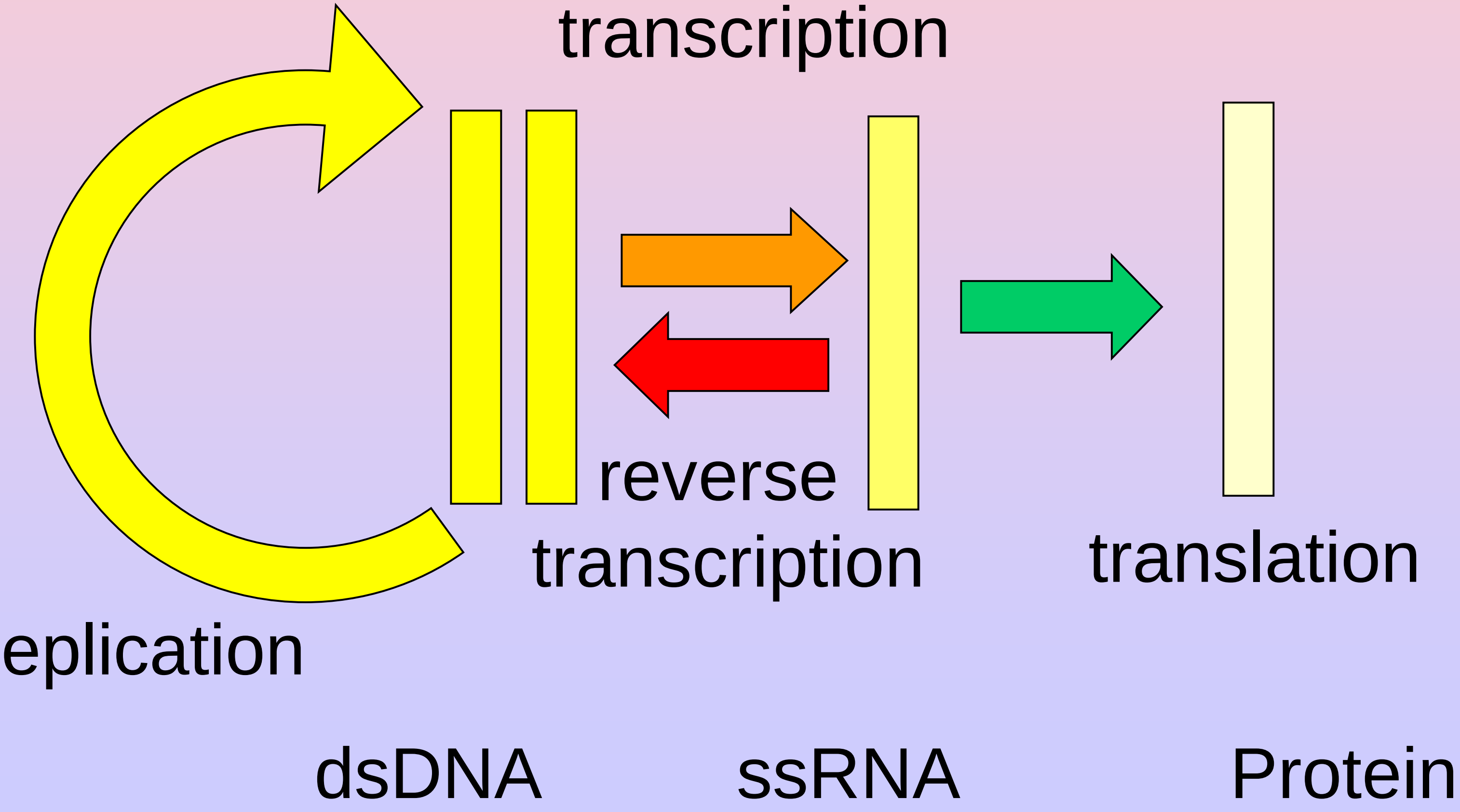
From gene to protein

Premedical biology

Central dogma

of Biology, Molecular Biology, Genetics



transcription

reverse transcription

translation

replication

dsDNA

ssRNA

Protein

RNA

- chemically similar to DNA, except it contains **ribose** instead of deoxyribose and **uracil** instead of **thymine**
- almost always consist of **a single strand**
- less stable

RNA

- some molecules are able to **self-replicate**
- mistakes in replication bring a variability = **family of closely related RNA sequences**
- some molecules are able to **self-catalyse**

example:

Ribosyms (ribosome, spliceosome)

Coenzymes - some are **ribonucleotids**, **rRNA, mRNA**

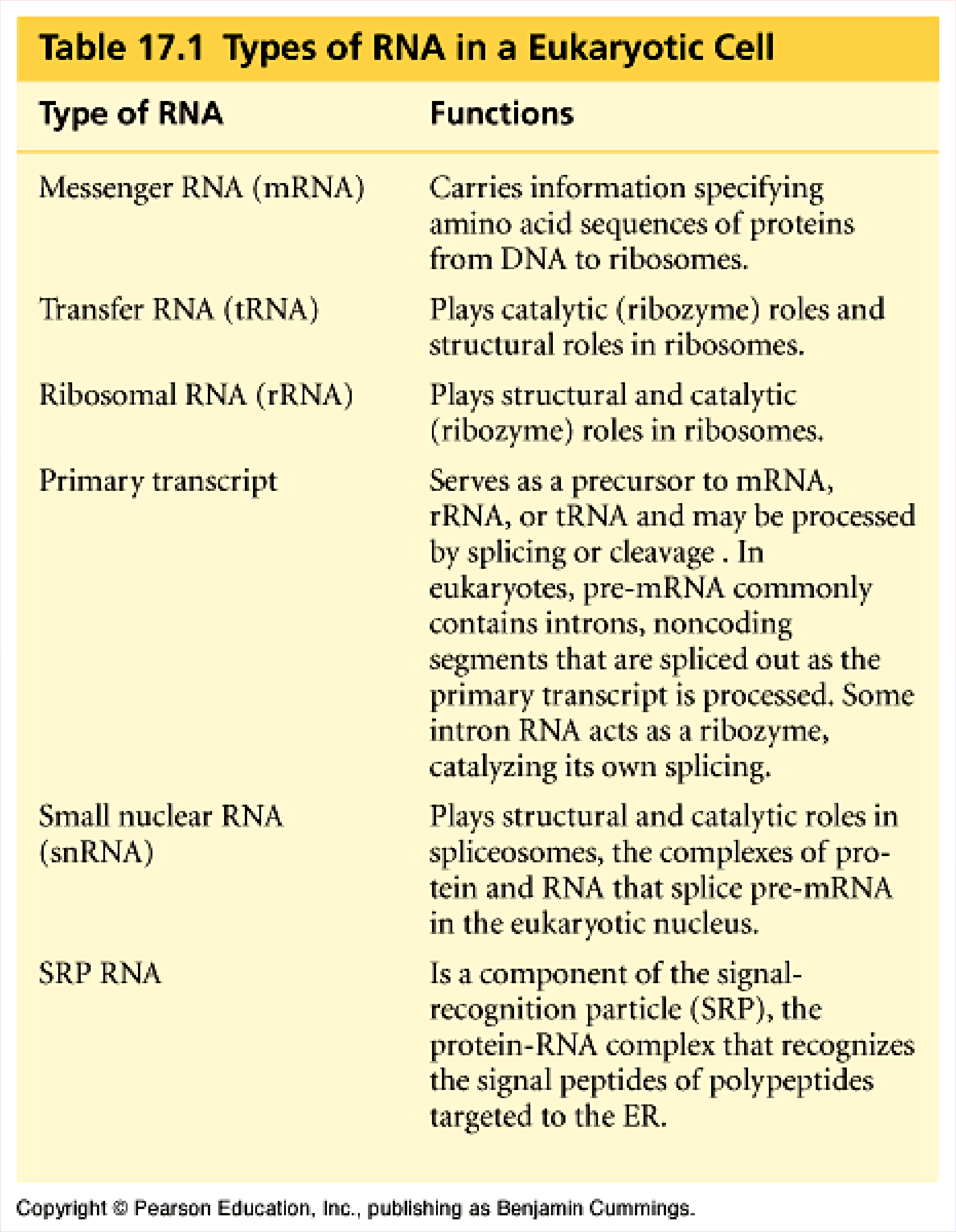


Table 17.1 Types of RNA in a Eukaryotic Cell

Type of RNA	Functions
Messenger RNA (mRNA)	Carries information specifying amino acid sequences of proteins from DNA to ribosomes.
Transfer RNA (tRNA)	Plays catalytic (ribozyme) roles and structural roles in ribosomes.
Ribosomal RNA (rRNA)	Plays structural and catalytic (ribozyme) roles in ribosomes.
Primary transcript	Serves as a precursor to mRNA, rRNA, or tRNA and may be processed by splicing or cleavage . In eukaryotes, pre-mRNA commonly contains introns, noncoding segments that are spliced out as the primary transcript is processed. Some intron RNA acts as a ribozyme, catalyzing its own splicing.
Small nuclear RNA (snRNA)	Plays structural and catalytic roles in spliceosomes, the complexes of protein and RNA that splice pre-mRNA in the eukaryotic nucleus.
SRP RNA	Is a component of the signal-recognition particle (SRP), the protein-RNA complex that recognizes the signal peptides of polypeptides targeted to the ER.

Transcription - eukaryotic

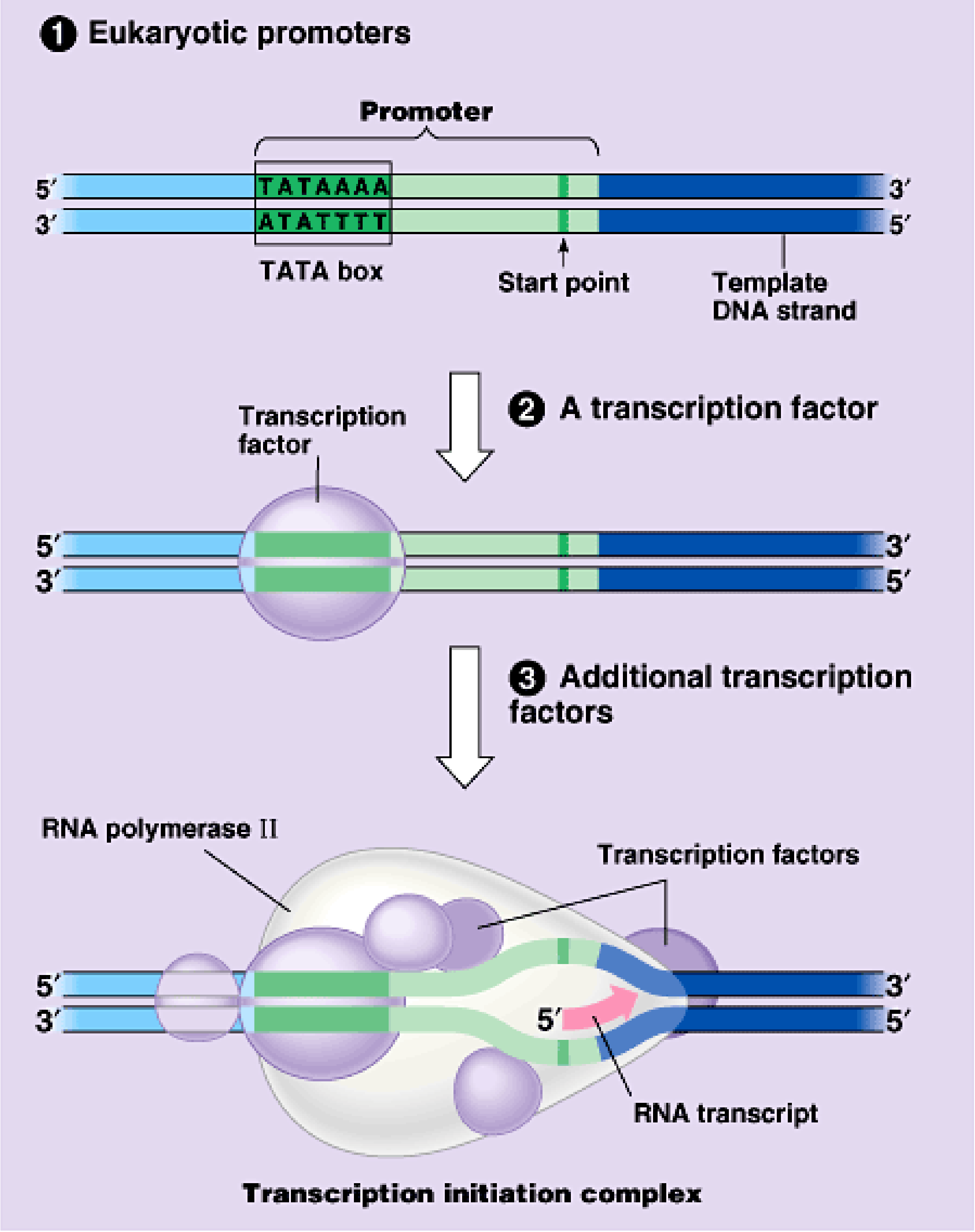
- Synthesis of RNA **under direction of DNA**
- Information is simply copied from one to another according to **complementarity** of bases
- enzyme **RNA polymerase (RNAP)**

- beginning = **promotor with initial code - AUG**
- **Initiation, elongation, termination phases with specific transcription factors (TF)**

Promoter

Typical promoter region for a protein-encoding eukaryotic gene.

The promoter is sequence, where RNAP binds to the DNA

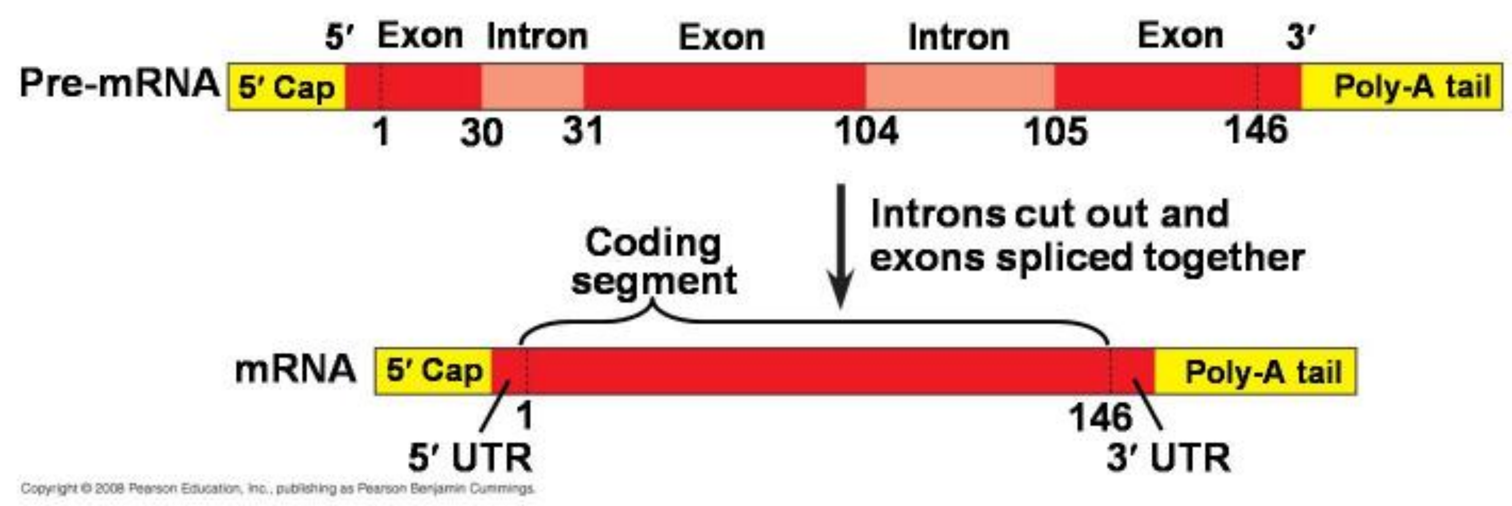


RNA processing – in nucleus

- the ***template strand*** is used as a template for RNA synthesis
- The product is ***pre-mRNA*** = **hnRNA** = primary transcript (eukaryotic cells)
- **7methyl guanosine cap** is added immediately to 5‘ end for protection from degradation by hydrolytic enzymes and serves as „attach“ sign (mark) for ribosomes
- **poly(A) tail - polyadenylatio**n of 3‘ end, which inhibit degradation of the RNA

RNA processing – in nucleus

- **exons** = encoding parts
- **introns** = non-coding parts, which are cut out
- removal of introns from mRNA precursors and the reattachment or annealing of exons = **splicing**
- in the **RNA processing** originates messenger RNA – **mRN**A
- *snRNPs* = **spliceosome cuts and regulates**



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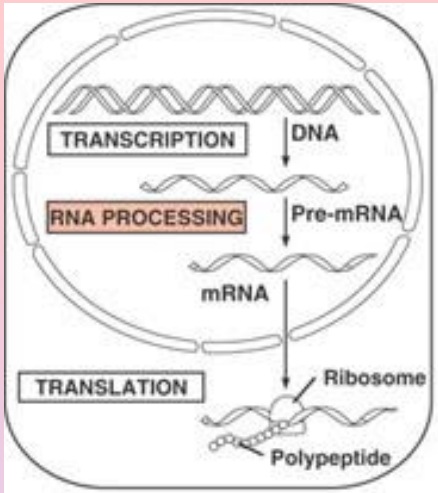
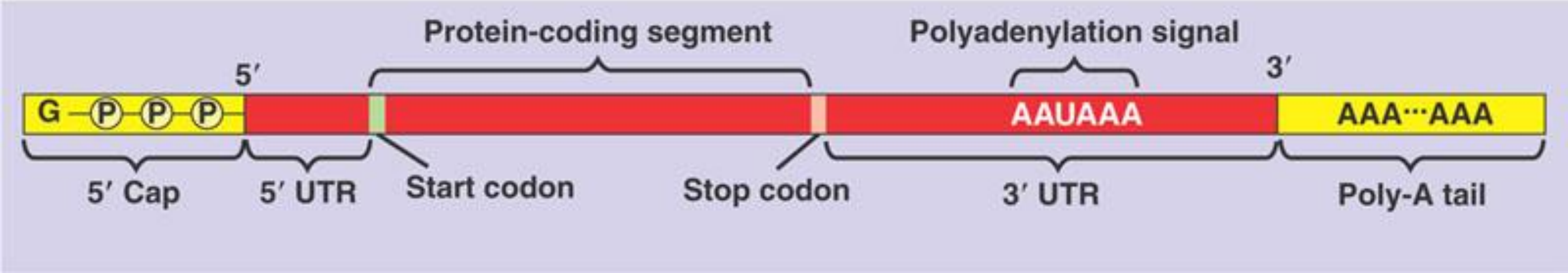
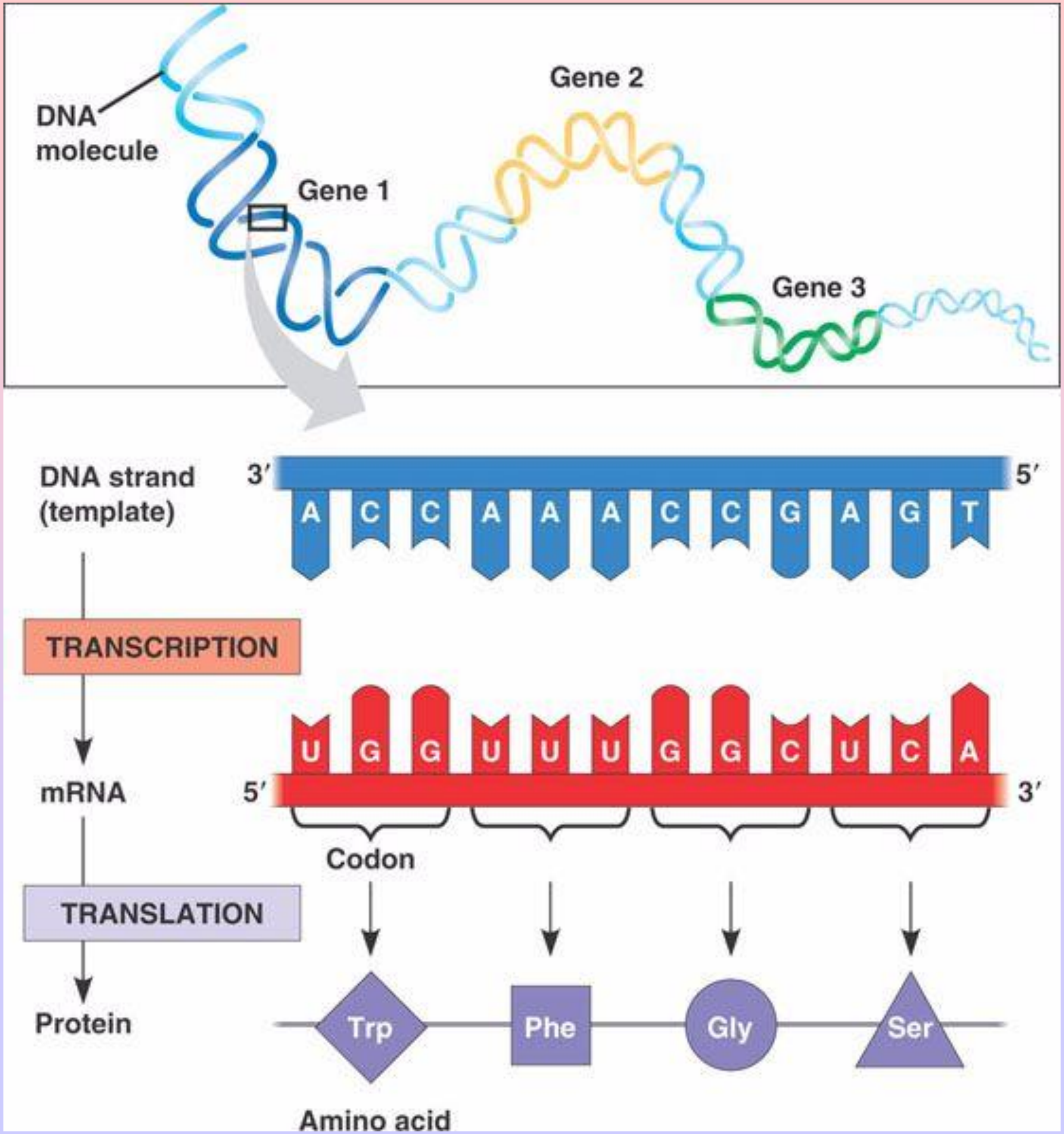
mRNA


TRANSCRIPTION
DNA
RNA PROCESSING
Pre-mRNA
mRNA
TRANSLATION
Ribosome
Polypeptide


Protein-coding segment
Polyadenylation signal
5′
3′
G
P
P
P
AAUAAA
AAA···AAA
5′ Cap
5′ UTR
Start codon
Stop codon
3′ UTR
Poly-A tail

The triplet code

Triplet code means three nucleotides in particular order.



Translation

eukaryotic in cytoplasm

Initiation, elongation, termination phase with specific factors

Translation requires **ribosomes, GTP,** translation factors

Origin of peptide bond – the **—CO—NH—** formed between the carboxyl group of one amino acid and the amino group of another.

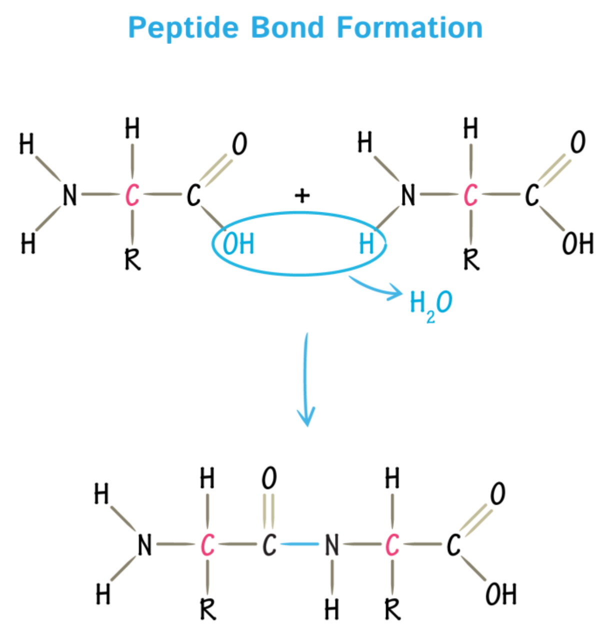
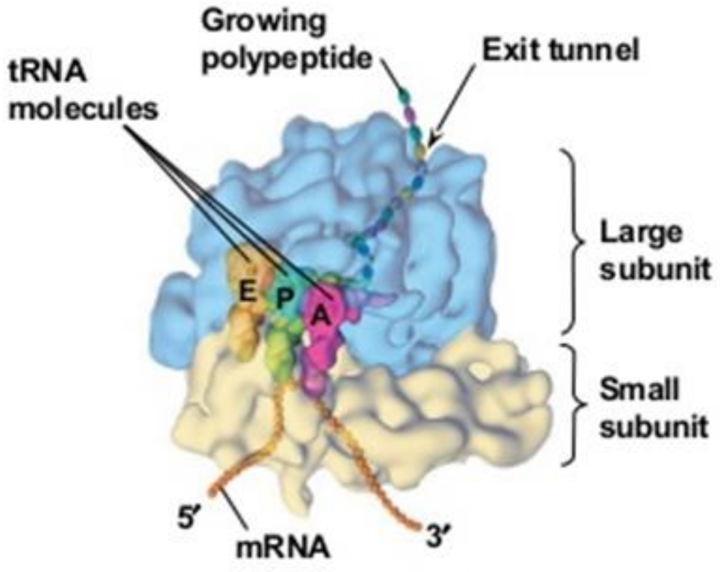
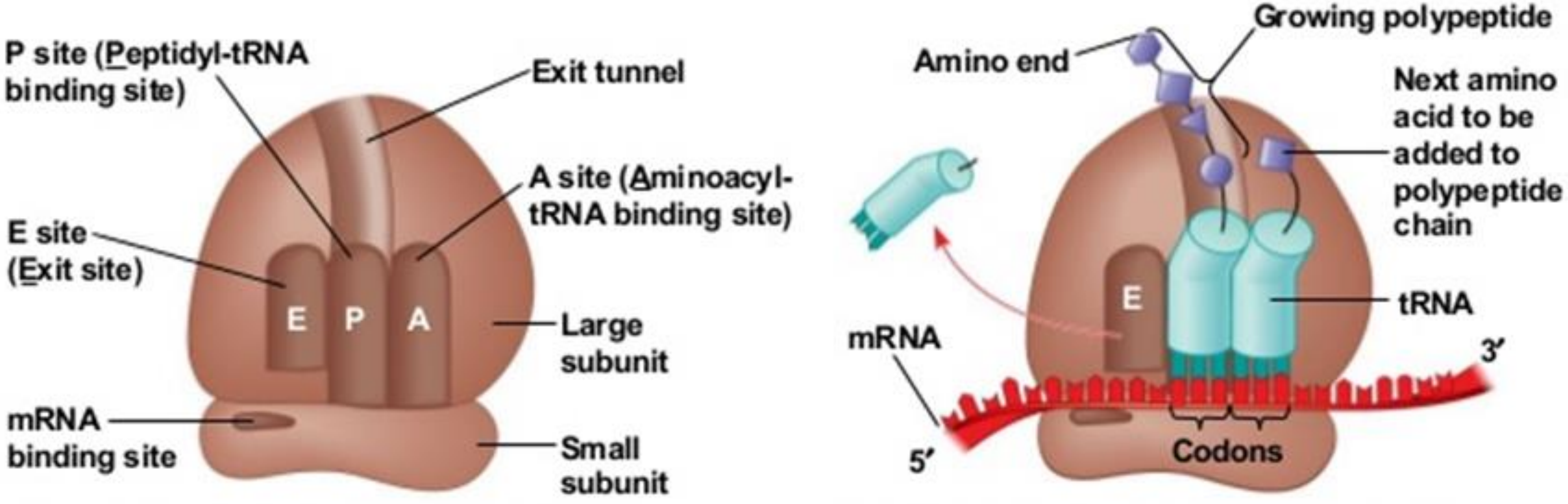

Peptide Bond Formation

Figure 17.17



(a) Computer model of functioning ribosome

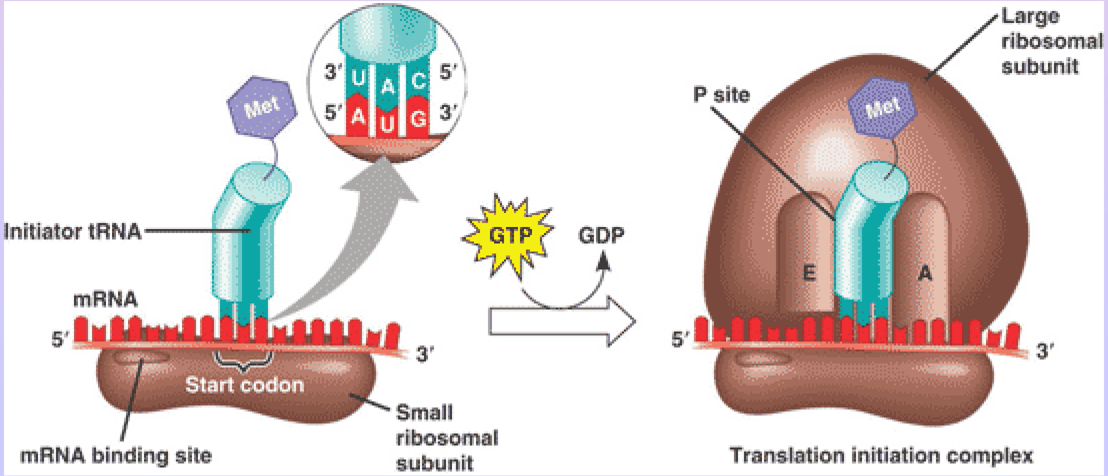


(b) Schematic model showing binding sites

(c) Schematic model with mRNA and tRNA

Ribosomes

- **subunits: proteins and ribosomal RNA** (made in nucleolus (eu))
- facilitate specific coupling of **anticodons in tRNA with codons in mRNA**
- Amino acid is added to the growing end of a polypeptide chain in ribosome.

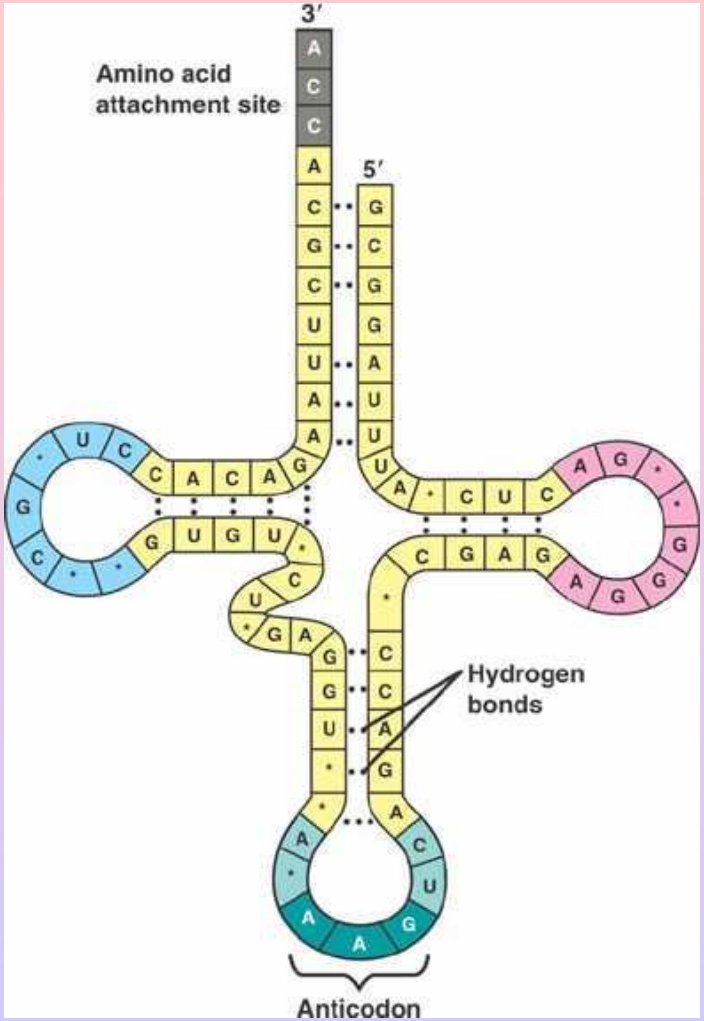


tRNA

mRNA sequences represent **codons.**

Interpreter is **transfer RNA, which** transfers amino acids to ribosome.

Nucleotide triplet called **anticodon in tRNA** links a particular mRNA codon



L-shape of tRNA three-dimensional structure

Genetic code

nucleotide triplets specify amino acids

We have 4 nucleotides together, which specify according to base-pairing rules 20 amino acids

in the form of **triplets.**

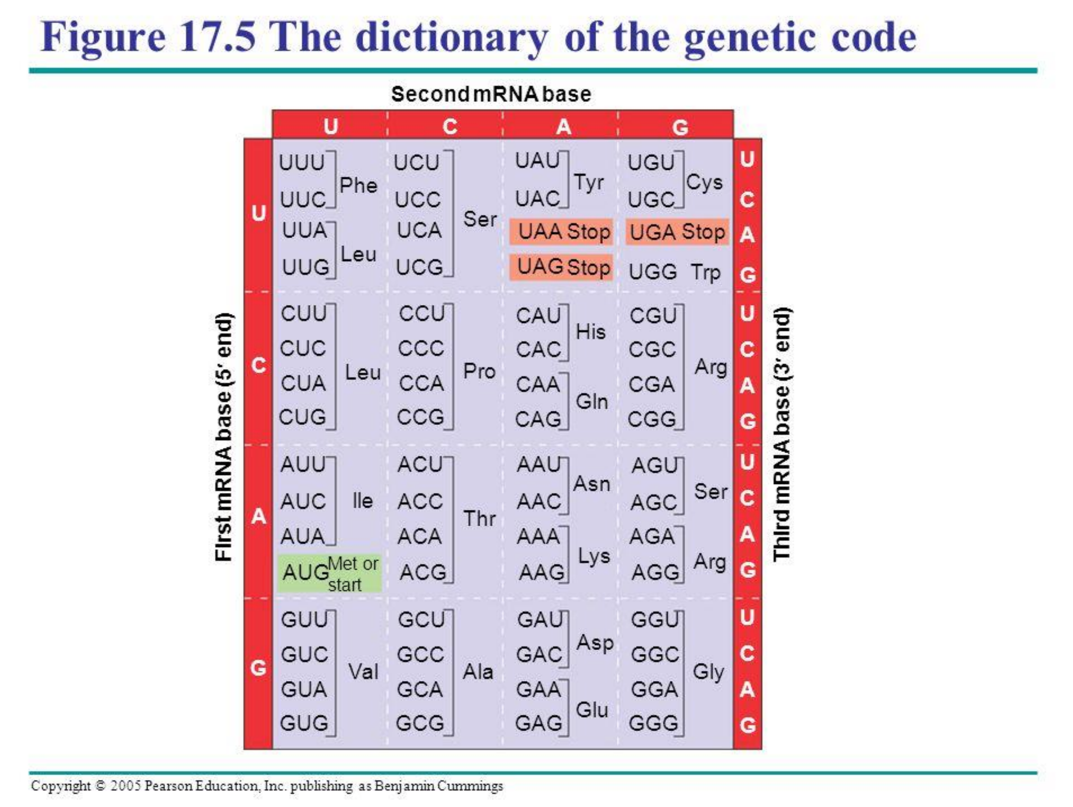
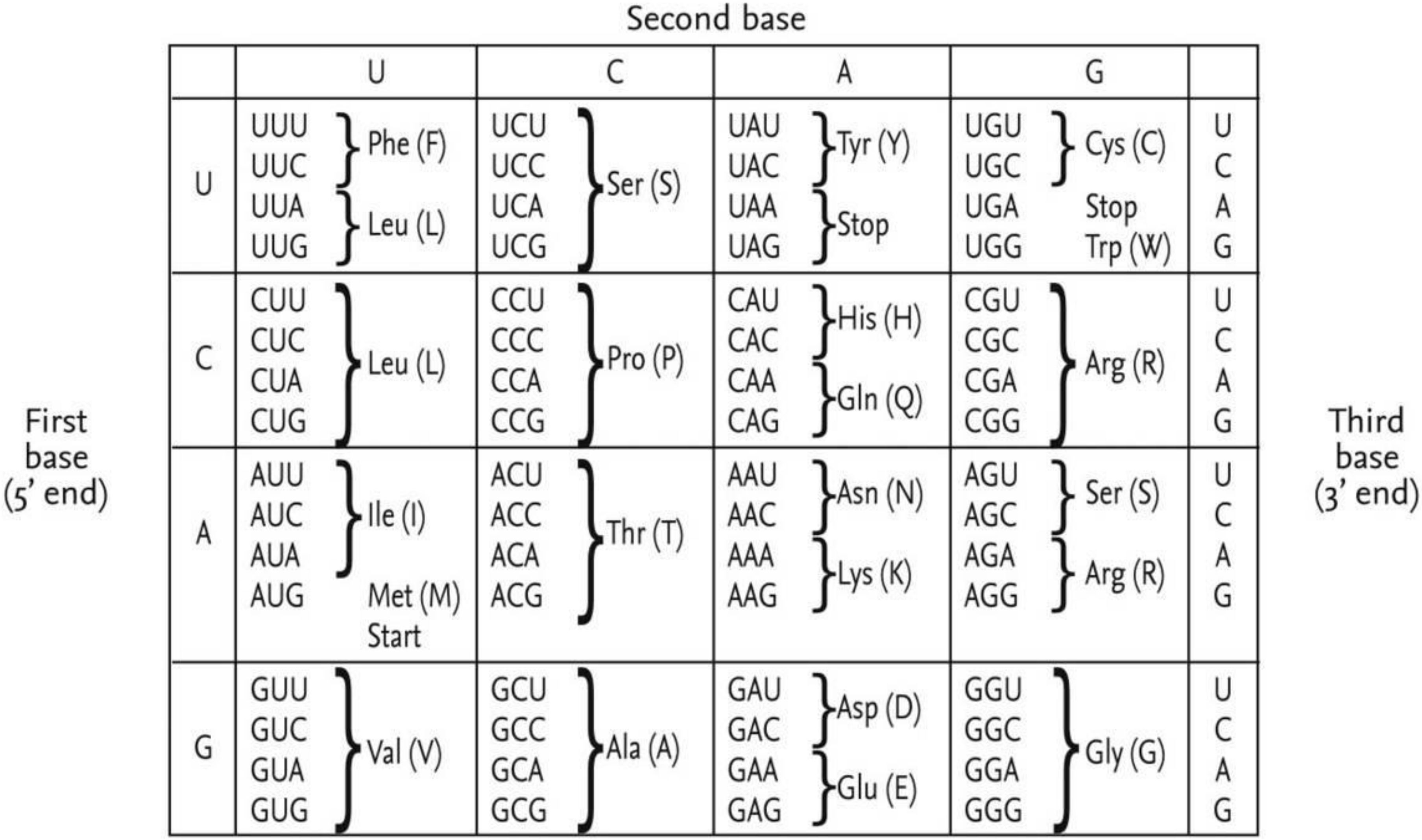


Figure 17.5 The dictionary of the genetic code

	Second mRNA base								
First mRNA base (5′ end)	U		C		A		G		Third mRNA base (3′ end)
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 or start	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

Genetic code



Second base

First base (5' end)	U		C		A		G		Third base (3' end)
U	UUU	Phe (F)	UCU	Ser (S)	UAU	Tyr (Y)	UGU	Cys (C)	U
	UUC		UCC		UAC		UGC		C
	UUA	Leu (L)	UCA		UAA	Stop	UGA	Stop	A
	UUG		UCG		UAG		UGG	Trp (W)	G
C	CUU	Leu (L)	CCU	Pro (P)	CAU	His (H)	CGU	Arg (R)	U
	CUC		CCC		CAC		CGC		C
	CUA		CCA		CAA	Gln (Q)	CGA		A
	CUG		CCG		CAG		CGG		G
A	AUU	Ile (I)	ACU	Thr (T)	AAU	Asn (N)	AGU	Ser (S)	U
	AUC		ACC		AAC		AGC		C
	AUA		ACA		AAA	Lys (K)	AGA	Arg (R)	A
	AUG	Met (M) Start	ACG		AAG		AGG		G
G	GUU	Val (V)	GCU	Ala (A)	GAU	Asp (D)	GGU	Gly (G)	U
	GUC		GCC		GAC		GGC		C
	GUA		GCA		GAA	Glu (E)	GGA		A
	GUG		GCG		GAG		GGG		G

Fig. 169 **Genetic code.** The mRNA codons of the genetic code arranged in a GENETIC DICTIONARY (see Fig. 27 for the AMINO ACID abbreviations).

Genetic code is almost universal.

The system is shared by the simplest bacteria to the most complex plants and animals

The genetic code must have evolved very early in the history of life.

AUG for methionine and it is **Initial codon**

AUG for formyl-methionine in prokaryotes

Initial codon in (mRNA) **is universal for all proteins of all organisms**

Termination codons:

UAA, UAG, UGA, (stop signals).These codons mean stop of translation, no amino acid is incorporated into peptide chain.

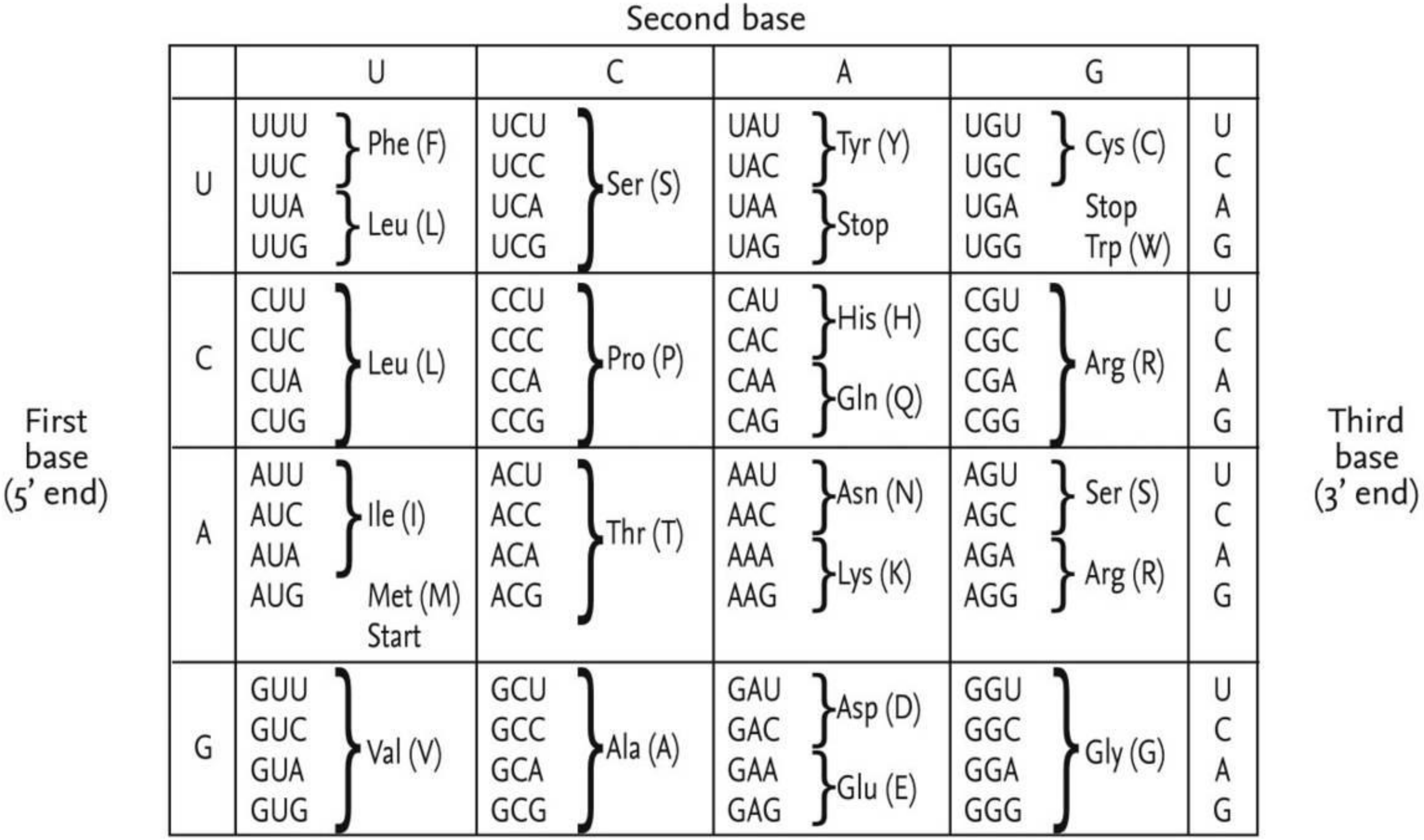
Genetic code is degenerated

61 of 64 triplets code for 20 amino acids.

There is **redundancy**, and it is not random.

Codons for the same amino acids differ in third base of triplet.

Genetic code



	Second base								
First base (5' end)	U		C		A		G		Third base (3' end)
U	UUU	Phe (F)	UCU	Ser (S)	UAU	Tyr (Y)	UGU	Cys (C)	U
	UUC		UCC		UAC		UGC		C
	UUA	Leu (L)	UCA		UAA	Stop	UGA	Stop	A
	UUG		UCG		UAG		UGG	Trp (W)	G
C	CUU	Leu (L)	CCU	Pro (P)	CAU	His (H)	CGU	Arg (R)	U
	CUC		CCC		CAC		CGC		C
	CUA		CCA		CAA	Gln (Q)	CGA		A
	CUG		CCG		CAG		CGG		G
A	AUU	Ile (I)	ACU	Thr (T)	AAU	Asn (N)	AGU	Ser (S)	U
	AUC		ACC		AAC		AGC		C
	AUA		ACA		AAA	Lys (K)	AGA	Arg (R)	A
	AUG	Met (M) Start	ACG		AAG		AGG		G
G	GUU	Val (V)	GCU	Ala (A)	GAU	Asp (D)	GGU	Gly (G)	U
	GUC		GCC		GAC		GGC		C
	GUA		GCA		GAA	Glu (E)	GGA		A
	GUG		GCG		GAG		GGG		G

Fig. 169 **Genetic code.** The mRNA codons of the genetic code arranged in a GENETIC DICTIONARY (see Fig. 27 for the AMINO ACID abbreviations).

Genetic code

Number **of tRNAs is 45**, some tRNAs have anticodons, that can recognize two or more different codons.

Important is correct **reading frame.**

Mutation as deletion or duplication (more or less than three triplets) **change reading frame = frame shift mutations.**

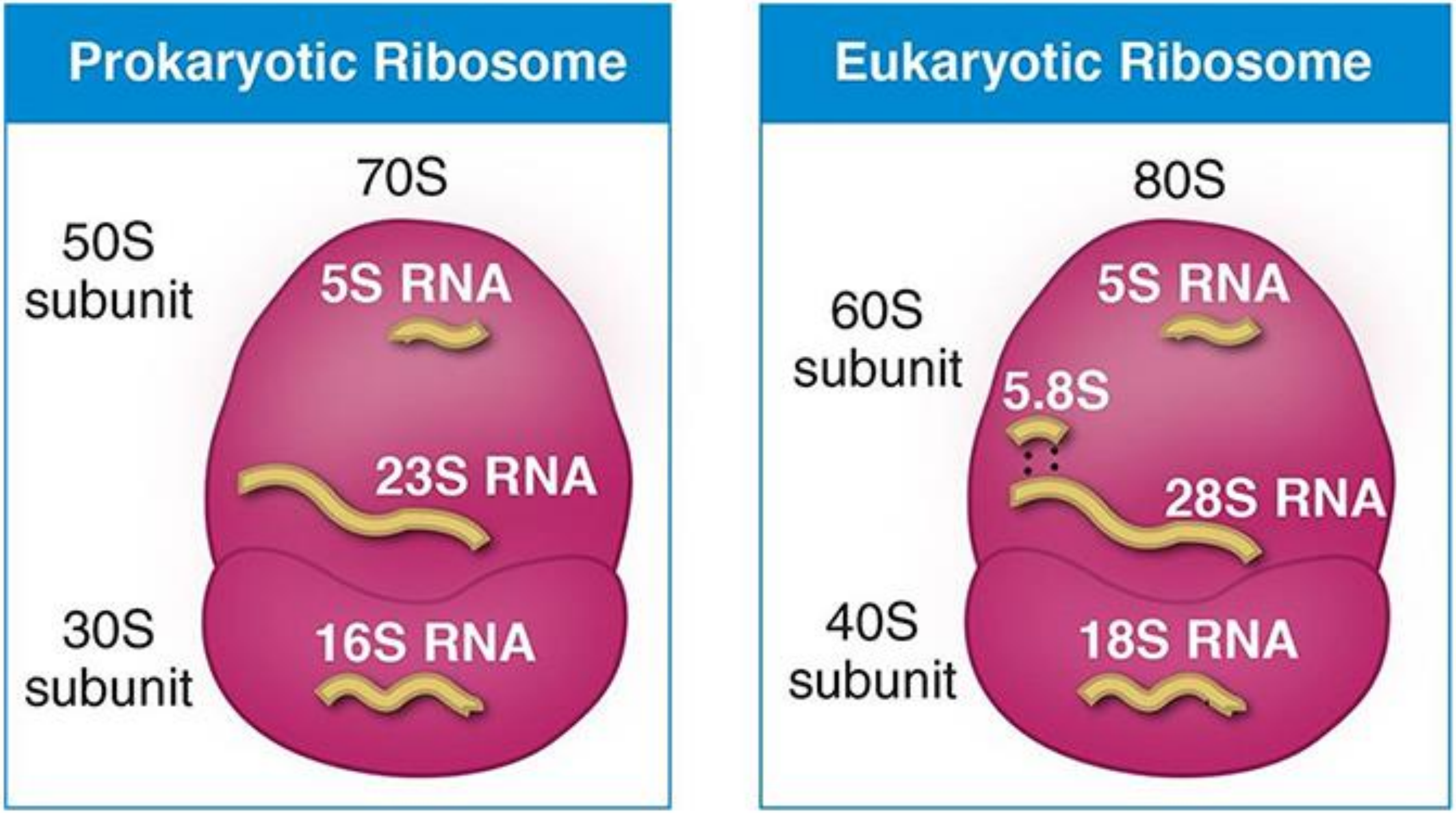
Comparing protein synthesis in prokaryotes and eukaryotes

It is very similar, but with certain differences.

There are **different polymerases.** Euk. transcription depends on transcription factors. **Ribosomes are different.** Transcription and translation simultaneously run at the same at the same time and place in Prokaryotes.

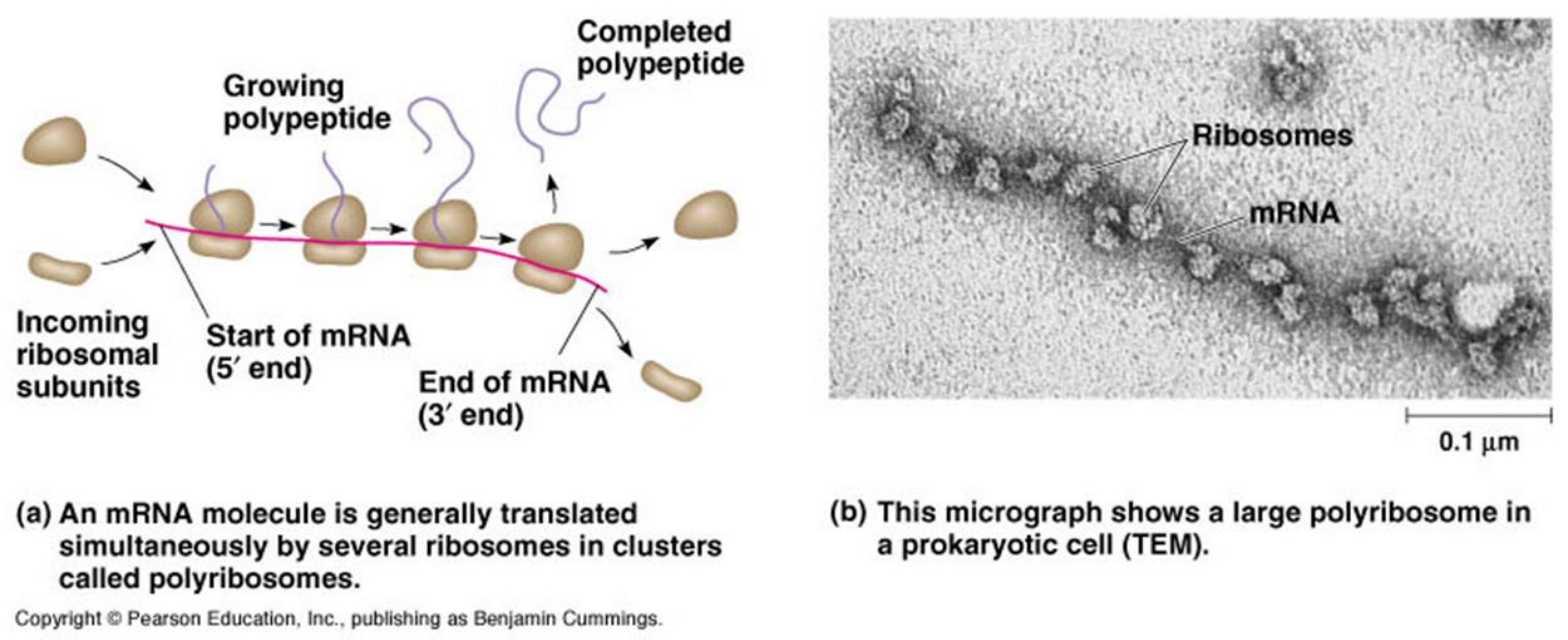
Nuclear envelope **segregates transcription and translation** in Eukaryotes.

Processing stages provide ways to regulate and coordinate proteosynthesis and gene expression in eukaryotic cells



A Svedberg unit is a unit for sedimentation coefficients. The Svedberg unit offers a measure of a particle's size indirectly based on its sedimentation rate under acceleration = how fast a particle of given size and shape settles to the bottom of a solution

Polyribosomes – in prokaryotes



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

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

Polyribosome (or **polysome**) is a cluster of ribosomes, bound to one mRNA molecule and read one strand of mRNA simultaneously.

ORFs

From polypeptide to functional protein – Euk.

One gene encodes one polypeptide, tRNA, rRNA

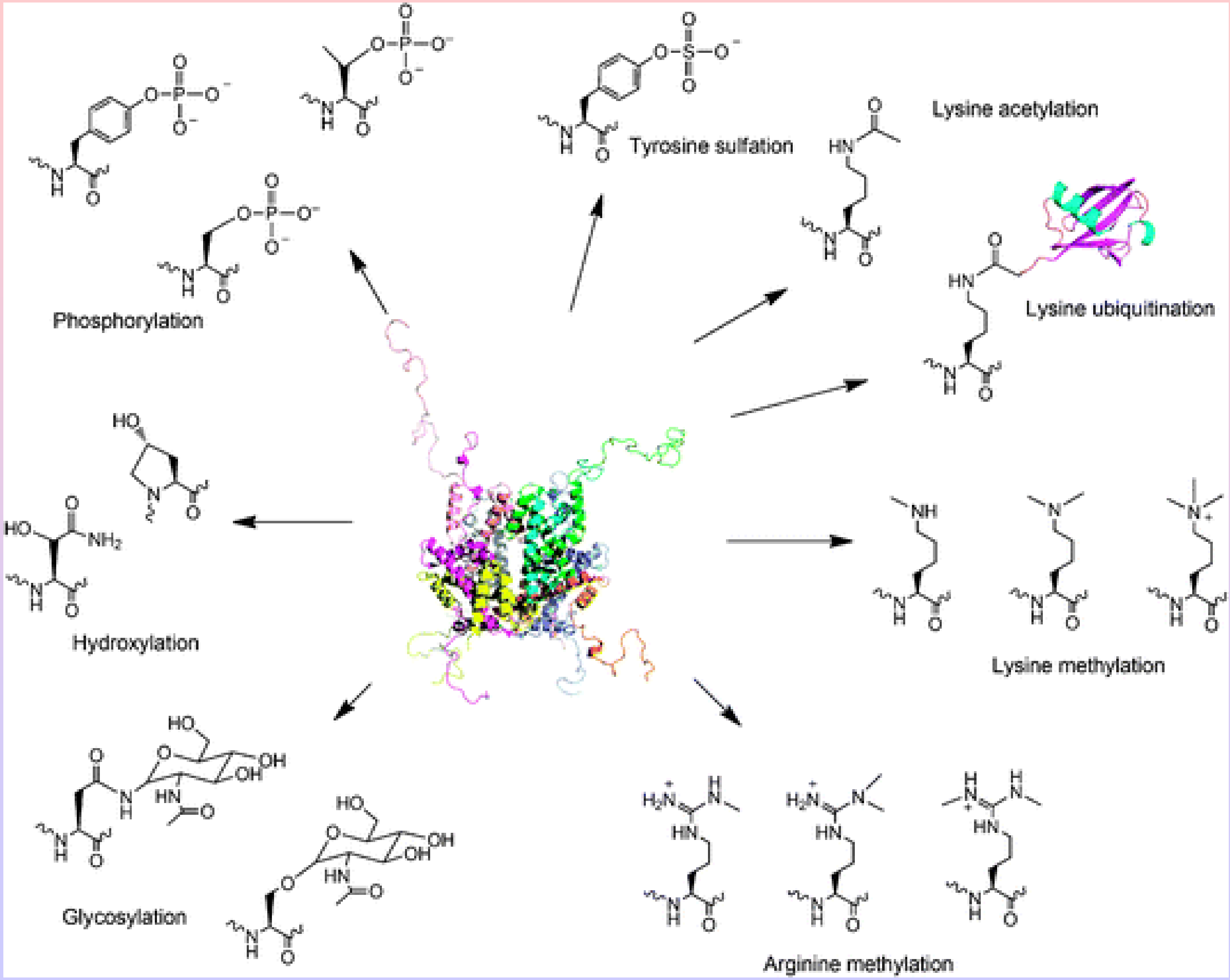
Genes determine the primary structure, the primary structure determines the conformation.

Coiling and folding are spontaneous actions given by chemical properties or aminoacids. Helpful are small specific proteins called **chaperones**.

Posttranslational modifications: certain amino acid are modified by attachment of sugars, lipids, phosphate groups.

Two or more polypeptides may join to become the **subunits of a protein.**

Posttranslational modifications



Mol Biosyst. 2011 Jan;7(1):38-47. doi: 10.1039/c0mb00216j. Epub 2010 Nov 19. :
Synthesis of proteins with defined posttranslational modifications using the genetic noncanonical amino acidincorporation approach.

Protein structures

Primary structure**:** amino acid sequences

Secondary structure**:** local structures stabilized by **hydrogen bonds**. The most common examples are the **alpha helix, beta sheet and turns.**

Tertiary structure**:** the overall shape of a single protein molecule; most commonly the formation of a hydrophobic core, but also through salt bridges, hydrogen bonds, disulfide bonds. The tertiary structure is what controls the basic function of the protein.

- also synonymous with the term ***fold***

Quaternary structure**:** the structure formed by several protein molecules (polypeptide chains), usually called *protein subunits* in this context, which function as a single protein complex.

Levels of Protein Structure

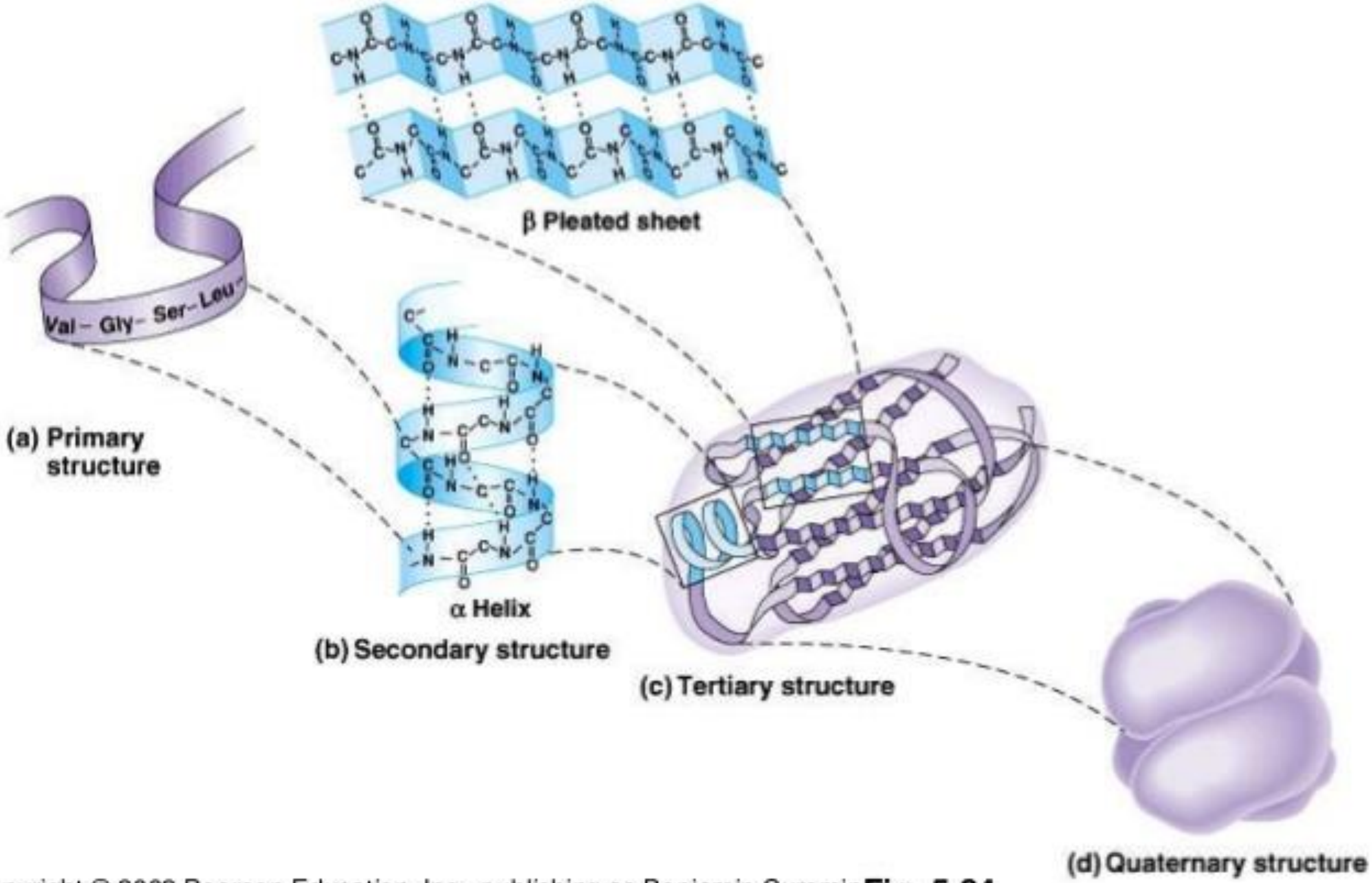


Fig. 5.24

Thank you for your attention

Campbell, Neil A., Reece, Jane B., Cain Michael L., Jackson, Robert B., Minorsky, Peter V., **Biology**, Benjamin-Cummings Publishing Company, 1996 –2010.