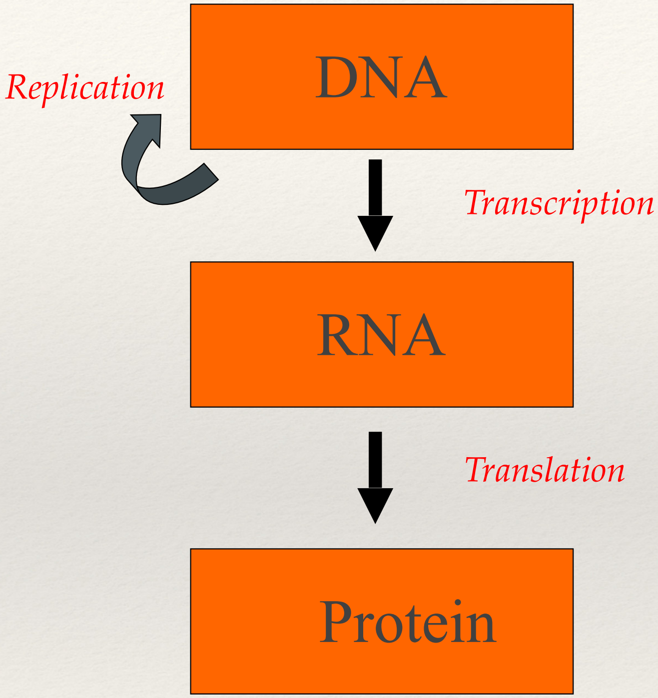
BIOMOLECULES

- ECS129
- Instructor: Patrice Koehl

Central Dogma



DNA

Replication

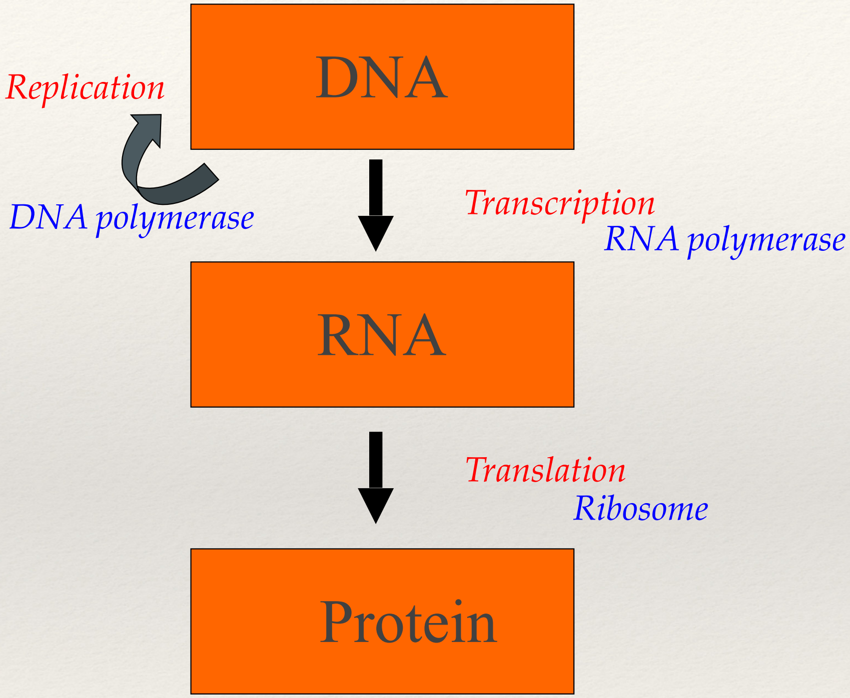
Transcription

RNA

Translation

Protein

Central Dogma



DNA

Replication

DNA polymerase

Transcription

RNA polymerase

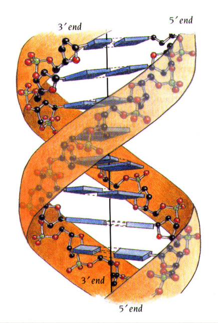
RNA

Translation

Ribosome

Protein

Central Dogma



DNA

Replication

DNA polymerase

Transcription

RNA polymerase

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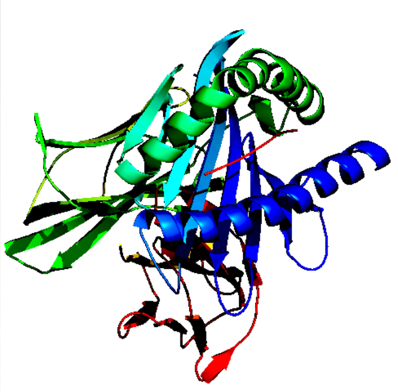
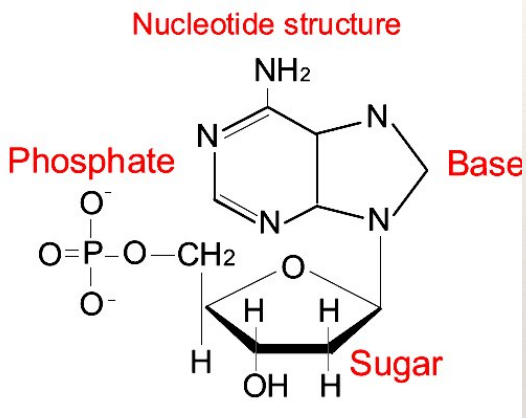
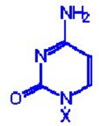
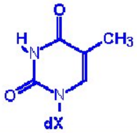
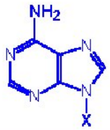
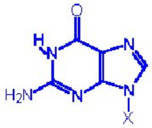
Ribosome

Protein



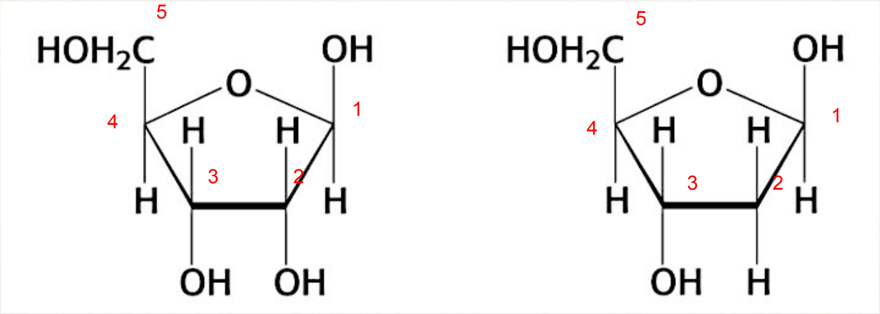
DNA



Base Formula	Base (X=H)	Nucleoside X=ribose or deoxyribose	Nucleotide X=ribose phosphate
	Cytosine, C	Cytidine, A	Cytidine monophosphate CMP
	Thymine, T	Thymidine, T	Thymidine monophosphate TMP
	Adenine, A	Adenosine, A	Adenosine monophosphate AMP
	Guanine, G	Guanosine, A	Guanosine monophosphate GMP

DNA

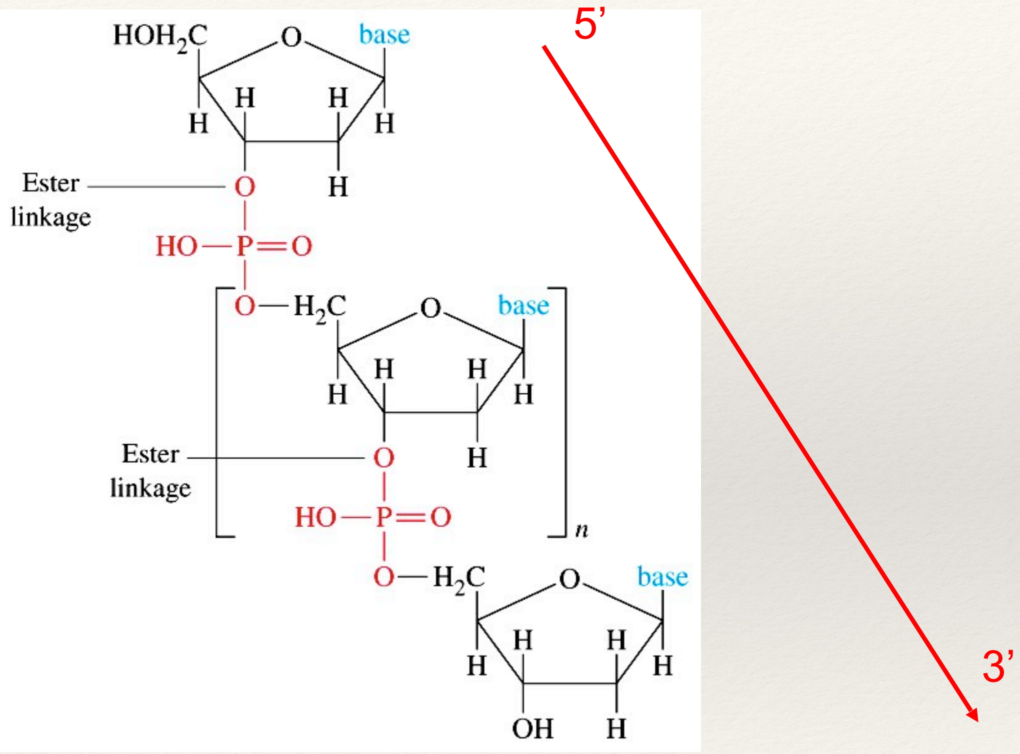
These “bases” are attached to sugar rings: ribose (RNA), deoxyribose (DNA):



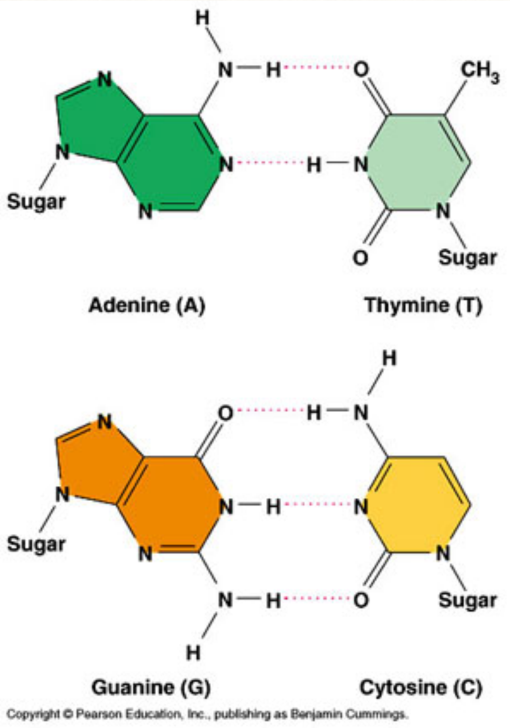
ribose

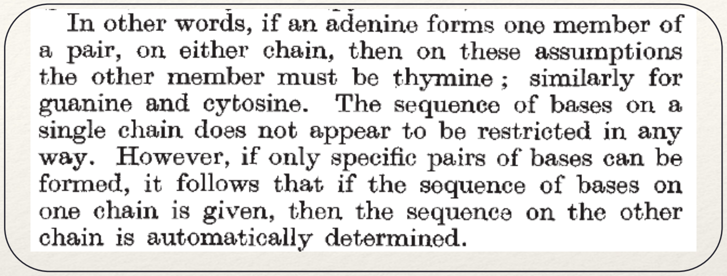
2-deoxyribose

DNA

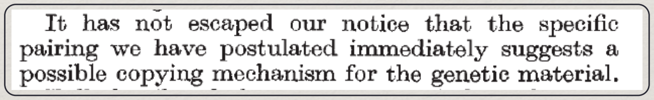

HOH$_2$C
O
base
H
H
H
H
H
Ester linkage
O
HO—P=O
O—H$_2$C
Ester linkage
n
OH
5'
3'

DNA





In other words, if an adenine forms one member of a pair, on either chain, then on these assumptions the other member must be thymine; similarly for guanine and cytosine. The sequence of bases on a single chain does not appear to be restricted in any way. However, if only specific pairs of bases can be formed, it follows that if the sequence of bases on one chain is given, then the sequence on the other chain is automatically determined.

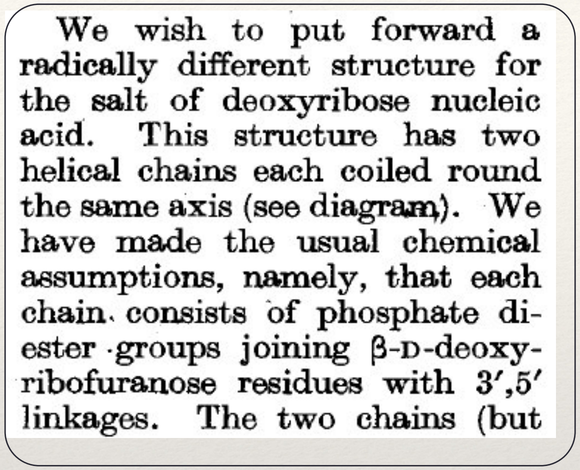


It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material.

Excerpt from Watson and Crick,

Nature, 4356, 737-728 (1953)

DNA


We wish to put forward a radically different structure for the salt of deoxyribose nucleic acid. This structure has two helical chains each coiled round the same axis (see diagram). We have made the usual chemical assumptions, namely, that each chain consists of phosphate diester groups joining β-D-deoxyribofuranose residues with 3′,5′ linkages. The two chains (but

Excerpt from Watson and Crick,

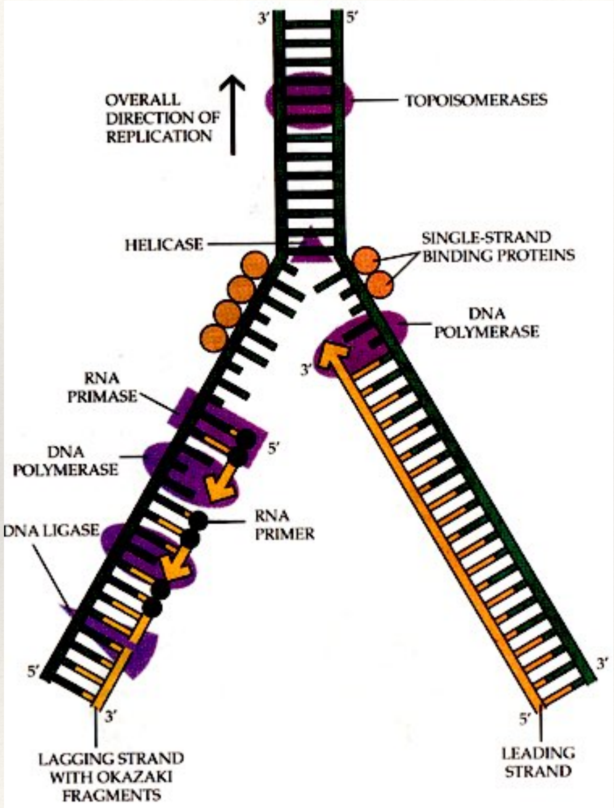
Nature, 4356, 737-728 (1953)

DNA → DNA

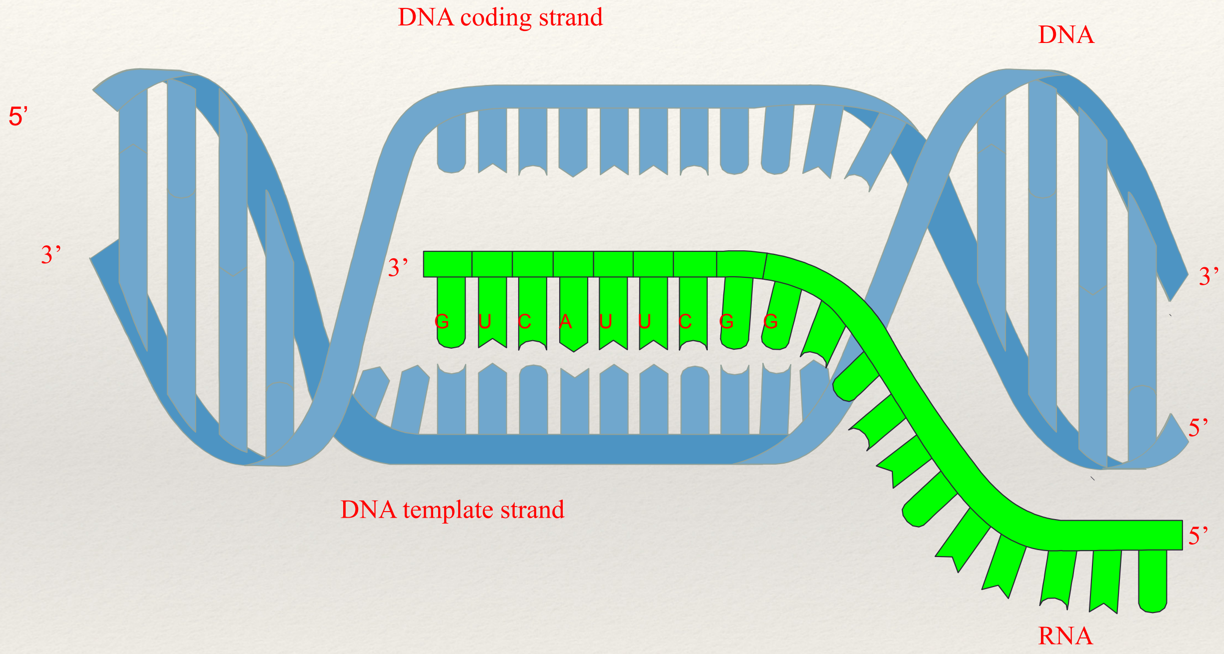
- **Helicase**: separates the two DNA strands, starting at replication origins (rich in A-T base pairs)

- **RNA primase**: inserts a starter of RNA nucleotides at the initiation point

- **DNA polymerase** binds a complementary leading strand of DNA nucleotides starting at the 3’end of the RNA prime



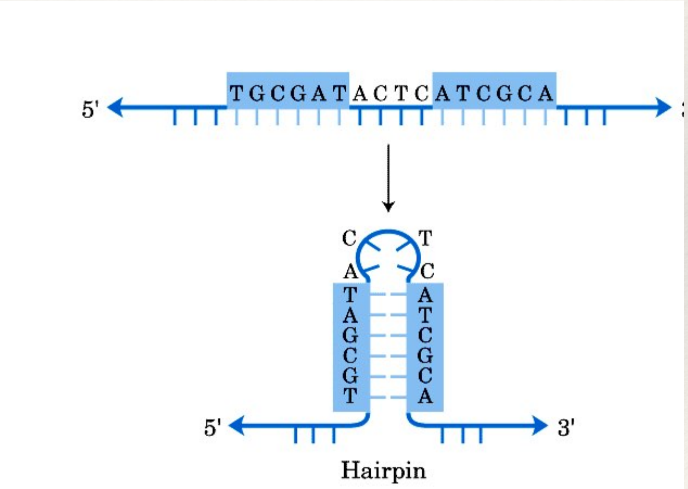
DNA → RNA

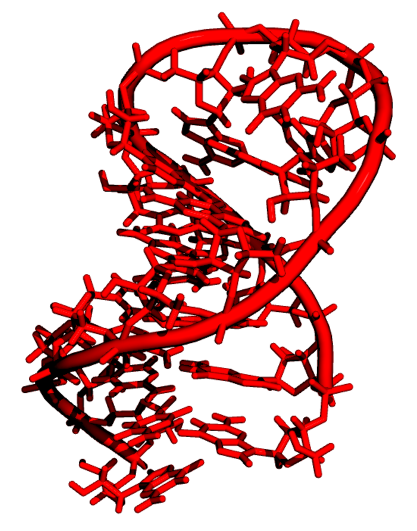

DNA coding strand
DNA
5’
3’
3’
G U C A U U C G G
3’
5’
5’
DNA template strand
RNA

RNA

Single stranded subsequences bounded by base pairs are called loops.

A loop at the end of a stem is called a hairpin loop. Simple substructures consisting of a single stem and loop are called stem loops, or hairpins.

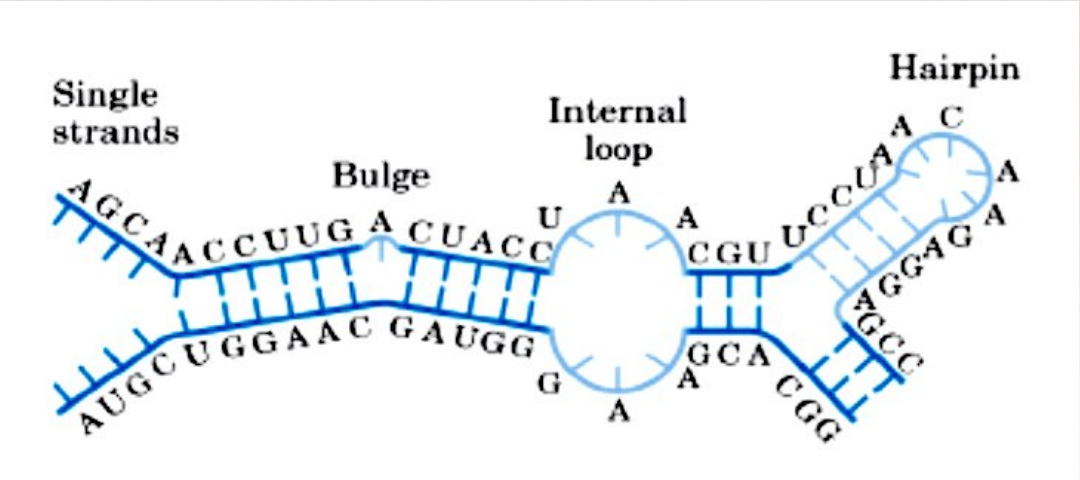




RNA

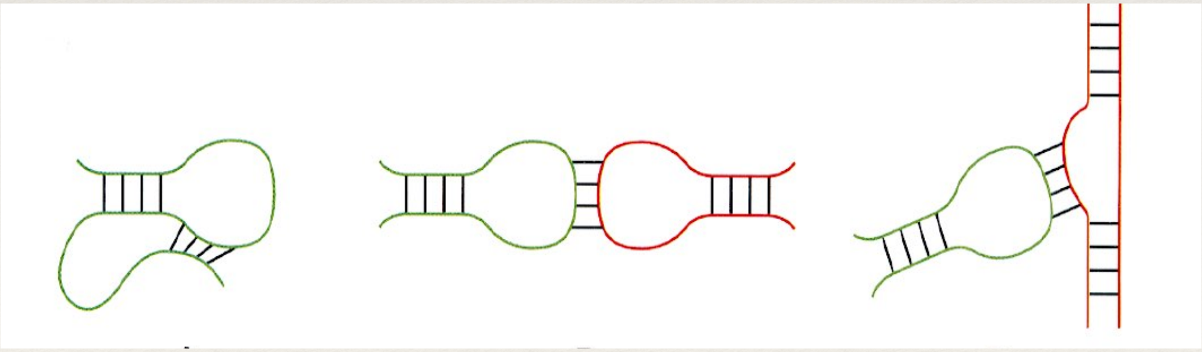
Single stranded bases within a stem form a bulge or bulge loop if the single stranded bases are on only one side of the stem.

If single stranded bases interrupt both sides of a stem, they form an internal (interior) loop.

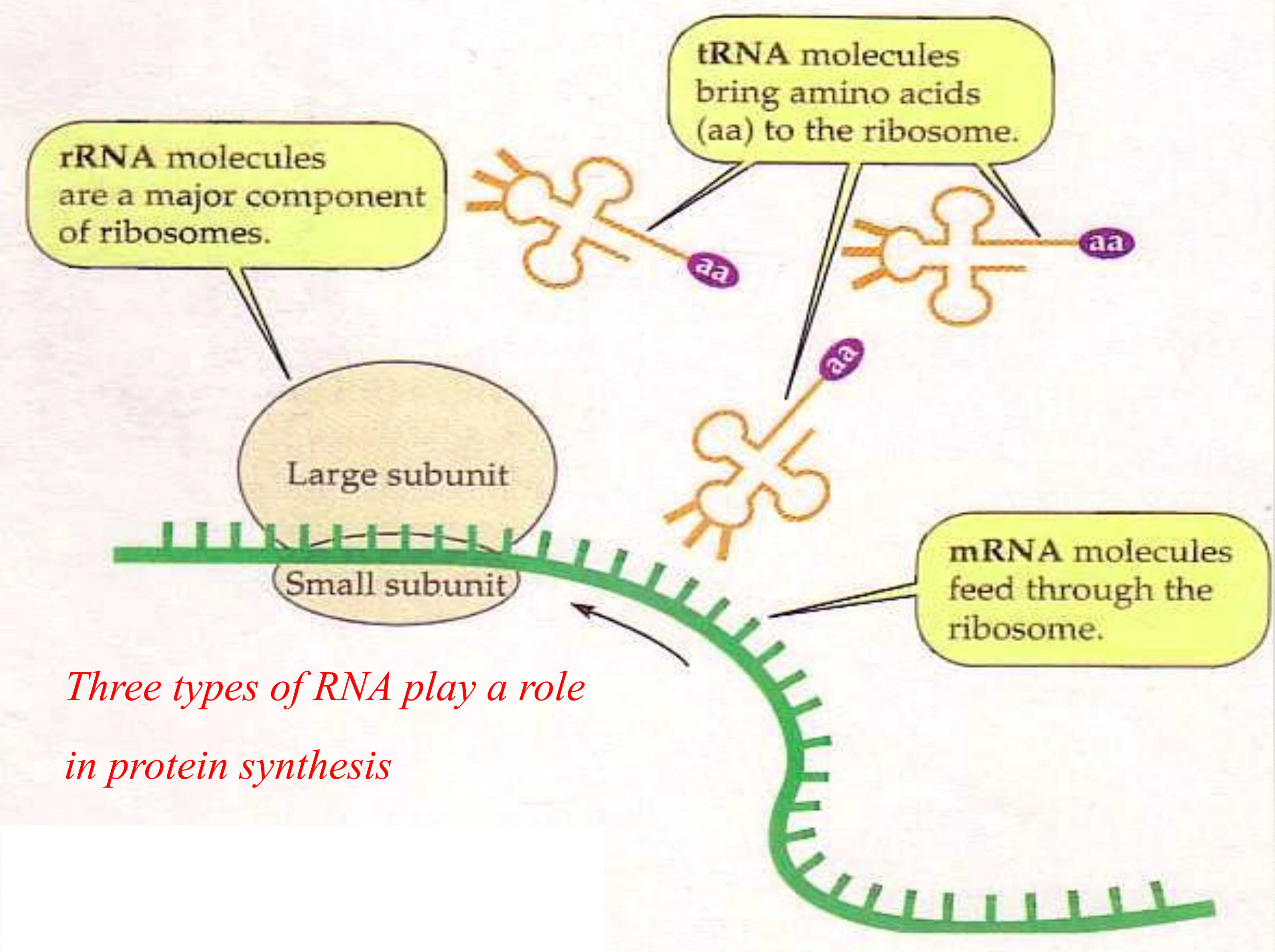


RNA

In addition to secondary structural interactions in RNA, there are also tertiary interactions, including: (A) pseudoknots, (B) kissing hairpins and (C) hairpin-bulge contacts.



Pseudoknot Kissing hairpins Hairpin-bulge



rRNA molecules are a major component of ribosomes.

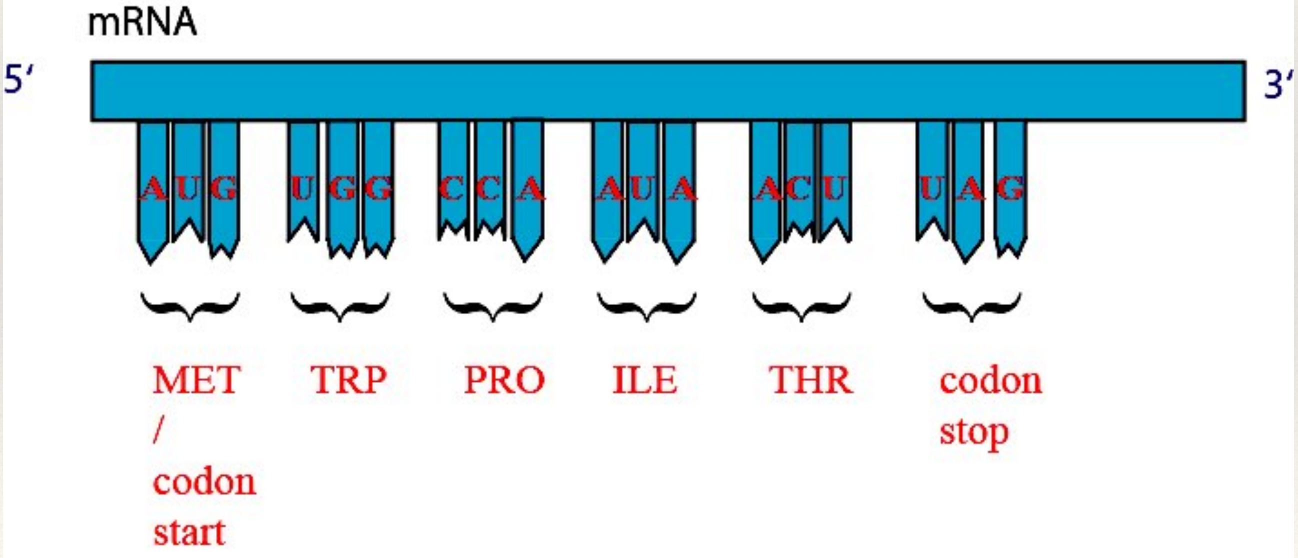
tRNA molecules bring amino acids (aa) to the ribosome.

mRNA molecules feed through the ribosome.

Three types of RNA play a role in protein synthesis

TRANSLATION

- The process of reading the mRNA sequence and creating the protein is called translation
- Protein are made of amino acids (20 different, 9 “essentials”)
- 3 bases or nucleotides make one codon
- Each codon specifies one amino acid : genetic code



RNA → Protein

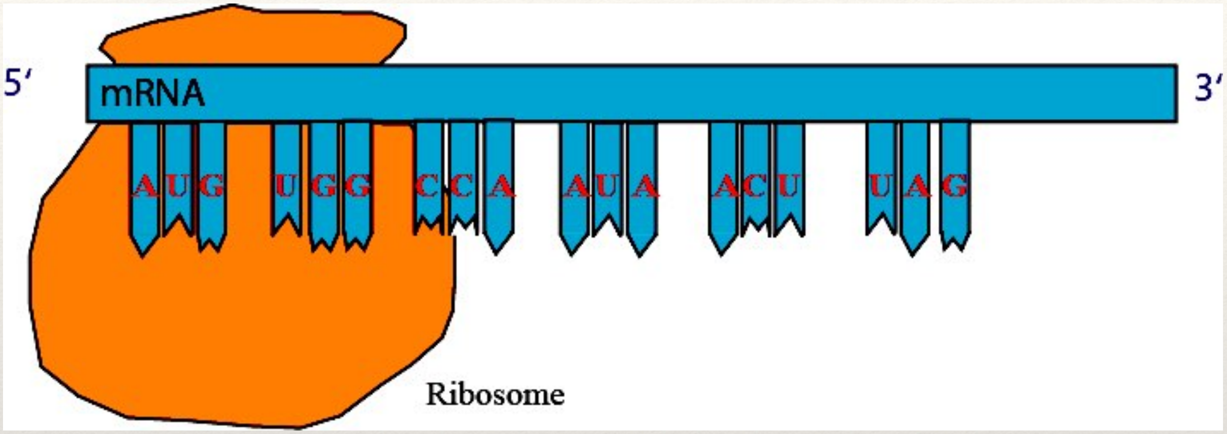
2nd base in codon

1st base in codon

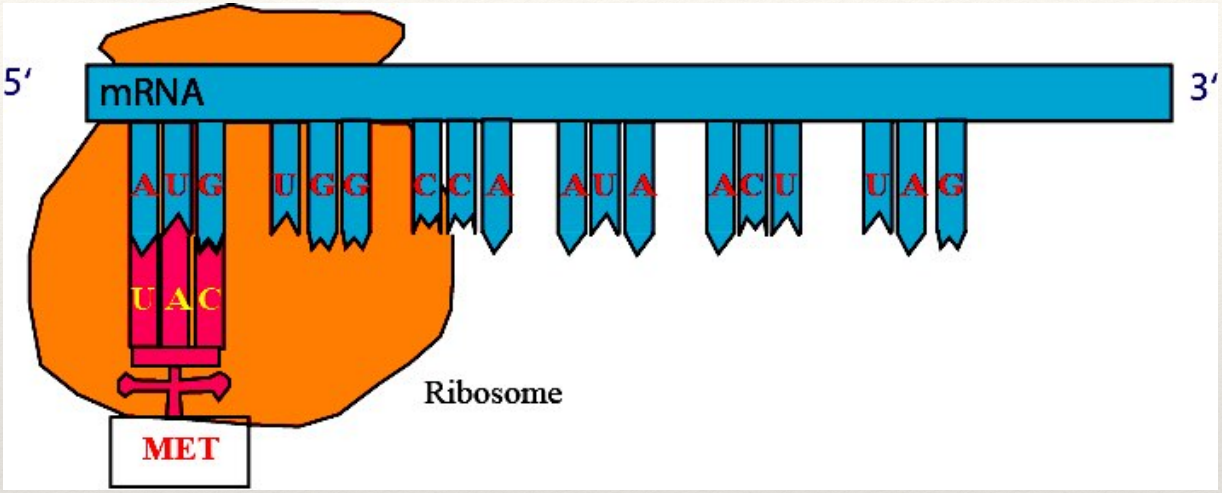
3rd base in codon

	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/Start	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

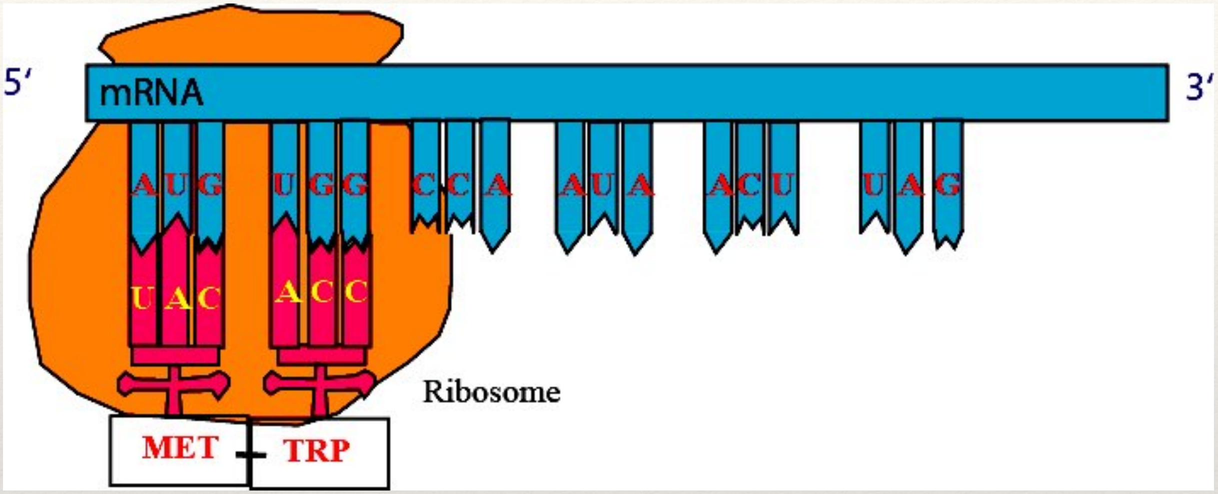
RNA → Protein



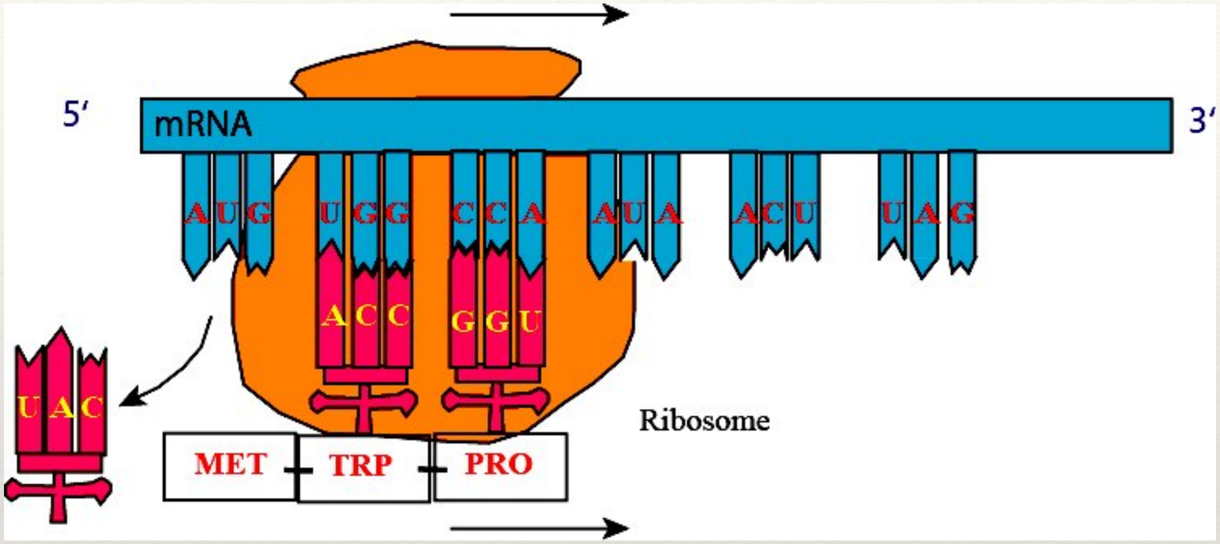
RNA → Protein



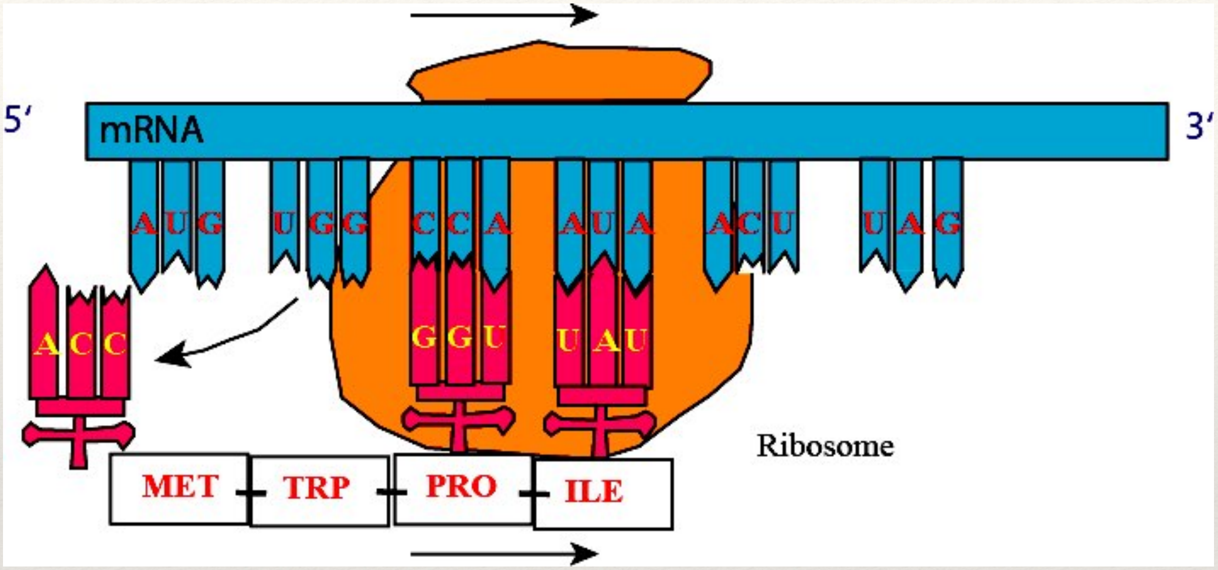
RNA → Protein



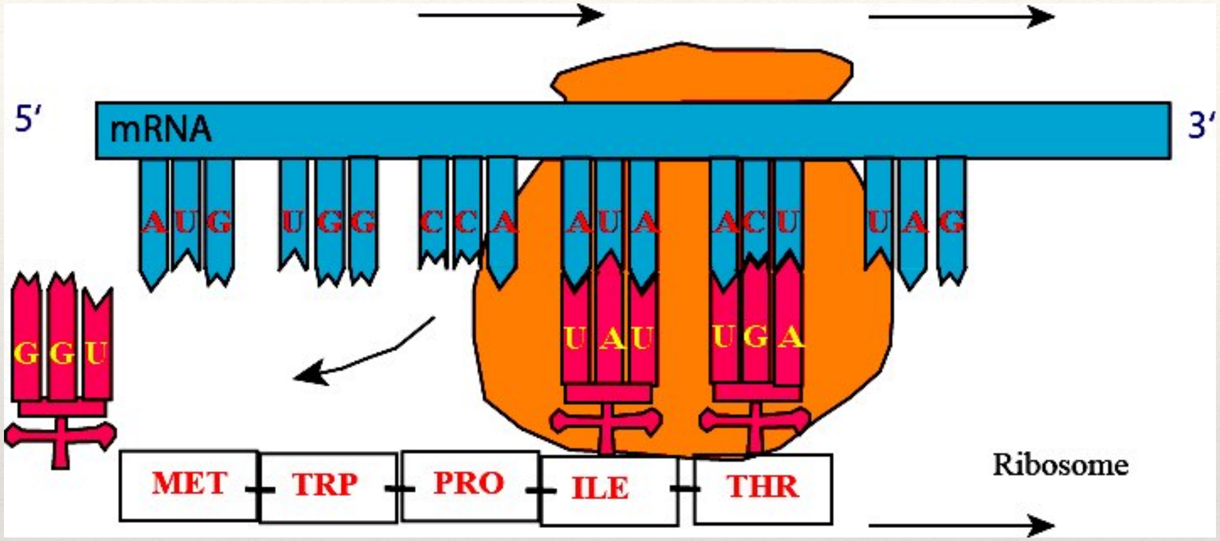
RNA → Protein


5'
mRNA
3'
A U G
U G G
C C A
A U A
A C U
U A G
A C C
G G U
U A C
Ribosome
MET
TRP
PRO

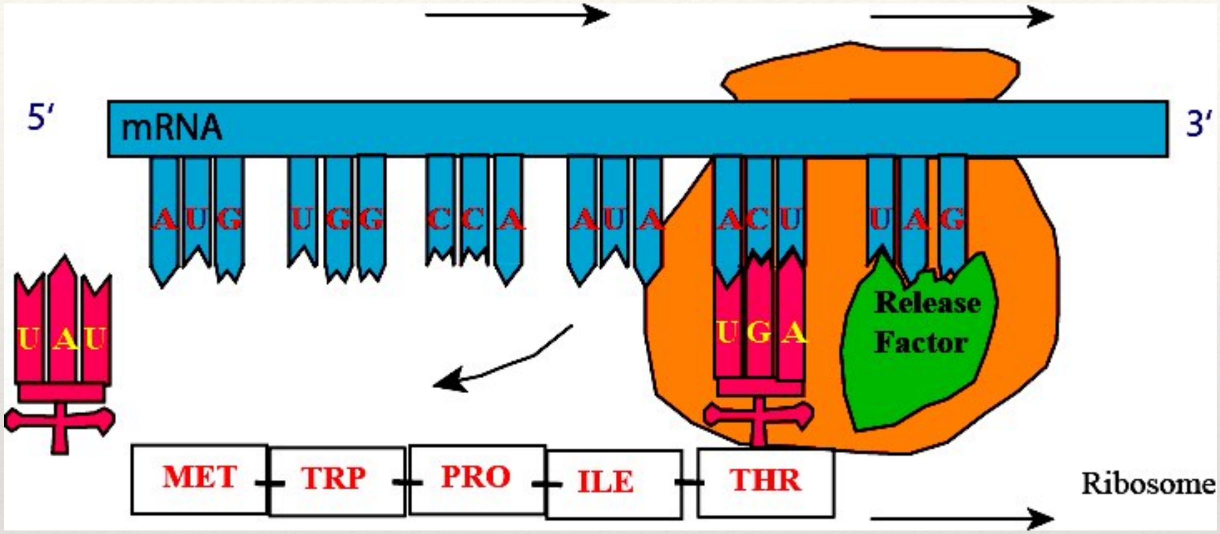
RNA → Protein


5′
mRNA
3′
A U G
U G G
C C A
A U A
A C U
U A G
A C C
G G U
U A U
MET
TRP
PRO
ILE
Ribosome

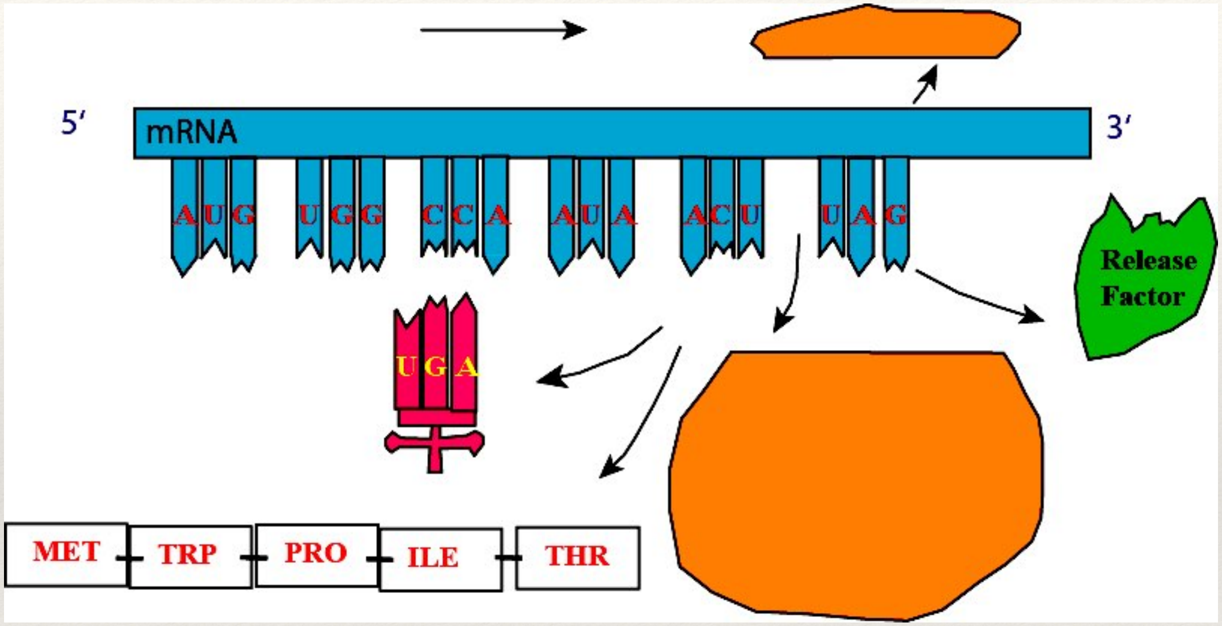
RNA → Protein


5′
mRNA
3′
A U G
U G G
C C A
A U A
A C U
U A G
G G U
U A U
U G A
MET
TRP
PRO
ILE
THR
Ribosome

RNA → Protein

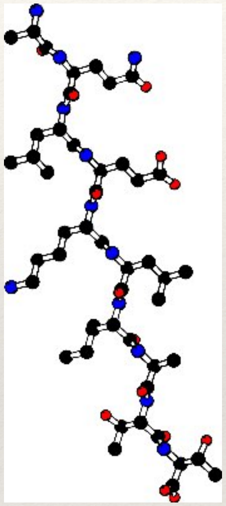

5′
mRNA
3′
A U G
U G G
C C A
A U A
A C U
U A G
U A U
U G A
Release Factor
MET
TRP
PRO
ILE
THR
Ribosome

RNA → Protein


5′
mRNA
3′
A U G
U G G
C C A
A U A
A C U
U A G
U G A
Release Factor
MET
TRP
PRO
ILE
THR

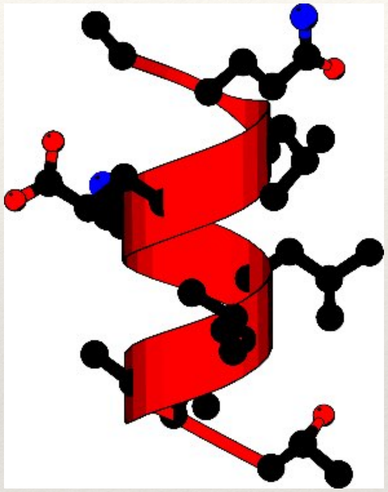
Protein

Primary structure



Sequence of Amino acids

Secondary Structure



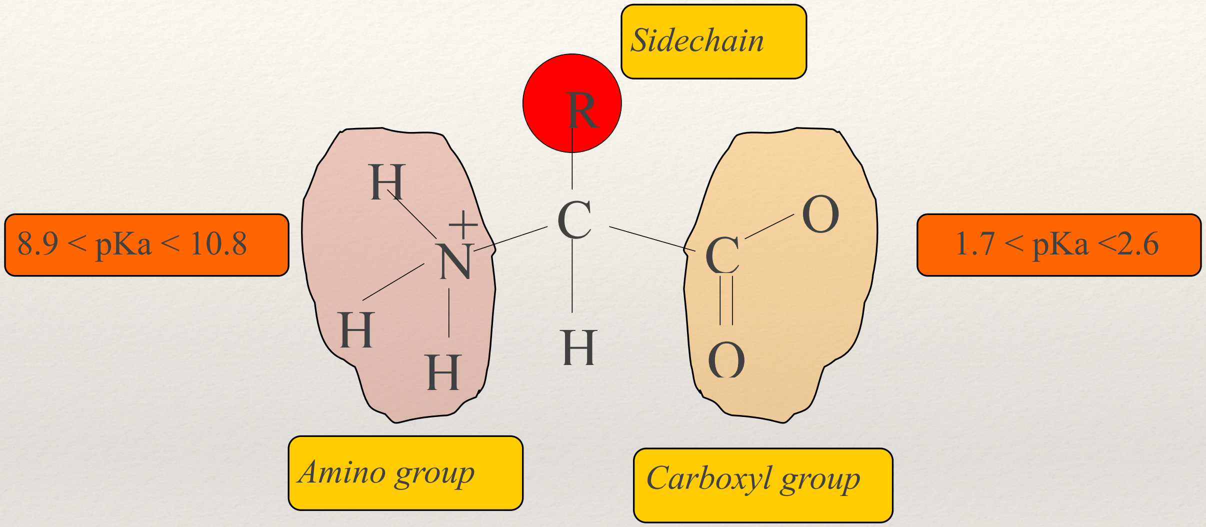
Local interactions

Tertiary Structure

Native protein

Protein

The Basic Block: Amino Acid



Sidechain

8.9 < pKa < 10.8

1.7 < pKa <2.6

Amino group

Carboxyl group

“zwitterion”

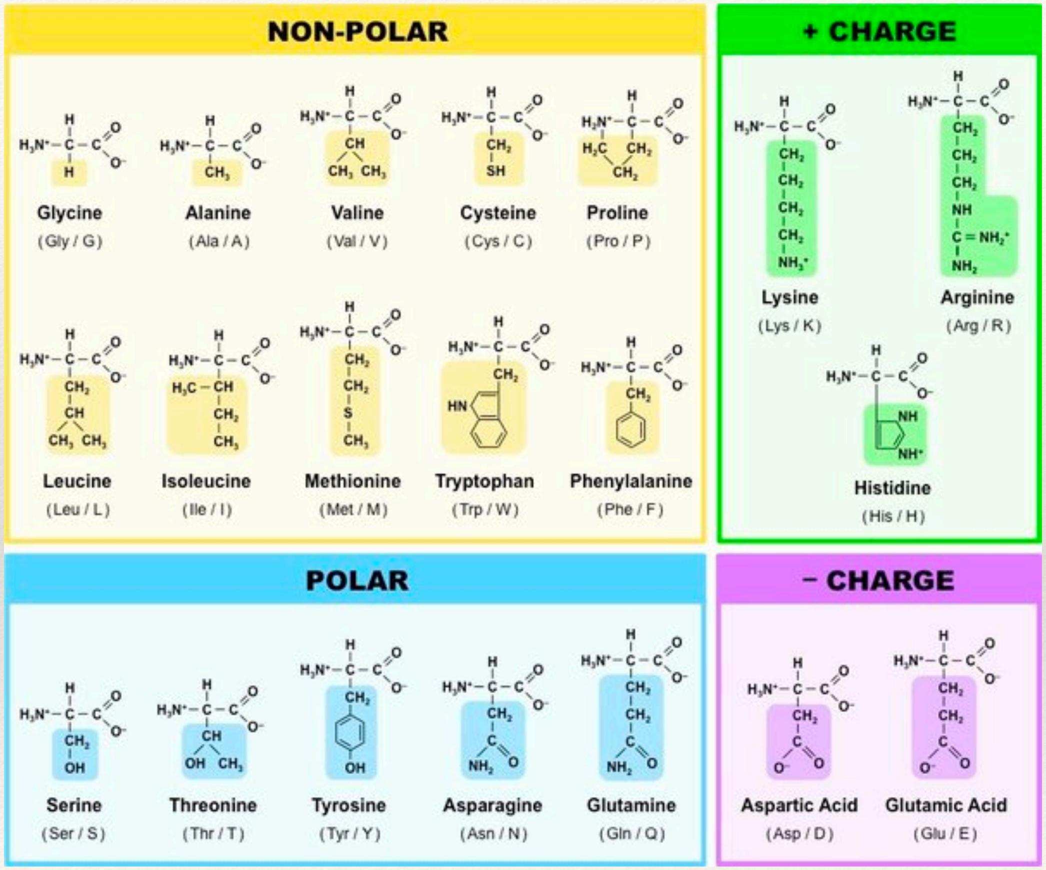
Protein

The 20 amino acids

1-letter	3-letter	Amino acid
A	Ala	Alanine
C	Cys	Cysteine
D	Asp	Aspartic Acid
E	Glu	Glutamic Acid
F	Phe	Phenylalanine
G	Gly	Glycine
H	His	Histidine
I	Ile	Isoleucine
K	Lys	Lysine
L	Leu	Leucine
M	Met	Methionine
N	Ask	Asparagine
P	Pro	Proline
Q	Gln	Glutamine
R	Arg	Arginine
S	Ser	Serine
T	The	Threonine
V	Val	Valine
W	Trp	Tryptophane
Y	Tyr	Tyrosine

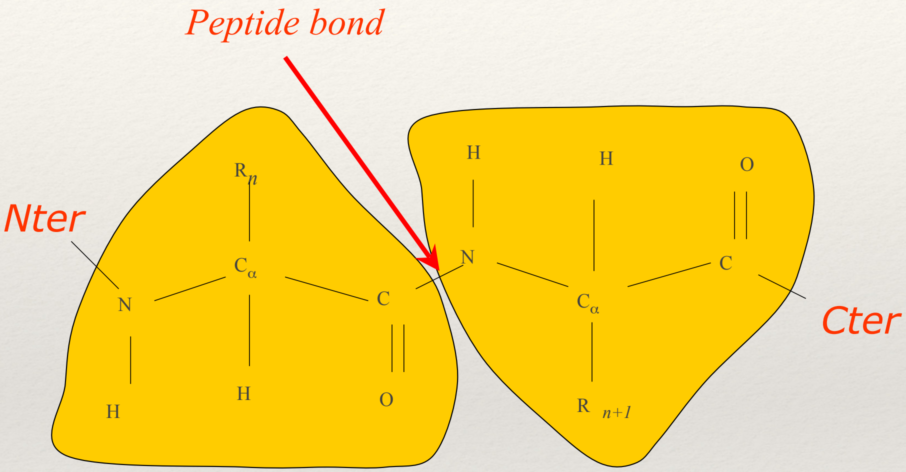
Protein

The 20 amino acids

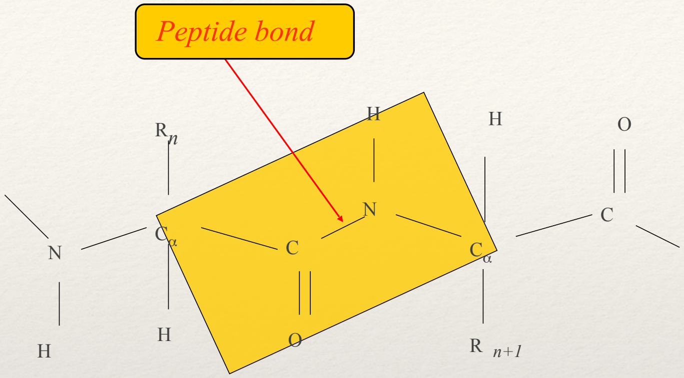


Protein

The Protein: A polymer of Amino acids

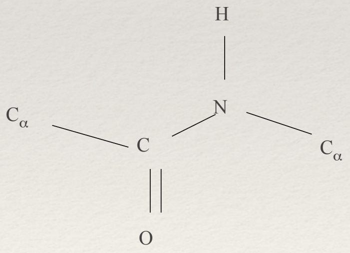


Protein

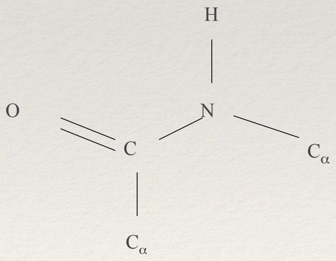


Peptide bond

The peptide bond is



Conformation “Trans”

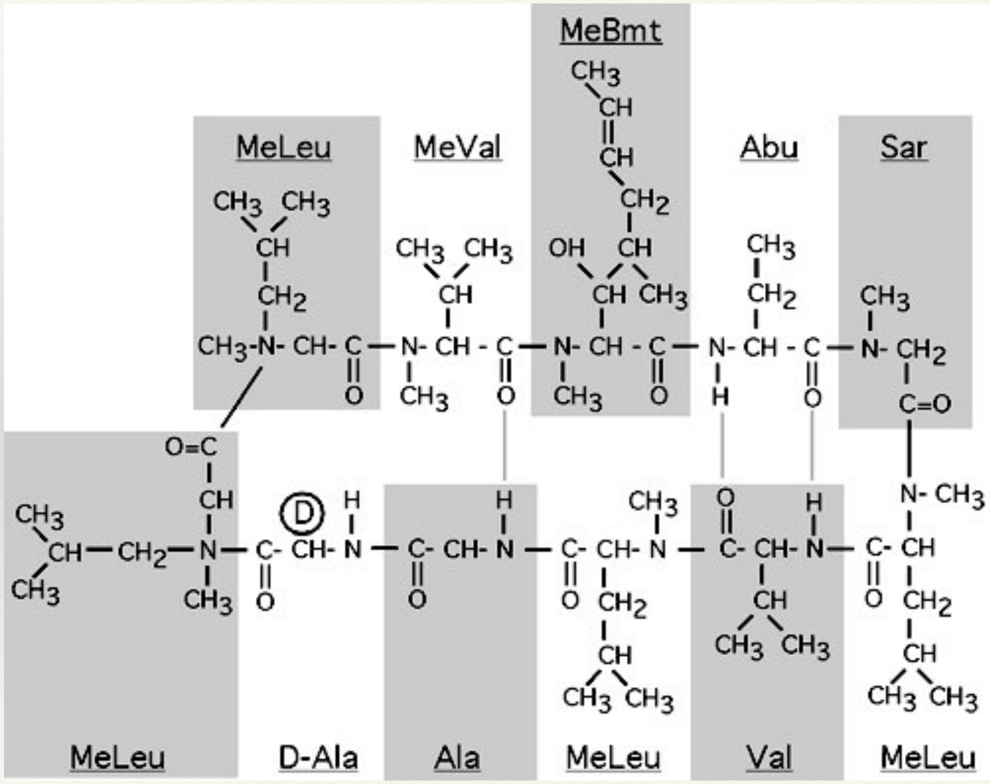


Conformation

Protein

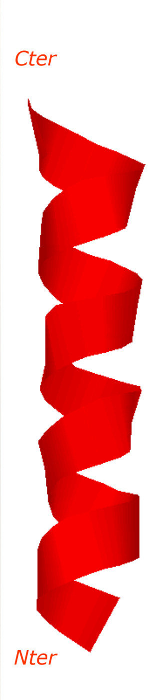
Unusual Amino Acids: Cyclosporin

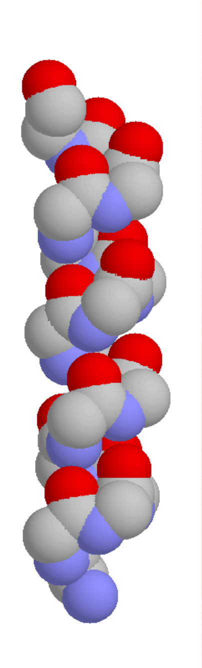
Where are the errors?

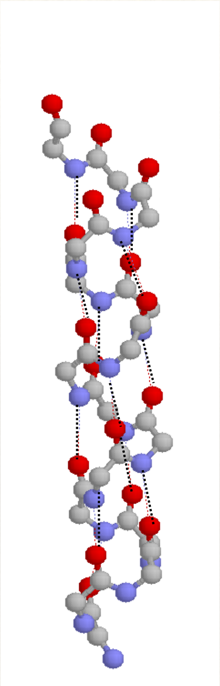


Protein

Helices



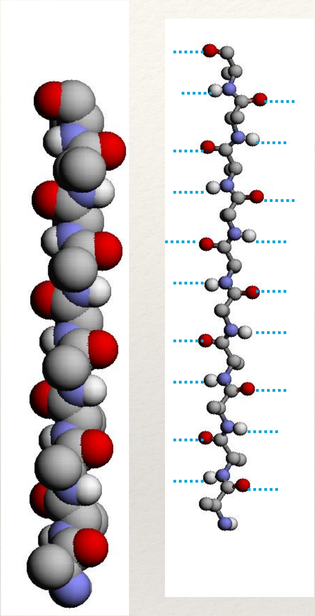




Hydrogen bonds: O (i) <-> N (i+4)

Protein

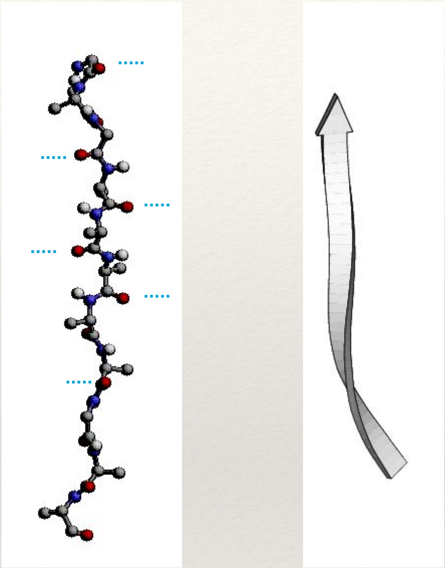
The β-strand



Extended chain is flat

N-H---O-C

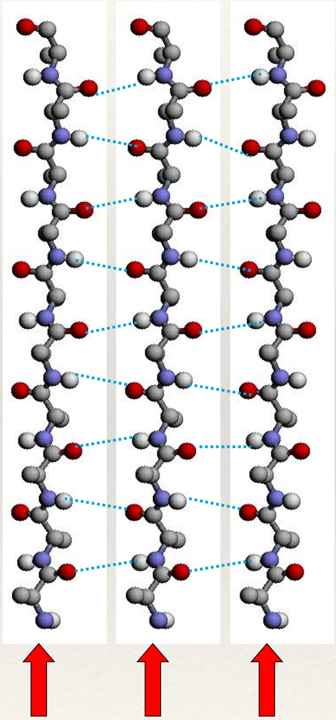
Hydrogen bonds



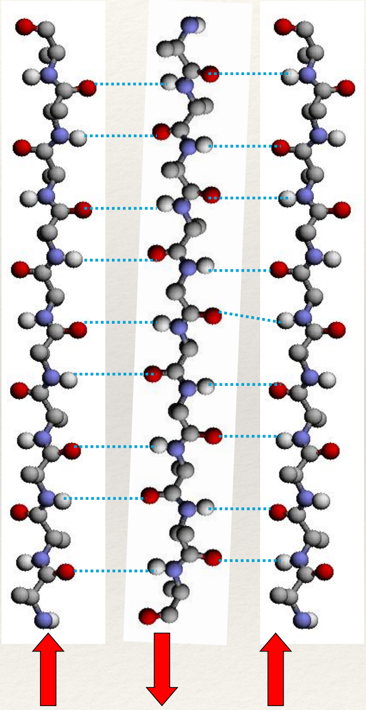
"Real β-strand is twisted"

Protein

Two types of β-sheets



Parallel



Anti-parallel

Protein

Protein Tertiary Structure

- All α proteins
- All β proteins
- Alpha and beta proteins:
  - α/β proteins (alternating α and β)
  - α + β proteins