MICROBIAL GENETICS

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Medical genetics in the past :

1. Minor subject in the school.
2. Related to uncommon diseases.
3. Only specialist and affected patients concern to the subject.

Medical genetics today :

- ❖ Explain underlying molecular pathobiology of many diseases.
- ❖ Mainstream of medical science and public health.
- ❖ Powerful tool to establish: diagnosis, classification, prognosis, prediction of complication, as well as response to the treatment.
- ❖ "Never ending story" subject.

MICROBIAL GENETICS

- The science of genetics define and analyzes heredity, or constancy and change in the vast array of physiologic function that form the poperties of organism
- The unit of hereditery is the GEN, a segment of DNA that carries in its nucleotide sequence information for a spesific biochemical or physiologic property

ORGANIZATION OF GENES

STRUCTURE OF NUCLEOTIDES:

DNA/RNA (DE-OXY RIBOSE / RIBOSE)

—›BASE PURINE : **Adenine (A)**

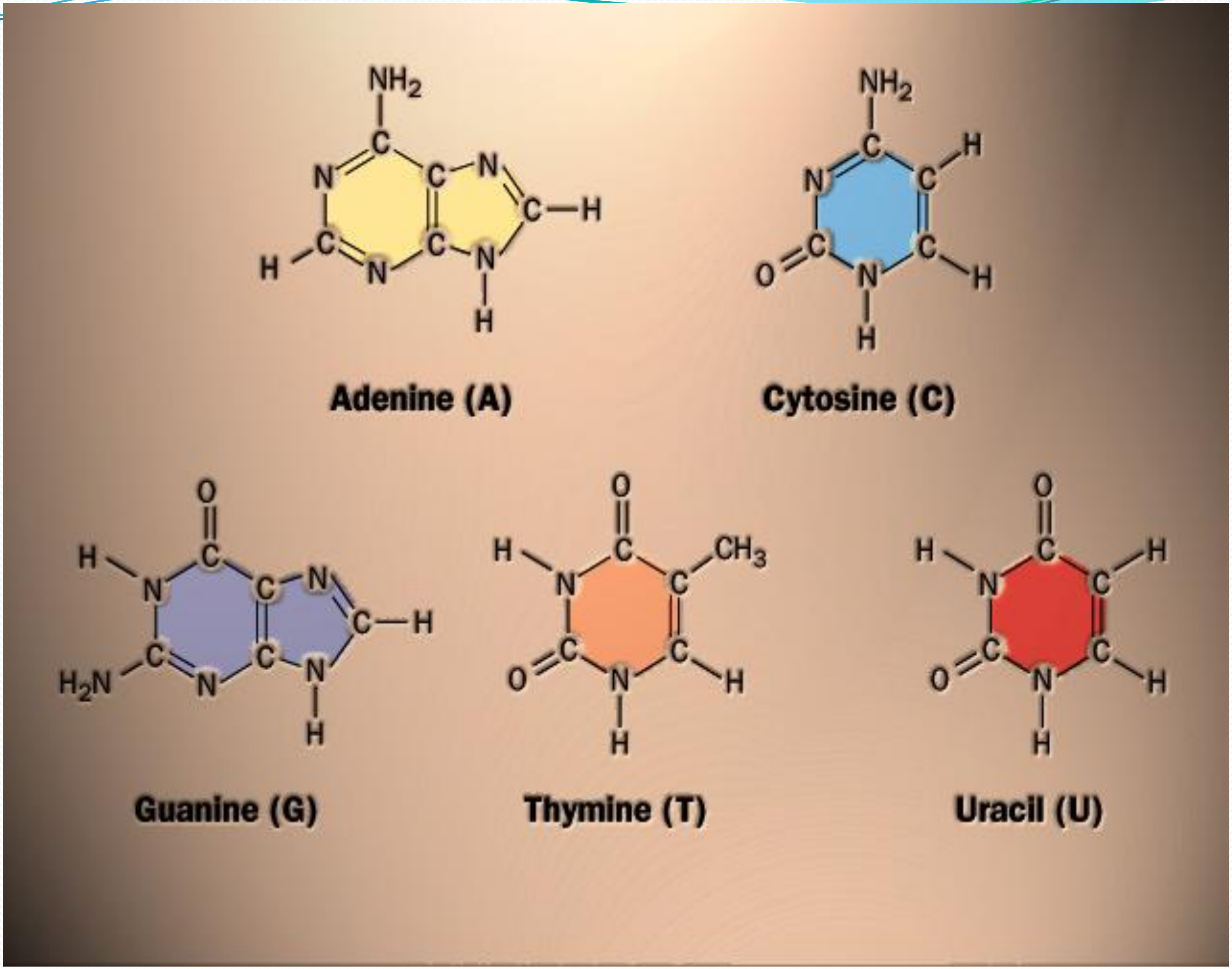
Guanine (G)

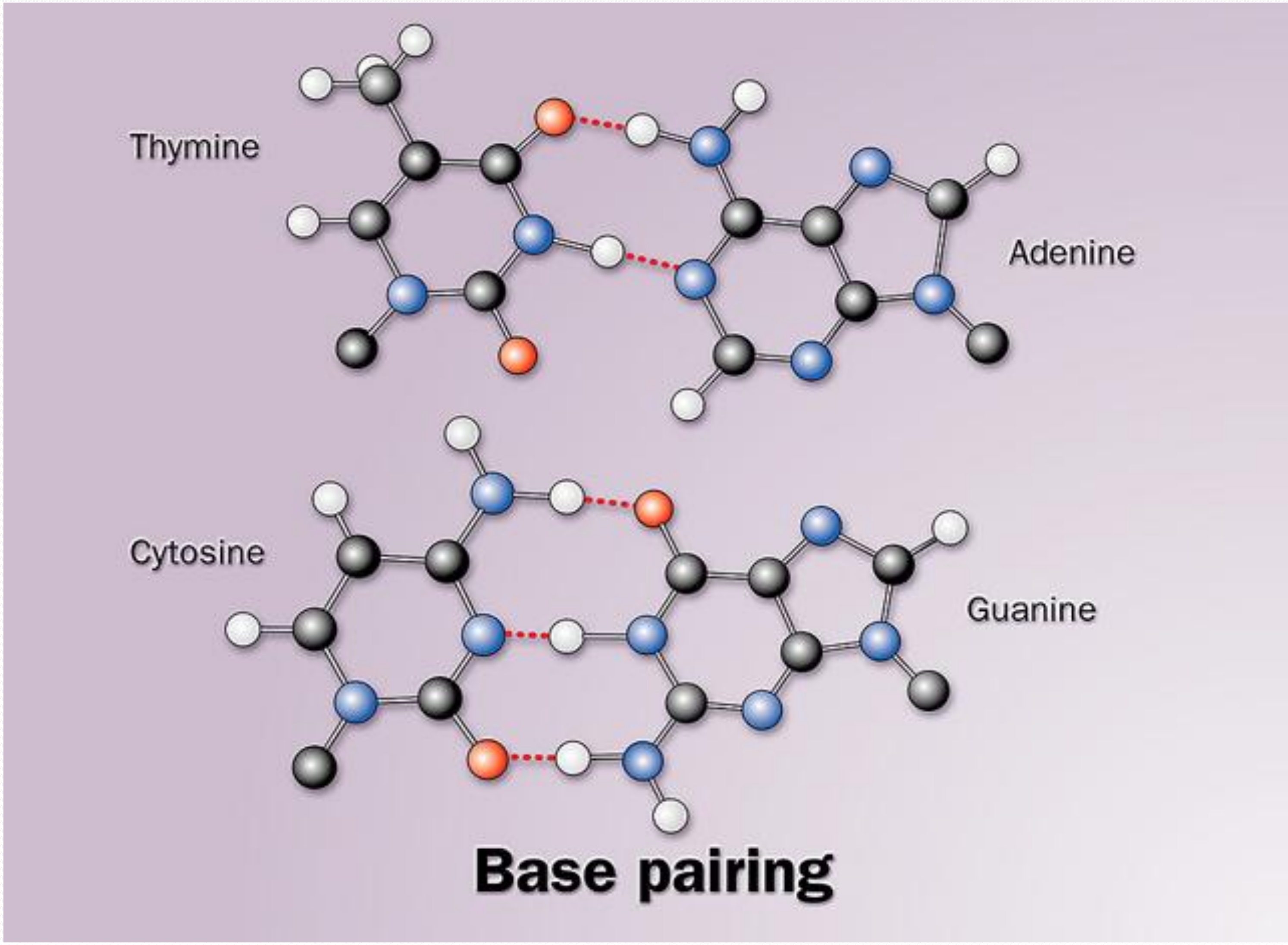
—› PYRIMIDINE : **Cytosin (C)**

(DNA) - Thymin (T)

(RNA) - Uracil (U)

*** Composition of bases of DNA from different organism varies greatly**


Adenine (A)
Cytosine (C)
Guanine (G)
Thymine (T)
Uracil (U)

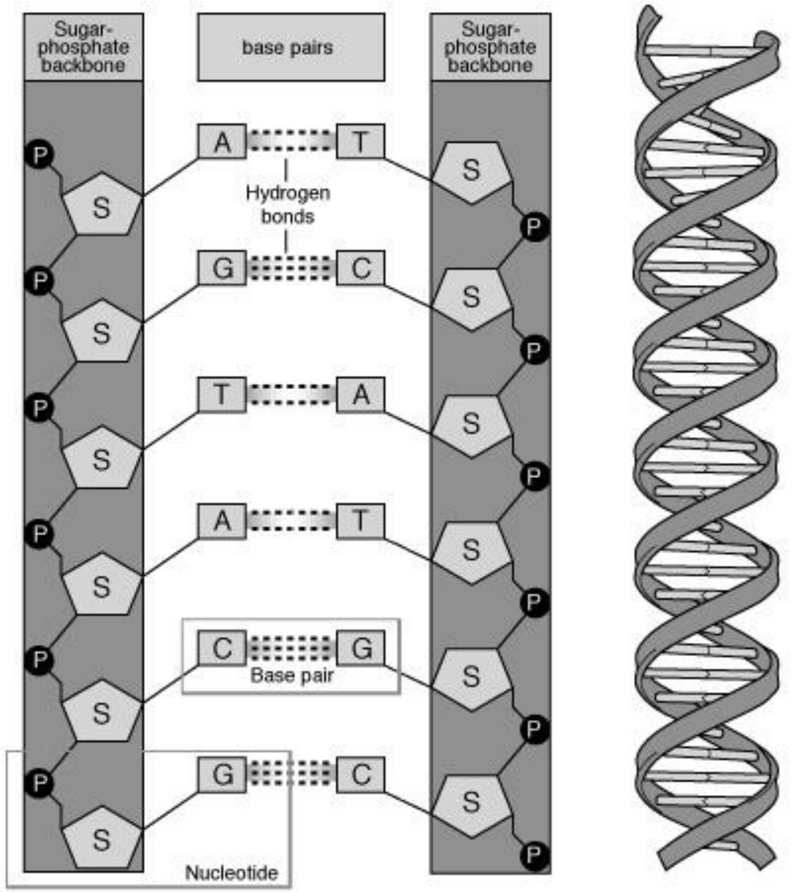

Thymine
Adenine
Cytosine
Guanine
Base pairing

ORGANIZATION OF GENES

The Structure of DNA:

- Most DNA molecules are double stranded
- Complementary bases (A-T; G-C) —› hydrogen bonding in the center of the molecule
- Each of the four bases is bonded to phospho-2’-deoxyribose—›nucleotide

Double helix of DNA



ORGANIZATION OF GENES

Structure of RNA:

- Most frequently occurs in single-stranded form
- In RNA the base Urasil (U)= base Thimin in DNA—› A-U; C-G

RNA $\Rightarrow$ m RNA
t RNA
r RNA

RNA function

mRNA$\Rightarrow$ transfer information from genes to protein - synthesizing machine

tRNA$\Rightarrow$ carries activated a.amino for protein synthetis

rRNA$\Rightarrow$ protein synthesis

Eukaryote versus Prokaryote

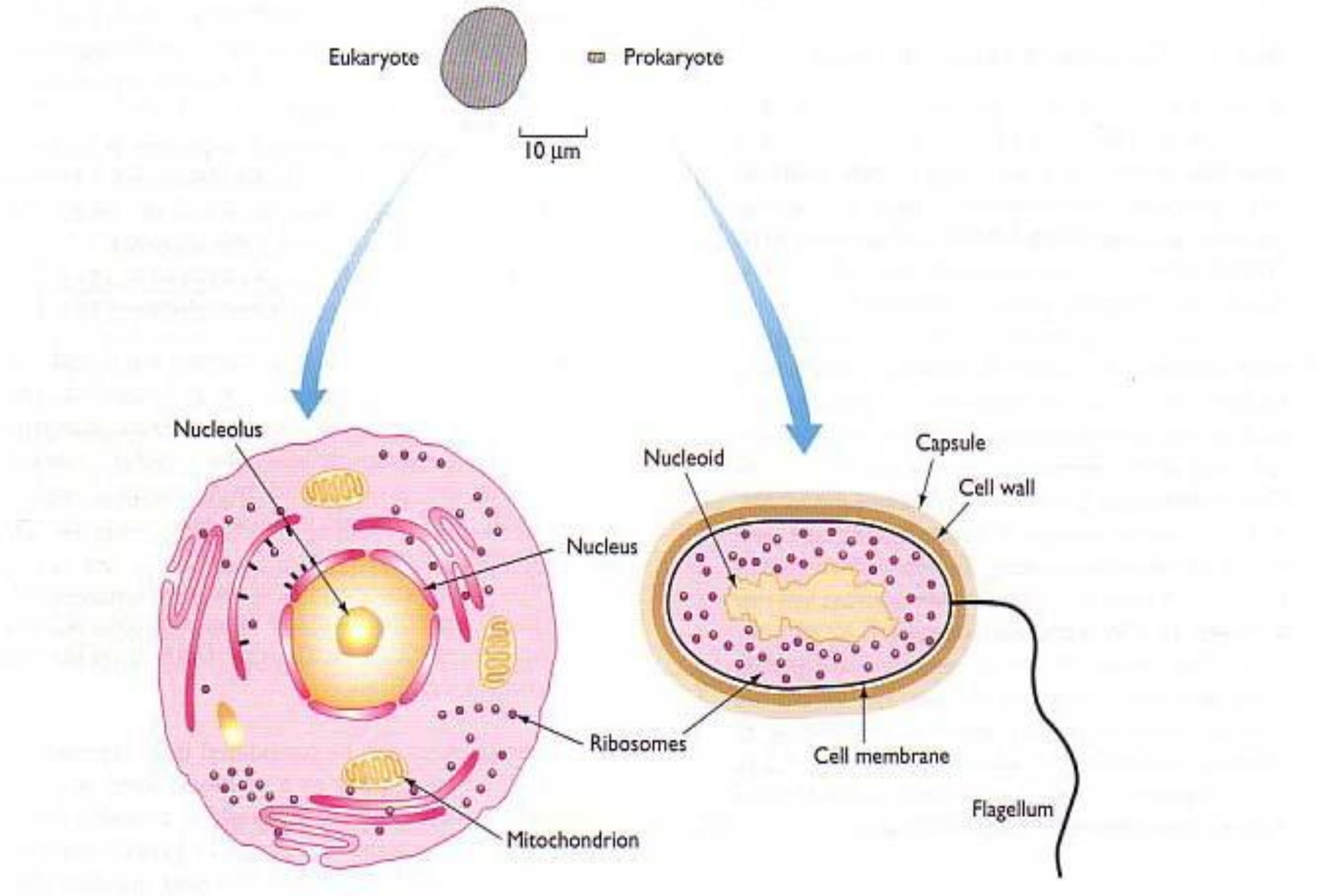


Figure 1.6 Cells of eukaryotes (left) and prokaryotes (right).

THE EUKARYOTIC GENOM

- Eukaryotic genome —›carried on 2 or more linear chromosomes, separated from cytoplasm within the membran of nucleus
- Diploid ⇒ contain two homologues
- Gene that doesn’t achieve phenotypic expression→***recessive***
- Gene that overrides the effect of its homologue→***dominan***
- Introns ⇒ intervening sequence of DNA, missing in mRNA, not translated

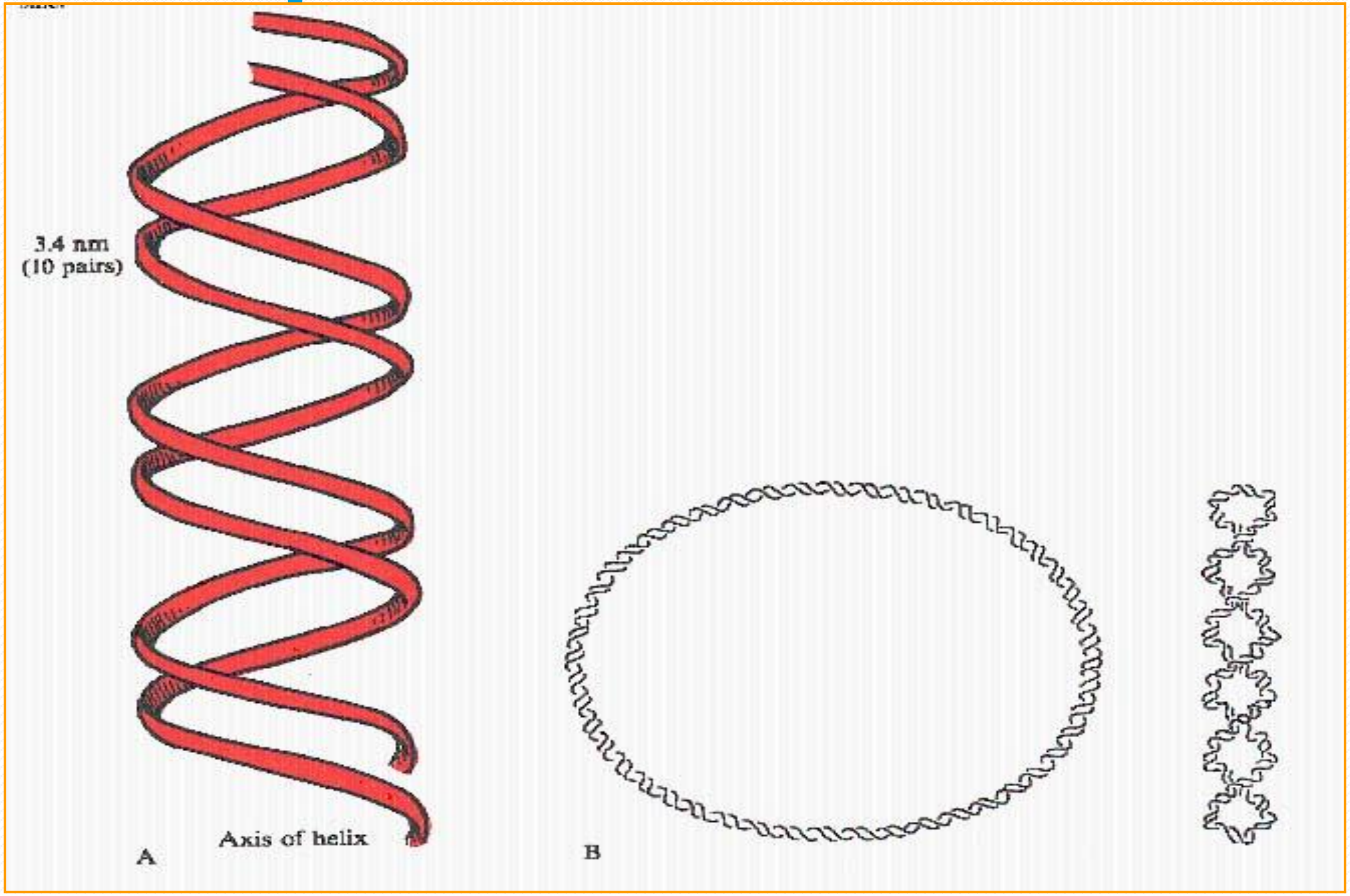
THE PROKARYOTIC GENOM

- Prokaryotic genes→bacterial chromosome, haploid
- **Plasmid** ⇒ small circles DNA, frequently in prokaryotes, amenable to genetic manipulation→genetic engineering
- **Transposons** ⇒genetic element, contain several kbp, include inform for migration→insertions mutations

THE DIFFERENT BETWEEN PROCARYOT& EUCARYOT

	PROCARYOT (Bacteria)	EUCARYOT
CHROMOSOMAL DNA	double helix, circular, usually single	double helix Linear;usually multiple
EXTRA CHROMOSOMAL DNA	Plasmid	Mitochondrial Chloroplast

Circular shape of microbial DNA



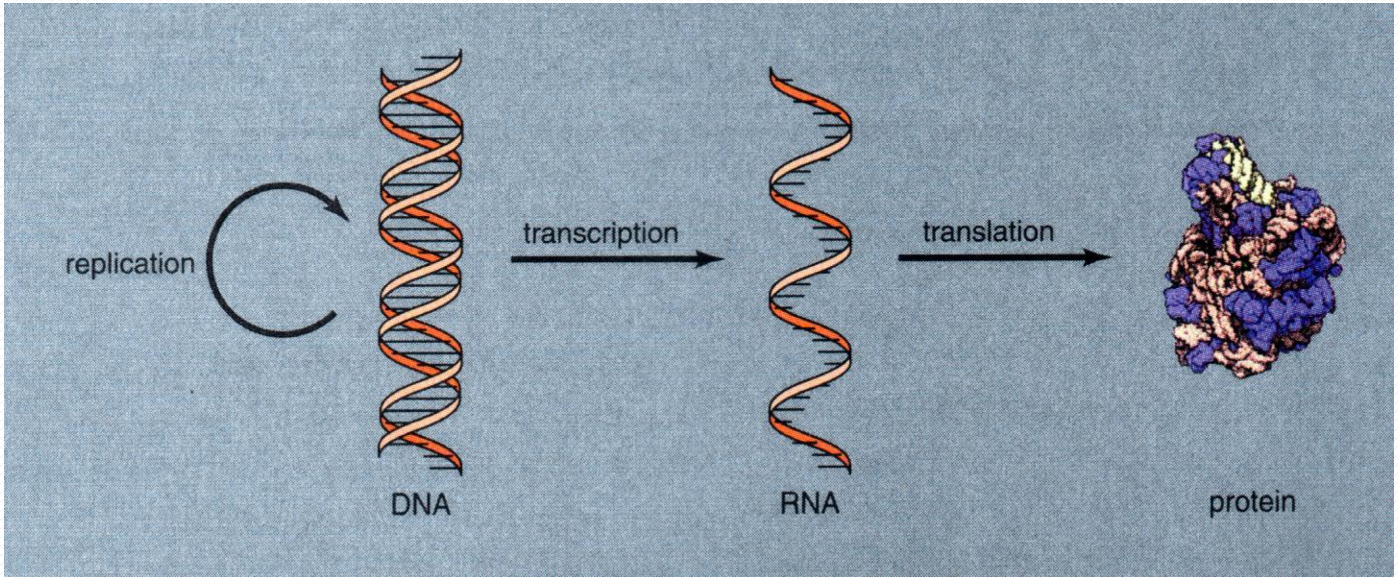
THE VIRAL GENOM

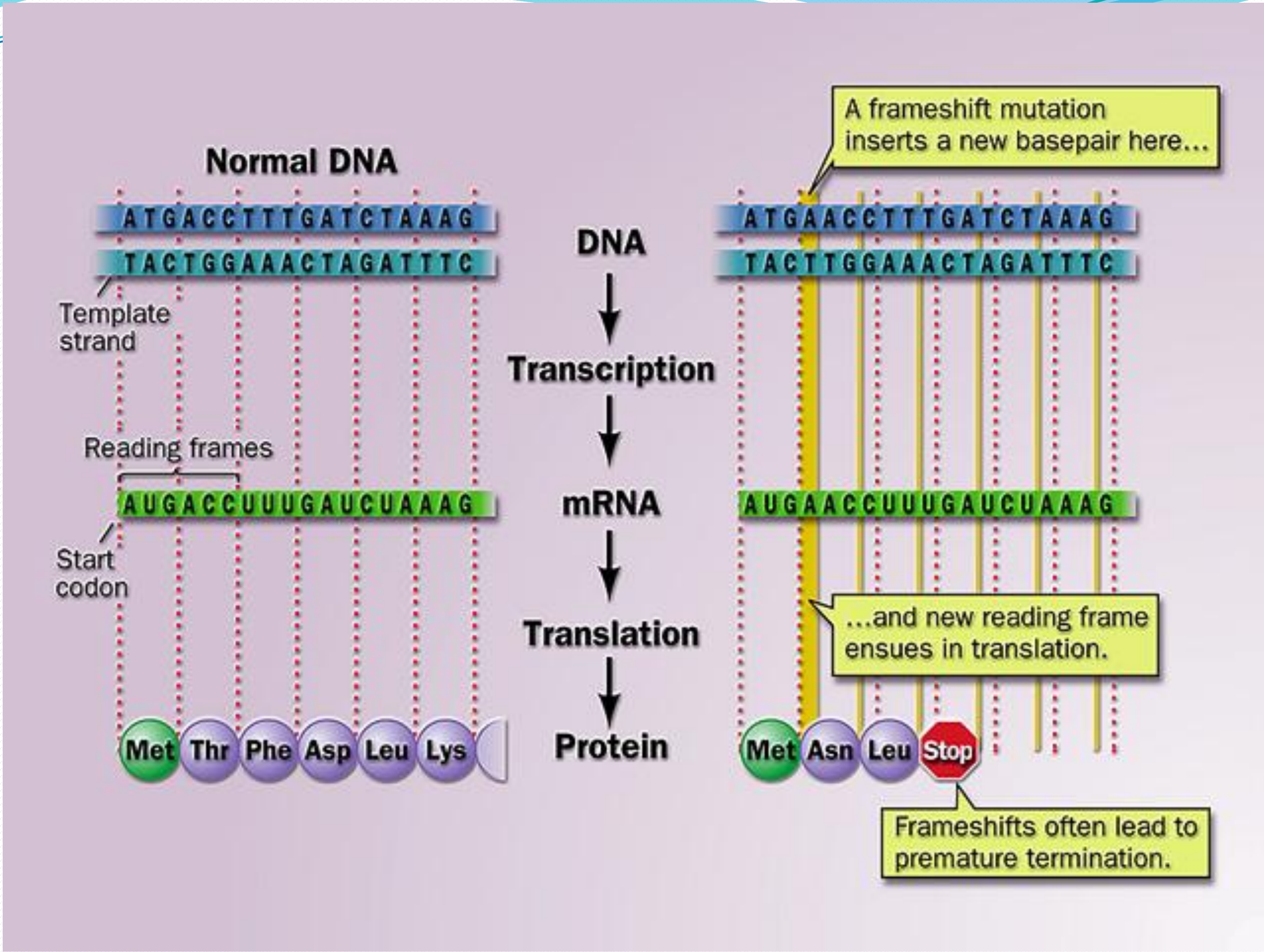
- Replication of viral genom→depends upon metabolic energy ‘n macromolecule syntesis of the host⇒ debilitation ‘n † of host cell
- Viruses associated with prokaryot⇒ **bacteriophage**
- Variability of phage⇒ contain double stranded DNA, single stranded RNA, single stranded DNA

THE VIRAL GENOM

- **Lytic phages:** produce m copies of themselves, kill host
- **Temperate phage**⇒ able enter a nonlytic prophagestate(e.g E. coli phage χ)

DOGMA CENTRAL





A frameshift mutation inserts a new basepair here...

...and new reading frame ensues in translation.

Frameshifts often lead to premature termination.

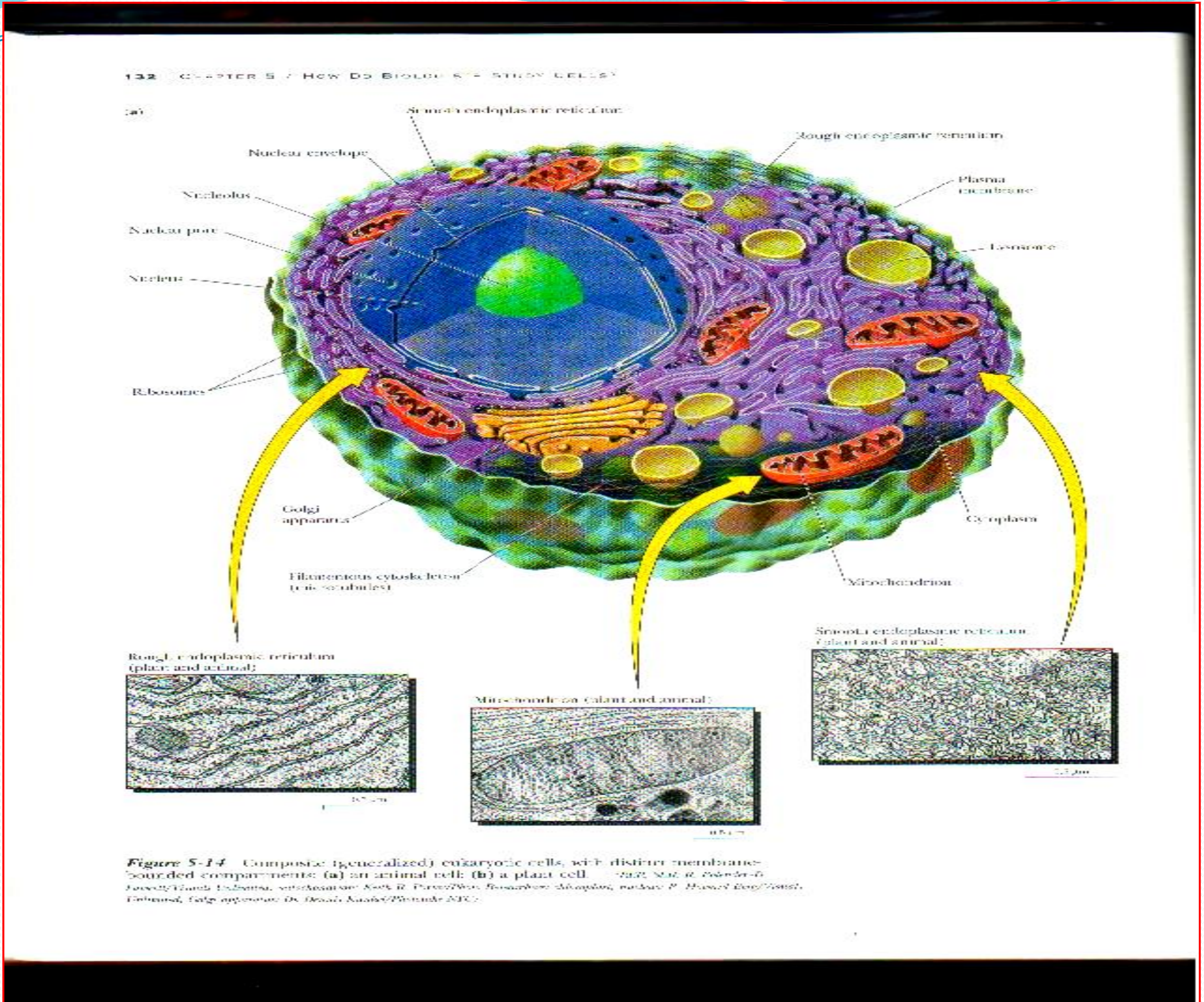
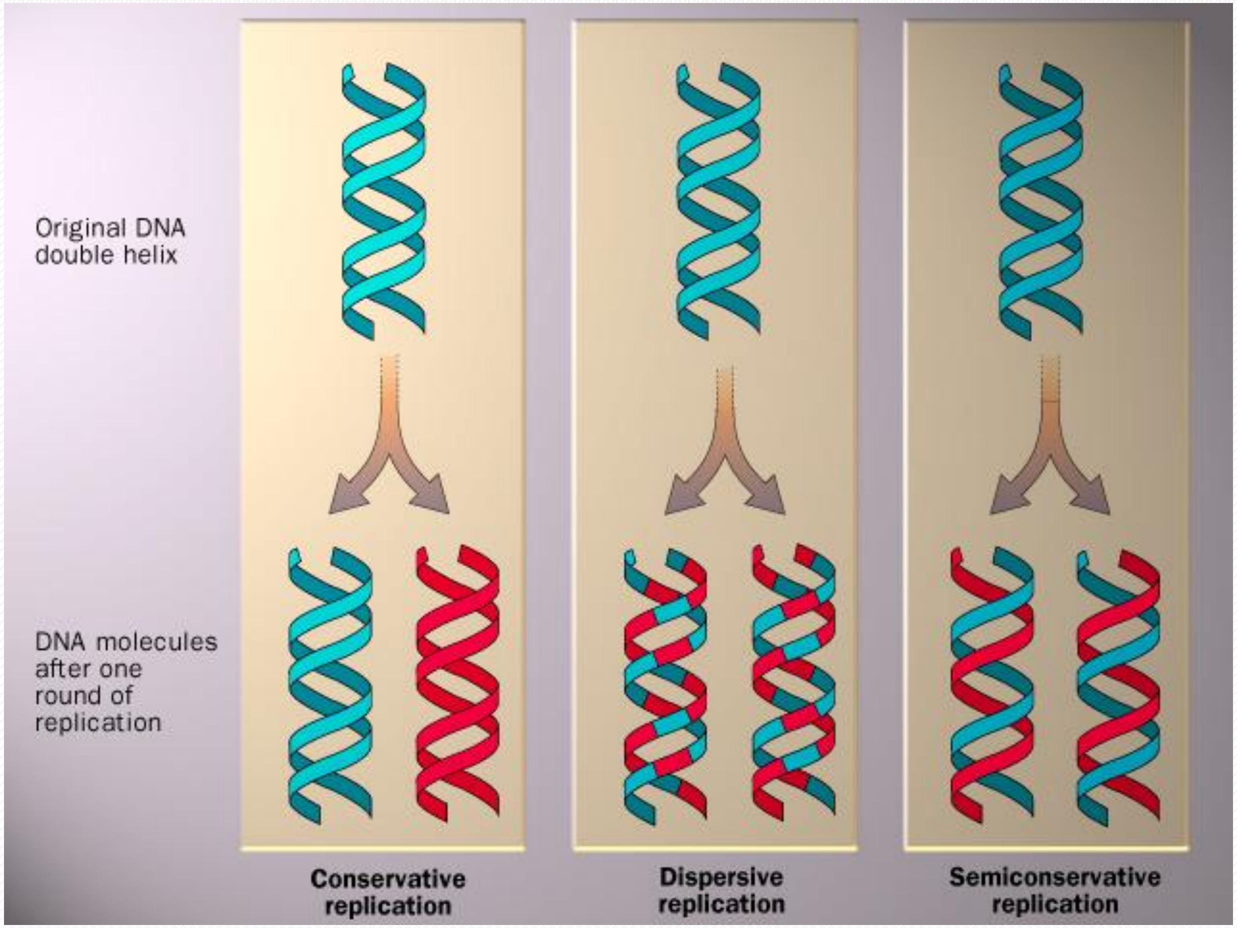


Figure 5-14 Composite (generalized) eukaryotic cells, with distinct membrane-bounded compartments: **(a)** an animal cell; **(b)** a plant cell.

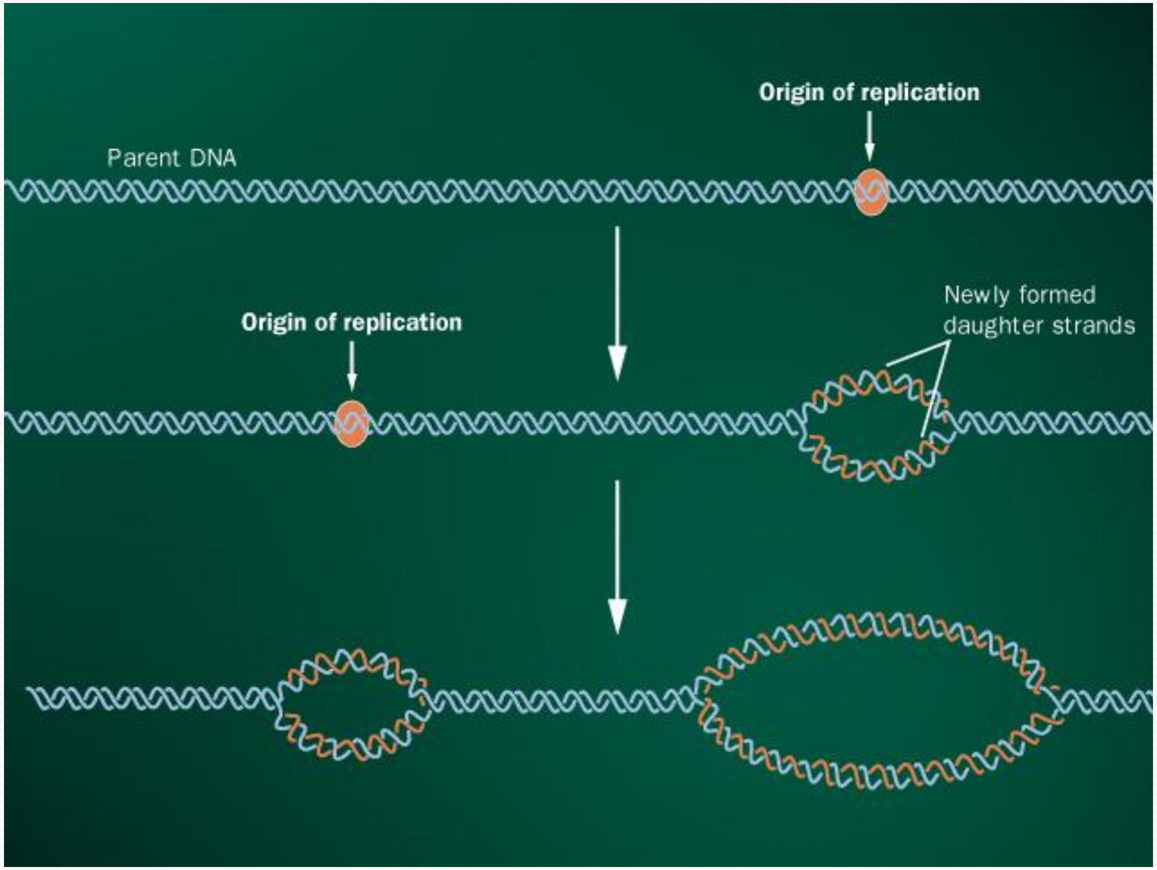
REPLICATION

- Double-stranded DNA
  ➔semi-konservative
- Enzym ➔ DNA Polymerase
- Require Primase ➔DNA Primer
- DNA Synthesis : 5’→ 3’
- DNA Eukaryot ➔ Origine of replication>>

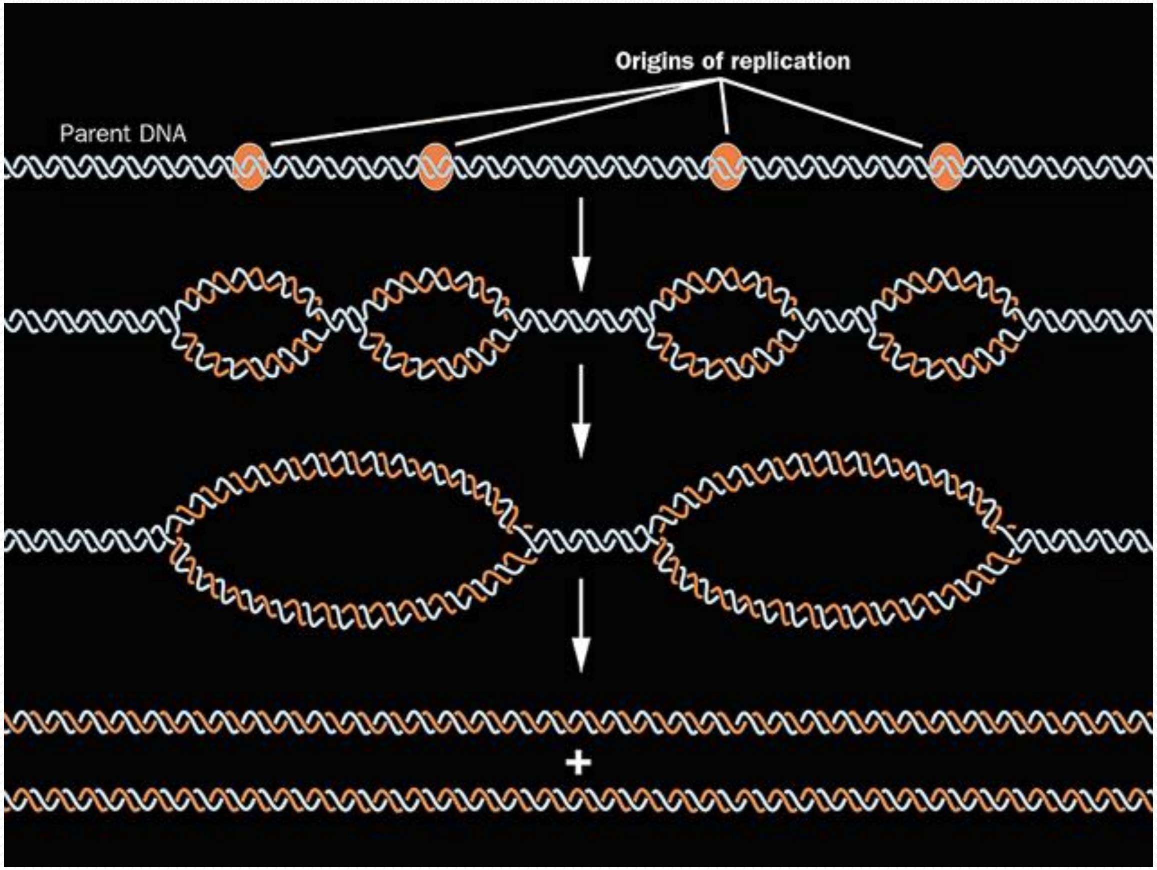
Replication type



STARTING POINT OF REPLICATION (DNA Eukariot)



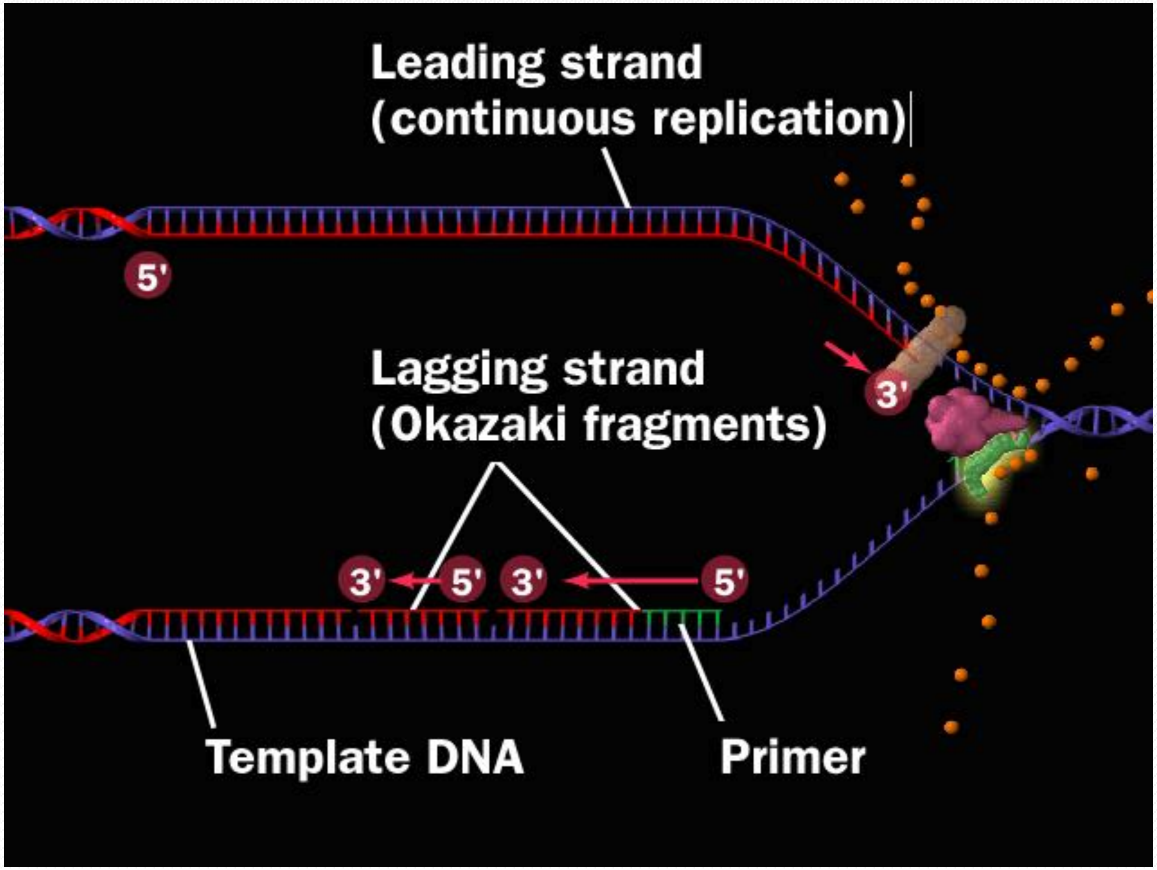
ORIGINE OF REPLICATION

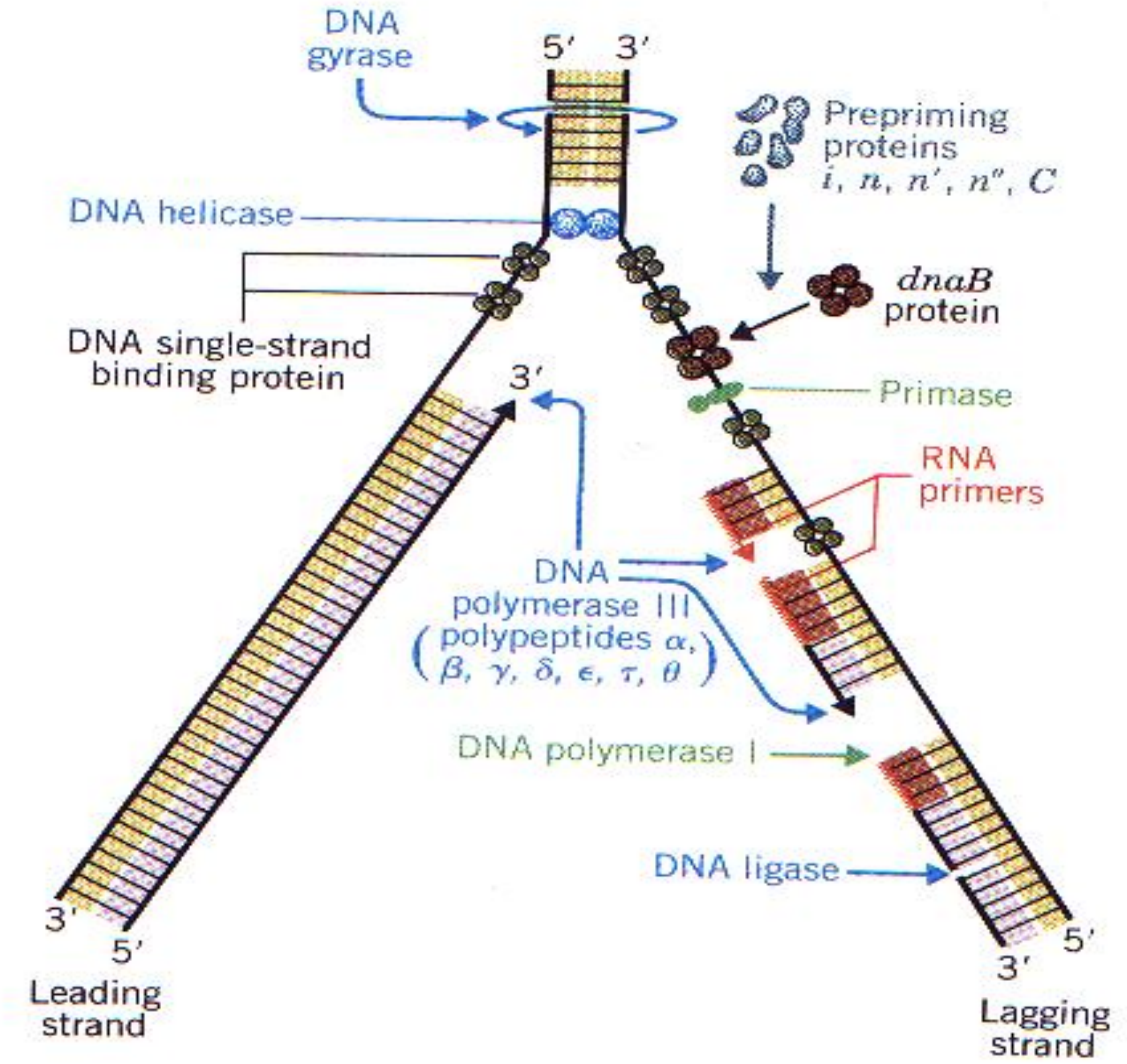


ORIGINE OF REPLICATION

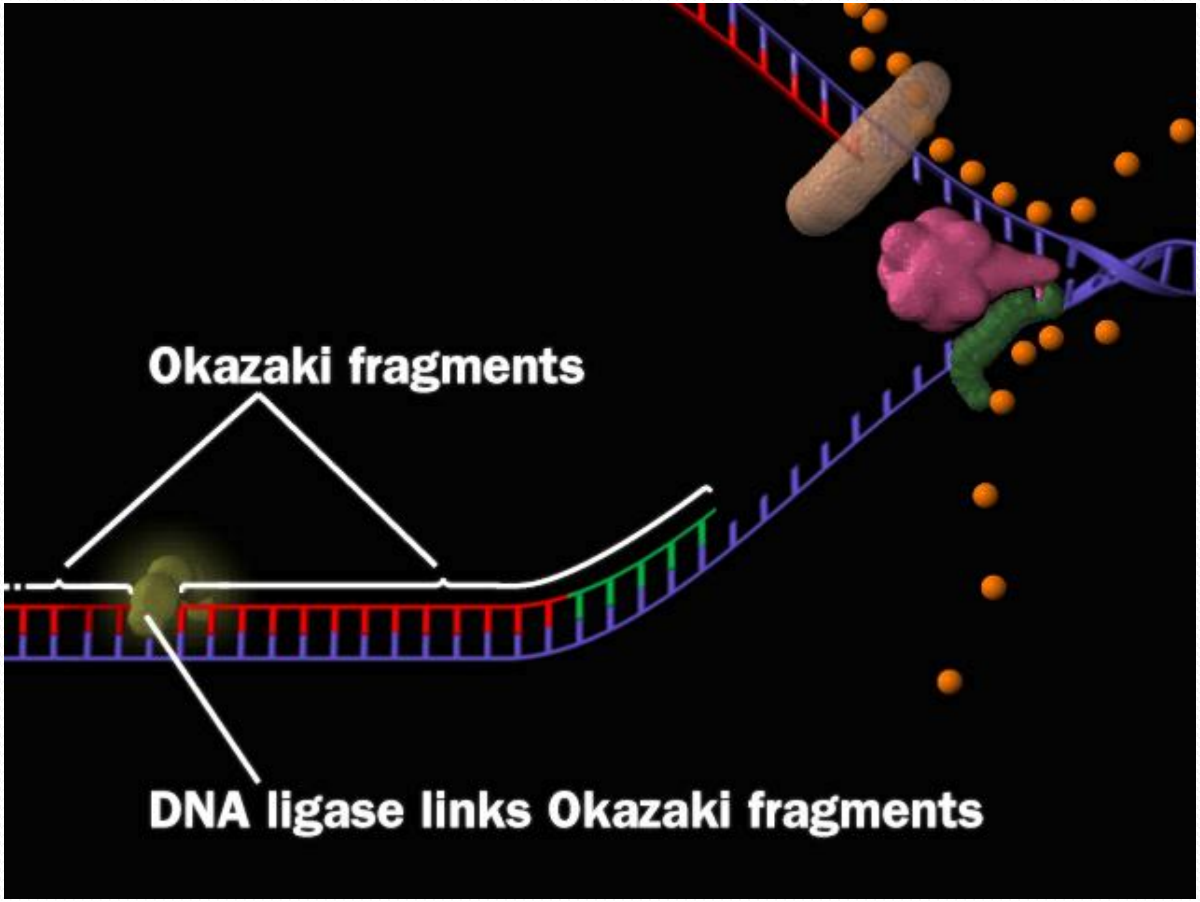
- Leading Strand
- Lagging Strand
  - ➔ Okazaki Fragmen
  - ➔ Ligase
- Helicase
- DNA binding protein
- Topoisomerase

LEADING STRAND AND LAGGING STRAND

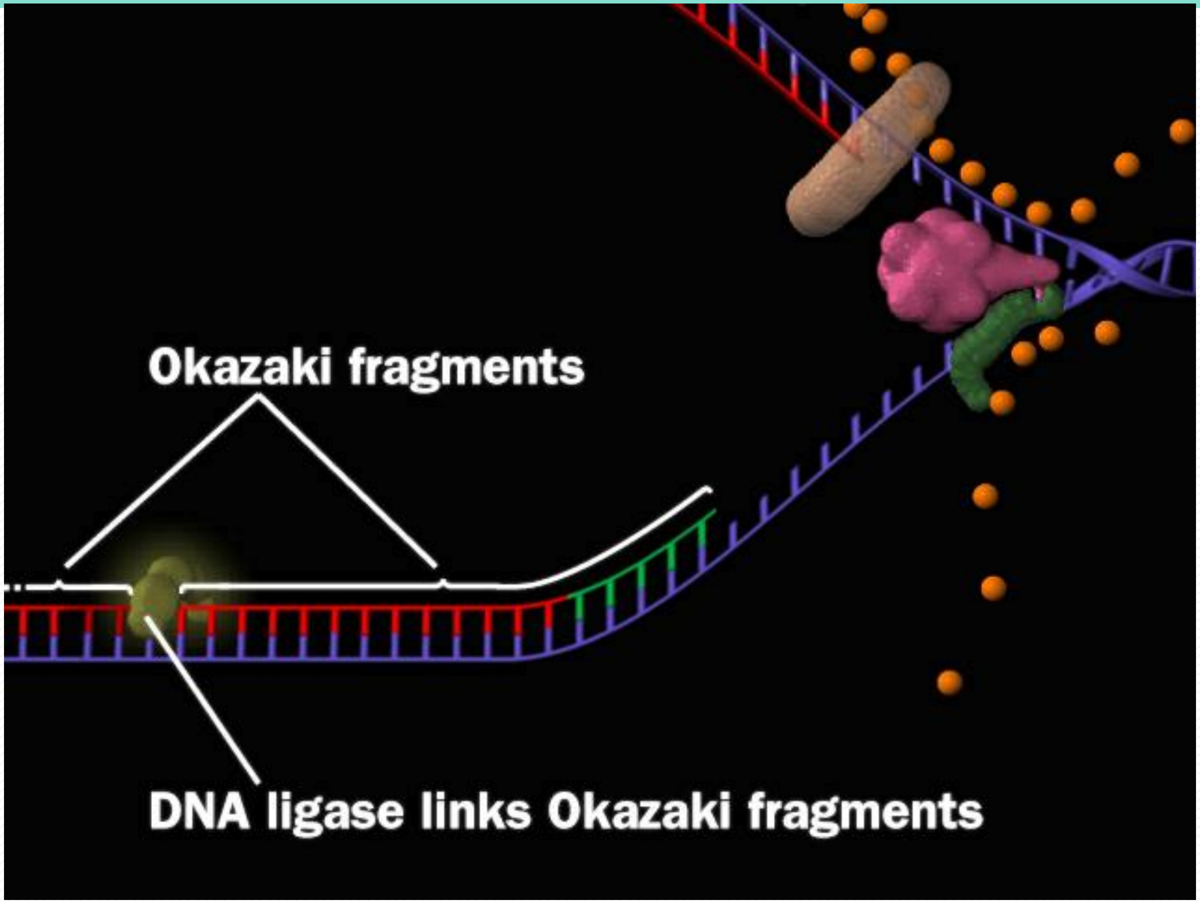



DNA gyrase
5′
3′
Prepriming proteins
i, n, n′, n″, C
DNA helicase
dnaB protein
DNA single-strand binding protein
3′
Primase
RNA primers
DNA polymerase III (polypeptides α, β, γ, δ, ε, τ, θ)
DNA polymerase I
DNA ligase
3′
5′
Leading strand
5′
3′
Lagging strand

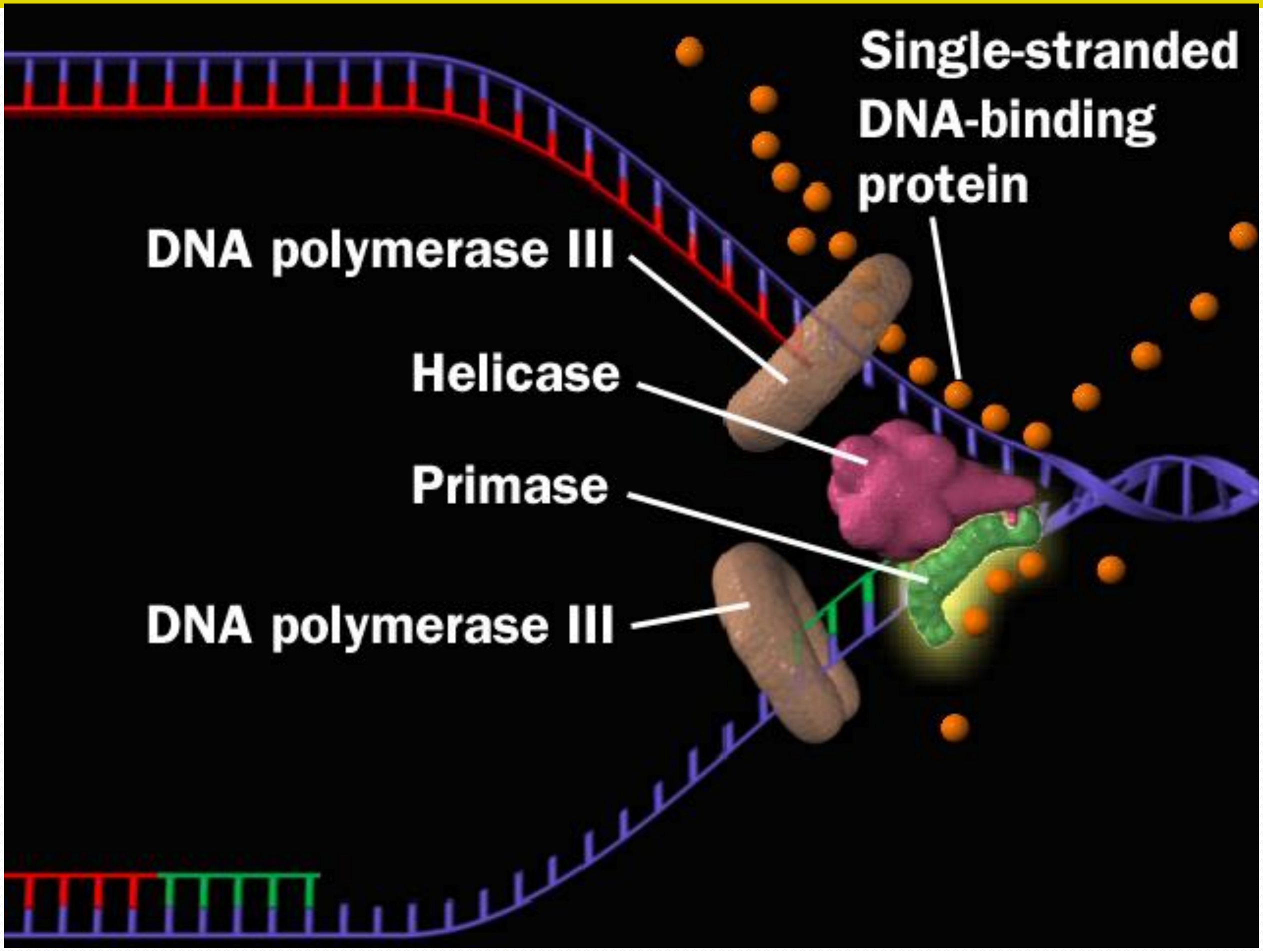
OKAZAKI FRAGMENTS



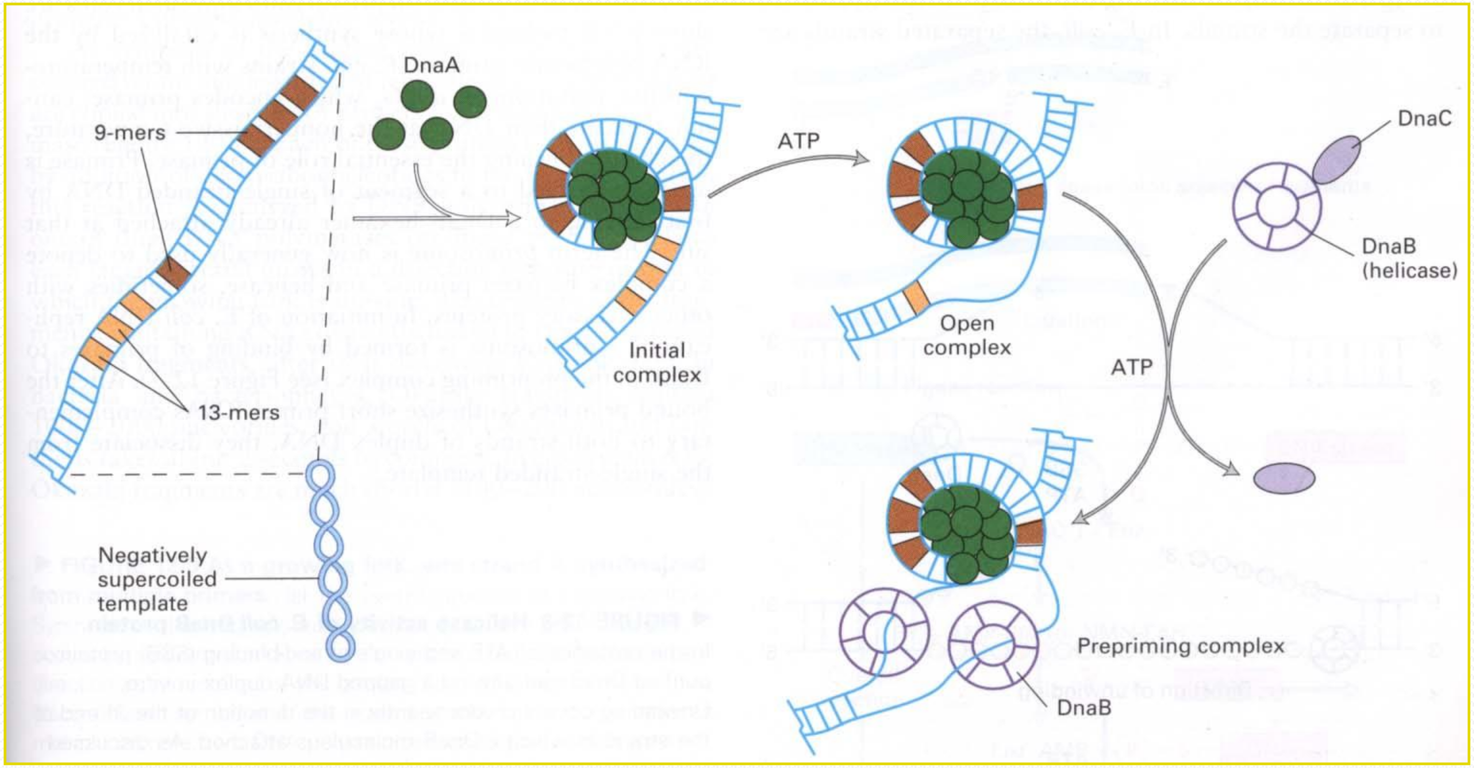
DNA LIGASE



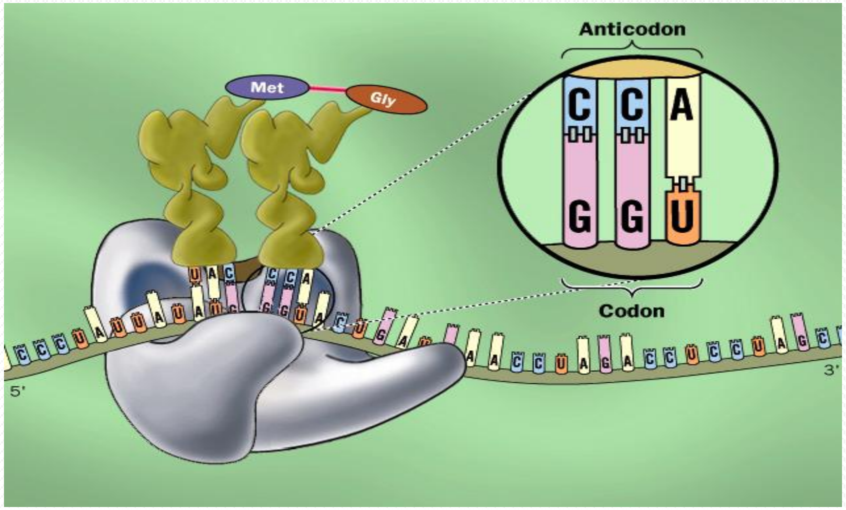
DNA BINDING PROTEIN



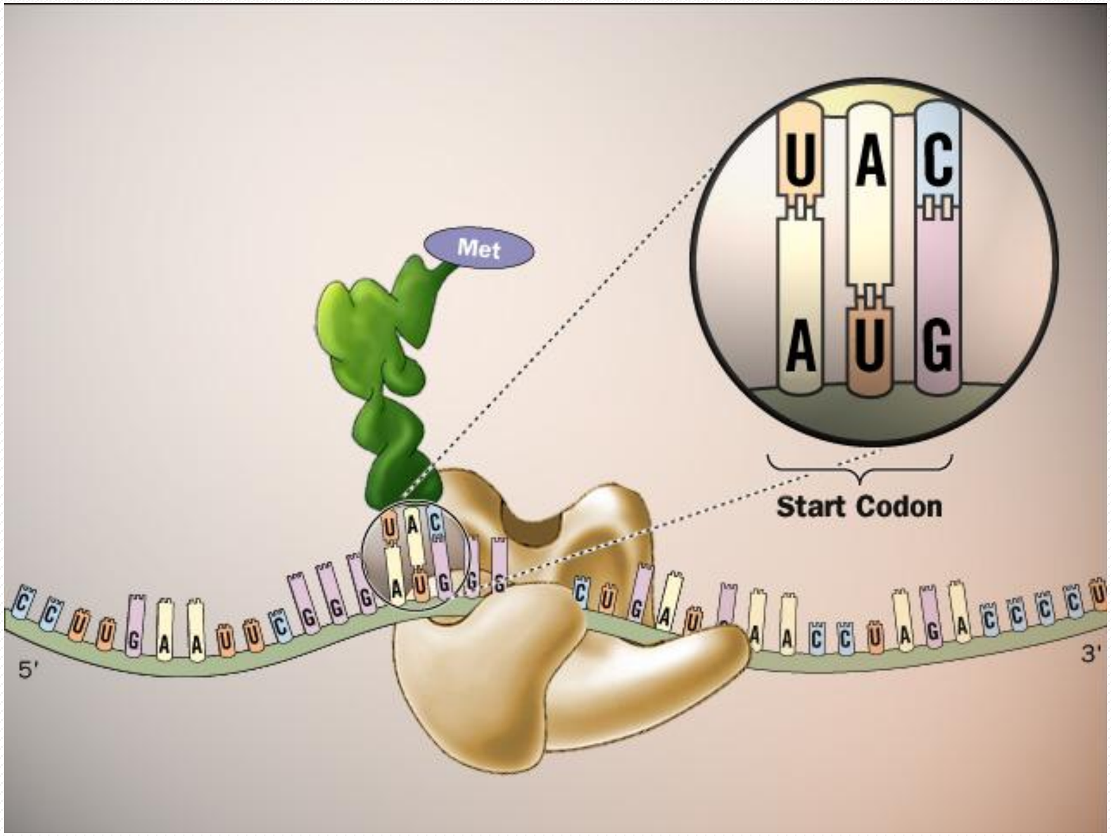
Model of initiation of replication at E.coli *oriC*



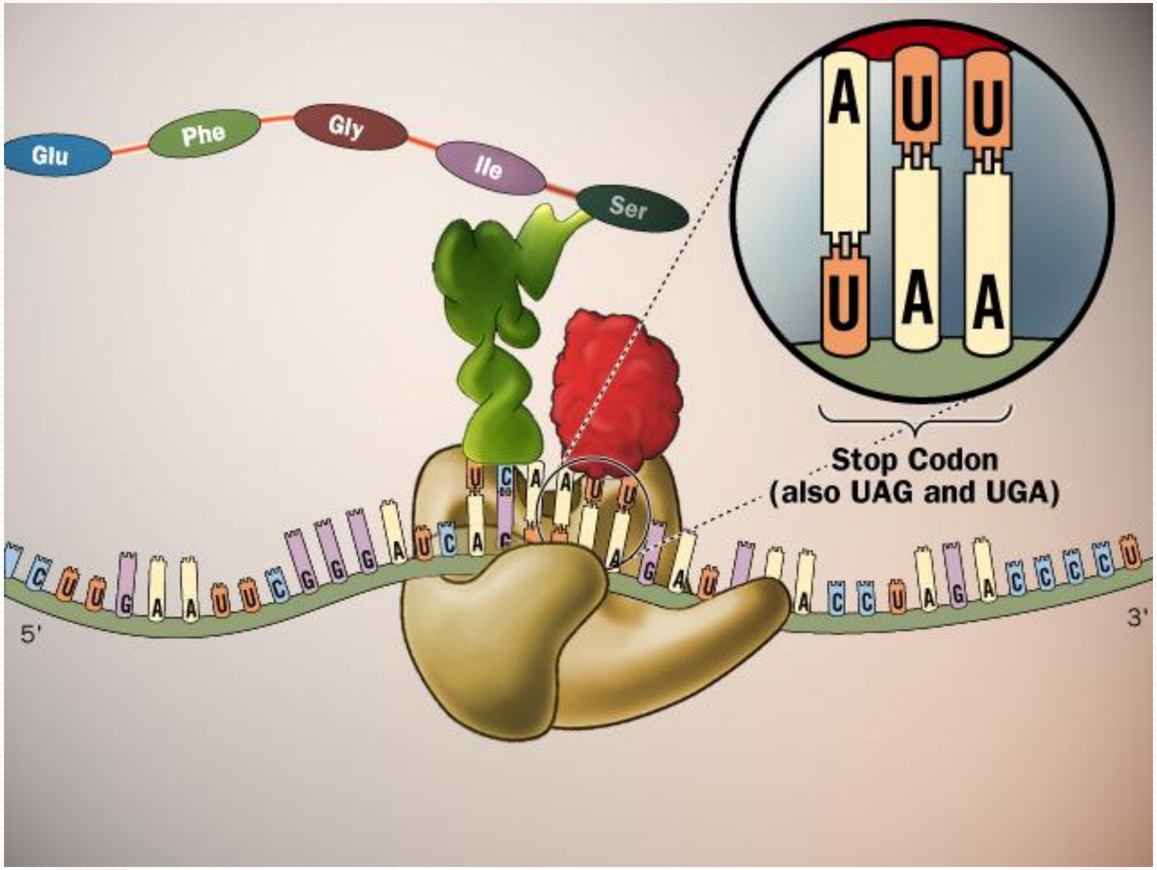
KODON AND ANTIKODON

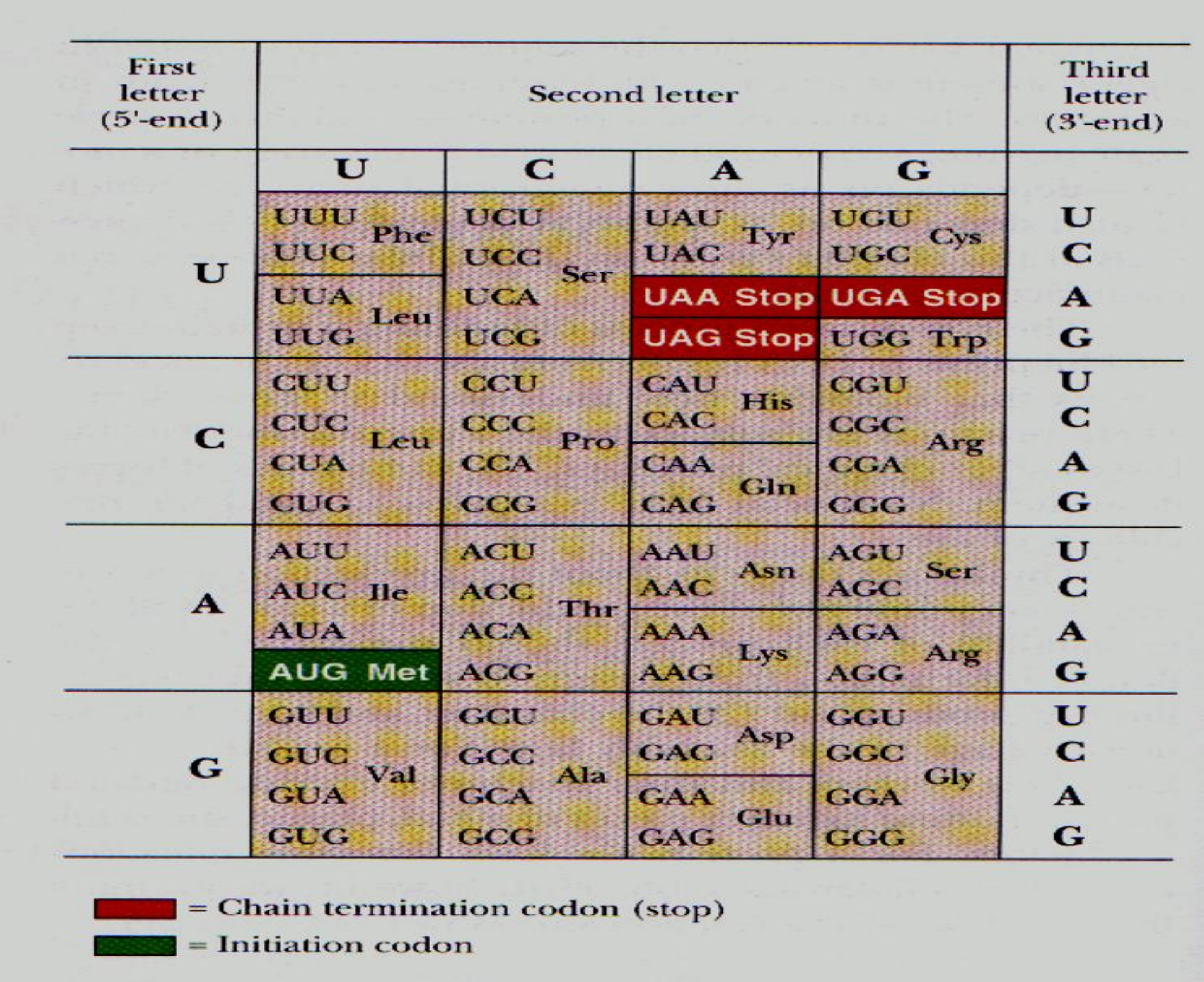


START KODON



STOP KODON

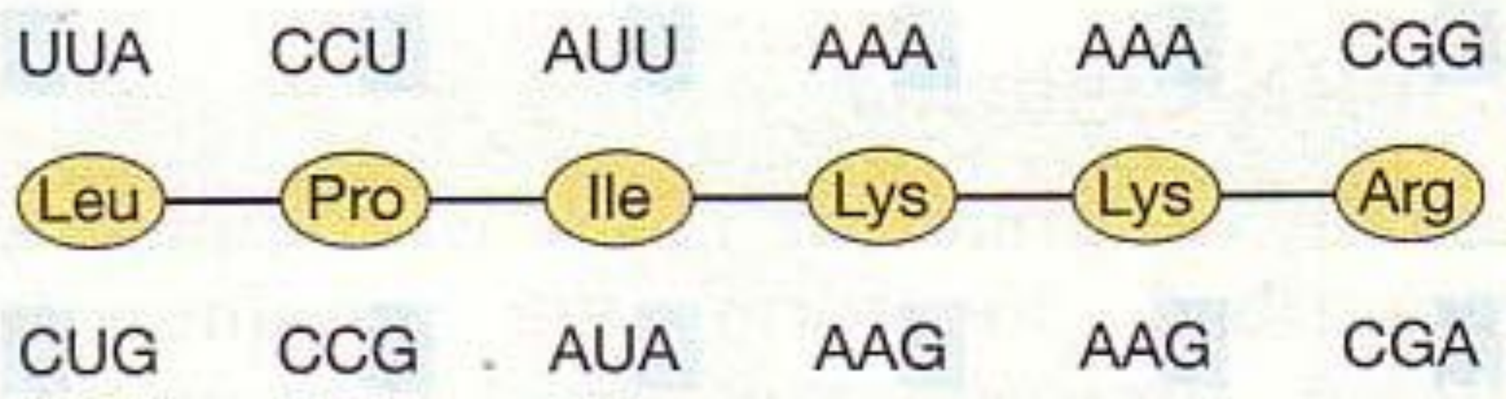




First letter (5'-end)	Second letter								Third letter (3'-end)
	U		C		A		G		
U	UUU	Phe	UCU	Ser	UAU	Tyr	UGU	Cys	U
	UUC		UCC		UAC		UGC		C
	UUA	Leu	UCA		UAA	Stop	UGA	Stop	A
	UUG		UCG		UAG	Stop	UGG	Trp	G
C	CUU	Leu	CCU	Pro	CAU	His	CGU	Arg	U
	CUC		CCC		CAC		CGC		C
	CUA		CCA		CAA	Gln	CGA		A
	CUG		CCG		CAG		CGG		G
A	AUU	Ile	ACU	Thr	AAU	Asn	AGU	Ser	U
	AUC		ACC		AAC		AGC		C
	AUA		ACA		AAA	Lys	AGA	Arg	A
	AUG	Met	ACG		AAG		AGG		G
G	GUU	Val	GCU	Ala	GAU	Asp	GGU	Gly	U
	GUC		GCC		GAC		GGC		C
	GUA		GCA		GAA	Glu	GGA		A
	GUG		GCG		GAG		GGG		G

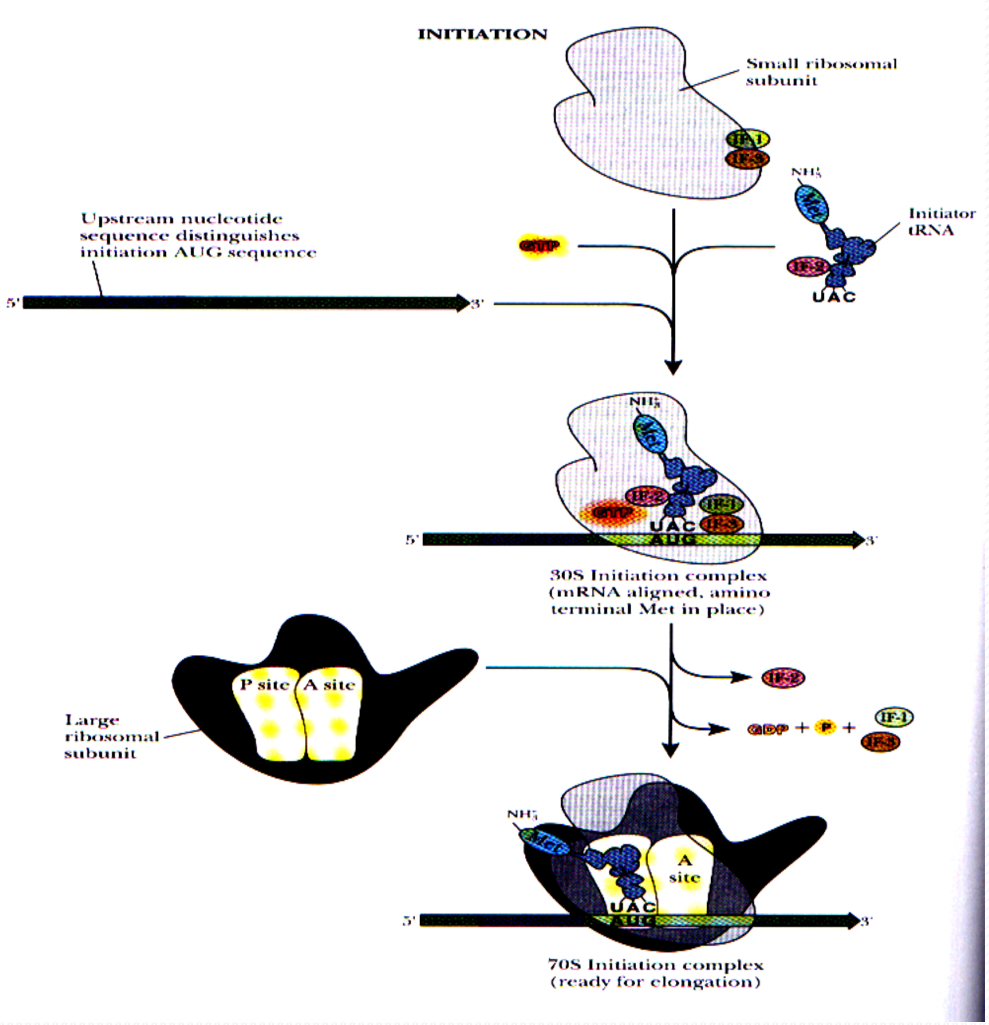
🟥 = Chain termination codon (stop)

🟩 = Initiation codon



D. Coding by similar nucleotide sequences

STEPS IN THE INITIATION PHASE OF PROTEIN SYNTHESIS



STEPS IN THE ELONGATION PHASE OF PROTEIN SYNTHESIS

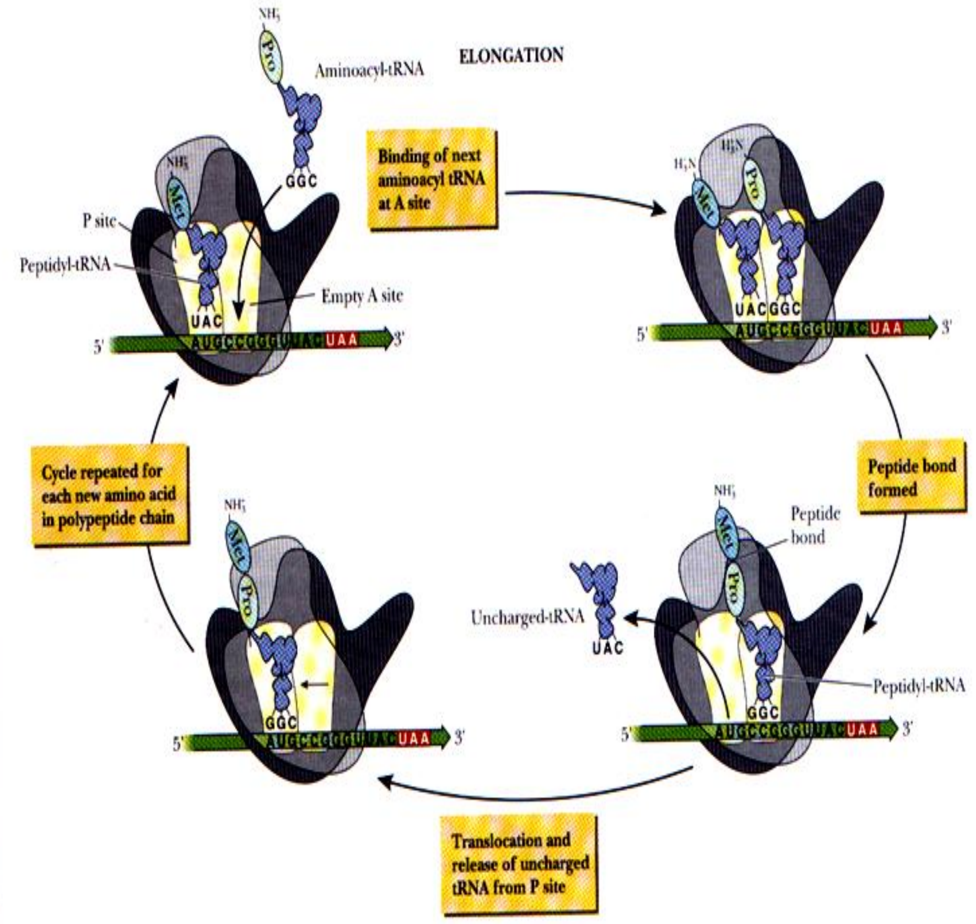


Figure 14-21 Steps in the elongation phase of protein synthesis.

STEPS IN THE TERMINATION PHASE OF PROTEIN SYNTHESIS

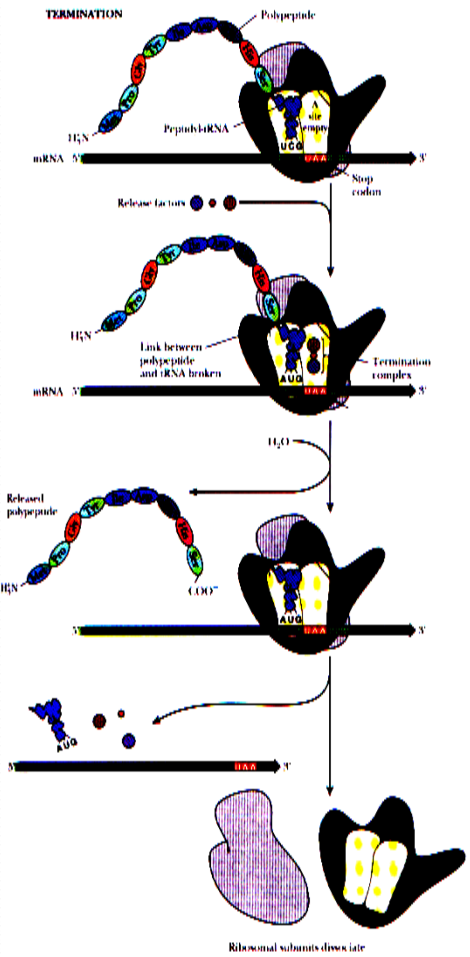
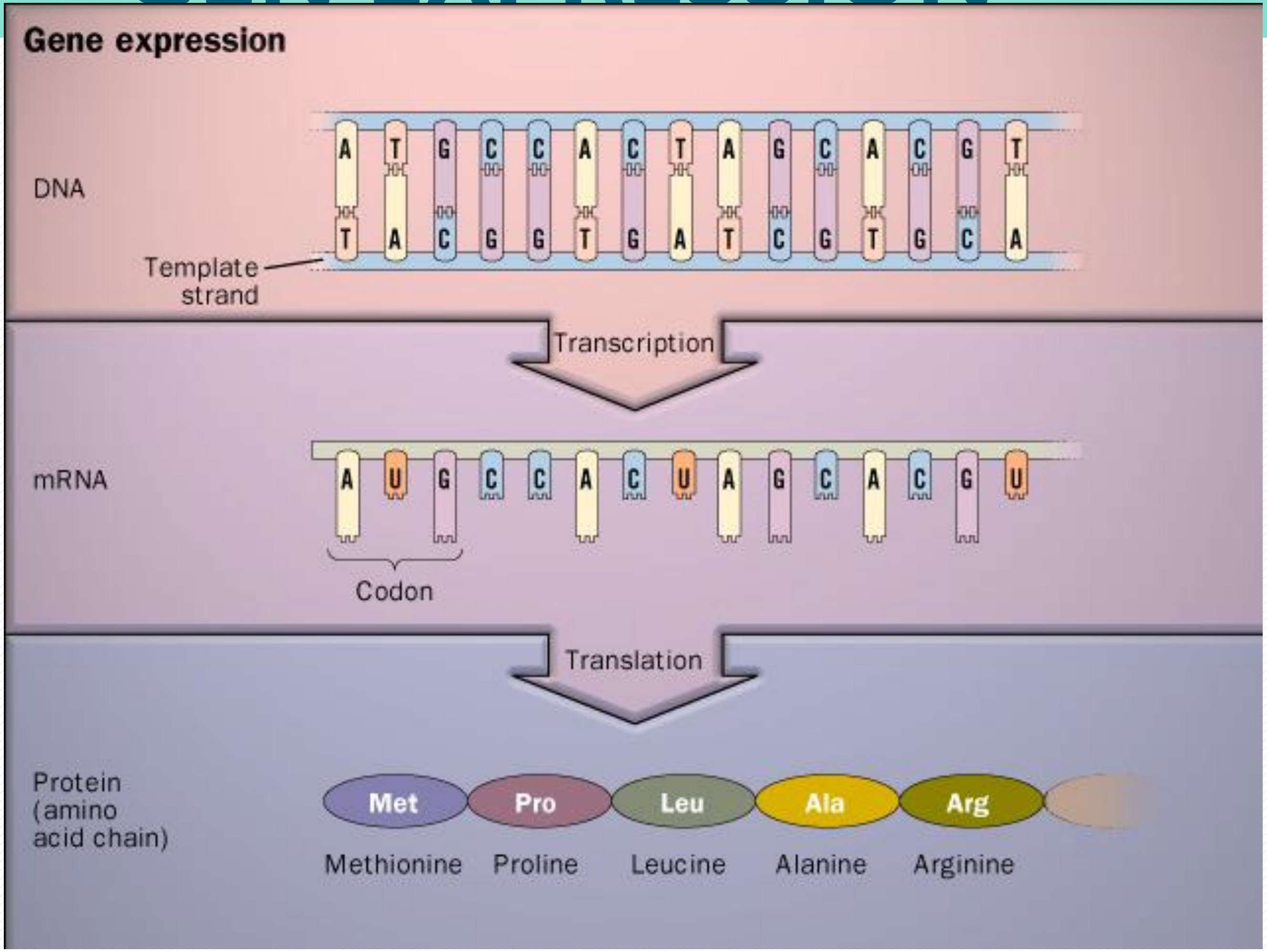
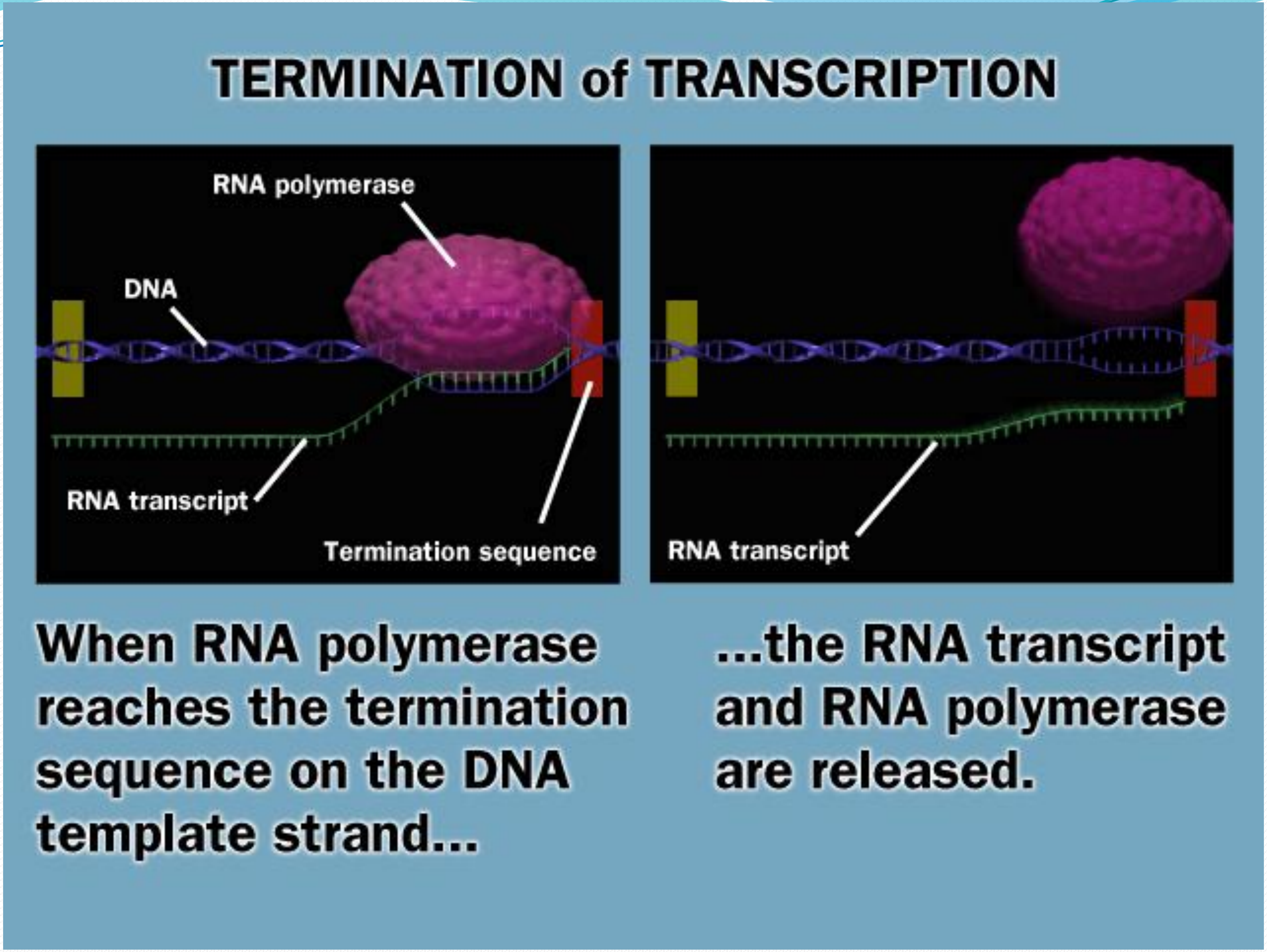


Figure 14-23 Steps in the termination phase of protein synthesis.

GEN EXPRESSION



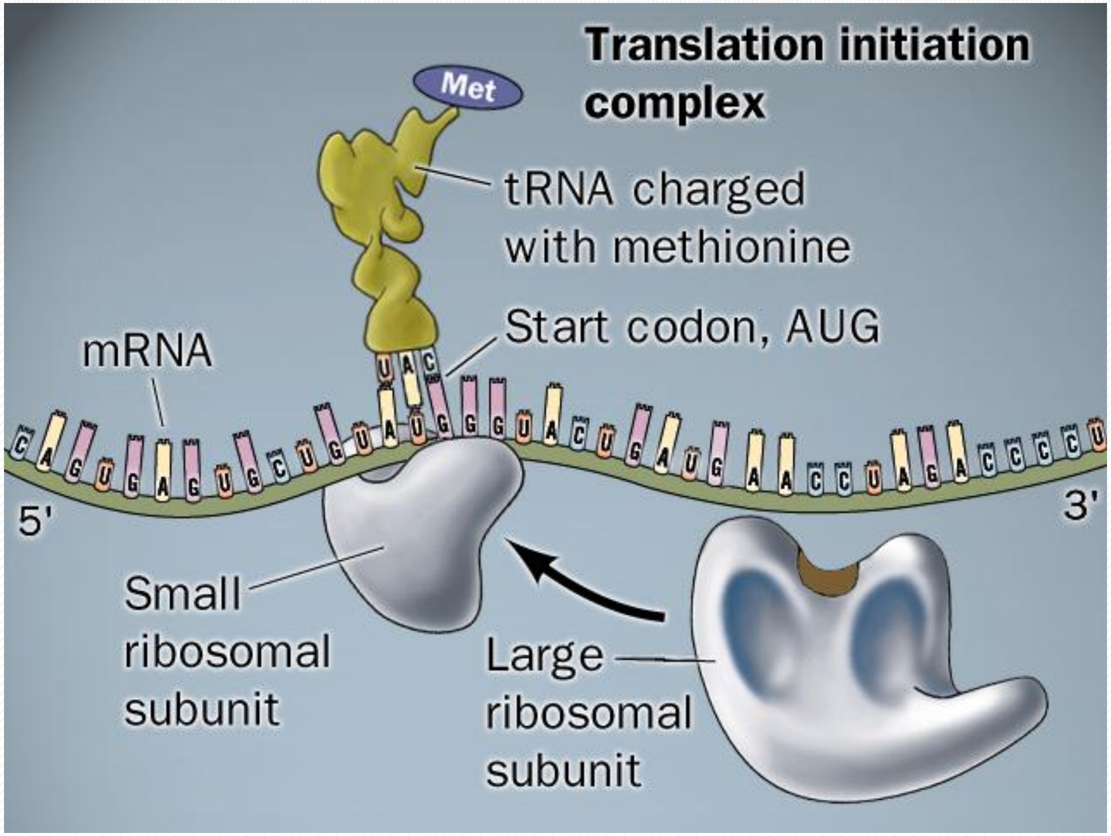


TERMINATION of TRANSCRIPTION

When RNA polymerase reaches the termination sequence on the DNA template strand…

…the RNA transcript and RNA polymerase are released.

TRANSLASI


Translation initiation complex
Met
tRNA charged with methionine
Start codon, AUG
mRNA
U A C
C A G U G A G U G C U G U A U G G G U A C U G A U G A A C C U A G A C C C C U
5'
3'
Small ribosomal subunit
Large ribosomal subunit

Terima Kasih