

Central dogma of molecular biology : a process of decoding

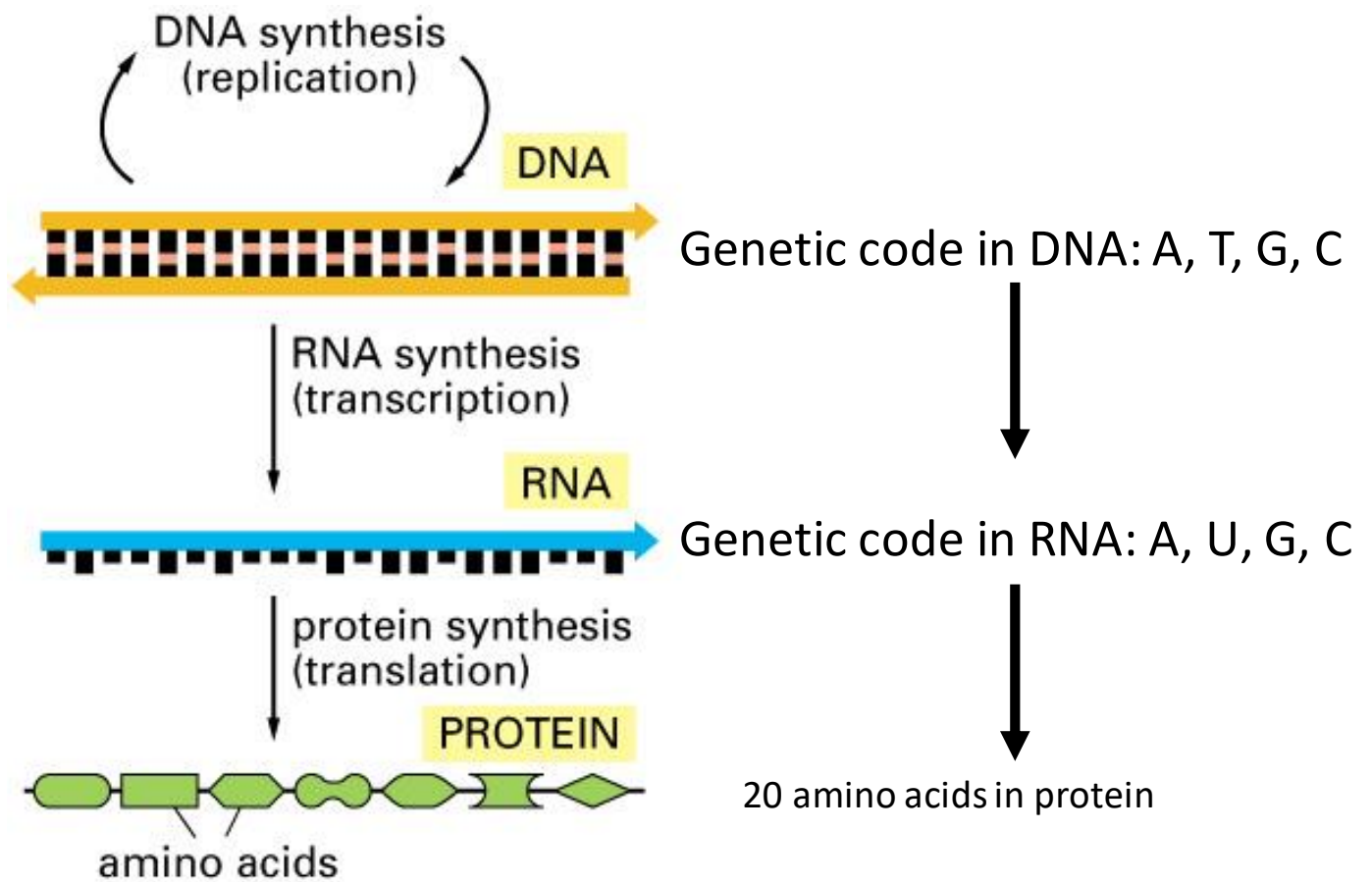


Figure 1-4. Molecular Biology of the Cell, 4th Edition.

DNA (genetic code)



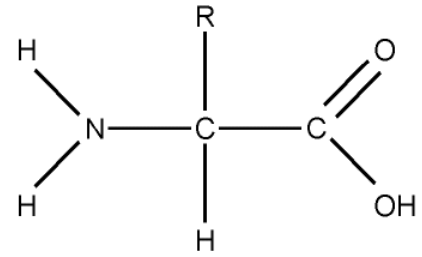
Gene expression

(Expression of information)

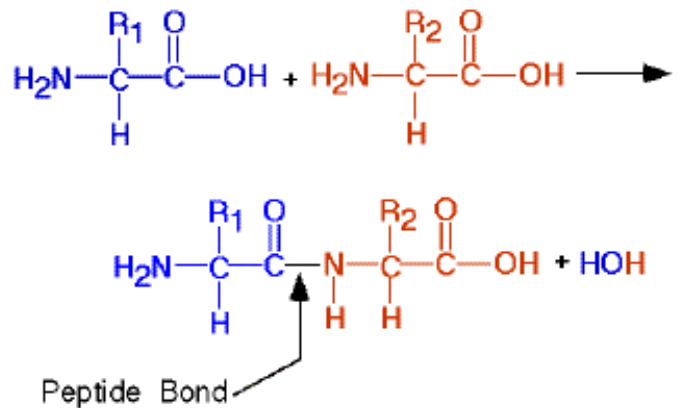
**To make a unique protein with a
specific amino acid sequence through
transcription and translation**

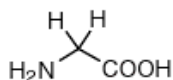
Amino Acids and Peptide Bonds

- There are 20 different amino acids coded in DNA.
- They all have an amino group (-NH_2) group on one end, and an acid group (-COOH) on the other end. Attached to the central carbon is an R group, which differs for each of the different amino acids.
- When polypeptides are synthesized, the acid group of one amino acid is attached to the amino group of the next amino acid, forming a peptide bond.

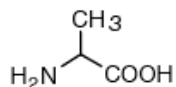


Peptide Bond Formation

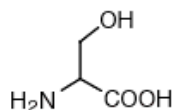


Small

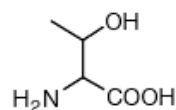
Glycine (Gly, G)
MW: 57.05



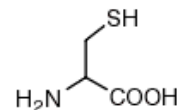
Alanine (Ala, A)
MW: 71.09



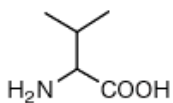
Serine (Ser, S)
MW: 87.08, pK_a ~ 16



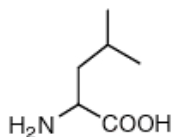
Threonine (Thr, T)
MW: 101.11, pK_a ~ 16



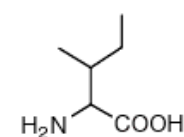
Cysteine (Cys, C)
MW: 103.15, pK_a = 8.35

Hydrophobic

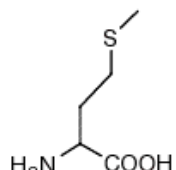
Valine (Val, V)
MW: 99.14



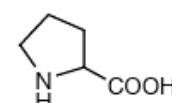
Leucine (Leu, L)
MW: 113.16



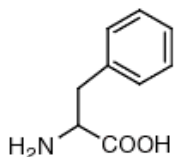
Isoleucine (Ile, I)
MW: 113.16



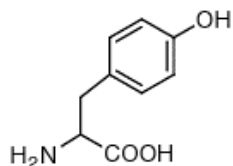
Methionine (Met, M)
MW: 131.19



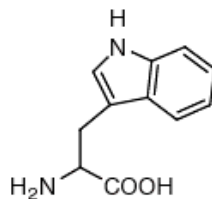
Proline (Pro, P)
MW: 97.12

Aromatic

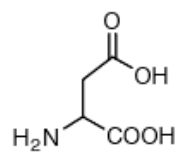
Phenylalanine (Phe, F)
MW: 147.18



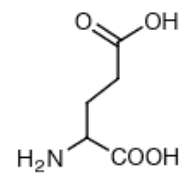
Tyrosine (Tyr, Y)
MW: 163.18



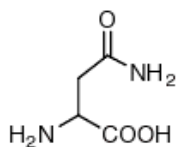
Tryptophan (Trp, W)
MW: 186.21

Acidic

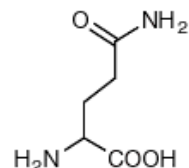
Aspartic Acid (Asp, D)
MW: 115.09, pK_a = 3.9



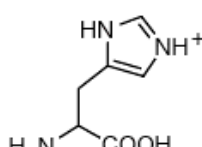
Glutamic Acid (Glu, E)
MW: 129.12, pK_a = 4.07

Amide

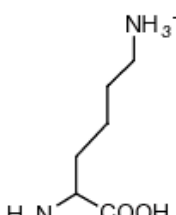
Asparagine (Asn, N)
MW: 114.11



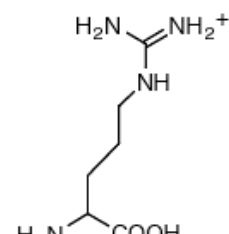
Glutamine (Gln, Q)
MW: 128.14

Basic

Histidine (His, H)
MW: 137.14, pK_a = 6.04



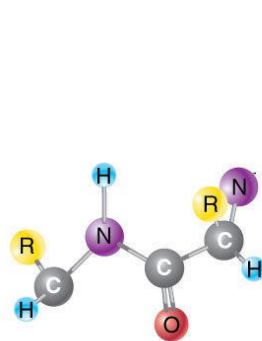
Lysine (Lys, K)
MW: 128.17, pK_a = 10.79



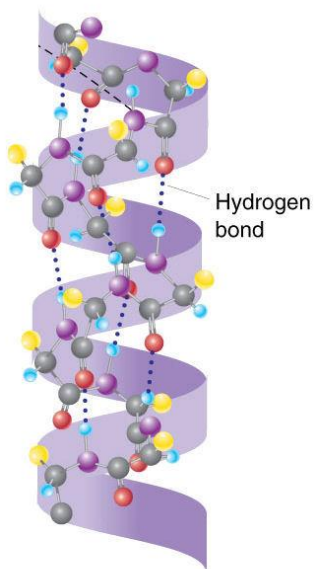
Arginine (Arg, R)
MW: 156.19, pK_a = 12.48

Protein

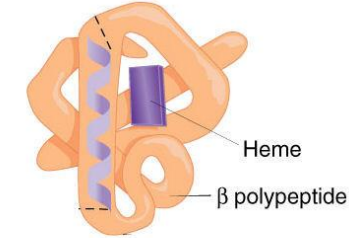
- Proteins (also known as polypeptides) are made of amino acids arranged in a linear chain and folded into a globular form.
- The sequence of amino acids in a protein is defined by the sequence of a gene, which is encoded in the genetic code.
- genetic code specifies 20 standard amino acids.



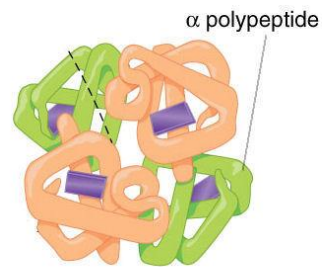
(a) Primary structure



(b) Secondary structure



c) Tertiary structure



(d) Quaternary structure—



The Nobel Prize in Chemistry 1972

Christian Anfinsen, Stanford Moore, William H. Stein

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The Nobel Prize in Chemistry 1972



Christian B. Anfinsen

Prize share: 1/2



Stanford Moore

Prize share: 1/4



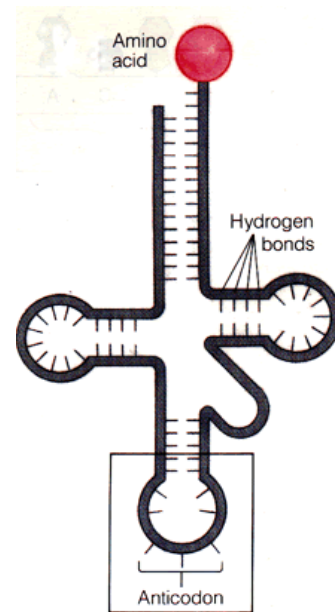
William H. Stein

Prize share: 1/4

The Nobel Prize in Chemistry 1972 was divided, one half awarded to Christian B. Anfinsen *"for his work on ribonuclease, especially concerning the connection between the amino acid sequence and the biologically active conformation"*, the other half jointly to Stanford Moore and William H. Stein *"for their contribution to the understanding of the connection between chemical structure and catalytic activity of the active centre of the ribonuclease molecule"*.

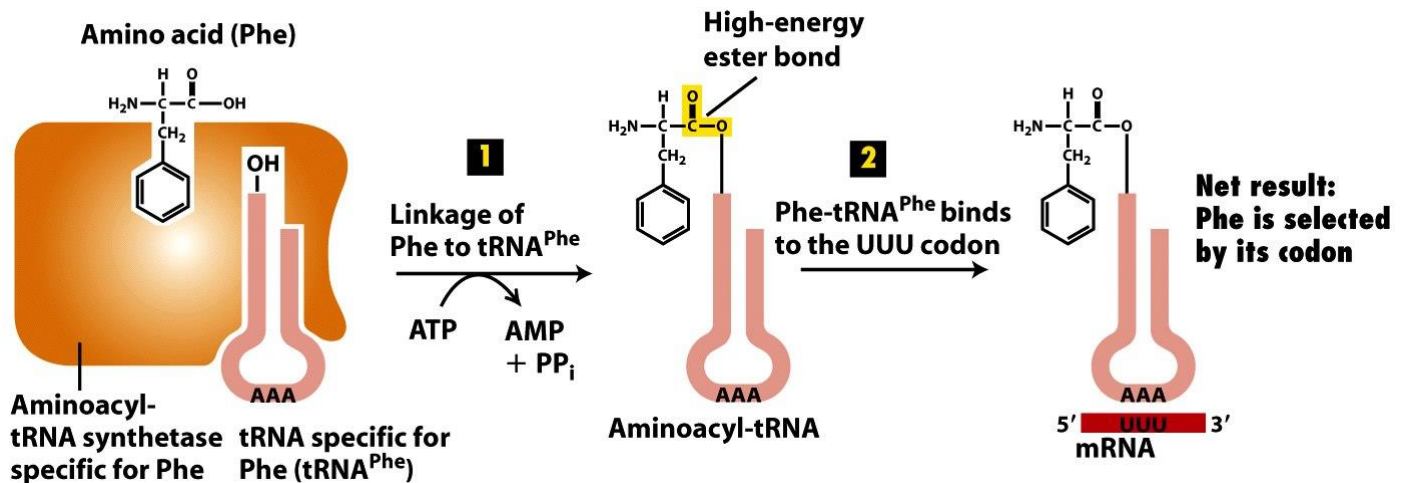
Transfer RNA

- Transfer RNA molecules are short RNAs that fold into a characteristic cloverleaf pattern. Some of the nucleotides are modified to become things like pseudouridine and ribothymidine.
- Each tRNA has 3 bases that make up the anticodon. These bases pair with the 3 bases of the codon on mRNA during translation.
- Each tRNA has its corresponding amino acid attached to the 3' end. A set of enzymes, the “aminoacyl tRNA synthetases”, are used to “charge” the tRNA with the proper amino acid.
- Some tRNAs can pair with more than one codon. The third base of the anticodon is called the “wobble position”, and it can form base pairs with several different nucleotides.



Two-step Process for mRNA Decoding

Amino acids are attached in ester linkage to the 3'-terminus of tRNA, forming aminoacyl-tRNAs (Fig. 4.19, step 1). The enzymes that carry out this ATP-driven reaction are known as aminoacyl-tRNA synthetases. Aminoacyl-tRNA synthetases are highly accurate (high fidelity) and this helps minimize translation errors. In step 2, the amino acid is added to the growing protein chain based on codon:anticodon interactions between mRNA and tRNA.



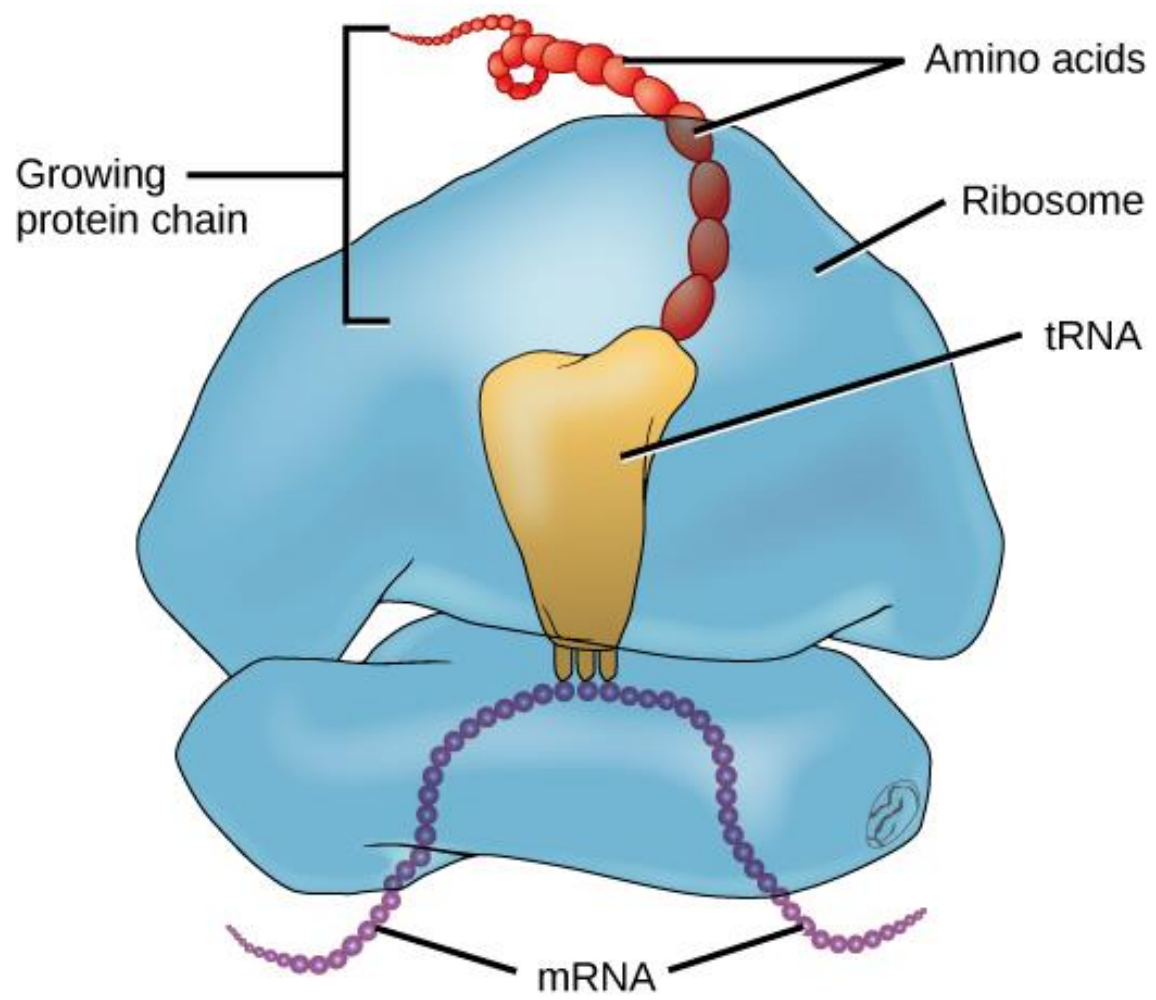
Bacteria synthesize 30-40 tRNAs, whereas eukaryotes may synthesize 50-100. Thus, a given amino acid often can be carried by more than one species of tRNA. Each aminoacyl-tRNA synthetase recognizes 1 amino acid and all of its cognate tRNAs.

The Genetic Code

- Each group of 3 nucleotides on the mRNA is a codon. Since there are 4 bases, there are $4^3 = 64$ possible codons, which must code for 20 different amino acids.
- More than one codon is used for most amino acids: the genetic code is “degenerate”. This means that it is not possible to take a protein sequence and deduce exactly the base sequence of the gene it came from.
- In most cases, the third base of the codon (the wobble base) can be altered without changing the amino acid.
- AUG is used as the start codon. All proteins are initially translated with methionine in the first position, although it is often removed after translation. There are also internal methionines in most proteins, coded by the same AUG codon.
- There are 3 stop codons, also called “nonsense” codons. Proteins end in a stop codon, which codes for no amino acid.

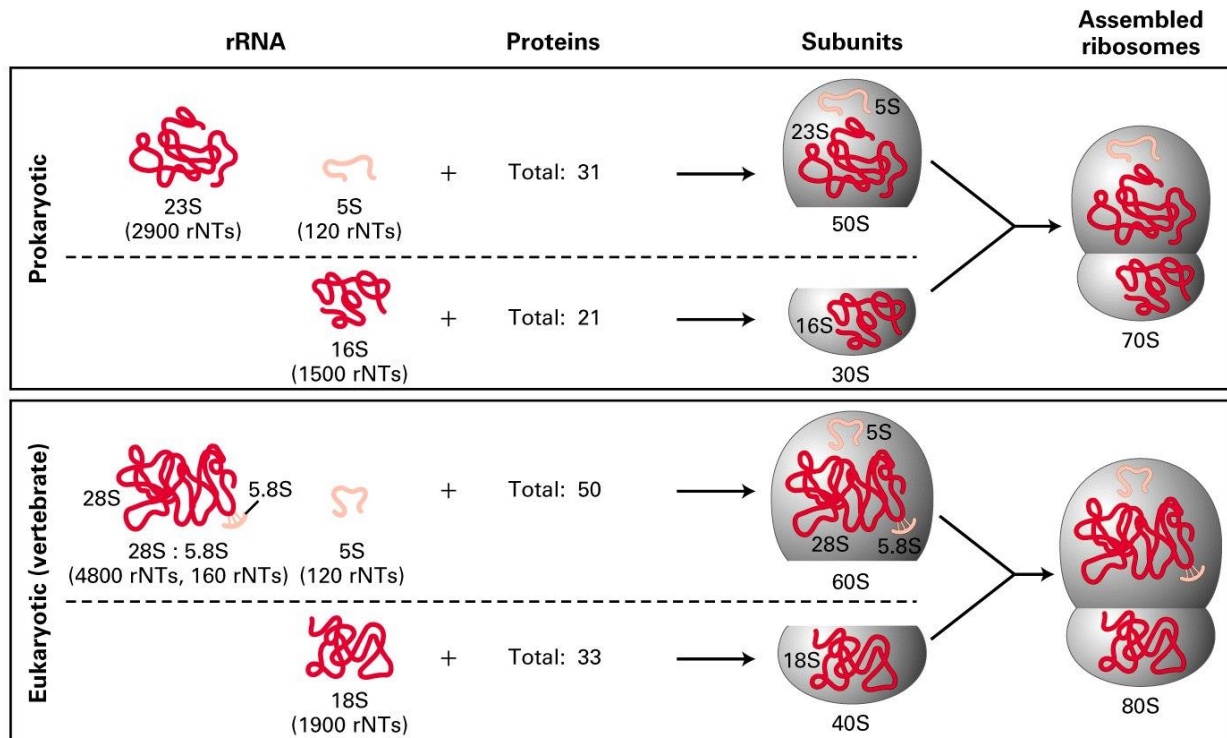
Genetic code

		Second base					
		U	C	A	G		
First base 5'	U	UUU } Phenyl- UUC } alanine UUA } UUG } Leucine	UCU } UCC } Serine UCA } UCG }	UAU } Tyrosine UAC } UAA } Stop codon UAG } Stop codon	UGU } Cysteine UGC } UGA } Stop codon UGG } Tryptophan	Third base 3'	U C A G
	C	CUU } CUC } Leucine CUA } CUG }	CCU } CCC } Proline CCA } CCG }	CAU } Histidine CAC } CAA } Glutamine CAG }	CGU } CGC } Arginine CGA } CGG }		U C A G
	A	AUU } AUC } Isoleucine AUA } AUG } Methionine start codon	ACU } ACC } Threonine ACA } ACG }	AAU } Asparagine AAC } AAA } Lysine AAG }	AGU } Serine AGC } AGA } Arginine AGG }		U C A G
	G	GUU } GUC } Valine GUA } GUG }	GCU } GCC } Alanine GCA } GCG }	GAU } Aspartic GAC } acid GAA } Glutamic GAG } acid	GGU } GGC } Glycine GGA } GGG }		U C A G



Ribosome Composition

Ribosomes are RNA-protein supramolecular complexes. They are the most abundant type of RNA-protein complex in cells. The compositions of prokaryotic and eukaryotic ribosomes are summarized in Fig. 4.22. Although proteins outnumber rRNAs, rRNAs comprise 60% of the ribosomal mass (see Fig. 4.23).

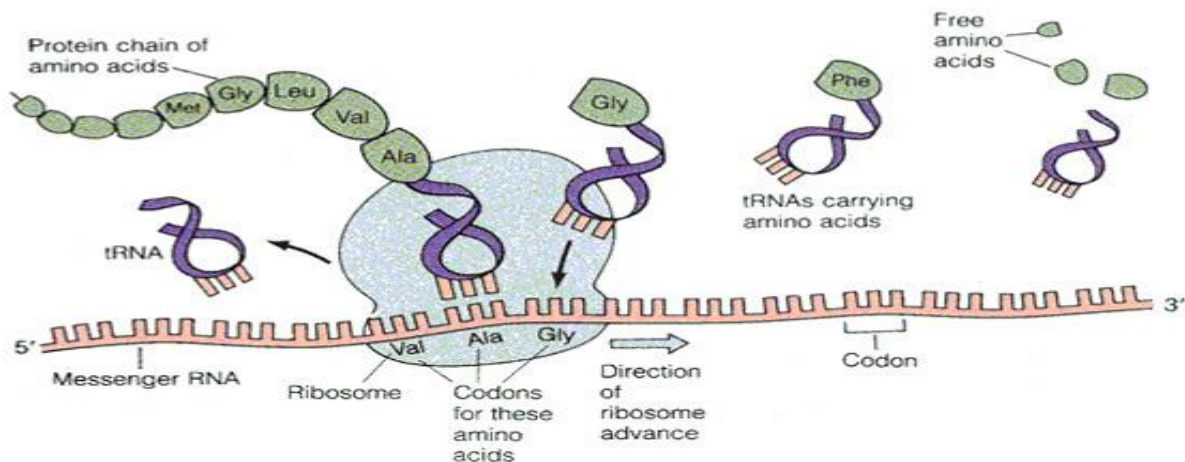


Translation

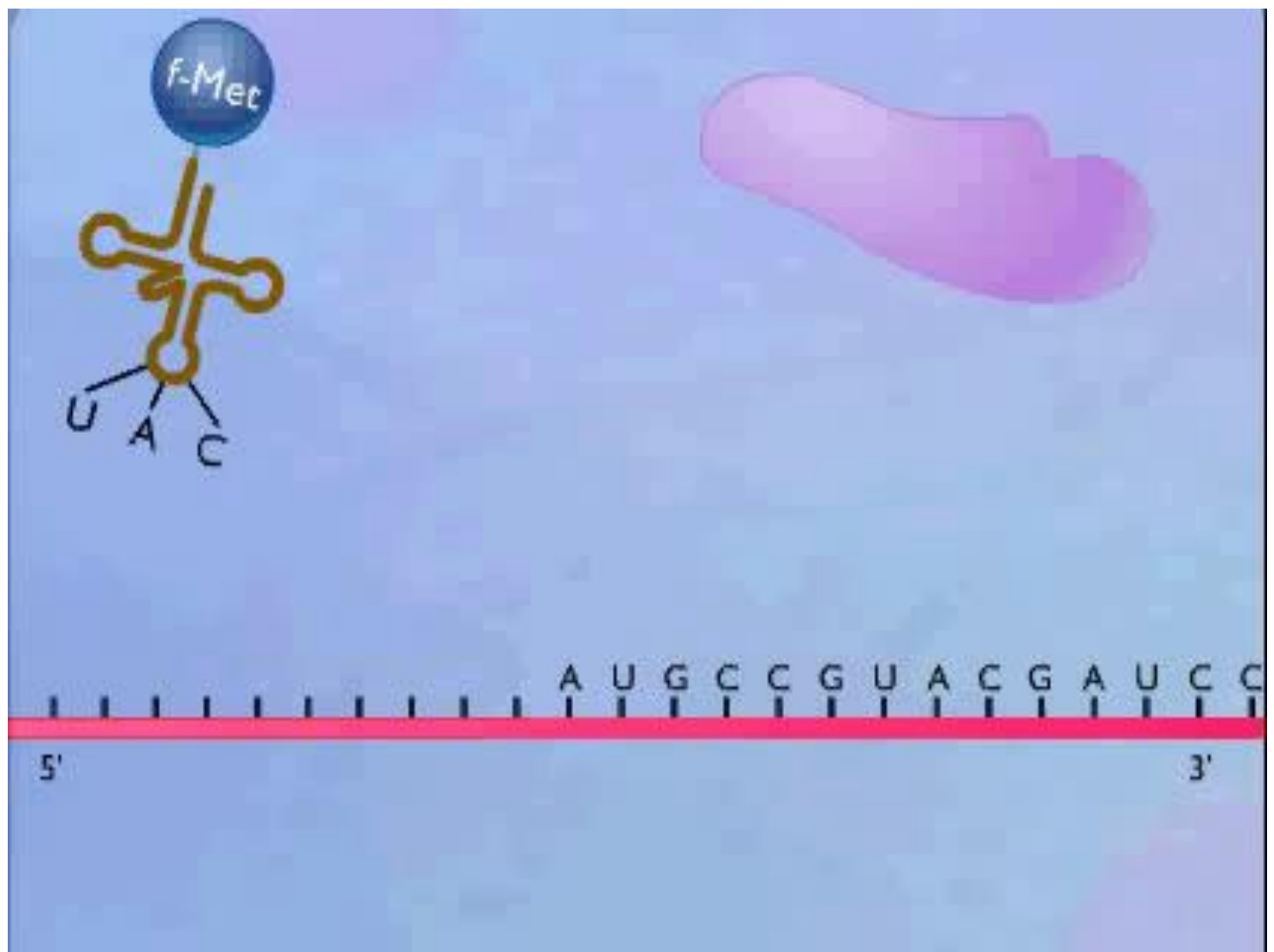
- Translation is the first stage of protein biosynthesis.
- In translation, (mRNA) produced by transcription is decoded by the ribosome to produce a specific amino acid chain, or polypeptide, that will later fold into an active protein.
- Translation occurs in the cell's cytoplasm, where the large and small subunits of the ribosome are located, and bind to the mRNA.

Translation process

- The ribosome facilitates decoding by inducing the binding of tRNAs with complementary anticodon sequences to mRNA.
- The tRNAs carry specific amino acids that are chained together into a polypeptide as the mRNA passes through and is "read" by the ribosome.



- the (Copyright © 2000 Benjamin/Cummings, an imprint of Addison Wesley Longman, Inc. e of the rough endoplasmic reticulum and release the nascent protein polypeptide inside for later vesicle transport and secretion outside of the cell.



Post-Translational Modification

- New polypeptides usually fold themselves spontaneously into their active conformation. However, some proteins are helped and guided in the folding process by chaperone proteins
- Many proteins have sugars, phosphate groups, fatty acids, and other molecules covalently attached to certain amino acids. Most of this is done in the endoplasmic reticulum.
- Many proteins are targeted to specific organelles within the cell. Targeting is accomplished through “signal sequences” on the polypeptide. In the case of proteins that go into the endoplasmic reticulum, the signal sequence is a group of amino acids at the N terminal of the polypeptide, which are removed from the final protein after translation.

