Tishk International University
Faculty of Nursing

GENETICS

3rd Grade- Spring Semester 2024-2025

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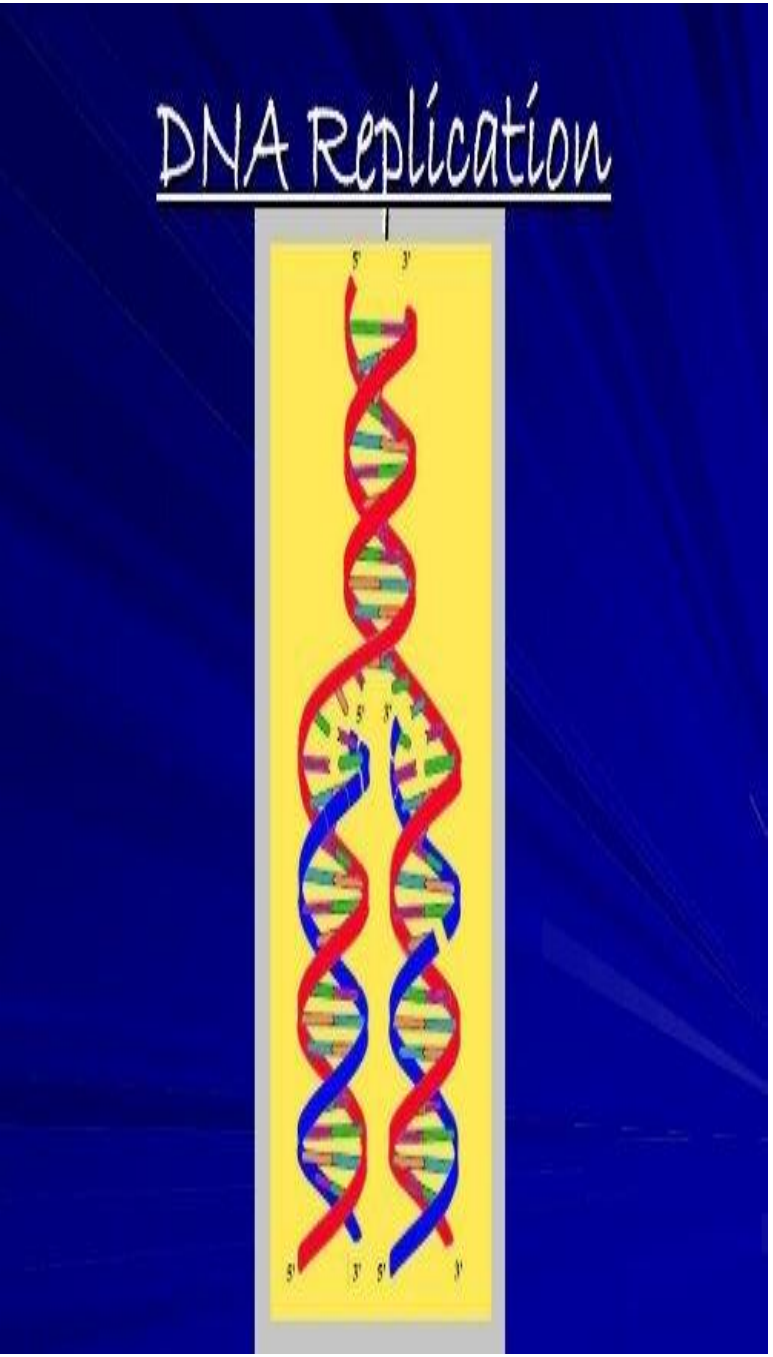


DNA Replication

How DNA Is Arranged in the Cell

DNA is a working molecule; it must be replicated when a cell is ready to divide, and it must be "read" to produce the molecules, such as proteins, to carry out the functions of the cell. For this reason,
the DNA is protected and packaged in very specific ways. In addition, DNA molecules can be very long. Stretched end-to-end,
the DNA molecules in a single human cell would come to a length of about 2 meters. Thus, the DNA for a cell must be packaged in a very ordered way
to fit and function within a structure (the cell) that is not visible to the naked eye. The chromosomes of prokaryotes are much simpler than those of eukaryotes in many of their features (**Figure**

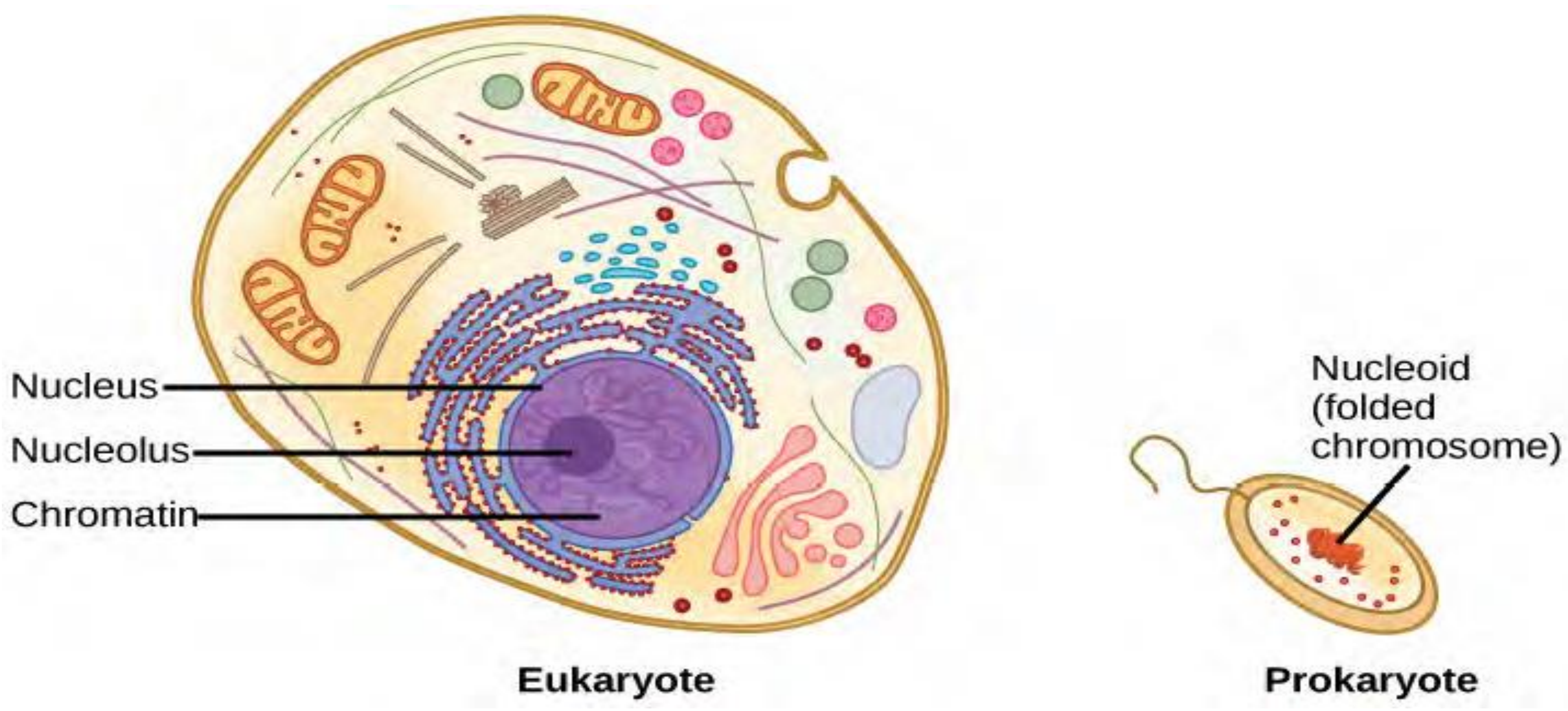


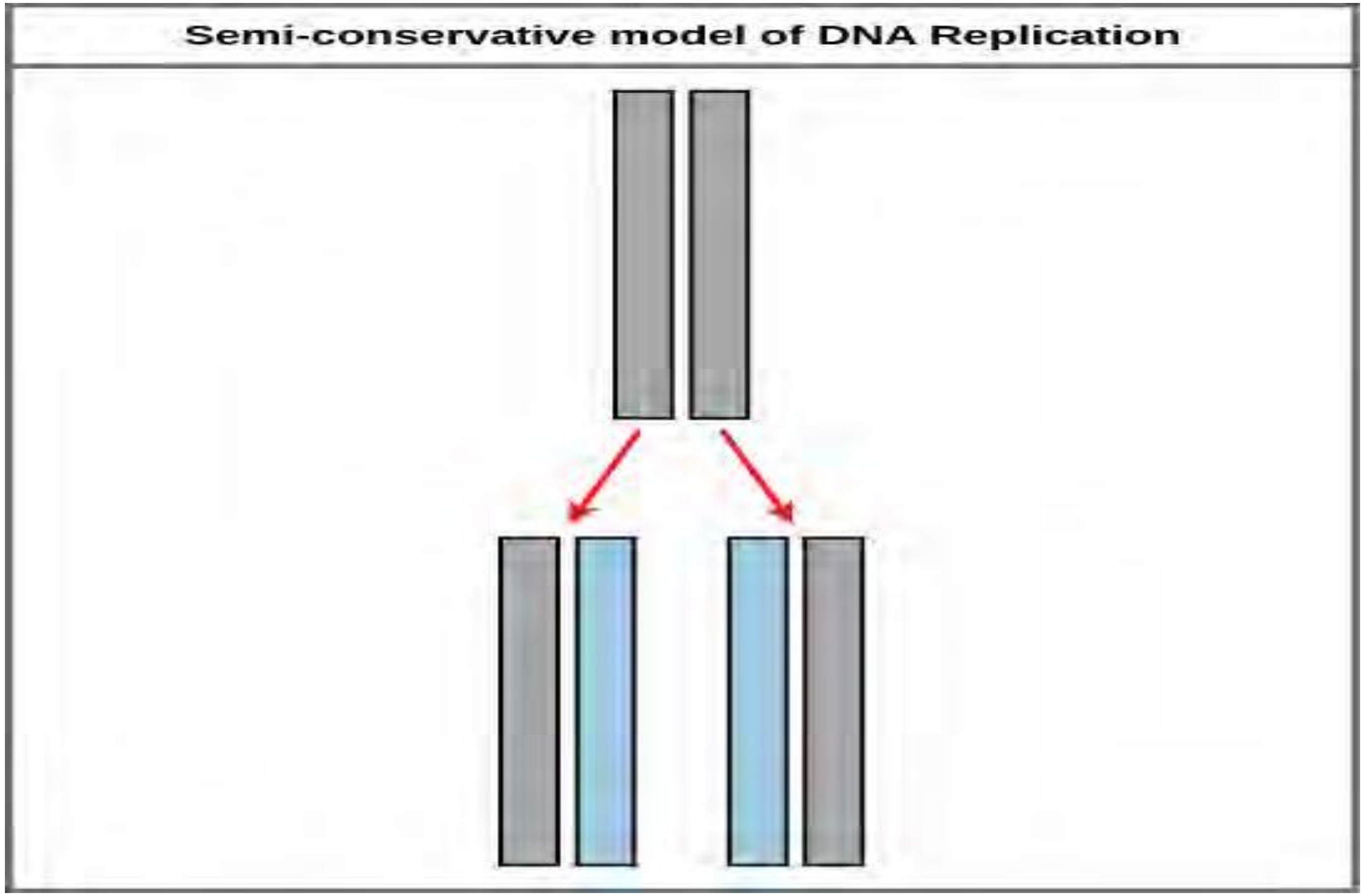
Figure : A eukaryote contains a well-defined nucleus, whereas in prokaryotes, the chromosome lies in the cytoplasm in an area called the nucleoid.

DNA Replication

By the end of this section, you will be able to:

- Explain the process of DNA replication
- Explain the importance of telomerase to DNA replication
- Describe mechanisms of DNA repair

When a cell divides, it is important that each daughter cell receives an identical copy of the DNA.
This is accomplished by the process of DNA replication. The replication of DNA occurs during the **synthesis phase, or S phase,** of the cell cycle, before the cell enters mitosis or meiosis.



The semiconservative model of DNA replication is shown. Gray indicates the original DNA strands, and blue indicates newly synthesized DNA.

DNA Replication in Eukaryotes

Because eukaryotic genomes are very complex, DNA replication is a very complicated process that involves several enzymes and other proteins. It occurs in three main stages: **initiation, elongation, and termination**.

eukaryotic DNA is bound to proteins known as histones to form structures called **nucleosomes.**

During initiation,

the DNA is made accessible to the proteins and enzymes involved in the replication process.

It turns out that there are specific nucleotide sequences called origins of replication at which replication begins. Certain proteins bind to the origin of replication while an enzyme called **helicase** unwinds and opens up the DNA helix. As the DNA opens up, Y-shaped structures called replication forks are formed .

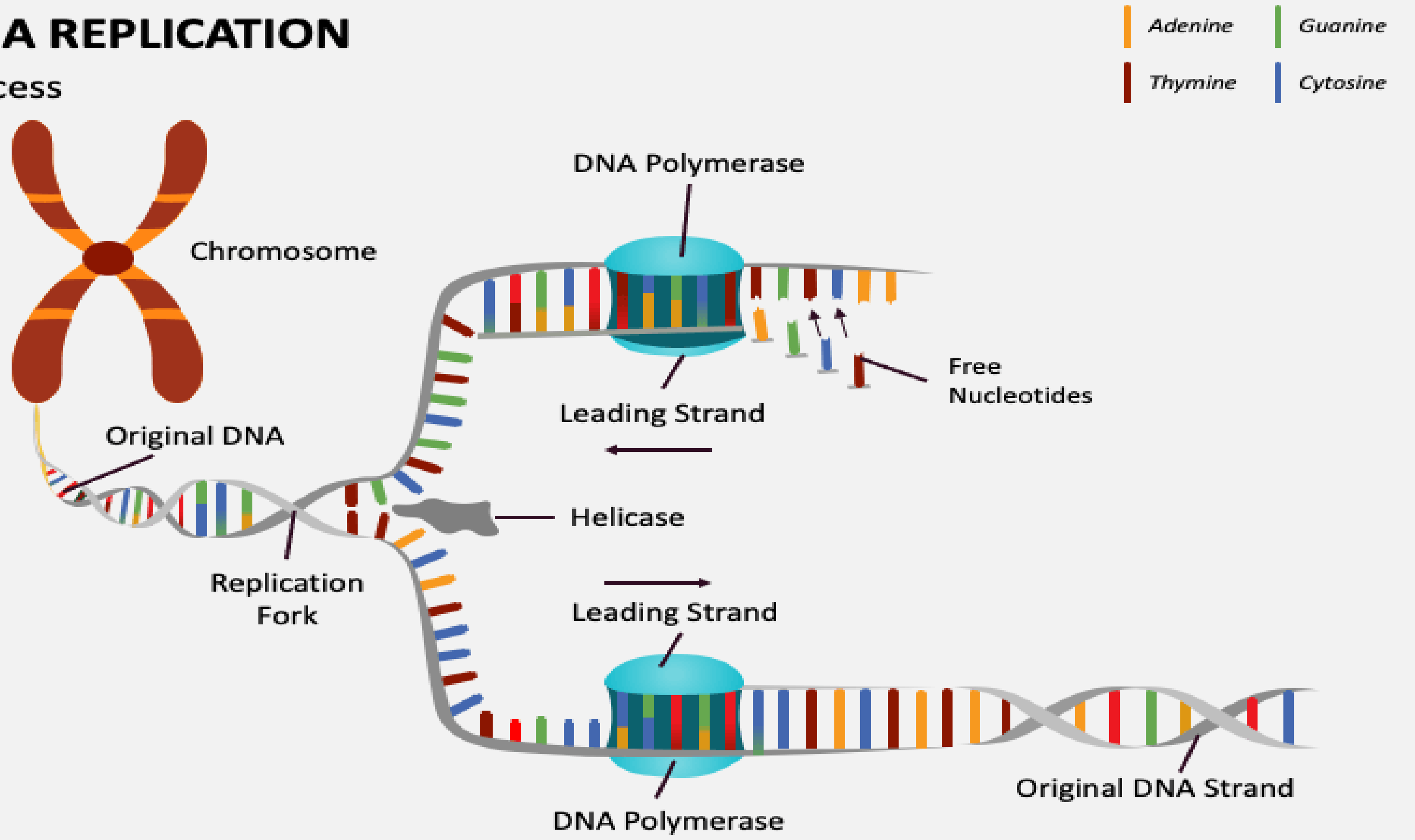
Two replication forks are formed at the origin of replication, and these get extended in both directions as replication proceeds.

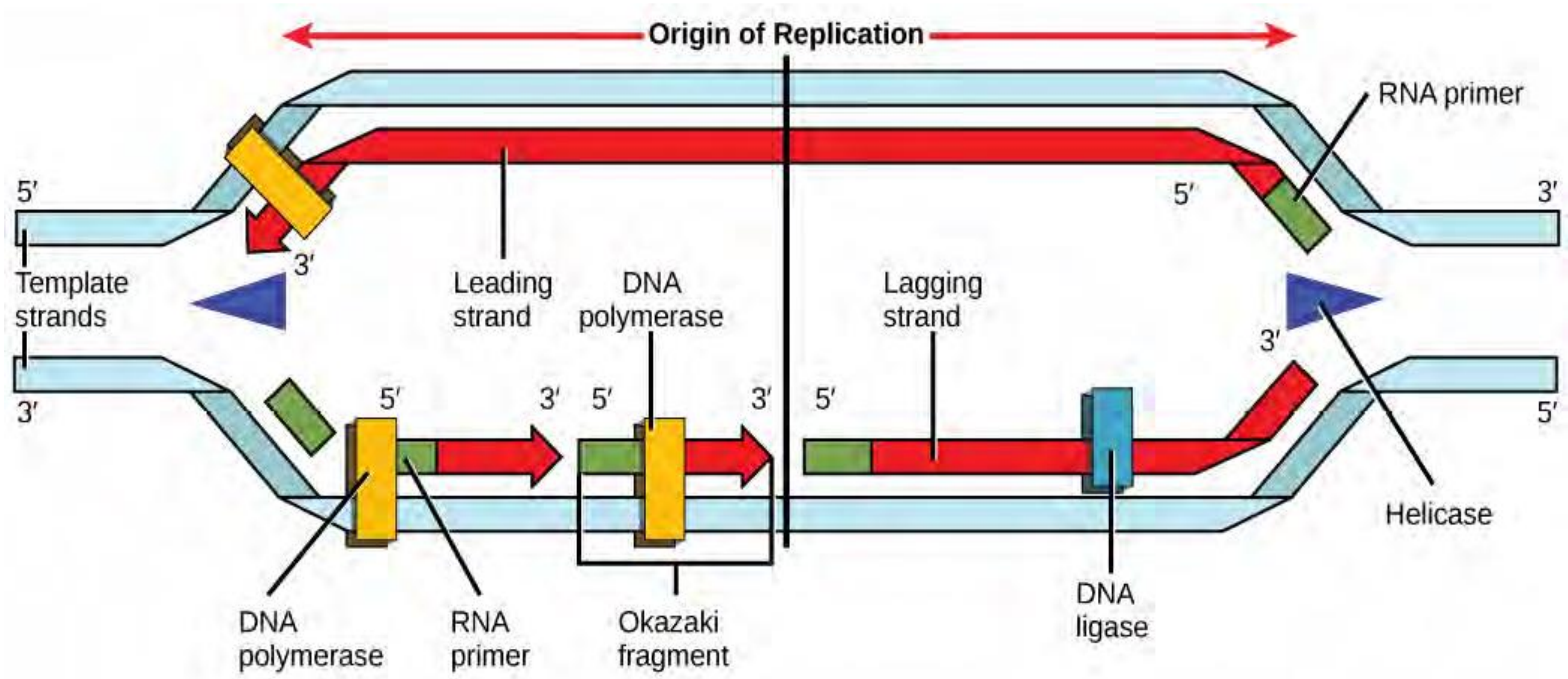
There are multiple origins of replication on the eukaryotic chromosome, such that replication can occur simultaneously from several places in the genome.

During elongation, an enzyme called DNA polymerase adds DNA nucleotides to the 3' end of the template. Because
DNA polymerase can only add new nucleotides at the end of a backbone, a primer sequence, which provides this starting
point, is added with complementary RNA nucleotides. This primer is removed later, and the nucleotides are replaced with DNA nucleotides.
One strand, which is complementary to the parental DNA strand, is synthesized continuously toward the replication fork so the polymerase can add nucleotides in this direction. This continuously synthesized strand is known as **the leading strand**. BecauseDNA polymerase can only synthesize DNA in a 5' to 3' direction, the other new strand is put
together in short pieces called **Okazaki fragments**. The Okazaki fragments each require a primer made of RNA to start
the synthesis. The strand with the Okazaki fragments is known as the **lagging strand**. As synthesis proceeds, an enzyme removes the RNA primer, which is then replaced with DNA nucleotides, and the gaps between fragments are sealed by an
enzyme called **DNA ligase**.

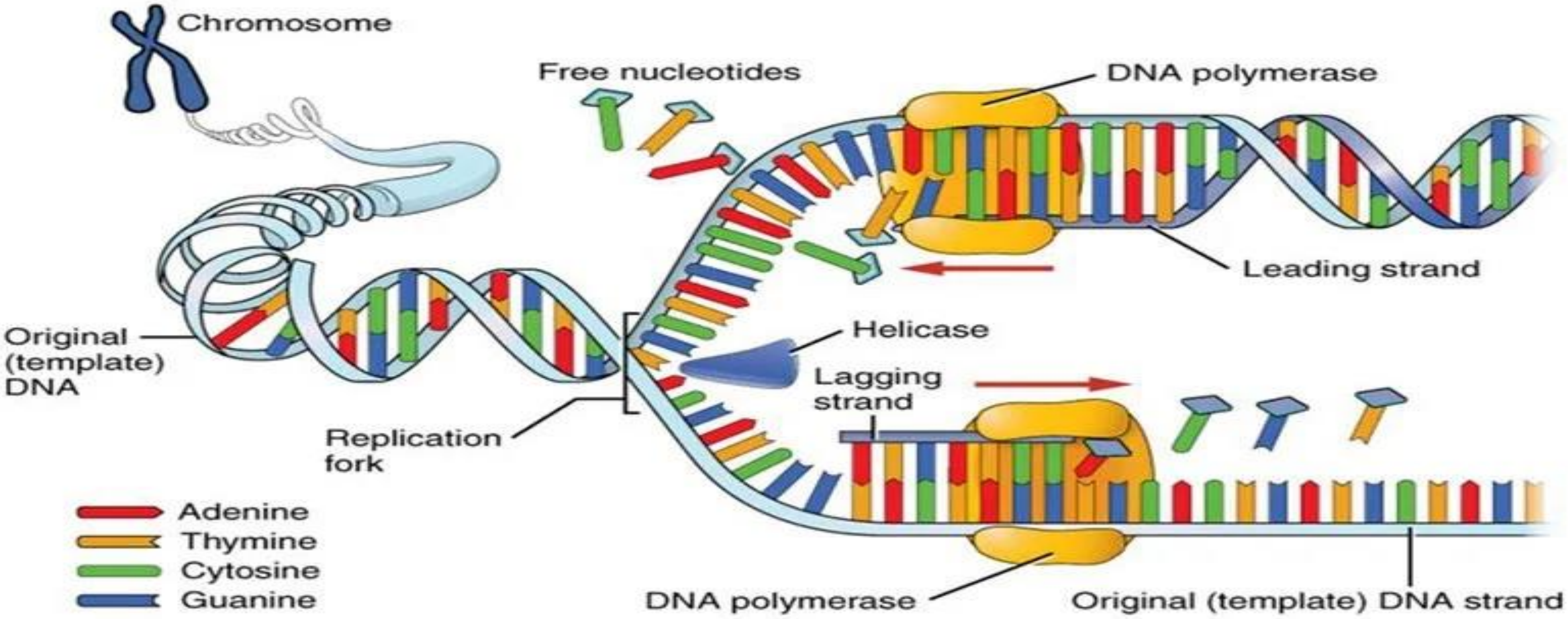
DNA REPLICATION

Process





replication fork is formed by the opening of the origin of replication, and helicase separates the DNA strands. An RNA primer is synthesized, and is elongated by the DNA polymerase. On the leading strand, DNA is synthesized continuously, whereas on the lagging strand, DNA is synthesized in short stretches. The DNA fragments are joined by DNA ligase.



Chromosome
Free nucleotides
DNA polymerase
Leading strand
Helicase
Lagging strand
Original (template) DNA
Replication fork
Adenine
Thymine
Cytosine
Guanine
DNA polymerase
Original (template) DNA strand

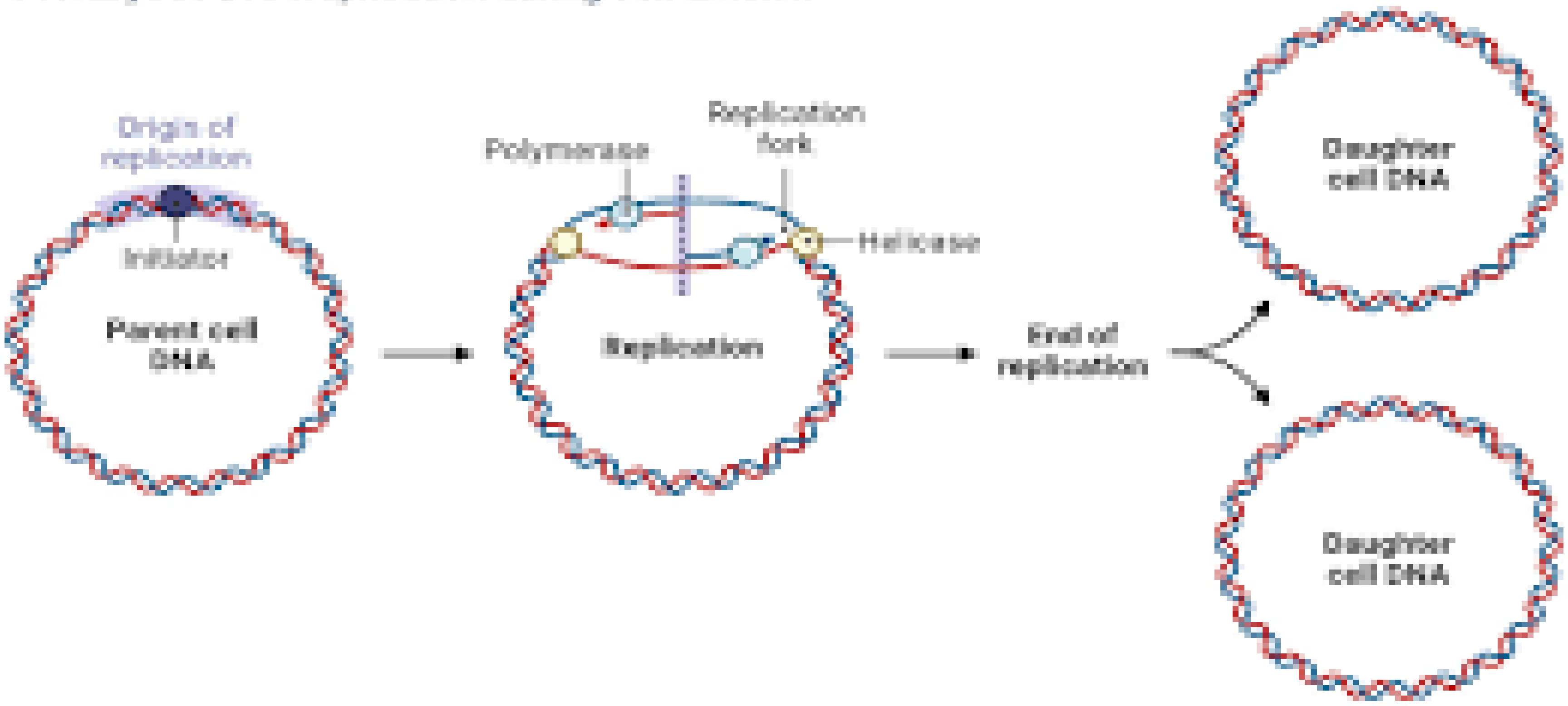
DNA Replication in Prokaryotes

prokaryotic chromosome is a circular molecule with a less extensive coiling structure than eukaryotic chromosomes. The eukaryotic chromosome is linear and highly coiled around proteins. While there are many similarities in the DNA replication process, these structural differences necessitate some differences in the DNA replication process in these two life forms.

DNA replication has been extremely well-studied in prokaryotes, primarily because of the small size of the genome and large number of variants available. Escherichia coli has 4.6 million base pairs in a single circular chromosome, and all of it gets replicated in approximately 42 minutes, starting from a single origin of replication and proceeding around the chromosome in both directions. This means that approximately 1000 nucleotides are added per second. The process is much more rapid than in eukaryotes.

DNA REPLICATION

Prokaryotic DNA replication during cell division



Termination In some DNA molecules, replication is terminated whenever two replication forks meet. In others, specific termination sequences block further replication. A termination protein, called Tus in *E. coli*, binds to these sequences. Tus blocks the movement of helicase, thus stalling the replication fork and preventing further DNA replication.

Table :Differences between Prokaryotic and Eukaryotic Replications

Property

property	prokaryotes	Eukaryotes
Origin of replication	single	multiple
Rate of replication	1000 nucleotide /S	50 to 100 nucleotide /S
Chromosome structure	circular	linear
telomerase	Not present	present

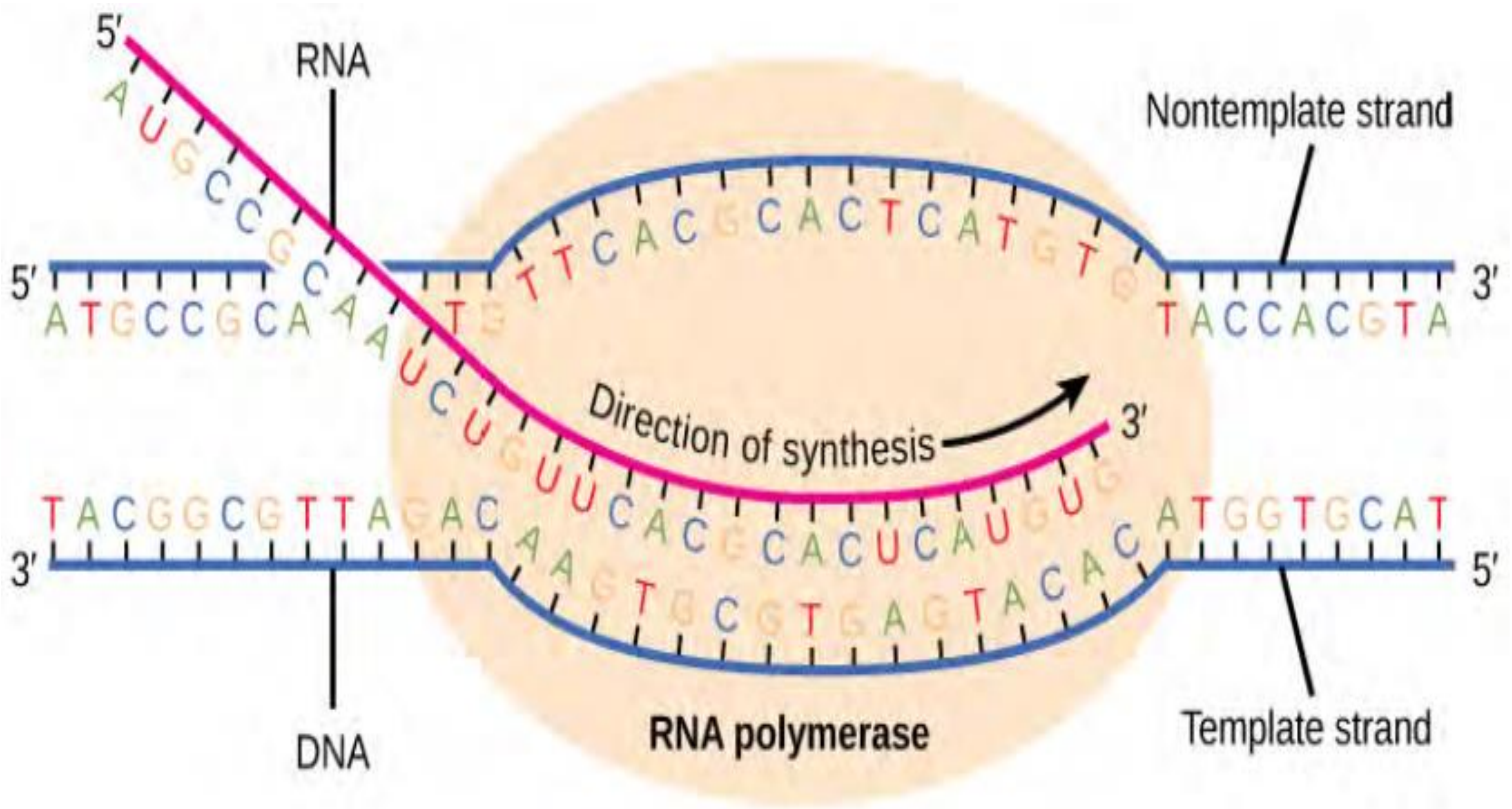
STEPS IN PROTEIN SYNTHESIS

- Several steps are involved in the synthesis of protein.
- The genetic information in cells flows in one way:

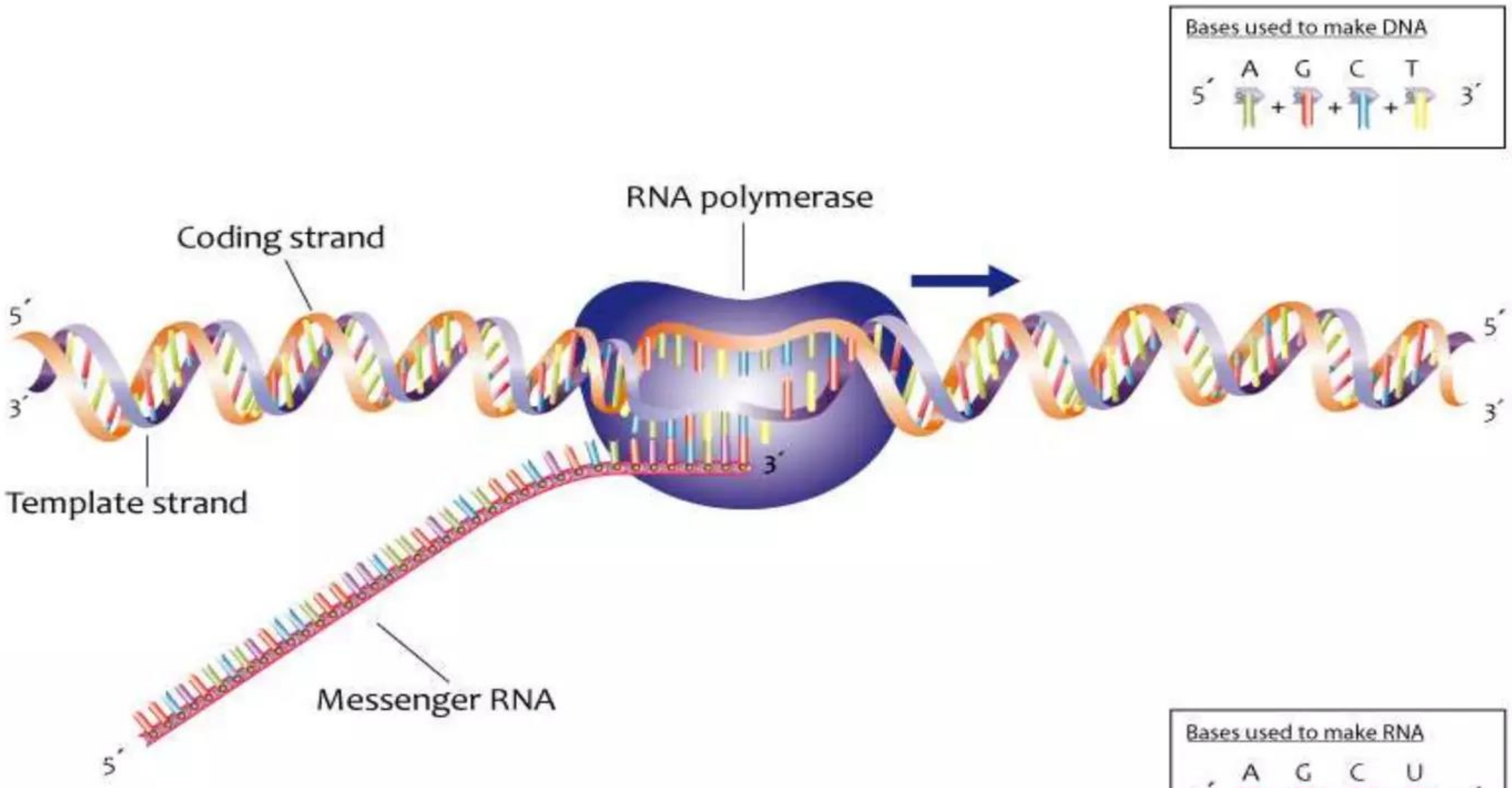
- DNA Specifies the synthesis of RNA
- RNA Specifies the synthesis of Amino Acids.
- The two main steps in protein synthesis are transcription and translation.

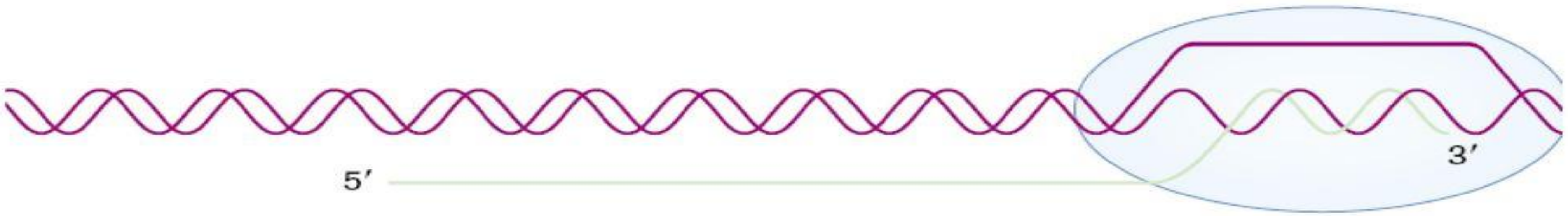
TRANSCRIPTION

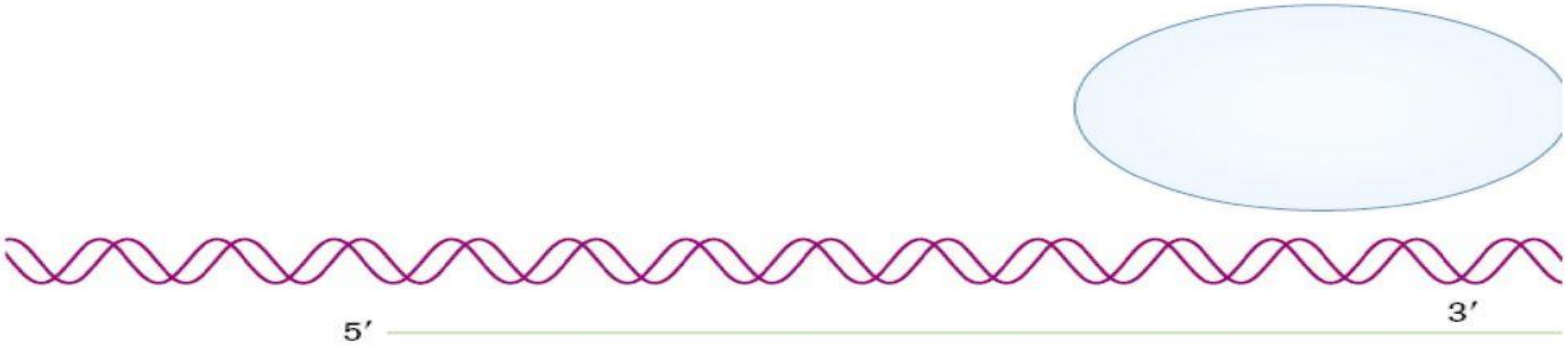
- Transcription is a process in which genetic information is transmitted from DNA to RNA .
- It is the first step in protein synthesis and occurs in the nucleus.
- When the genes are active, proteins called transcription factors are produced.
- These transcription factors binds to promoter or enhancer region of genes
- Transfer of the genetic information from DNA –dependent RNA polymerase **(Transcriptase)**
- It produces a new complimentary copy of the whole gene and is known as primary RNA molecule.
- The primary RNA molecule undergoes splicing in which introns are removed from exons, to produce single-stranded messenger ribonucleic acid (mRNA) molecule.
- The mRNA migrates from the nucleus to the cytoplasm and is used as a template for protein synthesis.



RNA
Nontemplate strand
5′
3′
Direction of synthesis
DNA
RNA polymerase
Template strand


Bases used to make DNA
A G C T
5´ 3´
RNA polymerase
Coding strand
5´
3´
5´
3´
3´
Template strand
Messenger RNA
5´
Bases used to make RNA
A G C U
5´ 3´


3′
5′


3′
5′

Post-transcription

- After transcription, the mRNA primary transcript must go to the cytoplasm to be translated.
- In eukaryotes, before it leaves the nucleus it needs a “cap” and a “tail” to protect it and prevent it from being broken down.

Eukaryotic RNA Processing

The newly transcribed eukaryotic mRNAs must undergo several processing steps before they can be transferred from the nucleus to the cytoplasm and translated into a protein. The additional steps involved in eukaryotic mRNA maturation create a molecule
that is much more stable than a prokaryotic mRNA. For example, eukaryotic mRNAs last for several hours, whereas the typical prokaryotic mRNA lasts no more than five seconds.

The mRNA transcript is first coated in RNA-stabilizing proteins to prevent it from degrading while it is processed and
exported out of the nucleus. This occurs while the pre-mRNA still is being synthesized by adding a special nucleotide “cap”to the 5' end of the growing transcript. In addition to preventing degradation, factors involved in protein synthesis recognize
the cap to help initiate translation by ribosomes.

Once elongation is complete, an enzyme then adds a string of approximately 200 adenine residues to the 3' end, called
the poly-A tail.

This modification further protects the pre-mRNA from degradation and signals to cellular factors that the transcript needs to be exported to the cytoplasm.

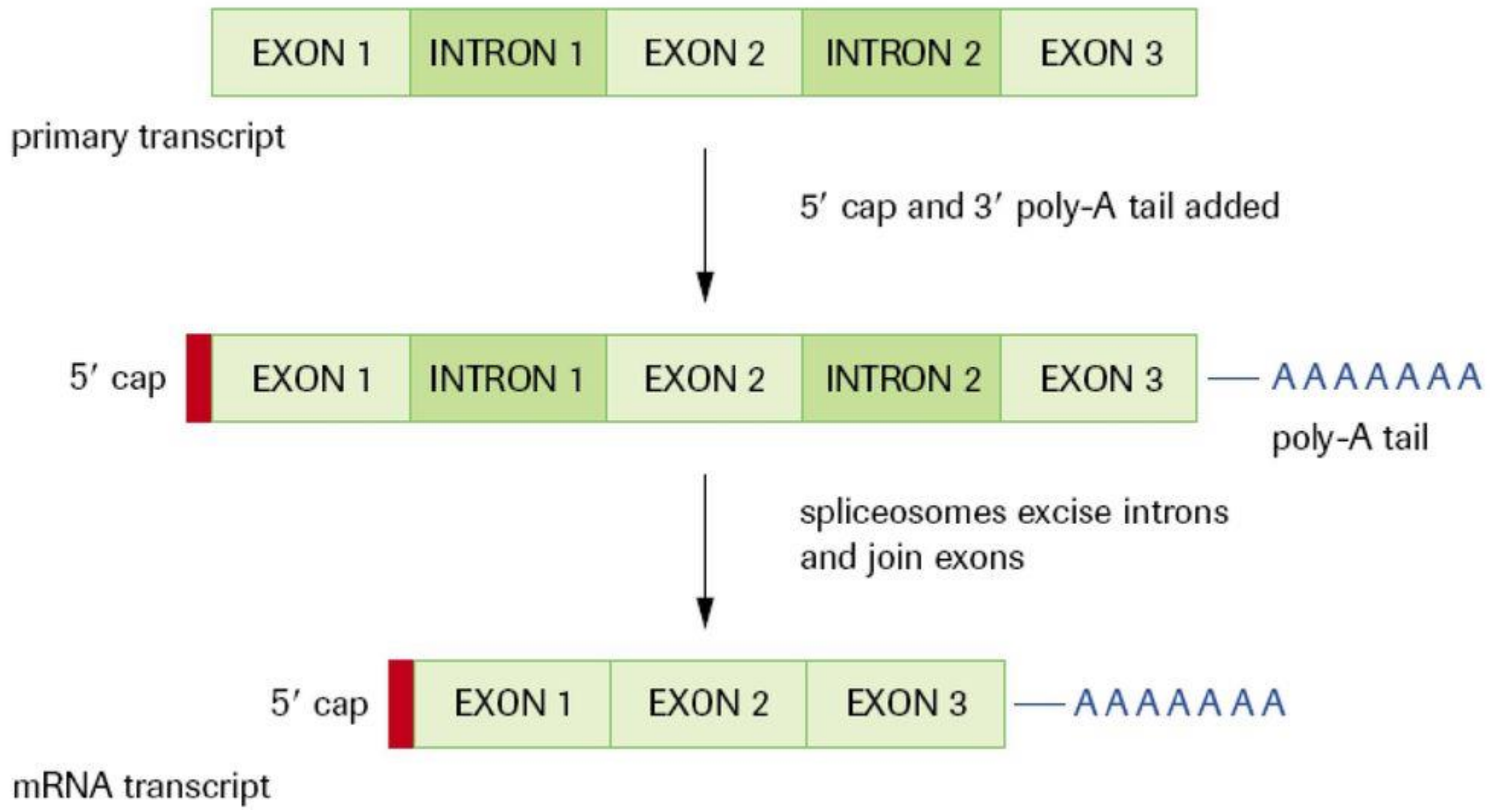
Poly-A tail

- A sequence of ~ 200 adenine ribonucleosides is added to the 3' end to protect the mRNA from breaking down
- This is called a poly-A tail
- The tail is added with the help of the enzyme poly-A polymerase

Exons and Introns

- In eukaryotic DNA, a gene consists of introns and exons
- EXONS: coding regions – they code for the specific protein
- INTRONS: noncoding - “filler DNA” that does not code for proteins.

- Before mRNA goes into the cytoplasm, the introns must be removed from the mRNA
- Proteins called spliceosomes cut the introns out and join the remaining exons together.


EXON 1
INTRON 1
EXON 2
INTRON 2
EXON 3
primary transcript
5′ cap and 3′ poly-A tail added
5′ cap
EXON 1
INTRON 1
EXON 2
INTRON 2
EXON 3
AAAAAAA
poly-A tail
spliceosomes excise introns
and join exons
5′ cap
EXON 1
EXON 2
EXON 3
AAAAAAA
mRNA transcript

mRNA transcript

- Once the cap and tail have been added, and the introns removed, the mRNA is called an mRNA transcript

- It can now go to the cytoplasm for translation