ZAPOROZHYE STATE MEDICAL UNIVERSITY
DEPARTMENT OF MEDICAL BIOLOGY

Molecular Basis of Heredity.

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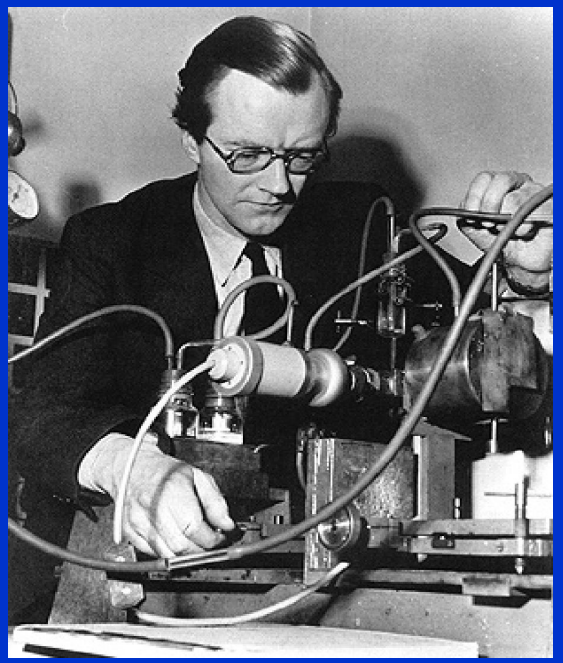
Zaporozhye - 2016

QUESTIONS

- -DNA – structure and function
- -Genetic Code and it properties
- -Gene Expression
- -Regulation of Gene action

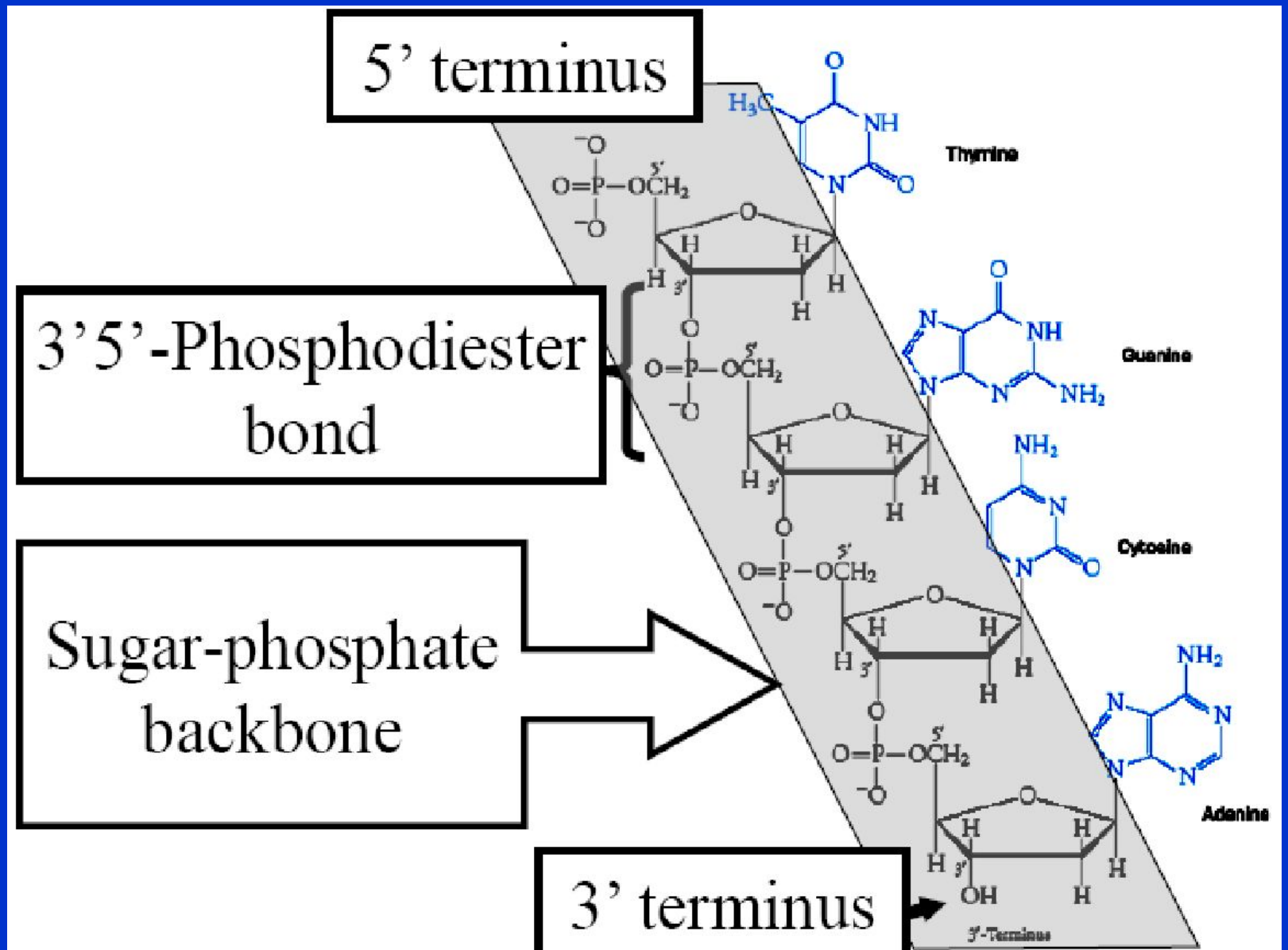

de FUMER
DANS LES DORTOIRS



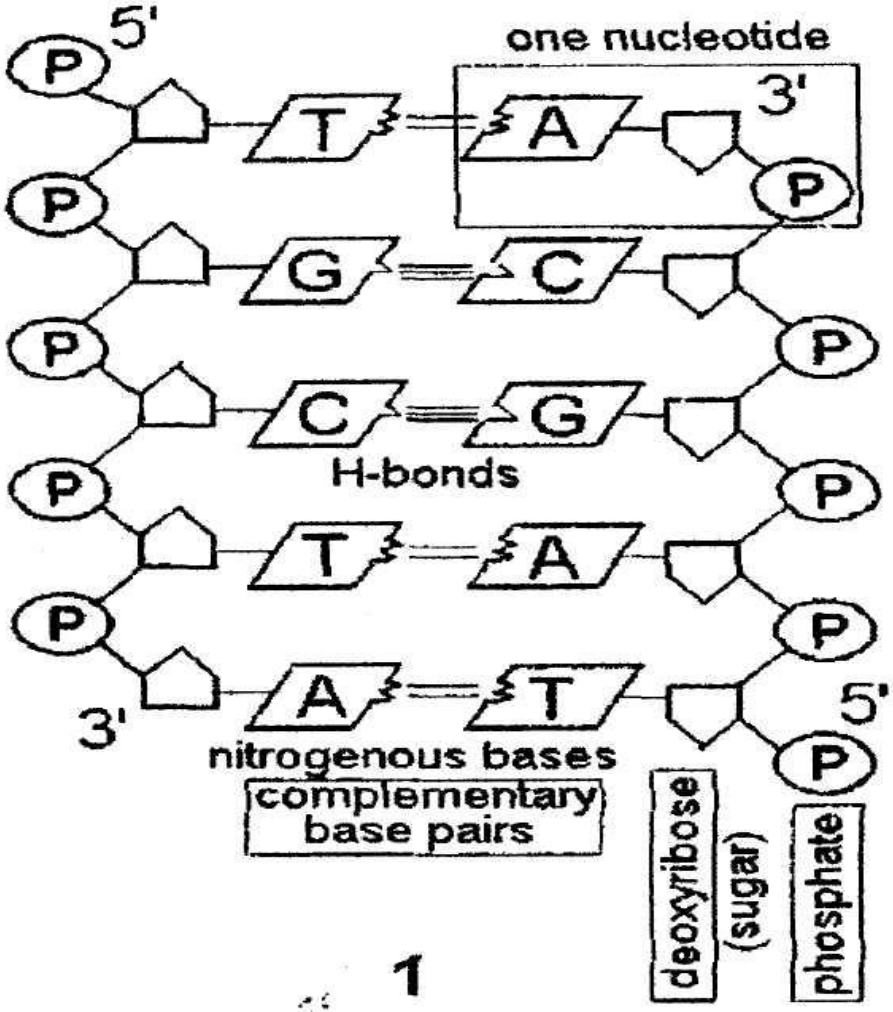
DNA.

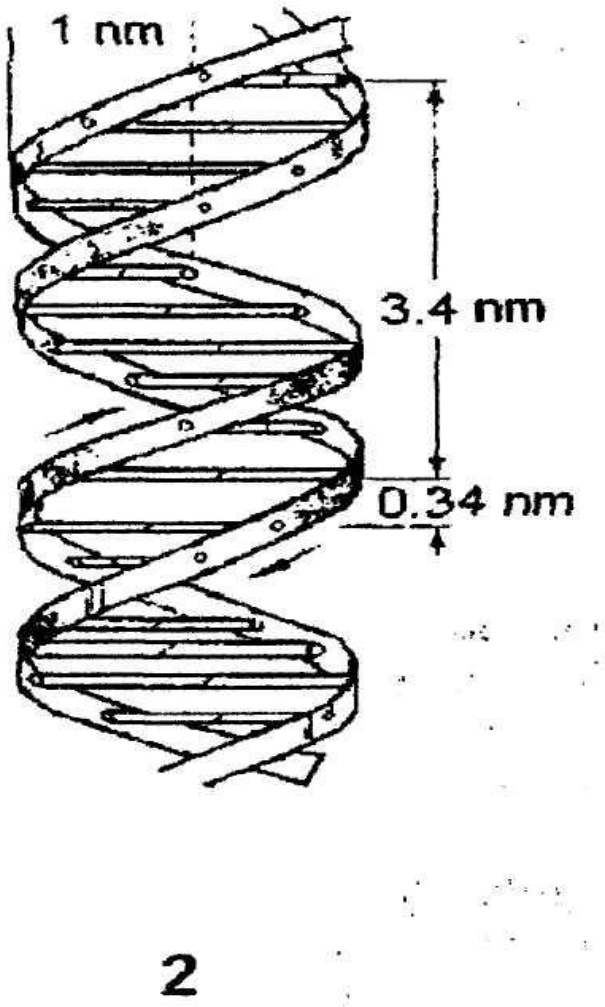
- It is a very long, thin, double helix in which two strands are wound around each other. Each strand is made up of a chain of nucleotides.
- It contains four organic bases: adenine, guanine, cytosine and thymine. The amount of guanine is usually equal to that of cytosine and the amount of adenine is usually equal to that of thymine.
- The two strands are held together by hydrogen bonds between adenine and thymine and between guanine and cytosine. This principle is called base paring.
- The two chains run in opposite direction i.e. are antiparallel.

DNA

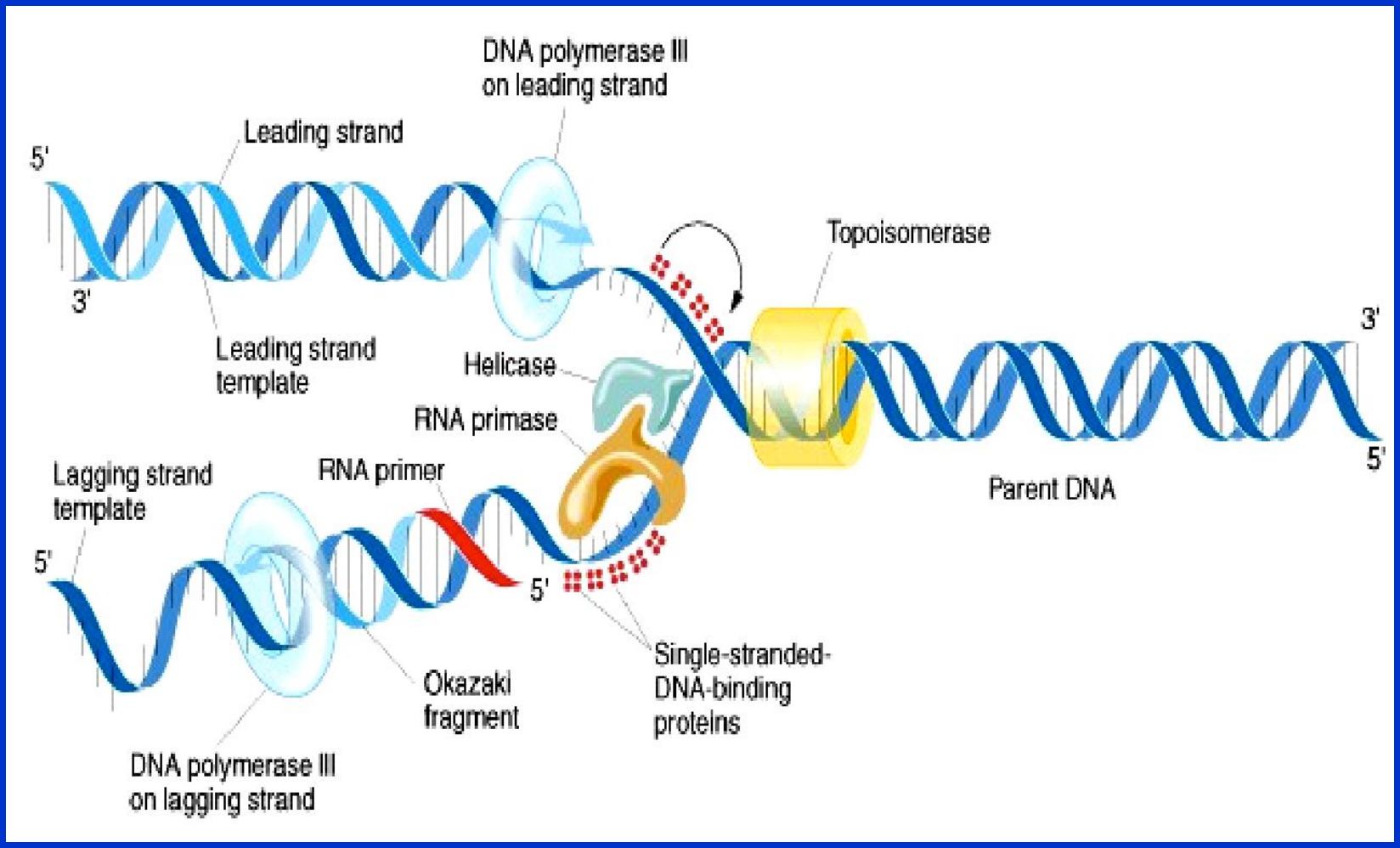

5’ terminus
3’5’-Phosphodiester bond
Sugar-phosphate backbone
3’ terminus
Thymine
Guanine
Cytosine
Adenine
5'-Terminus

DNA


5'
one nucleotide
3'
P
T
A
G
C
H-bonds
3'
5'
nitrogenous bases
complementary base pairs
deoxyribose (sugar)
phosphate
1


1 nm
3.4 nm
0.34 nm
2

DNA REPLICATION



Genetic code and its Properties.

Genetic code is a system of nucleotides placed in DNA molecule that controls amino-acids position sequence in protein molecule.

- The code is a triplet codon. Triplet is a name for three nucleotides which code one amino acid. Four nucleotides combined by three make 64 different codones. There are 61 informational triplets and three triplets which code no amino acids (UAG, UAA, UGA). They act as stop codons.

-The code is non-overlapping. It means that a base is not used for different codons.

-The code is collinear. It means that the sequences of nucleotides of DNA molecule defined the sequence of amino acids in a protein molecule.

-The code is degenerate. More than one codon may specify the same amino acid. All other 18 amino acids have more than one codon, except for tryptophan and methionine.

-The code is universal. Same genetic code is found valid for all organisms ranging from bacteria to man.

-The code is commaless. It means that no codon is reserved for punctuations: after one amino acid is coded, the second amino acid will be automatically coded by the next three letters and that no letters are wasted as the punctuation marks.

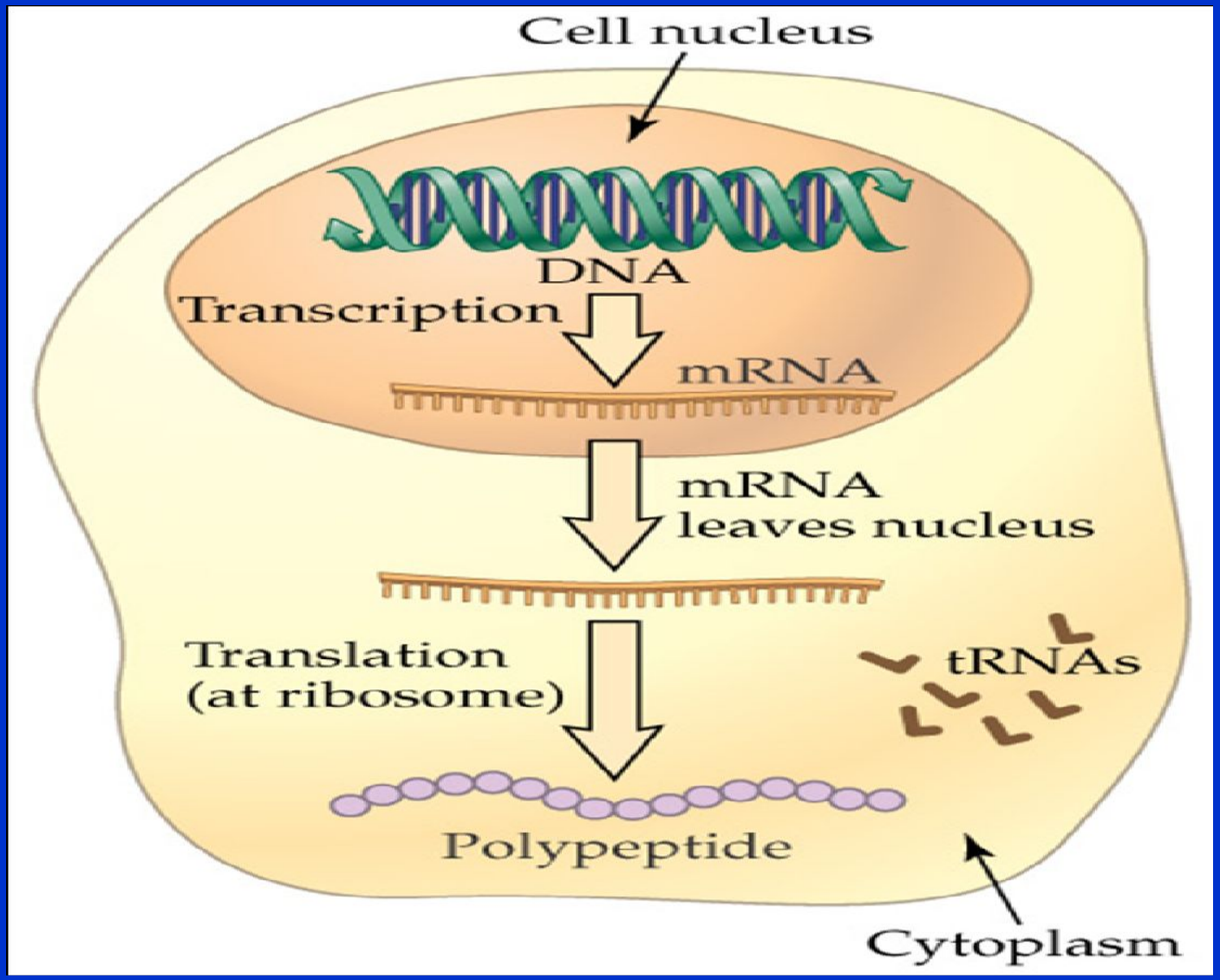
Gene Expression

Gene expression is the process by which a genes information is converted into the structures and functions of a cell by a process of producing a protein. Genes provide the instructions for making proteins.

Protein Systhesis is the process in which cells build proteins from information in a DNA gene in a two major steps:

1. Transcription.
2. Translation.

PROTEIN SYNTESIS



The three roles of RNA in protein synthesis

- Three types of RNA molecules
- perform different but
- complementary roles in
- protein synthesis (translation)
- **Messenger RNA (mRNA)**
- carries information copied from
- DNA in the form of a series of
- three base “words” termed codons

- **Transfer RNA (tRNA)**
- deciphers the code and delivers
- the specified amino acid
- **Ribosomal RNA (rRNA)**
- associates with a set of proteins
- to form ribosomes, structures that
- function as protein-synthesizing
- machines

Transcription:

synthesis of an RNA (mRNA) that is complementary to one of the strands of DNA.

Translation:

ribosomes read a messenger RNA and make protein accoding to its instruction.

Transcription

It is divided into 3 phases:Initiation, Elondation and Termination.

Initiation: The enzyme RNA polymerase recognizes a promoter site, binds to it causing the unwinding of the DNA molecule. This is followed by initiation of RNA synthesis at the starting point.

Elongation:

RNA polymerase directs the binding of ribonucleotides to the growing RNA chan in the 5'-3' direction.

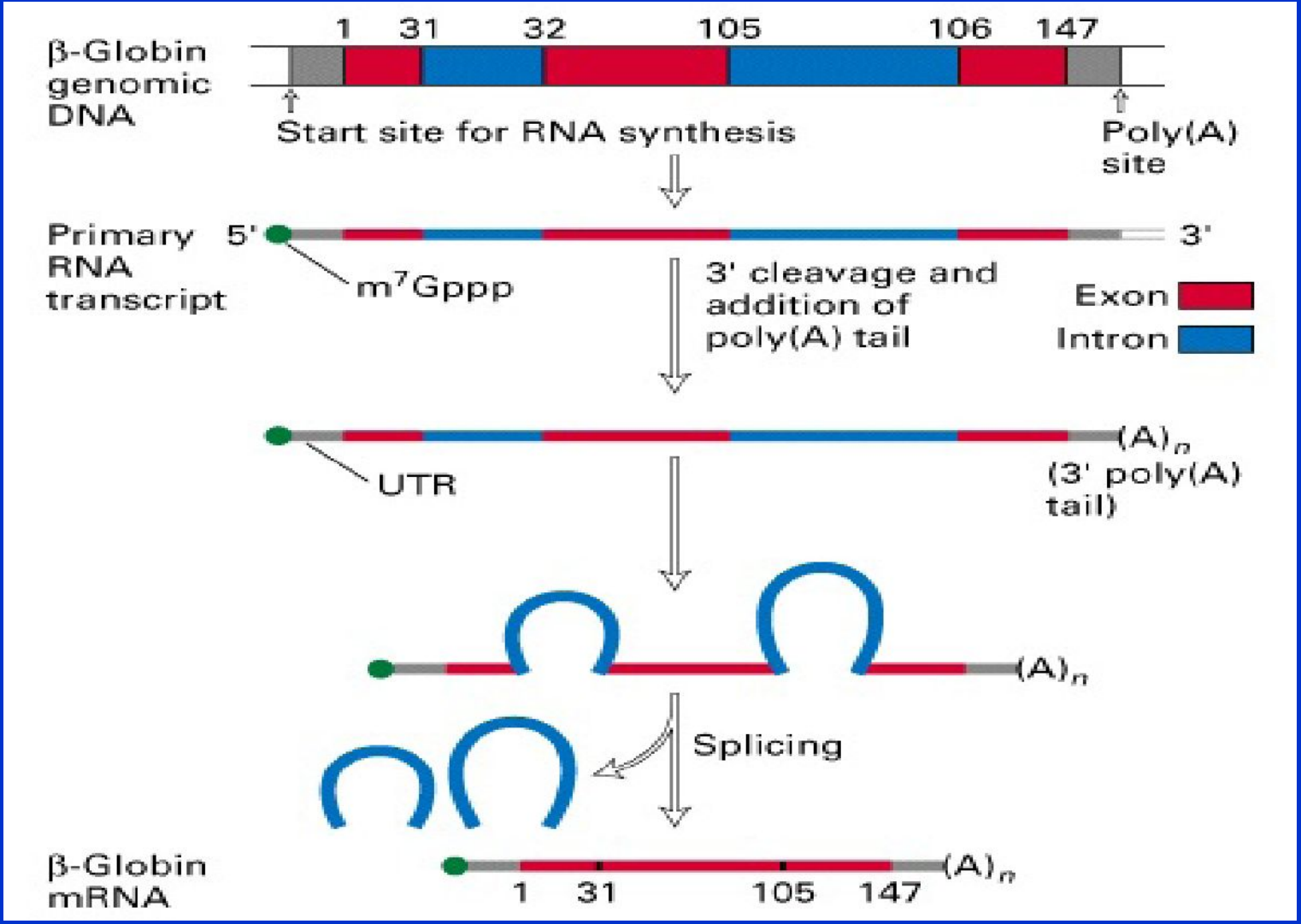
Termination:

The product is immature RNA or pre-mRNA (Primary transcript). Before the primary transcript leaves the nucleus it is modified in during RNA-processing.

RNA Processing (Pre-mRNA—mRNA)

- Splicing: step-by-step removal of introns and joining of the exons.
- Synthesis of the cap (capping) and poly (A) tail (polyadenylation) completes the m-RNA molecule (mature mRNA), which is now ready for translation.

Overview of RNA processing in eucaryotes



Translation:

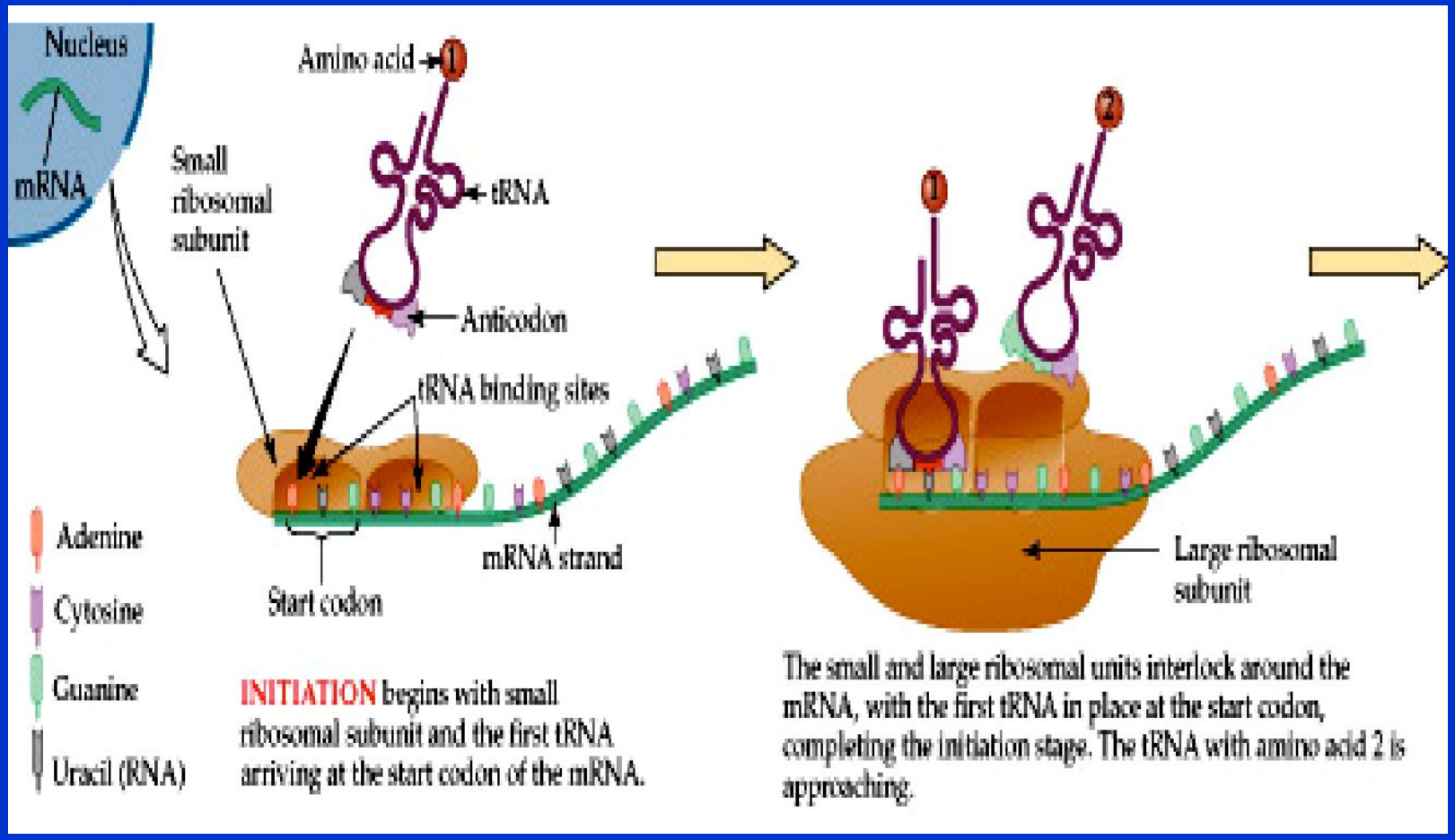
It is the process by which ribosomes read the genetic message in the mRNA and produce a protein molecules according to the message's instruction. It occurs in 3 phases:

1- Initiation: the ribosomes binds to the m-RNA;

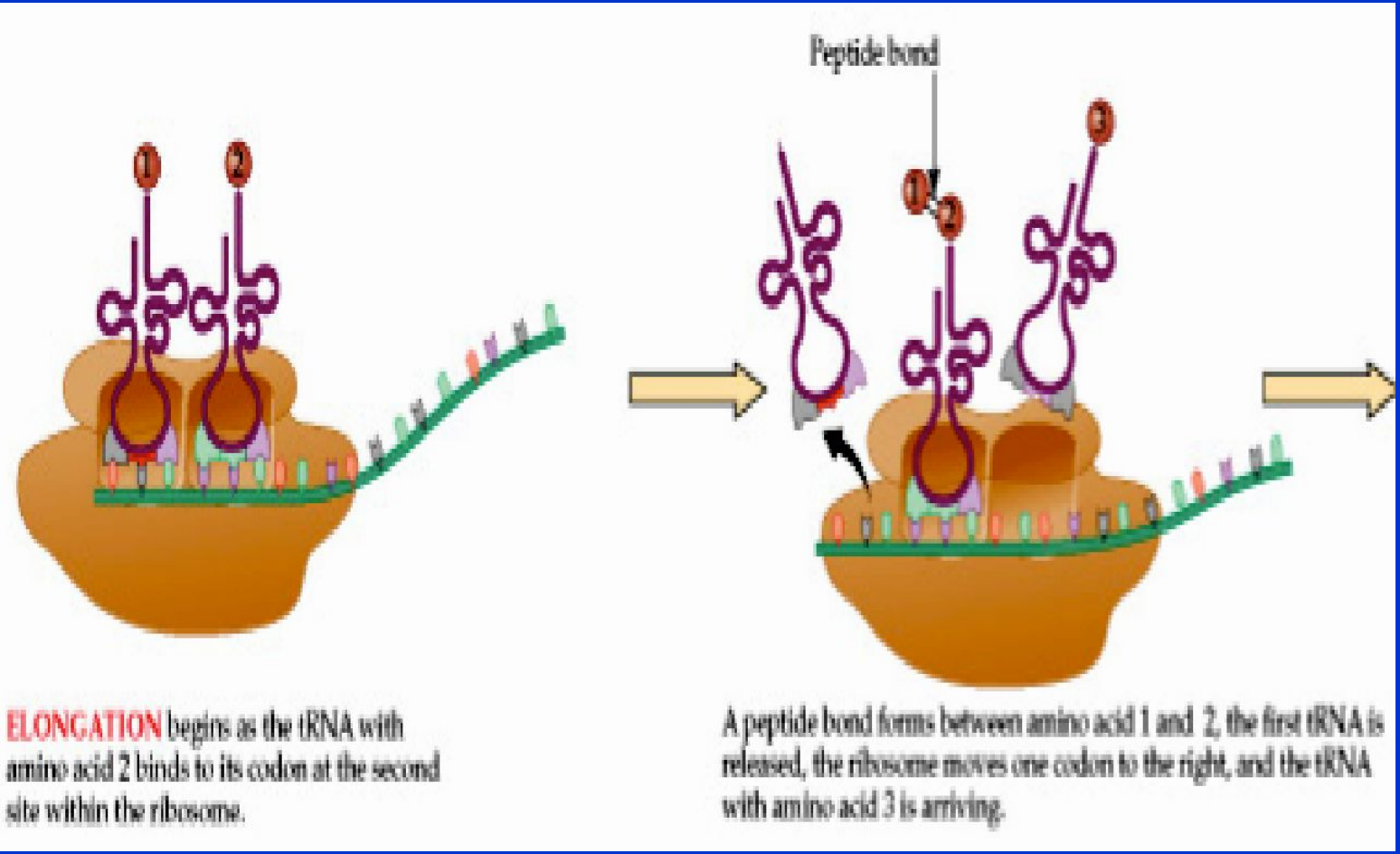
2-Elongation: the ribosomes add one amino-acid at a time to the growing polypeptide chain;

3-Termination- the ribosome releases the m-RNA and the polypeptide.

INITIATION


Nucleus
mRNA
Small ribosomal subunit
Amino acid
1
tRNA
Anticodon
tRNA binding sites
mRNA strand
Start codon
Adenine
Cytosine
Guanine
Uracil (RNA)
INITIATION begins with small ribosomal subunit and the first tRNA arriving at the start codon of the mRNA.
2
Large ribosomal subunit
The small and large ribosomal units interlock around the mRNA, with the first tRNA in place at the start codon, completing the initiation stage. The tRNA with amino acid 2 is approaching.

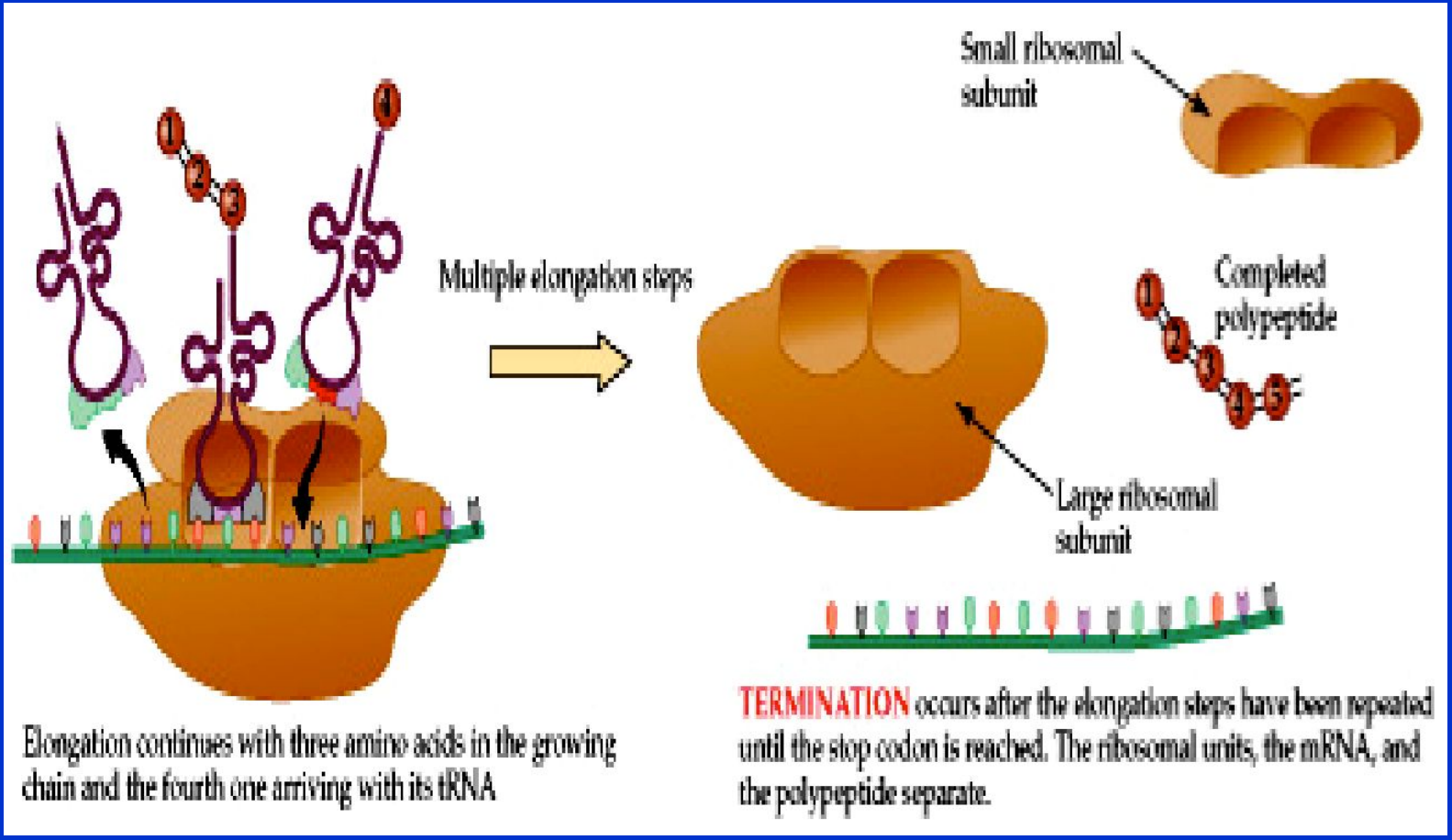
ELONGATION



ELONGATION begins as the tRNA with amino acid 2 binds to its codon at the second site within the ribosome.

A peptide bond forms between amino acid 1 and 2, the first tRNA is released, the ribosome moves one codon to the right, and the tRNA with amino acid 3 is arriving.

TERMINATION



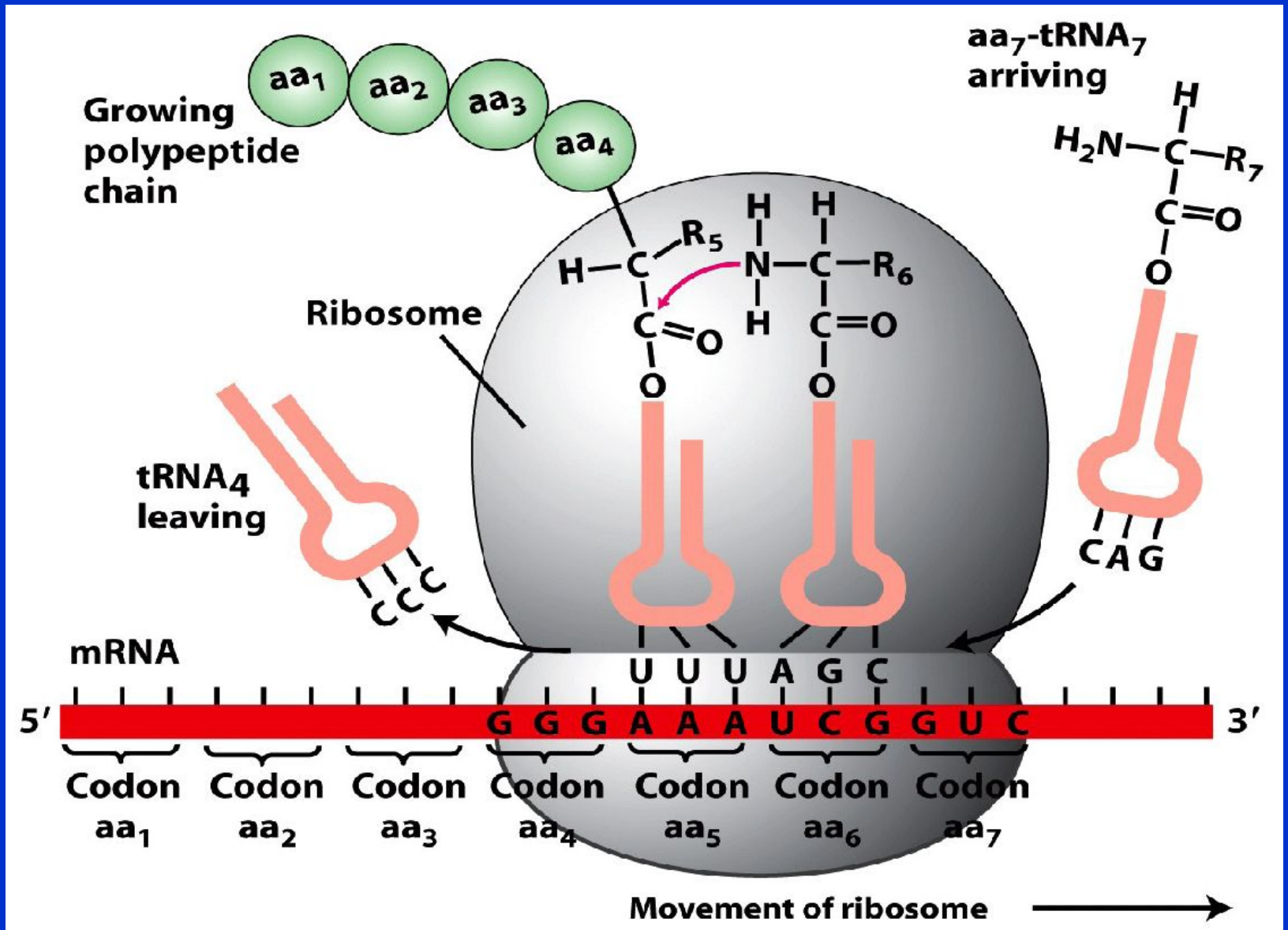


Figure 4-17
Molecular Cell Biology, Sixth Edition
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Prokaryotic Gene Expression. The Lac-Operon.

Operon is the coordinated unit of gene expression in bacteria.

This concept was introduced by Jacob and Monod in 1961. It was based on their observations on the regulation of lactose metabolism in E.coli.

Las operon has the following components:

-Promoter region where RNA-polymerase binds;

-Operator gene;

-Structural genes (Z,Y,A,).

The structural genes code:

-Z gene for B-galactosidase;

-Y gene codes for permease;

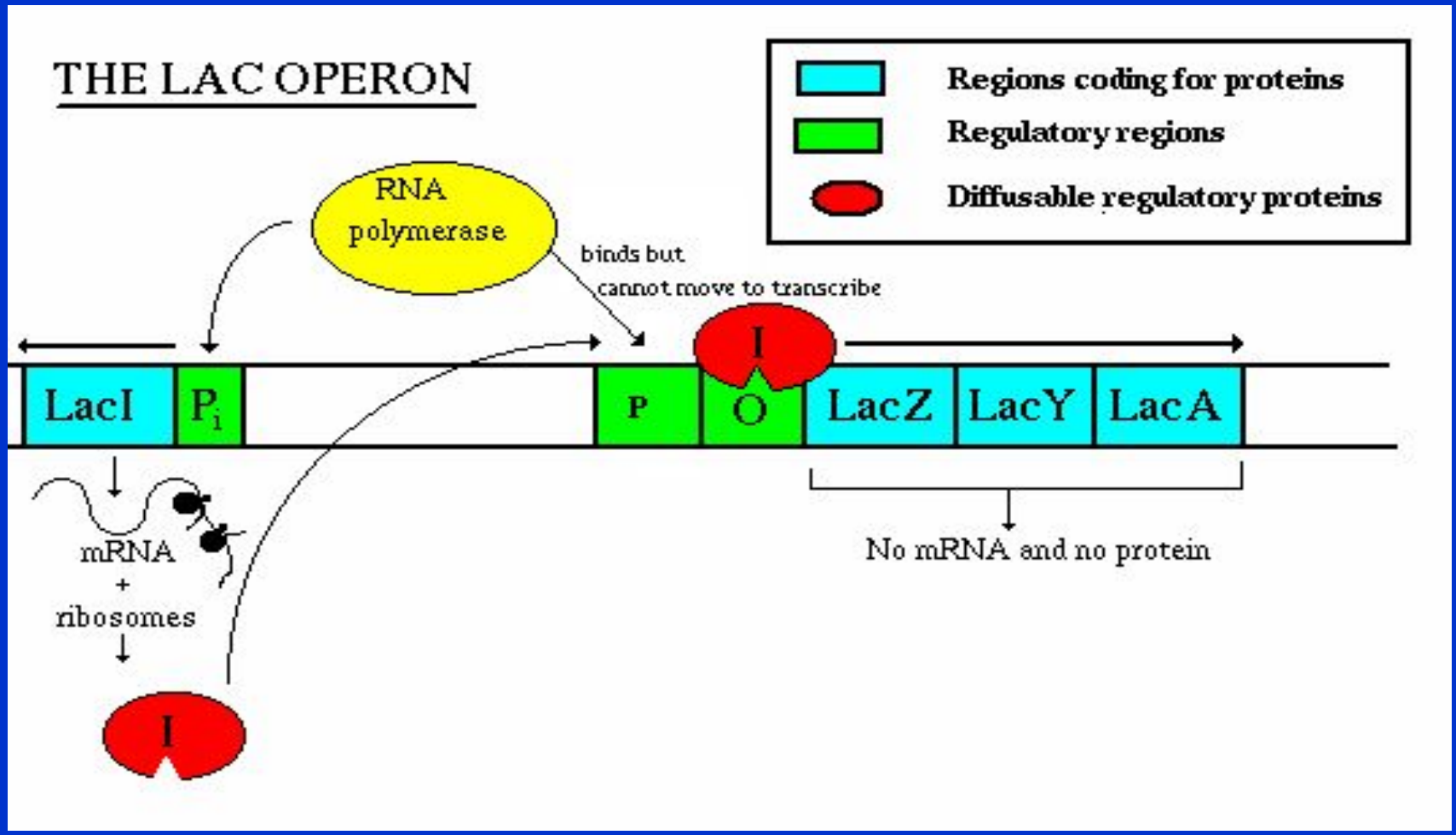
- A gene codes for acetylase.

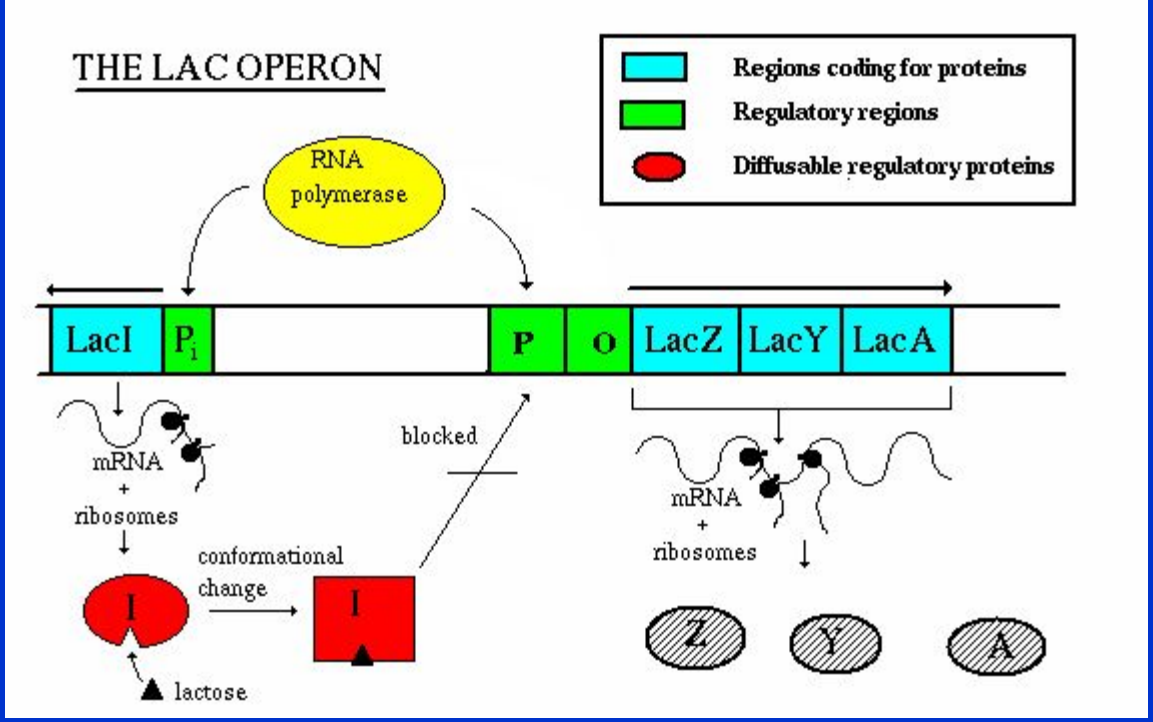
How does the system work?

Without lactose, the repressor protein (its synthesis is under the control of the regulatory gene) binds to the operator and prevents the read through of RNA polymerase into the three structural genes.

With lactose in the cell, lactose binds to the repressor. This causes a structural change in the repressor and it loses its affinity for the operator. RNA polymerase can bind to the promoter and transcribe the structural genes. (Lactose acts as an effector.)

Operation - If lactose is not present:
the repressor gene produces repressor, which binds to the operator. This blocks the action of RNA polymerase, thereby preventing transcription.





Operation - if lactose is present:

the repressor gene produces repressor, which has a site for binding with allolactose.

The allolactose/repressor compound is incapable of binding w/ the operator, so the RNA polymerase is uninhibited

once the concentration of lactose decreases, the repressor-allolactose complex falls apart and transcription is again inhibited

- **Gene Regulation in Eukaryotes**
- The latest estimates are that a human cell, a eukaryotic cell, contains approximately 35,000 genes.
- Some of these are expressed in all cells all the time. These so-called housekeeping genes are responsible for the routine metabolic functions (e.g. respiration) common to all cells.
- Some are expressed as a cell enters a particular pathway of differentiation.
- Some are expressed all the time in only those cells that have differentiated in a particular way. For example, a plasma cell expresses continuously the gene for the antibody it synthesizes.
- Some are expressed only as conditions around and in the cell change. For example, the arrival of a hormone may turn on (or off) certain genes in that cell.
- How is gene expression regulated?
- There are several methods used by eukaryotes.

- **Transcription Control**
  - The most common type of genetic regulation
  - Turning on and off of mRNA formation
- **Post-Transcriptional Control**
  - Regulation of the processing of a pre-mRNA into a mature mRNA
- **Translational Control**
  - Regulation of the rate of Initiation
- **Post-Tranlational Control**
  - Regulation of the modification of an immature or inactive protein to form an active protein