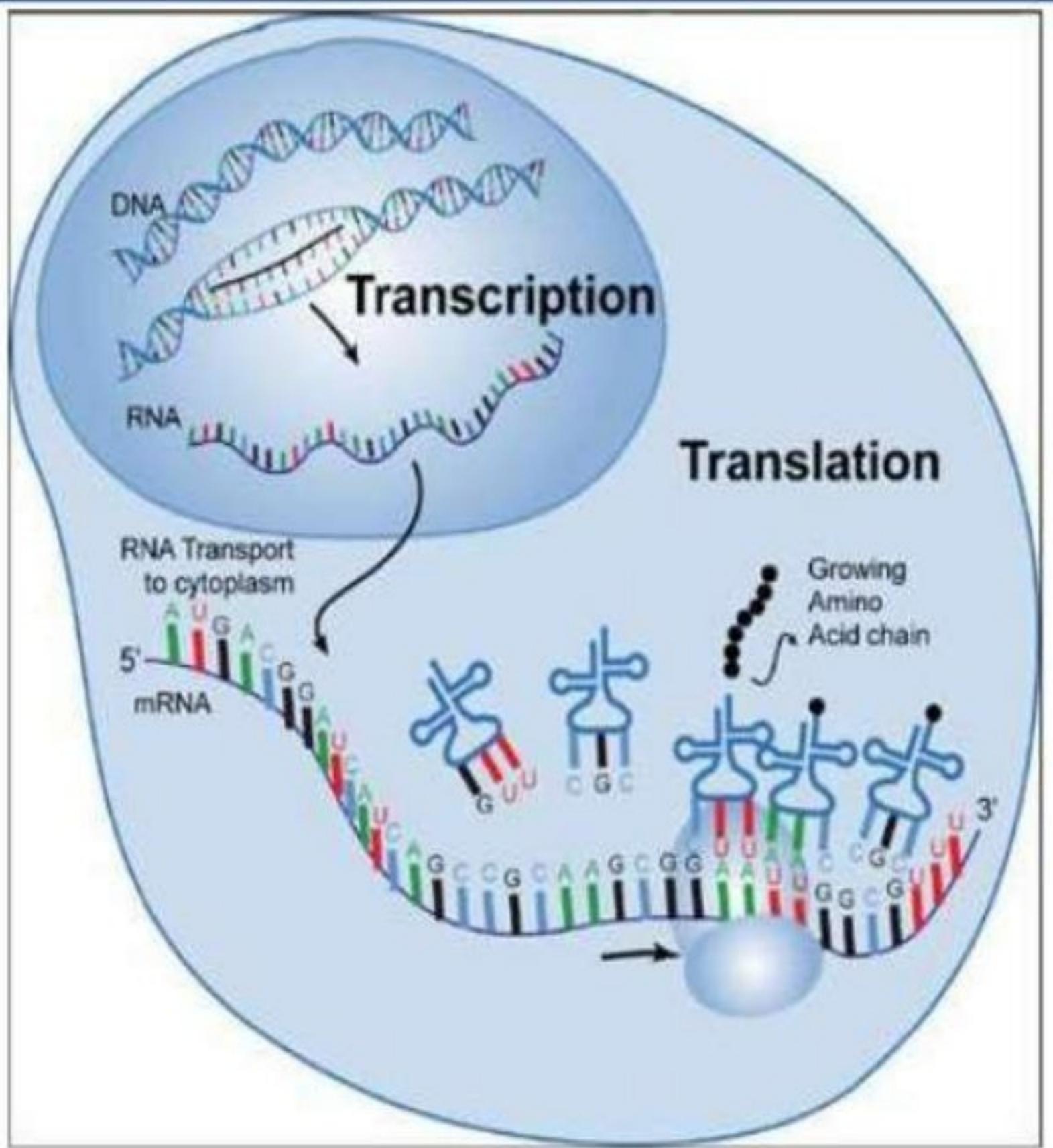




TRANSLATION



TRANSLATION



Components of the translational apparatus

- t-RNA - Structure and amino acid composition**
 - Basic features**

The ribosomes

- Prokaryotic ribosomes & components**
 - Eukaryotic ribosomes & components**
 - Functions of ribosomal units**

The mRNA & the Genetic code

- Features of prokaryotic & eukaryotic mRNA**
- The genetic code & its features**
- Wobbling & the genetic code**



- Amino acid activation & t-RNA loading
- Specificity & fidelity of amino acylation reaction
- Protein synthesis in prokaryotes
- The initiation complex & initiation factors
 - Initiation
 - Elongation & Translocation
 - Termination of translation
 - Antibiotics and prokaryotic protein synthesis

Eukaryotic translation

- Eukaryotic initiation factors & initiation complex- Initiation, Elongation, Termination
- Diphtheria toxin & its effects
- Iron & globin synthesis



Translation is the process in which a sequence of nucleotide triplets in a messenger RNA gives rise to a specific sequence of **amino acids during the synthesis of a **polypeptide chain (or) protein.****

- **Translation process occurs in cytosol and requires the involvement of protein synthesizing units - Ribosomes, mRNA, t-RNA, Amino acids, Aminoacyl-RNA synthetase and several other Proteins.**

CENTRAL DOGMA



5' -ATGCCTAGGTACCTATGA-3'

3' -TACGGATCCATGGATACT-5'

DNA

Transcription

5' -AUGCCUAGGUACCUAUGA-3'

mRNA

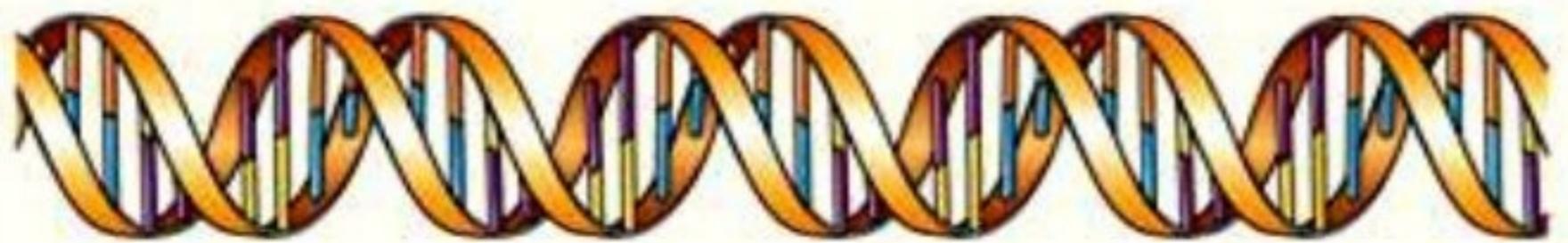
decoded as

5' -AUG CCU AGG UAC CUA UGA-3'

Translation

MET-PRO-ARG-TYR-LEU

Protein



Transcription into mRNA
 10^{-4}



Translation of mRNA
 10^{-4}



Selection of tRNAs by ribosomes
 $10^{-3}-10^{-5}$

Amino acid + tRNA



aaRS

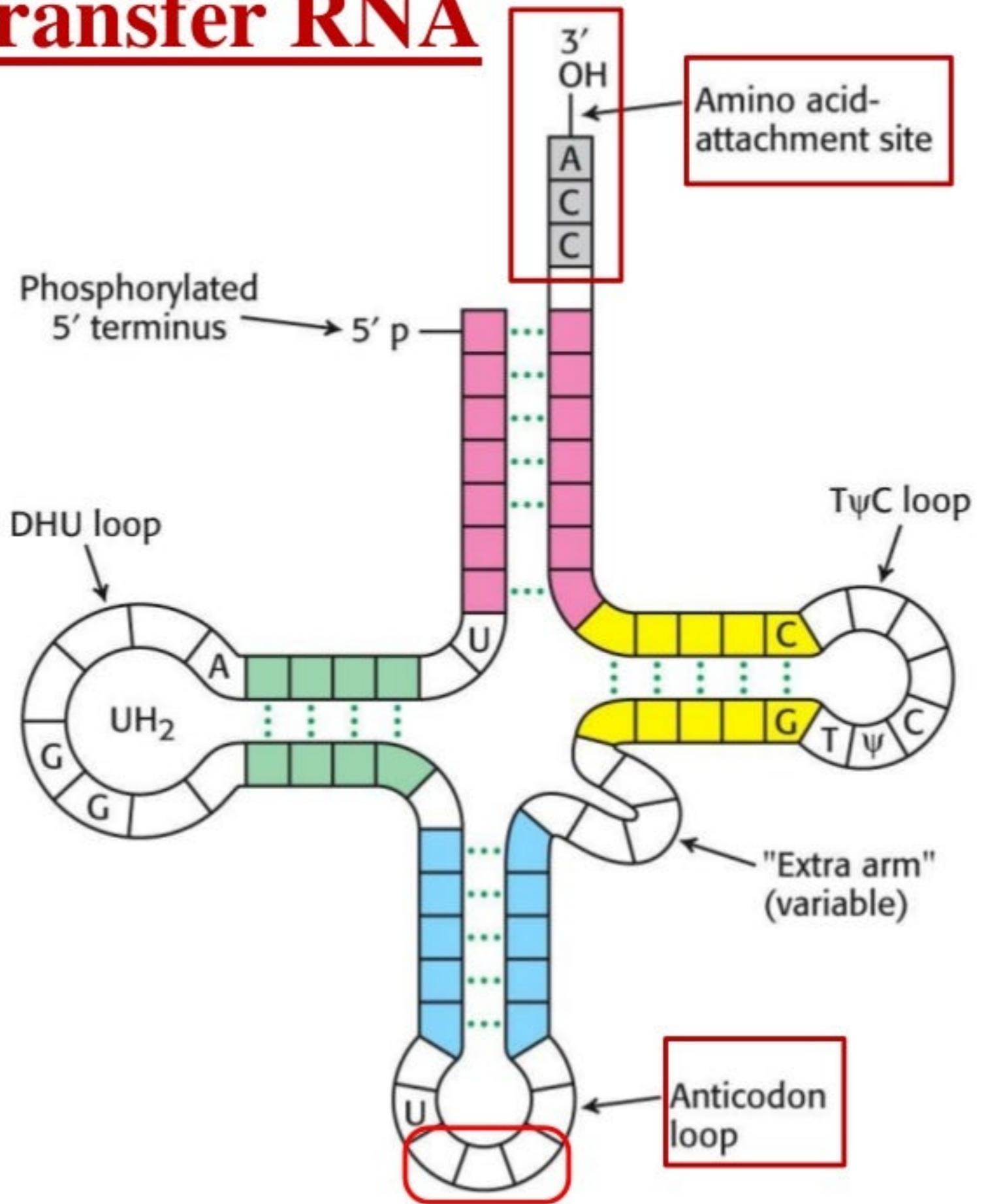
Aminoacylation of tRNA
 $10^{-3}-10^{-4}$

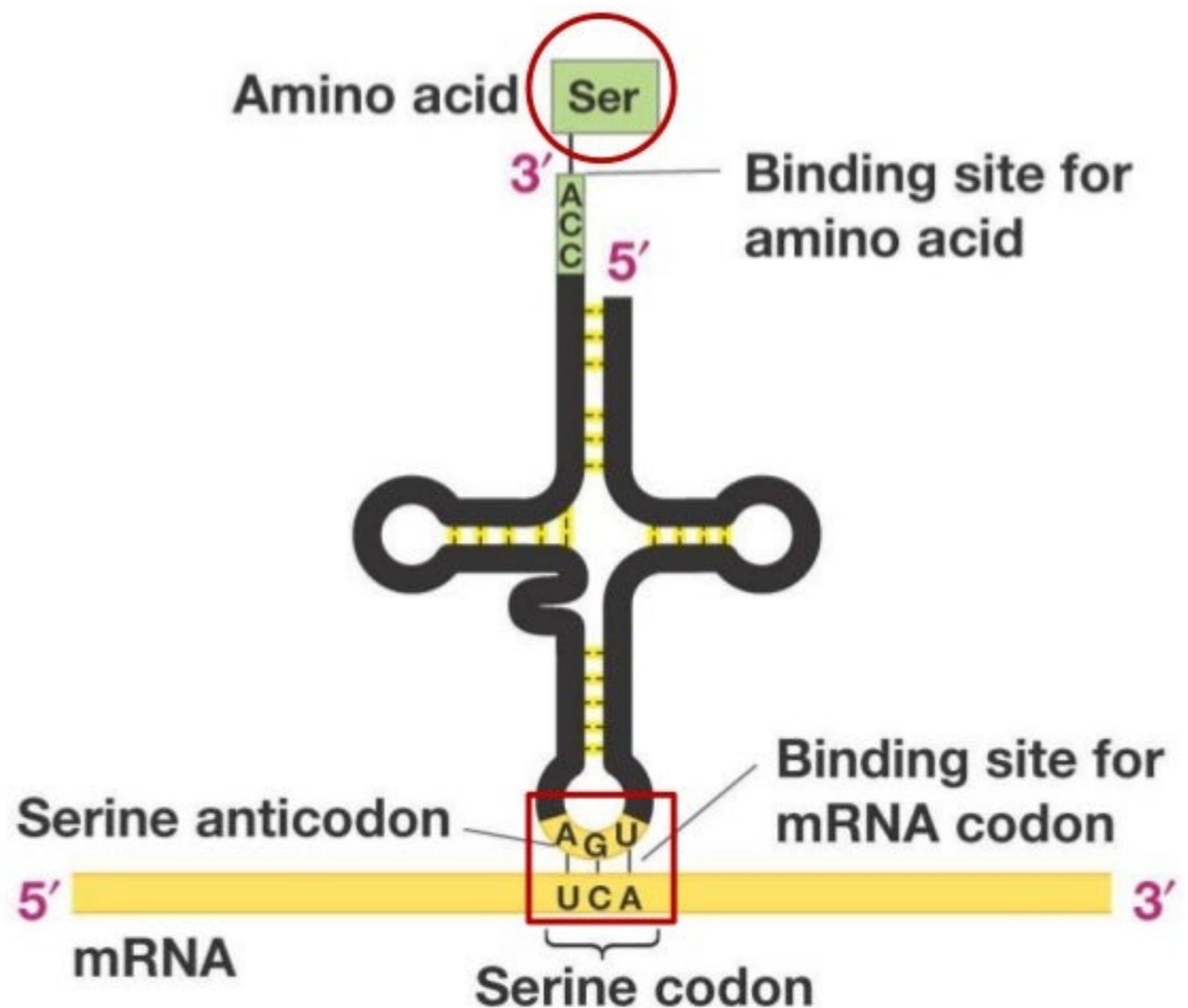


PROTEIN SYNTHESIS COMPONENTS

- mRNA (ORF)
- **Ribosomes**
- Amino acids (20)
- tRNA
- Mg²⁺
- Amino acyl tRNA Synthetases (I and II)
- Initiation, Elongation and Termination Factors

transfer RNA



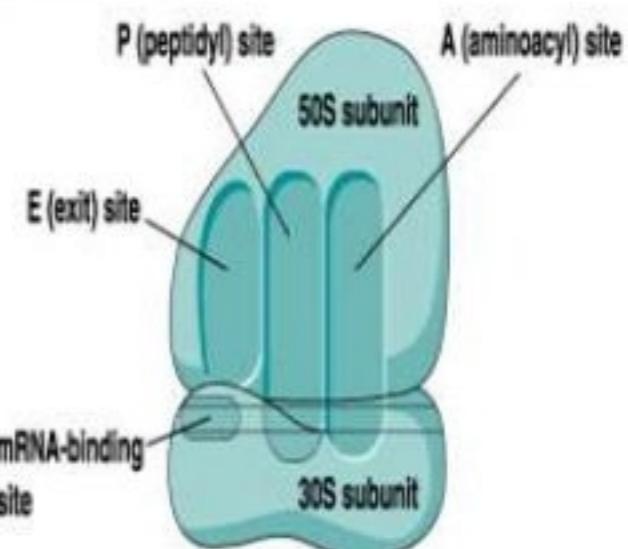
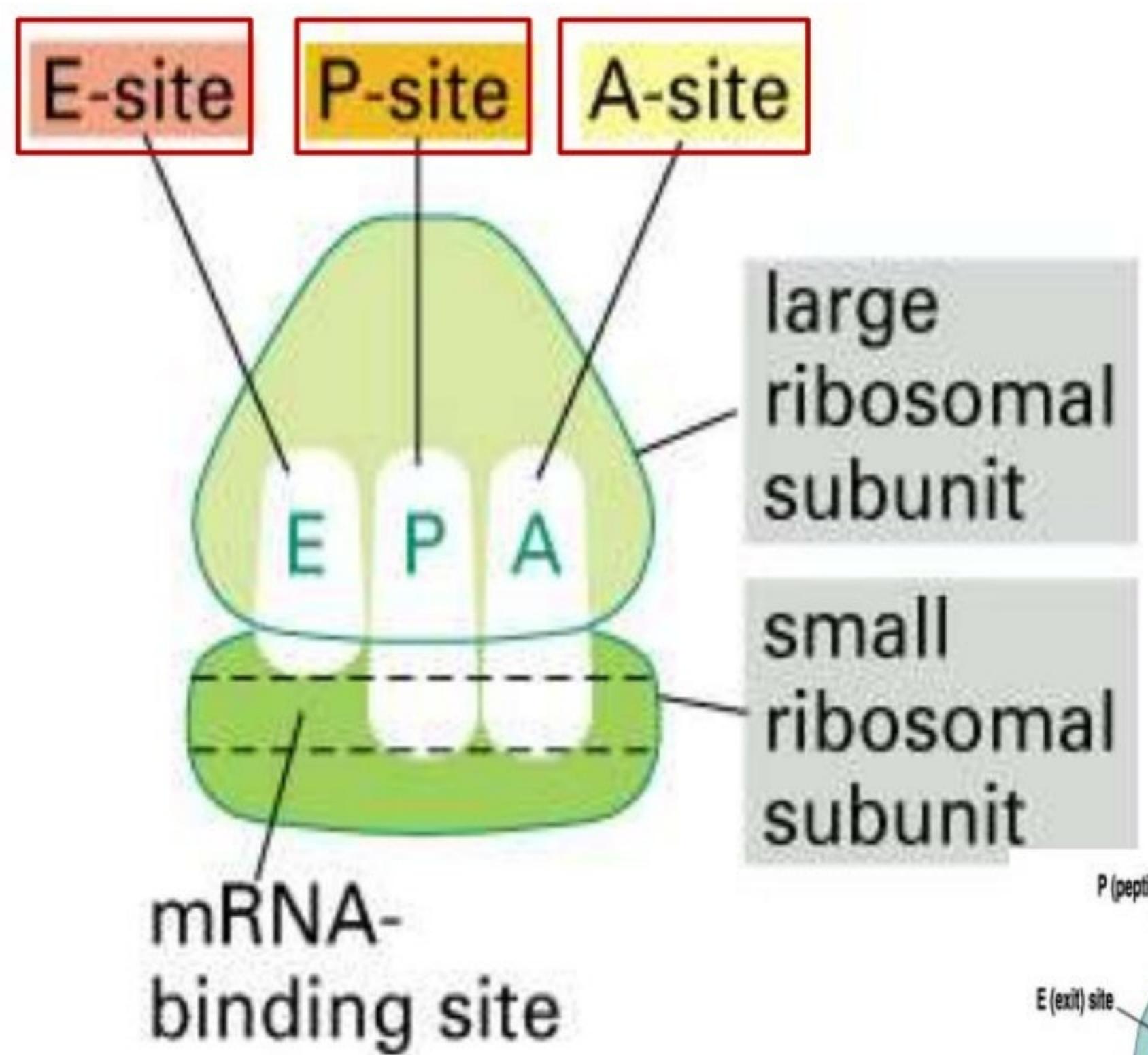


- **3' end of tRNA: binding site for amino acids.**
- **Anticodon loop at opposite end:**
 - Interacts with complementary codon on mRNA.



RIBOSOMES

- **Ribosomes are the macromolecular complex that directs the synthesis of proteins.**
- **These are the sites of protein synthesis, having**
 - **30% - 40% protein**
 - **60% - 70% RNA (rRNA)**
- **Each Ribosome having 2 ribosomal subunits –larger and smaller.**



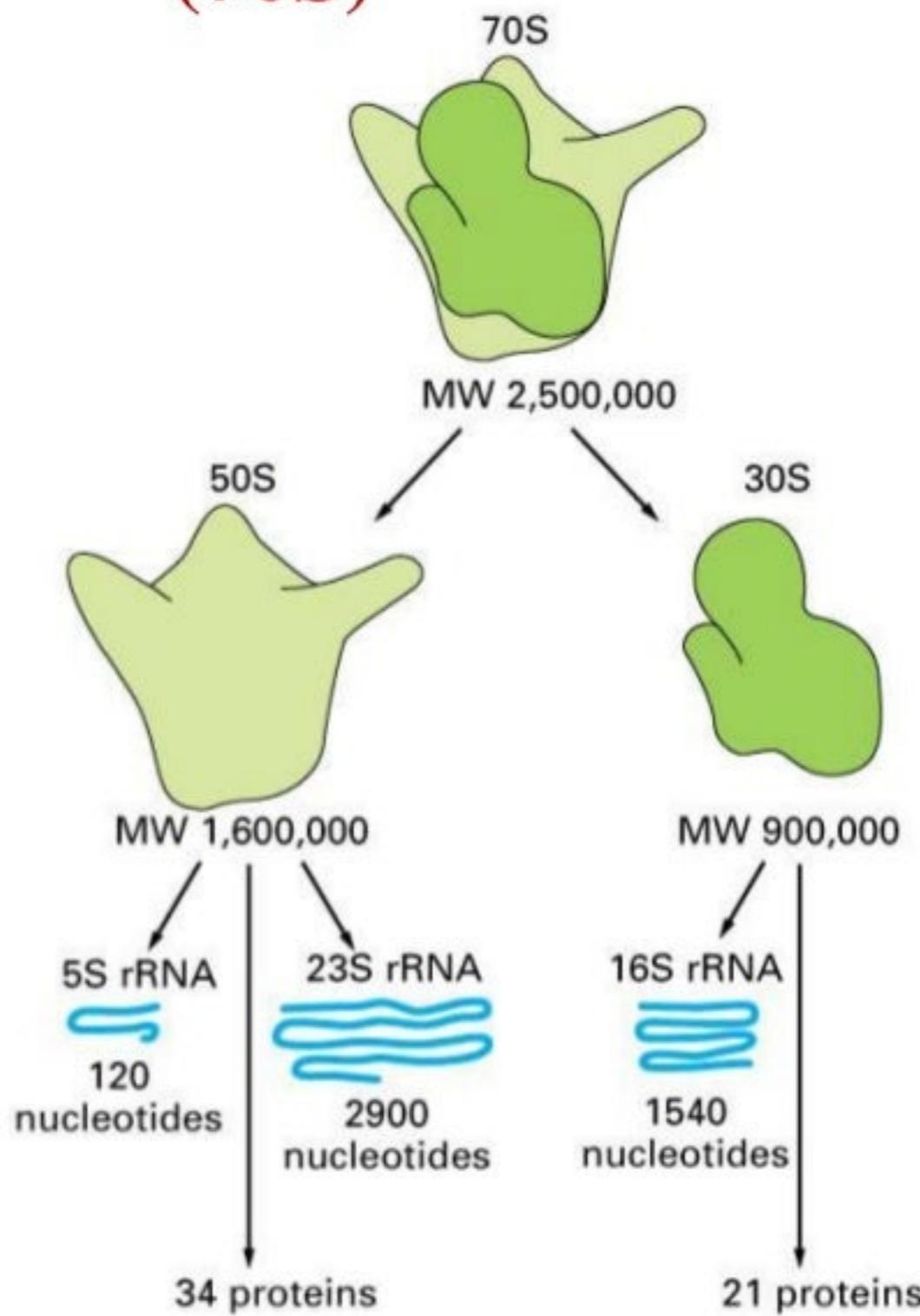


Ribosome has three tRNA binding sites

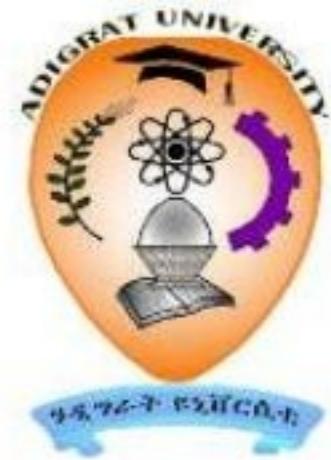
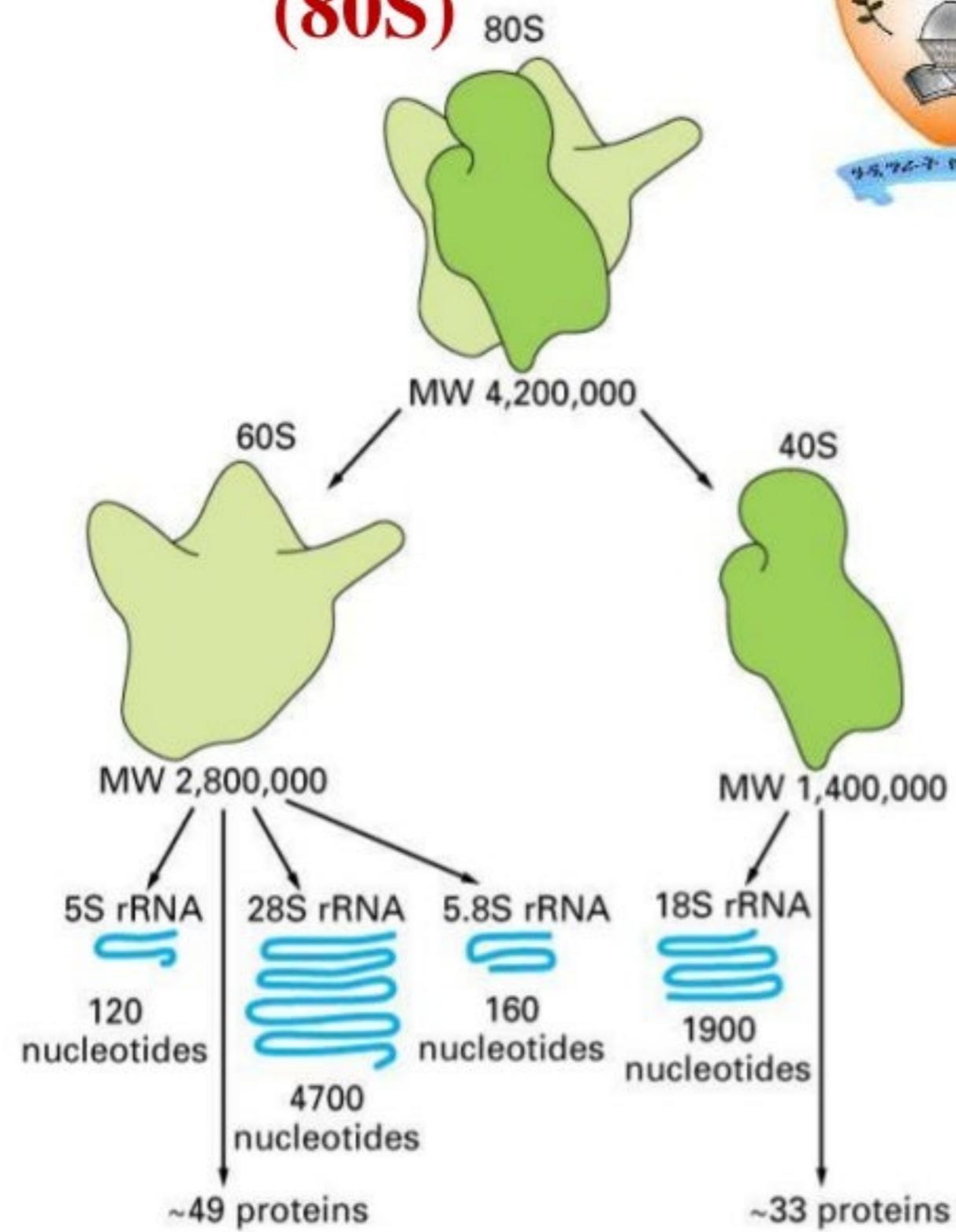
- 1) **A site** – binding site for first **aminocylated tRNA**
- 1) **P site** – binding site for the **peptidyl tRNA**
- 1) **E site** – binding site for the **uncharged tRNA**

These sites are present at the interface between the small and the large subunit of ribosome.

Prokaryotic Ribosome (70S)



Eukaryotic Ribosome (80S)





GENETIC CODE

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

GENETIC CODE

2nd base in codon

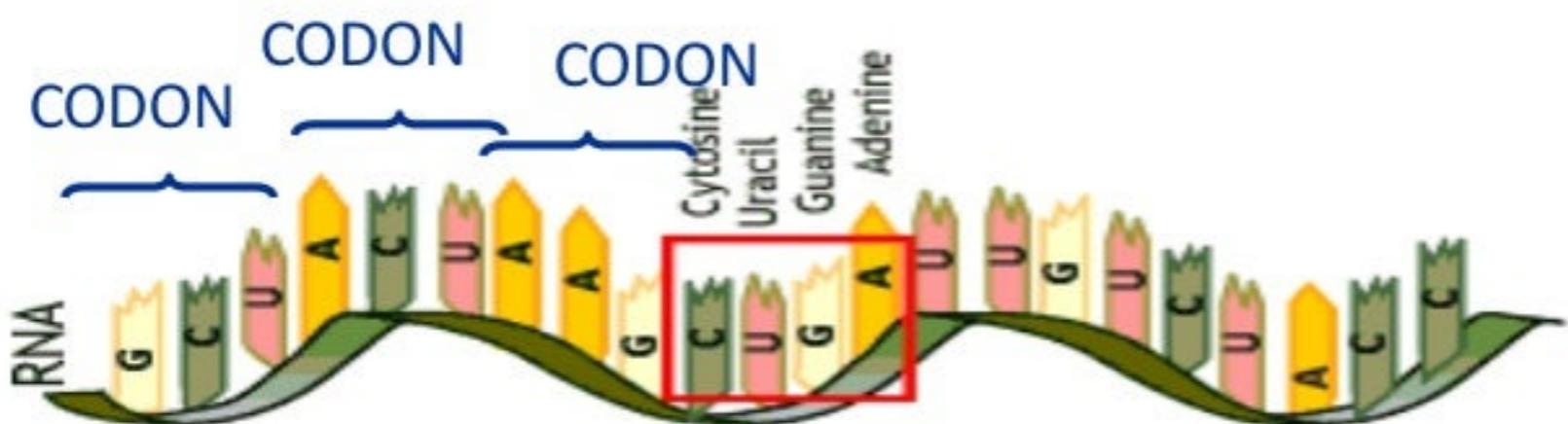
1st base in codon

3rd base in codon

	U	C	A	G	
U	Phe Phe Leu Leu	Ser Ser Ser Ser	Tyr Tyr STOP STOP	Cys Cys STOP Trp	U C A G
C	Leu Leu Leu Leu	Pro Pro Pro Pro	His His Gln Gln	Arg Arg Arg Arg	U C A G
A	Ile Ile Ile Met	Thr Thr Thr Thr	Asn Asn Lys Lys	Ser Ser Arg Arg	U C A G
G	Val Val Val Val	Ala Ala Ala Ala	Asp Asp Glu Glu	Gly Gly Gly Gly	U C A G

Even though there are only 20 amino acids exists, there are actually 64 possible Codons available.

$4 \times 4 \times 4 = 64$ possible combinations



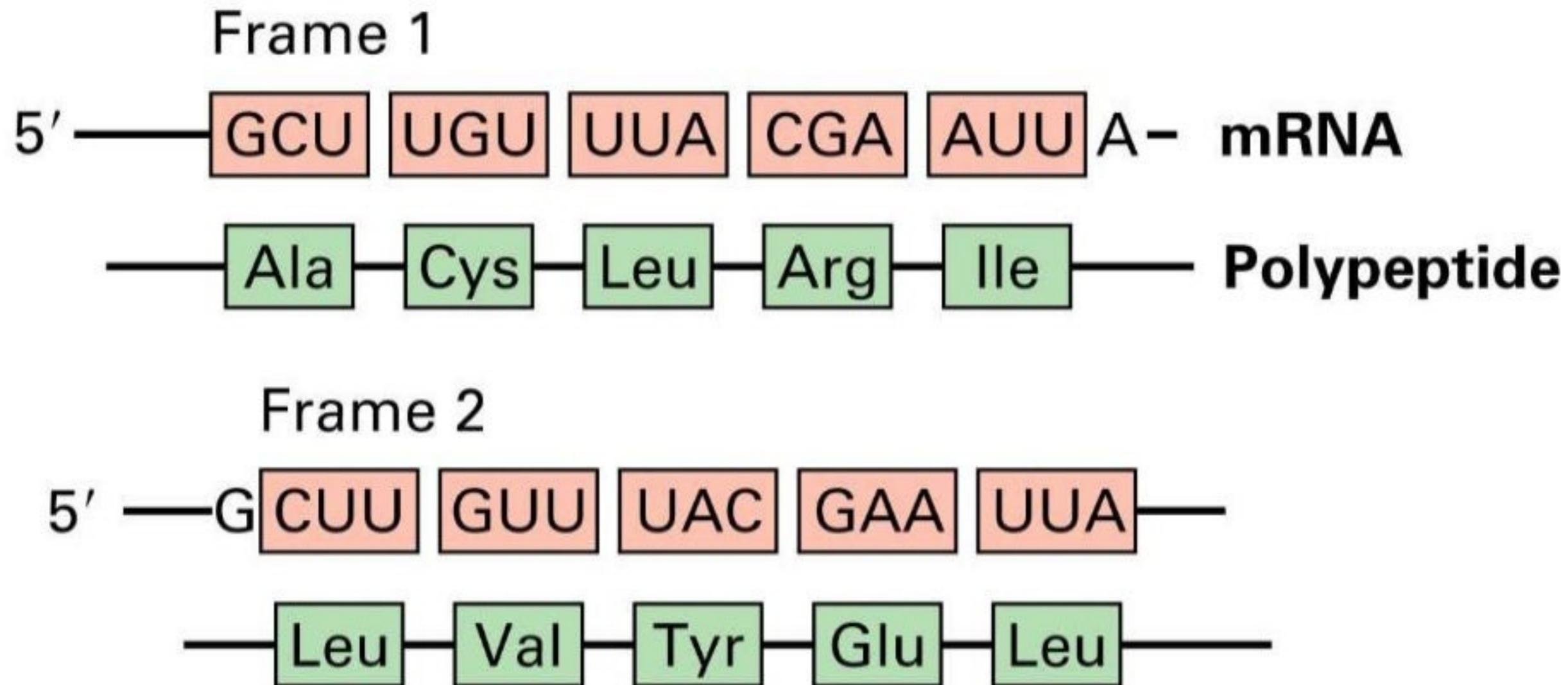
1 st NUCLEOTIDE

3 rd NUCLEOTIDE

GGU = Glycine

2 nd NUCLEOTIDE

3 letter code allows different reading frames

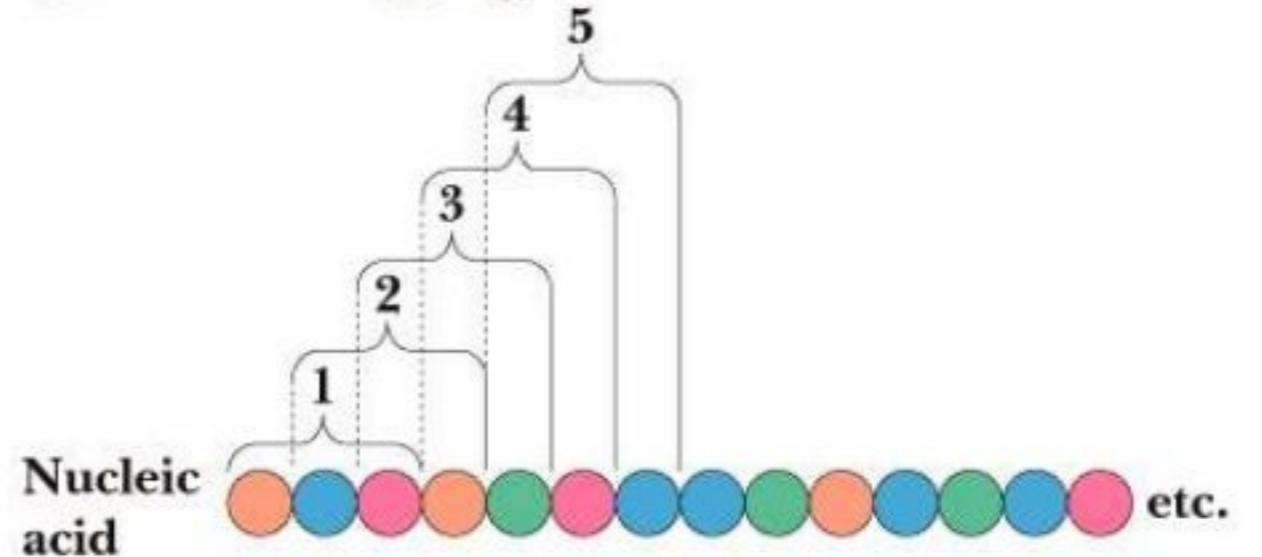




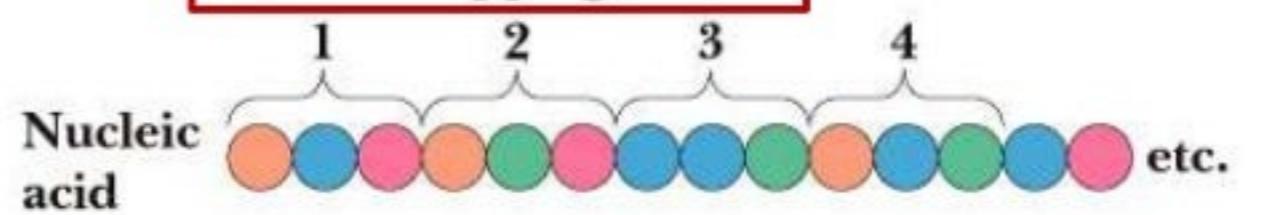
Characteristics of Genetic Code

- Triplet Codons
- Universal
- Non-overlapping
- Unambiguous
- Degenerate
- Stop or termination or nonsense codons

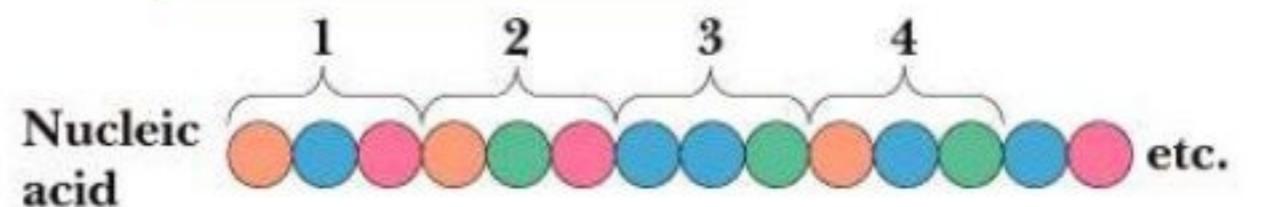
(a) Overlapping code



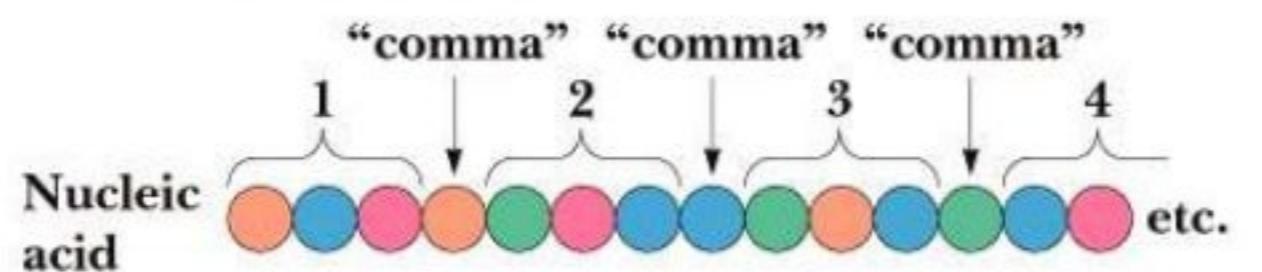
Nonoverlapping code



(b) Continuous code



Punctuated code





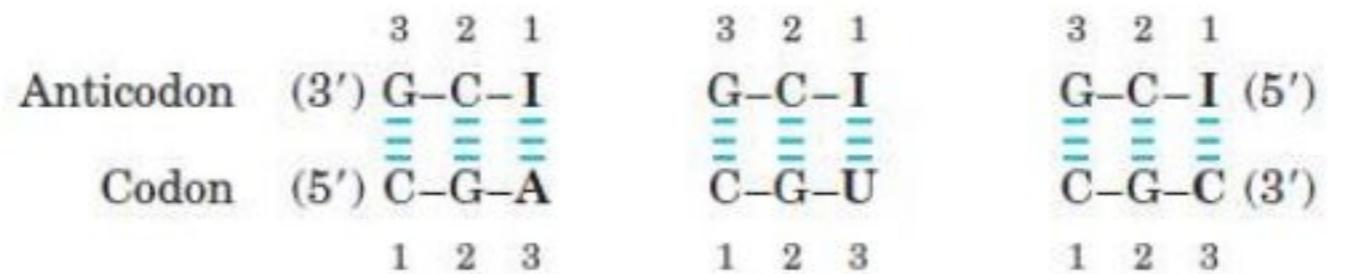
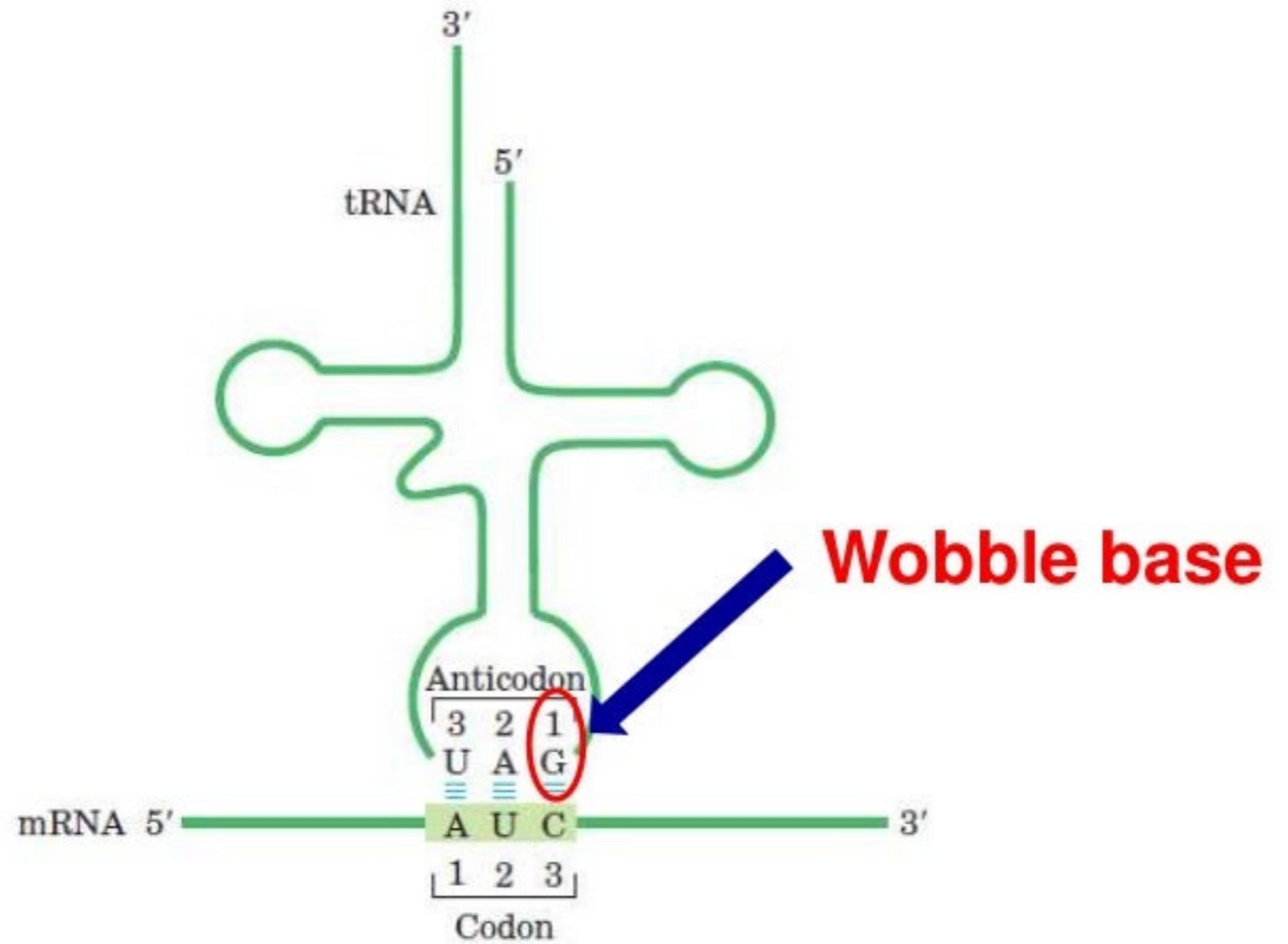
Some exceptions to the rule

Known Deviations from the Universal Genetic Code

Codon	Universal Code	Unusual Code*	Occurrence
UGA	Stop	Trp	<i>Mycoplasma, Spiroplasma, mitochondria of many species</i>
CUG	Leu	Thr	Mitochondria in yeasts
UAA, UAG	Stop	Gln	<i>Acetabularia, Tetrahymena, Paramecium, etc.</i>
UGA	Stop	Cys	<i>Euplotes</i>

Degeneracy of the Genetic Code

<i>Amino acid</i>	<i>Number of codons</i>	<i>Amino acid</i>	<i>Number of codons</i>
Met	1	Tyr	2
Trp	1	Ile	3
Asn	2	Ala	4
Asp	2	Gly	4
Cys	2	Pro	4
Gln	2	Thr	4
Glu	2	Val	4
His	2	Arg	6
Lys	2	Leu	6
Phe	2	Ser	6





How the Wobble Base of the Anticodon Determines the Number of Codons a tRNA Can Recognize

1. One codon recognized:

Anticodon

(3') X-Y-**C** (5')

Codon

(5') Y-X-**G** (3')

(3') X-Y-**A** (5')

(5') Y-X-**U** (3')

2. Two codons recognized

Anticodon

(3') X-Y-**U** (5')

Codon

(5') Y-X-**A**
G (3')

(3') X-Y-**G** (5')

(5') Y-X-**C**
U (3')

3. Three codons recognized

Anticodon

(3') X-Y-**I** (5')

Codon

(5') Y-X-**A**
U
C (3')

Note: X and Y denote bases complementary to and capable of strong Watson-Crick base pairing with X' and Y', respectively. Wobble bases—in the 3' position of codons and 5' position of anticodons—are shaded in pink.

Allowed Wobble Pairing Combinations in the Third Codon-Anticodon Position

5'-Anticodon Base	3'-Codon Base
C	G
A	U
U	A or G
G	U or C
I	U, C, or A

The base pair in the 3rd codon position can “wobble”



If these bases are in
first, or wobble, position of
anticodon

C	A	G	U	I	
G	U	C	A	C	then the tRNA may recognize codons in mRNA having these bases in third position



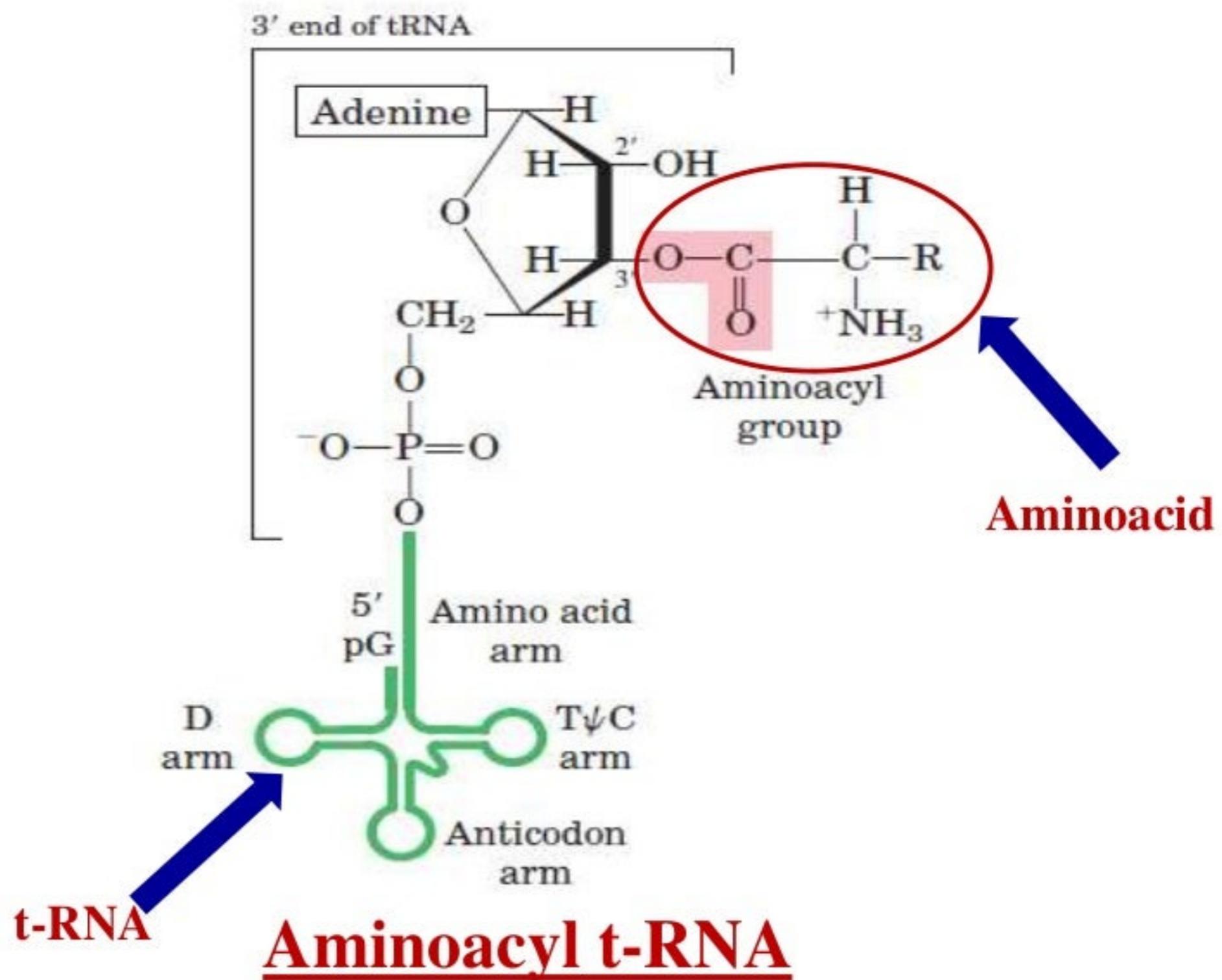
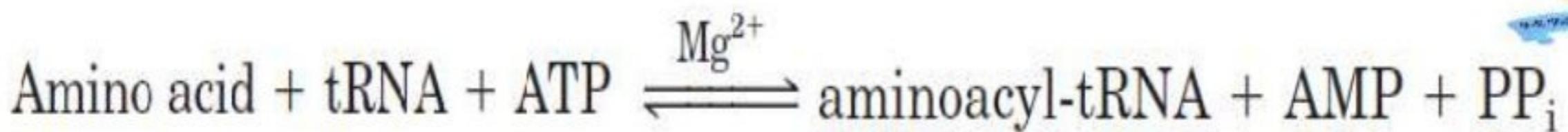
AGA	AGG									
GCA	CGA							GGA		
GCC	CGC							GGC		AUA
GCG	CGG	GAC	AAC	UGC	GAA	CAA	GGG	CAC	AUC	
GCU	CGU	GAU	AAU	UGU	GAG	CAG	GGU	CAU	AUU	
Ala	Arg	Asp	Asn	Cys	Glu	Gln	Gly	His	Ile	
A	R	D	N	C	E	Q	G	H	I	
UUA					AGC					
UUG					AGU					
CUA				CCA	UCA	ACA			GUA	
CUC				CCC	UCC	ACC			GUC	
CUG	AAA			CCG	UCG	ACG		UAC	GUG	
CUU	AAG	AUG	UUU	CCU	UCU	ACU	UGG	UAU	GUU	
Leu	Lys	Met	Phe	Pro	Ser	Thr	Trp	Tyr	Val	
L	K	M	F	P	S	T	W	Y	V	stop

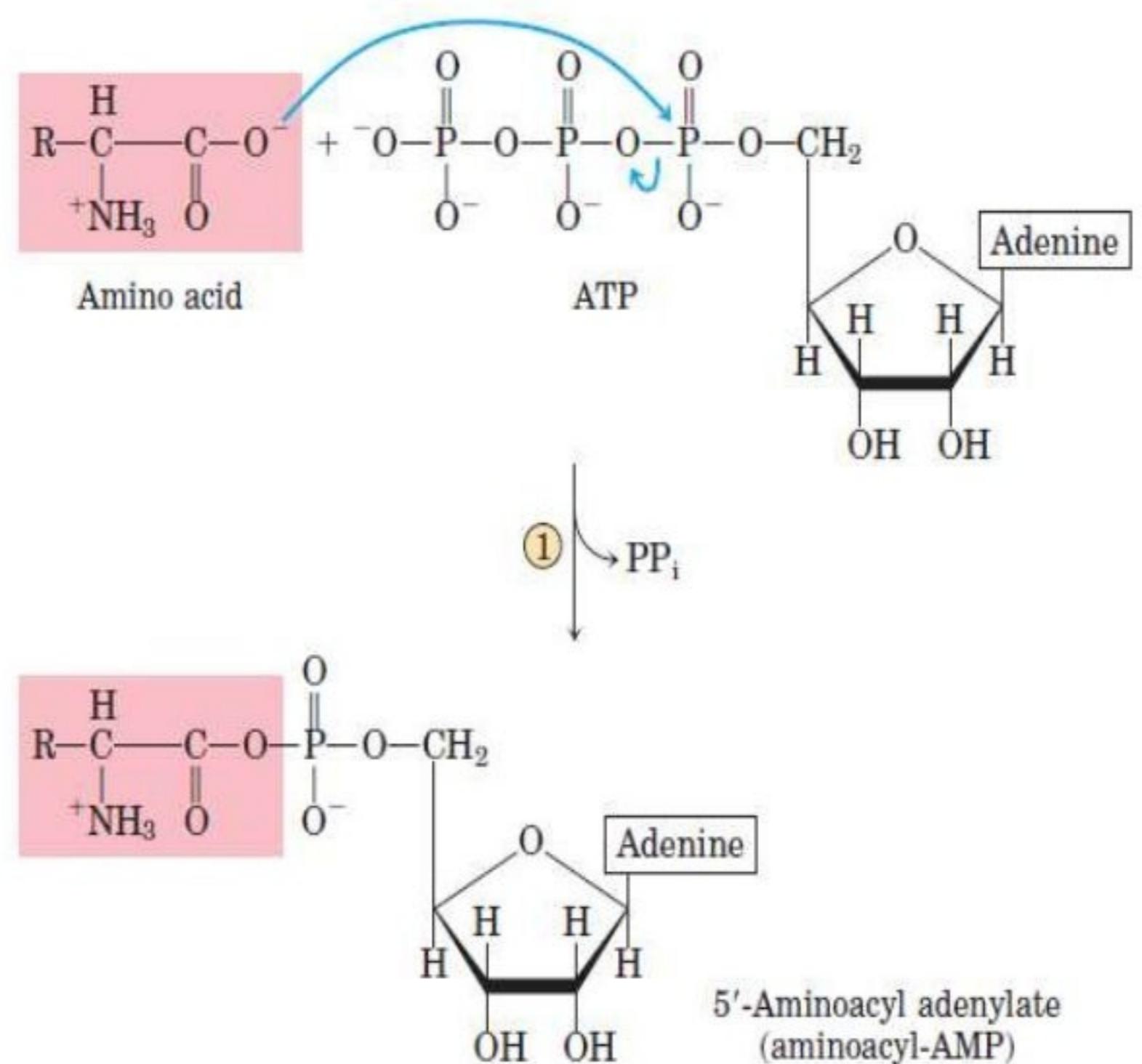
Figure 6–50. Molecular Biology of the Cell, 4th Edition.

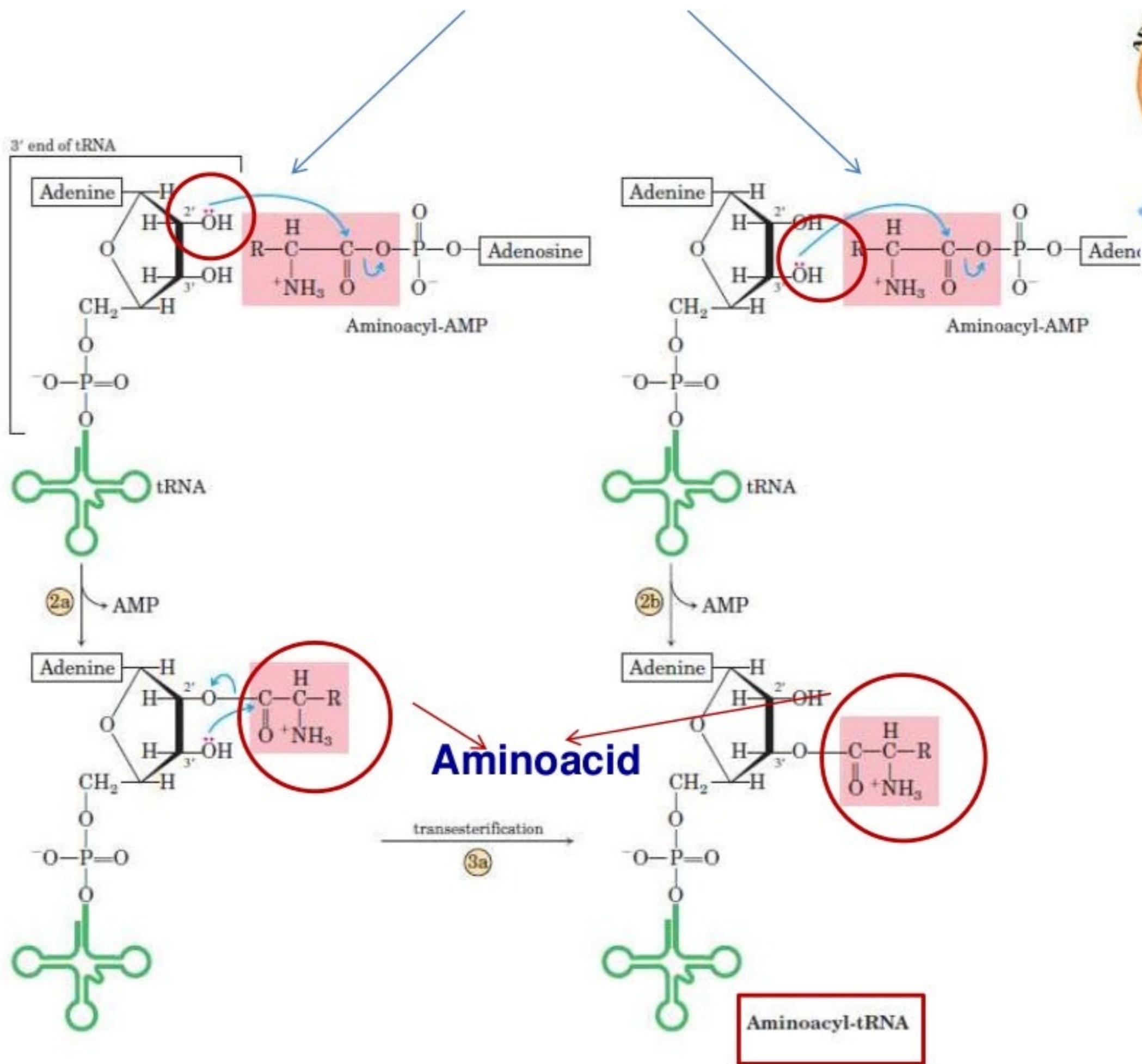
Components Required for the Five Major Stages of Protein Synthesis in *E. coli*

Stage	Essential components
1. Activation of amino acids	20 amino acids 20 aminoacyl-tRNA synthetases 32 or more tRNAs ATP Mg^{2+}
2. Initiation	mRNA <i>N</i> -Formylmethionyl-tRNA ^{fmet} Initiation codon in mRNA (AUG) 30S ribosomal subunit 50S ribosomal subunit Initiation factors (IF-1, IF-2, IF-3) GTP Mg^{2+}
3. Elongation	Functional 70S ribosome (initiation complex) Aminoacyl-tRNAs specified by codons Elongation factors (EF-Tu, EF-Ts, EF-G) GTP Mg^{2+}
4. Termination and release	Termination codon in mRNA Release factors (RF-1, RF-2, RF-3)
5. Folding and posttranslational processing	Specific enzymes, cofactors, and other components for removal of initiating residues and signal sequences, additional proteolytic processing, modification of terminal residues, and attachment of phosphate, methyl, carboxyl, carbohydrate, or prosthetic groups

Activation of Amino acid









Amino-acyl tRNA synthetases:

One synthetase for each amino acid a single synthetase may recognize multiple tRNAs or the same amino acid

Two classes of synthetases

Class I - monomeric, acylates the 2'-OH on the terminal ribose

Arg, Cys , Gln, Glu, Ile, Leu, Met, Trp Tyr, Val

Class II - dimeric, acylates the 3'-OH on the terminal ribose

Ala, Asn, Asp, Gly, His, Lys, Phe, Ser, Pro, Thr

Selection of the initiating AUG is determined by neighboring nucleotides



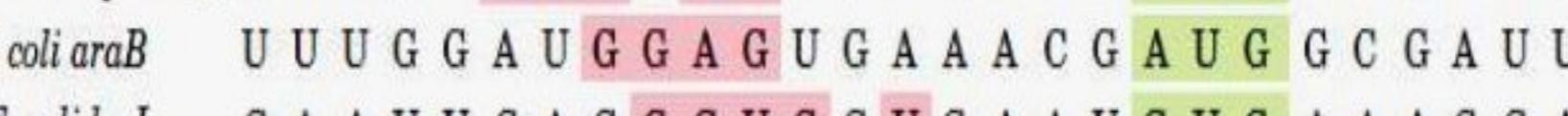
<u>Shine-Dalgarno</u>	<u>Initiation Codon</u>
5' AGCACCGAGGGGAAAU CUGAUGGAACGGCUAC	3' <i>E. coli trpA</i>
UUUGGAUGGGAGUGAAACGAUGGCGAUUGCA	<i>E. coli araB</i>
GGUAACCAGGUAAACAAACCAUGCGAGUGUUG	<i>E. coli thrA</i>
CAAUUCAGGGUGGUGAAUGUGAAACCAAGUA	<i>E. coli lacI</i>
AAUCUUGGAGGCCUUUJUUAUGGUUCGUUCU	φX174 phage A protein
UAACUAAGGAUGAAAUGCAUGUCUAAGACA	Q β phage replicase
UCCUAGGAGGUUUGACCUCUAUGCGAGCUUUU	R17 phage A protein
AUGUACUAAGGAGGUJGUUAUGGAACAAACGC	λ phage <i>cro</i>

Pairs with 16S rRNA

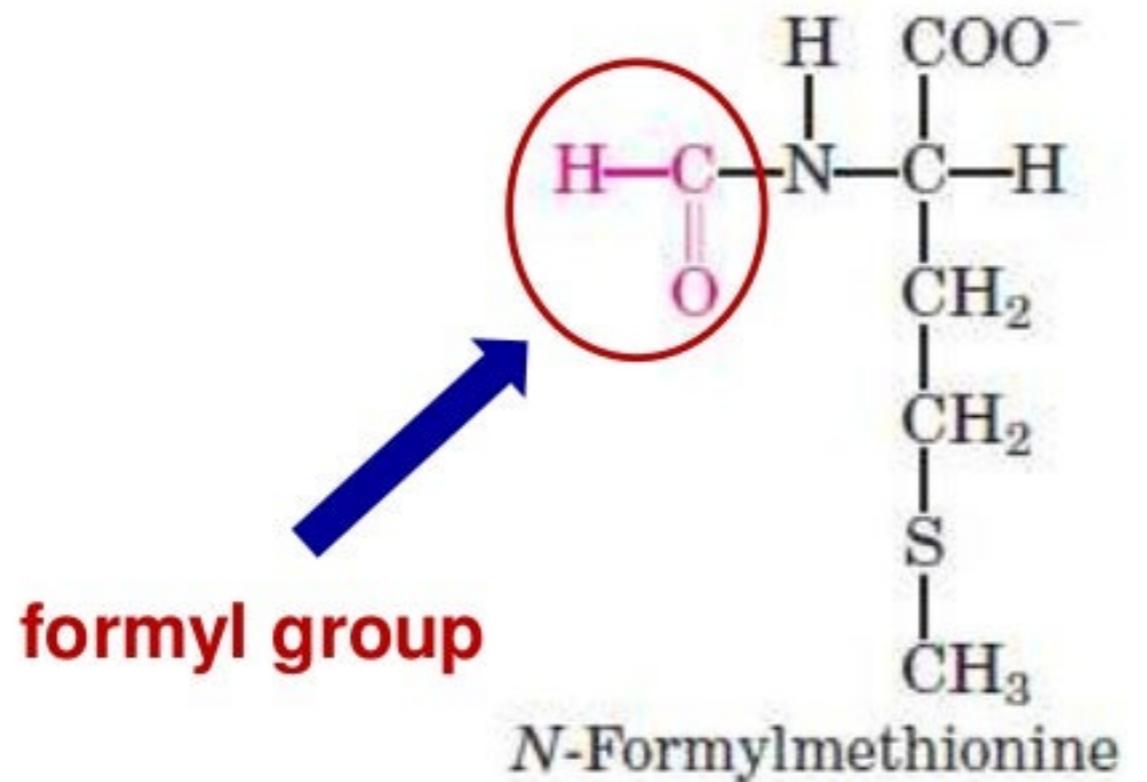
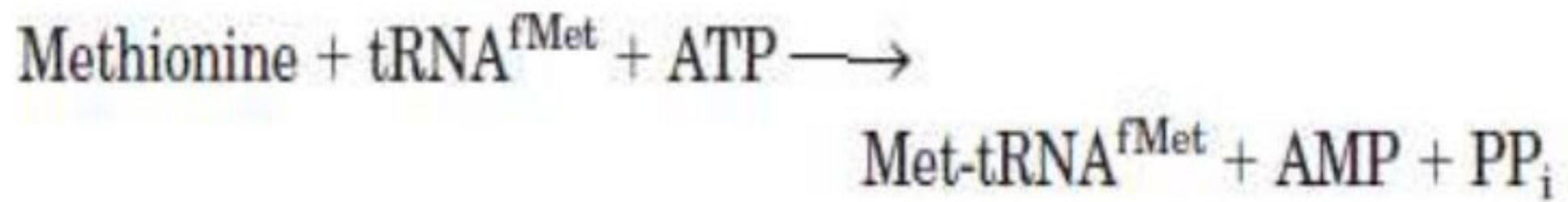
Pairs with initiator tRNA

In Eukaryotes: ACCAUGG (Kozak sequence)

<i>E. coli trpA</i>	(5') A G C A C G A G G G G A A A U C U G A U G G A A C G C U A C (3')
<i>E. coli araB</i>	U U U G G G A U G G A G U G A A A C G A U G G C G G A U U G C A
<i>E. coli lacI</i>	C A A U U C A G G G U G G U G A A U G U G G A A A C C A G U A
φX174 phage A protein	A A U C U U U G G A G G G C U U U U U U U A U G G U U C G U U C U
λ phage <i>cro</i>	A U G U A C U A A G G A G G U U G U A U G G A A C A A C G C



(a)

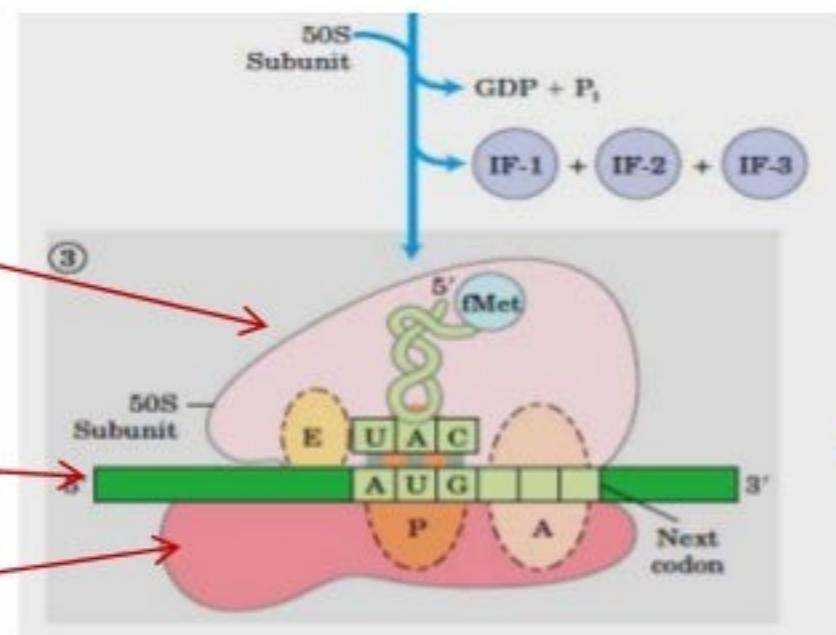
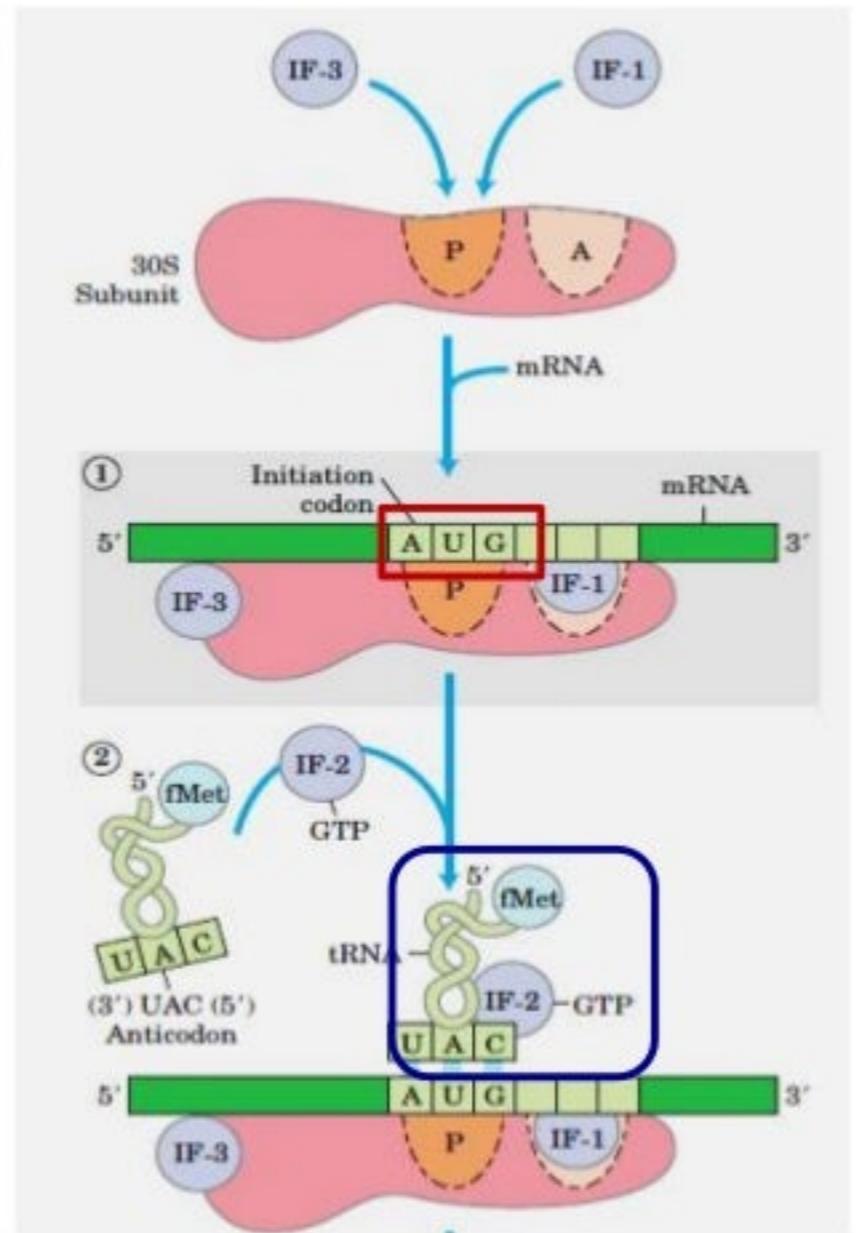
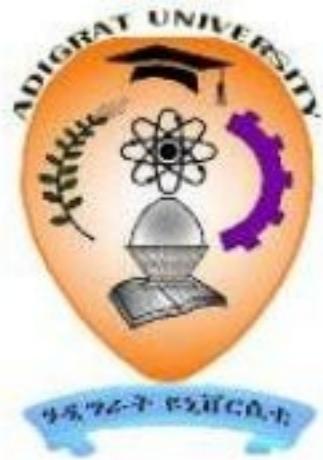


Protein Factors Required for Initiation of Translation in Bacterial and Eukaryotic Cells

Factor	Function
Bacterial	
IF-1	Prevents premature binding of tRNAs to A site
IF-2	Facilitates binding of fMet-tRNA ^{fMet} to 30S ribosomal subunit
IF-3	Binds to 30S subunit; prevents premature association of 50S subunit; enhances specificity of P site for fMet-tRNA ^{fMet}
Eukaryotic *	
elf2	Facilitates binding of initiating Met-tRNA ^{Met} to 40S ribosomal subunit
elf2B, elf3	First factors to bind 40S subunit; facilitate subsequent steps
elf4A	RNA helicase activity removes secondary structure in the mRNA to permit binding to 40S subunit; part of the elf4F complex
elf4B	Binds to mRNA; facilitates scanning of mRNA to locate the first AUG
elf4E	Binds to the 5' cap of mRNA; part of the elf4F complex
elf4G	Binds to elf4E and to poly(A) binding protein (PAB); part of the elf4F complex
elf5	Promotes dissociation of several other initiation factors from 40S subunit as a prelude to association of 60S subunit to form 80S initiation complex
elf6	Facilitates dissociation of inactive 80S ribosome into 40S and 60S subunits

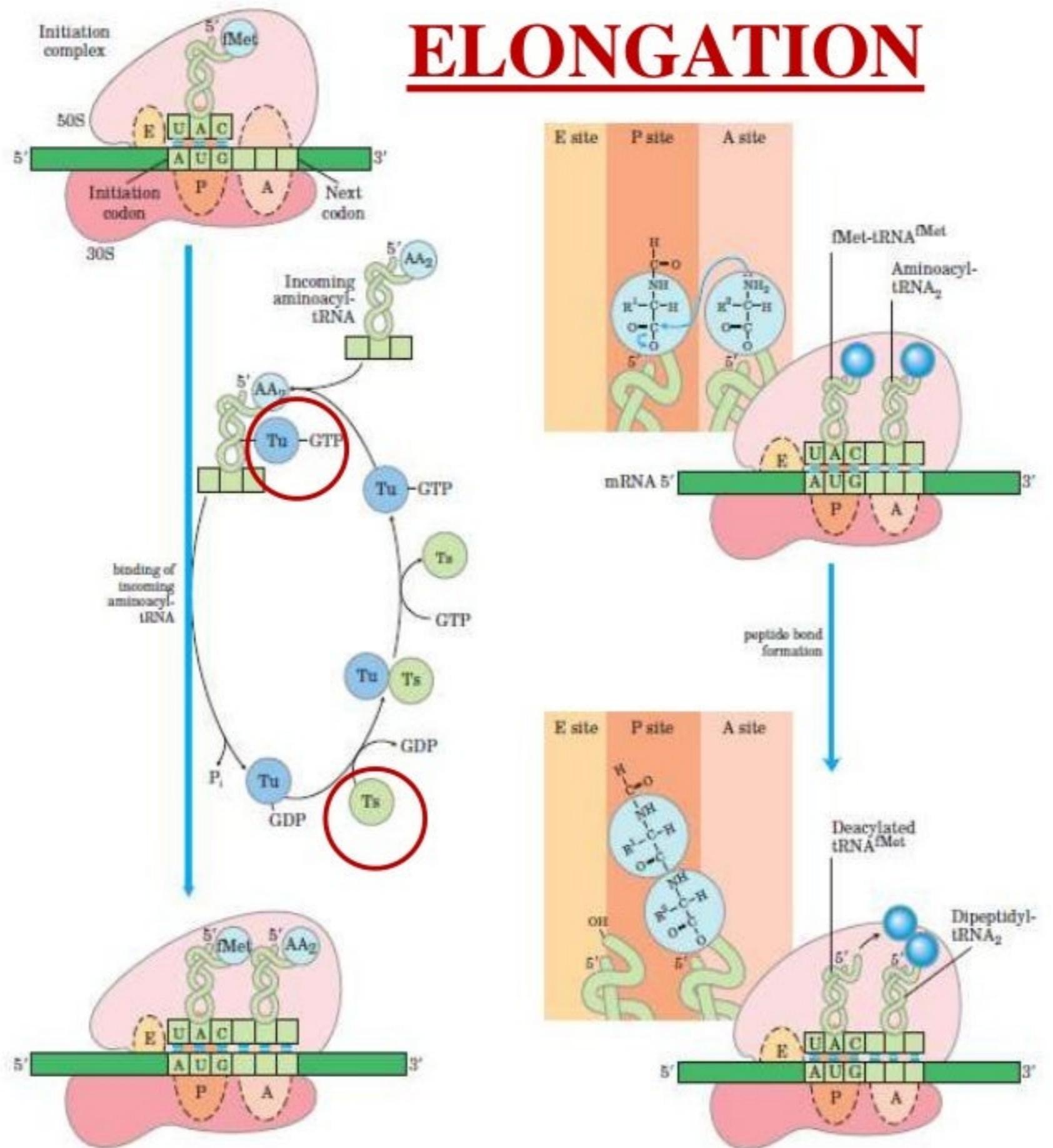
*The prefix "e" identifies these as eukaryotic factors.

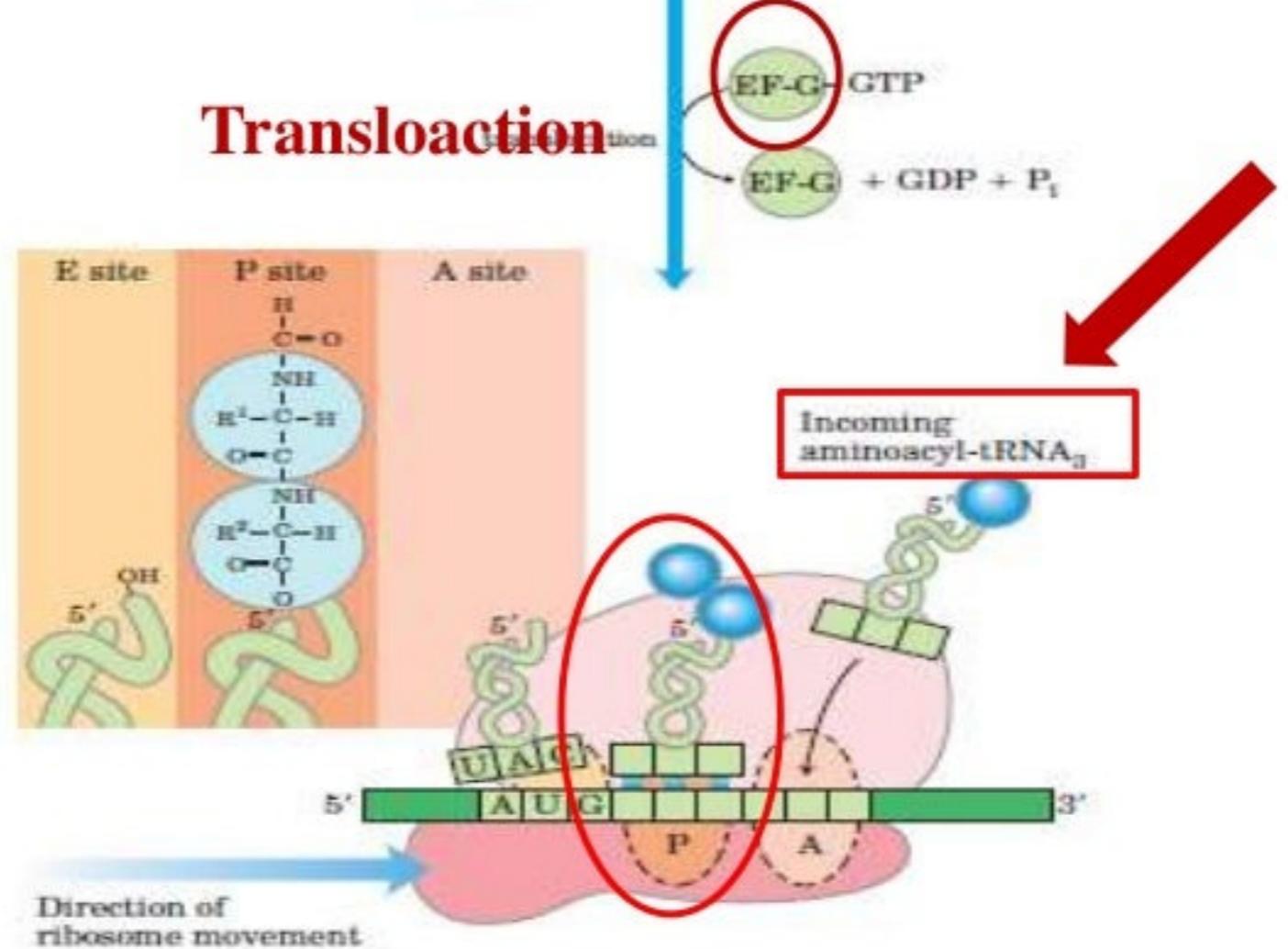
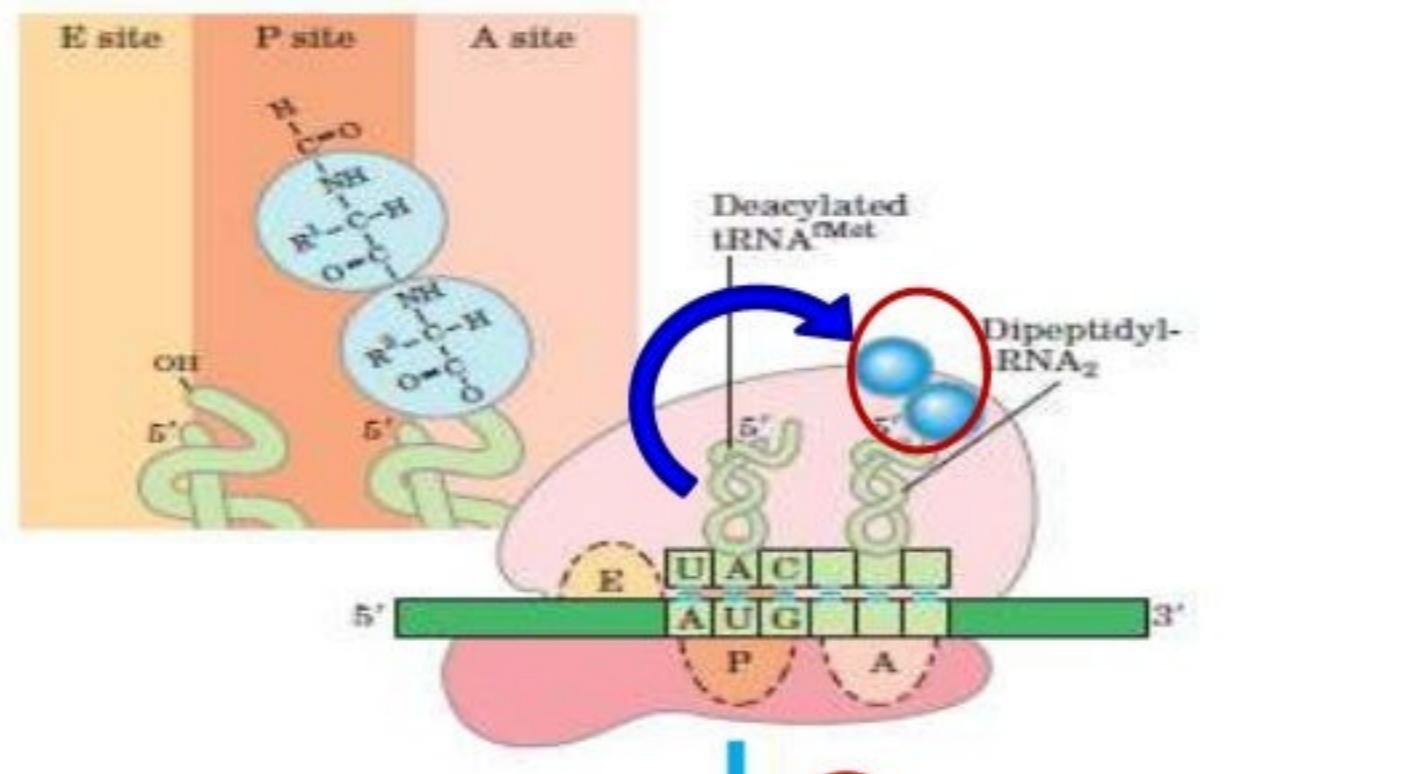
INITIATION



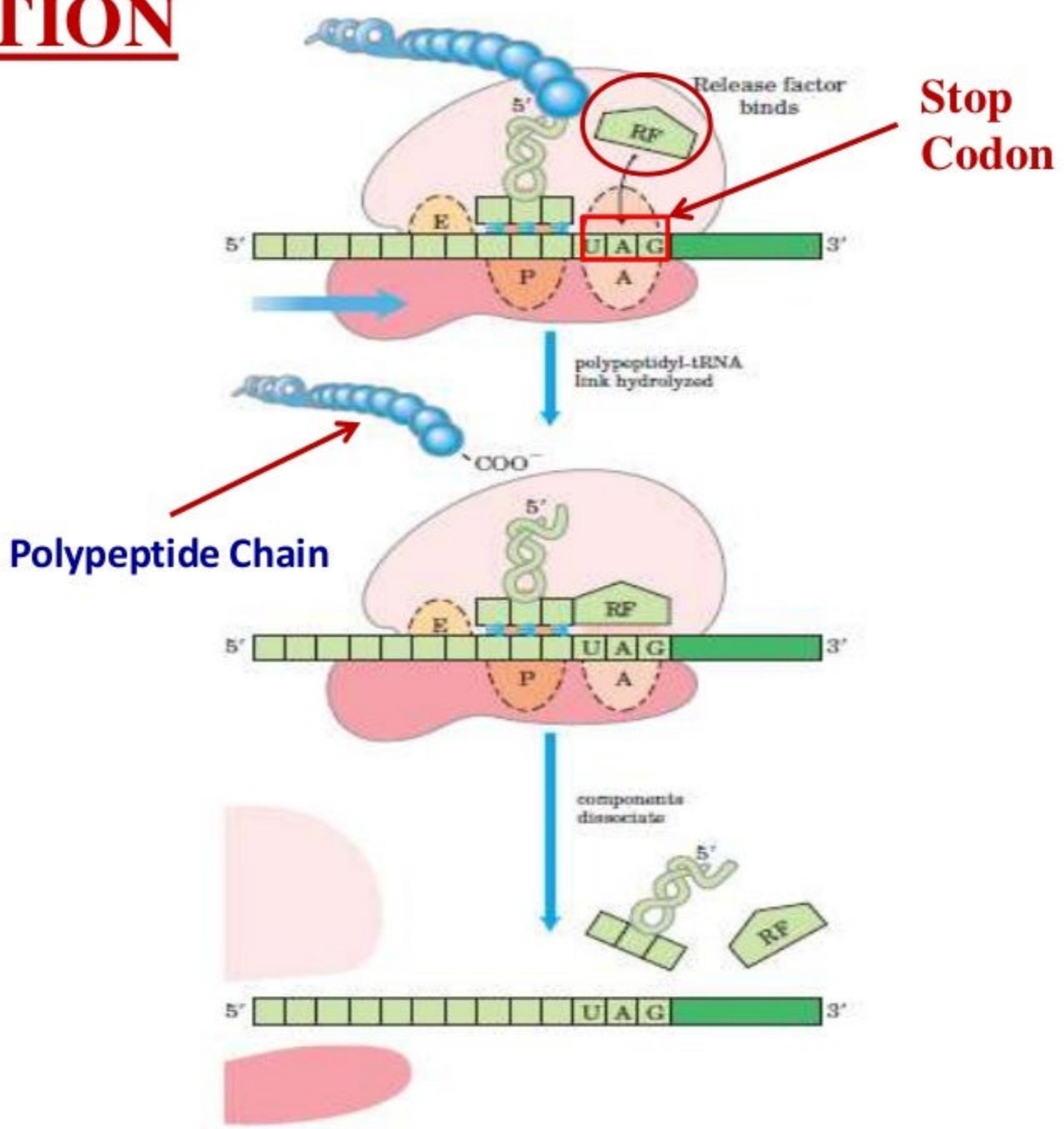
70S Initiation Complex

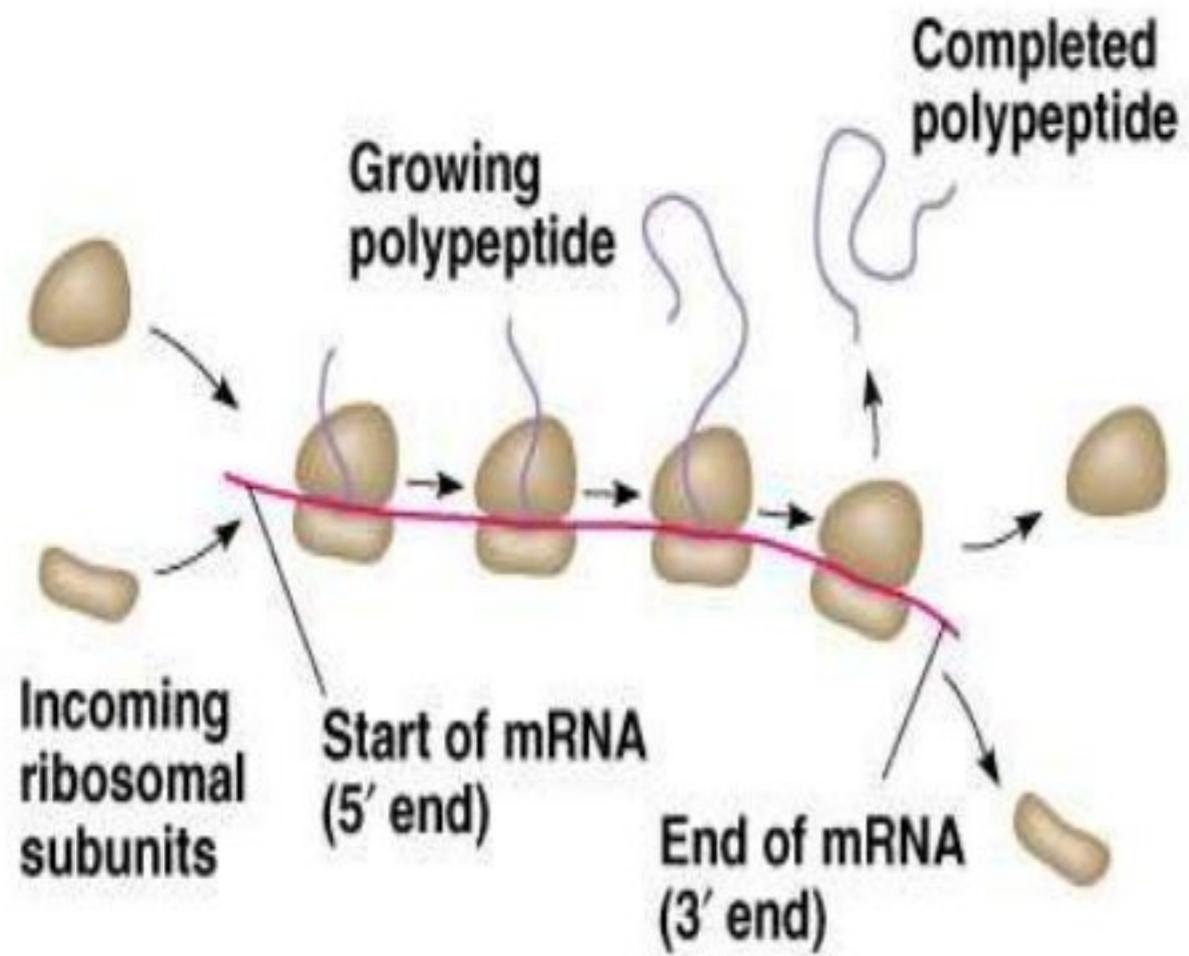
ELONGATION





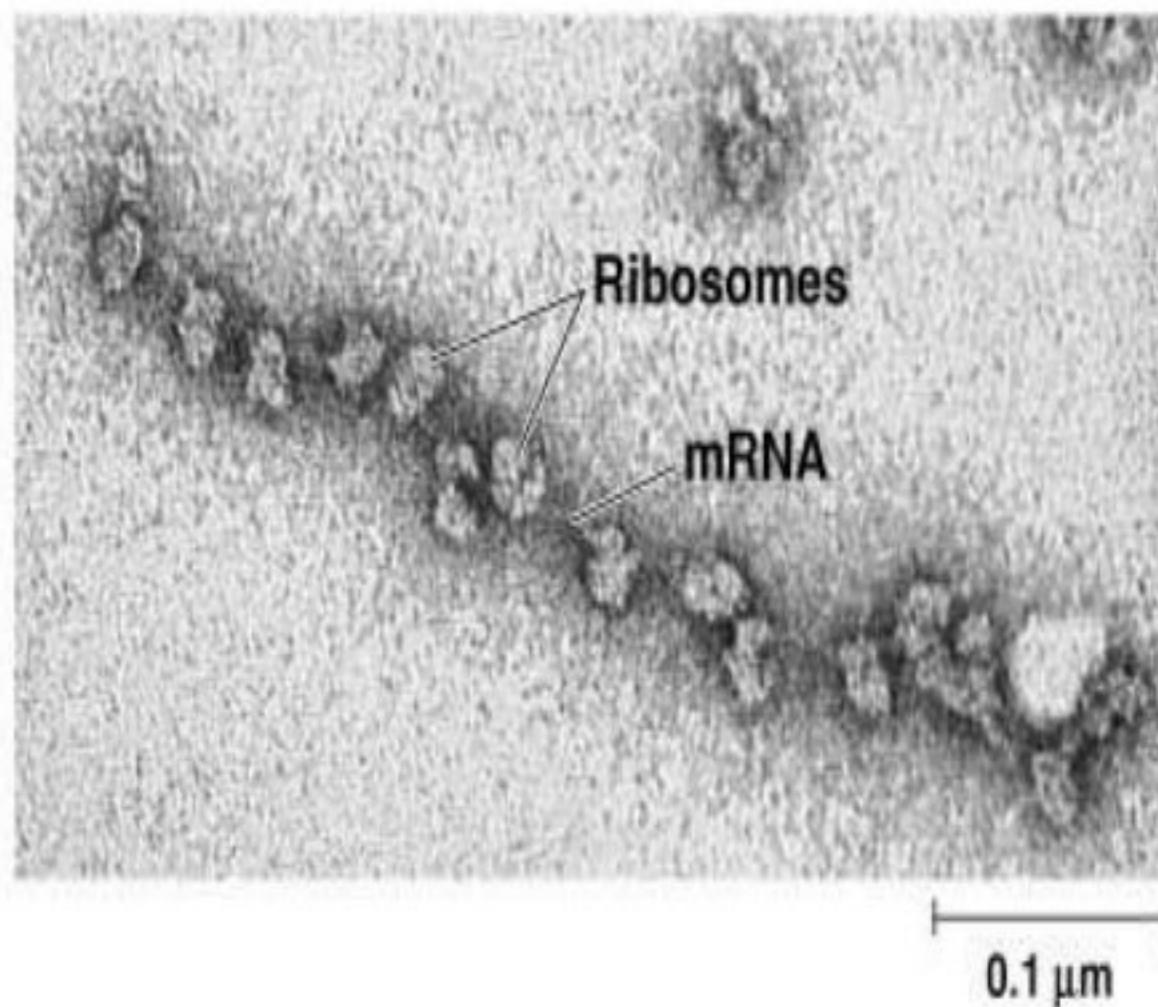
TERMINATION



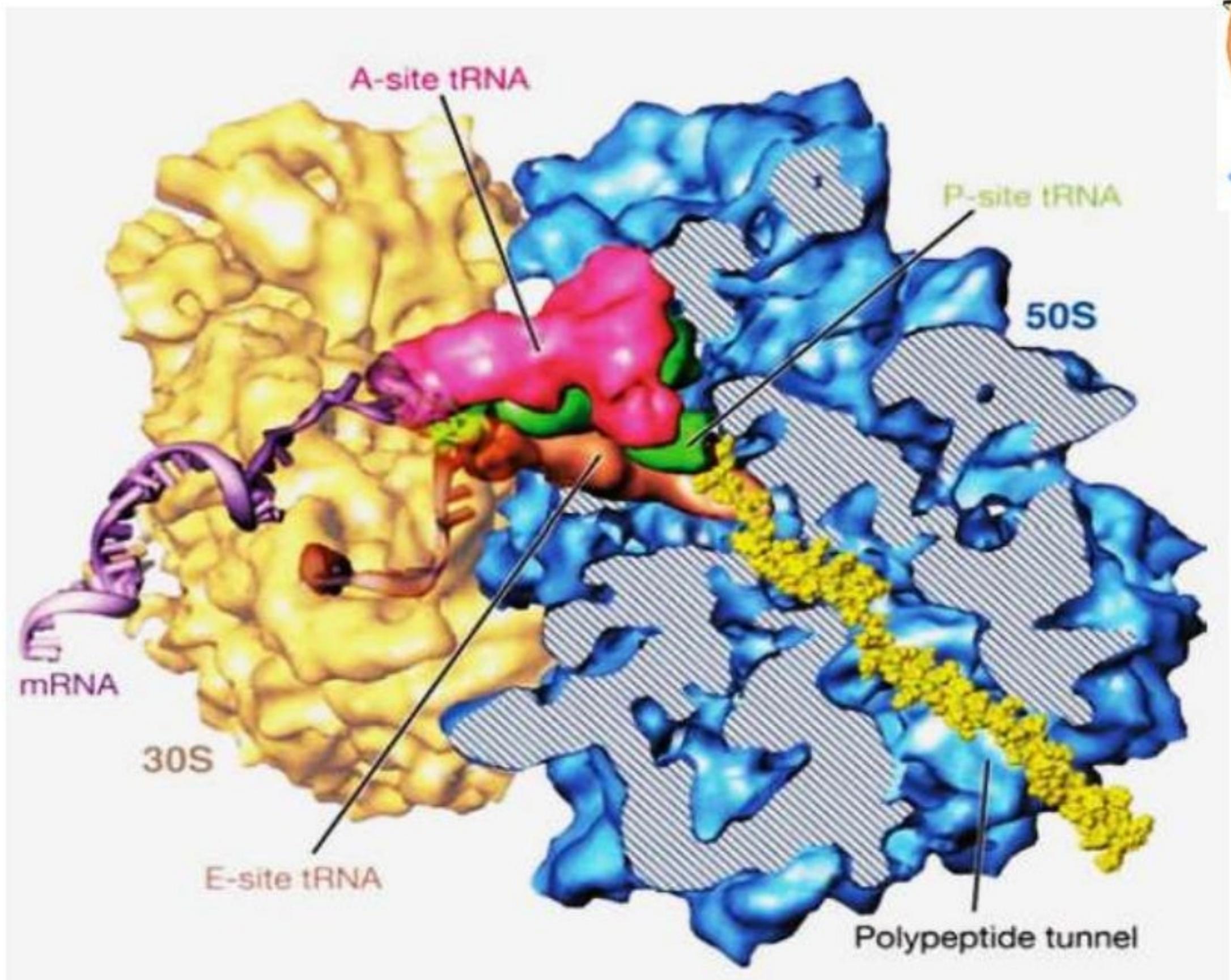


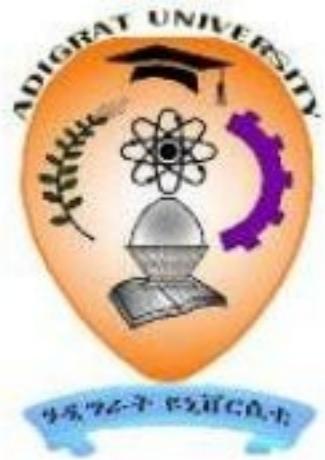
(a) An mRNA molecule is generally translated simultaneously by several ribosomes in clusters called polyribosomes.

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(b) This micrograph shows a large polyribosome in a prokaryotic cell (TEM).





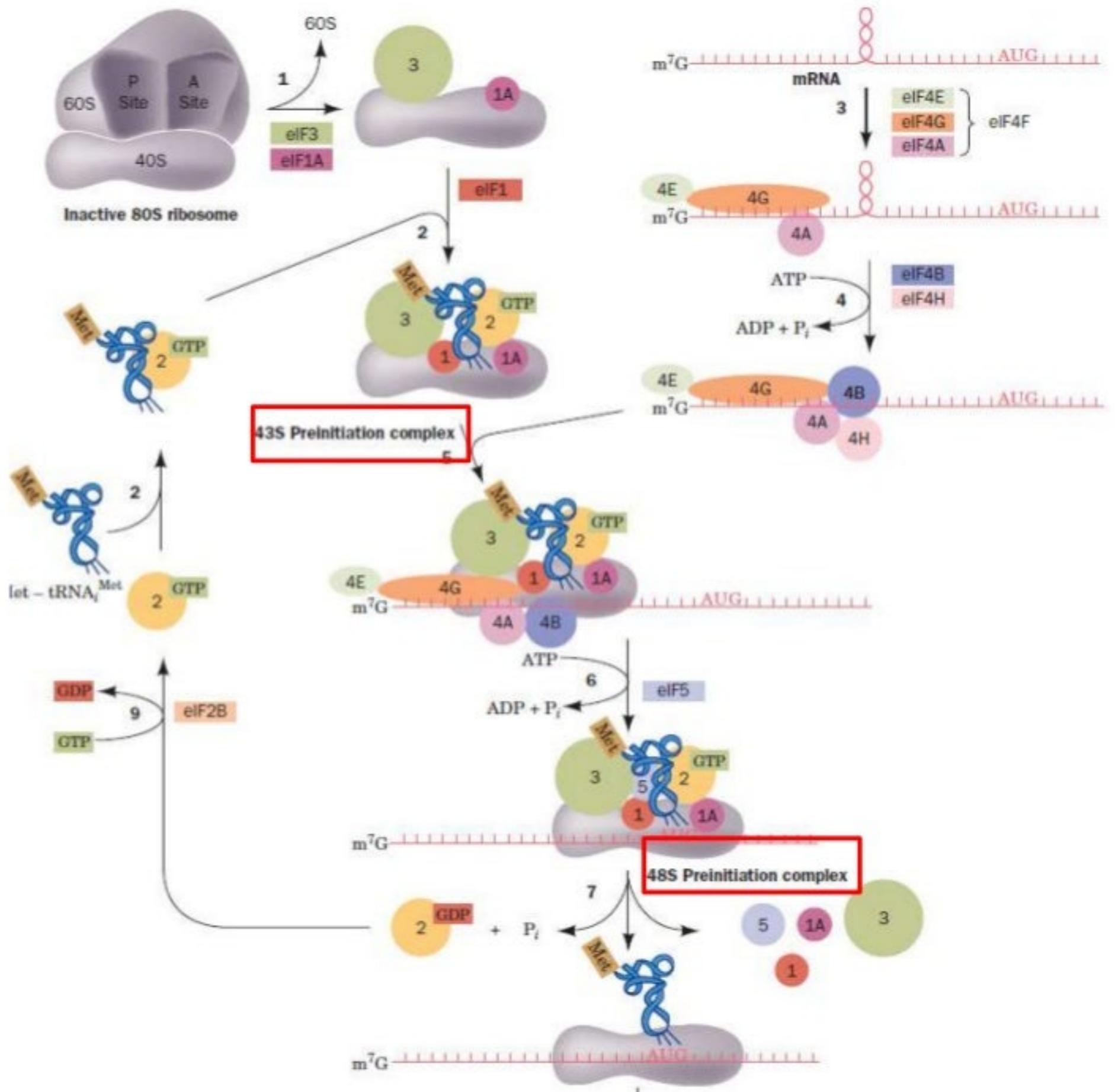
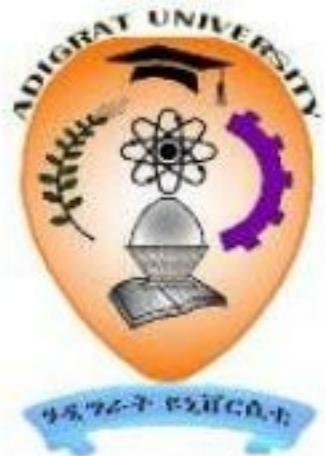
EUKARYOTIC PROTEIN SYNTHESIS

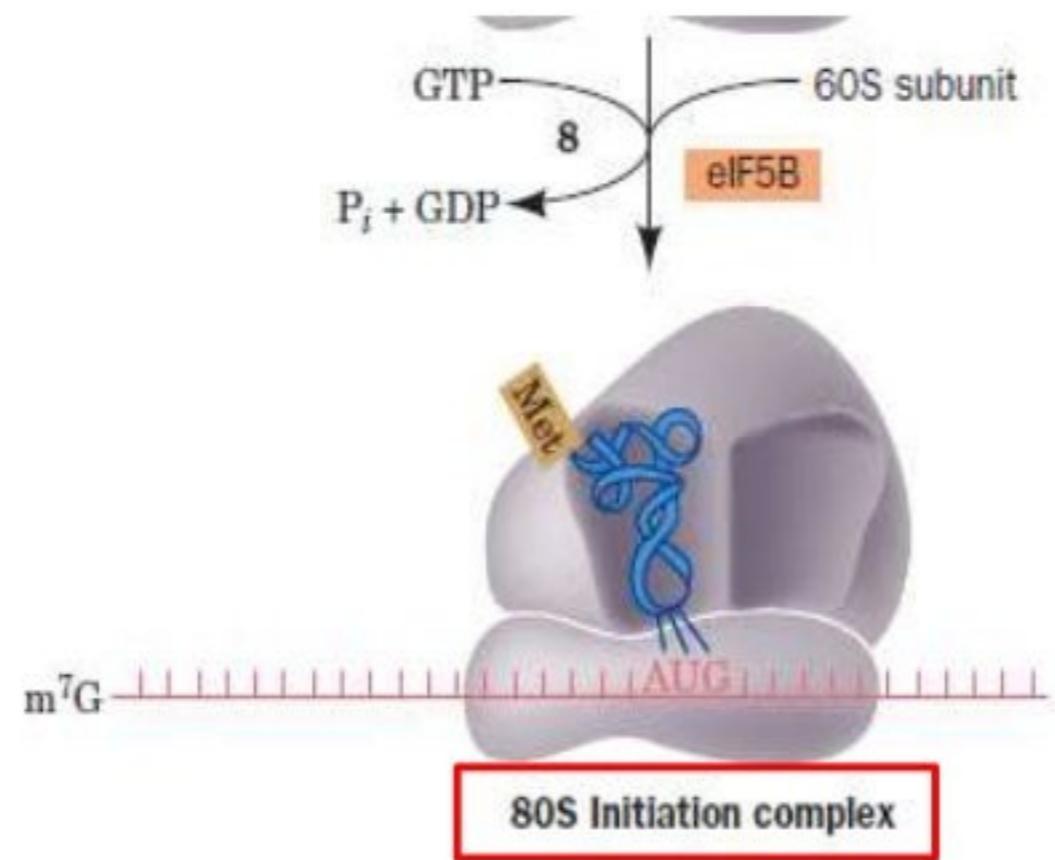


Eukaryotic Translation is similar to Prokaryotic process but much more complicated than that of Prokaryotes.

Like Prokaryotes it also occurs in **4 main Phases**:

- 1). Activation of Amino acids - Similar
- 2). Initiation – Similar but much complex
- 3). Elongation – Similar
- 4). Termination - Similar but simpler than Prokaryotes, only one **Releasing Factor (RF)** is required.

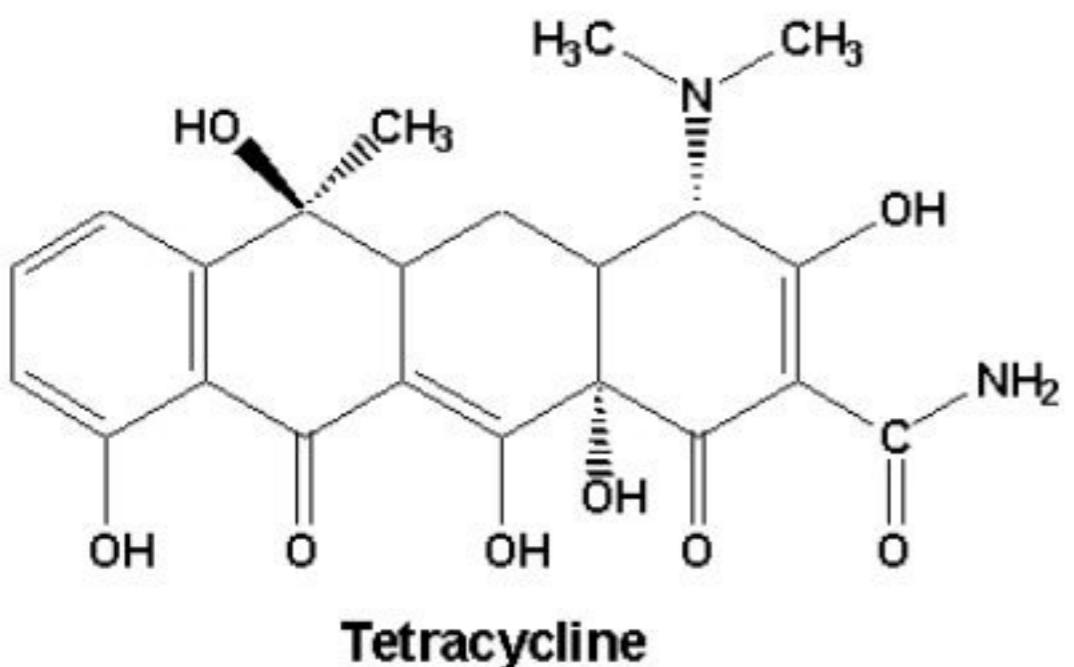




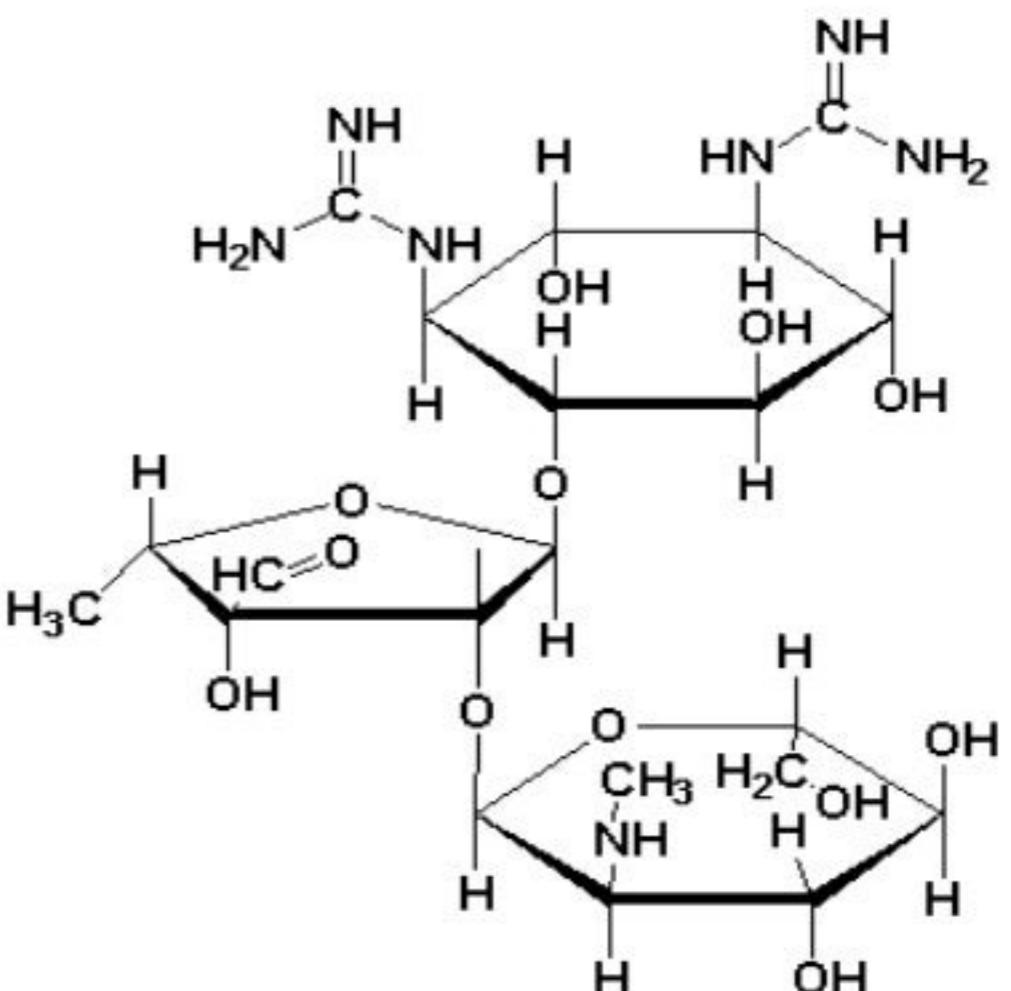
Elongation and Termination phases of Eukaryotic Protein synthesis is much similar Prokaryotes except that only one eRF (or) TF is sufficient to mediate the termination process.



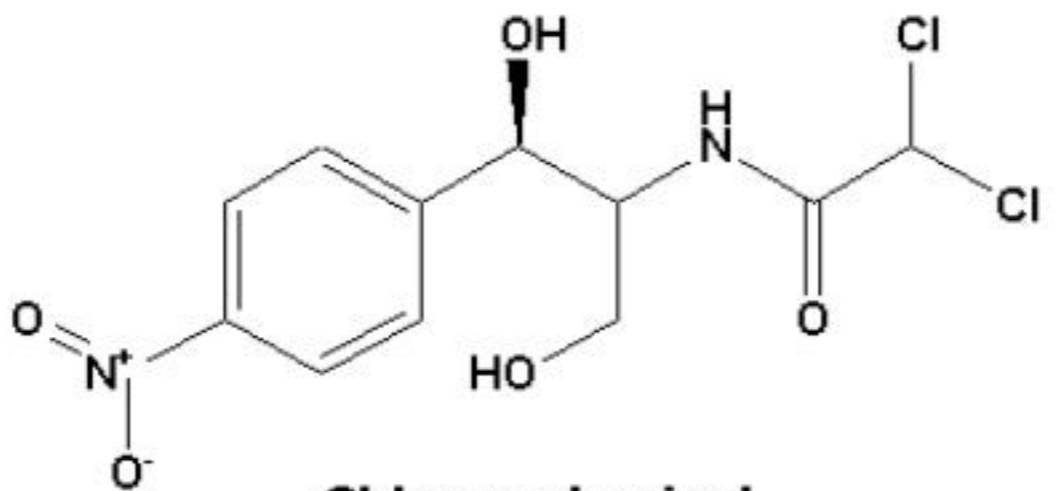
INHIBITORS



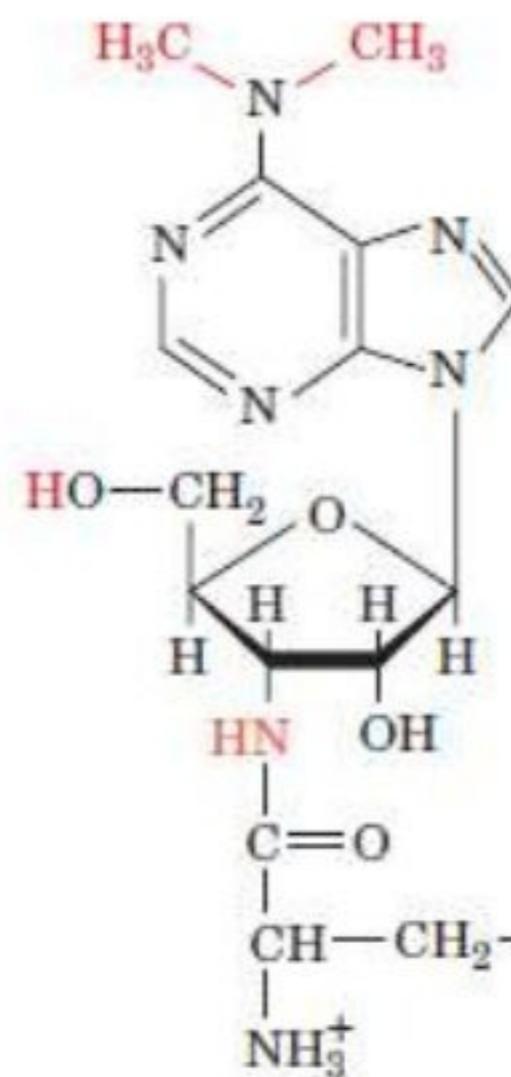
Tetracycline



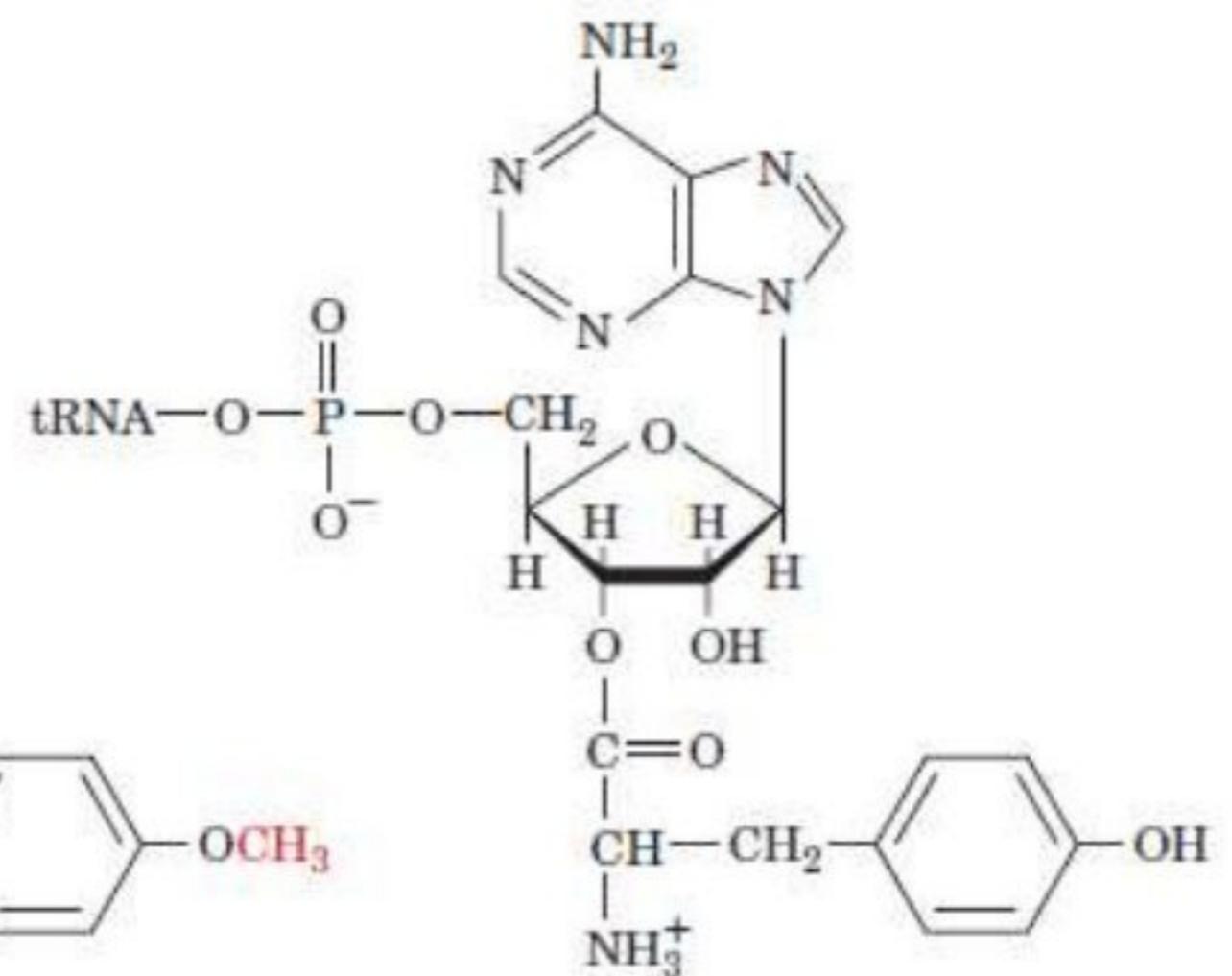
Streptomycin



Chloramphenicol



Puromycin



Tyrosyl-tRNA

Inhibitor	Action
Chloramphenicol	Inhibits peptidyl transferase on the prokaryotic large subunit
Cycloheximide	Inhibits peptidyl transferase on the eukaryotic large subunit
Erythromycin	Inhibits translocation by the prokaryotic large subunit
Fusidic acid	Inhibits elongation in prokaryotes by binding to EF-G · GDP in a way that prevents its dissociation from the large subunit
Paromomycin	Increases the ribosomal error rate

Puromycin

An aminoacyl-tRNA analog that causes premature chain termination in prokaryotes and eukaryotes

Streptomycin

Causes mRNA misreading and inhibits chain initiation in prokaryotes

Tetracycline

Inhibits the binding of aminoacyl-tRNAs to the prokaryotic small subunit

Diphtheria toxin

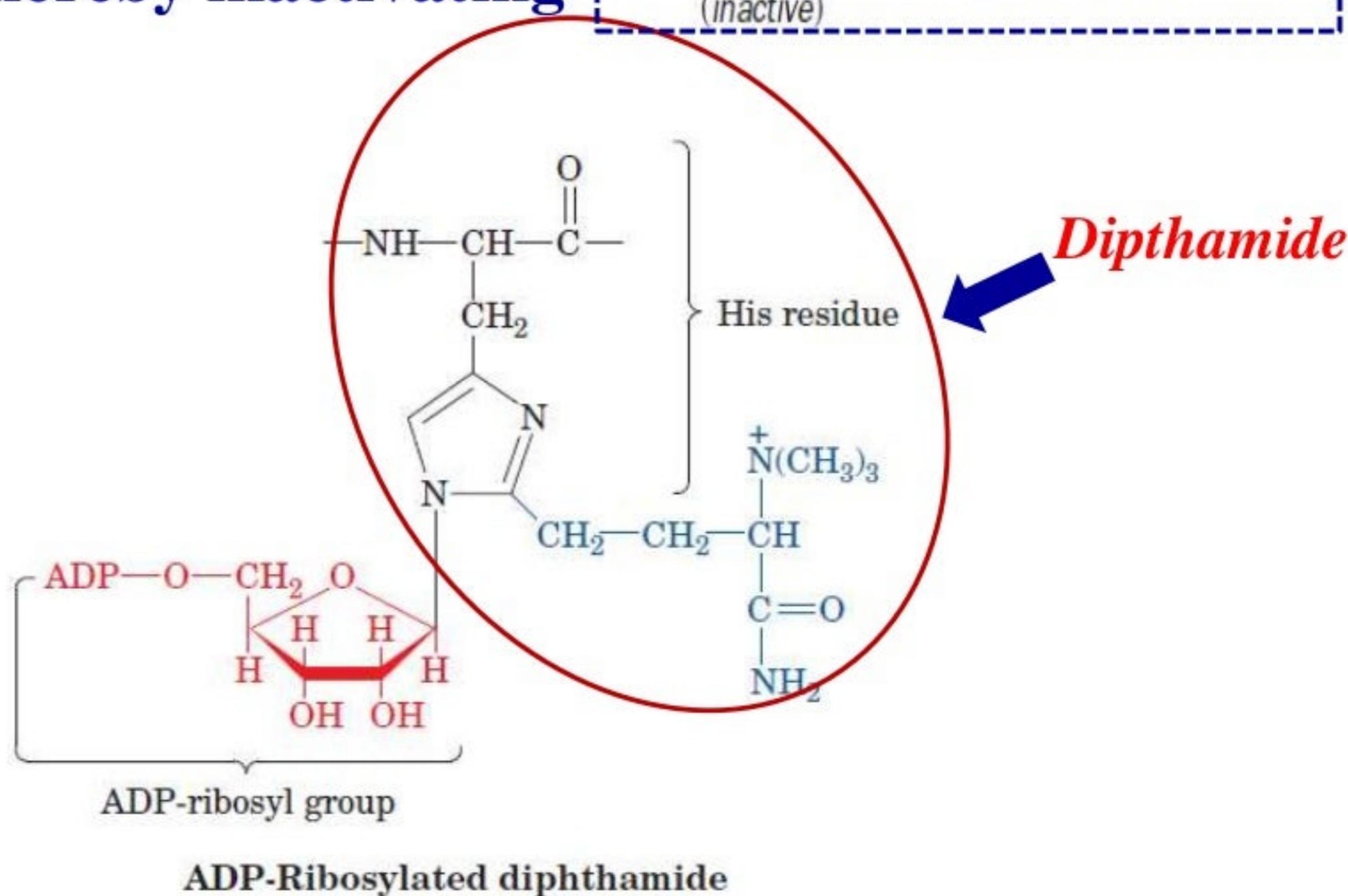
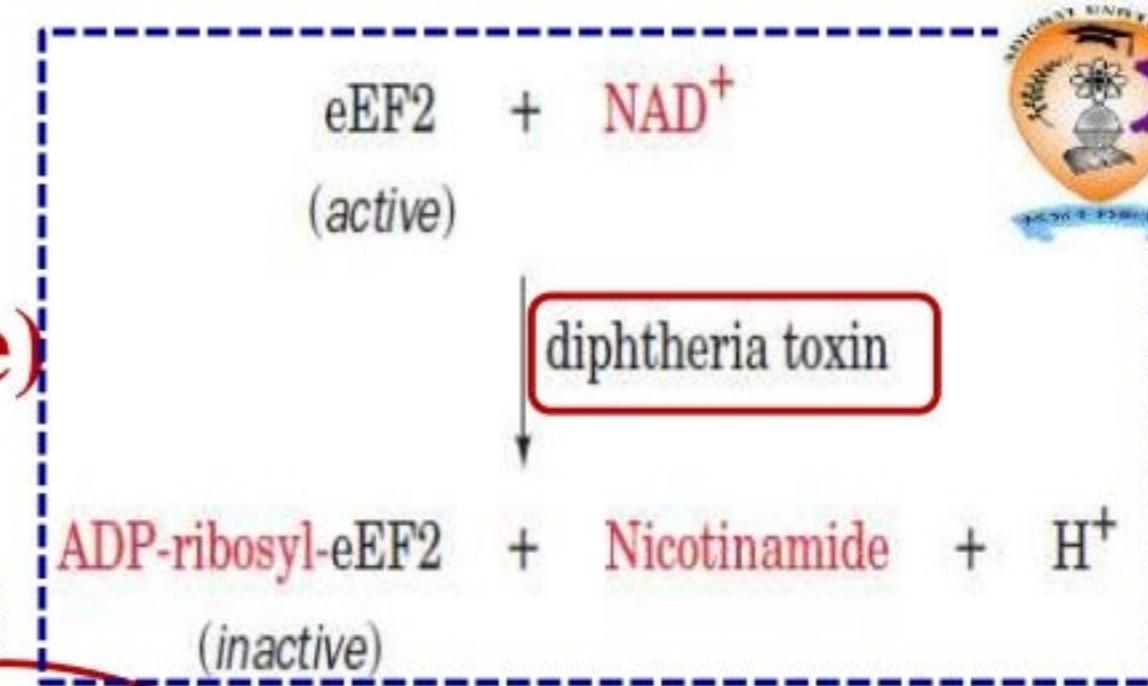
Catalytically inactivates eEF2 by ADP-ribosylation

Diphtheria Toxin



- **Diphtheria** is a disease resulting from bacterial infection by *Corynebacterium diphtheriae*.
- *Diphtheria toxin (DT)*, is a monomeric protein with **535 amino acid residues**, responsible for the disease's lethal effects.
- *Diphtheria toxin* specifically inactivates the eukaryotic elongation factor eEF2, thereby inhibiting eukaryotic protein synthesis.

Diphtheria toxin catalyzes the ADP-ribosylation of a *diphthamide* (a modified histidine) residue of eukaryotic elongation factor eEF2, thereby inactivating it.



Heme & Globin Synthesis Regulation

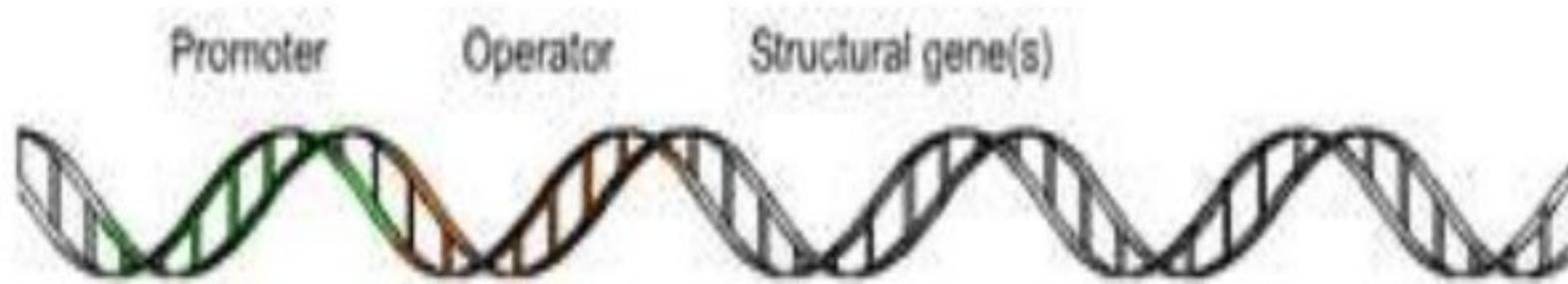


- In Eukaryotes the availability of **Heme** controls **Globin synthesis**.
- High levels of ***eIF2*** and **GTP** is essential for **Globin translation (or)synthesis**.
- **eIF2 kinase** named **heme-regulated inhibitor (HRI)** also called **heme-controlled repressor (HCR)** regulates the **Globin synthesis** based on presence and absence of **Heme**.

REGULATION OF GENE EXPRESSION IN PROKARYOTES

OPERON

- In genetics, an **operon** is a functioning unit of genomic DNA containing a **cluster of genes** under the control of a single promoter.
- Operons occur primarily in **prokaryotes**.
- An **operon** is made up of **several structural genes** arranged under a **common promoter** and regulated by a **common operator**.
- It is defined as a set of adjacent structural genes, plus the adjacent regulatory signals that affect transcription of the structural genes.



An operon is made up of **4 basic DNA components**:

Promoter (*p*) – a nucleotide sequence that enables a gene to be transcribed. The promoter is recognized by RNA polymerase, which then initiates transcription.

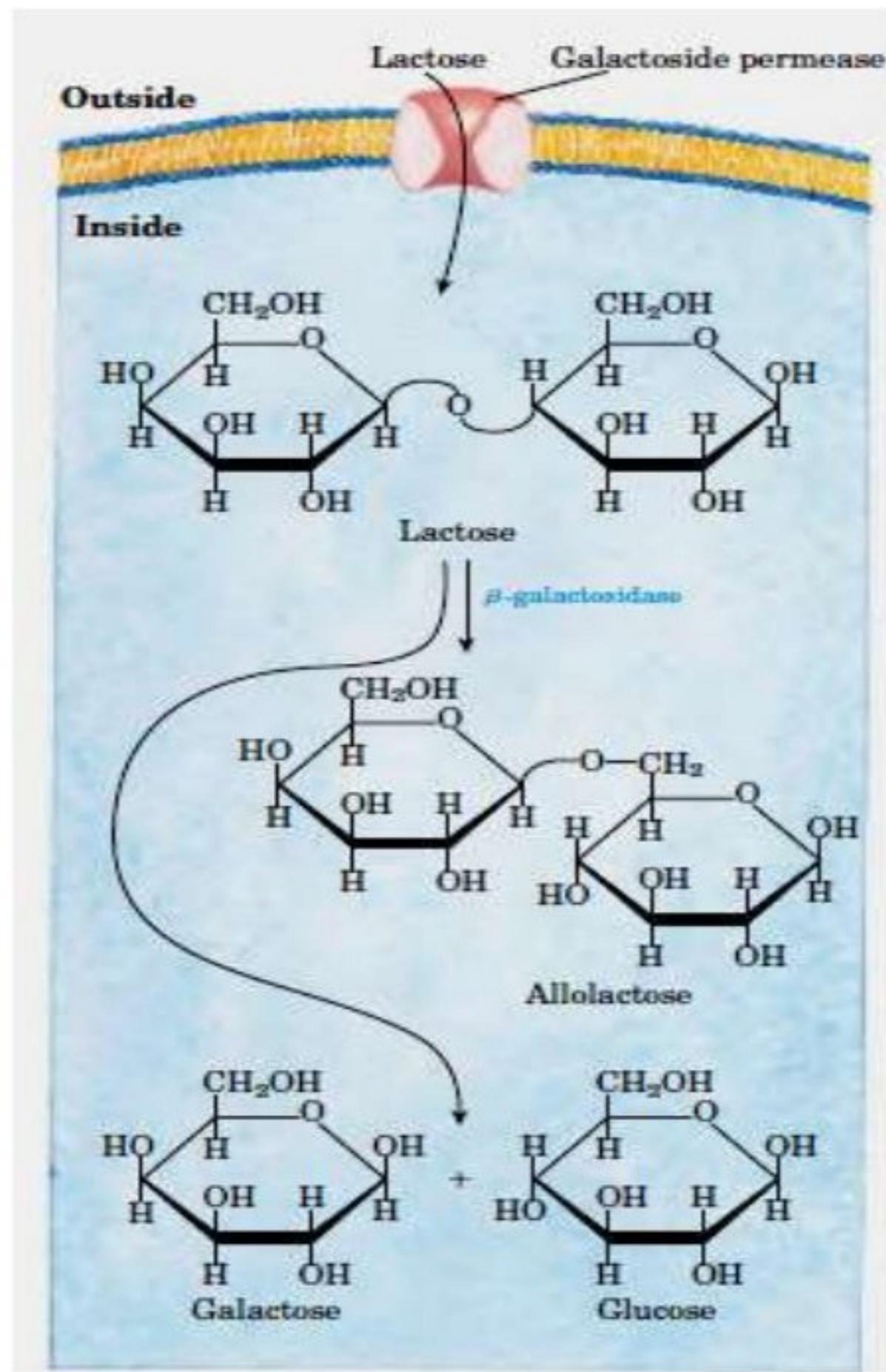
Regulator (*i*) – These genes control the operator gene in cooperation with certain compounds called **inducers and co-repressors** present in the cytoplasm.

Operator (*o*) – a segment of DNA that a **repressor** binds to. It controls the production of mRNA from structural genes.

Structural genes – the genes that are **co-regulated** by the operon.

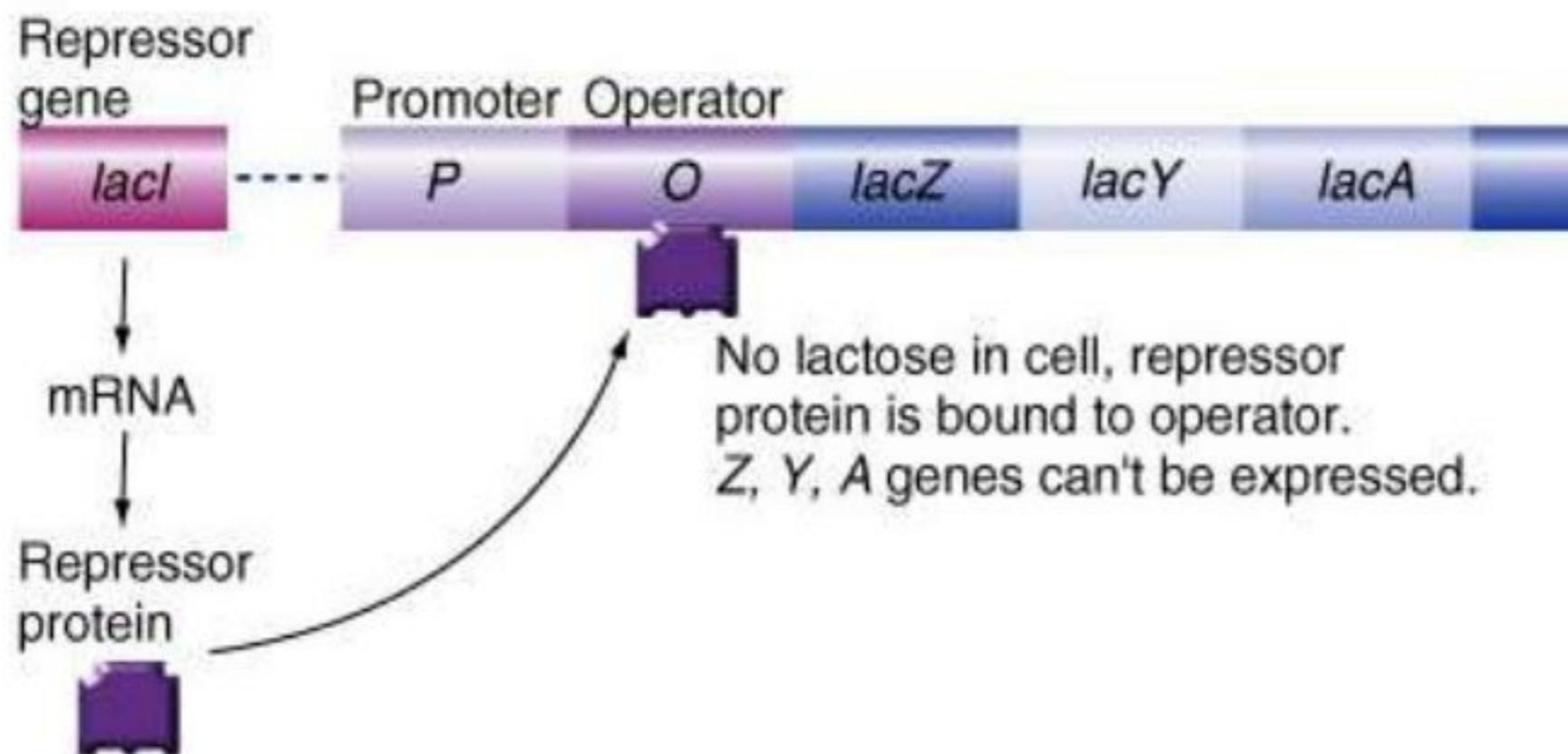
lac operon

- The *lac operon* contains genes for the use of lactose as an energy source.
- Regulatory regions of the operon include the CAP binding site, promoter, and the operator.
- The coding region contains genes for 3 enzymes:
 - β -galactosidase, permease, and transacetylase.



lac OPERON is an inducible Operon

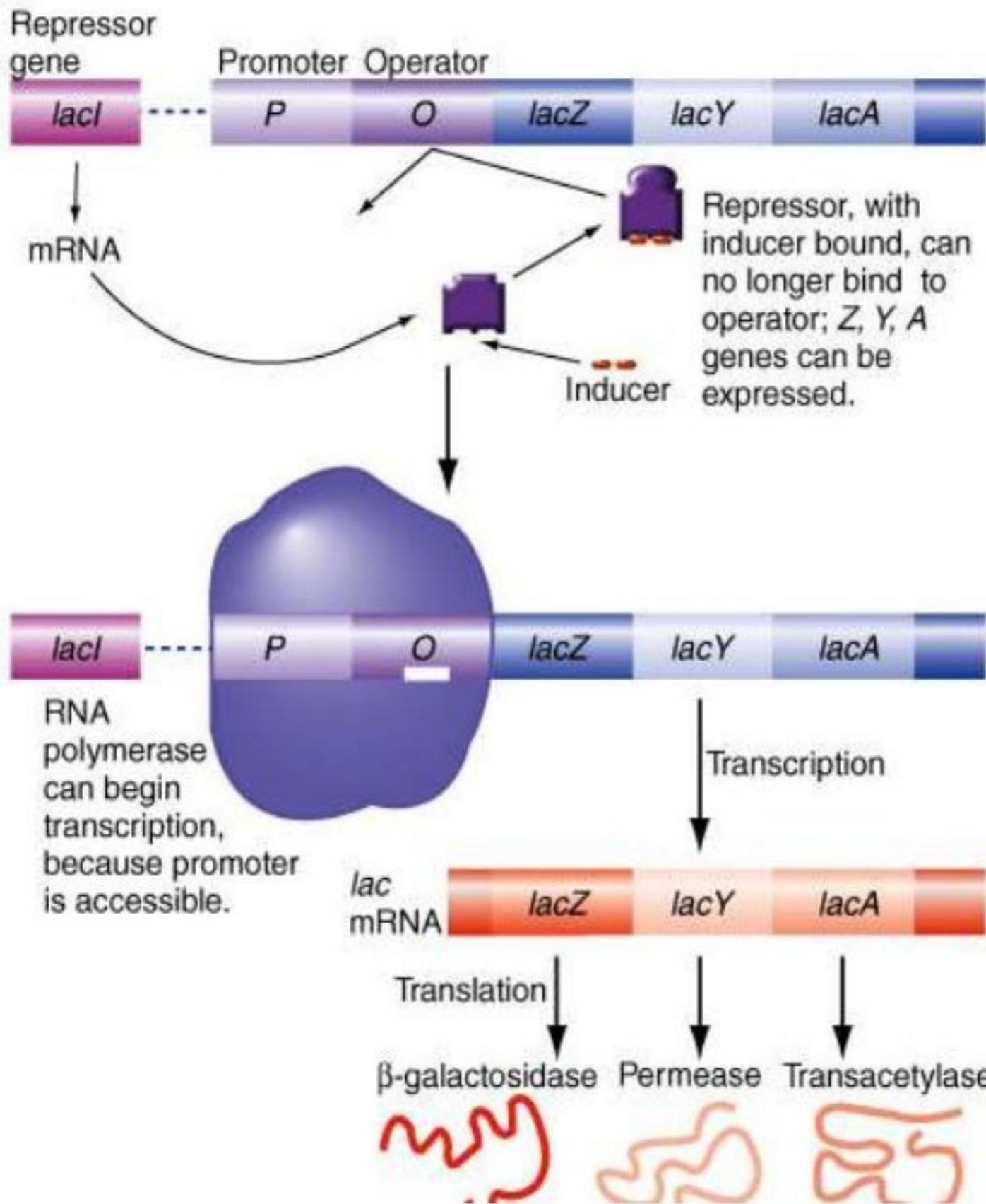
(b) Repression



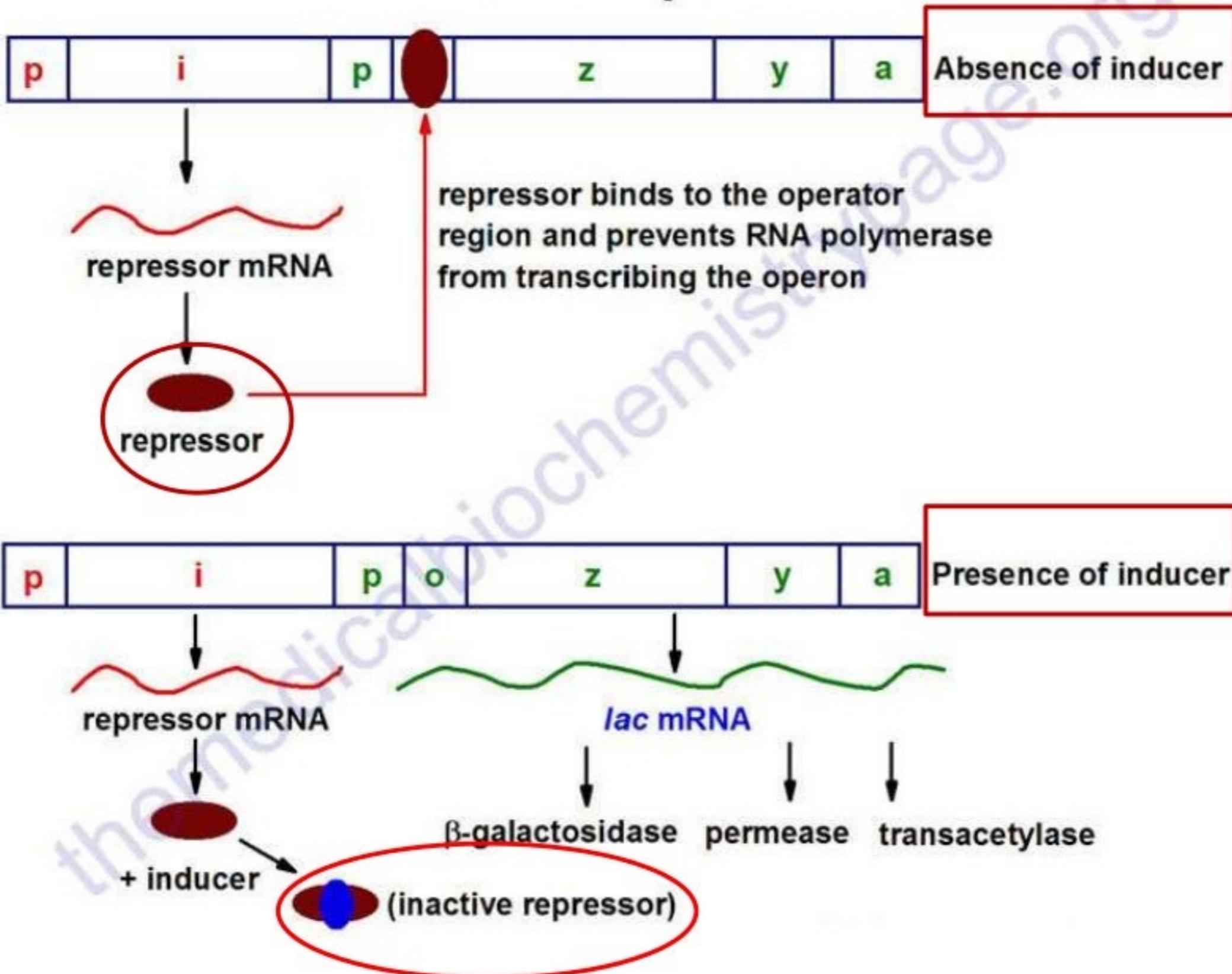
- **Repression**
 - In **absence of lactose**, repressor binds to operator which prevents transcription
 - Negative regulatory element.

Induction

- Lactose present
 - **Allolactose binds to repressor.**
 - **Repressor changes shape and can not bind to operator.**
 - **RNA polymerase binds to promoter and initiates transcription of polycistronic mRNA**



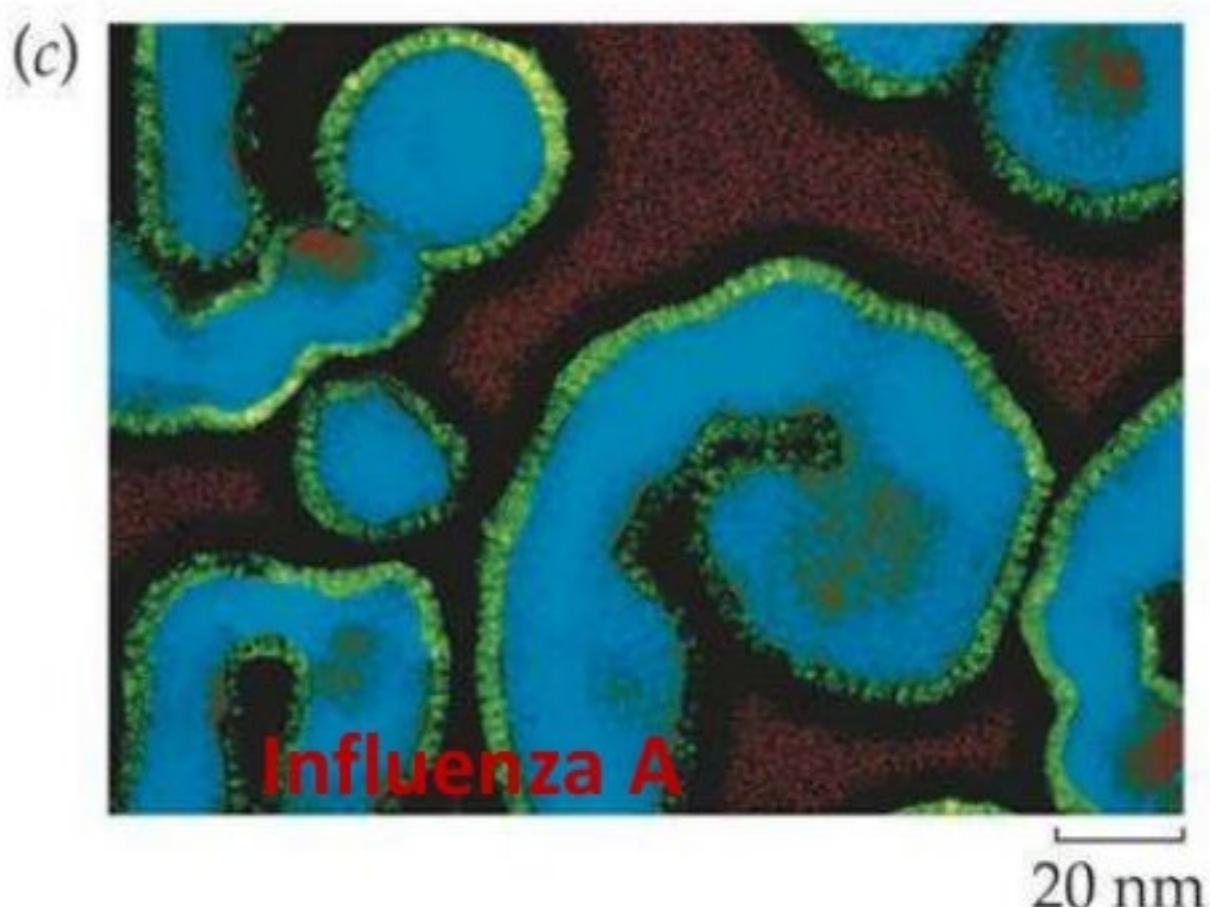
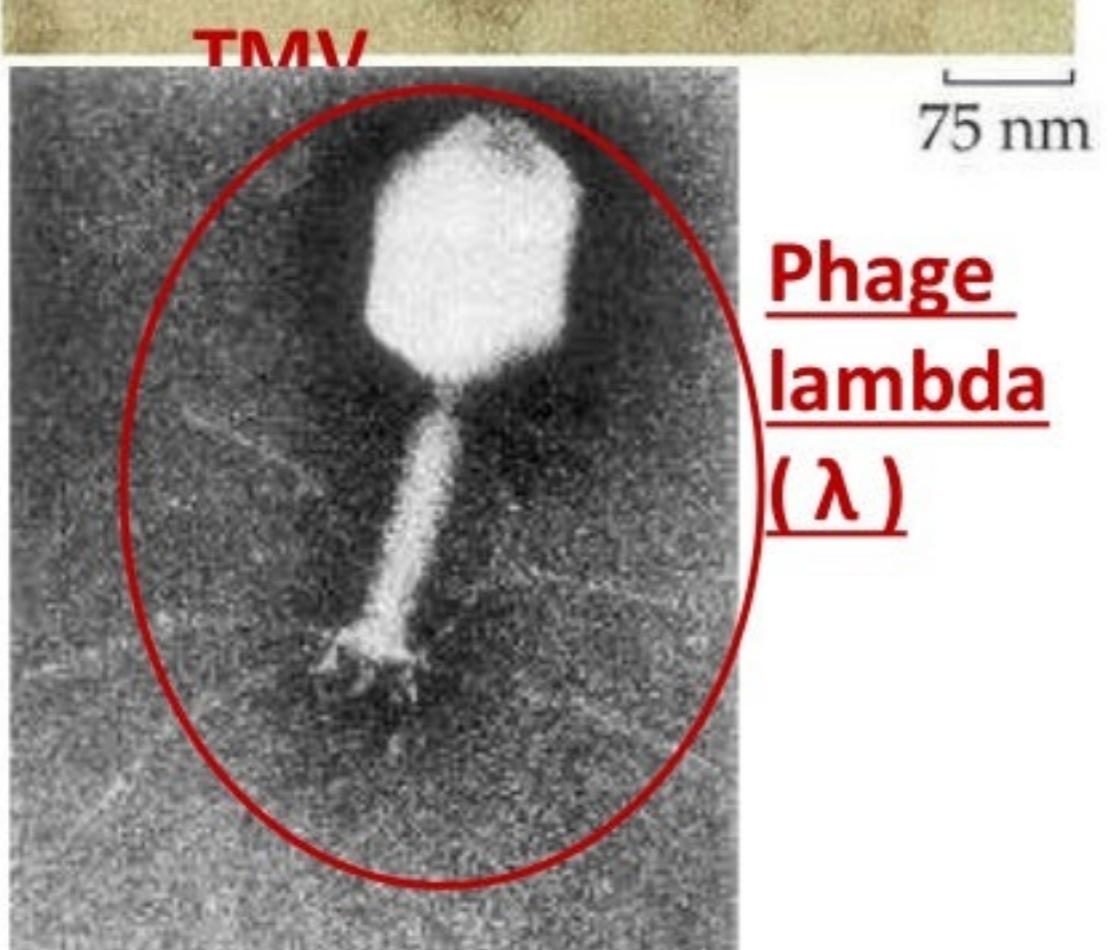
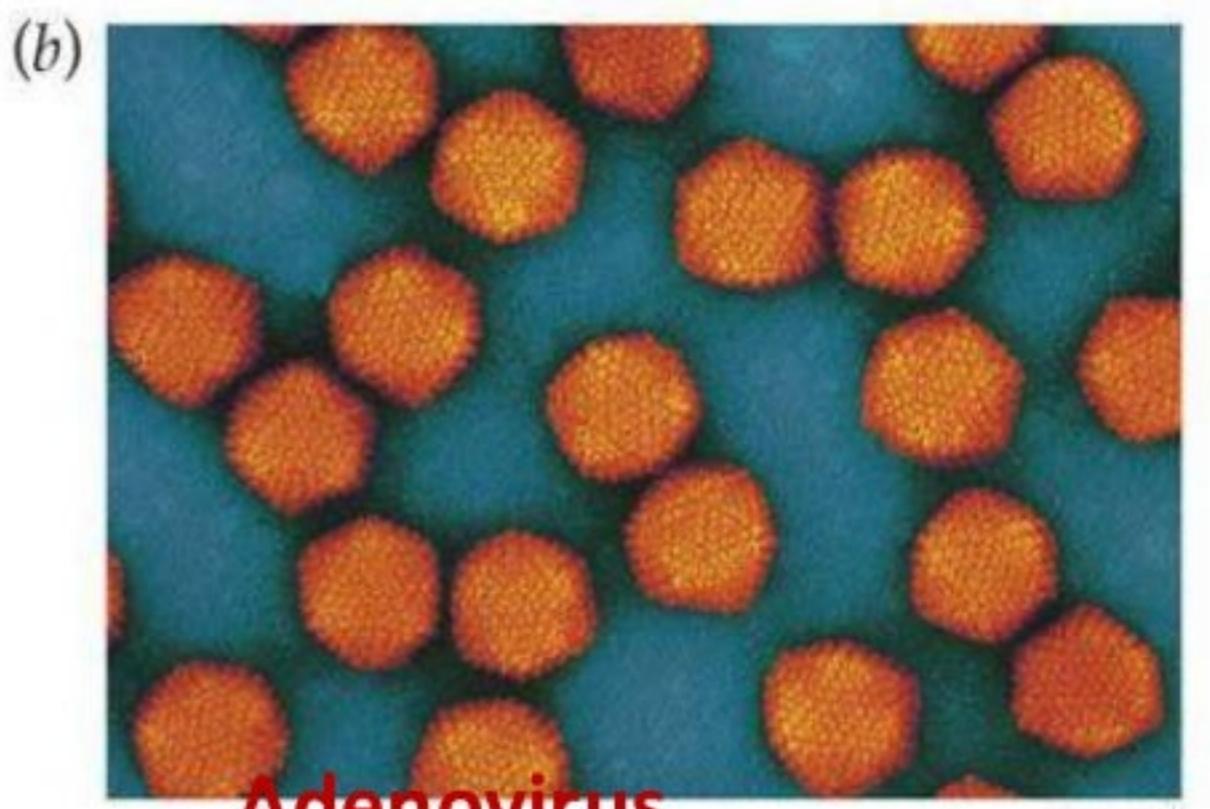
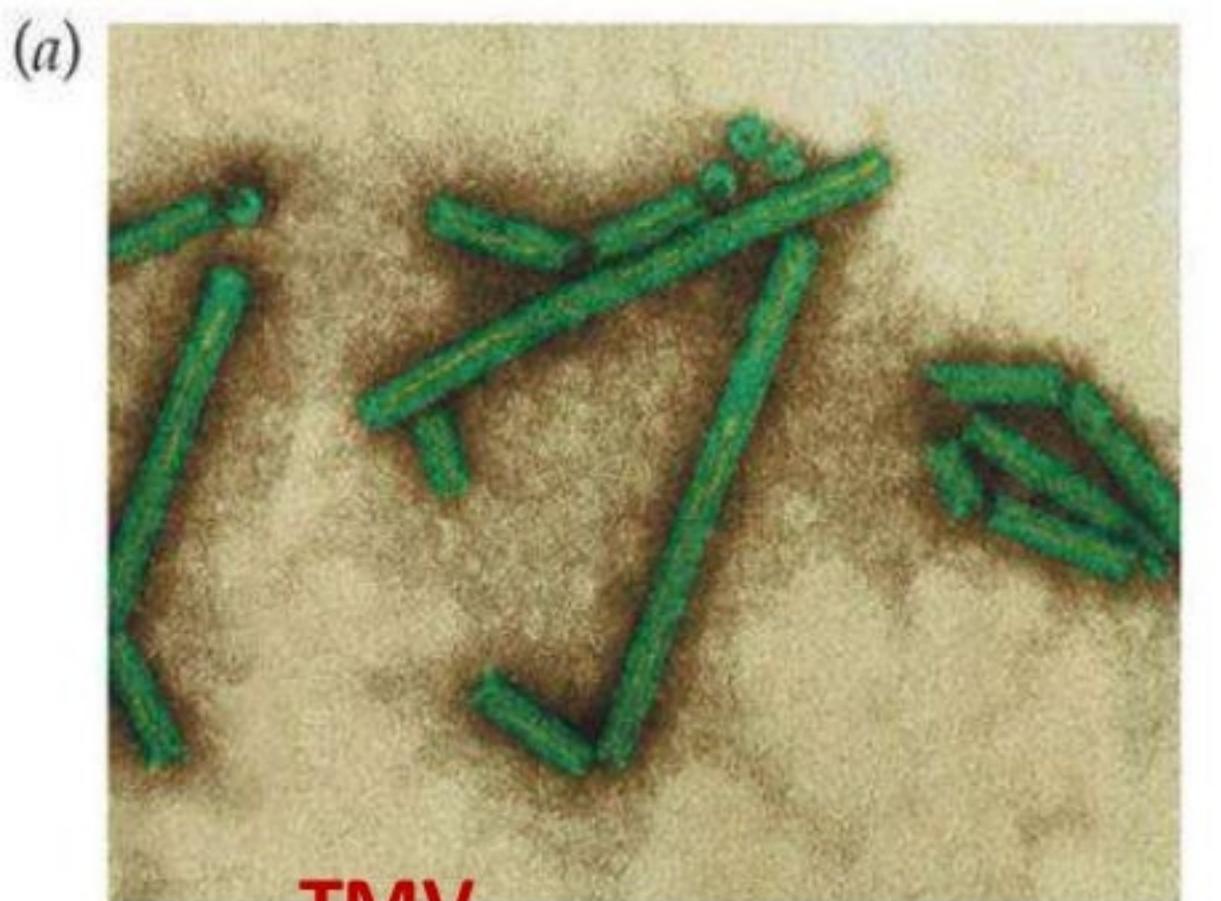
The *lac* Operon



Genetic switching in Bacteriophage

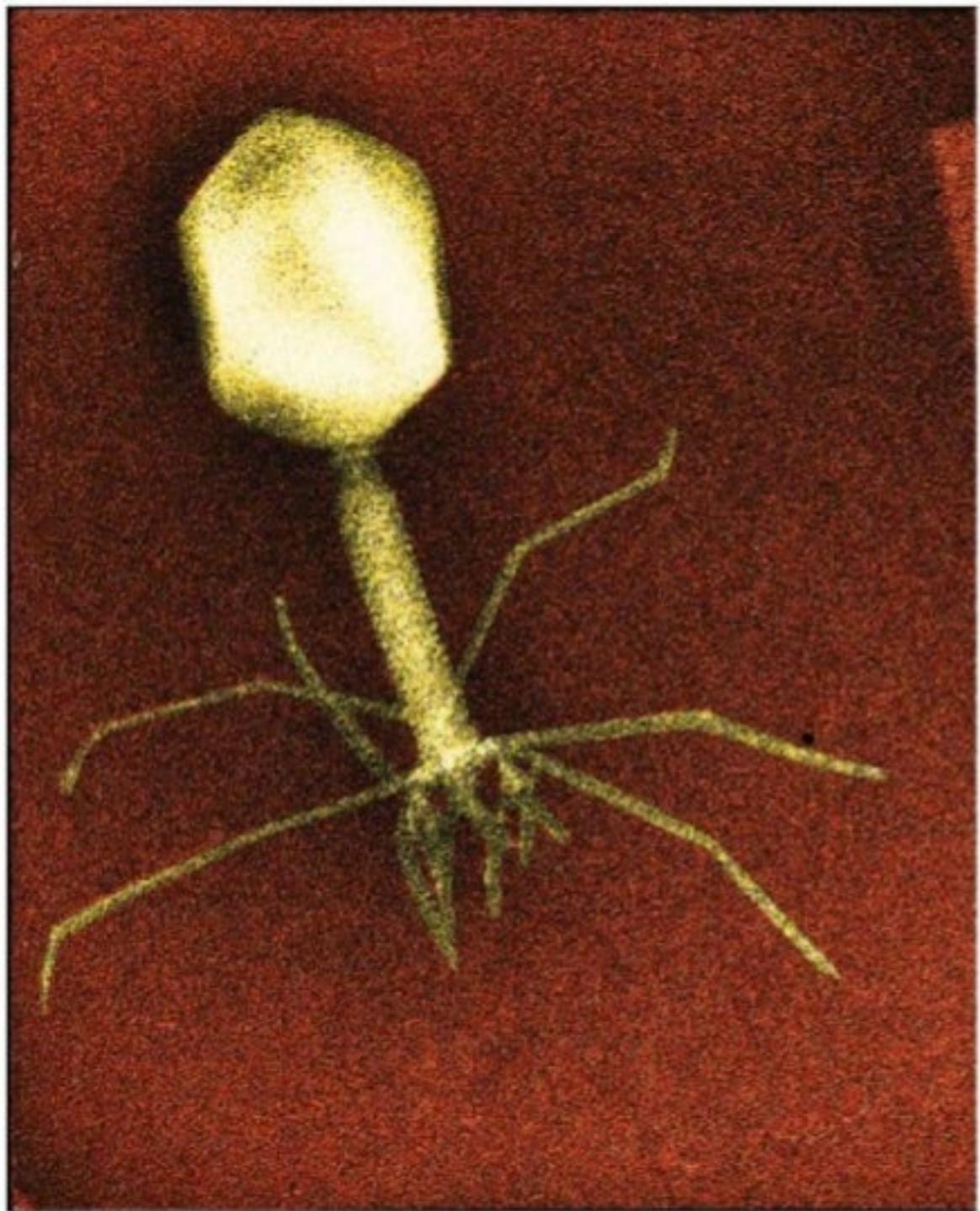
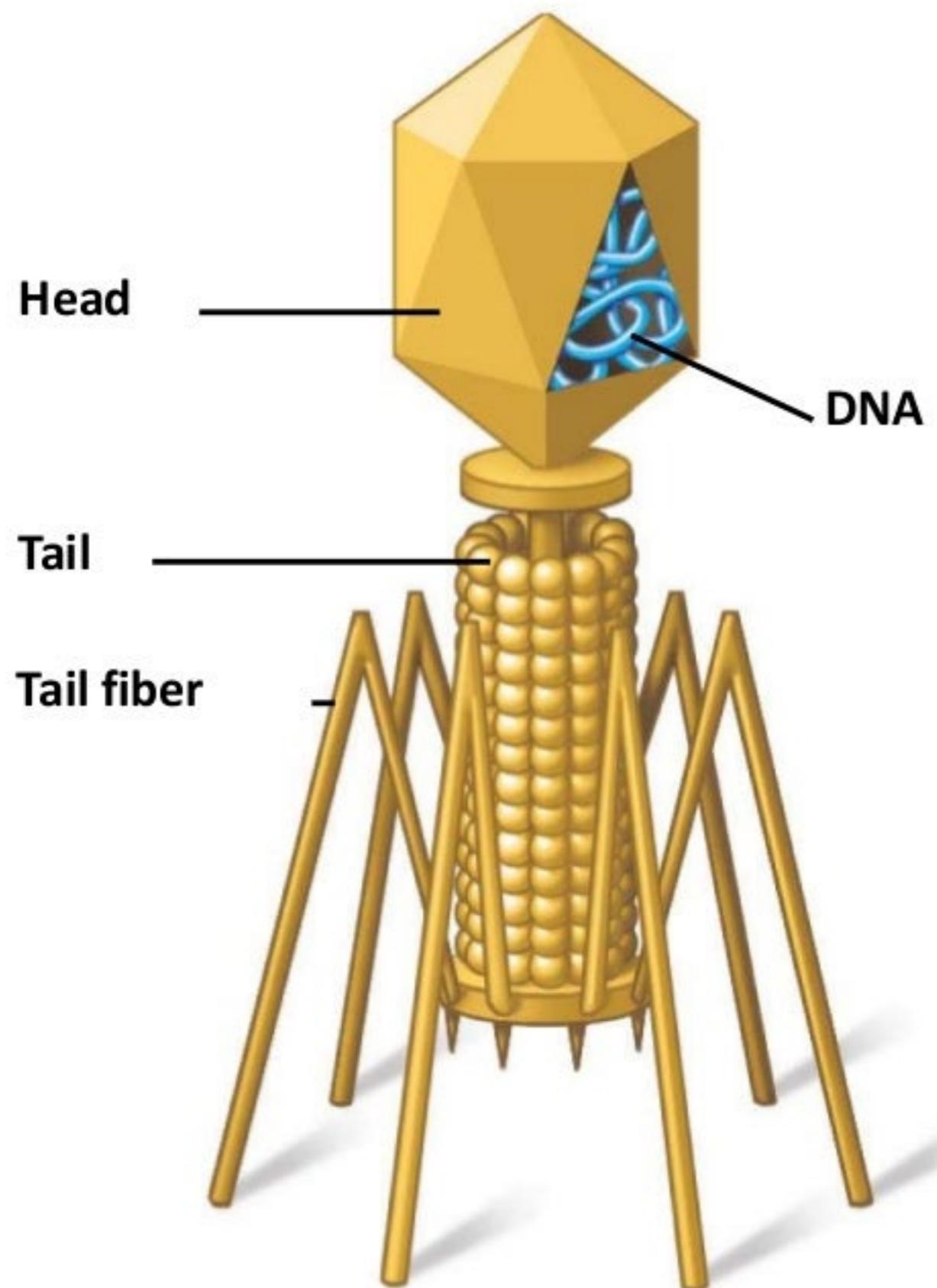
Viruses

- Viruses are a cellular.
- Composed of a nucleic acid and a few proteins
 - DNA or RNA
 - Coat proteins
 - Viral enzymes (e.g. reverse transcriptase)
- Do not carry out metabolism
 - obligate intracellular parasites
- Reproduce only in living cells
 - uses host cell's transcription/translation machinery
 - often integrate into host cell's chromosome(s)
- Progeny released from host cell
 - often destroy the host cell in the process

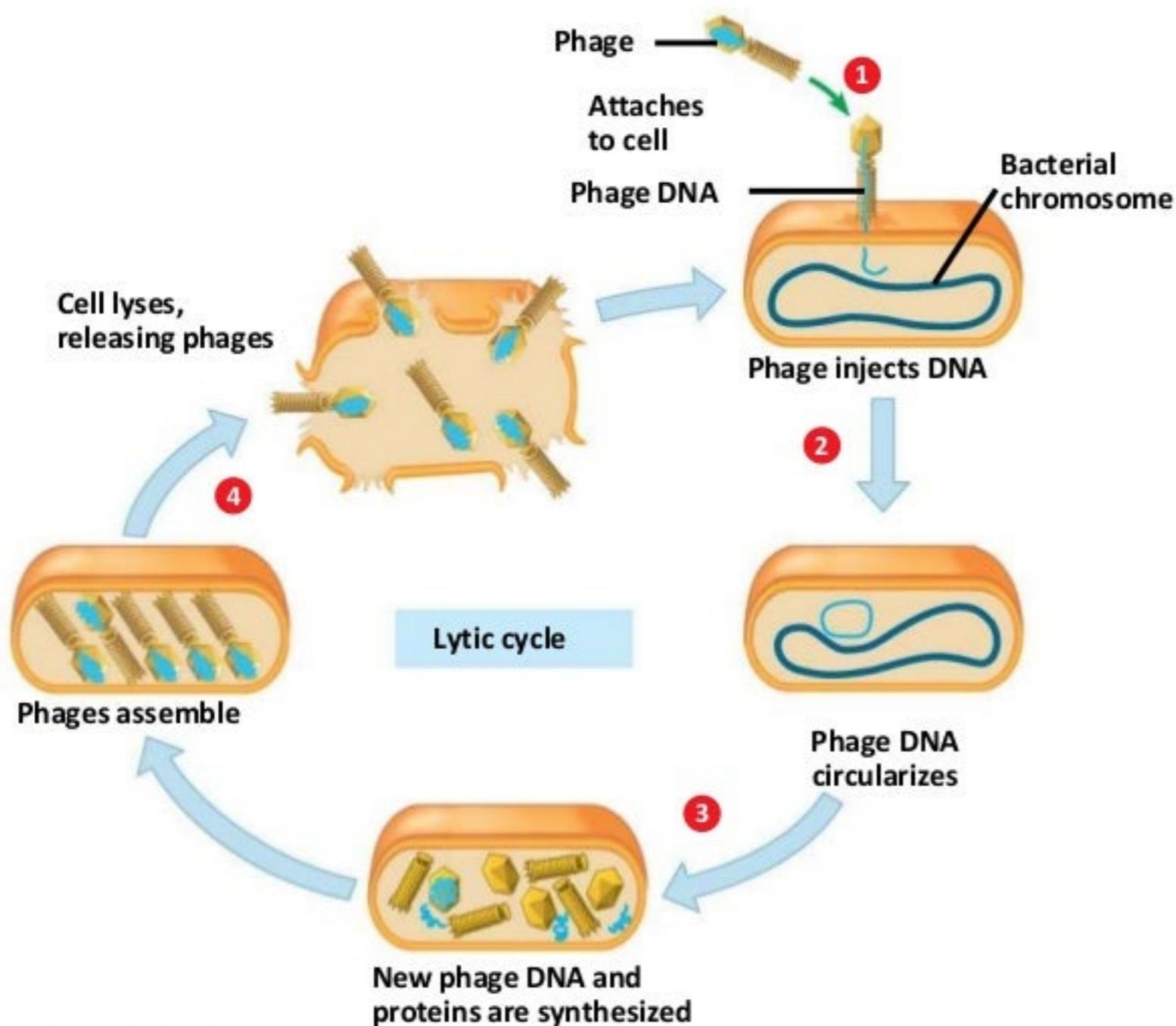


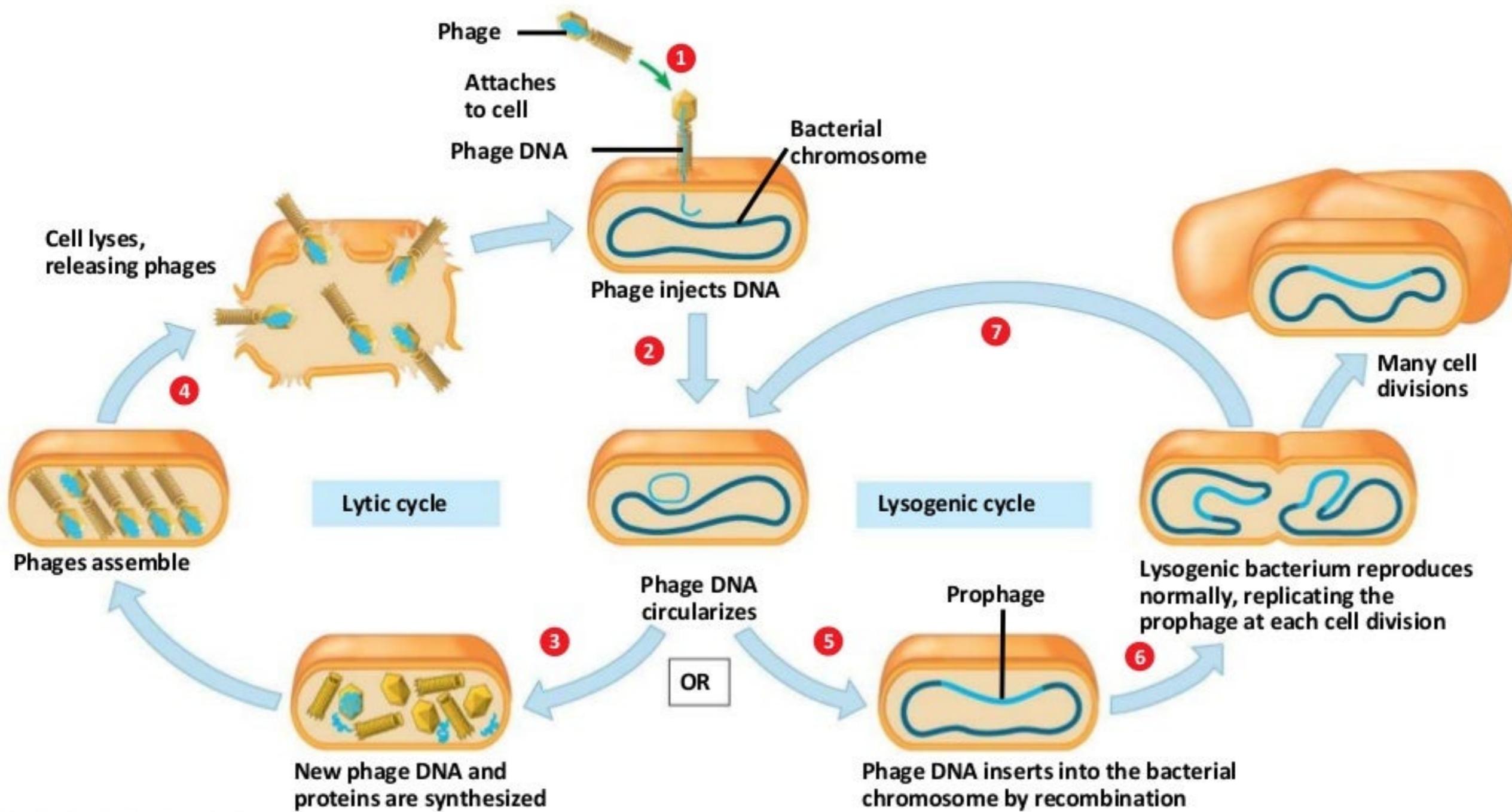
75 nm

20 nm



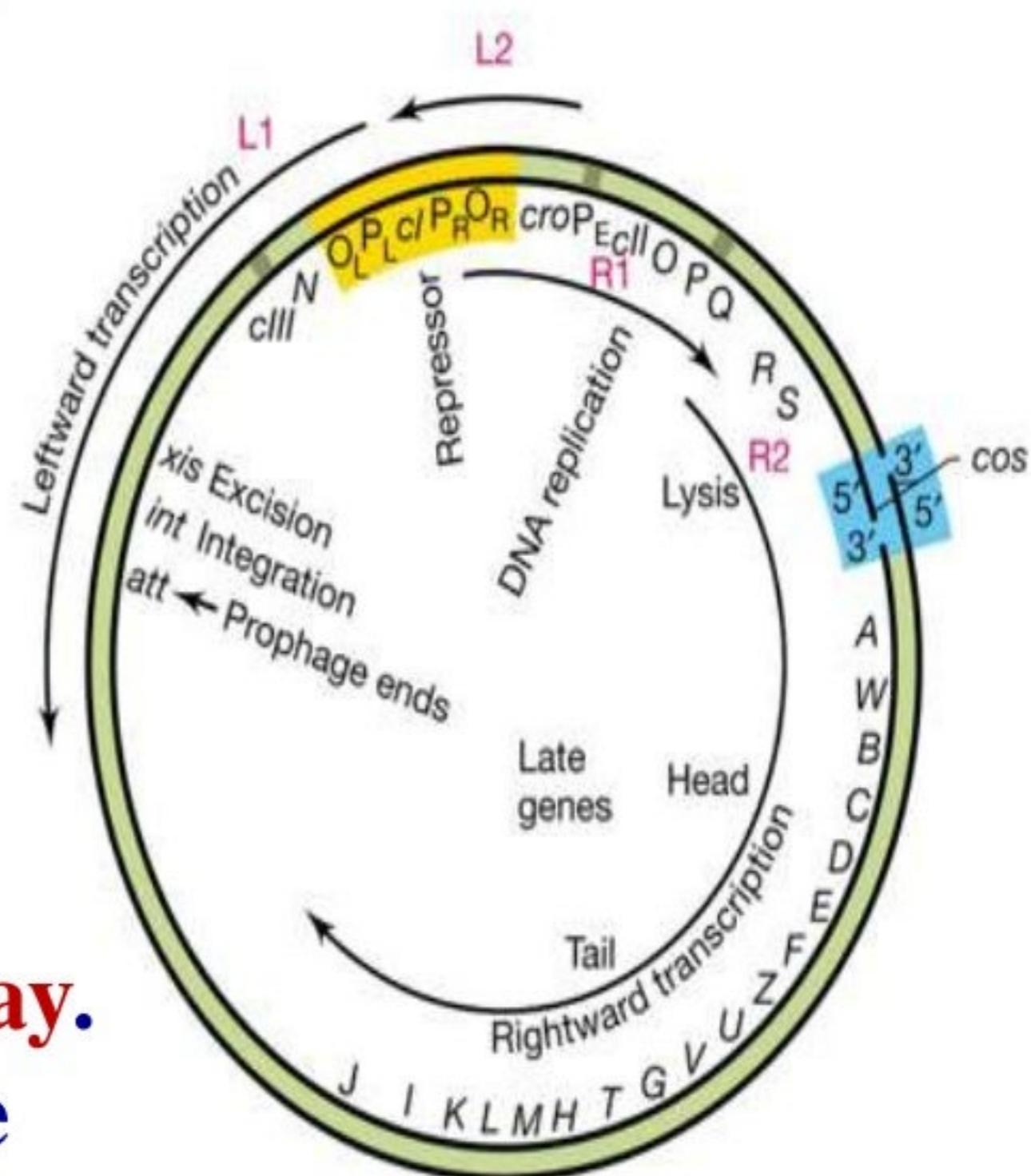
- Two types of reproductive cycles
- Lytic cycle - Immediate reproduction and lysis of host cell
- Lysogenic cycle - Integration into host chromosome with reproduction and lysis occurring later.
- Some phage are **only lytic** other **are both (temperate)**
- Most well studied Bacteriophage is Lambda (λ)

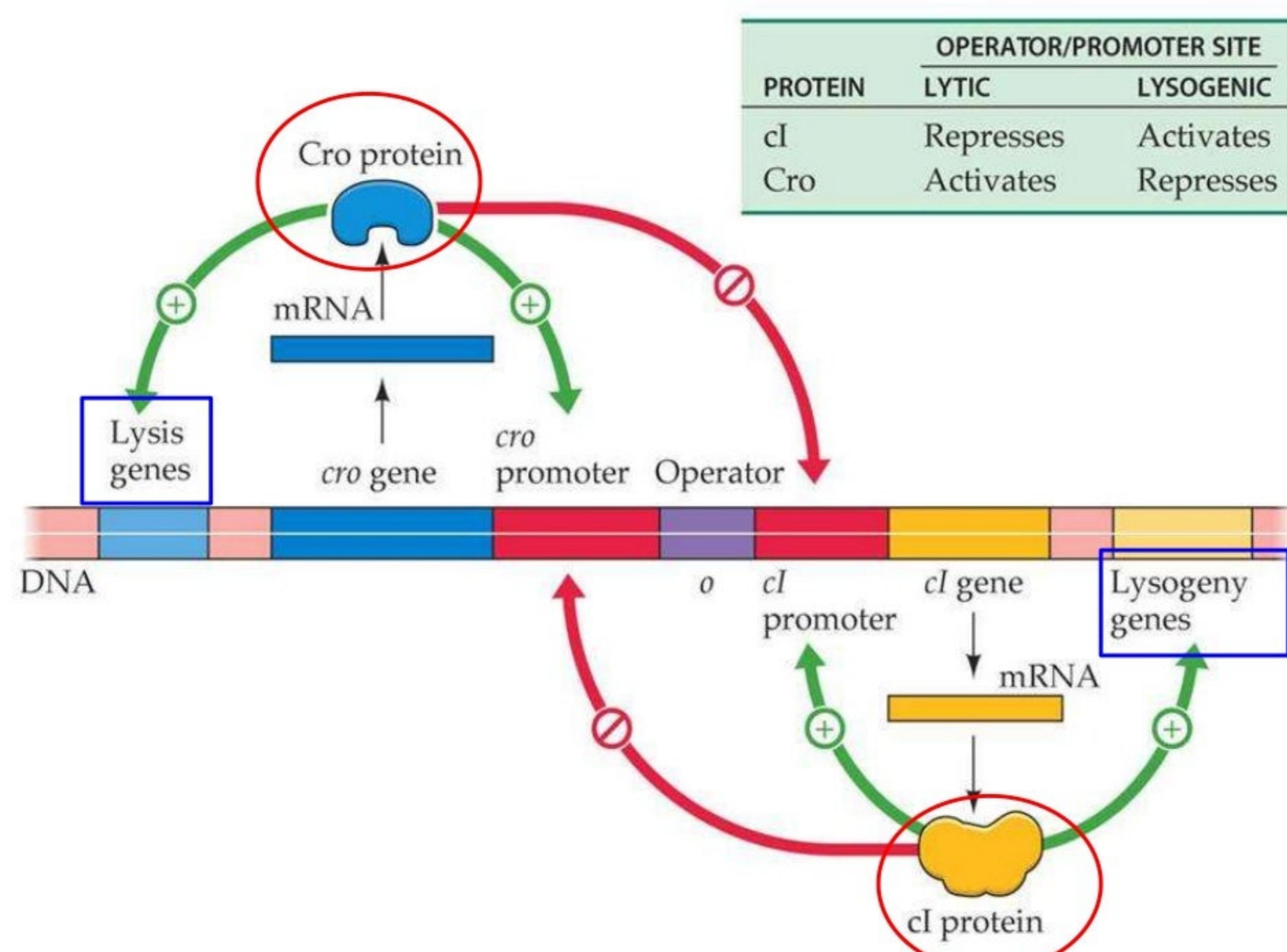




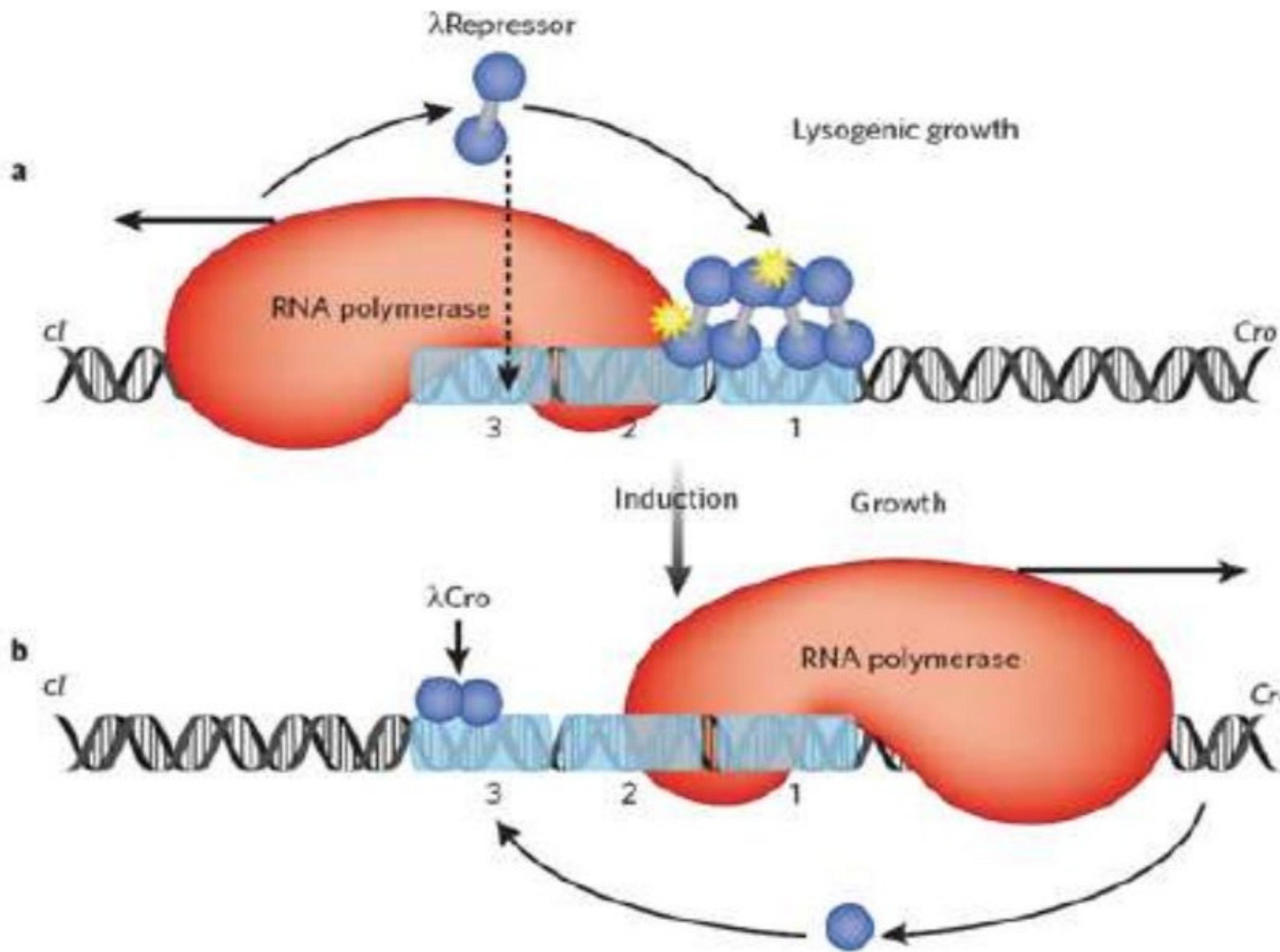
Lambda phage (λ) genome

- Two genes serve as the molecular switch.
- Lambda repressor protein (CI): activates the lysogenic pathway.
- Cro protein: activates the lytic pathway.
- This system is called the Lambda repressor switch.





LIFE: THE SCIENCE OF BIOLOGY, Seventh Edition, Figure 13.20 Control of Phage λ . Lysis and Lysogeny
© 2004 Sinauer Associates, Inc. and W. H. Freeman & Co.



Transcription factors bind to either [enhancer](#) or [promoter](#) regions of DNA adjacent to the genes that they regulate. Depending on the transcription factor, the transcription of the adjacent gene is either up- or down-regulated. Transcription factors use a variety of mechanisms for the regulation of gene expression.^[12] These mechanisms include:

stabilize or block the binding of RNA polymerase to DNA
catalyze the [acetylation](#) or deacetylation of [histone](#) proteins. The transcription factor can either do this directly or recruit other proteins with this catalytic activity. Many transcription factors use one or the other of two opposing mechanisms to regulate transcription:^[13]

[histone acetyltransferase](#) (HAT) activity – acetylates [histone](#) proteins, which weakens the association of DNA with [histones](#), which make the DNA more accessible to transcription, thereby up-regulating transcription

[histone deacetylase](#) (HDAC) activity – deacetylates [histone](#) proteins, which strengthens the association of DNA with histones, which make the DNA less accessible to transcription, thereby down-regulating transcription

recruit [coactivator](#) or [corepressor](#) proteins to the transcription factor DNA complex

General transcription factors are proteins that help form the pre-initiation complex responsible for the start of transcription in all class II genes.

Gene Specific transcription factors can be a wide variety of proteins involved in modulation of transcription processes, i.e inhibition, activation and can be classed according to structure and function

Basal transcription regulation[edit]

In [eukaryotes](#), an important class of transcription factors called [general transcription factors](#)(GTFs) are necessary for transcription to occur.^{[15][16][17]} Many of these GTFs don't actually bind DNA but are part of the large [transcription preinitiation complex](#) that interacts with [RNA polymerase](#) directly. The most common GTFs are [TFIIA](#), [TFIIB](#), [TFIID](#) (see also [TATA binding protein](#)), [TFIIE](#), [TFIIF](#), and [TFIIC](#).^[18] The preinitiation complex binds to [promoter](#)regions of DNA upstream to the gene that they regulate.

Differential enhancement of transcription[edit]

Other transcription factors differentially regulate the expression of various genes by binding to [enhancer](#) regions of DNA adjacent to regulated genes. These transcription factors are critical to making sure that genes are expressed in the right cell at the right time and in the right amount, depending on the changing requirements of the organism.

Development[edit]

Many transcription factors in [multicellular organisms](#) are involved in development.^[19] Responding to cues (stimuli), these transcription factors turn on/off the transcription of the appropriate genes, which, in turn, allows for changes in cell [morphology](#) or activities needed for [cell fate determination](#) and [cellular differentiation](#). The [Hox](#) transcription factor family, for example, is important for proper [body pattern formation](#) in organisms as diverse as fruit flies to humans.^{[20][21]} Another example is the transcription factor encoded by the [Sex-determining Region Y](#) (SRY) gene, which plays a major role in determining sex in humans

Genespecific Transcription Factors-Exampbles

Response to environment[edit]

Not only do transcription factors act downstream of signaling cascades related to biological stimuli but they can also be downstream of signaling cascades involved in environmental stimuli. Examples include [heat shock factor](#) (HSF), which upregulates genes necessary for survival at higher temperatures,^[25] [hypoxia inducible factor](#) (HIF), which upregulates genes necessary for cell survival in low-oxygen environments,^[26] and [sterol regulatory element binding protein](#) (SREBP), which helps maintain proper [lipid](#) levels in the cell.^[27]

Cell cycle control[edit]

Many transcription factors, especially some that are [proto-oncogenes](#) or [tumor suppressors](#), help regulate the [cell cycle](#) and as such determine how large a cell will get and when it can divide into two daughter cells.^{[28][29]} One example is the [Myc](#) oncogene, which has important roles in [cell growth](#) and [apoptosis](#).^[30]

Transcription factors are of clinical significance for at least two reasons: (1) mutations can be associated with specific diseases, and (2) they can be targets of medications.

Disorders[edit]

Due to their important roles in development, intercellular signaling, and cell cycle, some human diseases have been associated with [mutations](#) in transcription factors.^[74]

Many transcription factors are either [tumor suppressors](#) or [oncogenes](#), and, thus, mutations or aberrant regulation of them is associated with cancer. Three groups of transcription factors are known to be important in human cancer: (1) the [NF-kappaB](#) and [AP-1](#) families, (2) the [STAT](#) family and (3) the [steroid receptors](#).^[75]

Below are a few of the more well-studied examples:

Condition	Description	Locus
<u>Rett syndrome</u>	Mutations in the <u>MECP2</u> transcription factor are associated with <u>Rett syndrome</u> , a neurodevelopmental disorder. ^{[76][77]}	Xq28
<u>Diabetes</u>	A rare form of <u>diabetes</u> called <u>MODY</u> (Maturity onset diabetes of the young) can be caused by mutations in <u>hepatocyte nuclear factors</u> (HNFs) ^[78] or <u>insulin promoter factor-1</u> (IPF1/Pdx 1). ^[79]	multiple
	Mutations in the <u>FOXP2</u> transcri	

Alternative splicing is a regulated process during gene expression that results in a single gene coding for multiple proteins. In this process, particular exons of a gene may be included within or excluded from the final, processed messenger RNA (mRNA) produced from that gene.