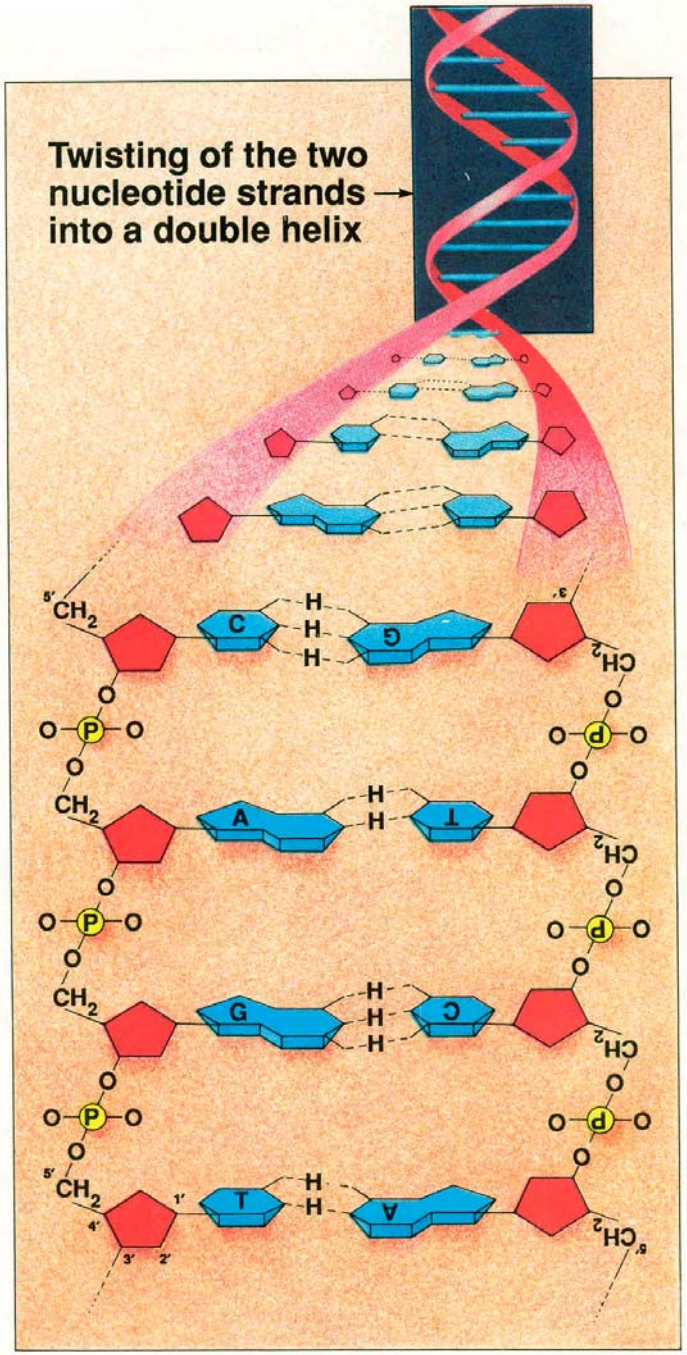
Cracking the genetic code

- Draw from the board

Genetic code

- The code is a language
- A Codon is a nucleotide triplet (like CAG)
- Codons specify particular amino acids (CAG specifies glutamine)



Genetic code

- There are 64 possible codons (4^3), but only 20 amino acids.
- The Genetic code is redundant

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

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

Translation

Ribosomes synthesize a polypeptide according to the genetic instructions in mRNA.

•tRNAs are adaptors that help the ribosome to translate genetic information into protein

The tRNA has an anti-codon that can base-pair with the codon in mRNA.

tRNAs are coupled to their appropriate amino acid

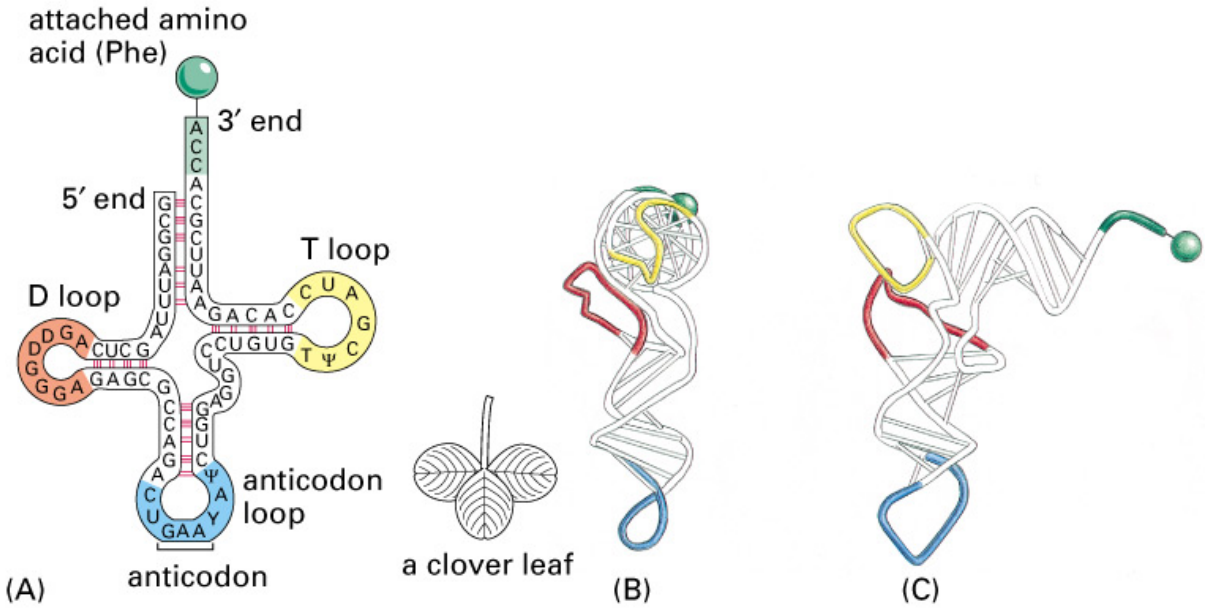
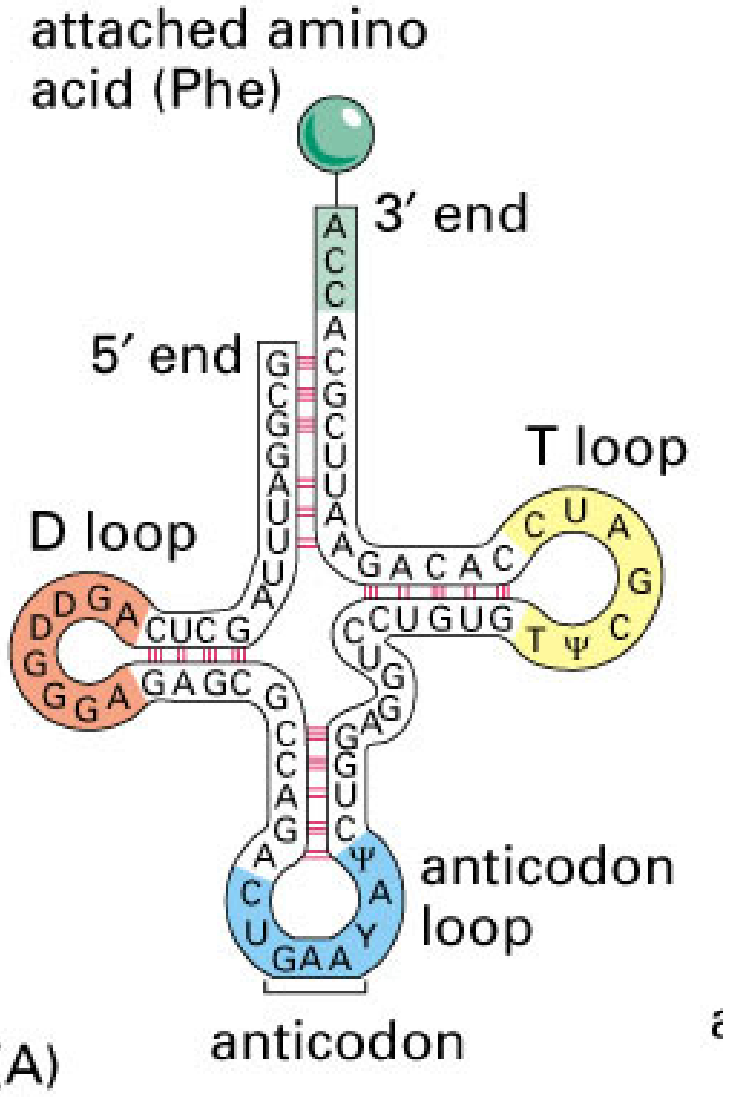


Figure 6–52. Molecular Biology of the Cell, 4th Edition.

tRNAs are coupled to their appropriate amino acid

- Binding of the amino acid is always to the 3’ terminal adenine of the tRNA
- A tRNA with a bound amino acid is “charged” and competent for translation



Aminoacyl-tRNA synthetases

- Synthetases catalyze the addition of amino acids to tRNA
- ATP energy is required
- There are 20 synthetases, one for each amino acid

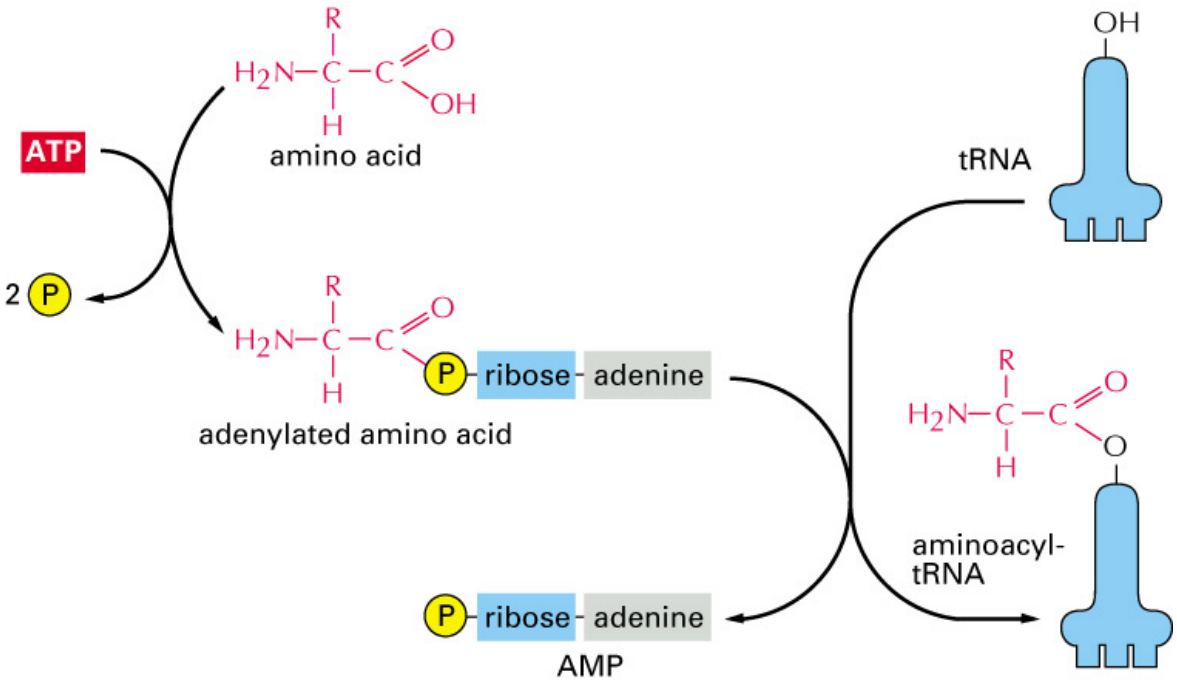


Figure 6–56. Molecular Biology of the Cell, 4th Edition.

The specificity of the tRNA-aminoacyl synthetases and of codon-anticodon basepairing is essential to the high fidelity of translation

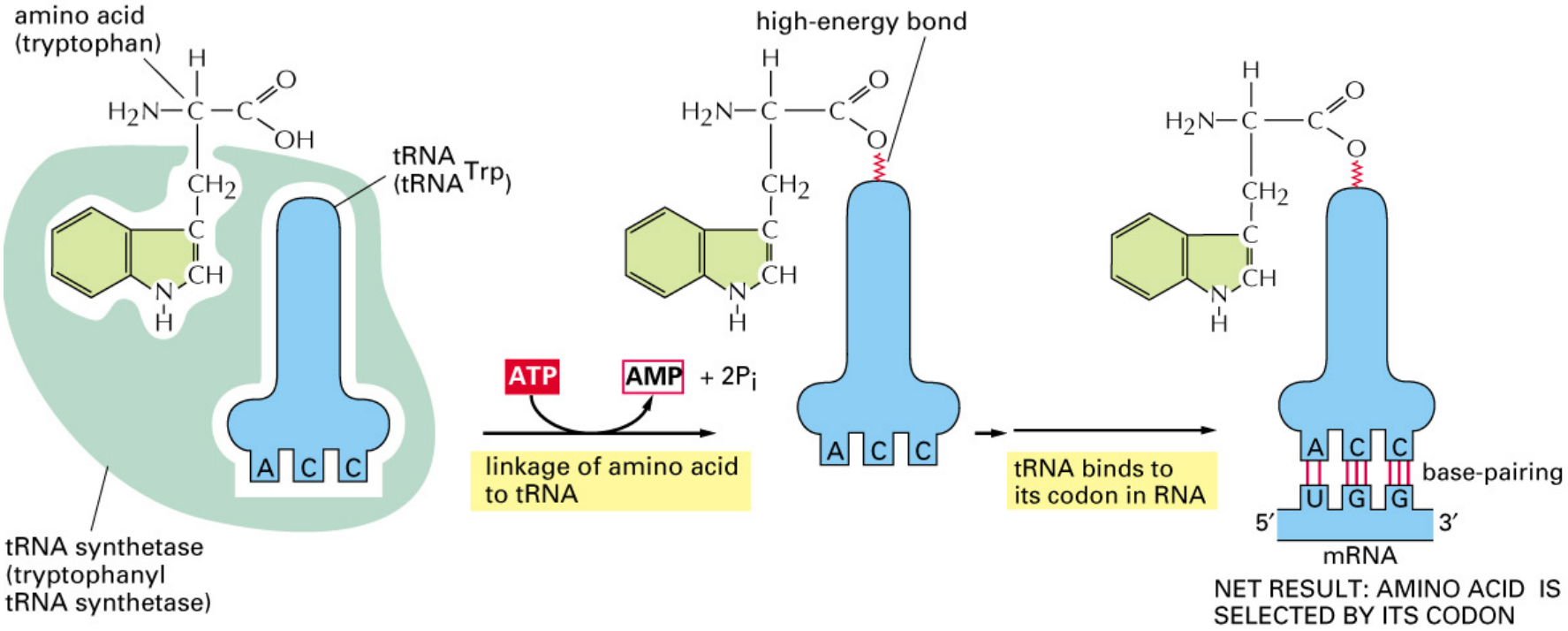


Figure 6–58 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

Figure 6–58 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

Ribosomes are composed of rRNA and proteins, and exist as 2 subunits

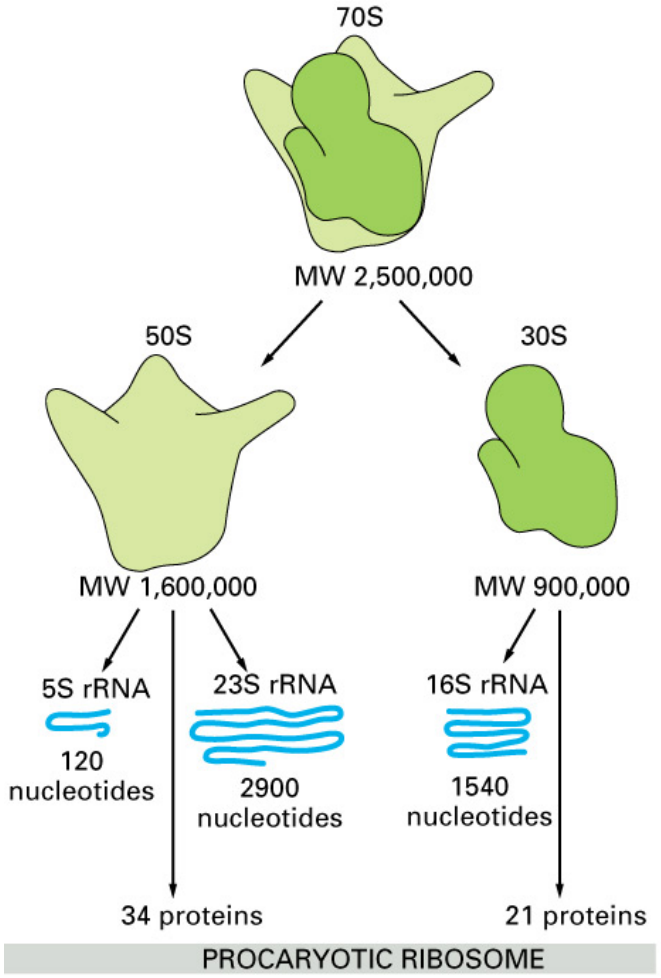


Figure 6–63 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

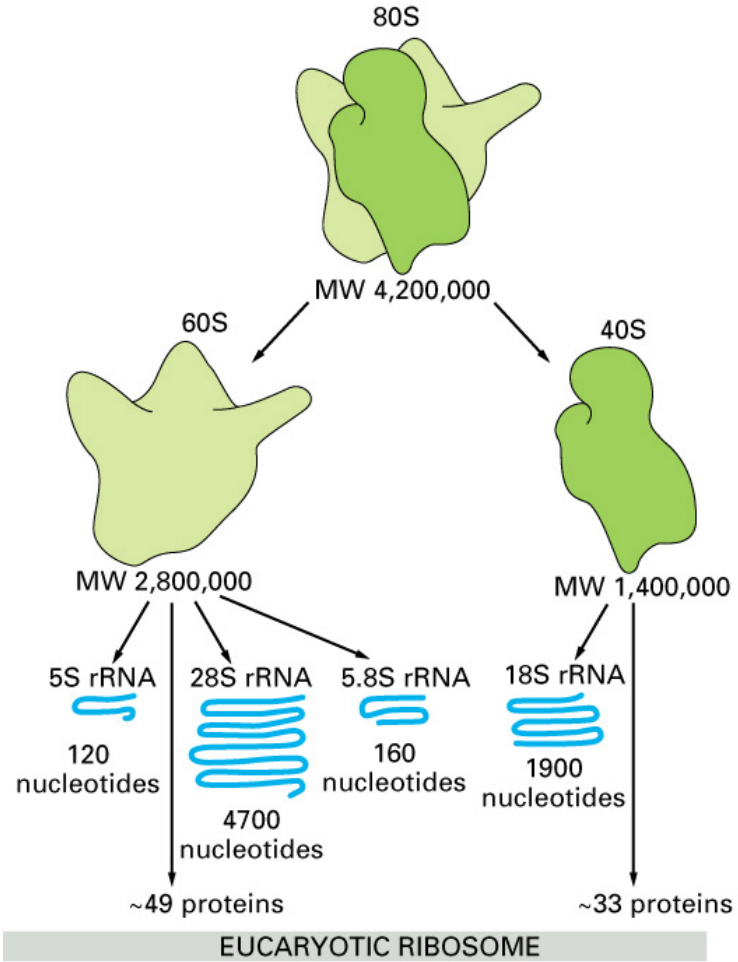


Figure 6–63 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

The complex secondary structure of rRNA forms the structural core of the ribosome.

rRNA has catalytic activity (peptidyl transferase), thus the ribosome is a ribozyme (RNA enzyme)

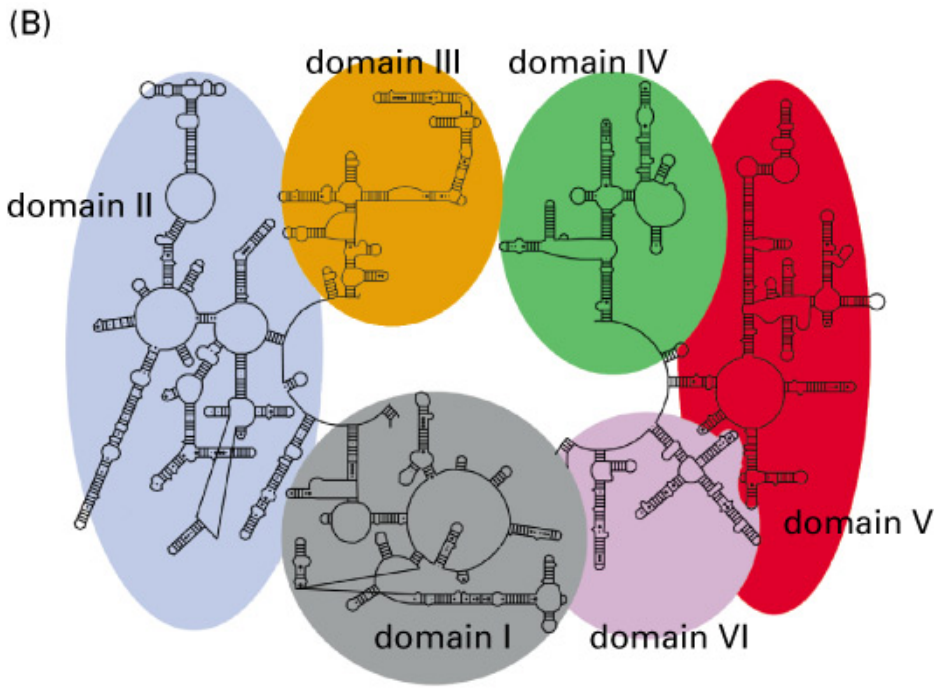


Figure 6–67 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

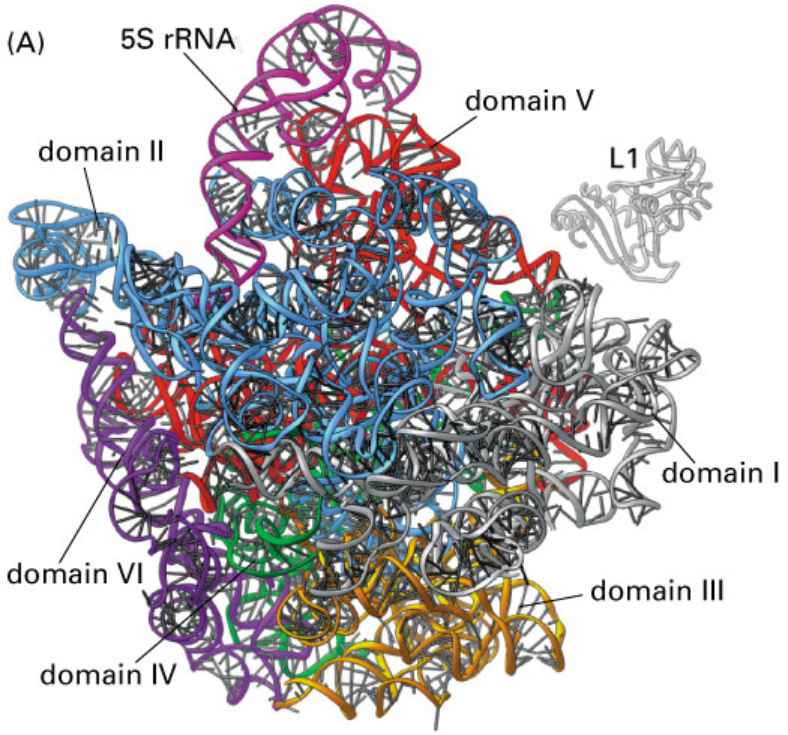
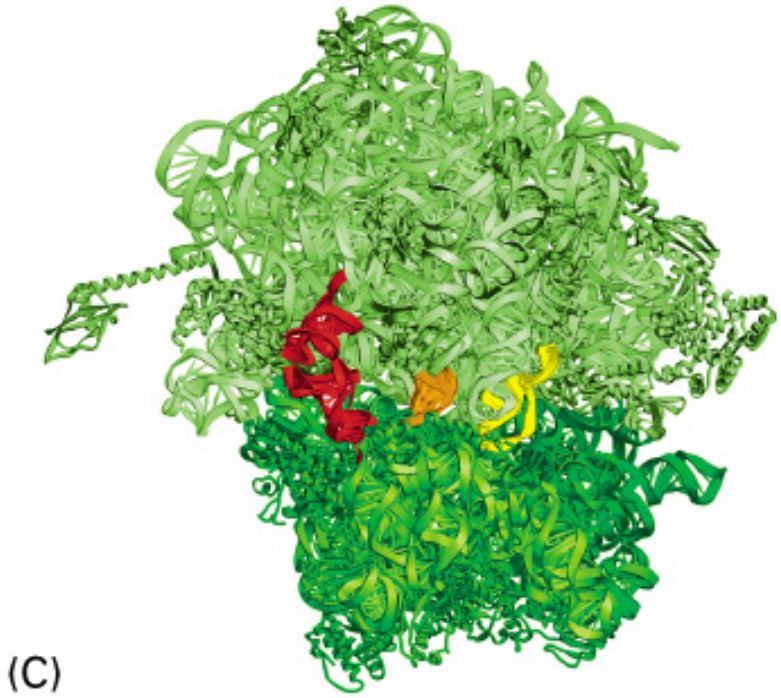


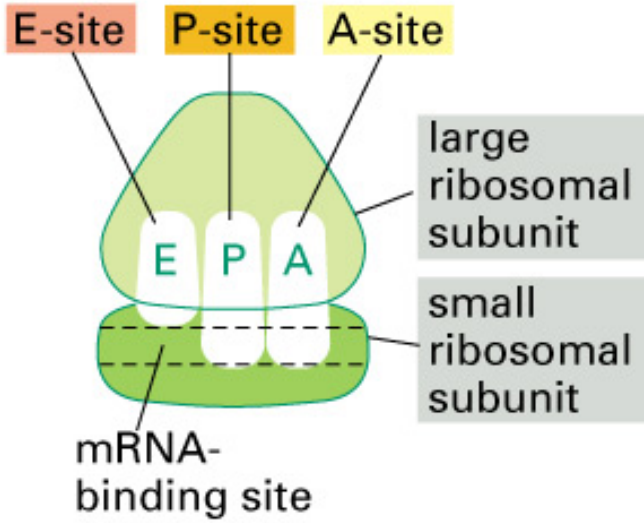
Figure 6–67 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

The Ribosome has 4 RNA binding sites

- A = aminoacyl-tRNA site
- P = peptidyl-tRNA site
- E = exit site
- mRNA binding site



(C)



(D)

Figure 6–64 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

Translation occurs in 3 steps

1. Initiation
    - Ribosome binds to mRNA and initiates at an AUG (methionine) codon

2. Elongation
    - The polypeptide is lengthened one amino acid at a time

3. Termination
    - Synthesis of the polypeptide terminates and the ribosome dissociates from the mRNA and the polypeptide

Reading Frames in mRNA

- mRNAs have three possible “reading frames”, but only one frame encodes the correct polypeptide.
- Translation initiation mechanisms ensure use of the correct frame.

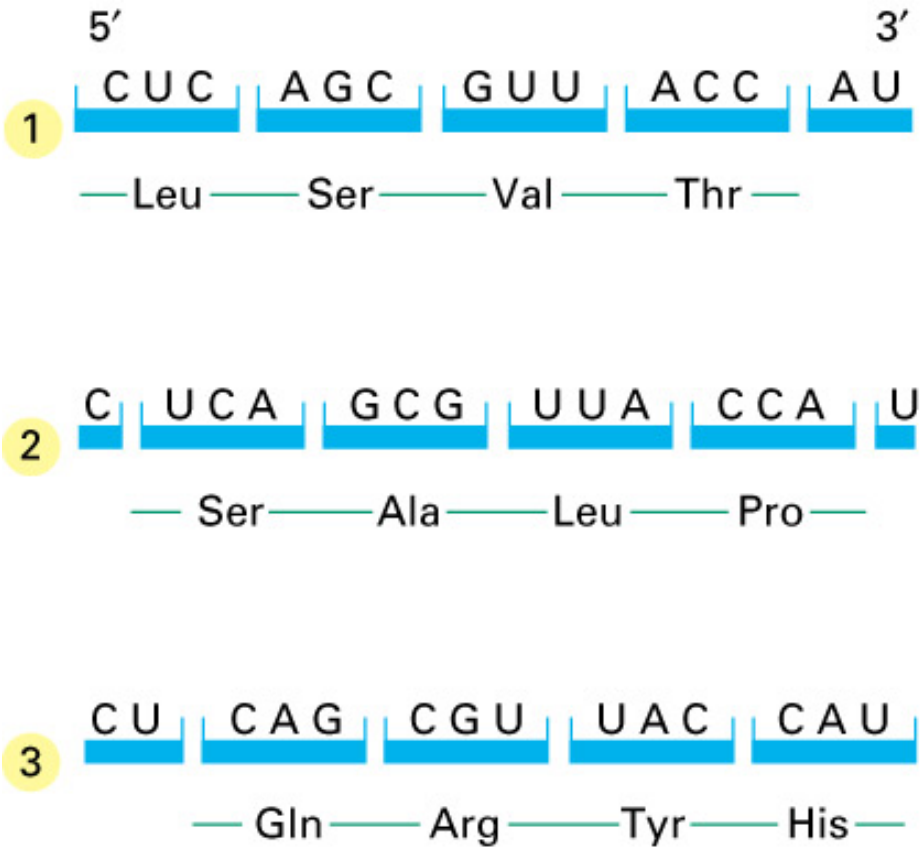
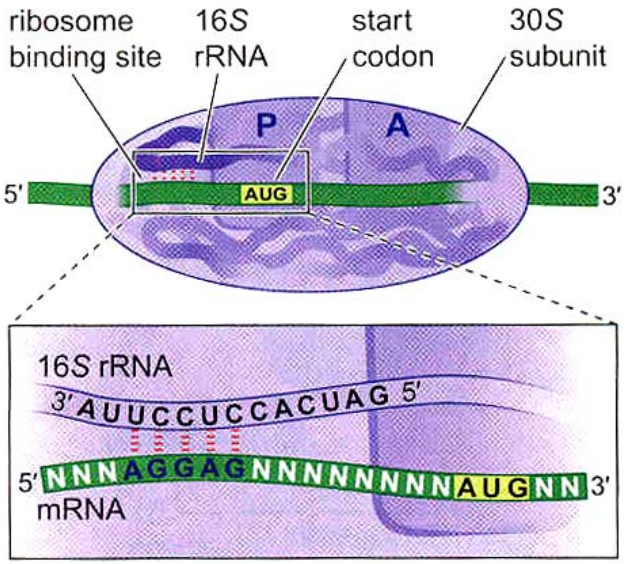


Figure 6–51. Molecular Biology of the Cell, 4th Edition.

Translation

- Draw the process of Translation from the blackboard. This drawing can be related to the text on the following pages.

Translation Initiation in Prokaryotes



The initiator tRNA binds to the small ribosomal subunit (30S)

This initiation complex binds to the mRNA at the Shine-Delgarno sequence, which base-pairs with the 16S rRNA and positions the ribosome at the correct AUG initiator codon.

The Large ribosomal subunit (50S) binds to form the functional 70S ribosome.
An incoming aminoacyl-tRNA binds to the A-site

- Peptidyl transferase catalyzes a peptide bond between the new amino acid and methionine while breaking the bond between methionine and the initiator-tRNA
- The ribosome translocates one codon toward the 3’ end of the mRNA.
- The initiator tRNA moves into the E site before exiting the ribosome.

Elongation of Translation

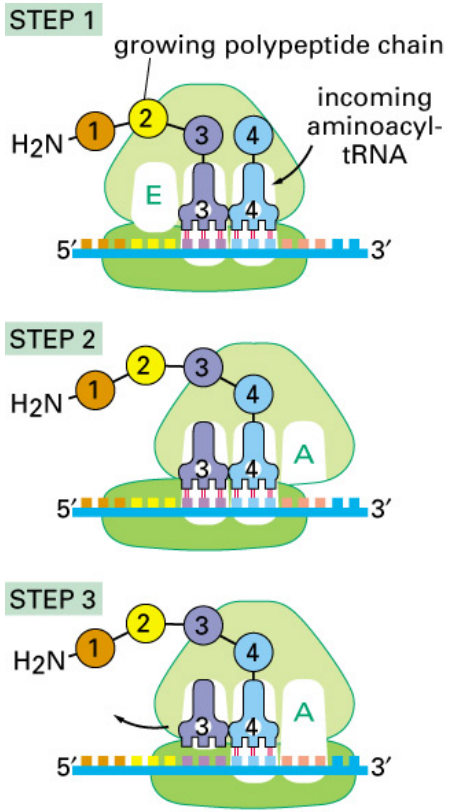
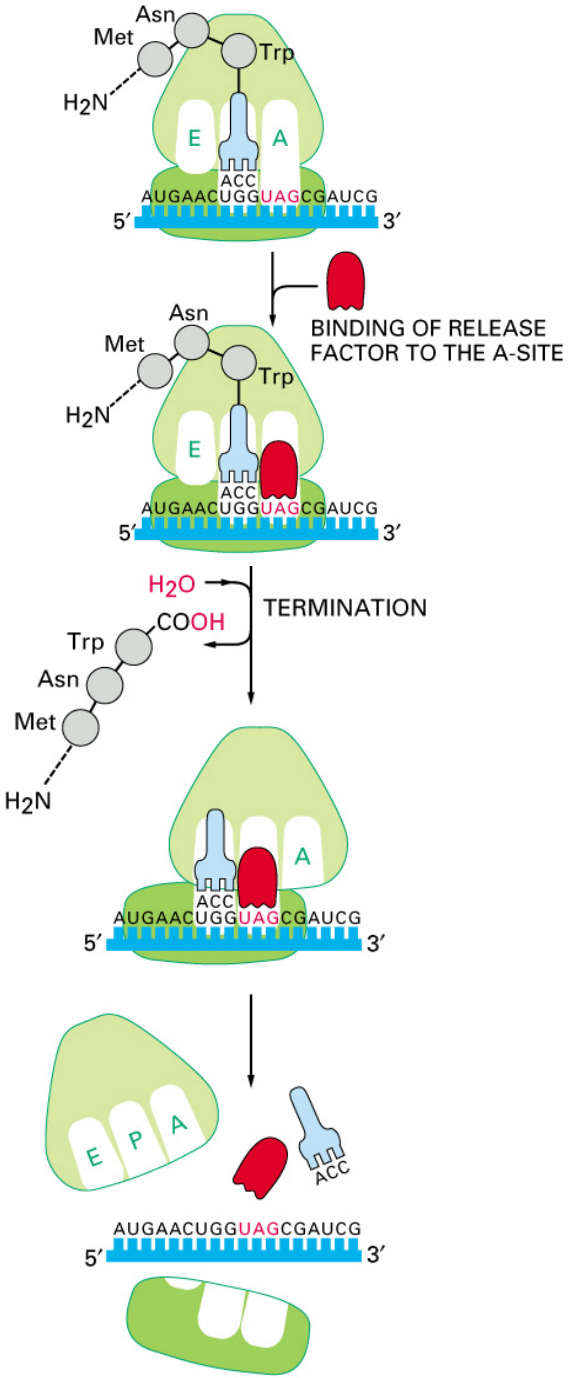


Figure 6–65 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

- The nascent (growing) polypeptide is bound to the peptidyl-tRNA in the P-site
- The incoming aminoacyl-tRNA binds to the A-site
- Peptidyl transferase catalyzes a peptide bond between the new amino acid and the nascent polypeptide and breaks the bond between the nascent chain and the peptidyl-tRNA
- The ribosome translocates by one codon along the mRNA toward the 3’ end
- The A site receives the next incoming aminoacyl-tRNA
- A peptide bound is formed and the cycle continues until termination

Termination of Translation



- Releasing factors bind to termination codons (UAG, UAA, UGA) in the A-site.
- Releasing factors facilitate hydrolysis of the nascent polypeptide from the peptidyl-tRNA thus freeing the polypeptide from the ribosome.
- Release of the polypeptide is followed by dissociation of the ribosomal subunits from the mRNA

Figure 6–73 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

Releasing factors are proteins that mimic the shape of tRNAs

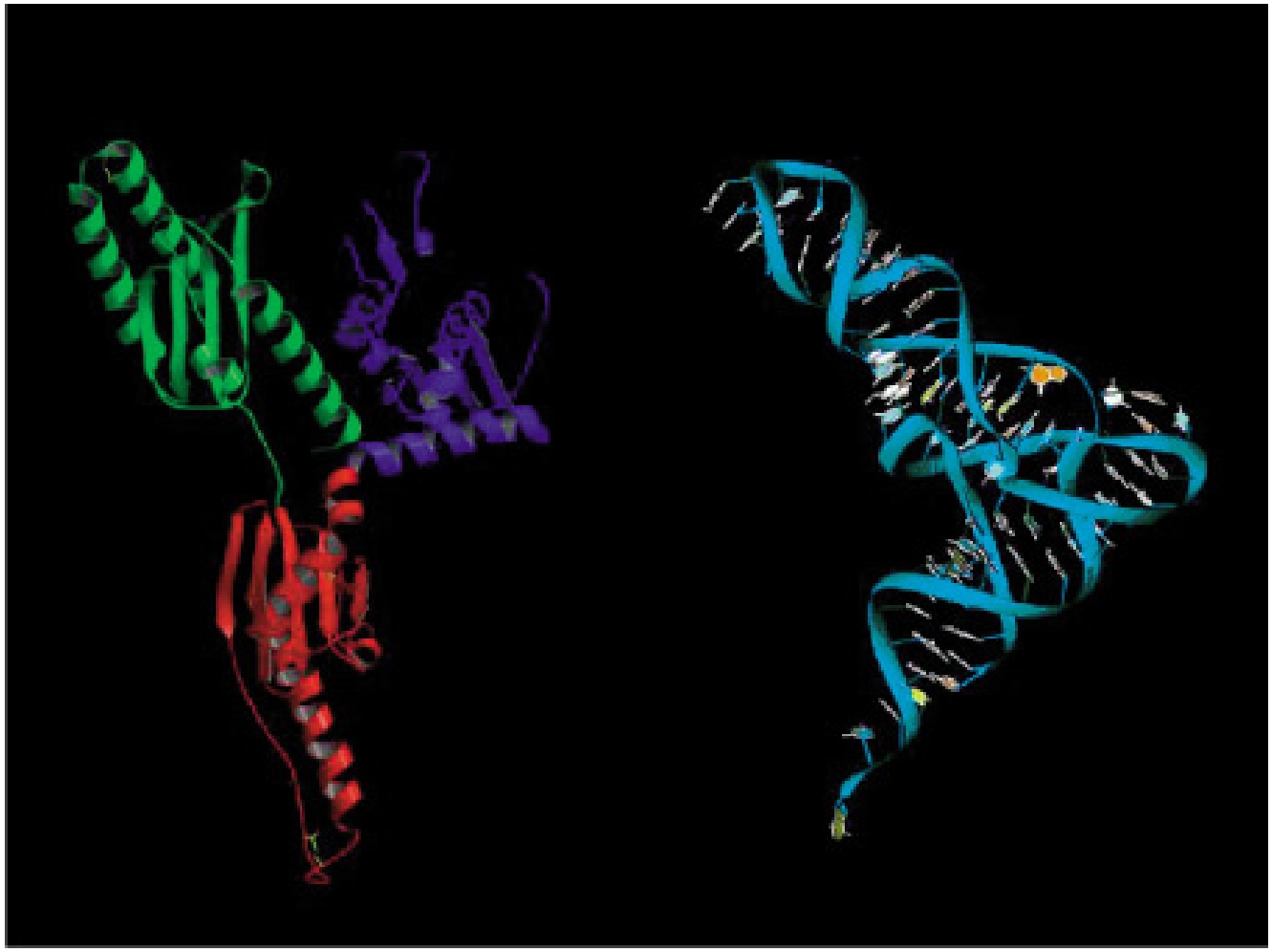


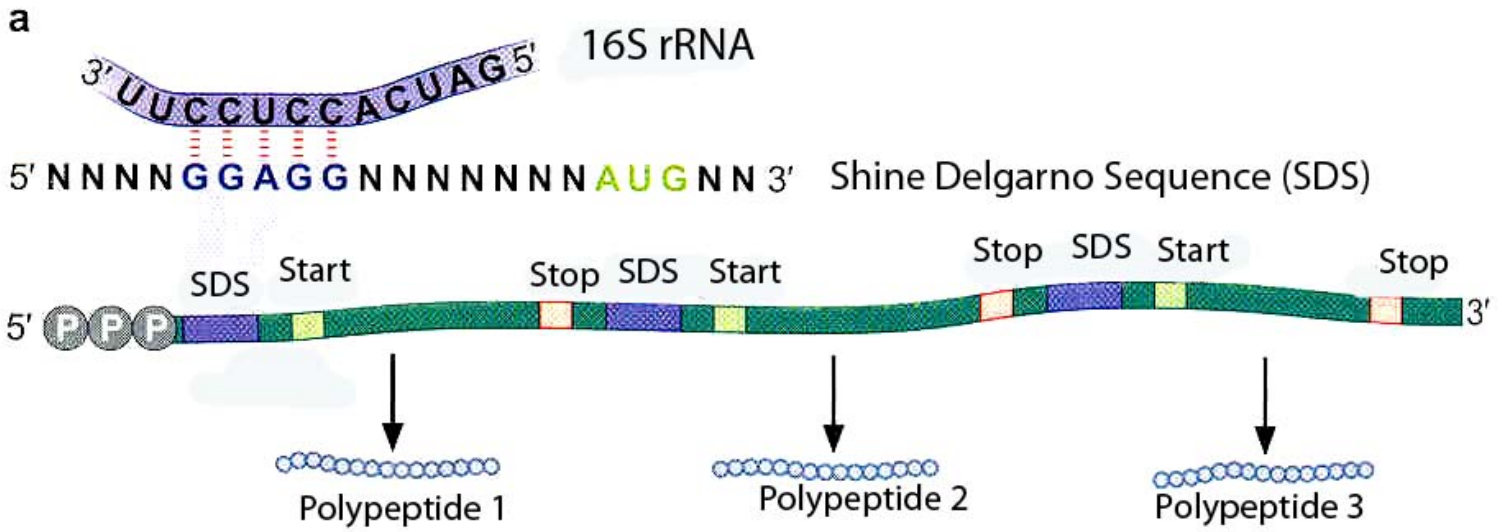
Figure 6–74. Molecular Biology of the Cell, 4th Edition.

Mono Vs Polycistronic mRNAs

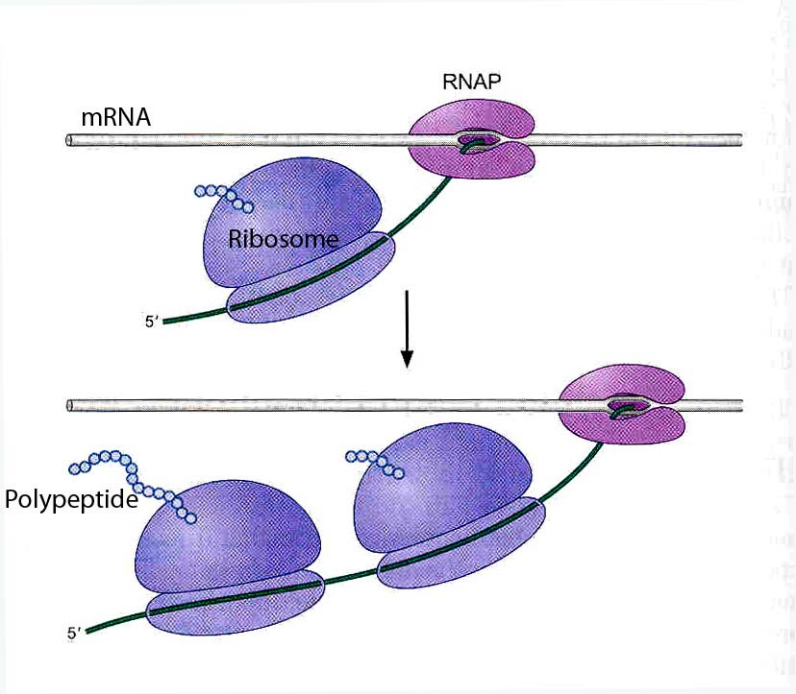
- In prokaryotes, ribosomes bind internally on the mRNA and a single mRNA may be polycistronic (encoding multiple polypeptide)

Polycistronic mRNA code for several different polypeptides

- Prokaryotic ribosomes bind internally on mRNA at Shine Delgarno Sequences (SDS).
- One mRNA may contain several coding regions (cistrons) for distinct polypeptides. Each cistron is preceded by a SDS.
- Such mRNAs are termed polycistronic



Transcription and Translation are coupled in Prokaryotes



- Prokaryotes lack a nucleus, therefore there is no physical separation of DNA from ribosomes.
- As soon as mRNA is produced by RNA polymerase it is bound by ribosomes and translation begins.
- In this manner, transcription and translation occur simultaneously.