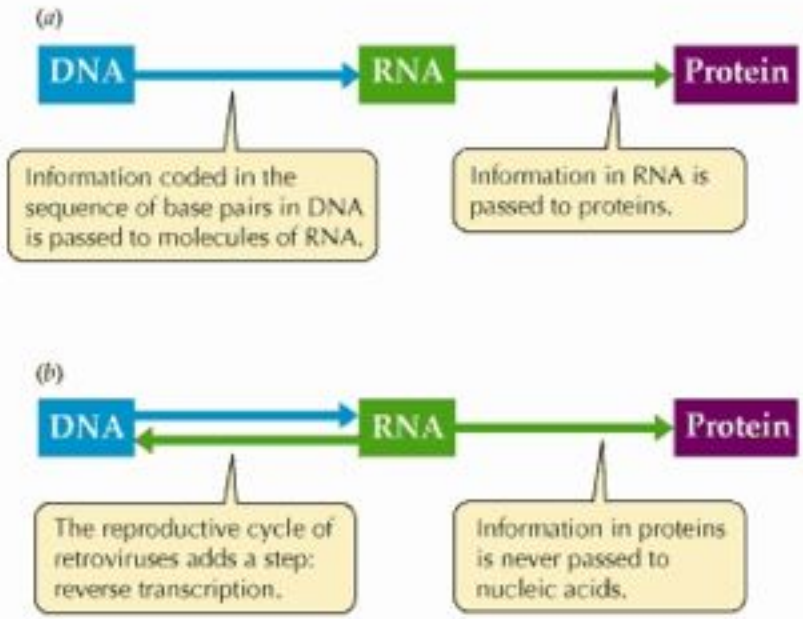
BTEC 101

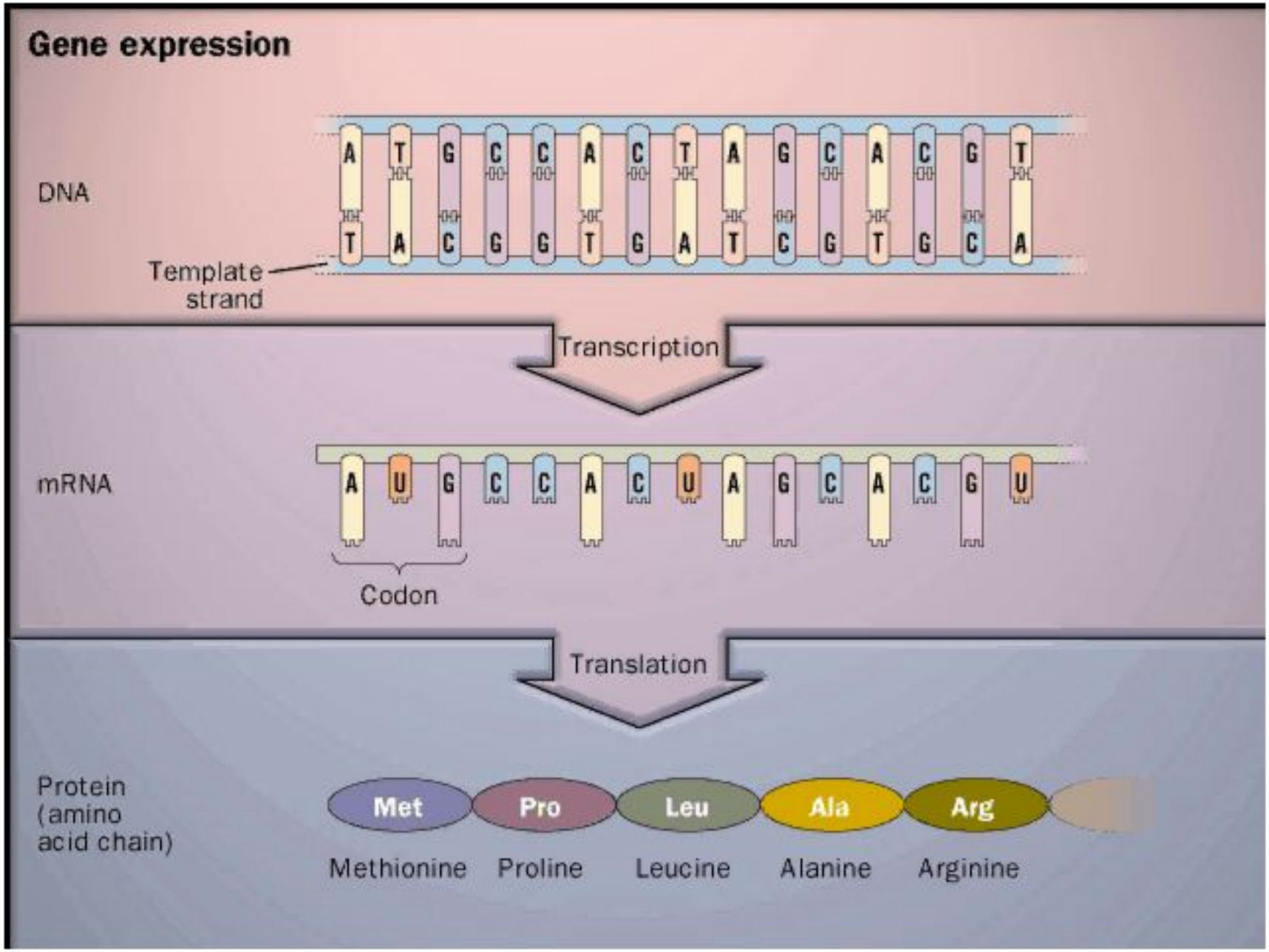
Protein Folding

Protein Basics

- Proteins are the workers of the cells
- Proteins are encoded by DNA (Central Dogma)
- Form follows function.

The Central Dogma



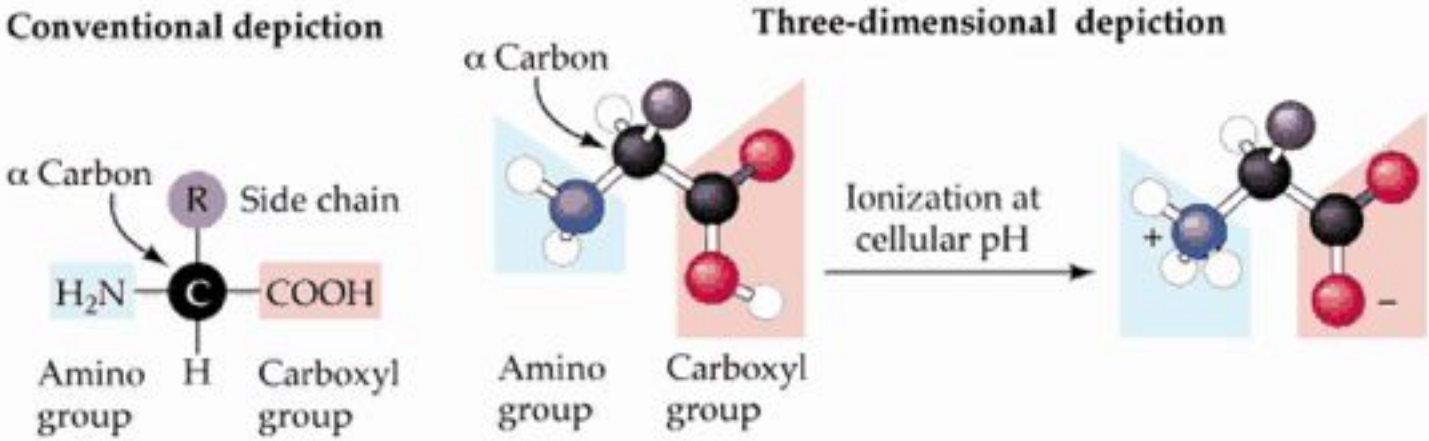

Gene expression
DNA
A T G C C A C T A G C A C G T
T A C G G T G A T C G T G C A
Template strand
Transcription
mRNA
A U G C C A C U A G C A C G U
Codon
Translation
Protein (amino acid chain)
Met Pro Leu Ala Arg
Methionine Proline Leucine Alanine Arginine

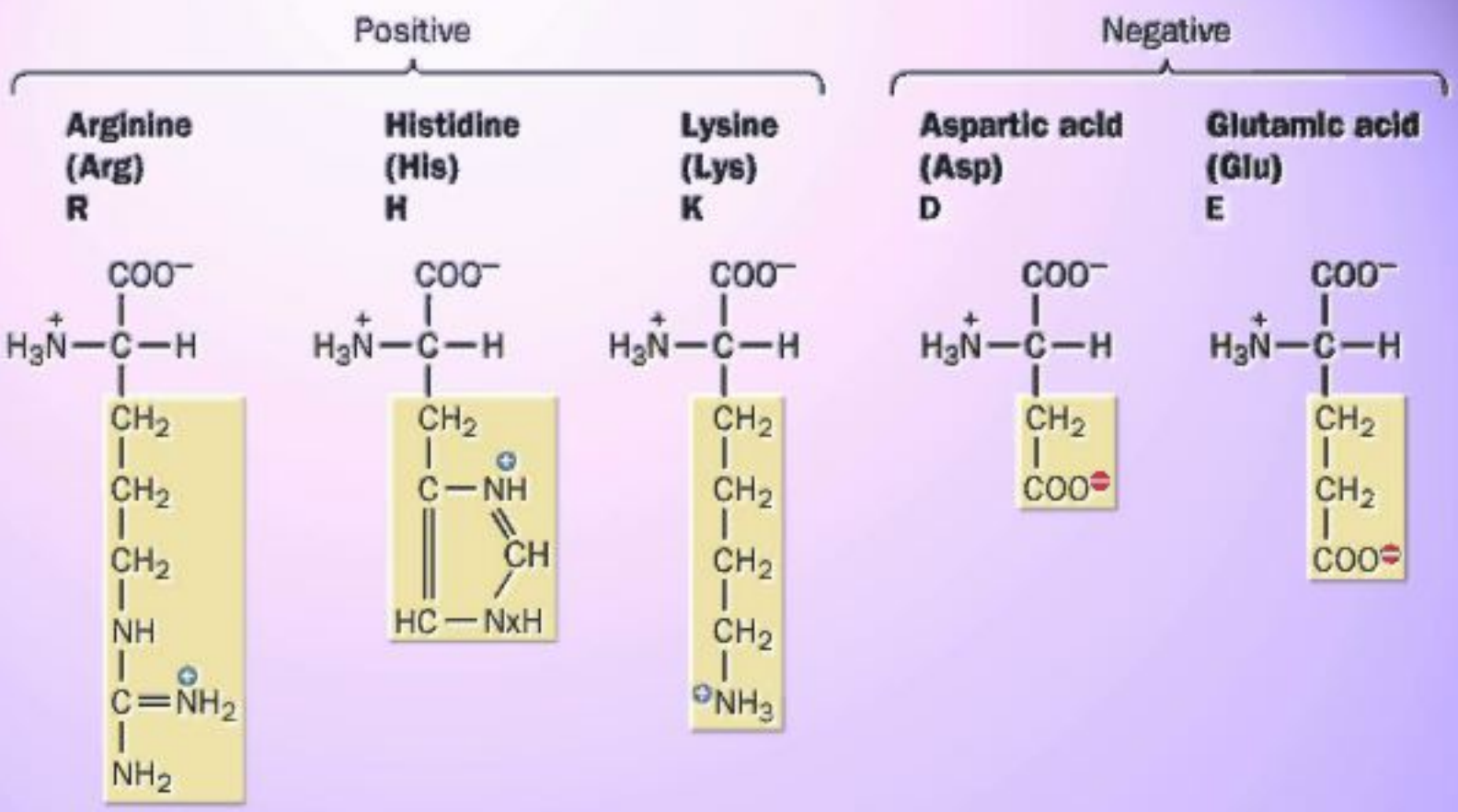
First base	Second base: U	Second base: C	Second base: A	Second base: G	Third base
U	UUU Phe	UCU Ser	UAU Tyr	UGU Cys	U
	UUC Phe	UCC Ser	UAC Tyr	UGC Cys	C
	UUA Leu	UCA Ser	UAA Stop	UGA Stop	A
	UUG Leu	UCG Ser	UAG Stop	UGG Trp	G
C	CUU Leu	CCU Pro	CAU His	CGU Arg	U
	CUC Leu	CCC Pro	CAC His	CGC Arg	C
	CUA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

Protein structure

- Proteins are a composite of amino acids.
- Amino acids have a general structure as seen on the next slide.
- The order of the amino acids determines the proteins conformation.
- Form follows function.

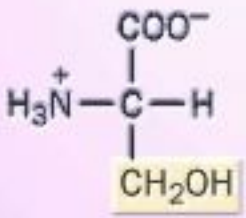
Amino Acids


Conventional depiction
α Carbon
R
Side chain
H_2N
C
COOH
Amino group
H
Carboxyl group
Three-dimensional depiction
α Carbon
Amino group
Carboxyl group
Ionization at cellular pH
+
–

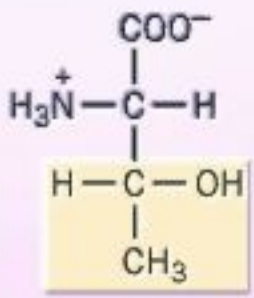


Amino acids with electrically charged side chains

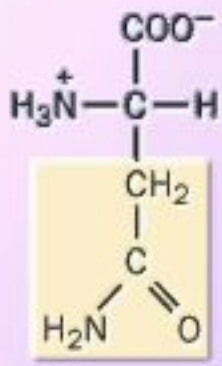
Serine
(Ser)
S



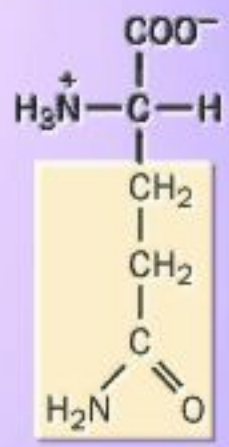
Threonine
(Thr)
T



Asparagine
(Asn)
N

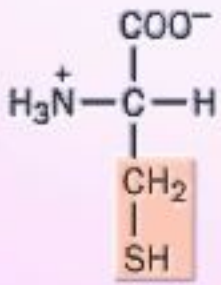


Glutamine
(Gln)
Q

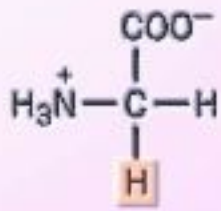


Amino acids with polar but uncharged side chains

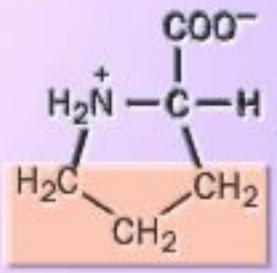
Cysteine
(Cys)
C



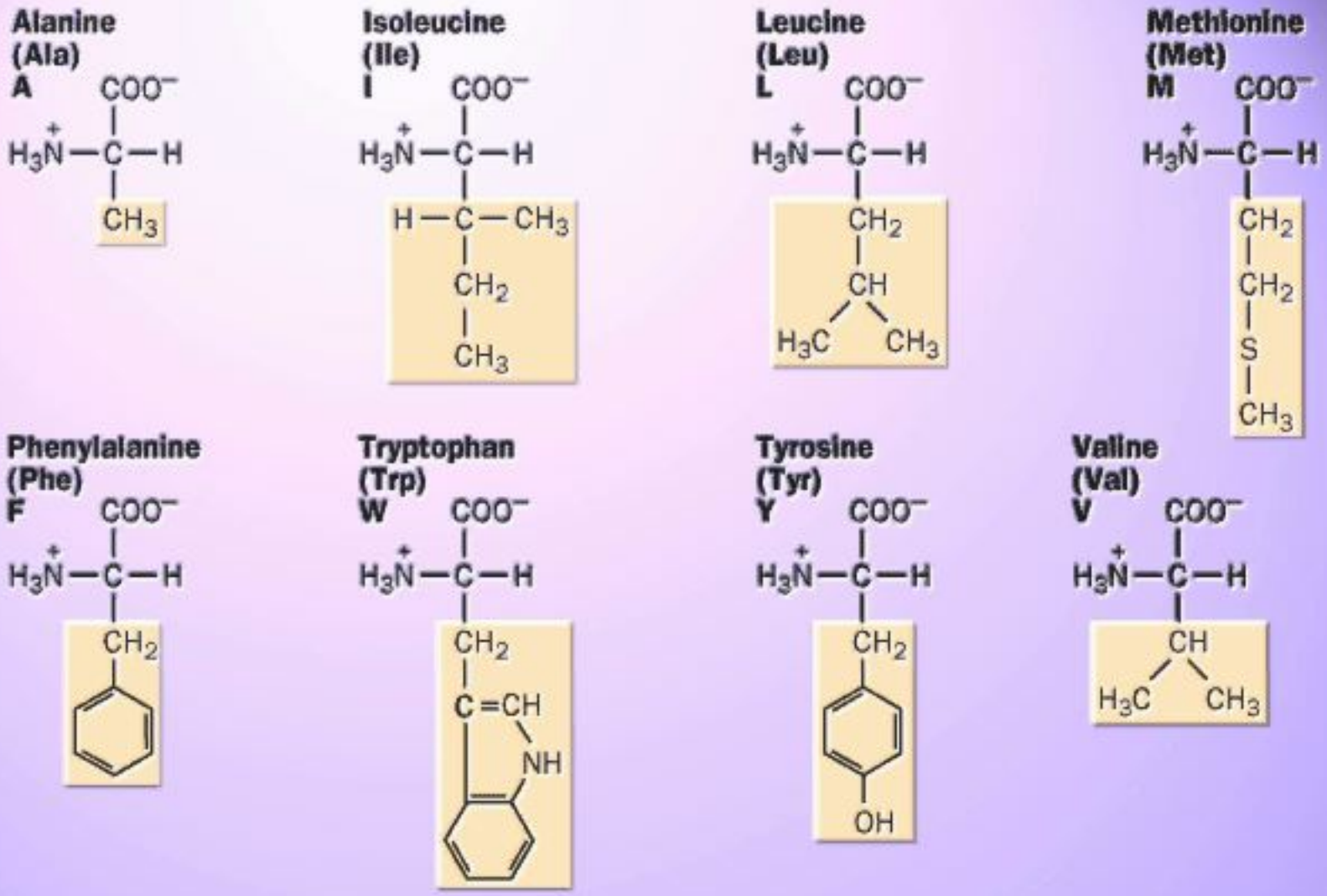
Glycine
(Gly)
G



Proline
(Pro)
P

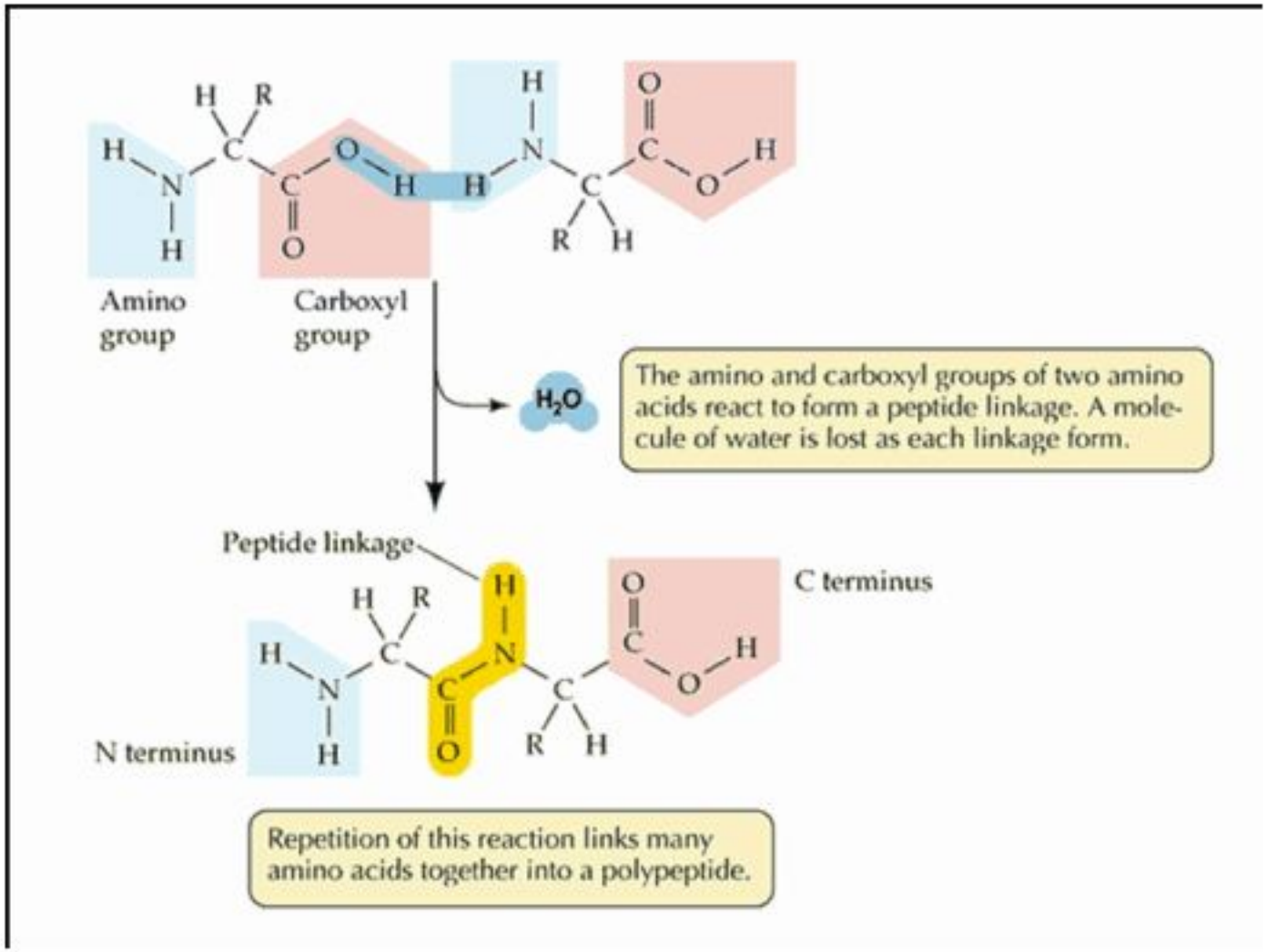


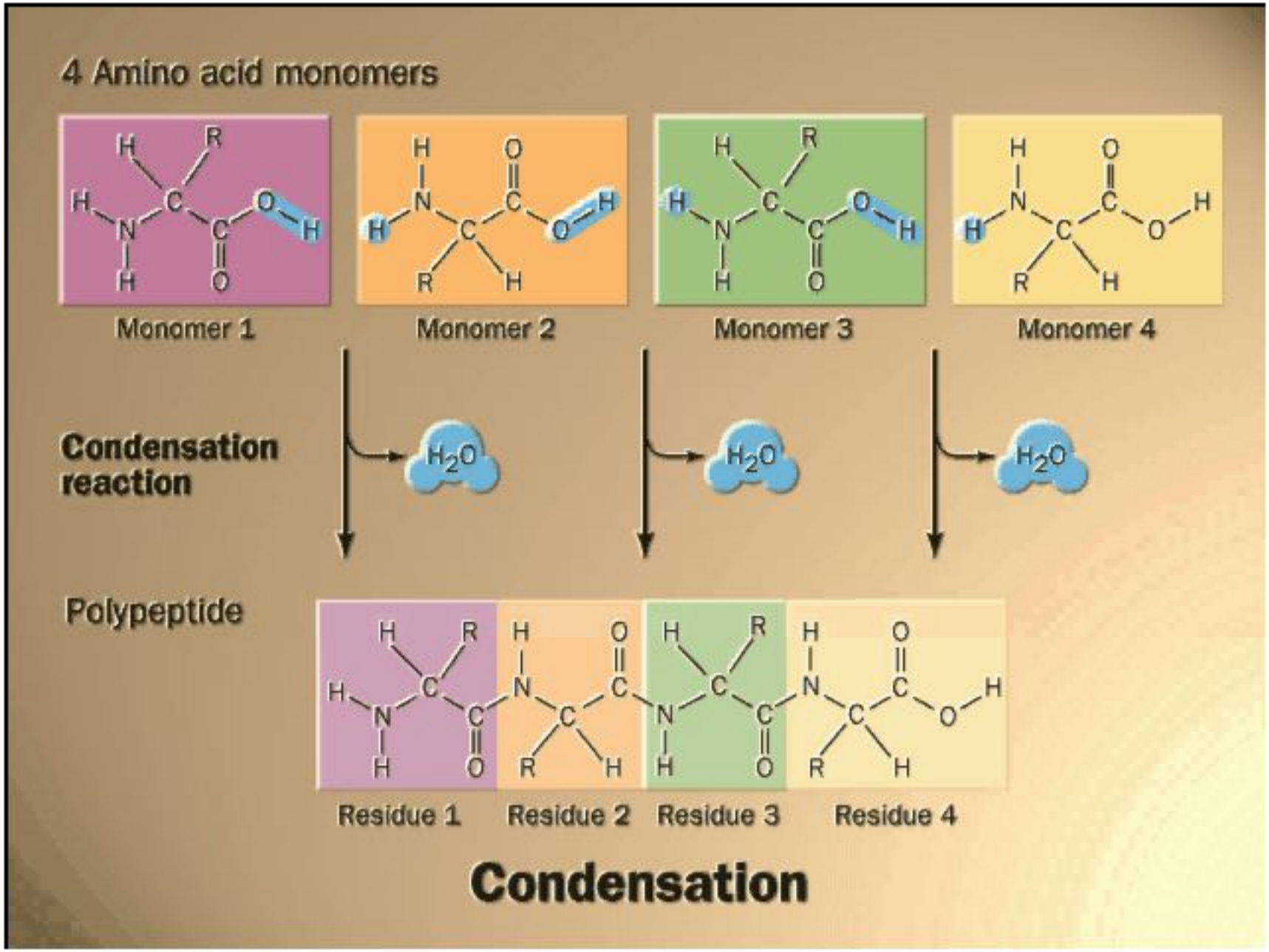
Special cases



Amino acids with hydrophobic side chains

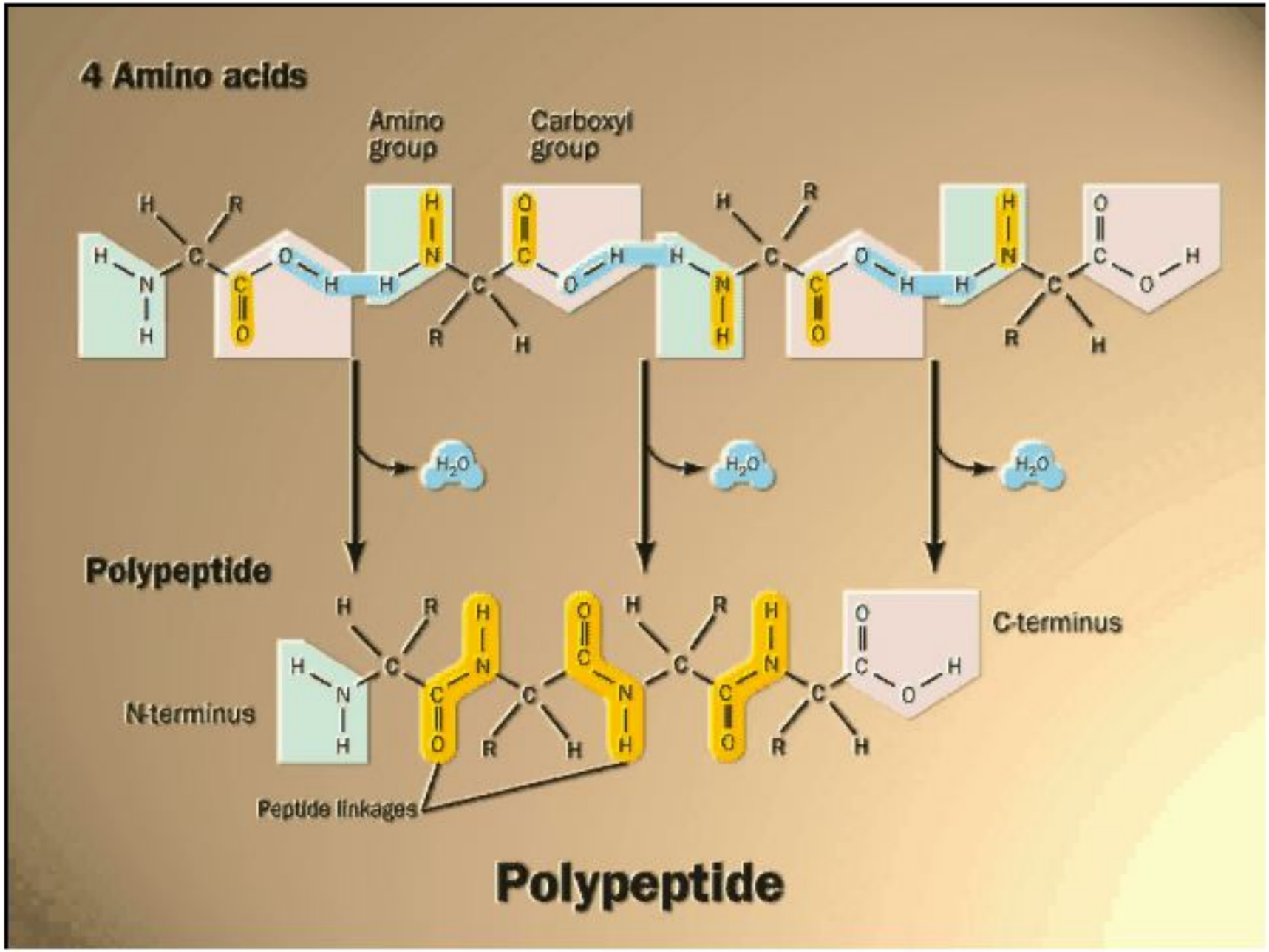
Peptide bonds

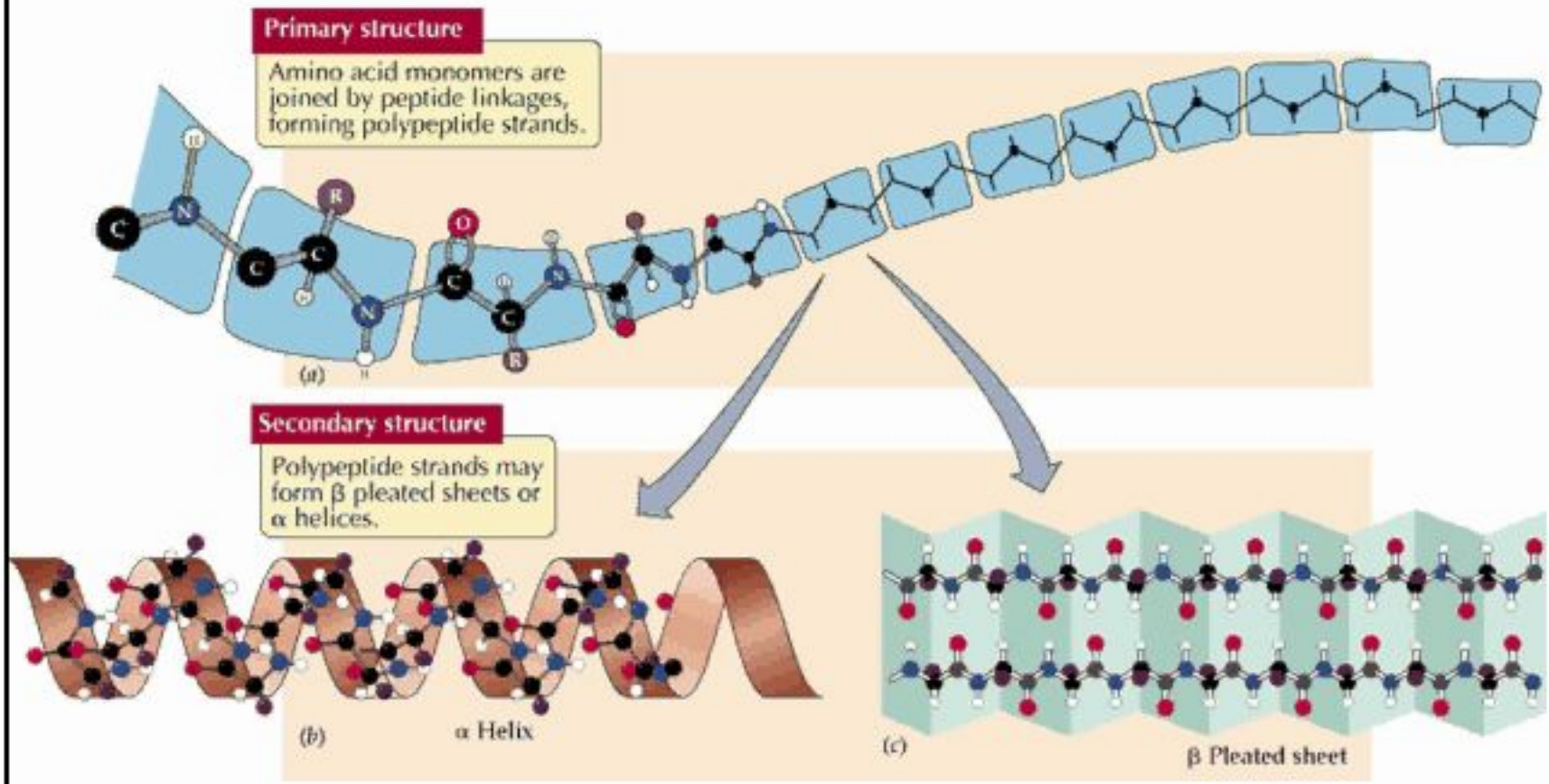



4 Amino acid monomers
Monomer 1
Monomer 2
Monomer 3
Monomer 4
Condensation reaction
H_2O
H_2O
H_2O
Polypeptide
Residue 1
Residue 2
Residue 3
Residue 4
Condensation

Peptide bonds

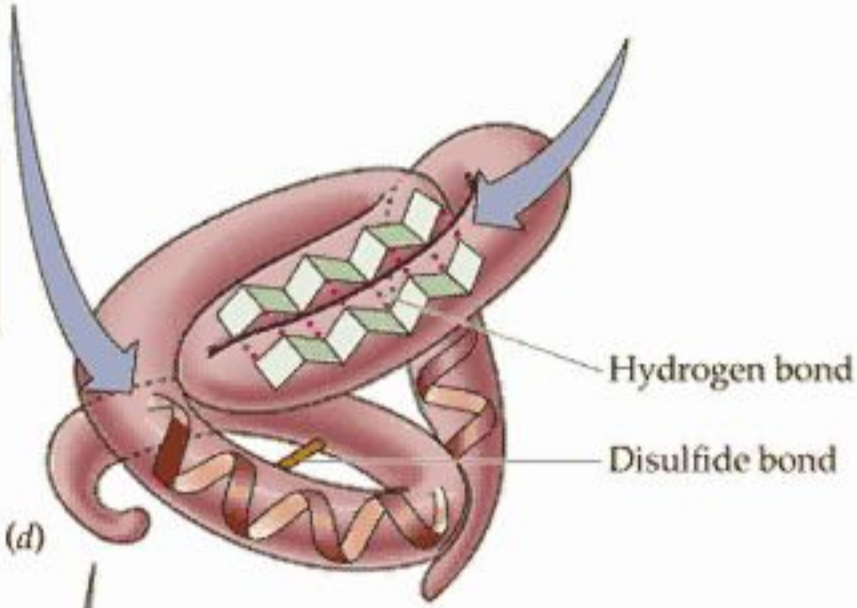
- Formed by the ribosomes in the cell, it is a dehydration reaction.
- Order of the amino acid is encoded in the mRNA.
- Order of the amino acids will determine the function of the protein.


4 Amino acids
Amino group
Carboxyl group
H_2O
Polypeptide
N-terminus
C-terminus
Peptide linkages
Polypeptide


Primary structure
Amino acid monomers are joined by peptide linkages, forming polypeptide strands.
(a)
Secondary structure
Polypeptide strands may form β pleated sheets or α helices.
(b)
α Helix
(c)
β Pleated sheet

Tertiary structure

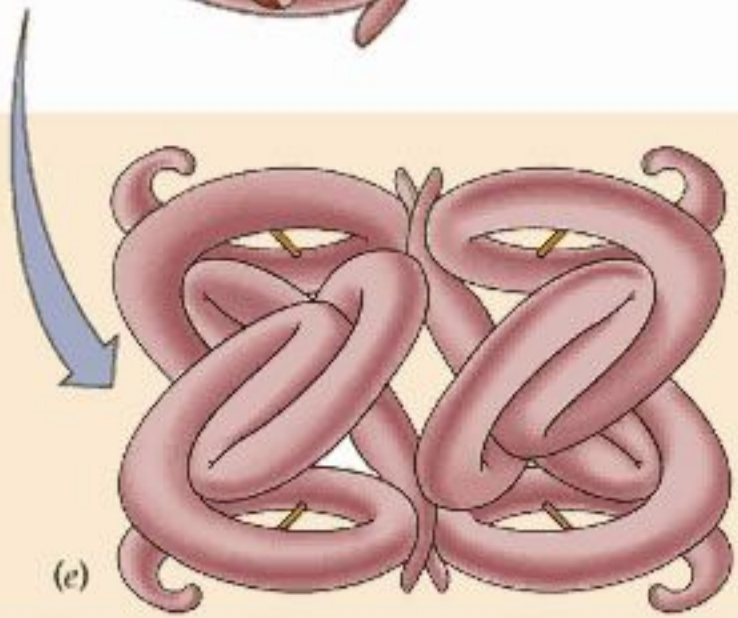
Polypeptides fold, forming specific shapes. Folds are stabilized by bonds, including hydrogen and disulfide bonds.



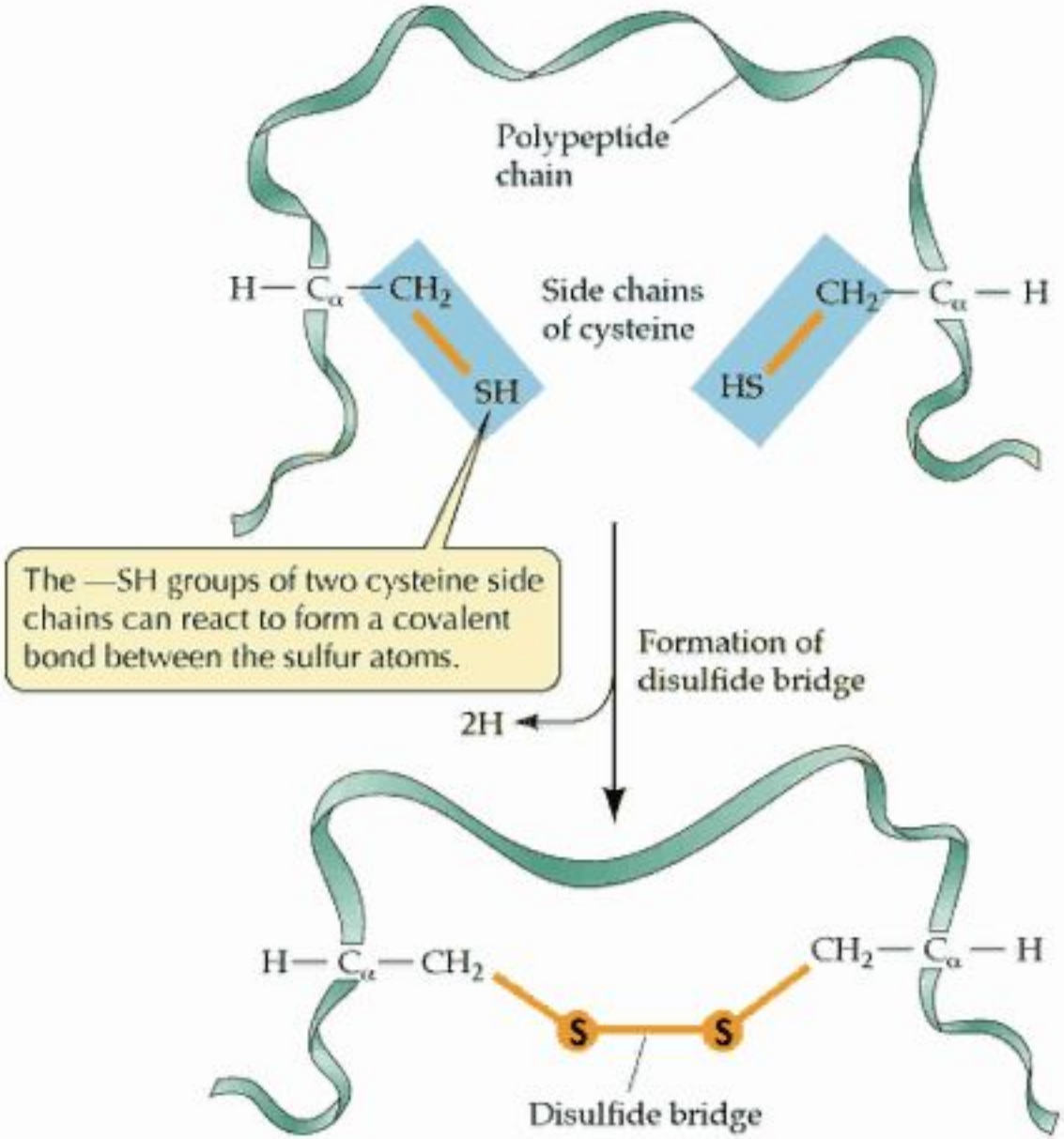
(*d*)

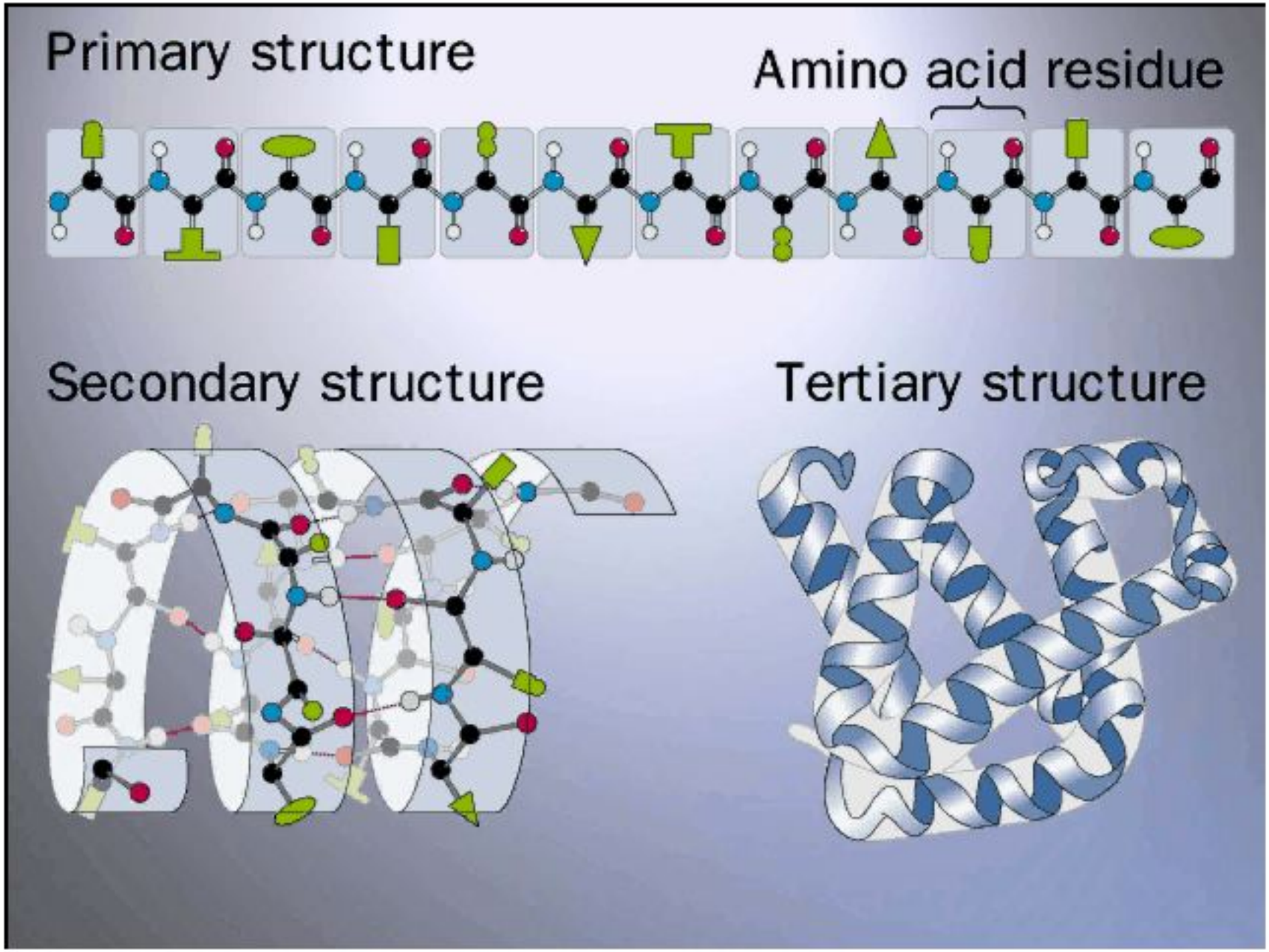
Quaternary structure

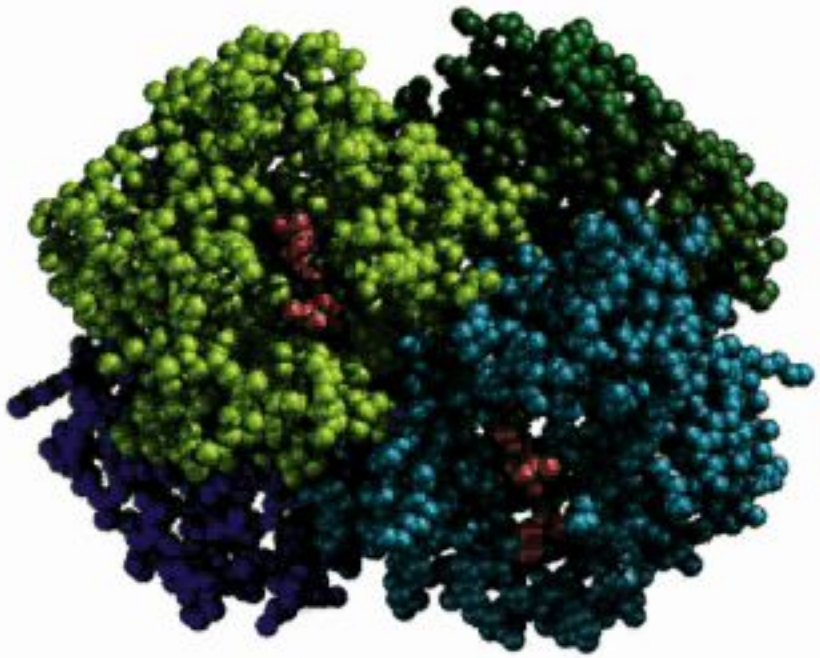
Two or more polypeptides assemble to form larger protein molecules. The hypothetical molecule here is a tetramer, made up of four polypeptides.

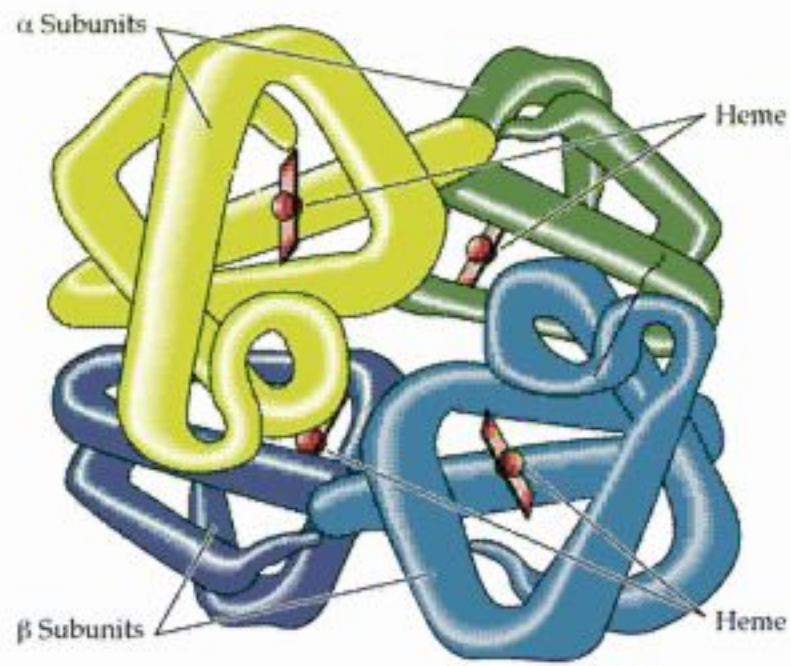


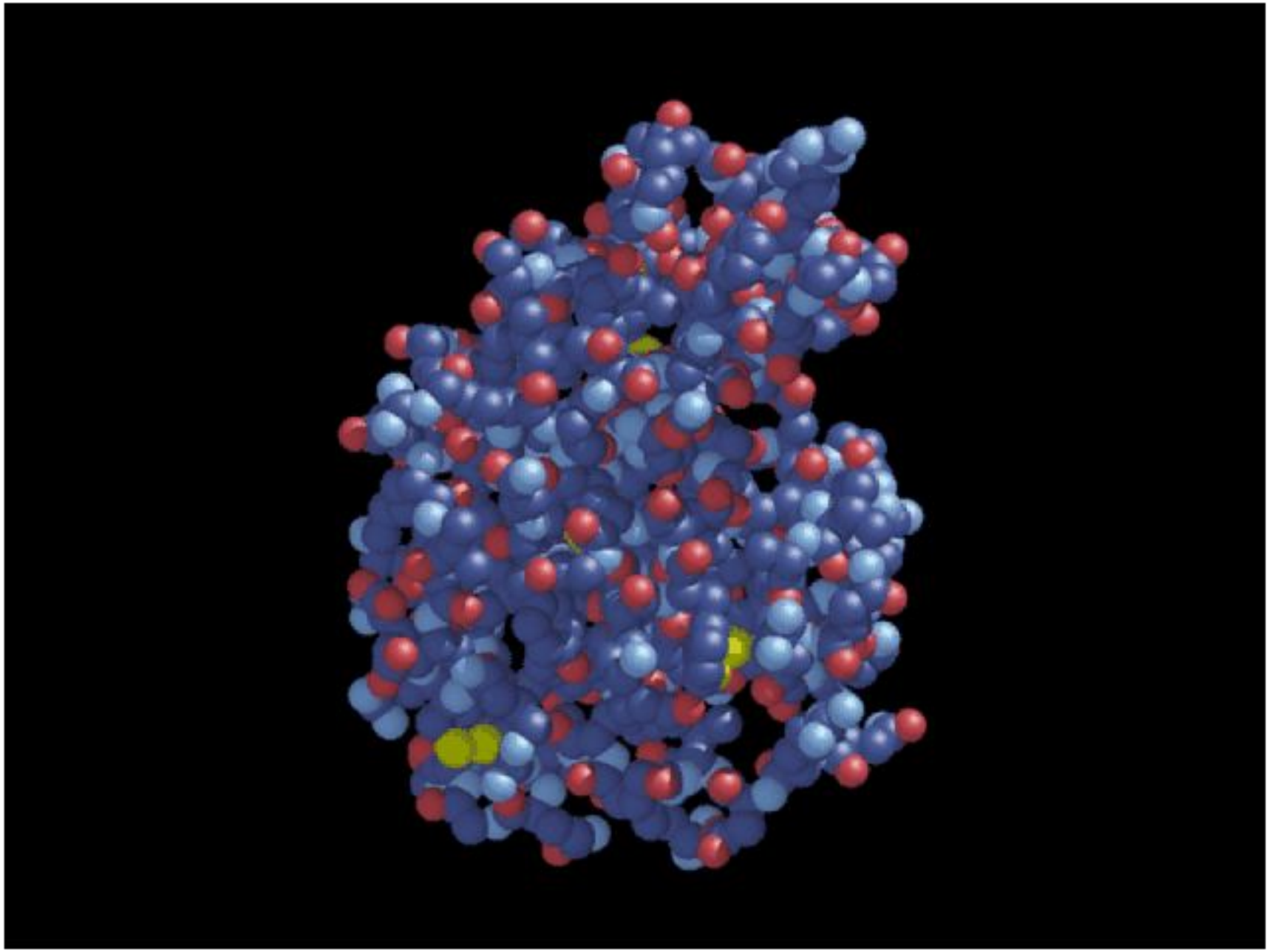
(*e*)

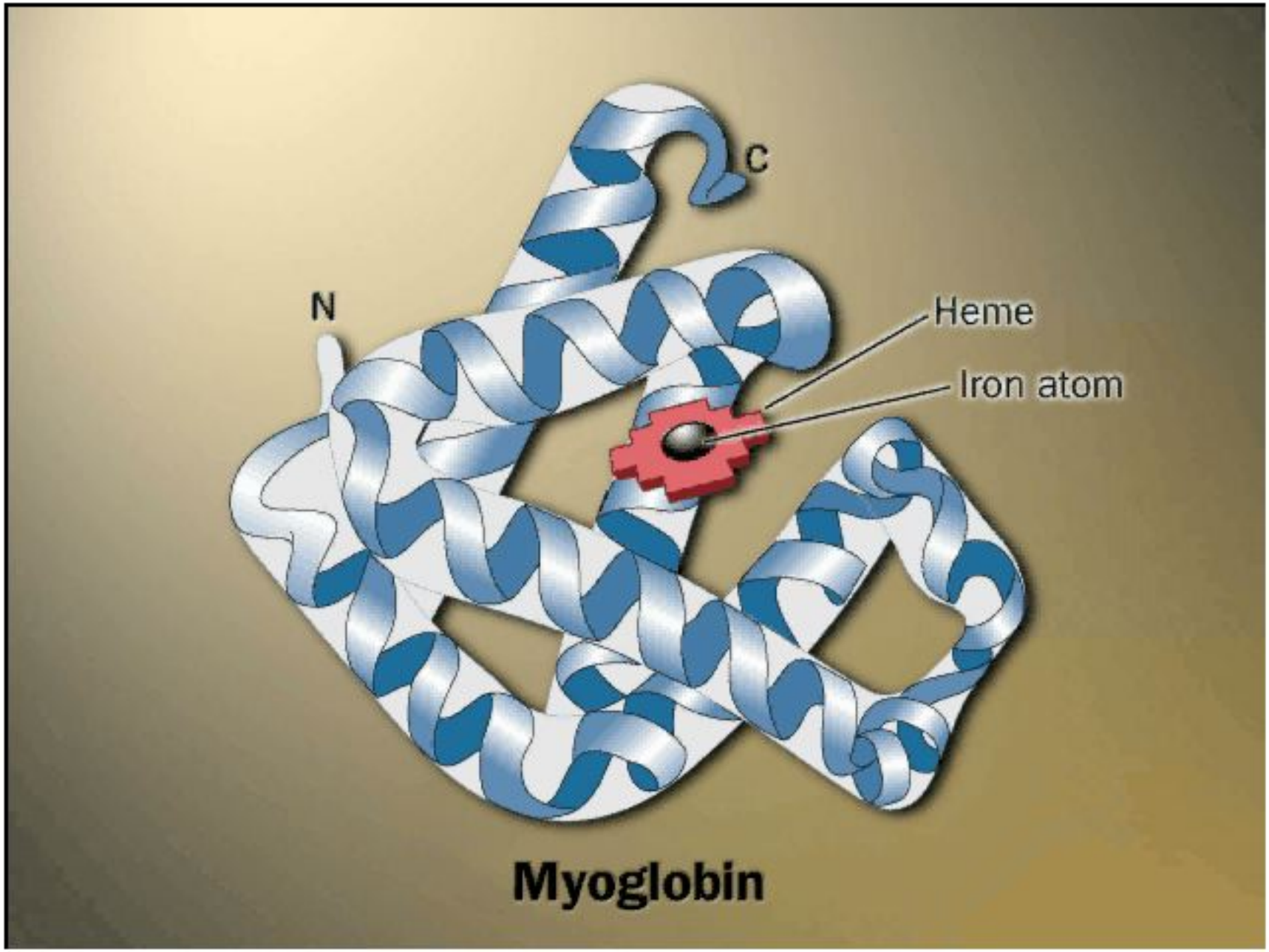

Polypeptide chain
H— Cα —CH2
Side chains of cysteine
CH2— Cα — H
SH
HS
The —SH groups of two cysteine side chains can react to form a covalent bond between the sulfur atoms.
Formation of disulfide bridge
2H
H— Cα —CH2
CH2— Cα — H
S
S
Disulfide bridge

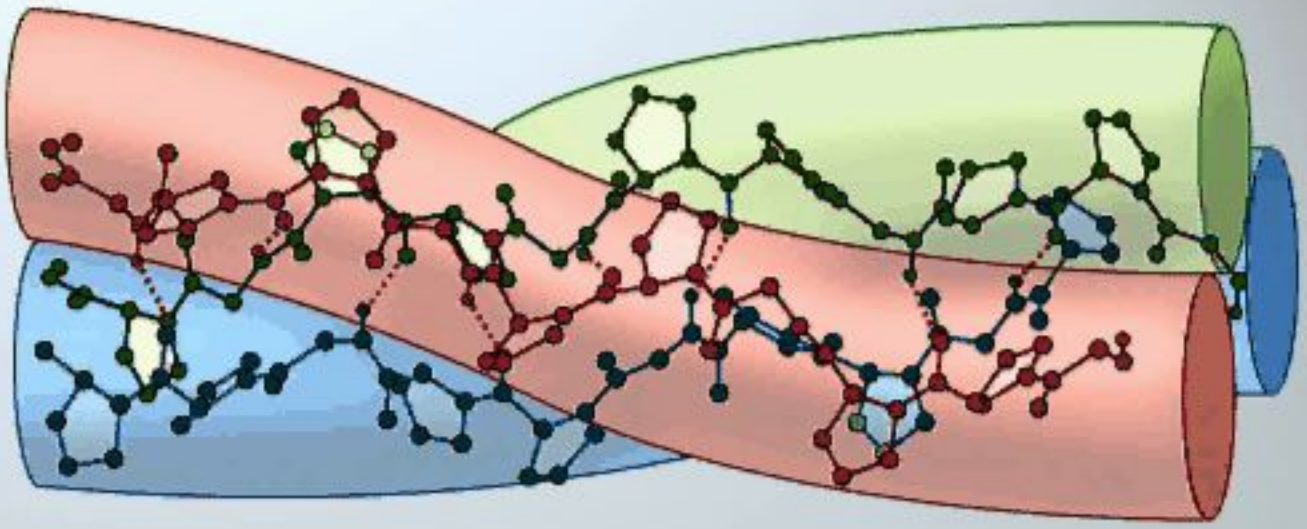

Primary structure
Amino acid residue
Secondary structure
Tertiary structure



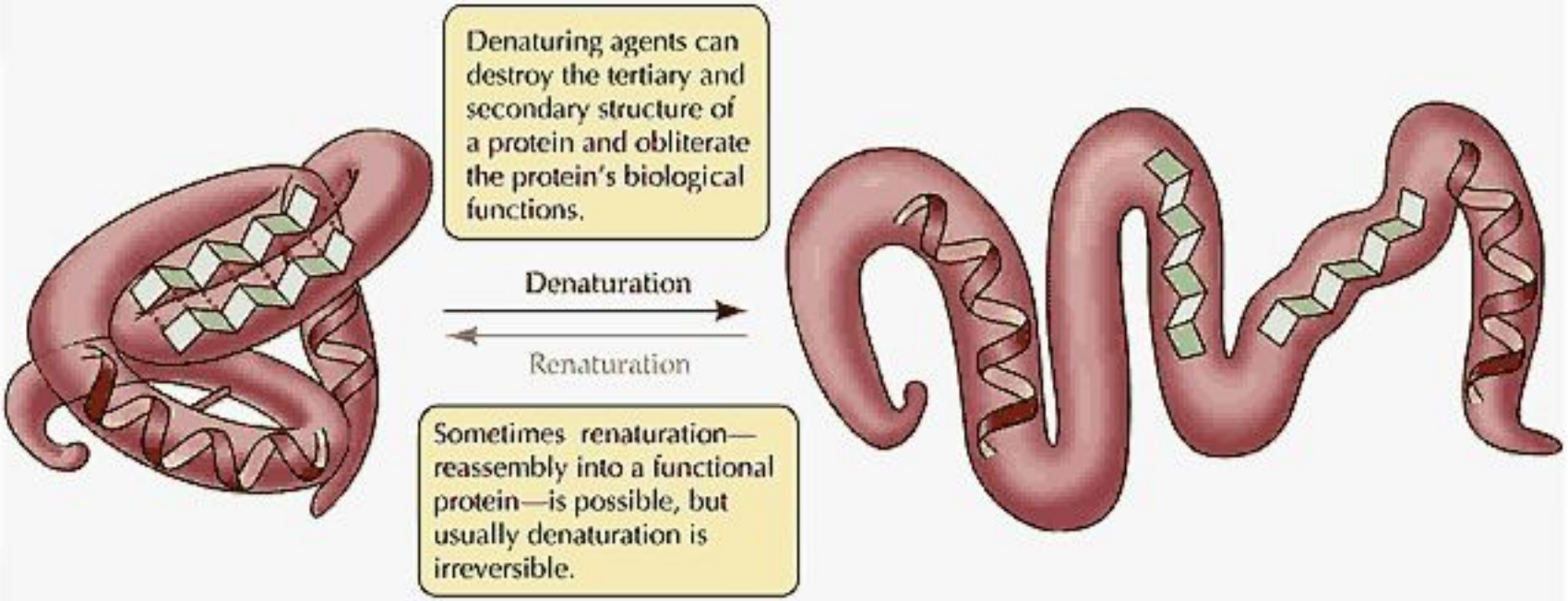

α Subunits
Heme
β Subunits
Heme




C
N
Heme
Iron atom
Myoglobin



Collagen


Denaturing agents can destroy the tertiary and secondary structure of a protein and obliterate the protein's biological functions.
Denaturation
Renaturation
Sometimes renaturation—reassembly into a functional protein—is possible, but usually denaturation is irreversible.