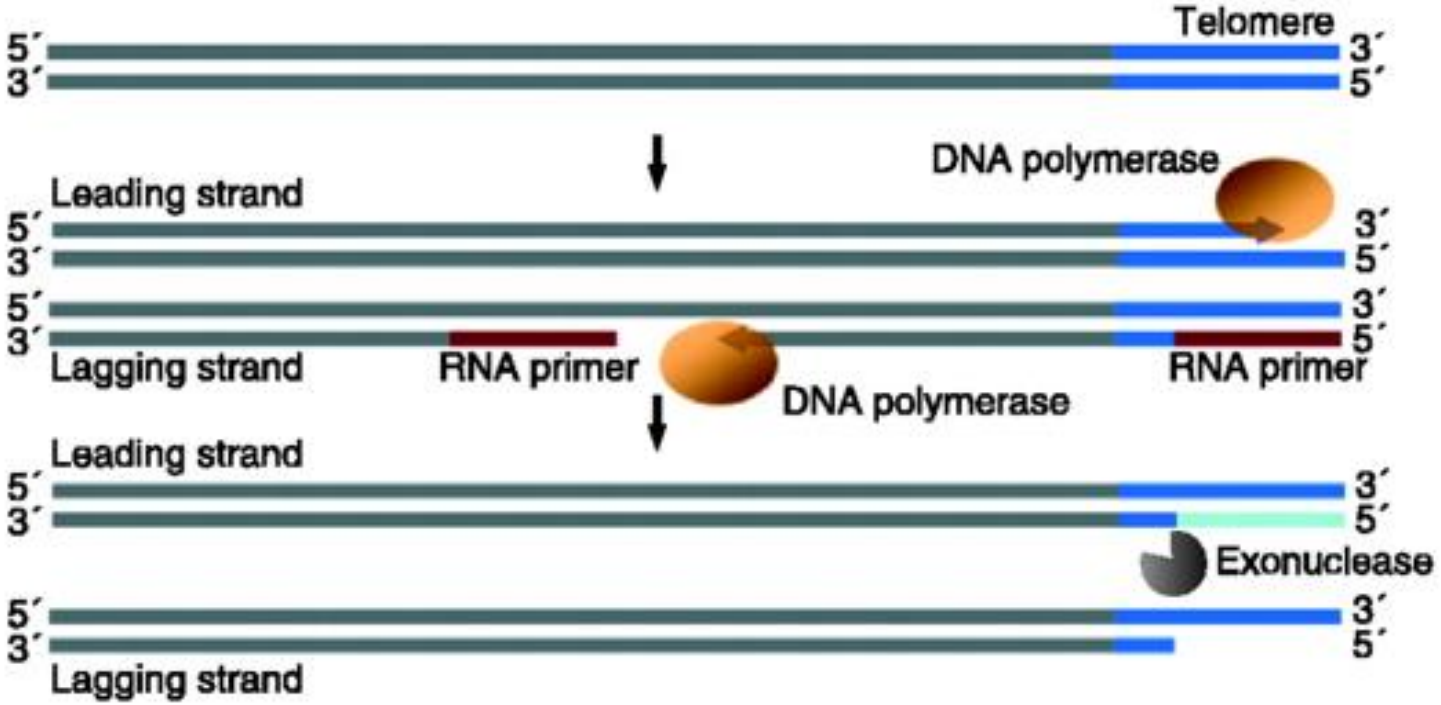
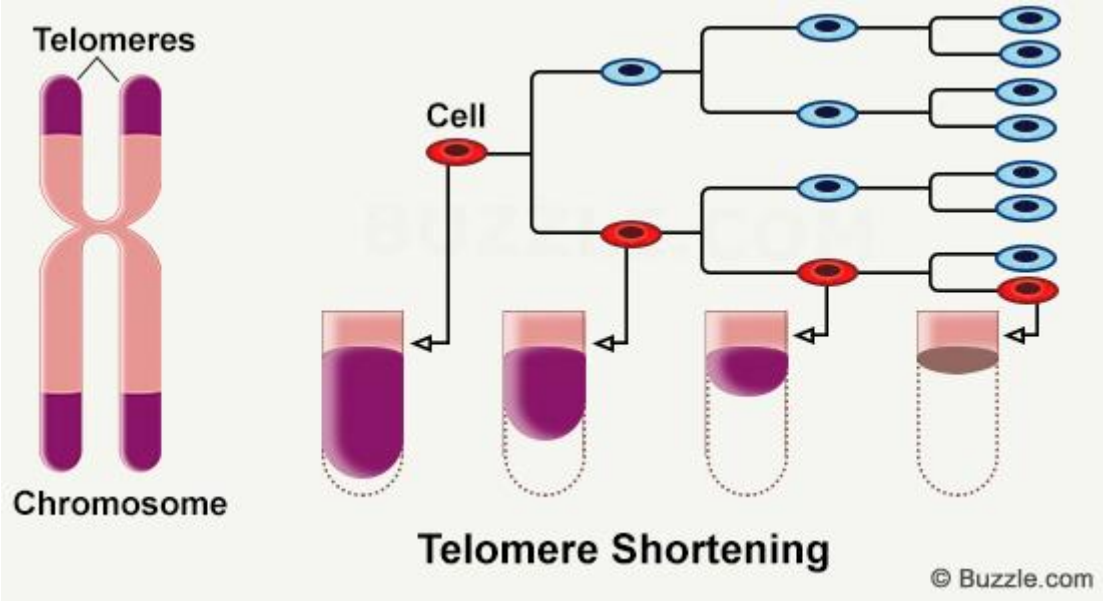


Figure 11.6 Binary fission in a bacterium

- **Bacterial** chromosome is circular, thus its replication terminates in the same way as replication of plasmid DNA – trhough simple resolution of two daughter DNA molecules.
- **Eukaryotic chromosomes are linear.** Unidirectional (5’ to 3’) nature of DNA replication creates a problem of potential chromosome end truncation. The problem is solved in nature by adding special regions called *telomeres* to the ends of eukaryotic chromosomes.


Telomere
5′
3′
3′
5′
DNA polymerase
Leading strand
5′
3′
3′
5′
5′
3′
3′
5′
Lagging strand
RNA primer
RNA primer
DNA polymerase
Leading strand
5′
3′
3′
5′
Exonuclease
5′
3′
3′
5′
Lagging strand

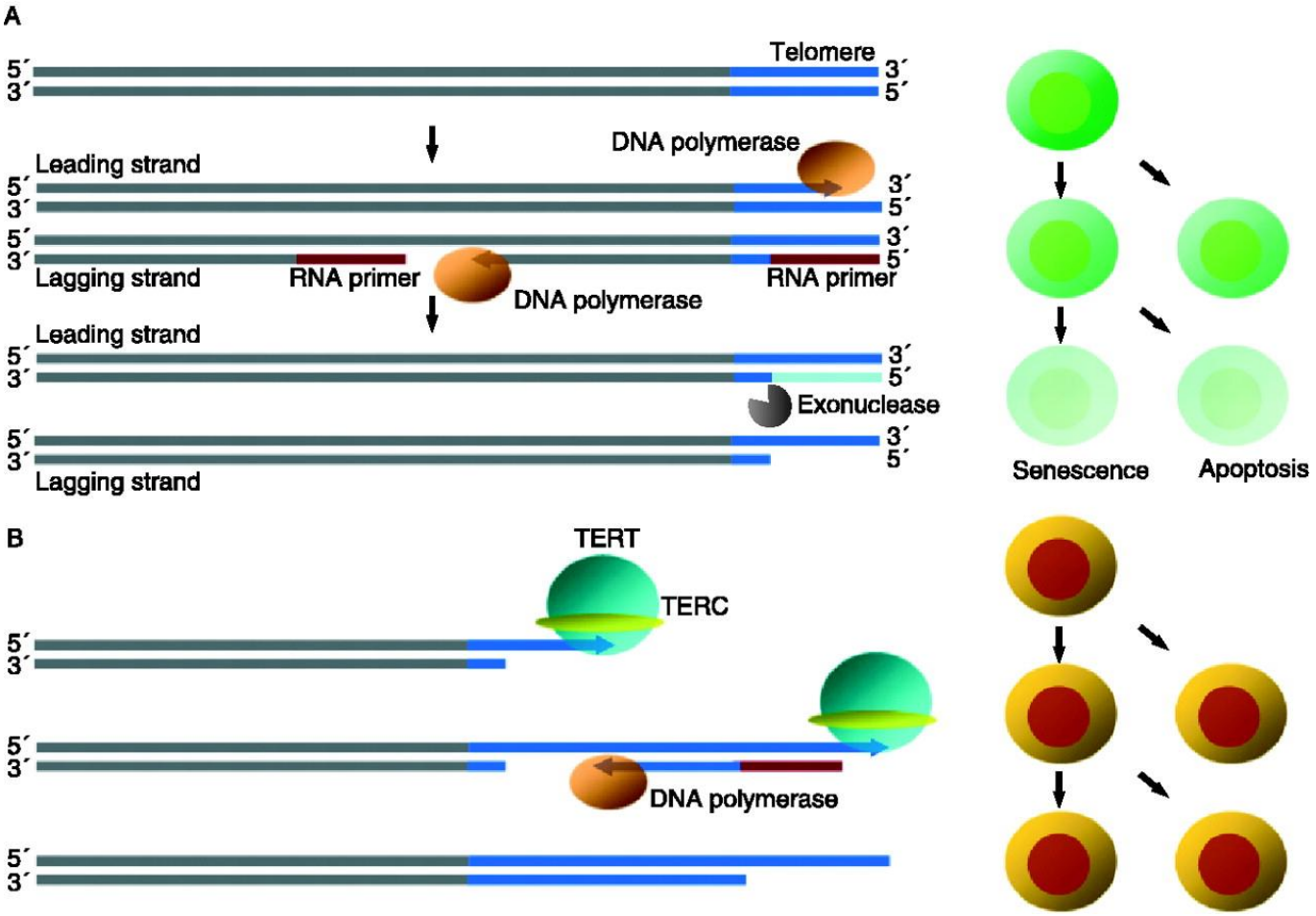
Telomere shortening



Telomerase

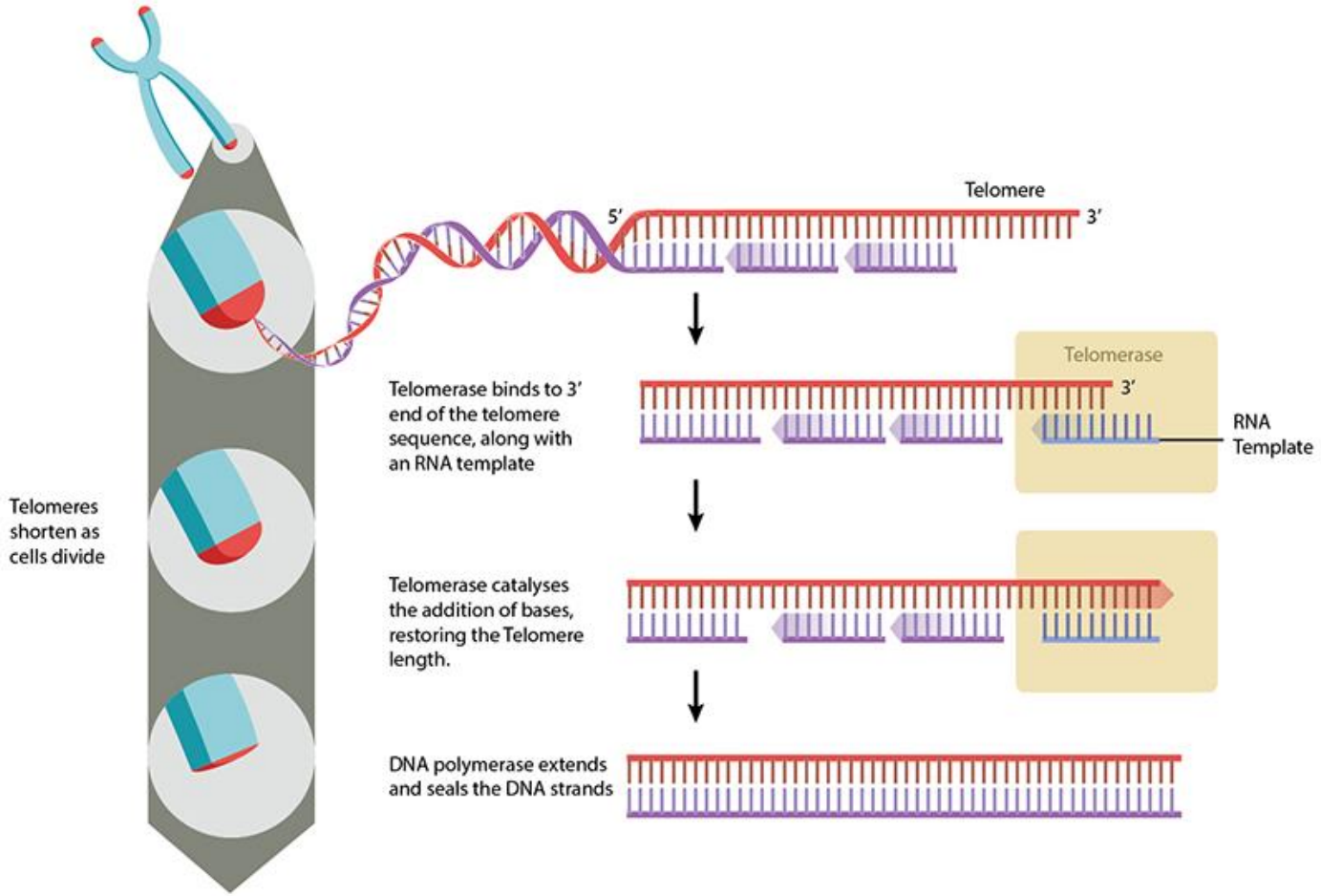
- Many organisms have an enzyme called *telomerase*, which carries out the task of adding repetitive nucleotide sequences to the ends of the DNA. Telomerase "replenishes" the telomere "cap." In most multicellular eukaryotic organisms, telomerase is active only in germ cells, some types of stem cells such as embryonic stem cells, and certain white blood cells.

Telomerase


A
Telomere
5′
3′
3′
5′
DNA polymerase
Leading strand
Lagging strand
RNA primer
RNA primer
DNA polymerase
Exonuclease
B
TERT
TERC
DNA polymerase
Senescence
Apoptosis

- Telomerase is a reverse transcriptase enzyme
- Telomerase is a ribonucleoprotein. It carries its own RNA molecule which is used as a template when it elongates telomeres.
- Sequence of the small RNA which is a part of telomerase depends on the organism species. For example in *Trypanosoma brucei* the sequence is 3’-CCCAAUCCC-5’

Telomerase


Telomeres shorten as cells divide
Telomere
5′
3′
Telomerase binds to 3′ end of the telomere sequence, along with an RNA template
Telomerase
3′
RNA Template
Telomerase catalyses the addition of bases, restoring the Telomere length.
DNA polymerase extends and seals the DNA strands

- Telomerase is active in germ cells but is normally absent from, or at very low levels in, most somatic cells.
- Reactivation of telomerase in somatic cells can lead to cancer. Indeed in the majority of cancer cells telomerase is actively expressed.
- Telomerase can be reactivated and telomeres reset back to an embryonic state by *somatic cell nuclear transfer*. This process is used in cloning of mammalian organisms.