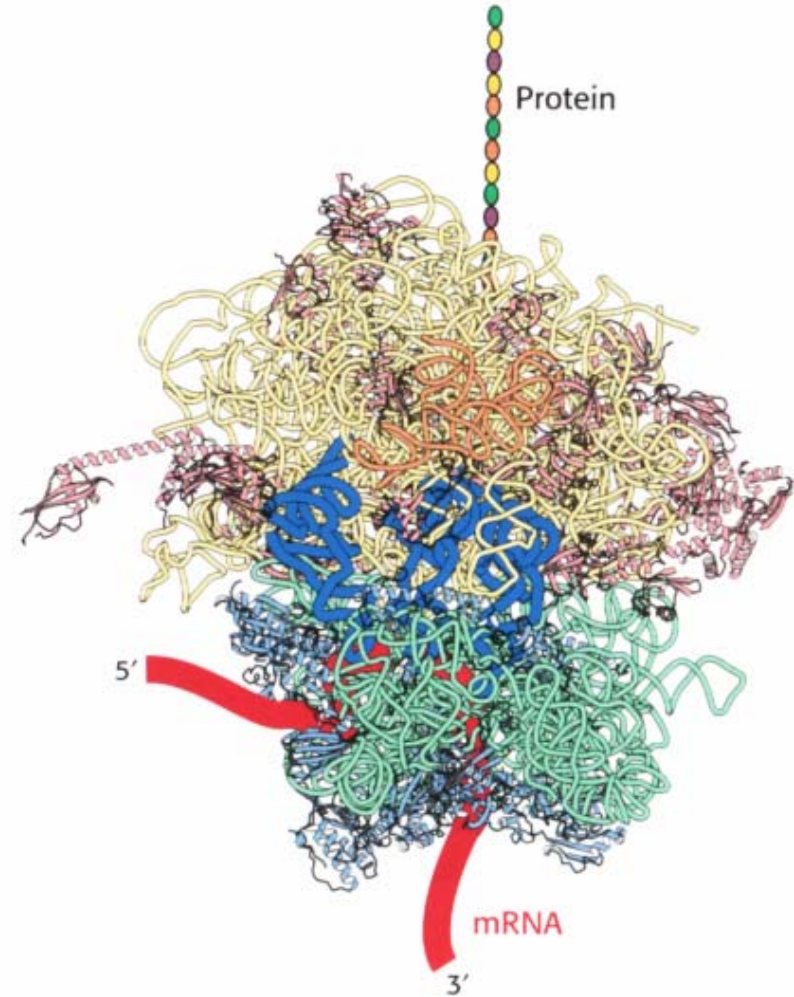
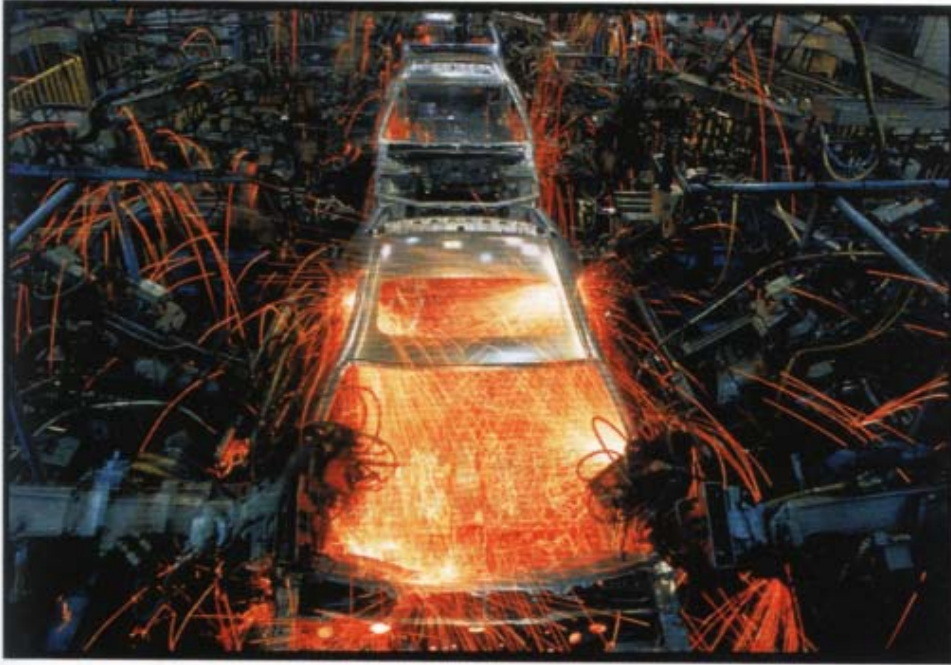


# Protein Synthesis Factory



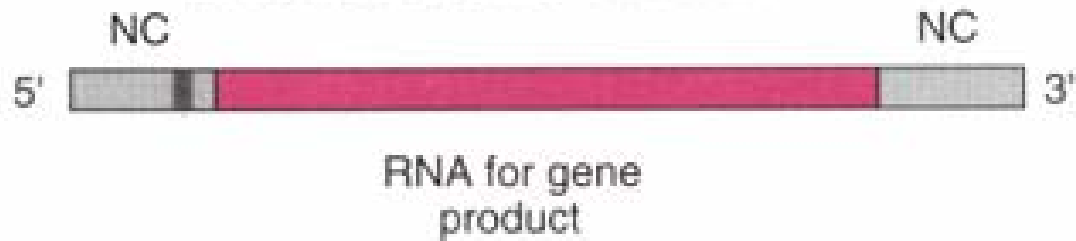
# Components required for translation

- mRNA
- Amino acids
- tRNA
- Aminoacyl-tRNA synthetases
- Ribosomes
- Protein factors

# mRNA

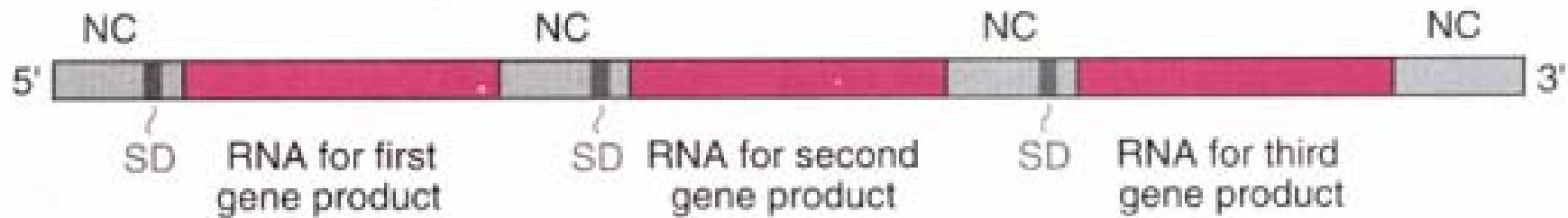
**A**

## Monocistronic mRNA

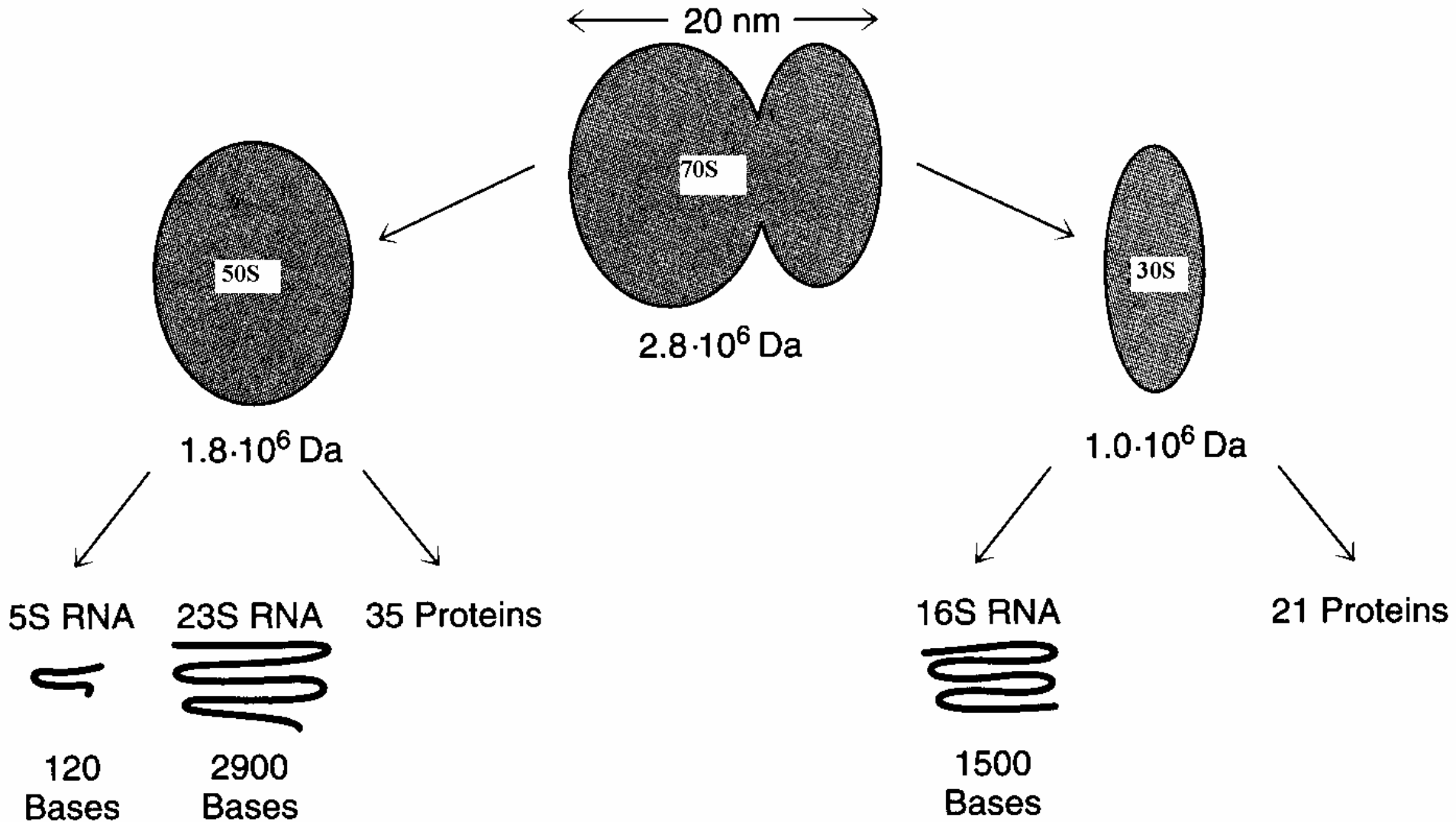


**B**

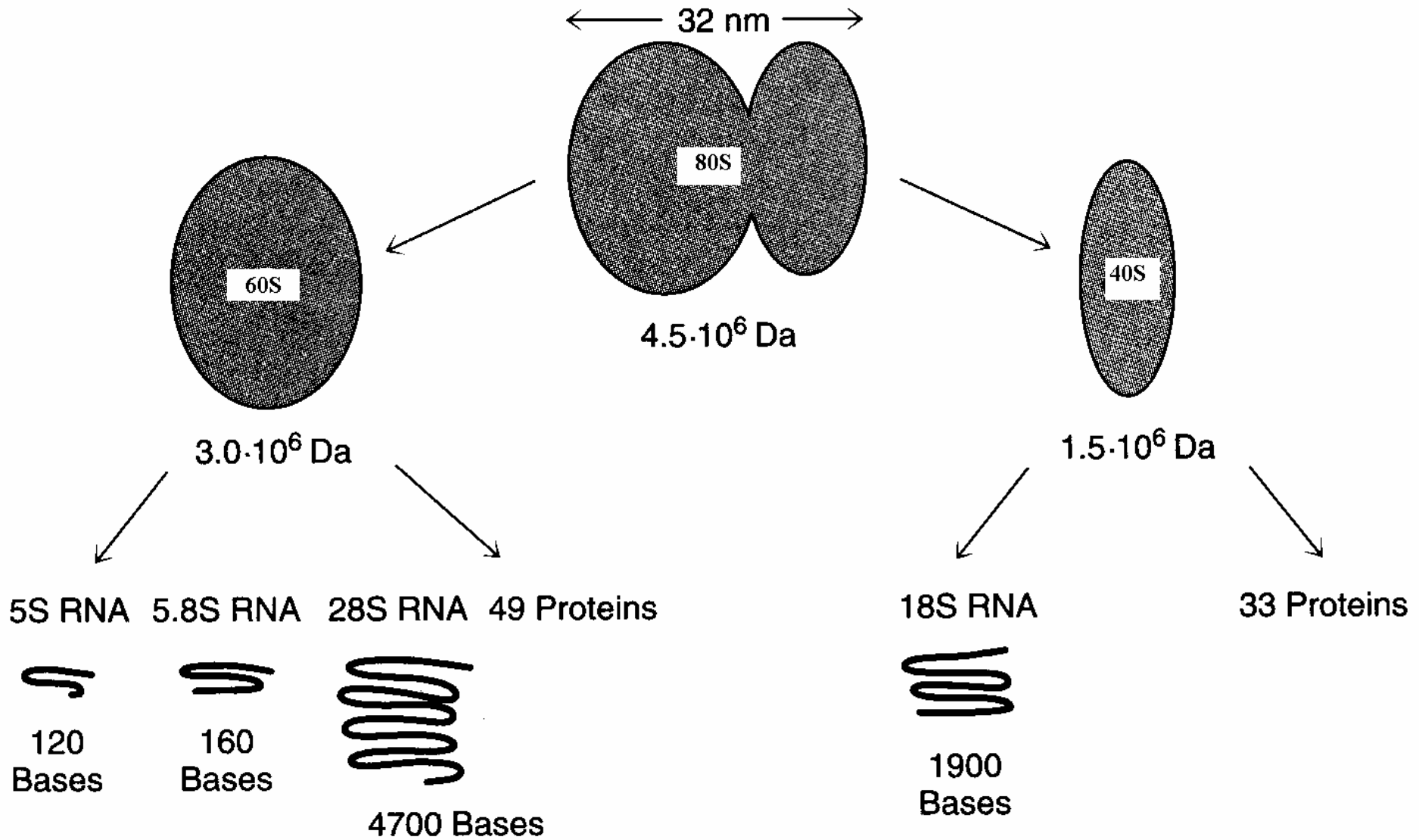
## Polycistronic mRNA



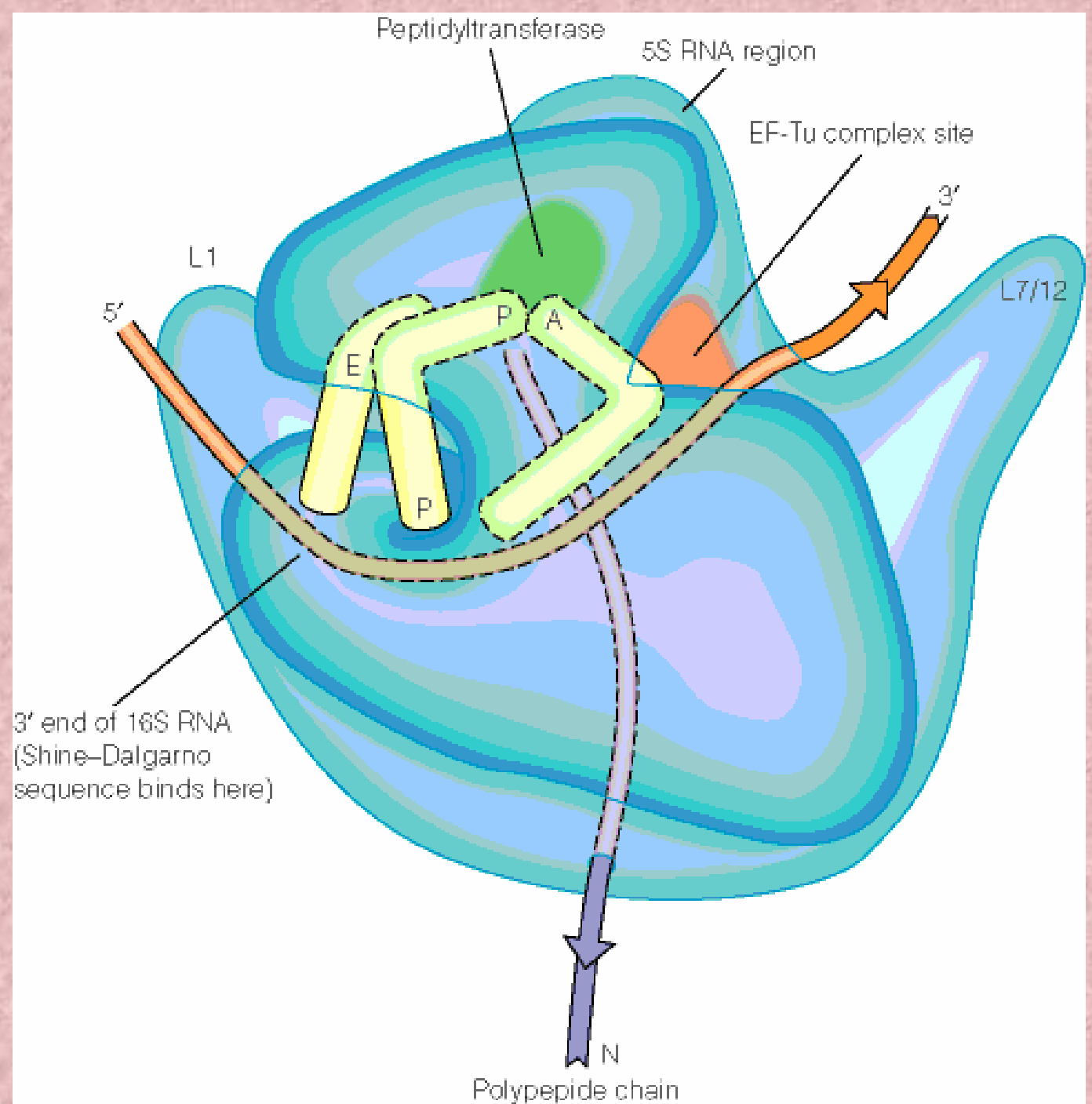
# Prokaryotic Ribosome



# Eukaryotic Ribosome



# Functional domains of a ribosome



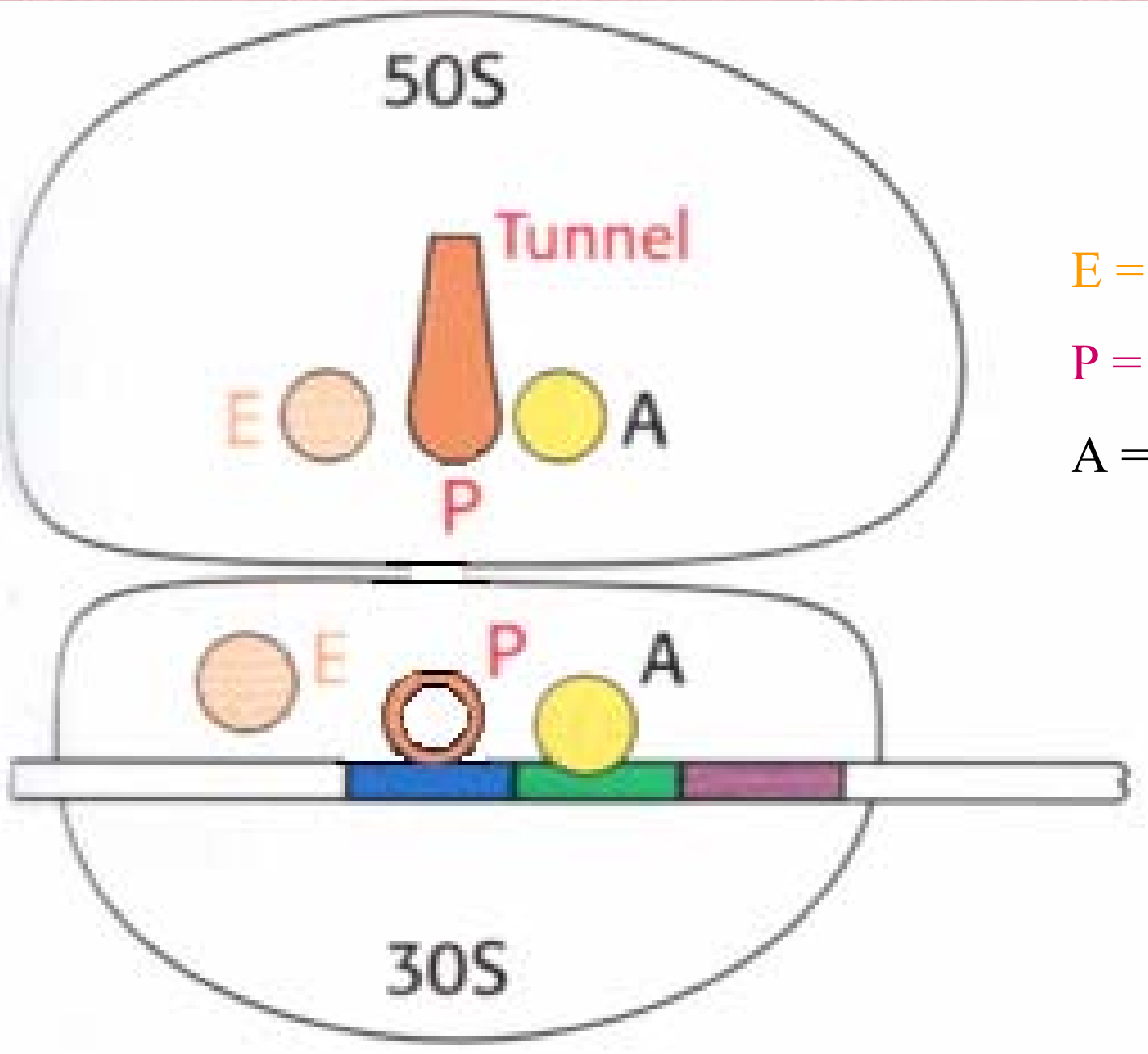
# 70S ribosome peptide synthesis domains

Sites

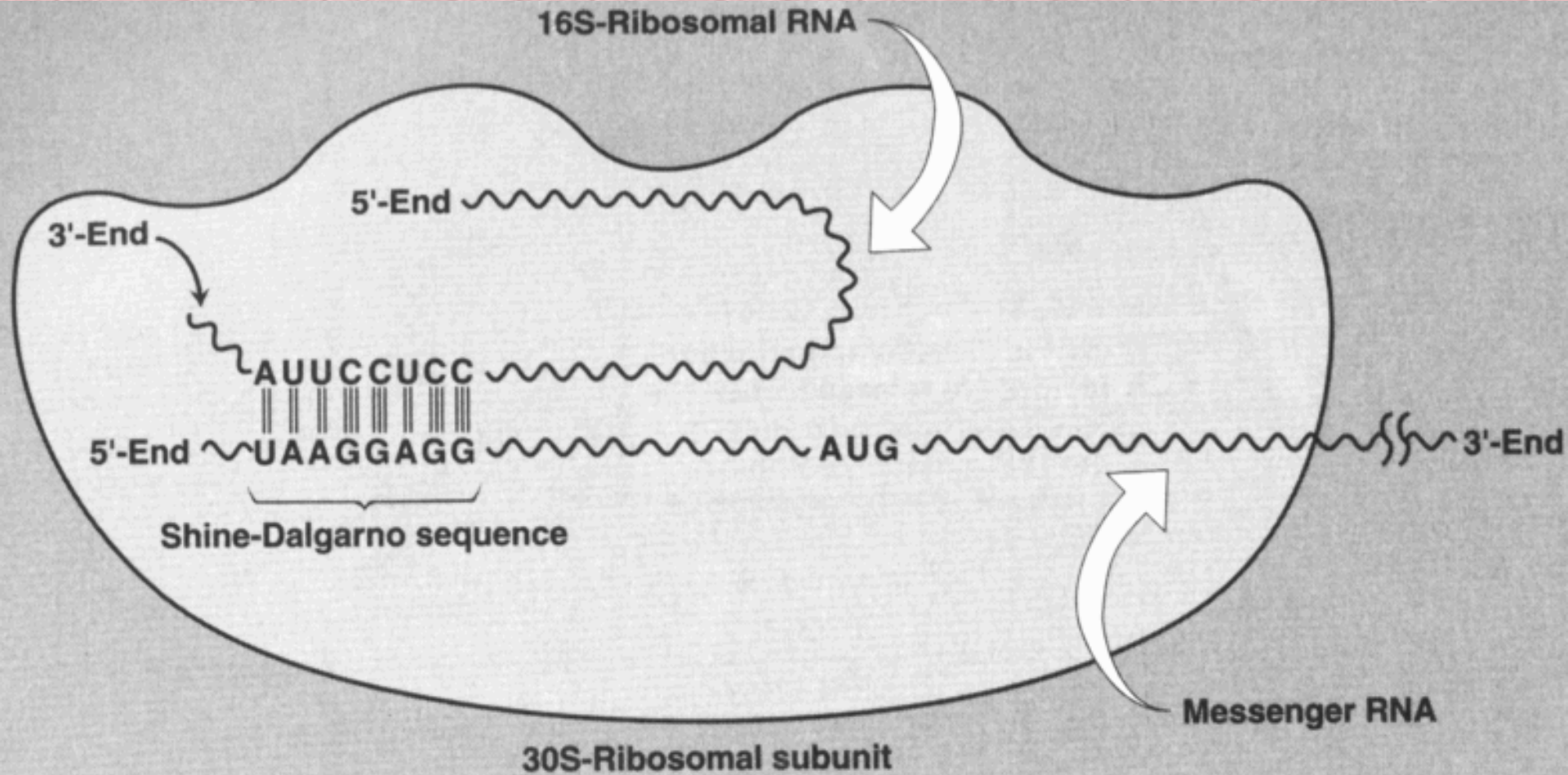
E = Exit

P = Peptidyl

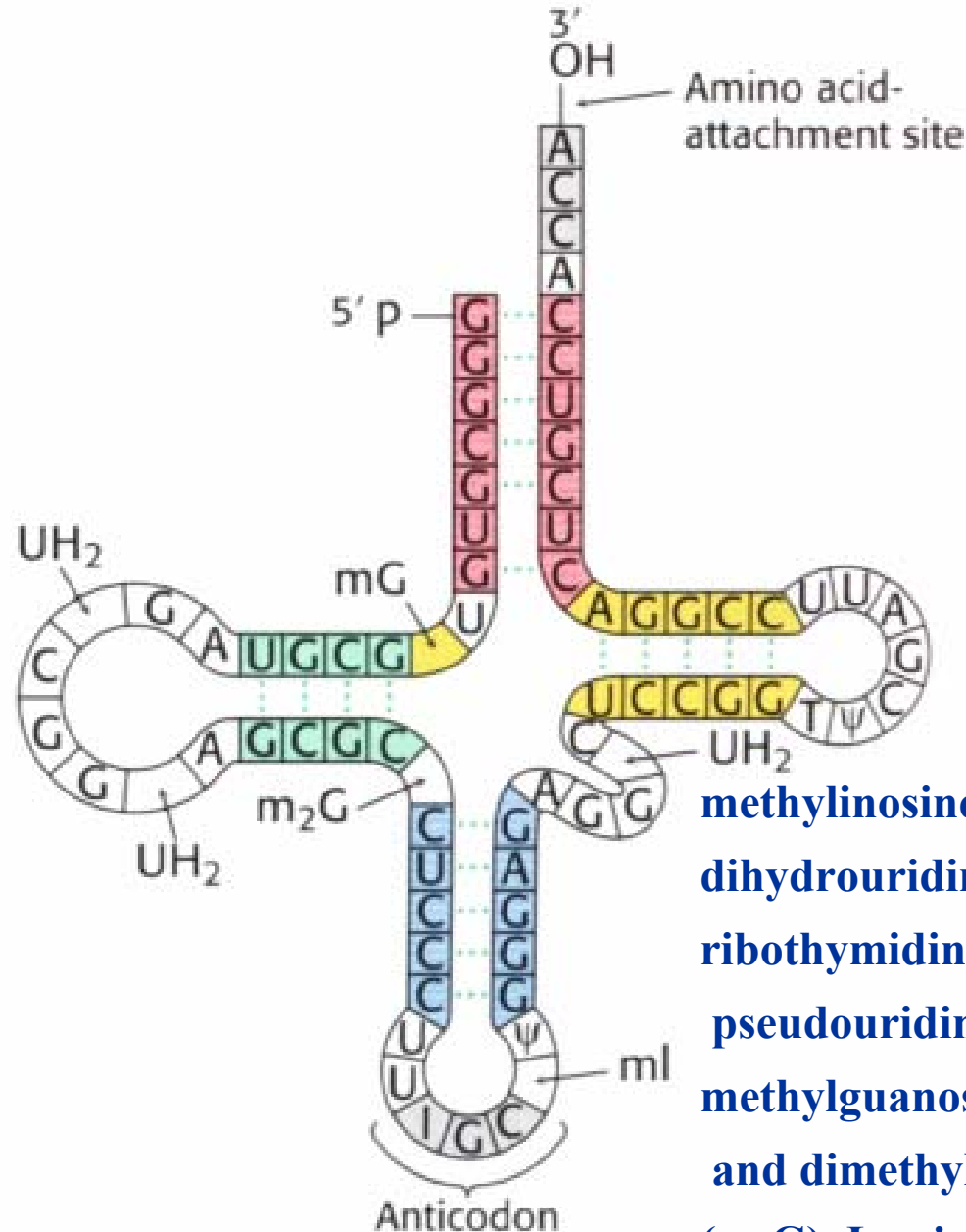
A = Aminoacyl



# Shine Dalgarno sequence

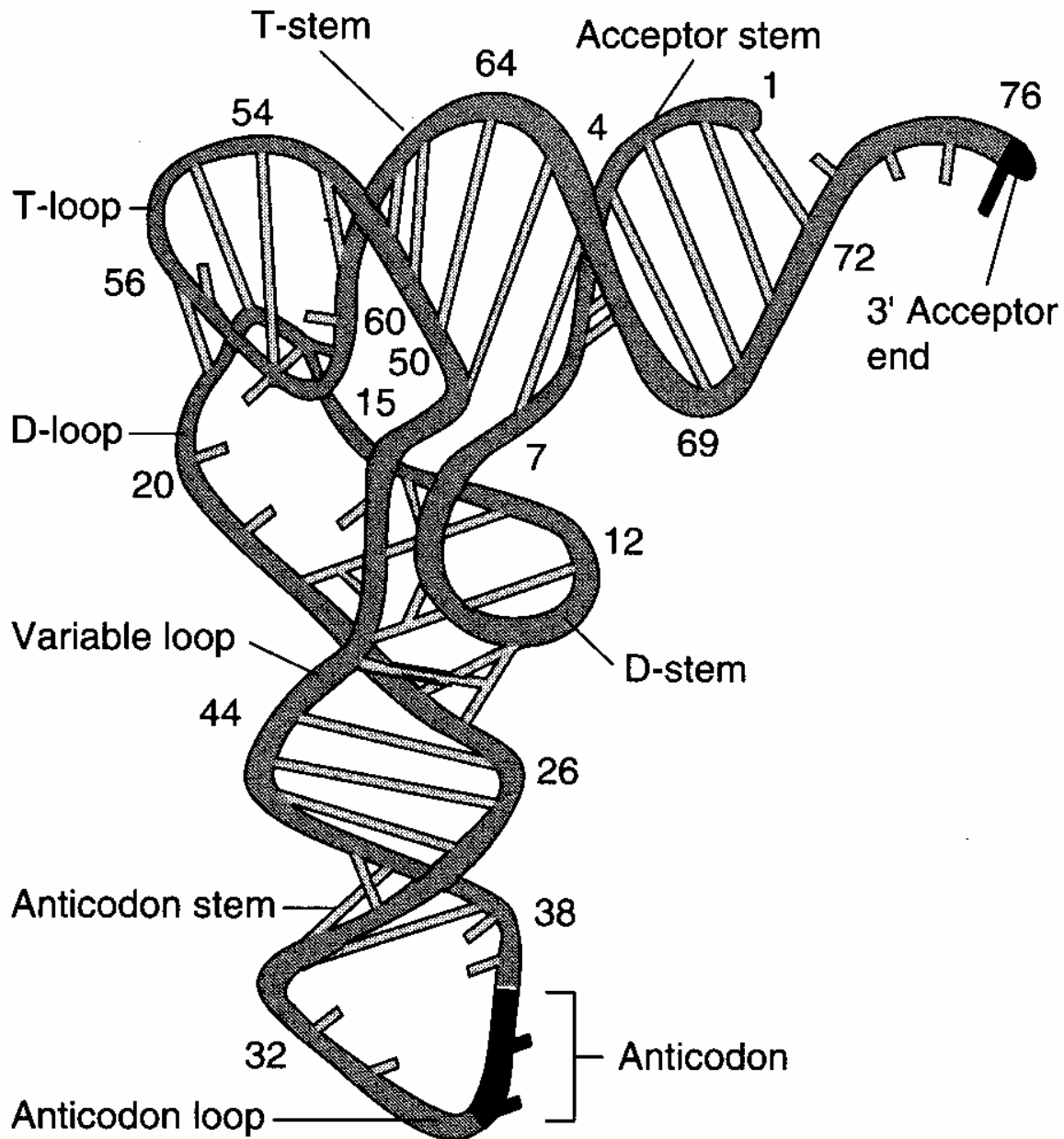


# tRNA Sequence



**methylinosine (ml),  
dihydrouridine (UH<sub>2</sub>),  
ribothymidine (T),  
pseudouridine (ψ),  
methylguanosine (mG),  
and dimethylguanosine (m<sub>2</sub>G). Inosine (I),**

# tRNA Structure

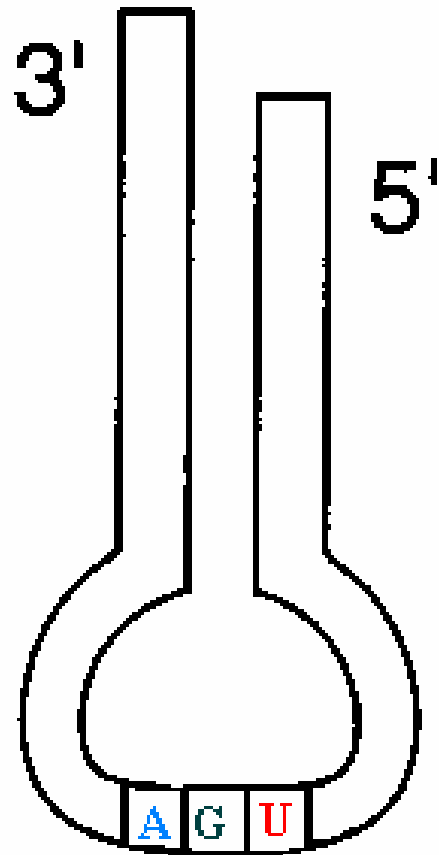


# The Genetic Code

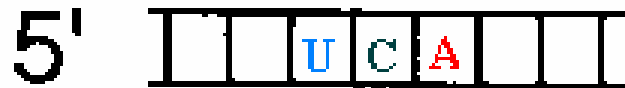
First position (5' end)	Second position				Third position (3' end)
	U	C	A	G	
U	UUU	UCU	UAU	UGU	U C A G
	UUC <b>Phe</b>	UCC <b>Ser</b>	UAC <b>Tyr</b>	UGC <b>Cys</b>	
	UUA <b>Leu</b>	UCA <b>Ser</b>	UAA <b>Stop</b>	UGA <b>Stop</b>	
	UUG <b>Leu</b>	UCG <b>Ser</b>	UAG <b>Stop</b>	UGG <b>Trp</b>	
C	CUU	CCU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

# “Wobble” hypothesis

tRNA

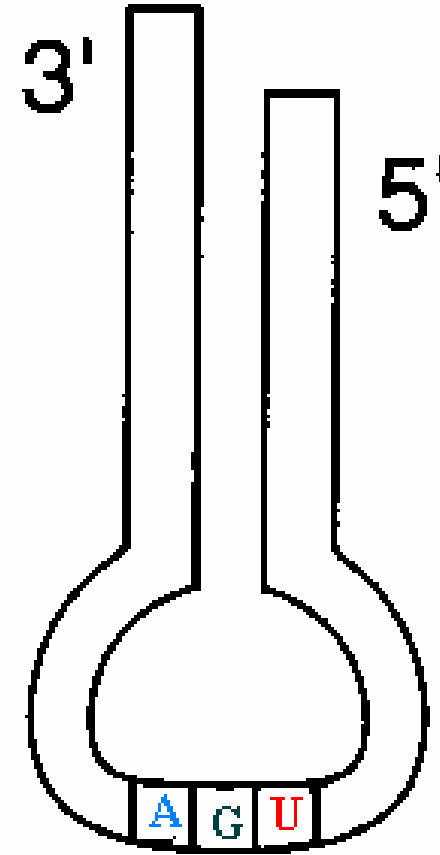


t m  
A U  
G C  
U A  
C G

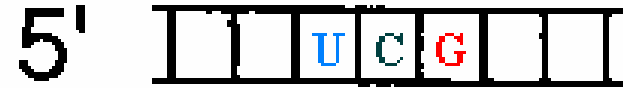


mRNA

tRNA

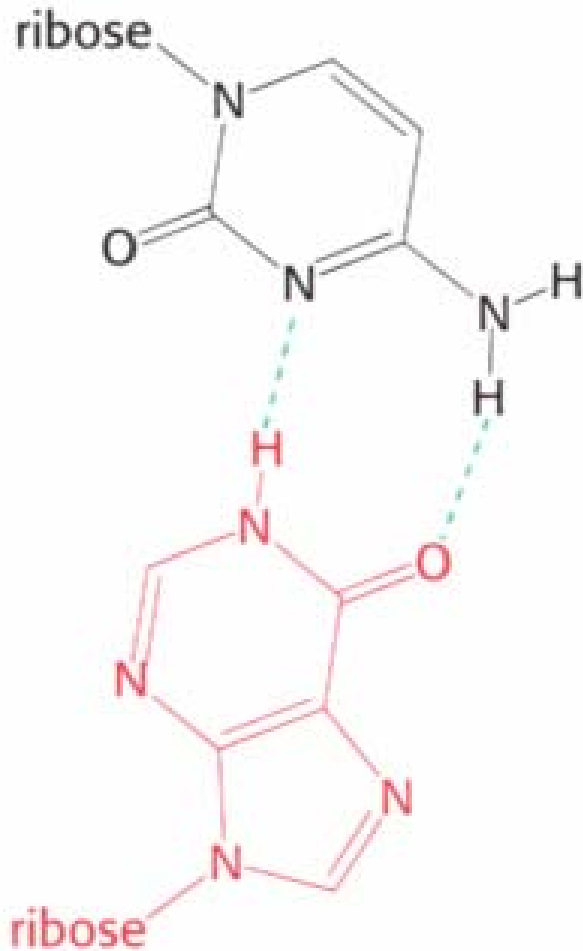


t m  
A U  
G C U  
U A G  
C G  
I U C A

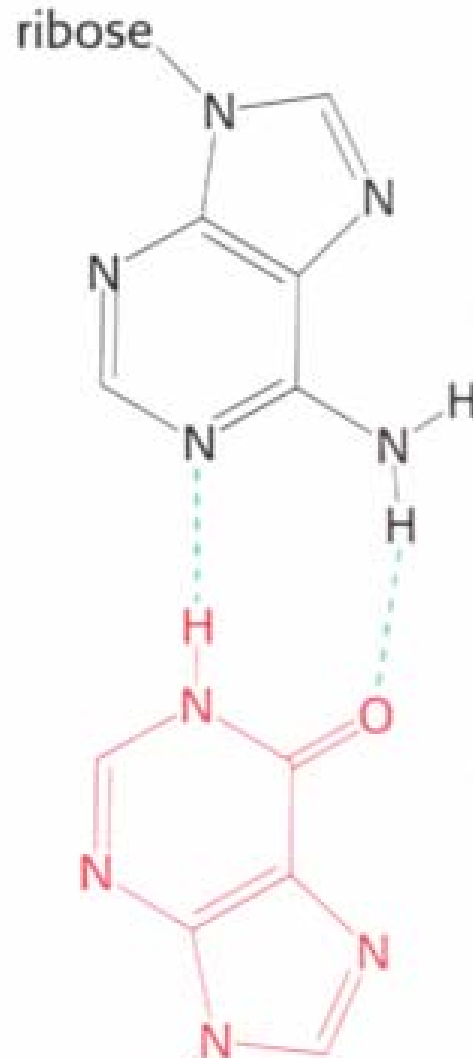


mRNA

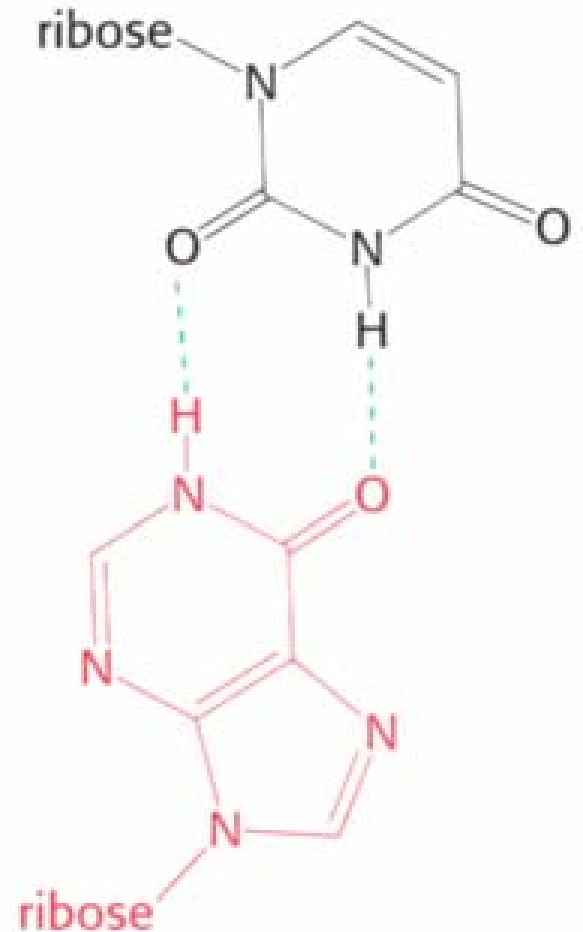
# Non-Watson-Crick base pairing



Inosine-cytidine  
base pair



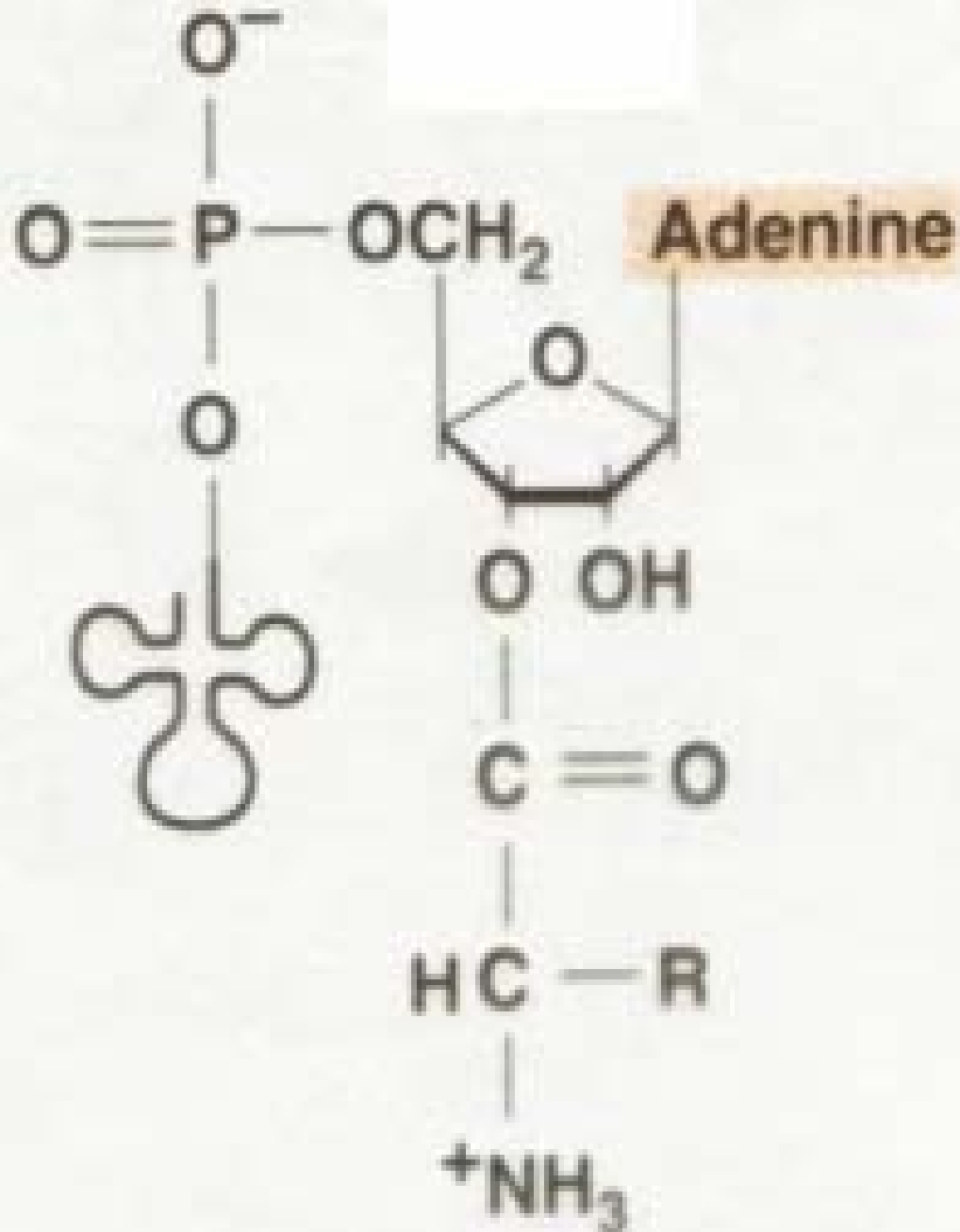
Inosine-adenosine  
base pair



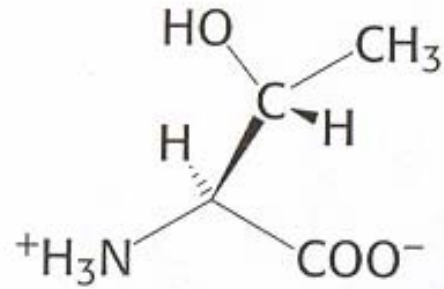
Inosine-uridine  
base pair



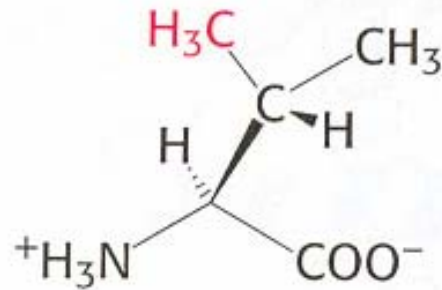
# 3'-O aminoacyl-tRNA



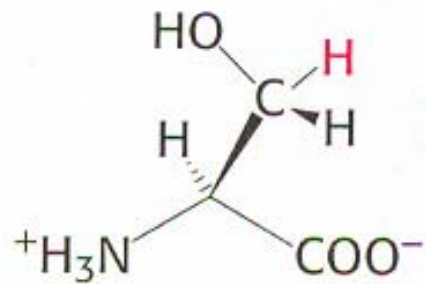
# Threonyl-tRNA formation



**Threonine**

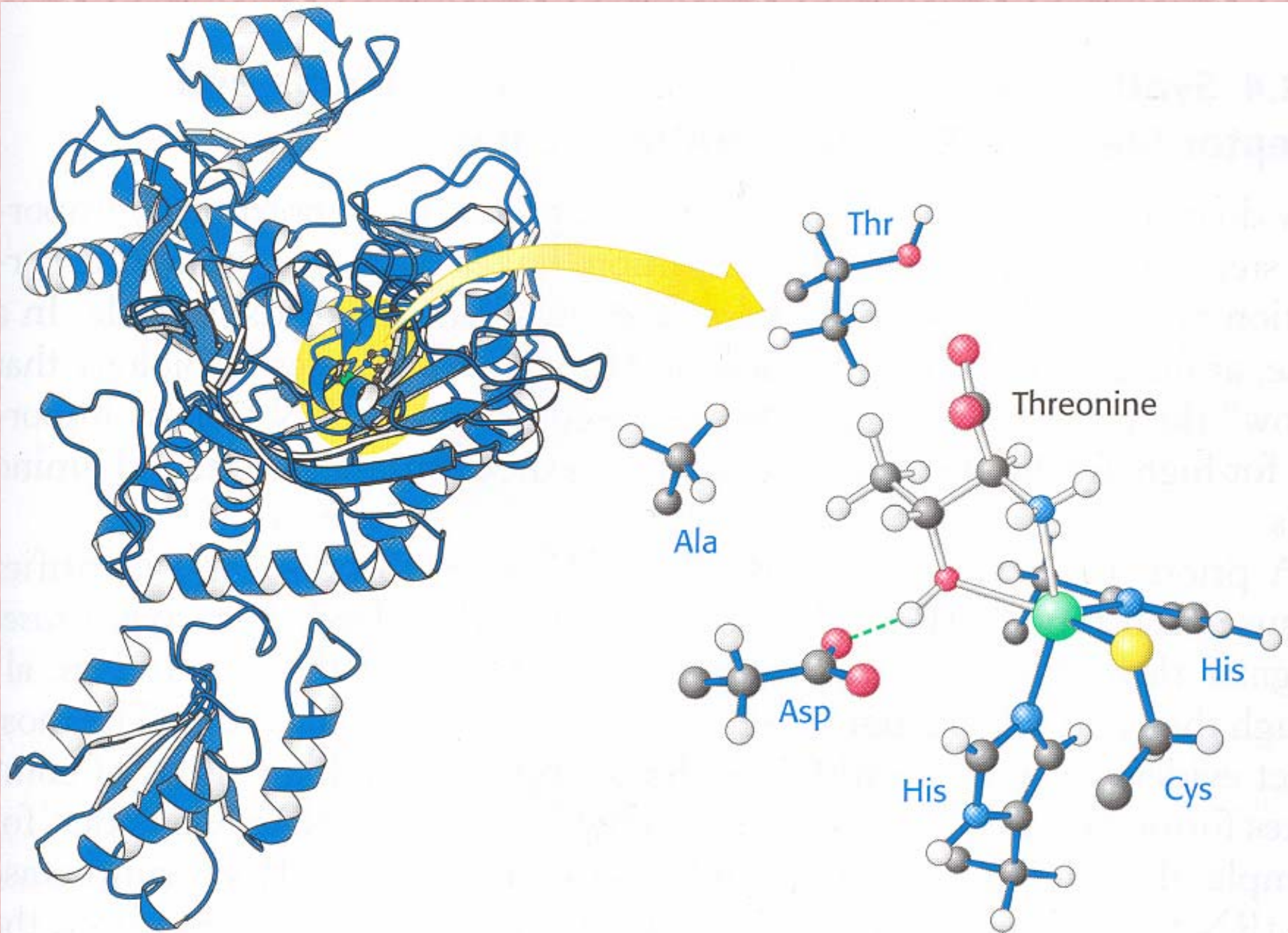


**Valine**

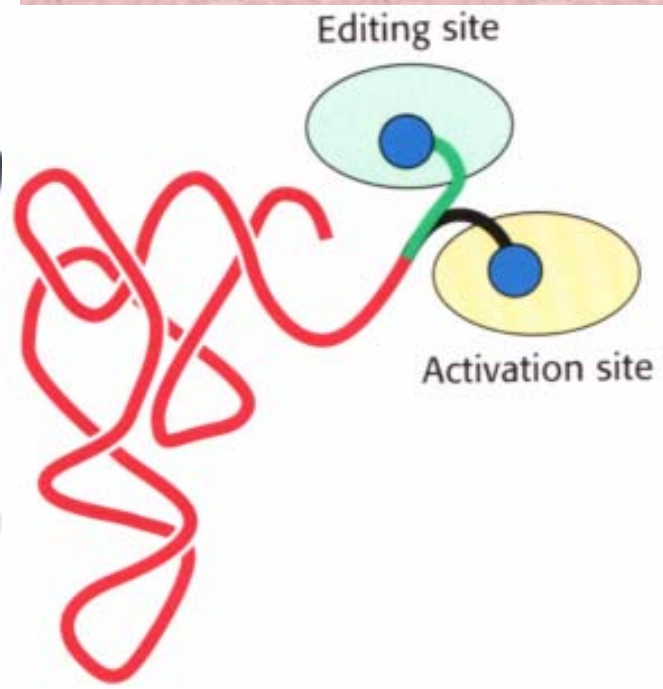
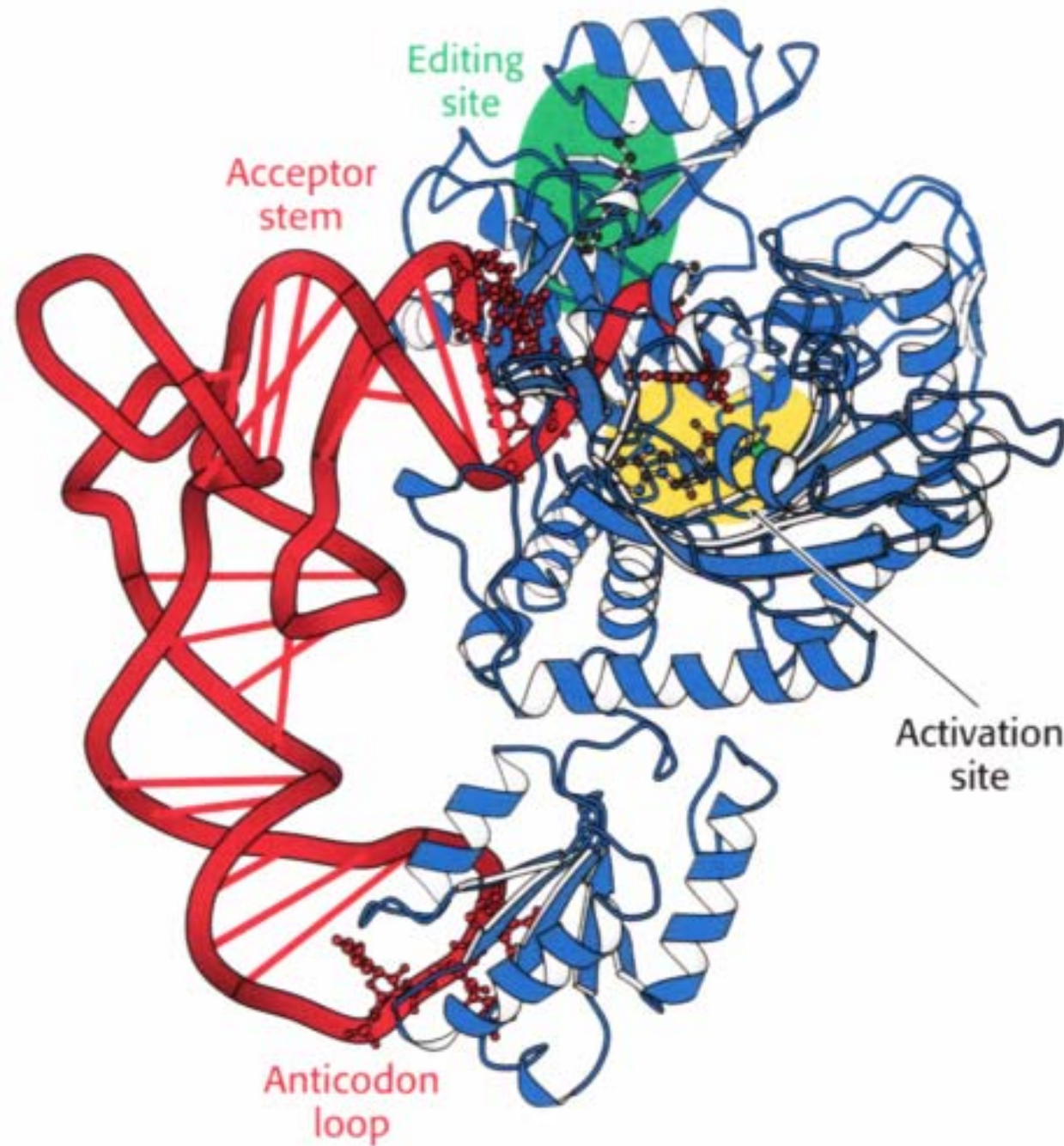


**Serine**

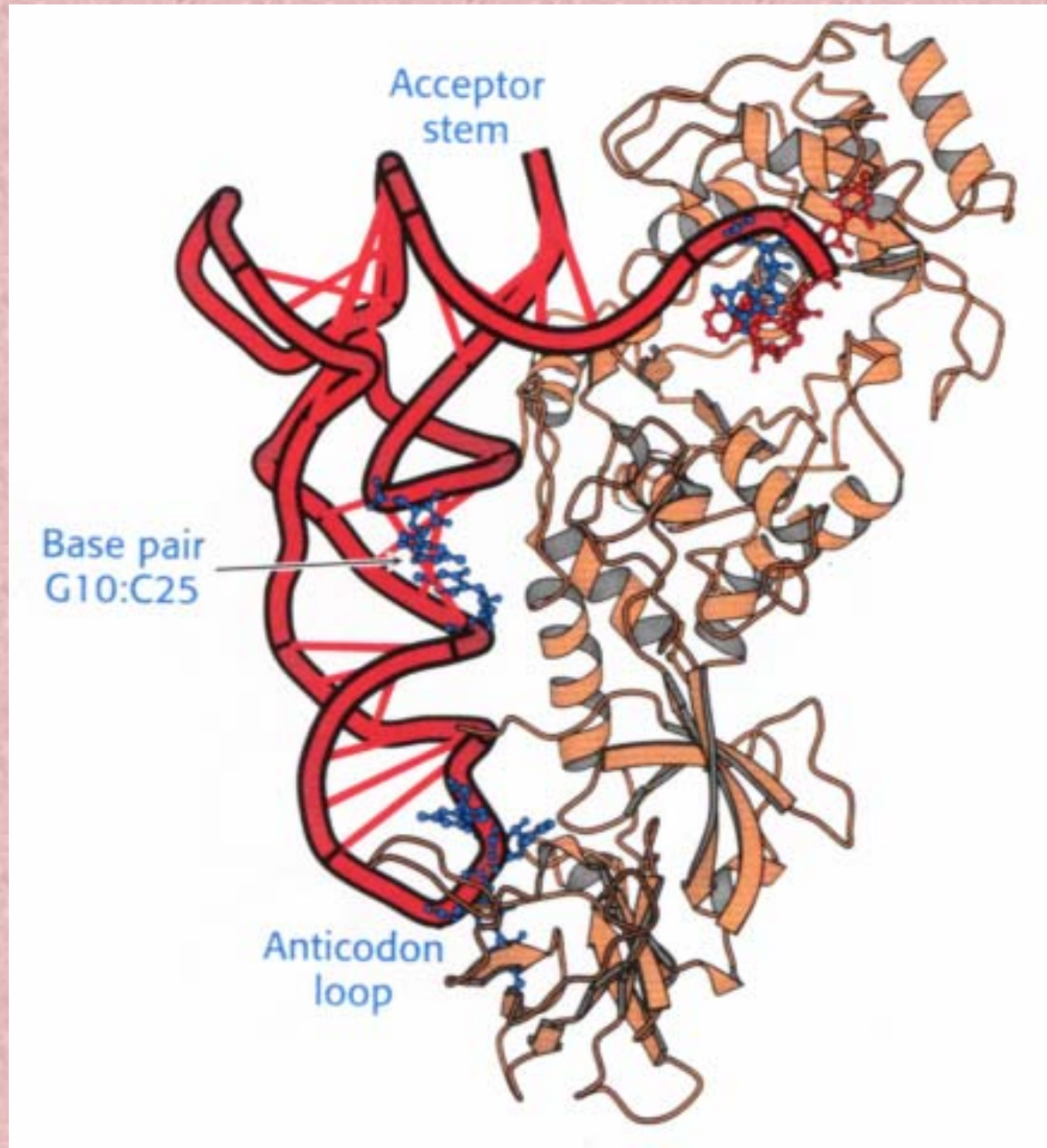
# Threonyl-tRNA Synthetase



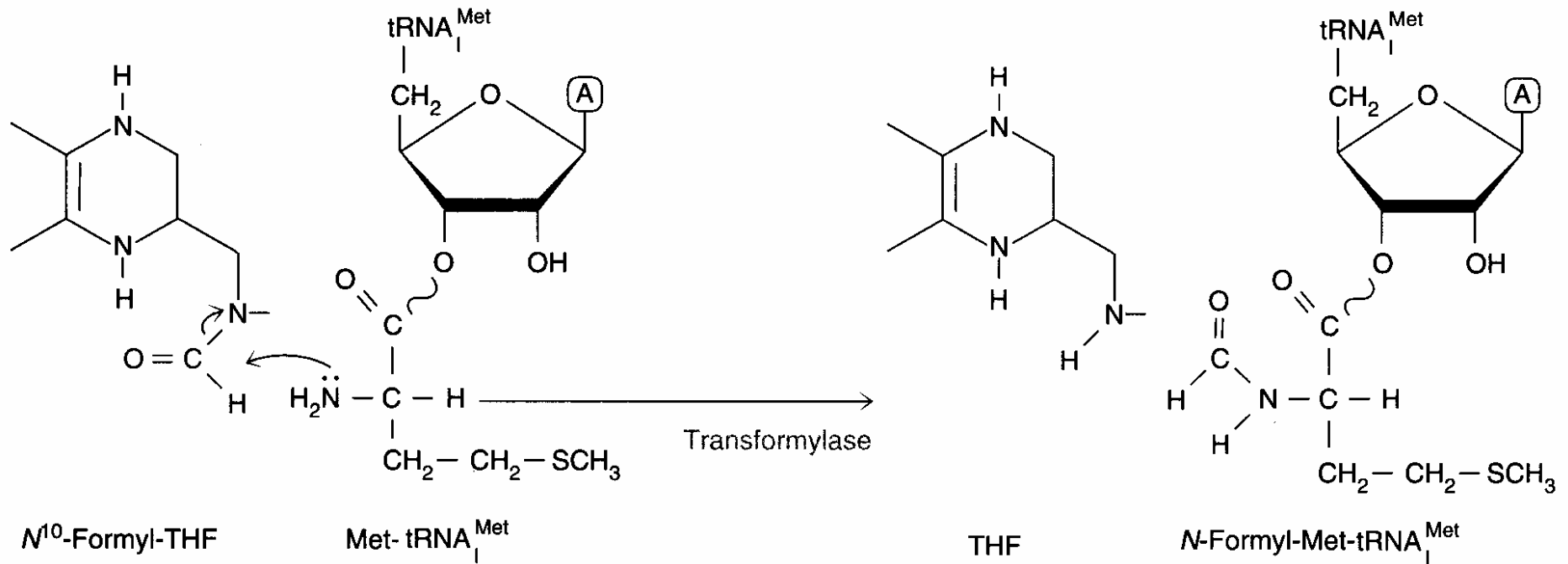
# Aminoacyl-tRNA synthetase and tRNA



# Glutaminyl-tRNA synthetase complex



# Met formylation



# Protein Translation

## Components required for translation

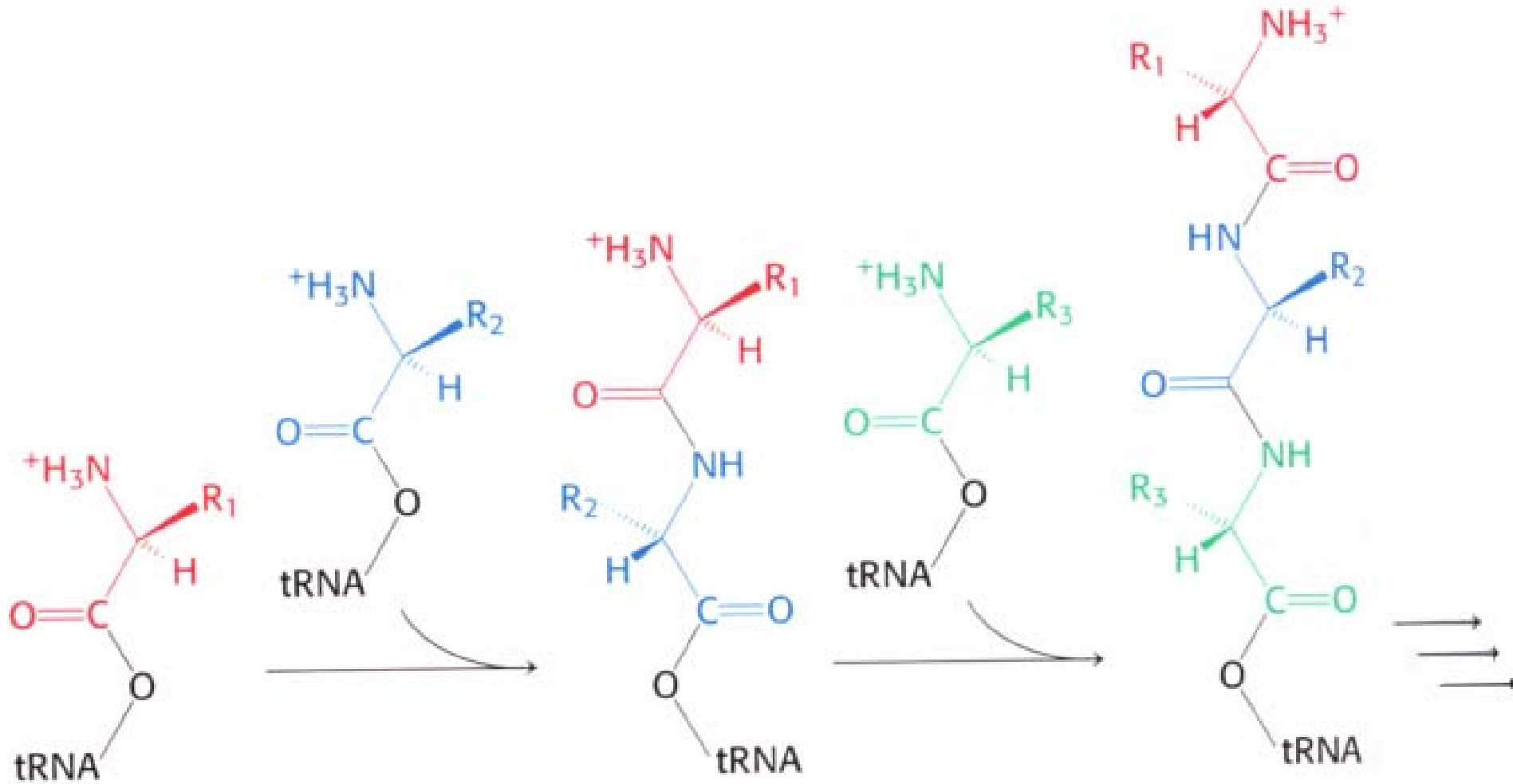
- mRNA
- Amino acids
- tRNA
- Aminoacyl-tRNA synthetases
- Ribosomes
- Protein factors

# Protein Translation

## Protein translation steps

- Initiation
- Elongation
- Termination

# Polypeptide Chain Growth



Proteins are synthesized by the successive addition of amino acids to the carboxyl terminus

# Protein Synthesis Initiation Factors

---

**Factor**

**Function**

---

## •Initiation factors

**IF1**

**Keeps ribosome subunits dissociated**

**IF2**

**Binds GTP and formyl-Met-tRNA<sup>fMet</sup>**

**IF3**

**Prevents association of the small and large subunits**

---

# Translation Initiation in Prokaryotes

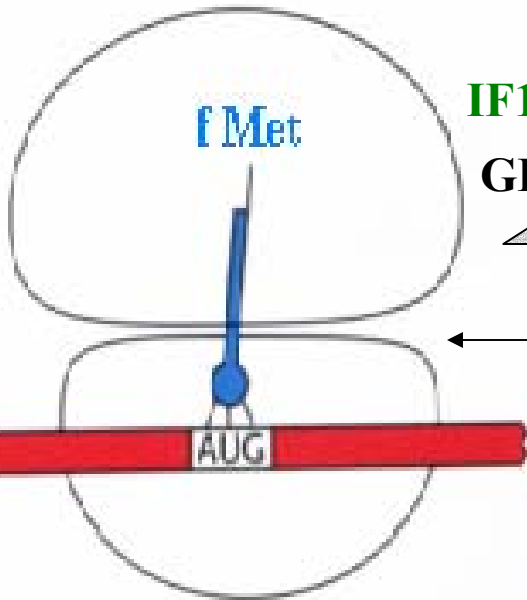
30s ribosomal subunit

Initiation factors

30s.IF1.IF3

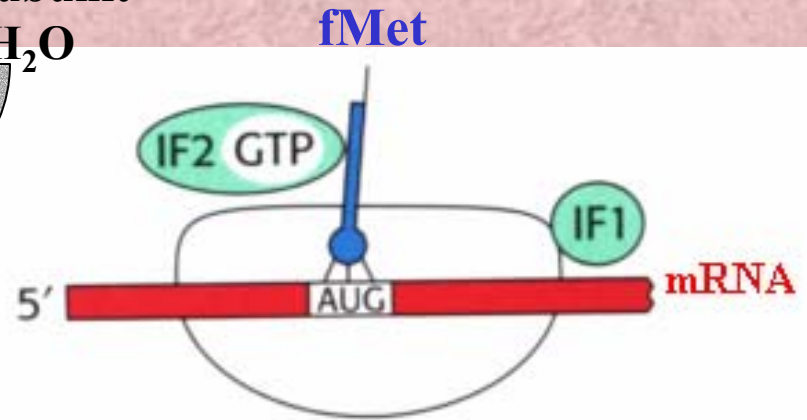
IF2(GTP).fMet-tRNA<sub>f</sub>  
+ mRNA

IF3



IF1 + IF2,  
GDP + P<sub>i</sub>

50S subunit  
+ H<sub>2</sub>O



30S initiation complex

70S initiation complex

# Protein Synthesis Elongation Factors

---

**Factor**

**Function**

---

## •Elongation factors

**EF-T**

***Transfer***

**EF-Tu**

***unstable; binds aminoacyl tRNA . GTP***

**EF-Ts**

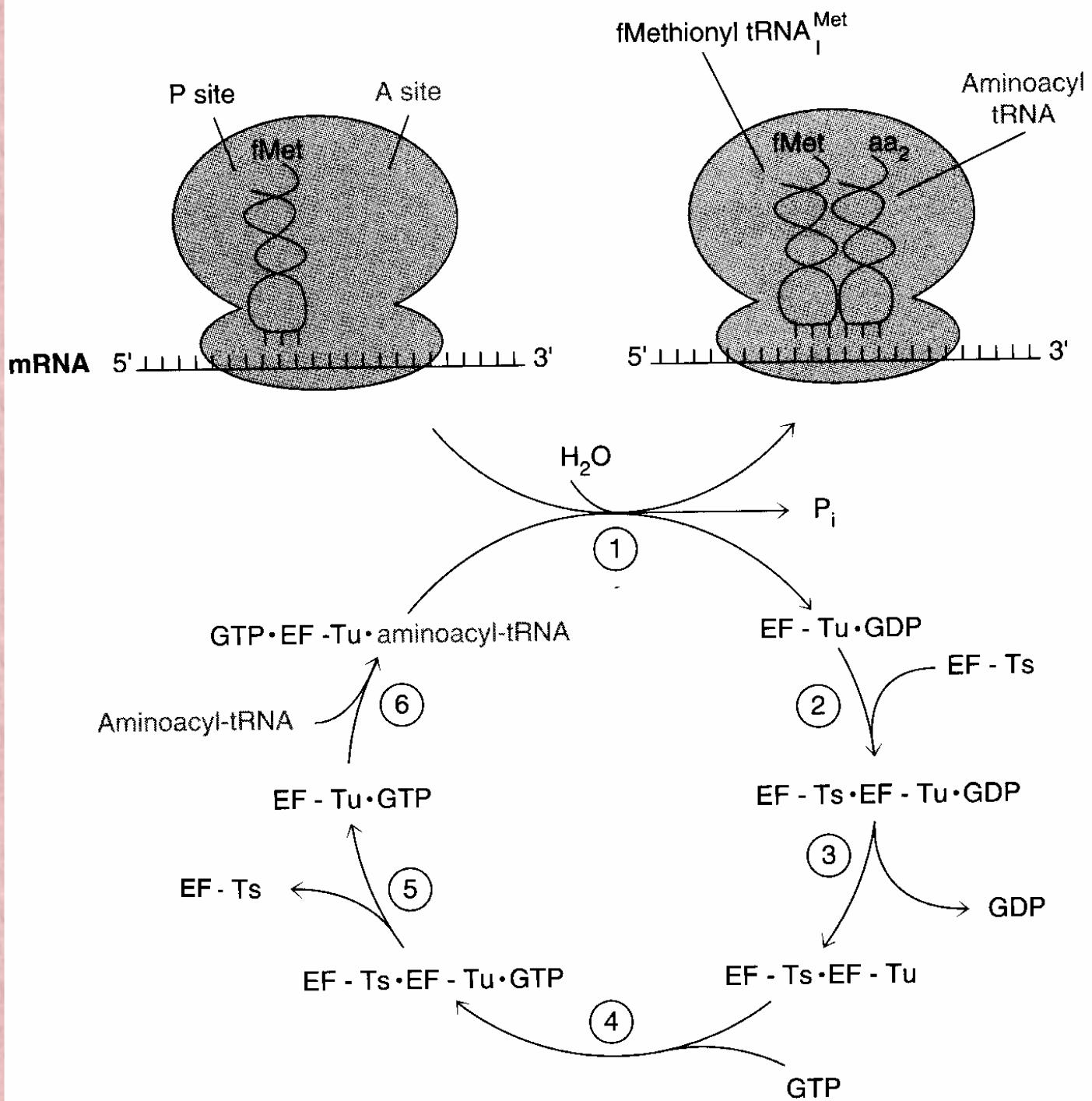
***stable; displaces GDP***

**EF-G**

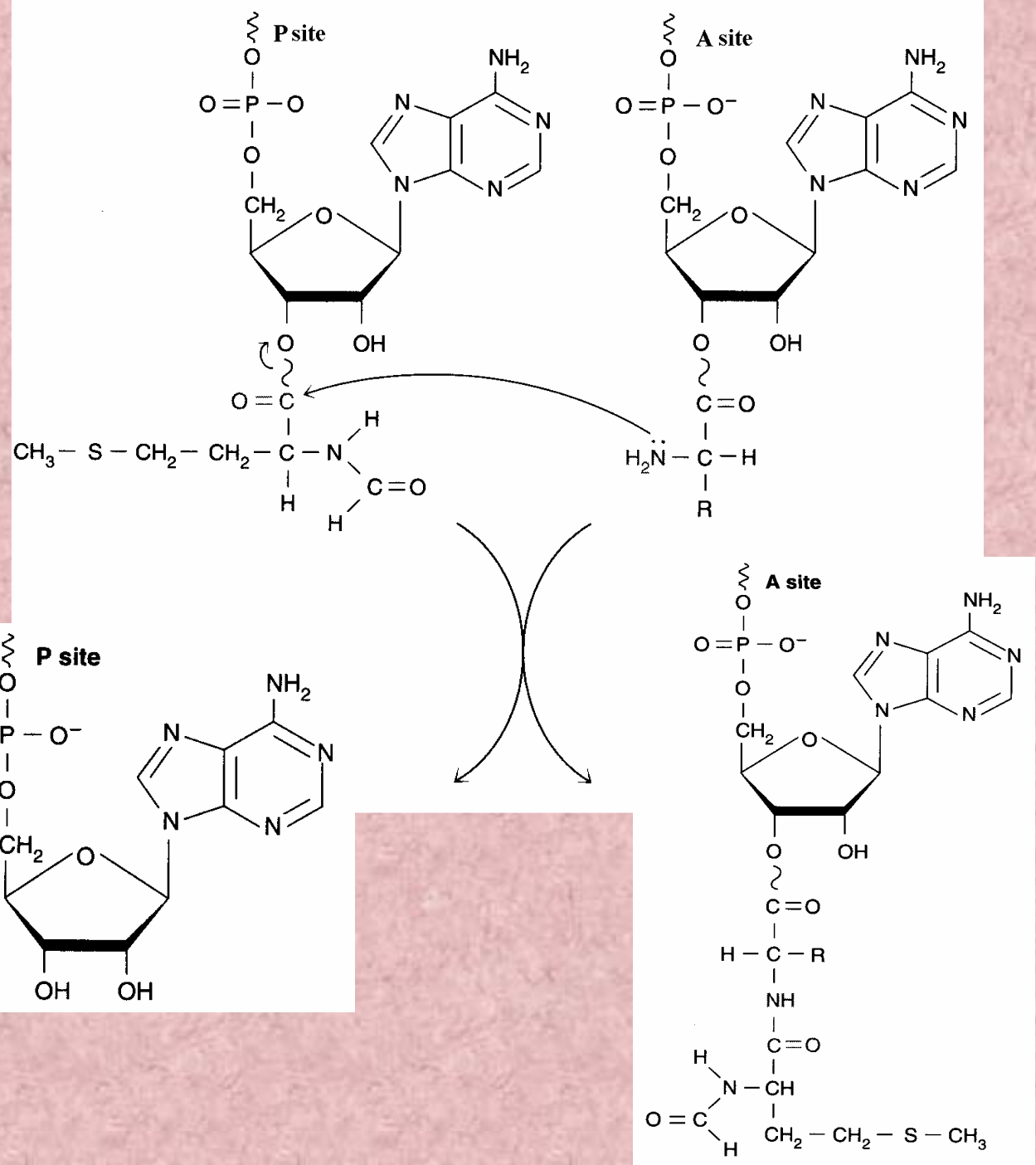
***GTPase; translocates mRNA along  
Ribosome (Homologous to tRNA  
bound to EF-Tu)***

---

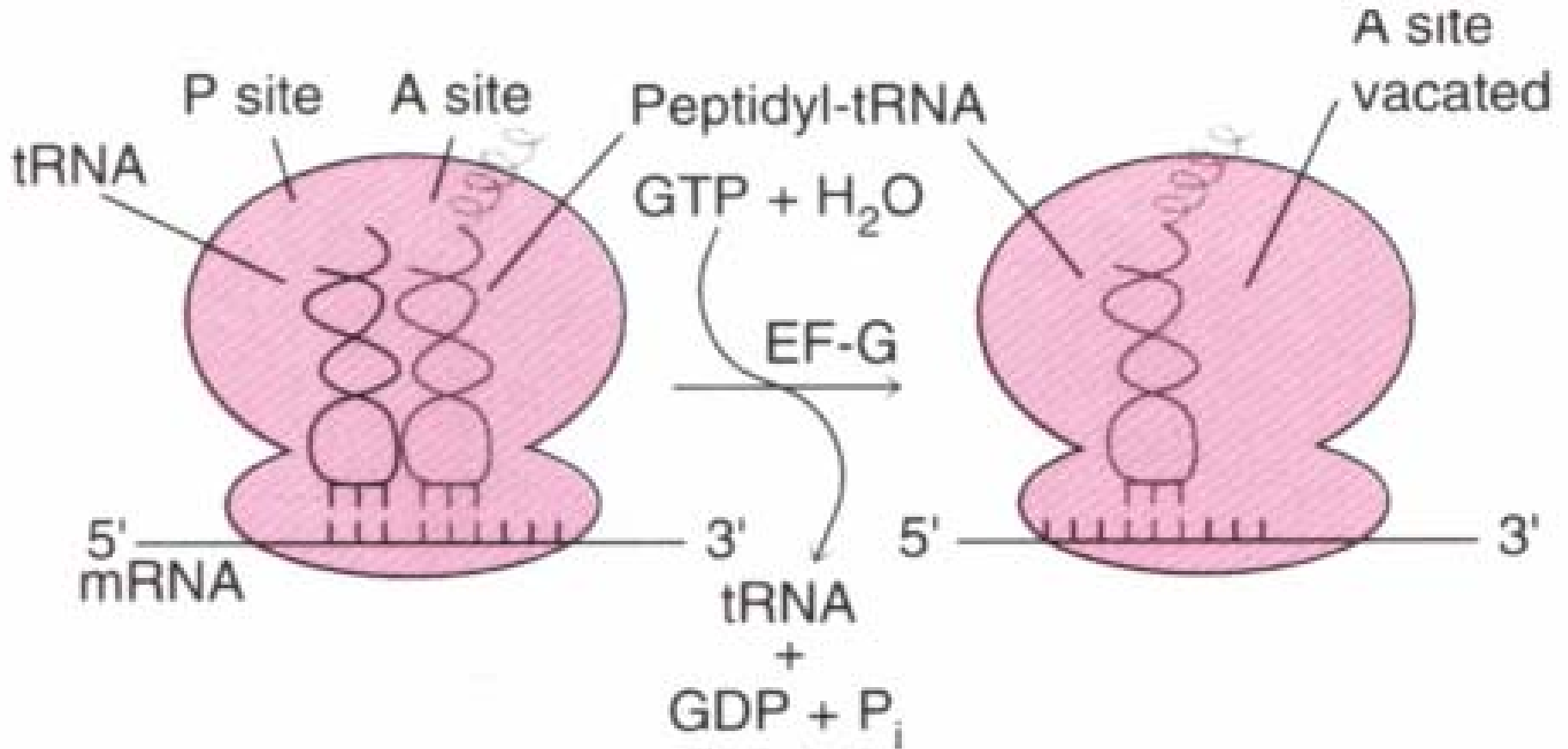
# Elongation



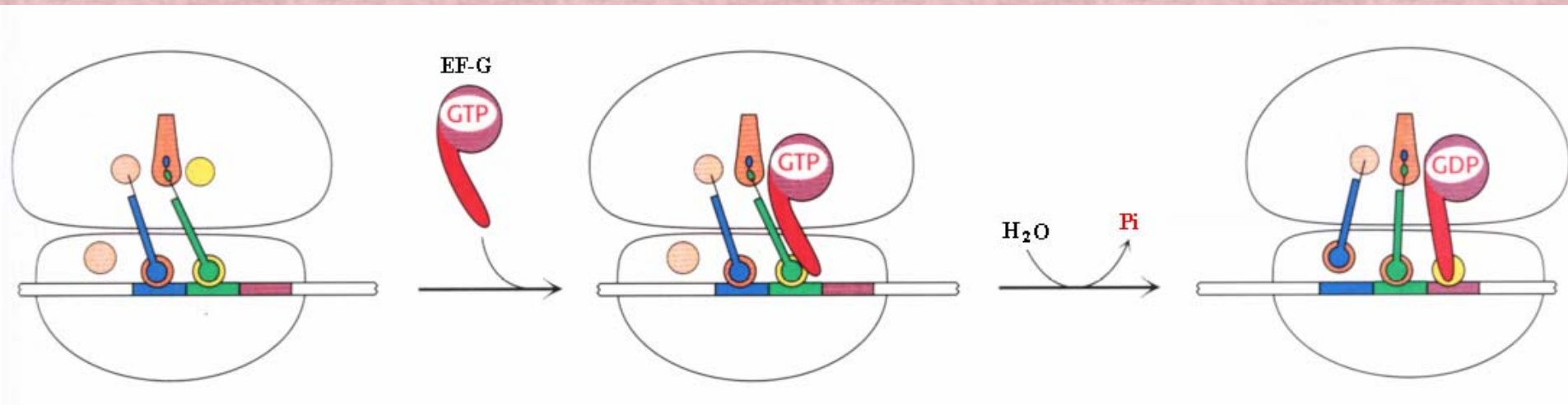
# Peptide bond formation



# Translocation

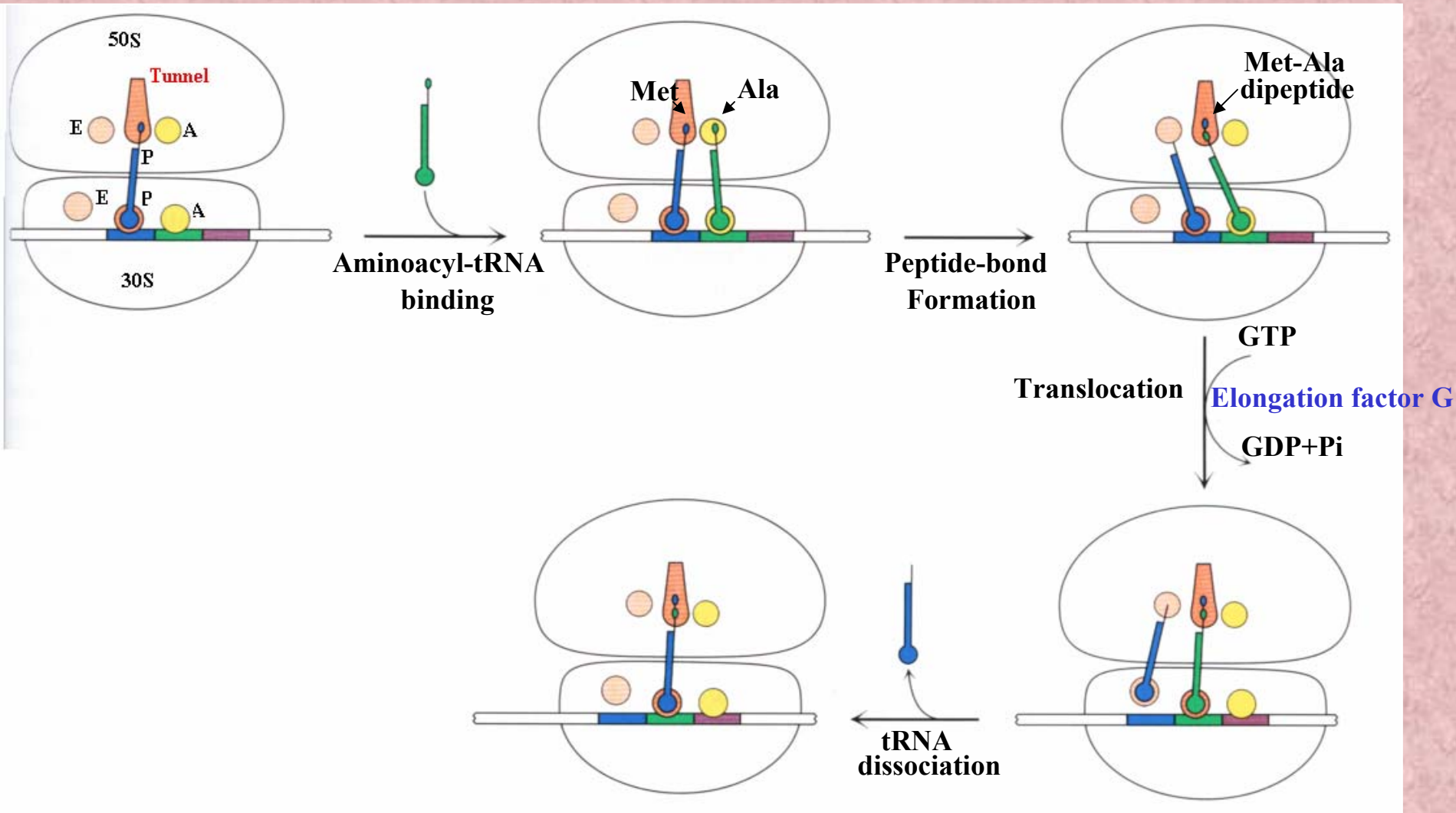


# Translocation Mechanism



**In the GTP form, EF-G binds to the EF-Tu binding site on the 50S subunit. This stimulates GTP hydrolysis, inducing a conformational change in EF-G, and driving the stem of EF-G into the A site on the 30S subunit. To accommodate this domain, the tRNAs and mRNA move through the ribosome by a distance corresponding to one codon.**

# Mechanism of Protein Synthesis



# Protein Synthesis Release Factors

---

**Factor**

**Function**

---

## •Release factors

**RF1**

**Recognizes UAA, UAG**

**RF2**

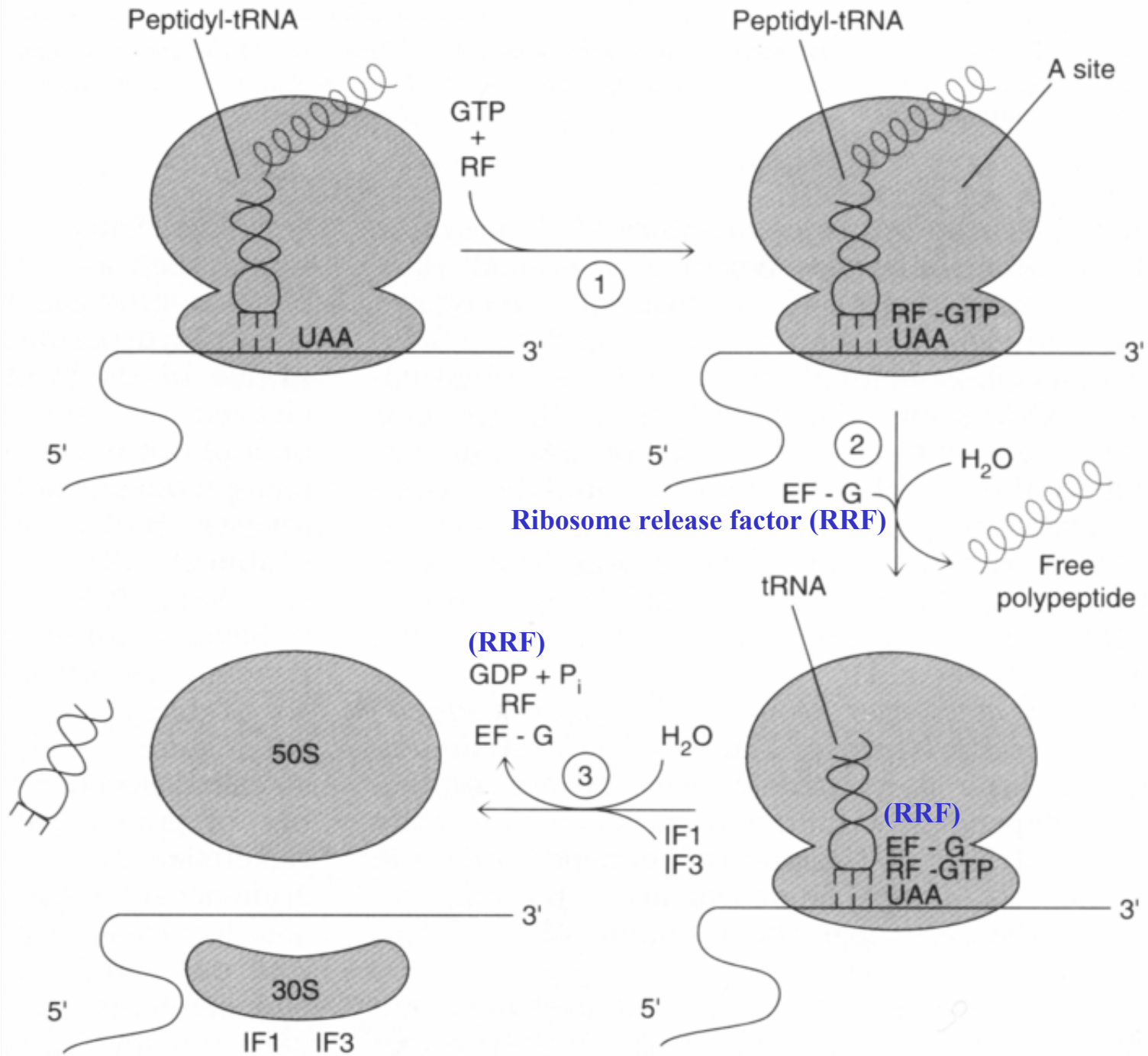
**Recognizes UAA, UGA**

**RF3**

**Binds GTP and interacts with RF1  
and RF2 (Homolog of EF-Tu)**

---

# Termination



# Protein Translation

## Components required for translation

- mRNA, Amino acids, tRNA, Aminoacyl-tRNA synthetases, Ribosomes & Protein factors

## Protein translation steps

- Initiation
- Elongation
- Termination

# Protein Translation

## Translation overview

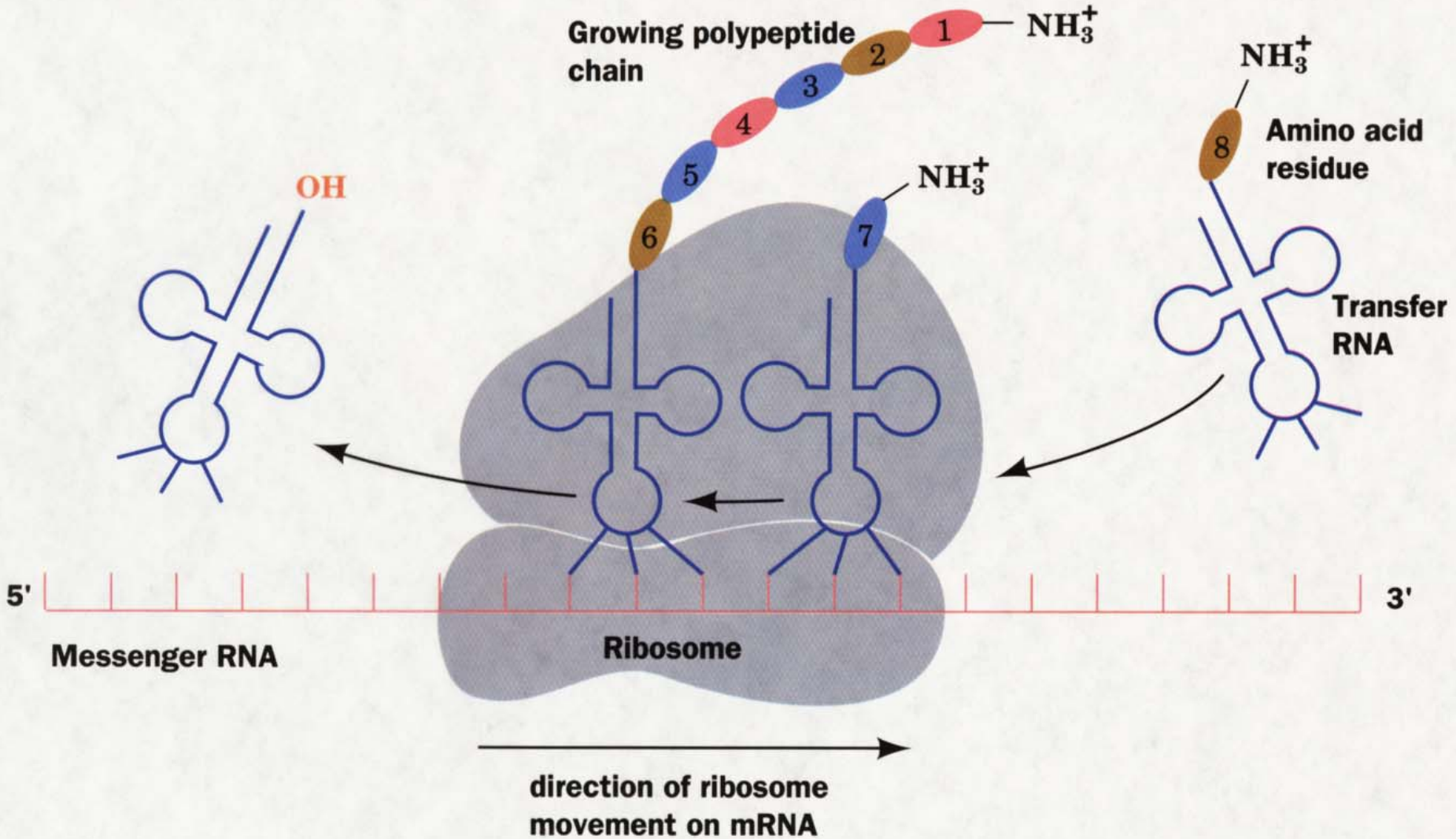
- Prokaryotes
- Eukaryotes

## Post-translational modifications

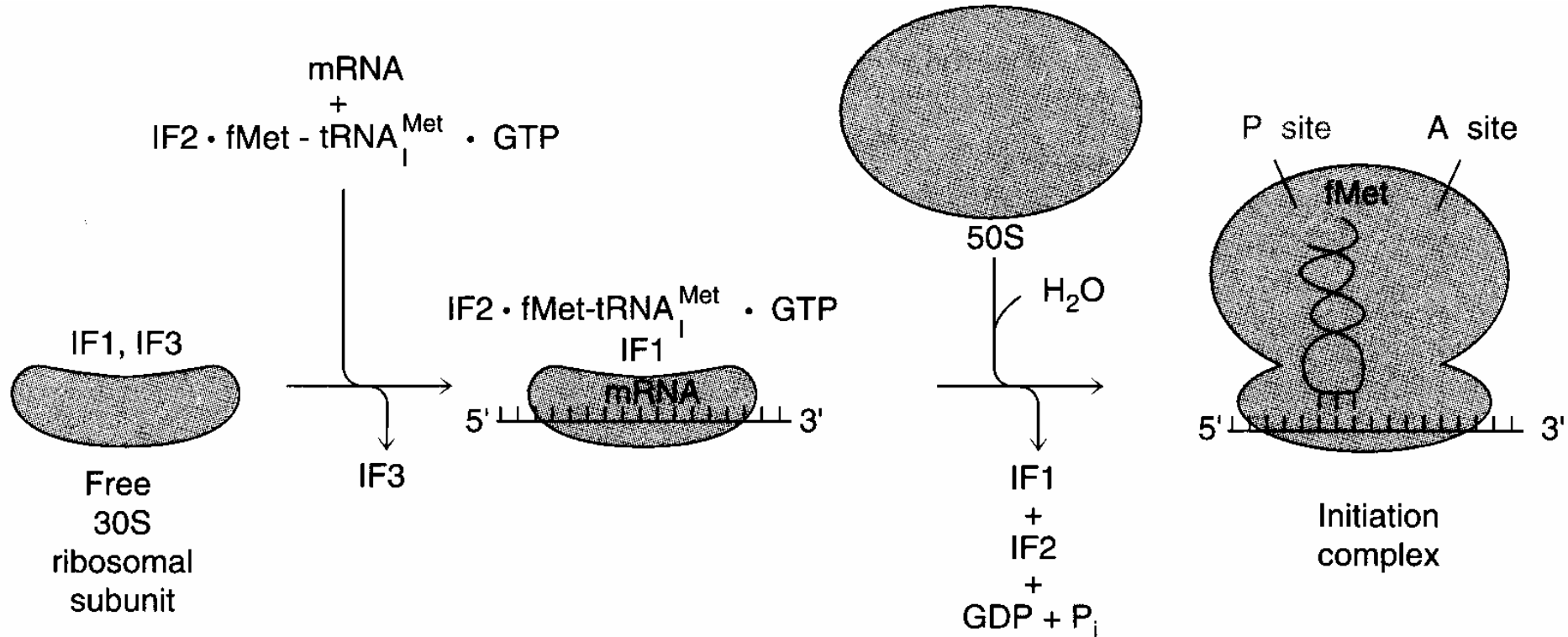
## Protein targeting

## Protein synthesis inhibition by Anti-biotics

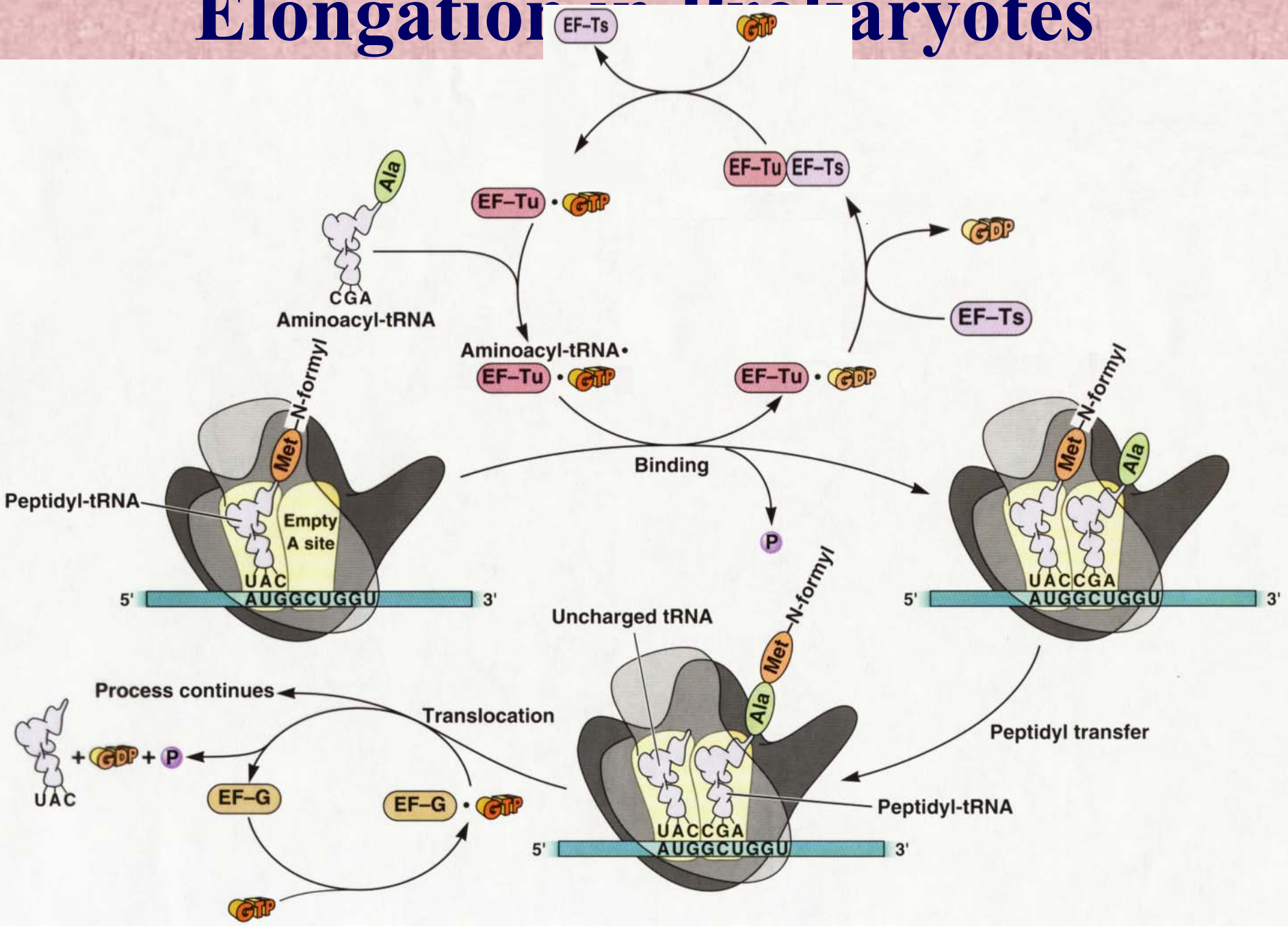
# Translation



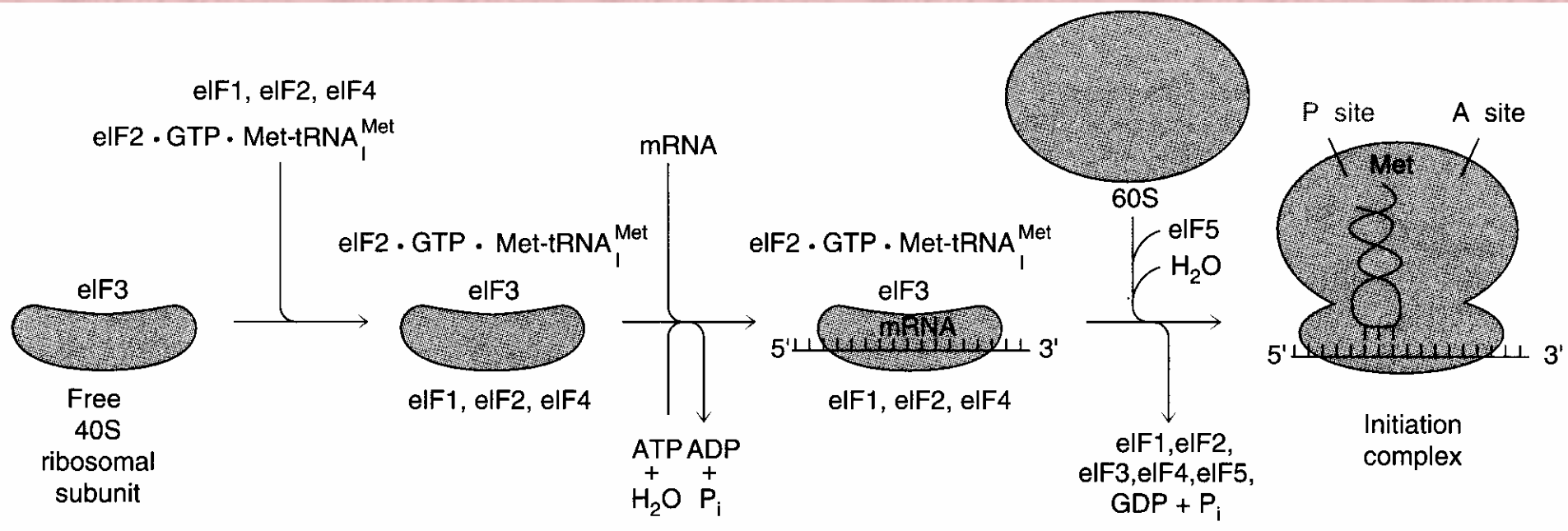
# Initiation in Prokaryotes



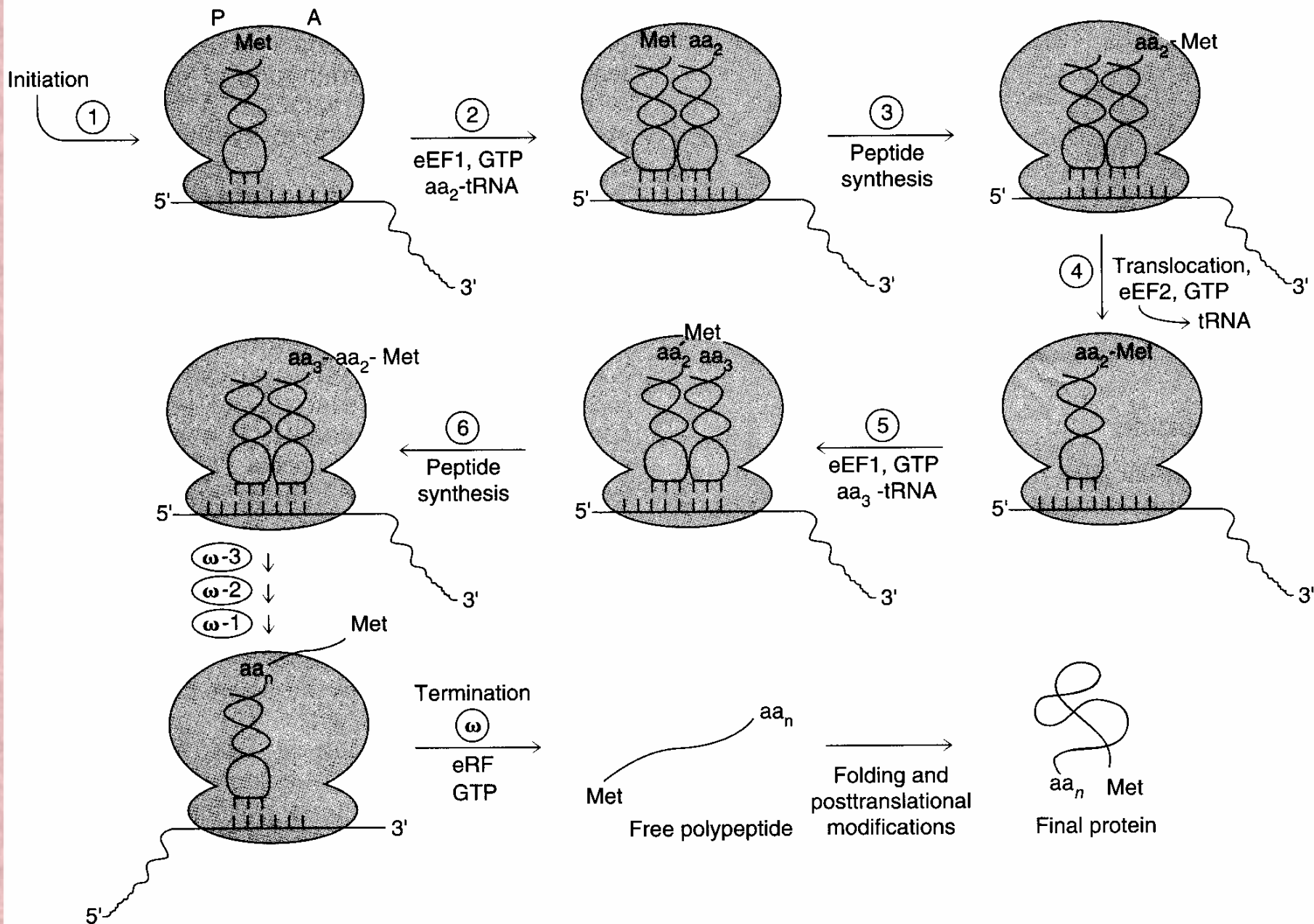
# Elongation in Prokaryotes



# Initiation in Eukaryotes



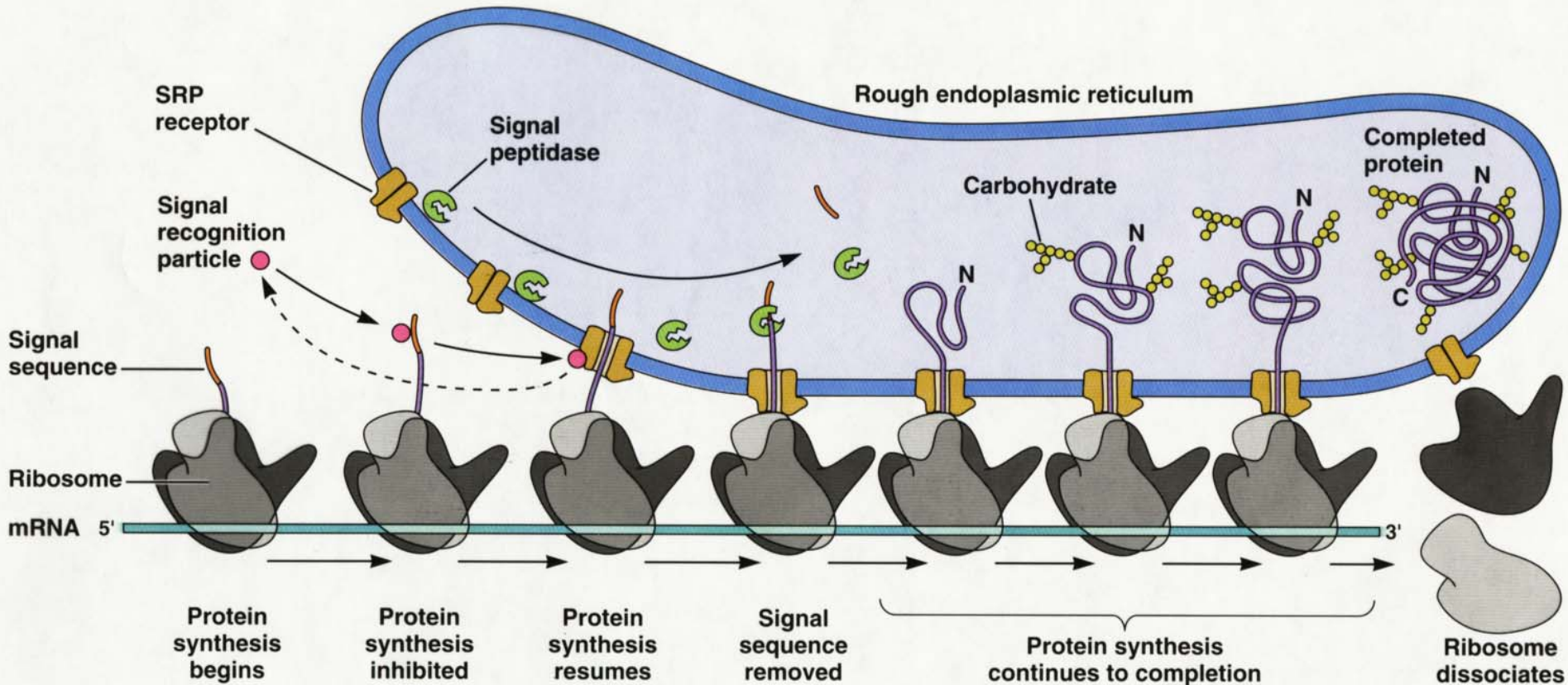
# Protein Synthesis in Eukaryotes



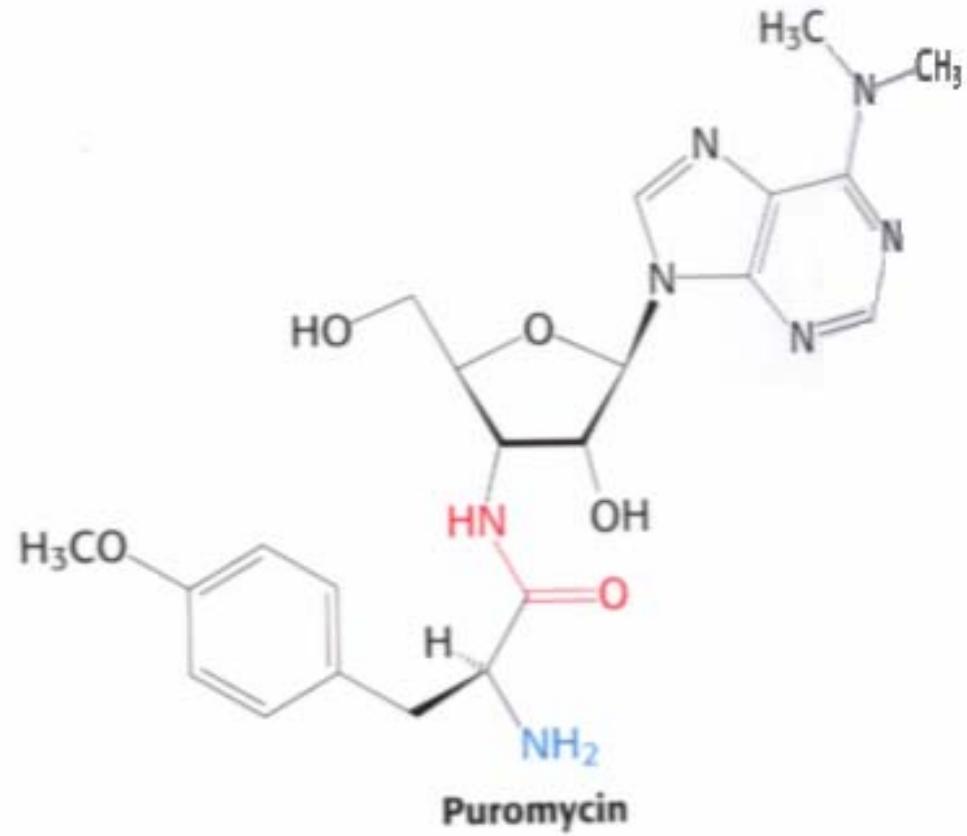
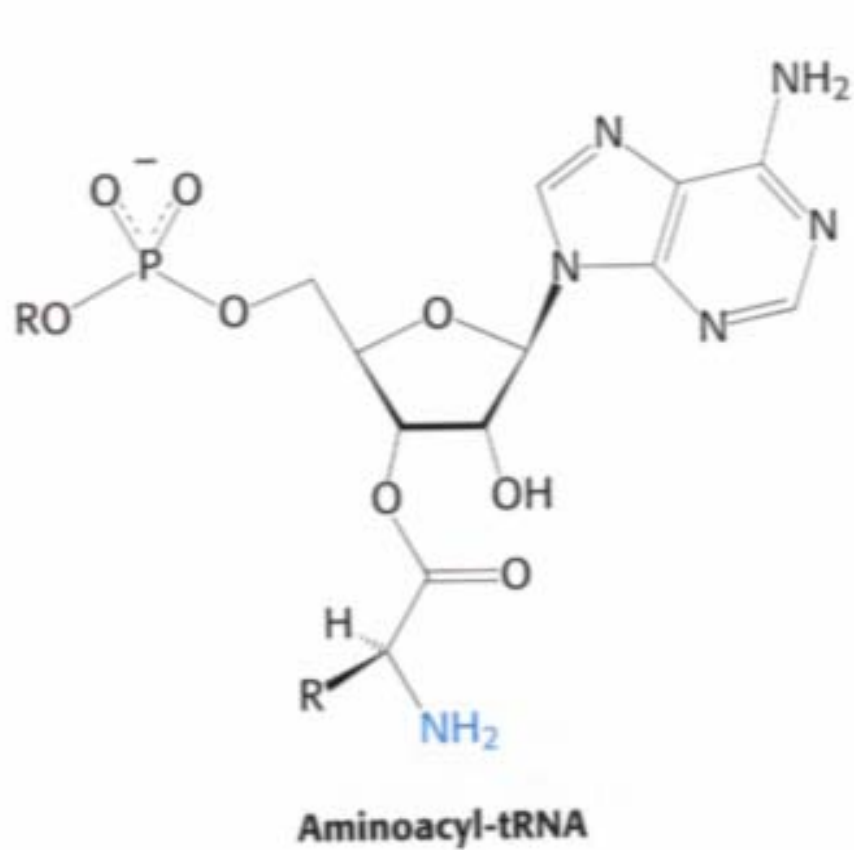
# Post-Translational Modification of Proteins

- Trimming
  - Zymogens
- Covalent alterations
  - Phosphorylation (Ser & Thr)
  - Hydroxylation (Pro & Lys)
  - Glycosylation (Ser & Thr----O linked  
Asn----N linked)

# Protein targeting



# Antibiotic Action of Puromycin



# Bacterial Protein Synthesis Inhibition by Antibiotics

Antibiotic	Mechanism
<b>Aminoglycoside</b> (streptomycin, gentamycin)	<b>Inhibits initiation;</b> <b>produces translation</b> <b>errors</b>
<b>Chloramphenicol</b>	<b>Inhibits</b> <b>peptidyltransferase activity</b>
<b>Erythromycin &amp; Fusidic acid</b>	<b>Inhibit translocation</b>
<b>Tetracycline</b>	<b>Inhibits aminoacyl-tRNA</b> <b>binding to the A site</b>
<b>Cycloheximide</b>	<b>Inhibits peptidyltransferase</b> <b>activity</b>
<b>Puromycin</b>	<b>Aminoacyl-tRNA analog</b> <b>causes premature chain</b> <b>termination</b>