CHEMISTRY OF PROTEINS

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What are proteins?

- Proteins are necklaces of amino acids – long chains molecules.
- Proteins are the basis of how biology get this done. As enzymes, they are the driving force behind all the biochemical reactions which make biology work.
- As structural elements, they are main constituents of our bones, muscles, hair, skin, and blood vessels.
- As antibodies, they recognize invading elements and allow the immune system to get rid of the unwanted invaders.
- For these reasons, scientists have sequenced the human genome – the blueprint for all of the proteins in biology.

General Characteristics of Proteins

- **They are the most complex and most diverse in chemical composition, conferring upon the different tissues.**
- **Protein molecule contains elements of C, H, O,N, S, and P together with traces of Fe, Cu, I, Mn, and Zn.**
- **It has a molecular weight of 5,000 to 3,000,000**
- **They are the most important of the biologic substances being the fundamental constituent of cell cytoplasm.**
- **They supply not only heat and energy but also material for building and repair.**
- **Unlike carbohydrates and lipids, only small amounts of protein is temporarily stored in the body, and which can be quickly used up upon demand.**

Classificati

Based on Composition:

- Simple proteins – composed of entirely amino acids only.

  Ex. Albumin, Globulin

- Complex or Conjugated proteins – made up of amino acids and other organic compounds. The non-amino acid group is termed as the prosthetic group.

  Ex. Nucleoproteins, lipoproteins,

  glycoproteins, metalloproteins

Classification of Proteins

Based on Axial Ratio:

Axial ratio is the ratio of the length to the breath.

- **Globular proteins** – with axial ratio less than 10 but not below 3 or 4. They are compactly folded and coiled.

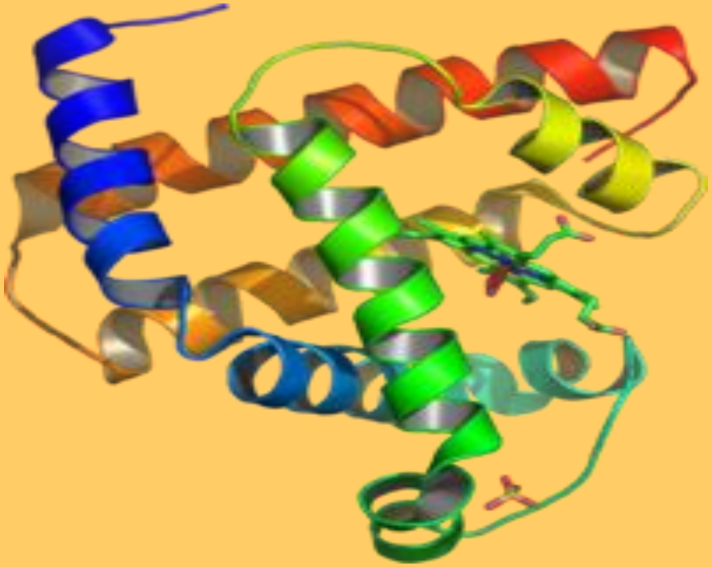
  Ex. Insulin, plasma albumin, globulin,

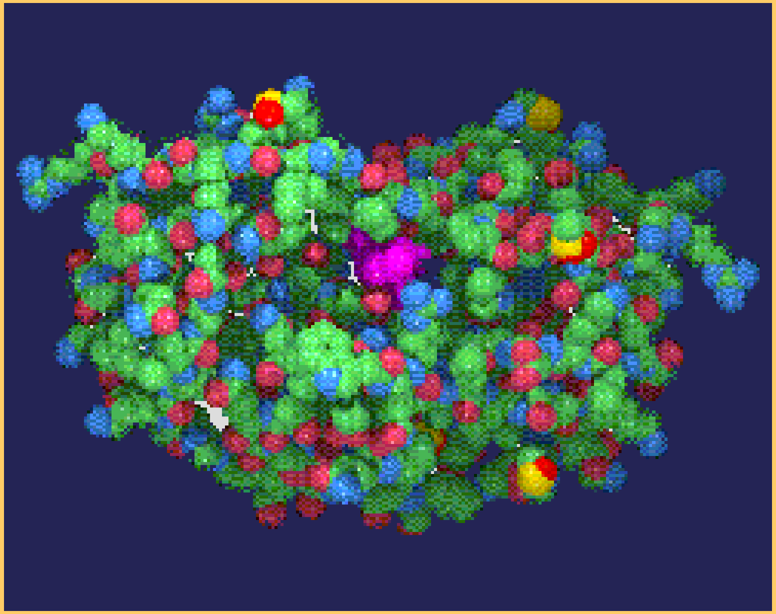
  enzymes

- **Fibrous proteins** – with axial ratio greater than 10. They are spiral and helical and are cross linked by disulfide and hydrogen bonds.

Ex. Keratin, myosin, elastin, collagen

Globular Proteins

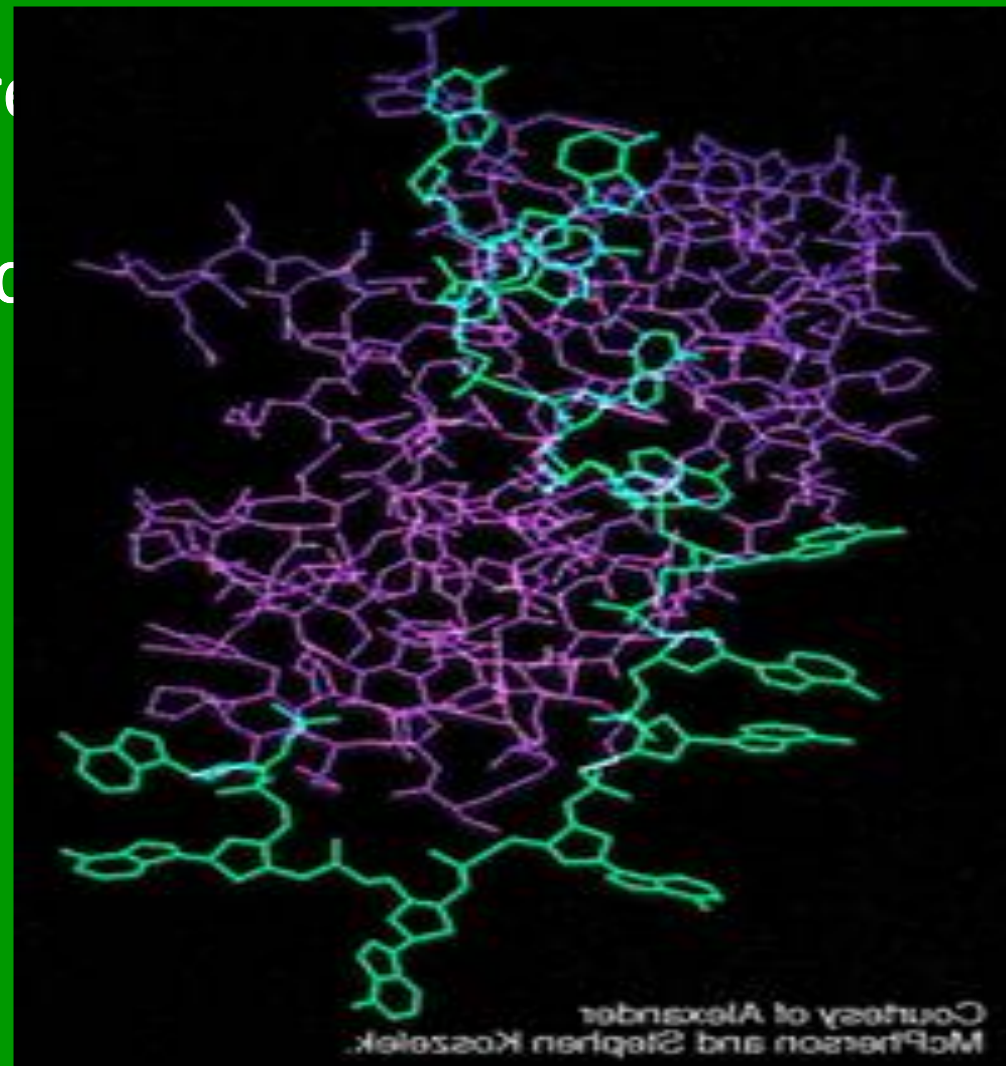




- Globular proteins have their axial ratio less than 10 but not below 3 or 4. They are compactly folded and coiled.
- Examples are insulin, plasma albumin, globulin, enzymes

Fibrous Proteins

- Fibrous proteins are spiral and helical and are cross linked by disulfide and hydrogen bonds
- Examples are keratin, myosin, elastin, collagen



Based on Biologic Functions

- **Structural proteins**: collagen, elastin, keratin, fibroin **of** silk and webs
- **Transport proteins:** hemoglobin, myoglobin, lipoproteins
- **Protective proteins:** immunoglobulins, fibrinogen**,** thrombin, snake venoms, bacterial toxins
- **Contractile proteins:** actin, myosin, tubulin
- **Catalytic proteins:** enzymes
- **Regulatory proteins**: hormones
- **Storage proteins:** ferritin, hemosiderin, gluten, casein, ovalbumin
- **Reception of Stimuli:** rhodopsin, membrane receptor proteins, acethylcholine, insulin
- **Germicidal proteins**: Polymyxin B1, Gramicidin S

Amino Acids

- **Proteins when hydrolyzed either by boiling with acids or through the action of enzymes like trypsin, are broken down into their component amino acids.**
- **The amino acids are of the α-form, that is the amine group (NH_2) is attached to the C atom next to the carboxyl group (-COOH).**
- **Amino acids are classified as:**

1. Neutral amino acids

a) Alipathic amino acids

b) Aromatic amino acids

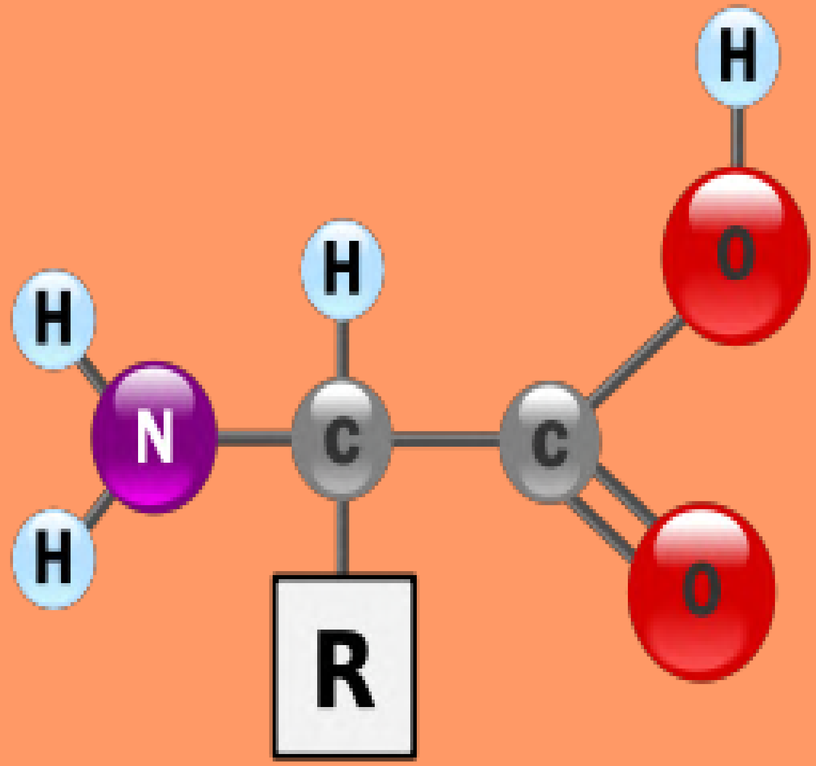
c) Thionine group

d) Secondary amino acids

2. Acid amino acids

3. Basic amino acids

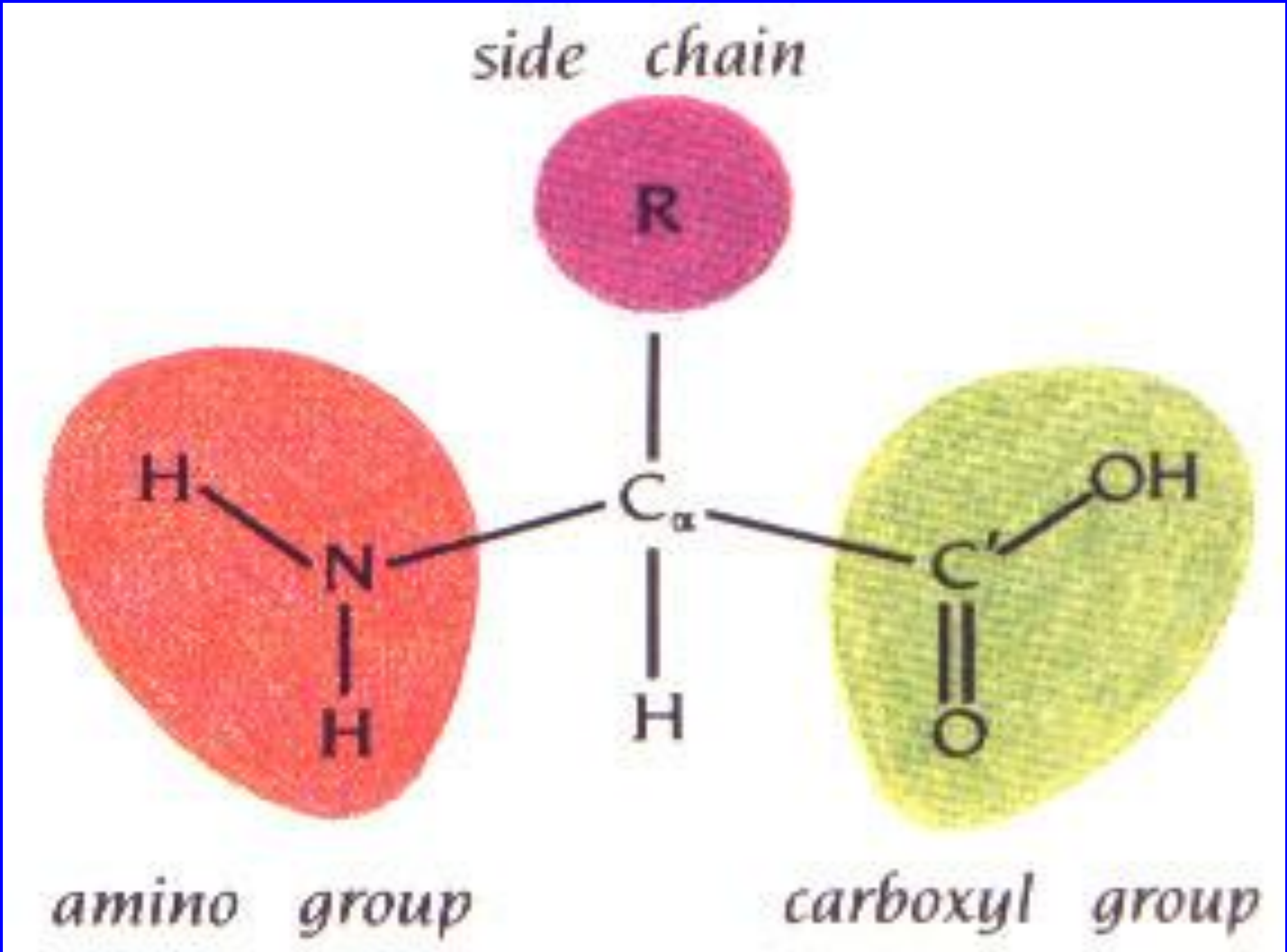
General Structure of Amino Acids



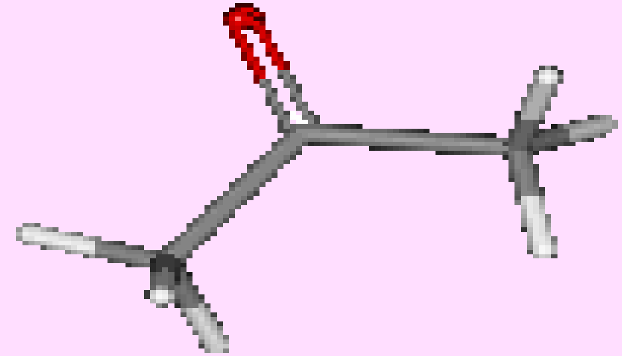
- The amino group is attached to the

  α- carbon which is next to the carboxyl group; hence the name

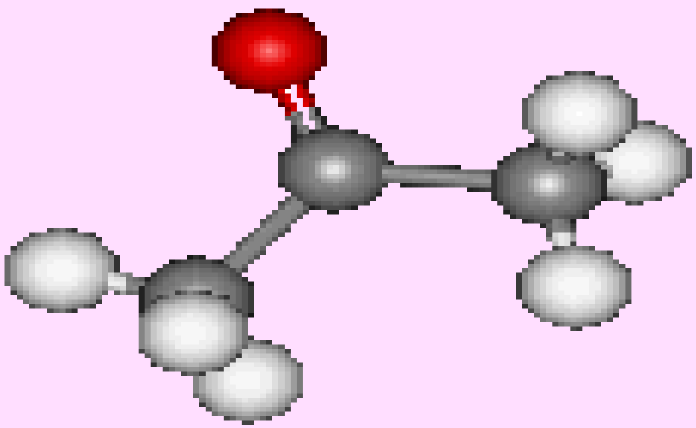
  α-amino acid


side chain
R
H
N
H
C_α
H
C'
OH
O
amino group
carboxyl group

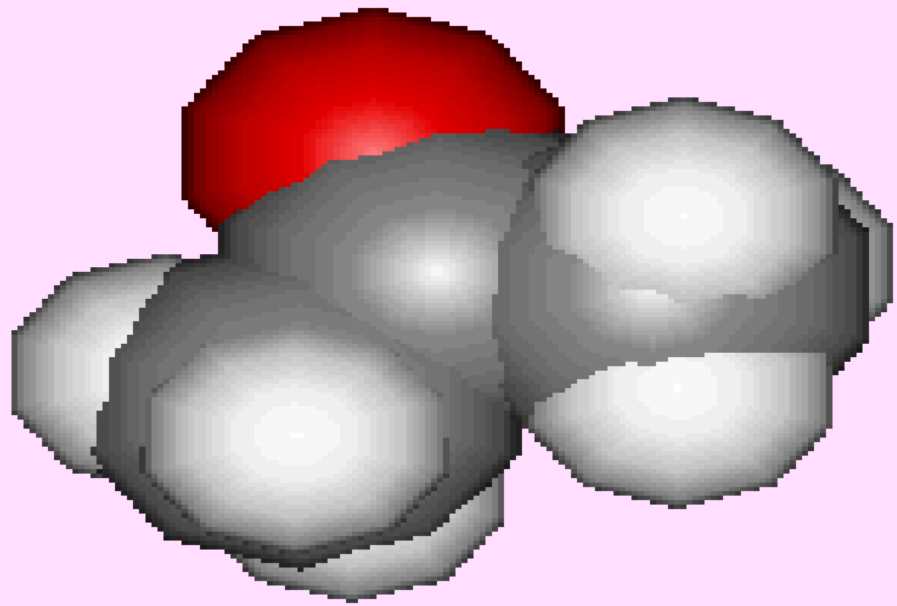
Wireframe



Sticks



Ball&Stick



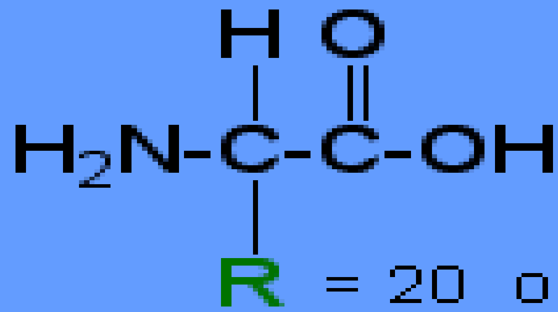
Spacefill

Amino Acids

- Amino acids are the basic structural units of proteins.
- Proteins when hydrolyzed either by boiling with acids or by the action of enzymes like trypsin are broken down into amino acids.
- All amino acids are ampholytes; each contains an amino and carboxyl group.
- H and –COOH groups bound to the alpha C are both acidic
- The basic characteristic of the amino acid is due to the lone pair of electrons of the amino group.
- Naturally occurring amino acids belong to the α-configuration.

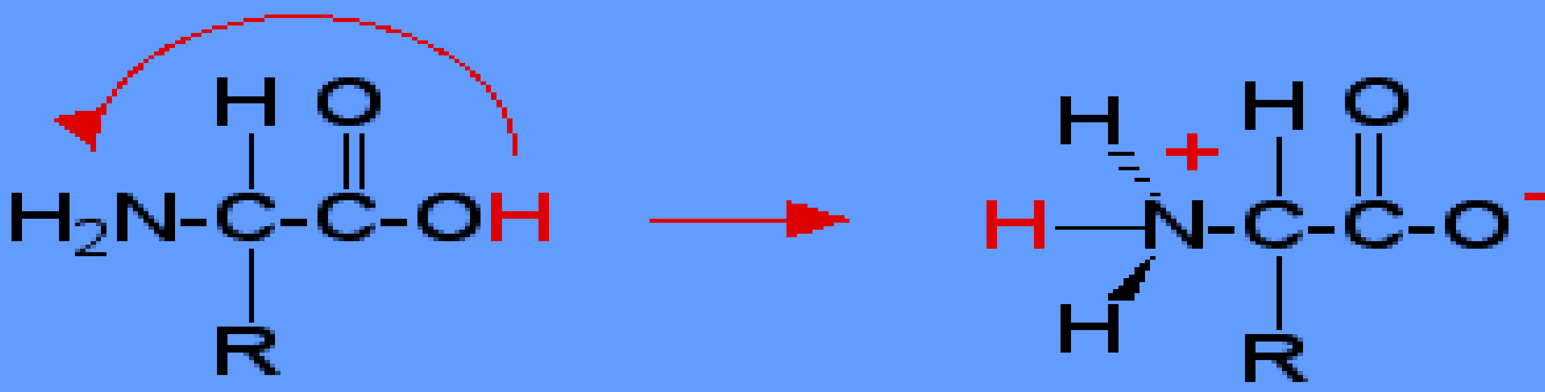
Amino Acid Structure

amine



acid

= 20 or more variations of amino acid "side chain"



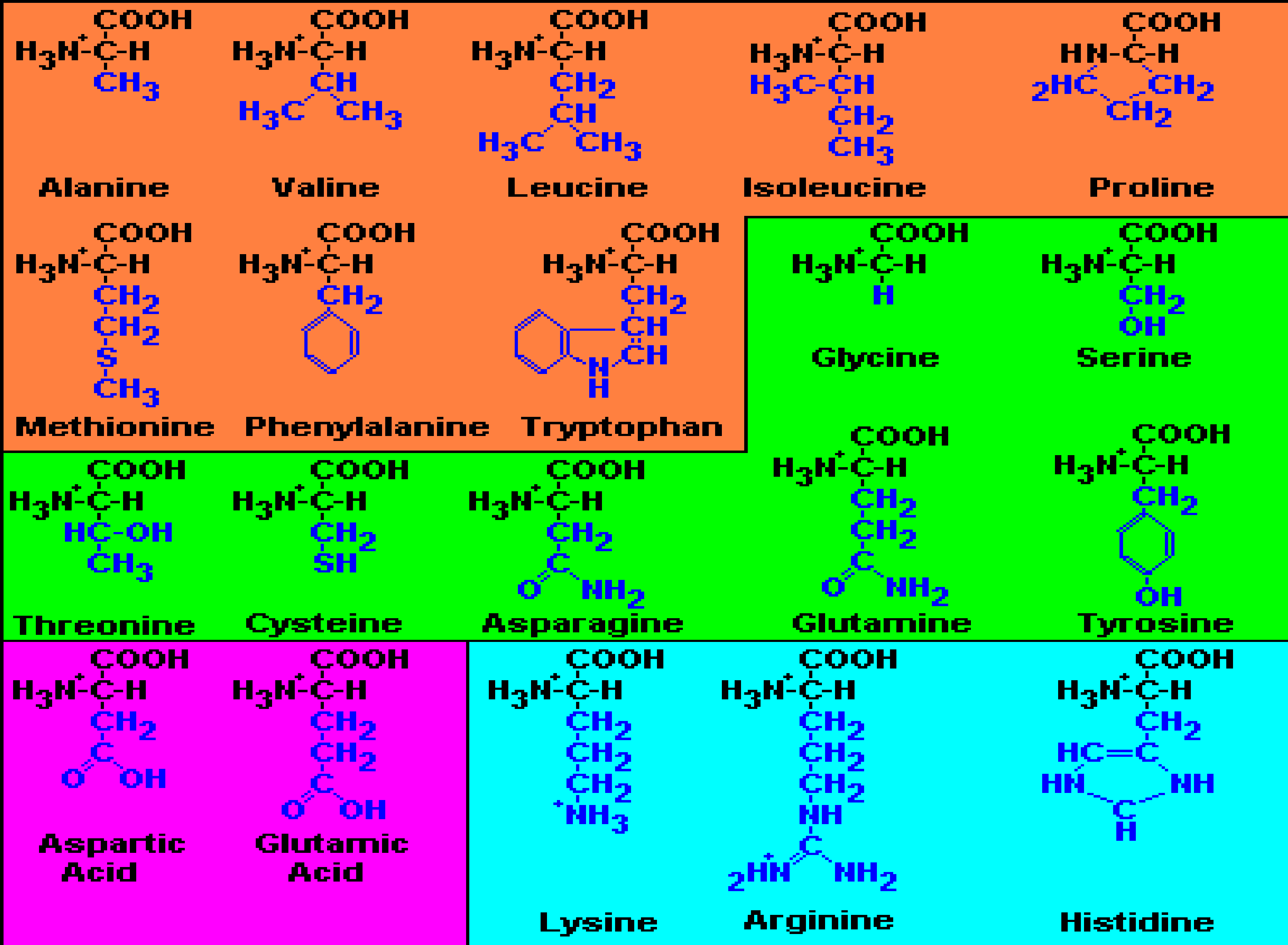
Zwitterion

Amino Acids found in Proteins

Amino acids	1-Letter Abbreviation	3-letter Abbreviation
Alanine	A	Ala
Arginine	R	Arg
Asparagine	N	Asn
Aspartic acid	D	Asp
Cysteine	C	Cys
Glutamine	Q	Gln
Glutamic acid	E	Glu
Glycine	G	Gly
Histidine	H	His

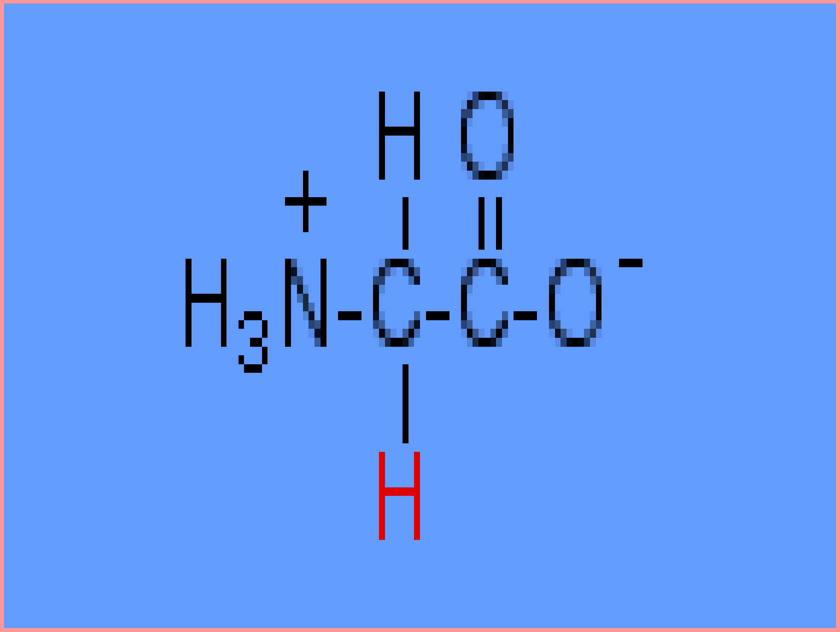
Amino Acids found in Proteins

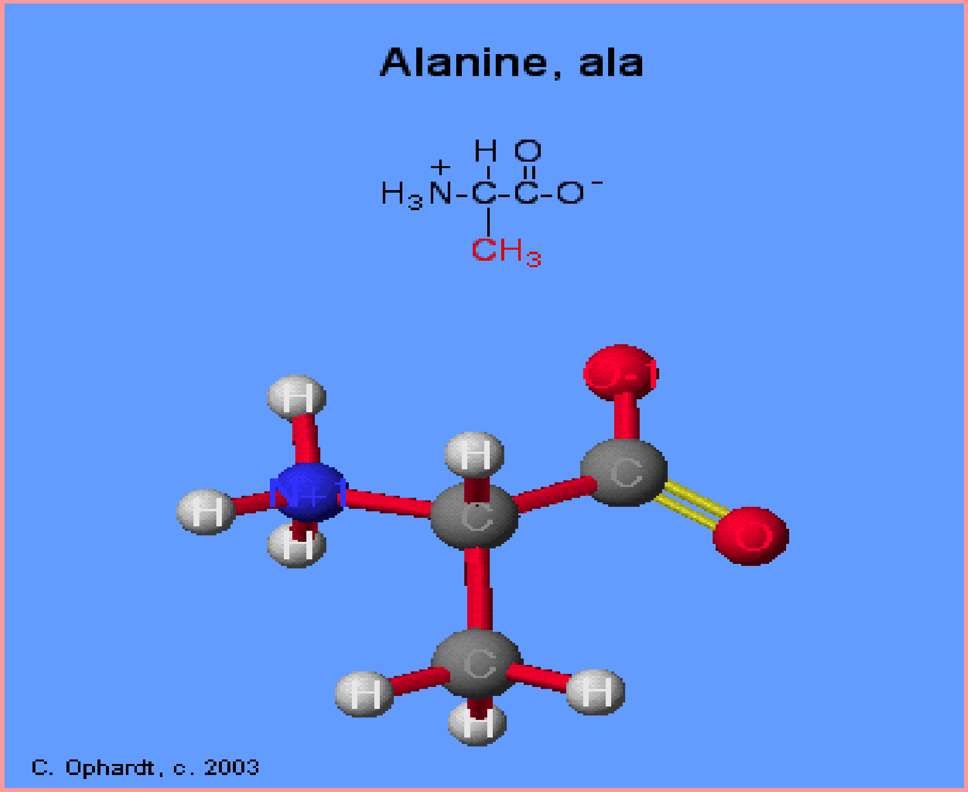
Isoleucine	I	Ile
Leucine	L	Leu
Lysine	K	Lys
Methionine	M	Met
Phenylalanine	F	Phe
Proline	P	Pro
Serine	S	Ser
Threonine	T	Thr
Tryptophan	W	Trp
Tyrosine	Y	Tyr
Valine	V	Val


Alanine
Valine
Leucine
Isoleucine
Proline
Methionine
Phenylalanine
Tryptophan
Glycine
Serine
Threonine
Cysteine
Asparagine
Glutamine
Tyrosine
Aspartic Acid
Glutamic Acid
Lysine
Arginine
Histidine

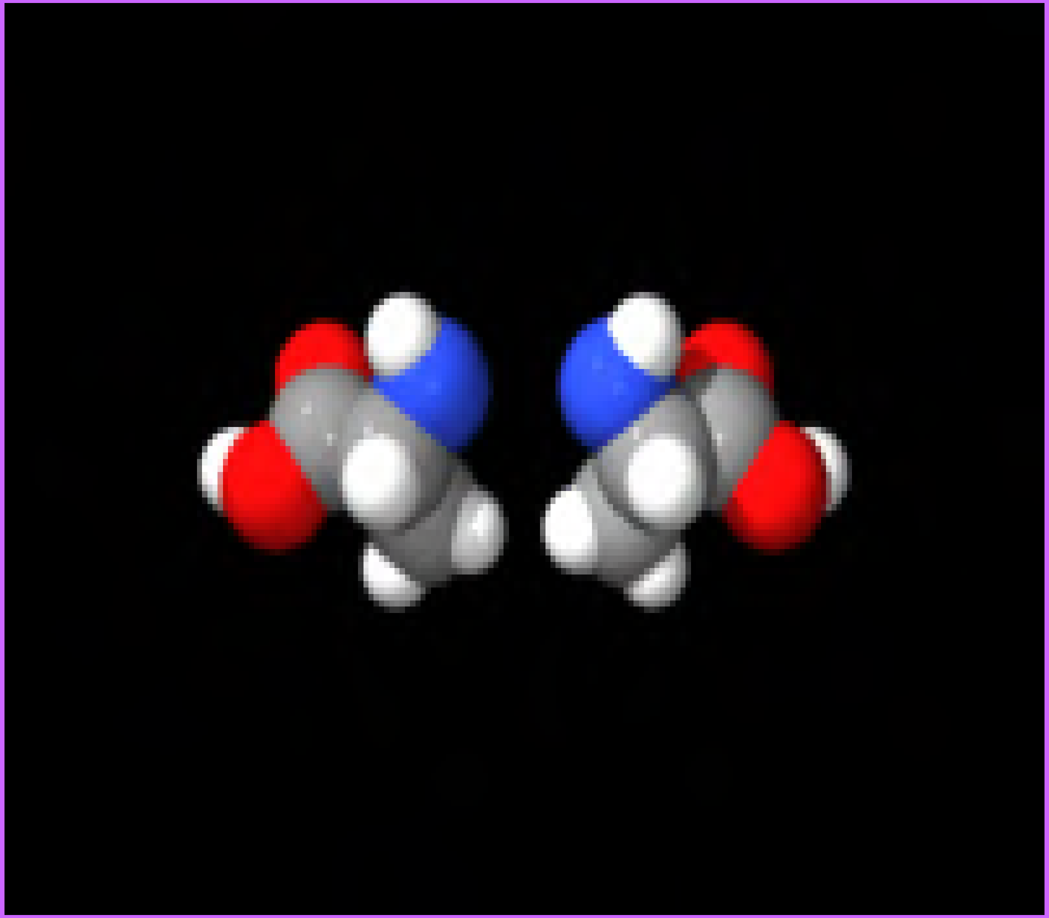
Neutral Amino Acids

- Alipathic Amino acids:
- Glycine, Alanine, Valine, Leucine, Isoleucine



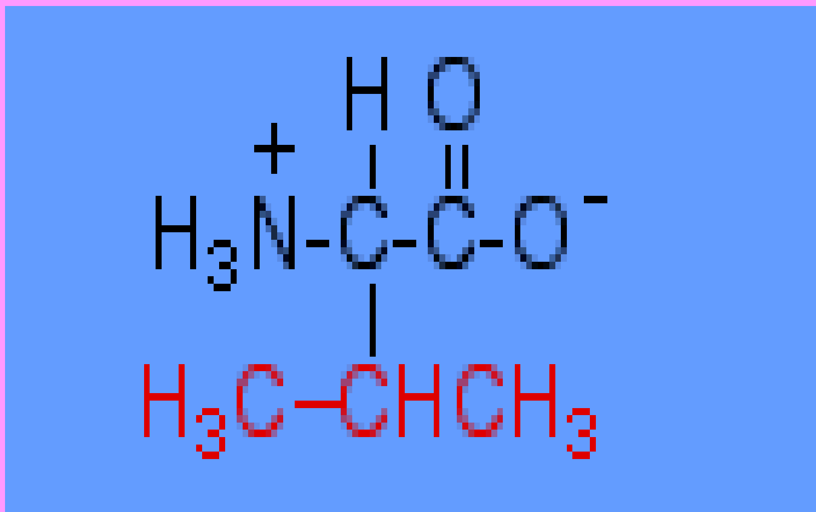


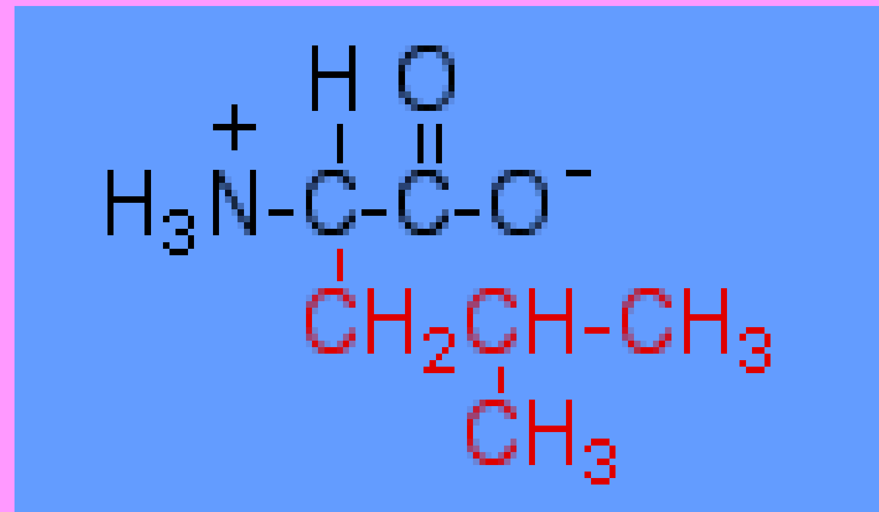
Streoisomers of Alanine

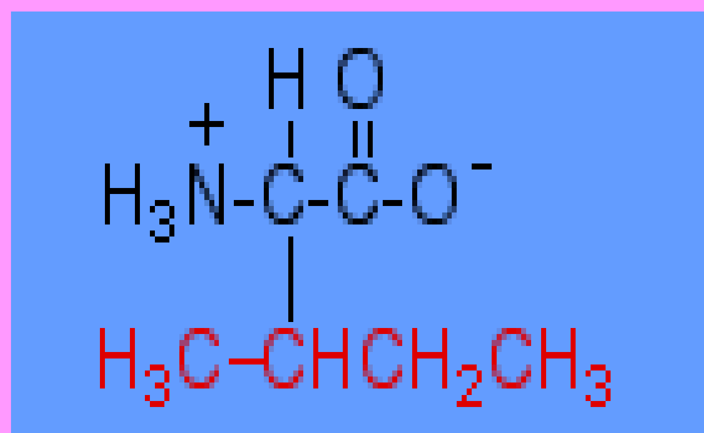


- α-alanine and its enantiomer D-alanine are shown here as mirror images which are not superimposable.
- All α-amino acids except glycine contain a assymmetric α-carbon and thus have D and L enatiomers.
- Only L-enantiomer are found in proteins.

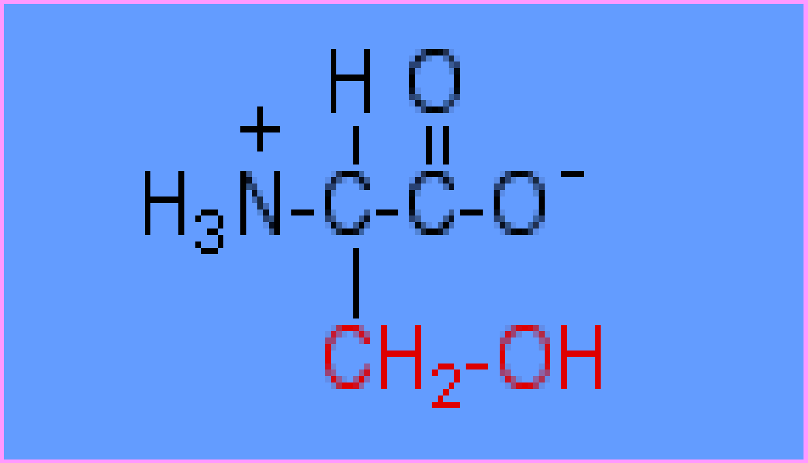
Valine, Leucine, Isoleucine

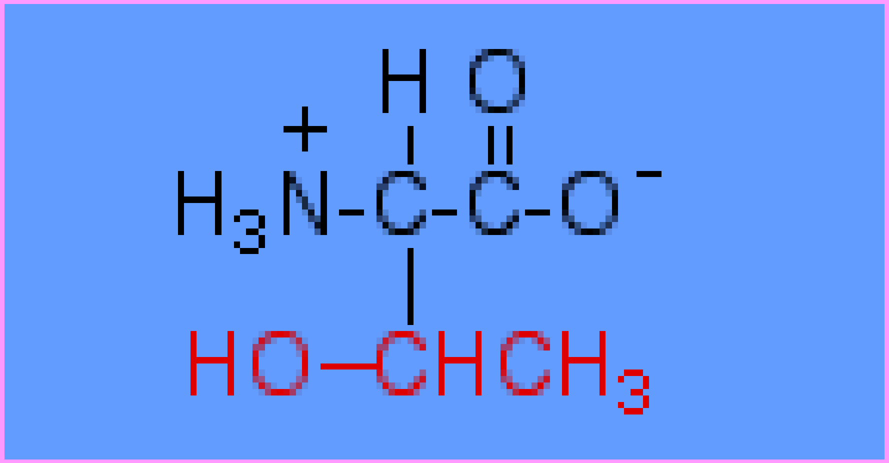






Amino Acids with Hydroxyl





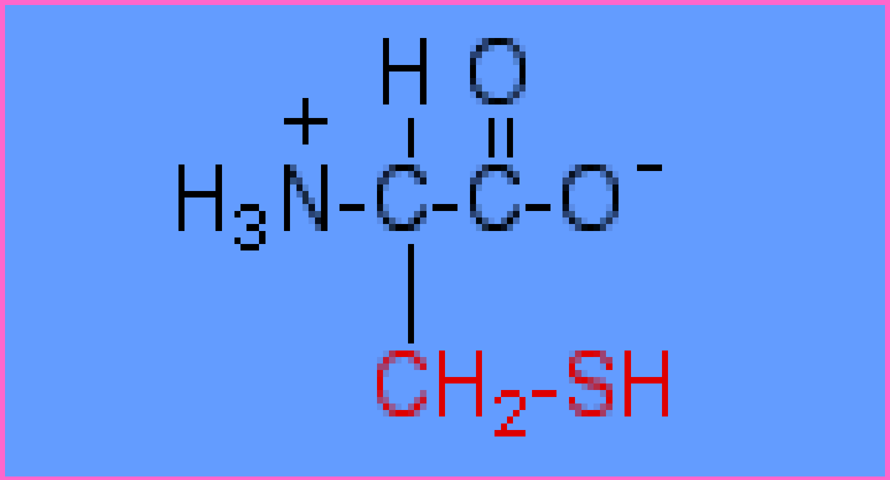
Serine

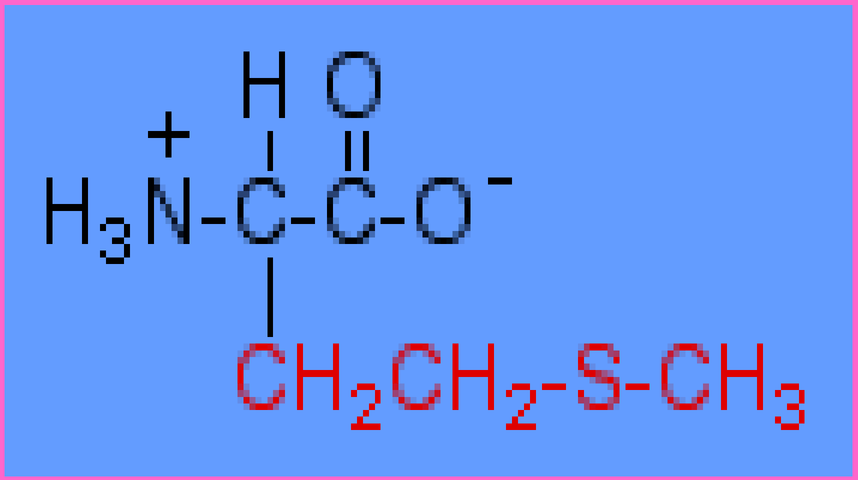
(α-amino β-hydroxy propanoic acid)

Threonine

(α-amino b-y-propionic hydroxy butyric) acid)

Sulfur-containing Amino Acids





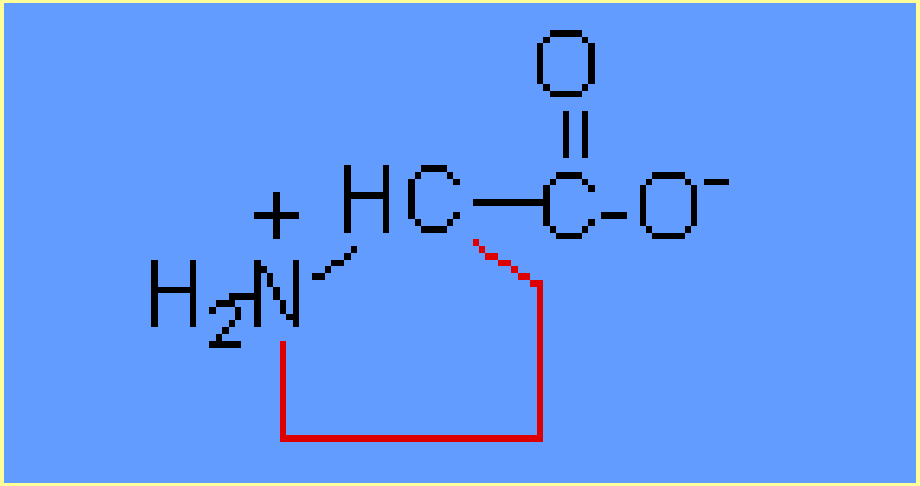
Cysteine

(α-amino β-thio propionic acid)

Methionine

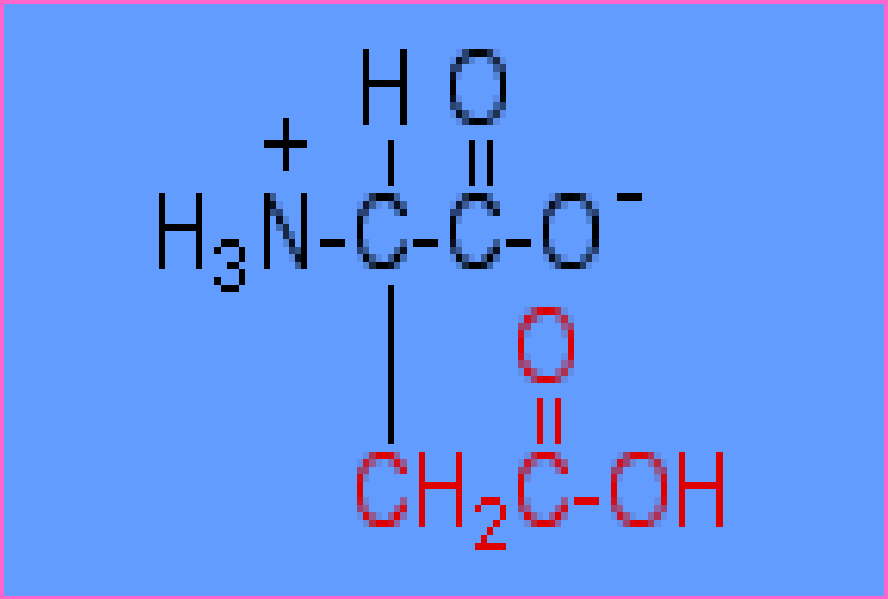
(α-amino g-methyl thiobutyric acid)

Secondary Amino Acids



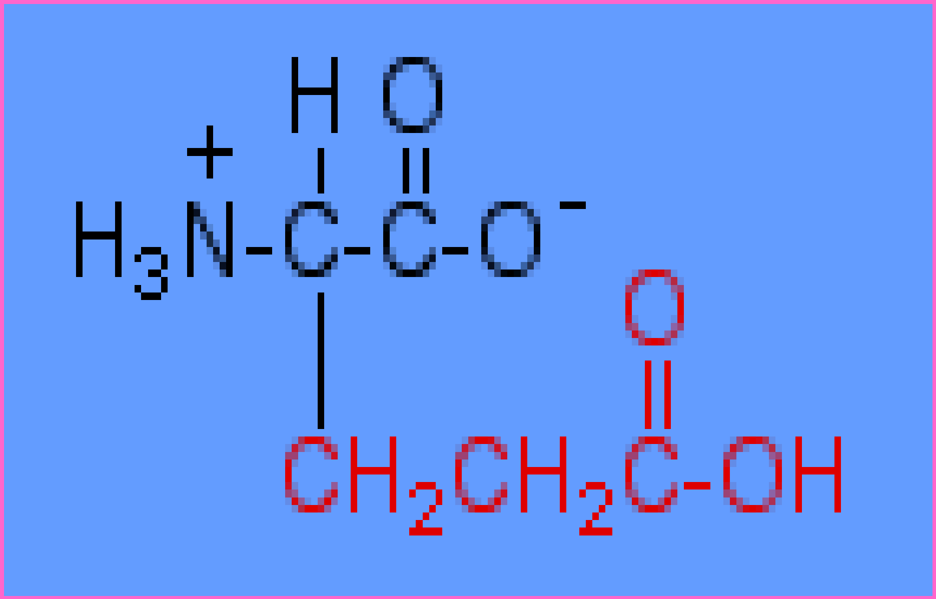
- Proline (pyrrolidine carboxylic acid)

Acid Amino Acids



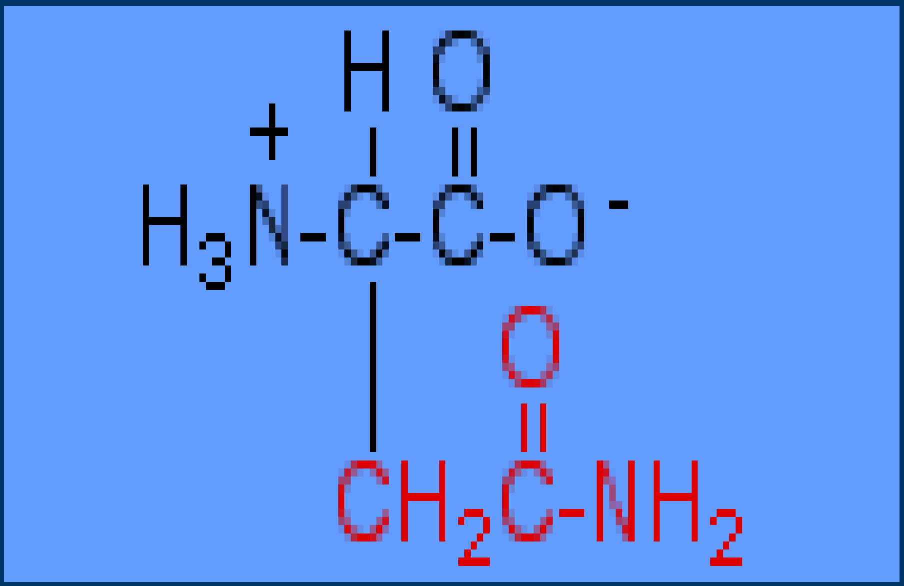
Aspartic Acid

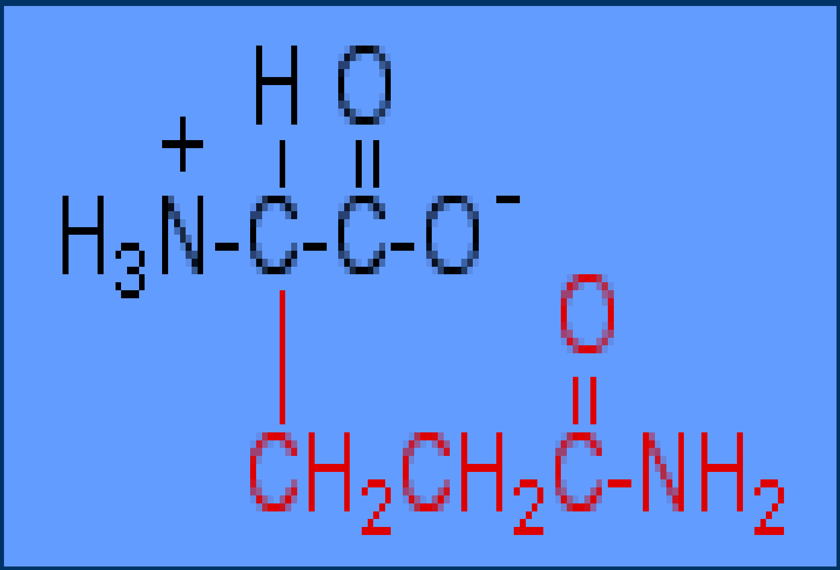
(amino succinic acid)



Glutamic Acid

(α-amino glutaric acid)





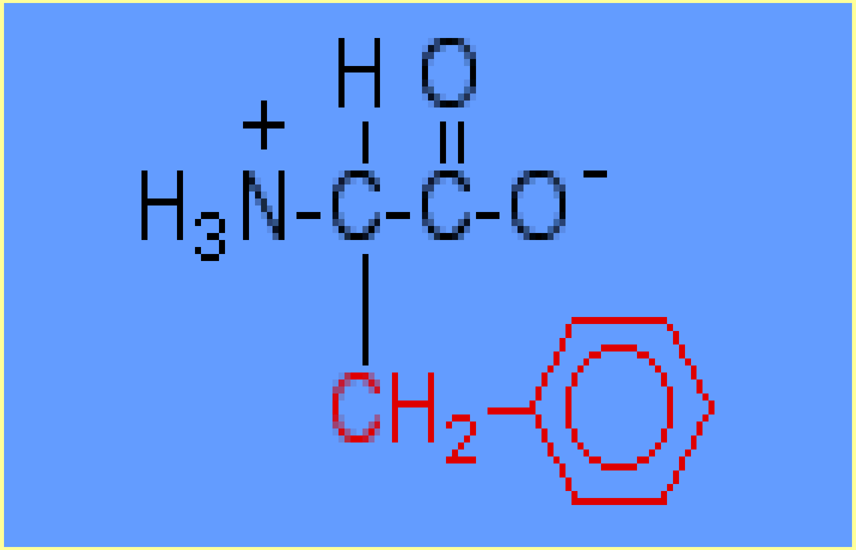
Asparagine

(β-amide of aspartic acid)

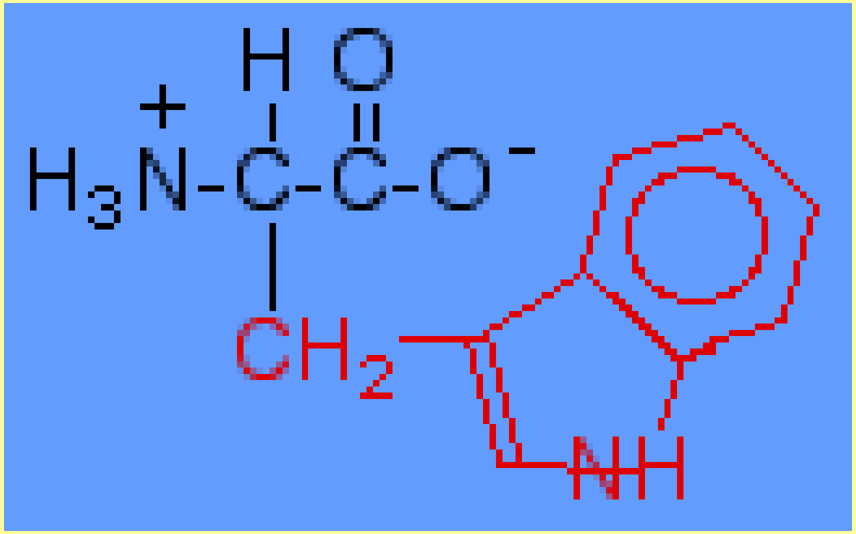
Glutamine

(y-amide of glutamic acid)

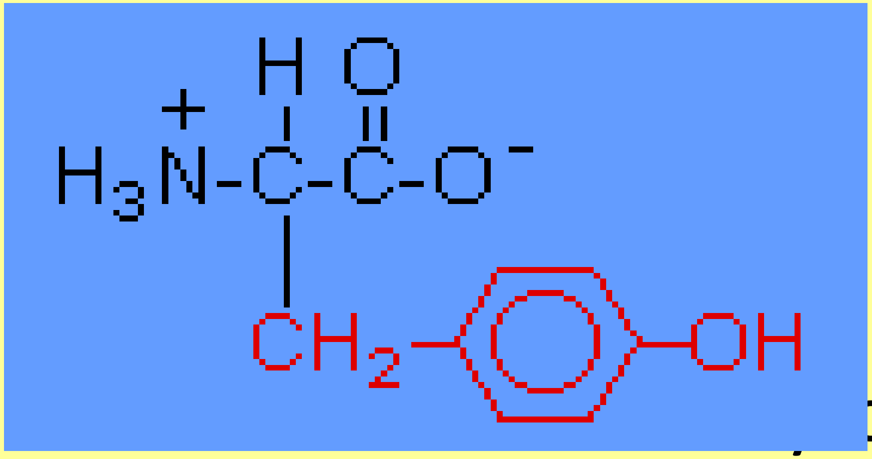
Aromatic Amino Acids



Phenylalanine

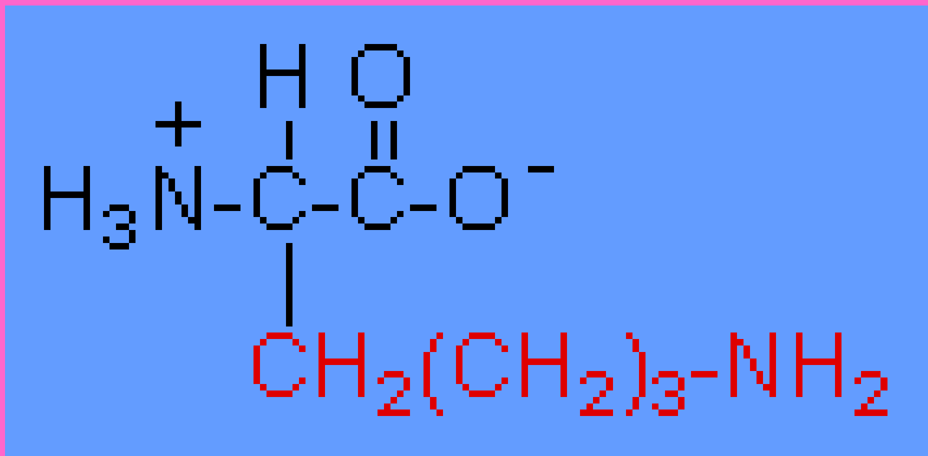


Tryptophan



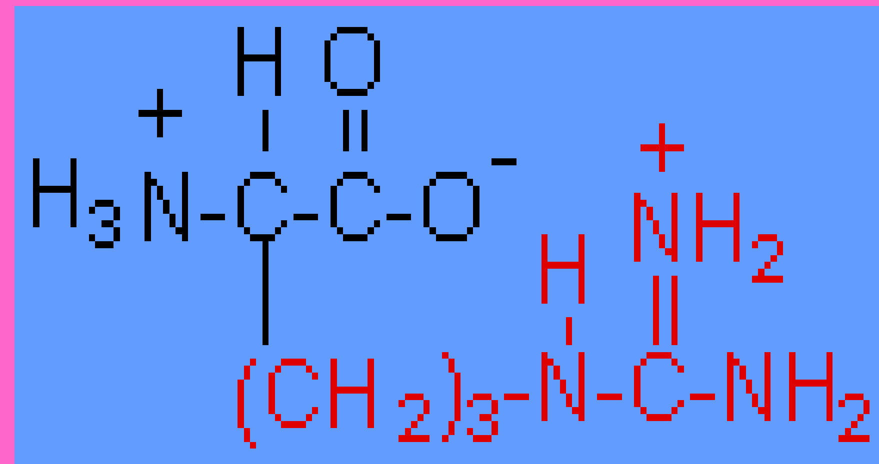
osine

Basic Amino Acids



Lysine

(α-e-diamino caproic acid)



Arginine

(α-amino d-guanido valeric acid)

How many types of proteins are in our body?

- The proteins in our bodies are made of **20 different amino acids** strung together like beads on a string.
- All 20 have a part in common: a central C attached to a carbonyl, an amino and a H atom
- The 20 AA contain, in their 20 different side chains, a remarkable collection of chemical groups.
- It is this diversity of the monomers that allows proteins to exhibit such a great variety of structures and properties.

Biochemical Importance of Amino Acids

Amino Acids	Systematic name	Importance
Glycine	Aminoetha-noic acid	▪Helps trigger the release of oxygen to the energy requiring cell-making process ▪Important in the manufacture of hormones for strong immune system
Alanine	α-amino propanoic acid	▪Important AA as it is an energy source for the liver, muscles, and CNS ▪Strengthens the immune system by producing antibodies ▪Helps in the metabolism of sugars and organic acids

Valine	α-amino 3-methylbutanoic acid	▪Essential AA ▪Promotes mental vigor, muscle coordination and calm emotions
Leucine	α-amino 4-methyl pentanoic acid	▪Essential AA ▪Provides necessary substances for energy production ▪Stimulants to the upper brain and helps to be more alert
Isoleucine	α-amino 3-methylpentanoic acid	▪Essential AA ▪Same functions as leucine

Phenylalanine	α-amino 3-phenylpropanoic acid	▪Essential AA ▪Used by the brain to produce norepinephrine, ▪Reduces hunger pains ▪Functions as antidepressant ▪Helps improve memory
Tyrosine	α-amino 3-(4-hydroxyphenyl)propanoic acid	▪ Transmits nerve impulses to the brain; helps overcome depression; improves memory; increases mental alertness; promotes the healthy functioning of the endocrine glands
Tryptophan	α-amino 3-indole propanoic acid	▪Essential AA ▪A natural relaxant, helps alleviate insomia by inducing normal sleep ▪Reduces anxiety and depression ▪Helps in the treatment of migraines and headaches ▪Helps stabilize the immune system ▪Helps reduce risk of artery and heart spasms ▪Works with lysine in reducing cholesterol levels

Methionine	**α-amino 4-methyl thiol butanoic acid**	▪**Essential AA** ▪**Principal supplier of sulfur which prevents disorder of the hair, skin and nails** ▪**Helps lower cholesterol levels by increasing the liver's production of lecithin** ▪**A natural chelating agent for heavy metals** ▪**Regulates the formation of ammonia and creates ammonia-free urine which reduces bladder irritation** ▪**Influences hair follicles and promotes hair growth**

Cysteine	2-amino 3-mercaptopropanoic acid	▪Functions as an antioxidant and is a powerful aid to the body in protecting against radiation and pollution ▪Helps slow down the aging process, deactivate free radicals, neutralizes toxins ▪Aids in protein synthesis and promotes cellular repair ▪Necessary for skin formation, in the recovery from burns and surgical operations
Serine	2-amino 3 hydroxy propanoic acid	▪A storage source of glucose by the liver and muscles ▪Helps strengthen immune system by providing antibodies ▪Synthesizes fatty acid sheath around nerve fibers
Threonine	2-amino 3 hydroxy butanoic acid	▪Essential AA ▪Important constituent of collagen, ▪Assists metabolism and assimilation ▪Helps the digestive and intestinal tracts functions normally ▪Helps prevents fat build-up in the liver

Histidine	α-amino 3 (1H-imidazol-4-yl) propanoic acid	▪Essential AA ▪Found abundantly in hemoglobin ▪Used in the treatment of rheumatoid arthritis, allergic diseases, ulcers, anemia
Lysine	2,6 diamino hexanoic acid	▪Essential AA ▪Insures adequate absorption of calcium ▪Helps form collagen (which makes up bone and cartilages) ▪Aids in the production of antibodies, hormones and enzymes
Arginine	α-amino 5-guanidino pentanoic acid	▪Helps improve immune responses to bacteria, viruses and tumor cells ▪Promotes wound healing and regeneration of the liver ▪Causes the release of growth hormones ▪Crucial for optimal muscle growth and tissue repair

Aspartic Acid	α-amino butanedioic acid	▪Most easily used as energy source ▪Aids in the expulsion of toxic ammonia from the body ▪Located most closely to the TCA cycle, the site of energy production ▪Found in increased levels in people with epilepsy and in decreased amounts in some cases of depression
Glutamic acid	α-amino pentanedioic acid	▪Considered to be nature's "brain food" by improving mental capacities ▪Helps speed the healing of ulcers; gives a "lift" from fatigue ▪Helps control alcoholism, schizophrenia and the craving of sugar, Parkinson's disease, mental retardation, and muscular dystrophy
Asparagine	α-amino 3 carbamoyl propanoic acid	▪Found in the surfaces of proteins where they can interact with water molecules

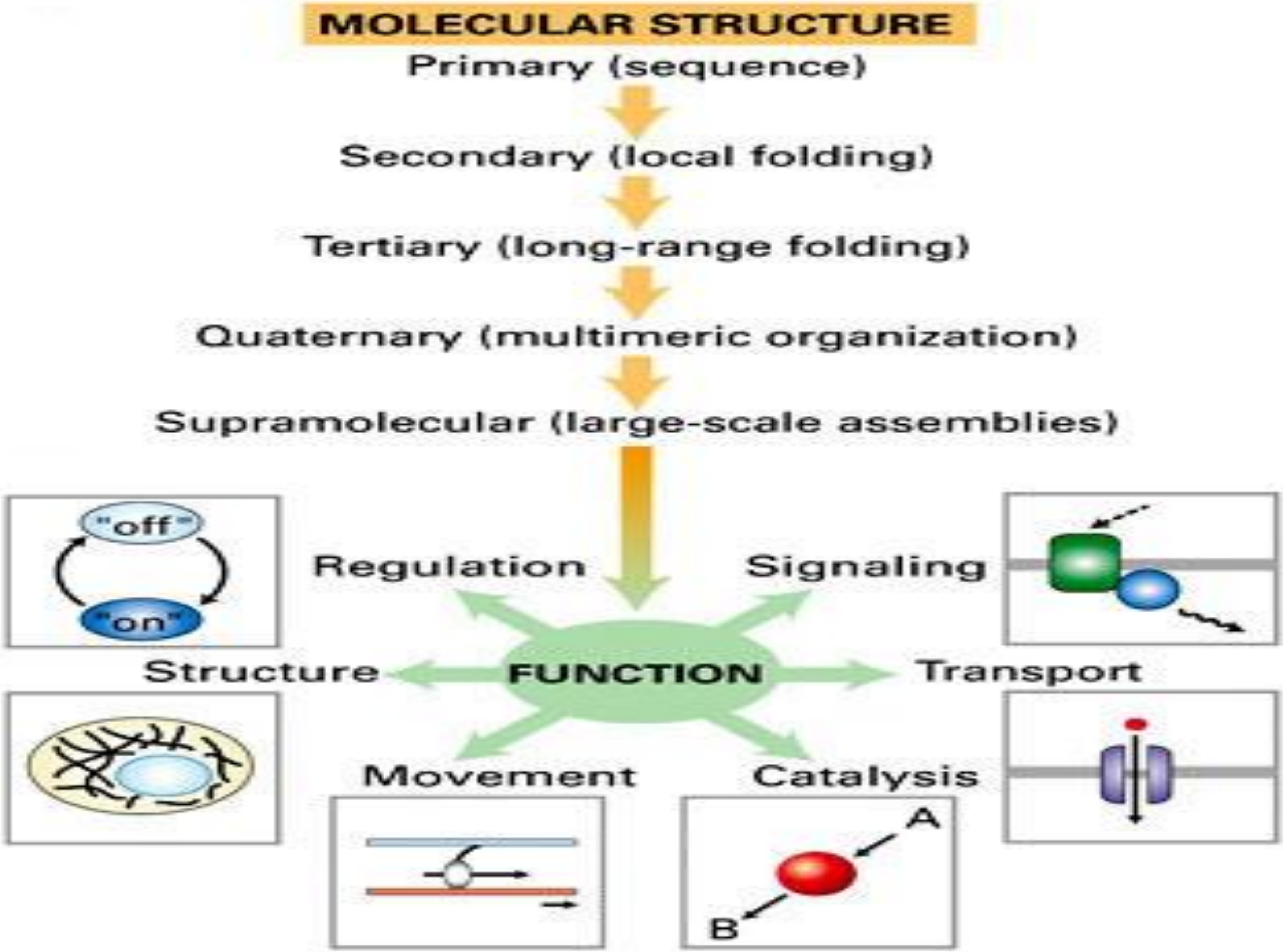
Glutamine	α-amino 4 carbamoyl butanoic acid	▪Found in the surfaces of proteins where they can interact with water molecules ▪The polar amide groups can also form hydrogen bonds with atoms in the side chains of other polar amino acids
Proline	Pyrrolidine-2-carboxylic acid	▪Non-essential AA ▪Important for the proper functioning of joints and tendons ▪Helps maintain and strengthen heart muscles ▪Helps repair processes after cell injury or for any type of wound healing
Hydroxy lysine	Hydroxy hexanoic acid	▪It is a hydroxy derivative of lysine. ▪It is most widely known as a component of collagen

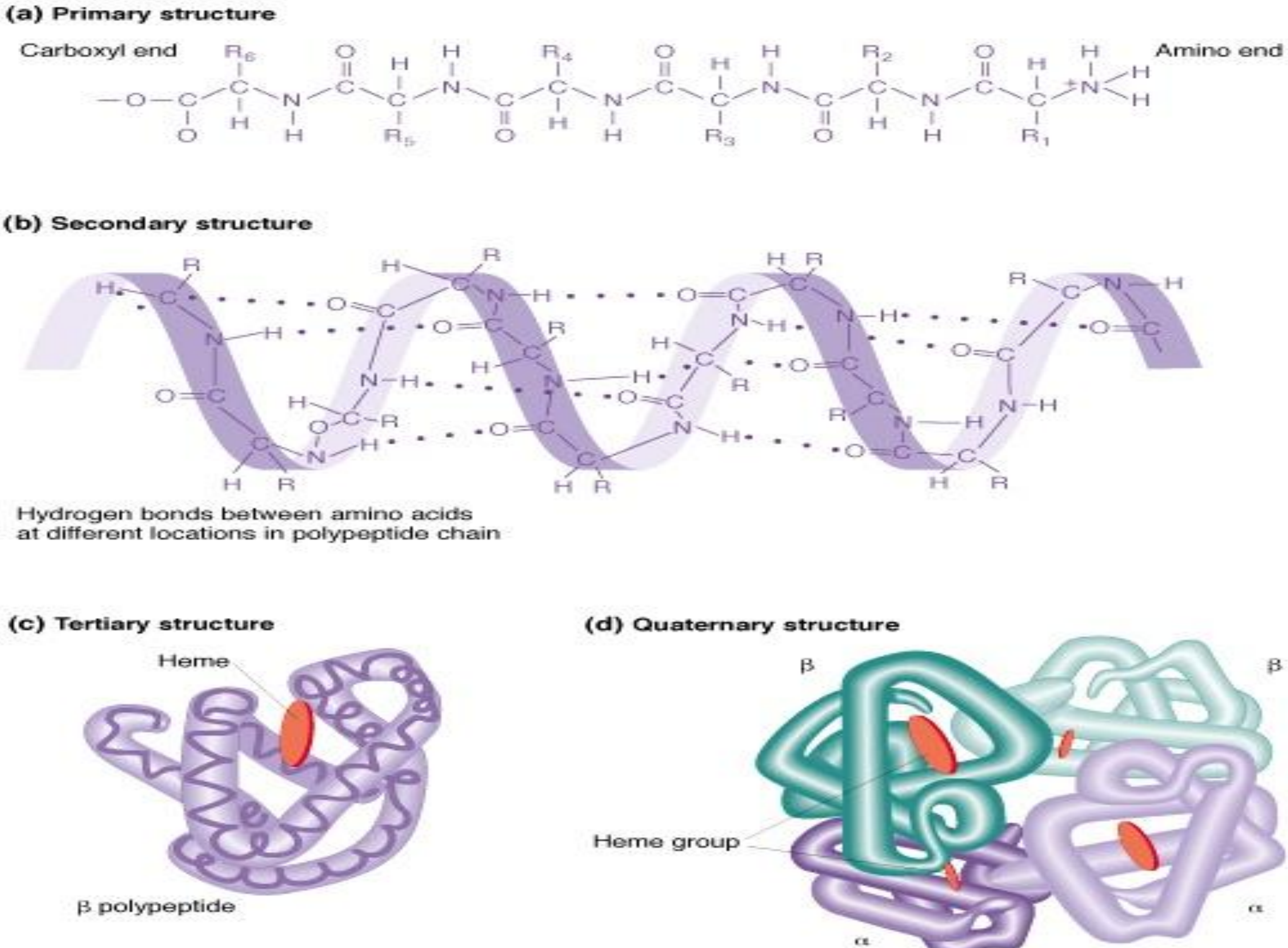
Biologically Important Proteins

Protein	No. of AA	Function
Insulin	51	Enzyme for sugar metabolism
Cytochrome C	104	Enzyme for cell respiration
Growth hormone	191	Used as anti-aging treatment
Hemoglobin	574	Oxygen transport in blood
Hexokinase	730	Enzyme for glycolysis
Gamma globulin	1320	Part of immune system in blood
Myosin	6100	Muscle action

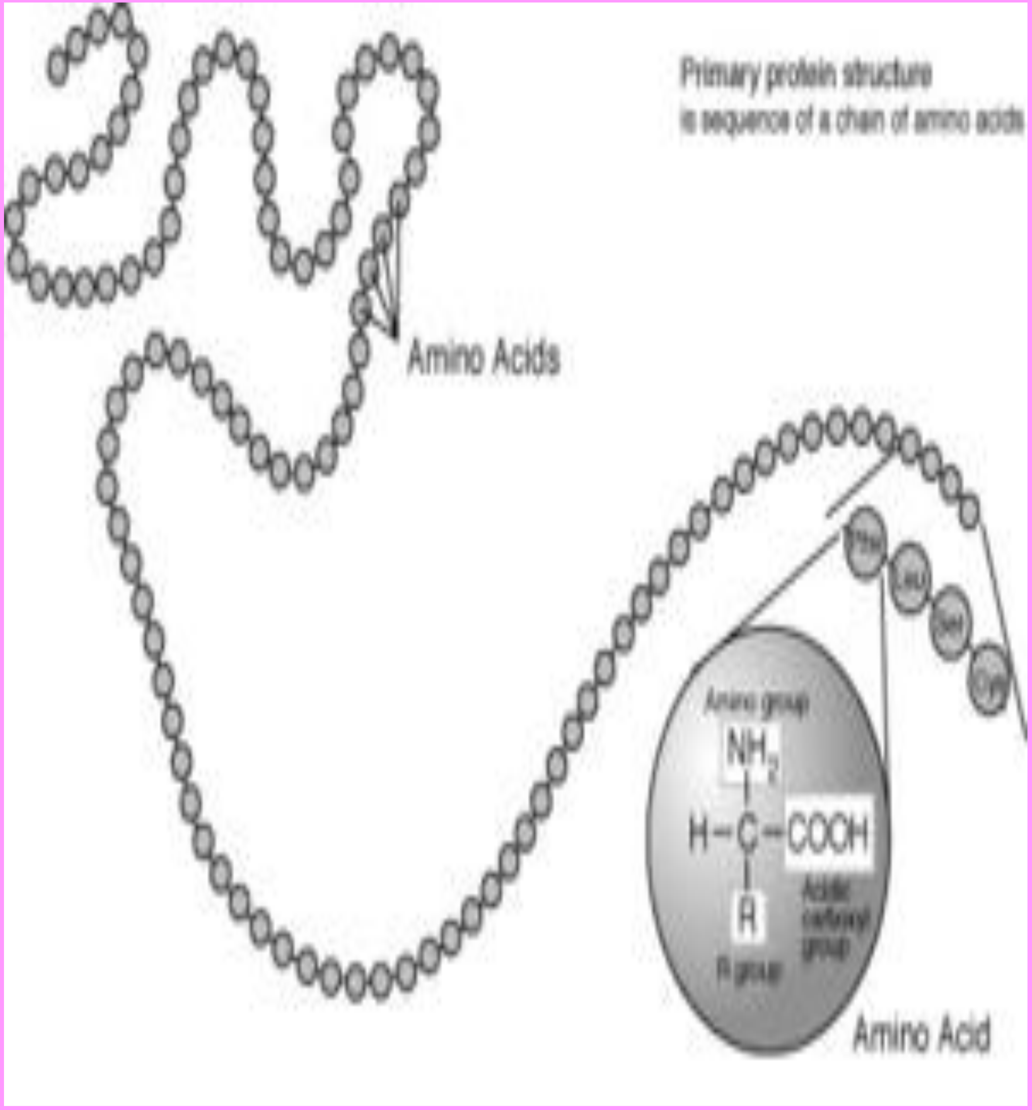
Blood Proteins

Albumins	Create osmotic pressure and transport other molecules
Immunoglobulins	Participate in immune system
Fibrinogens	Blood coagulation
Alpha-1-Antitrypsin	Neutralize trypsin that has leaked from the digestive system
Regulatory proteins	Regulation of gene expression


MOLECULAR STRUCTURE
Primary (sequence)
Secondary (local folding)
Tertiary (long-range folding)
Quaternary (multimeric organization)
Supramolecular (large-scale assemblies)
"off"
"on"
Regulation
Signaling
Structure
FUNCTION
Transport
Movement
Catalysis
A
B


(a) Primary structure
Carboxyl end
Amino end
(b) Secondary structure
Hydrogen bonds between amino acids
at different locations in polypeptide chain
(c) Tertiary structure
Heme
β polypeptide
(d) Quaternary structure
β
β
Heme group
α
α

Four Levels of Architectural Organization of Proteins

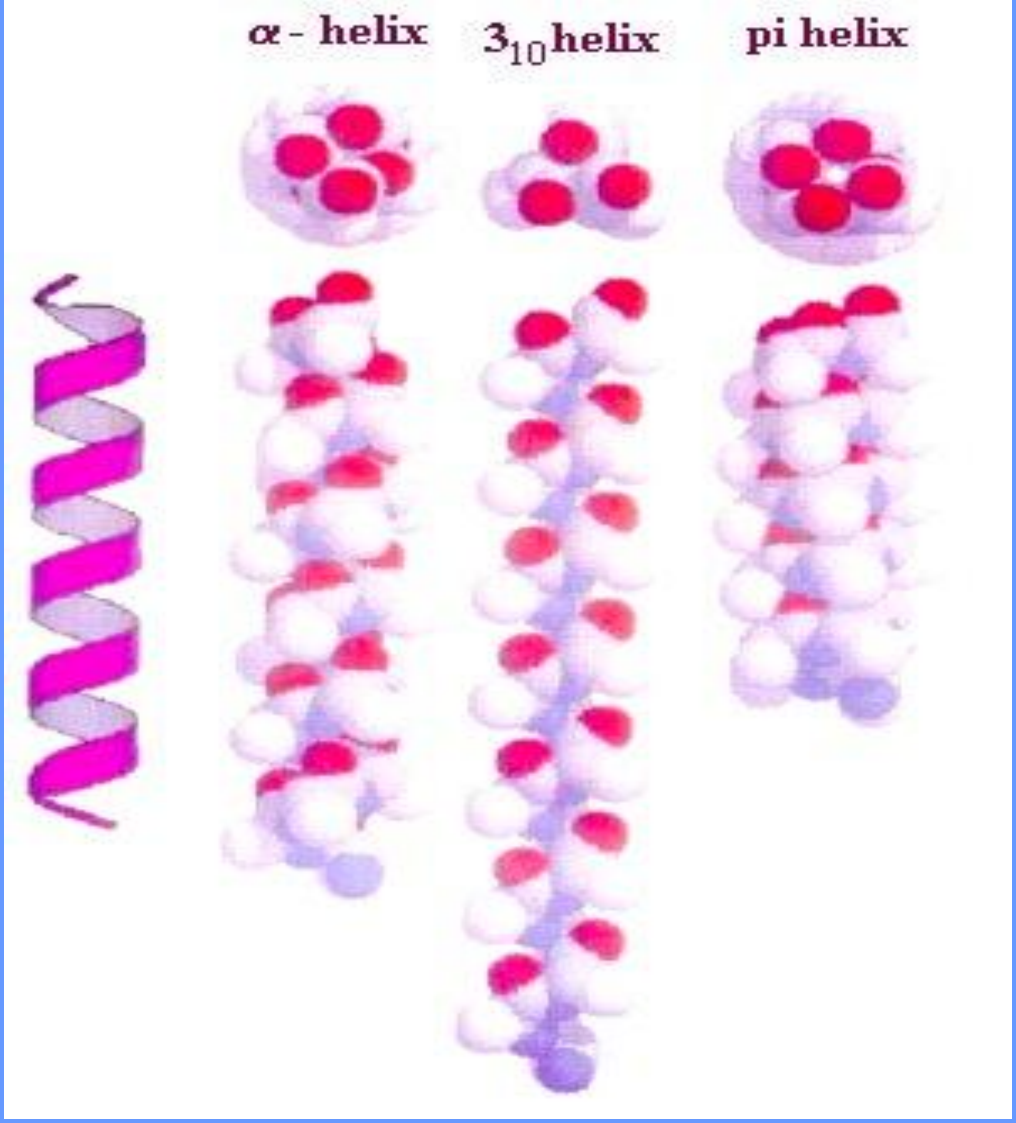


Primary Structure

It is the sequence of amino acids that make up a protein

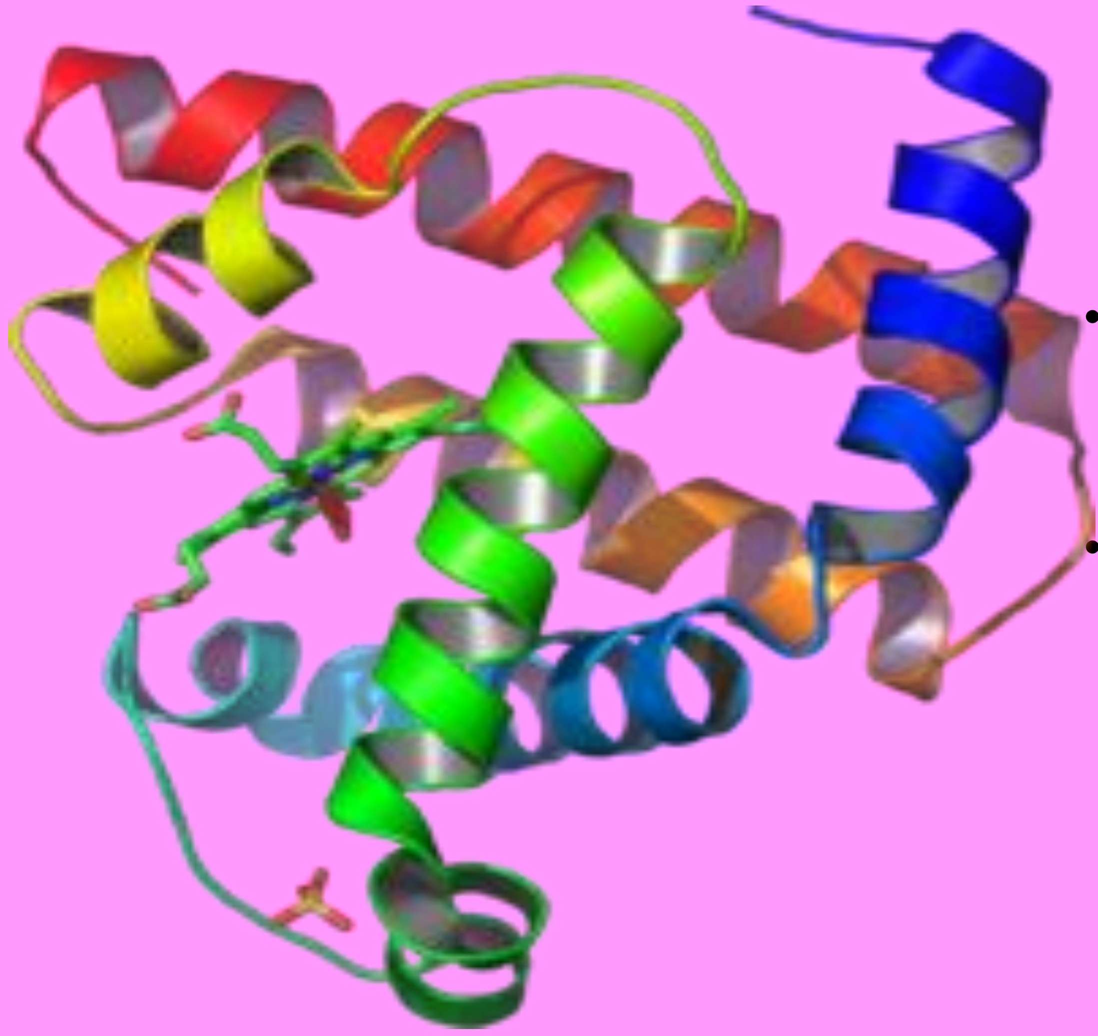
It is stabilized by peptide bonds (non-specific attractive forces that occur between adjacent –COOH and NH_2 groups)

Secondary Structure of Proteins

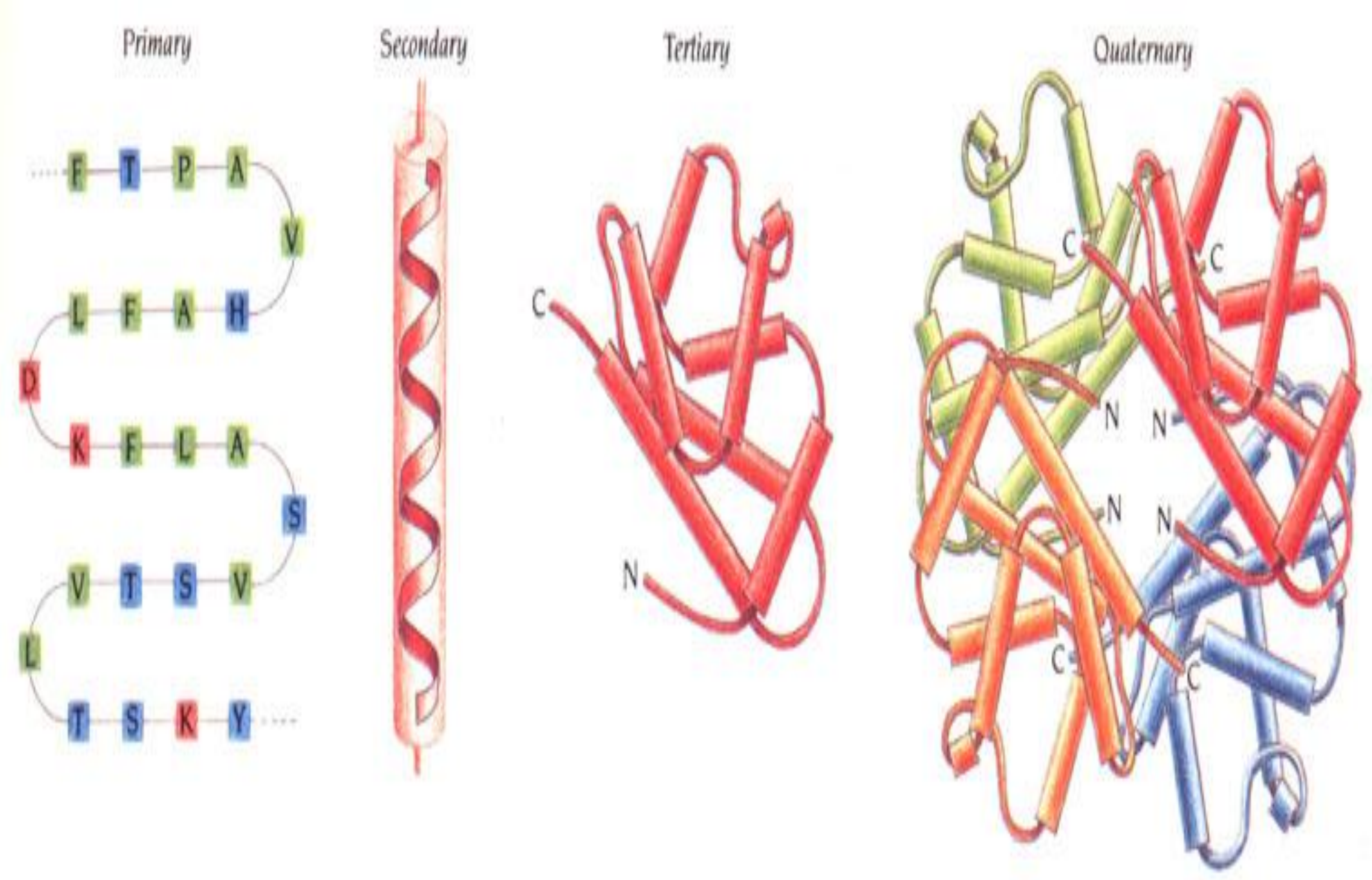


- Refers to the steric relationship of amino acid residues that arte close to one another in a linear sequence.
- It is stabilized by hydrogen bonding between carbonyl group of 1 peptide chain and the amino group of another chain.
- The polypeptide chain can change its orientation because of free rotation around the polypeptide backbone (-N-C-C).
- The hydrogen bonding produces a regular coiled arrangement called helix.

3D Structure of Myoglobin



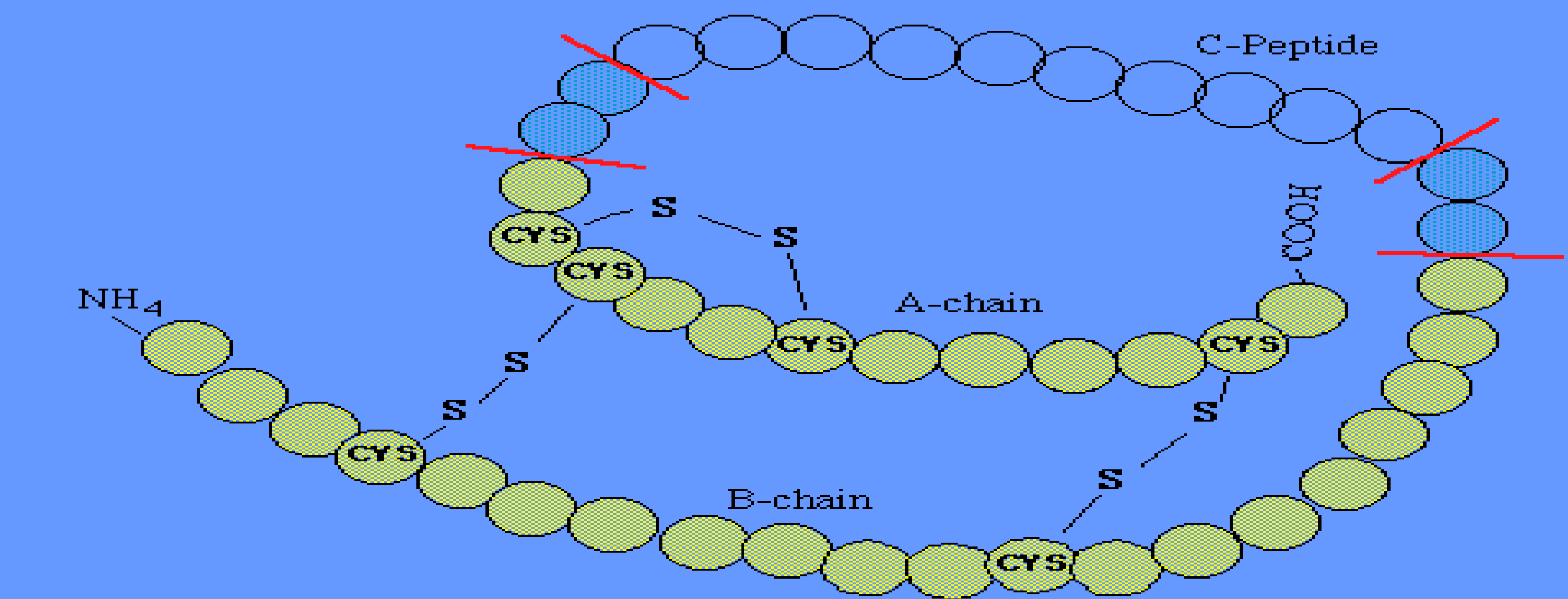
- Tertiary structure -
  refers to the steric relationship of amino acid residue that are far apart in the linear sequency.
- It also refers to how the polypeptide chain is bent or folded in 3 dimensions.
- It is stabilized by non-covalent bonds, hydrohobic bonds, electrostatic bons, hydrogen bonding, Van der Waals forces, and covalent disulfide bonds.



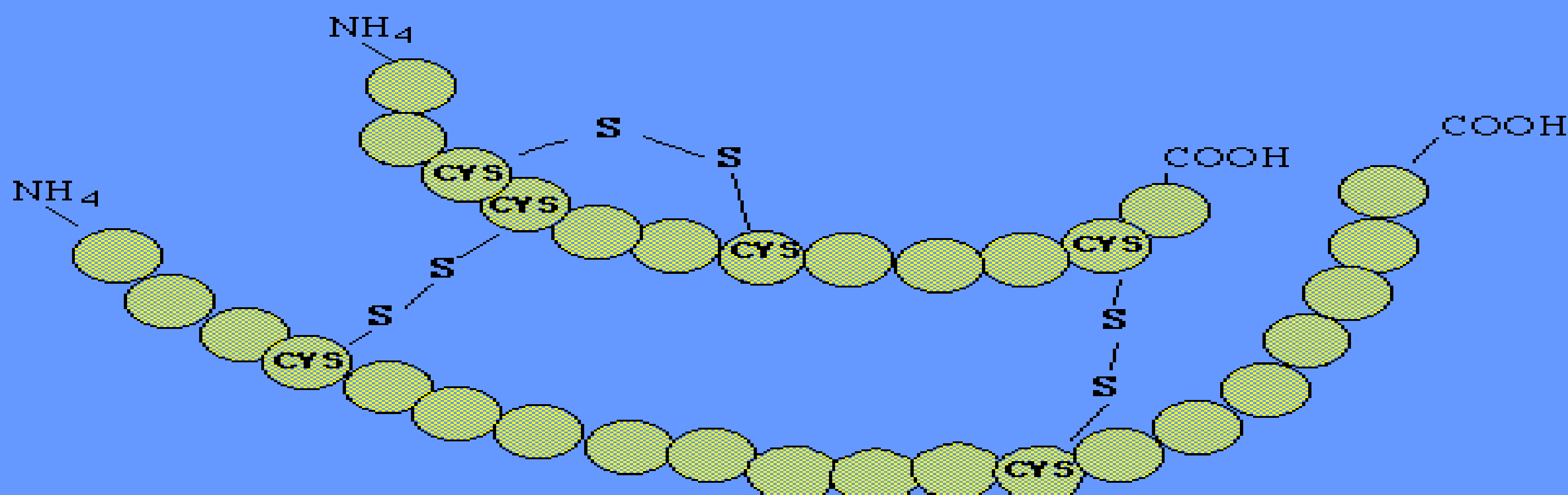
Primary
Secondary
Tertiary
Quaternary
F
T
P
A
V
L
F
A
H
D
K
F
L
A
S
V
T
S
V
L
T
S
K
Y
C
N
C
C
N
N
N
N
C
C

Quaternary Structure

- Contains more than one polypeptide chains stabilized by the same bonds as in tertiary structure
- Quaternary level donates the way the chains are packed together in a protein.
- Each chain in a protein is called a subunit or domain (protomers).
- Proteins with more than 1 chain are called oligomers.

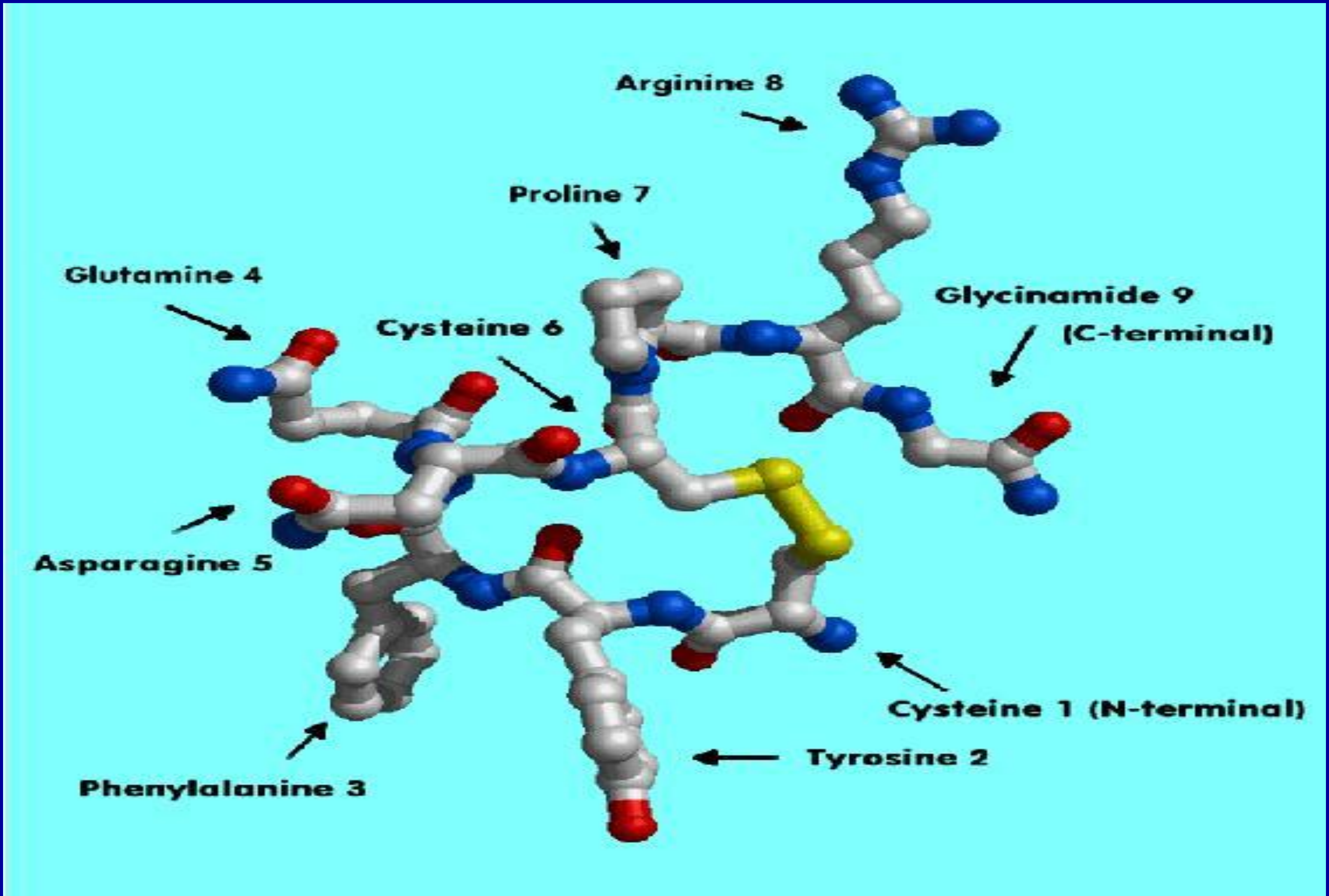


Proinsulin



Insulin

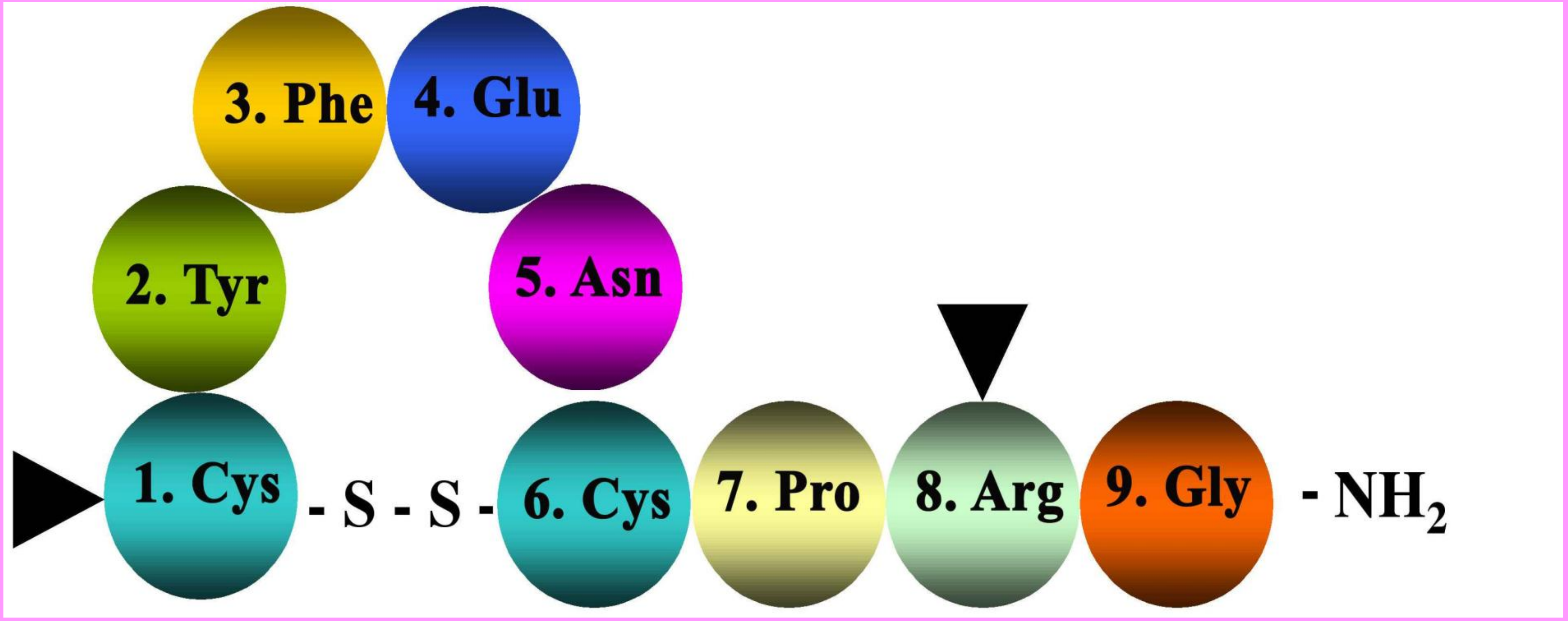
Vasopressin



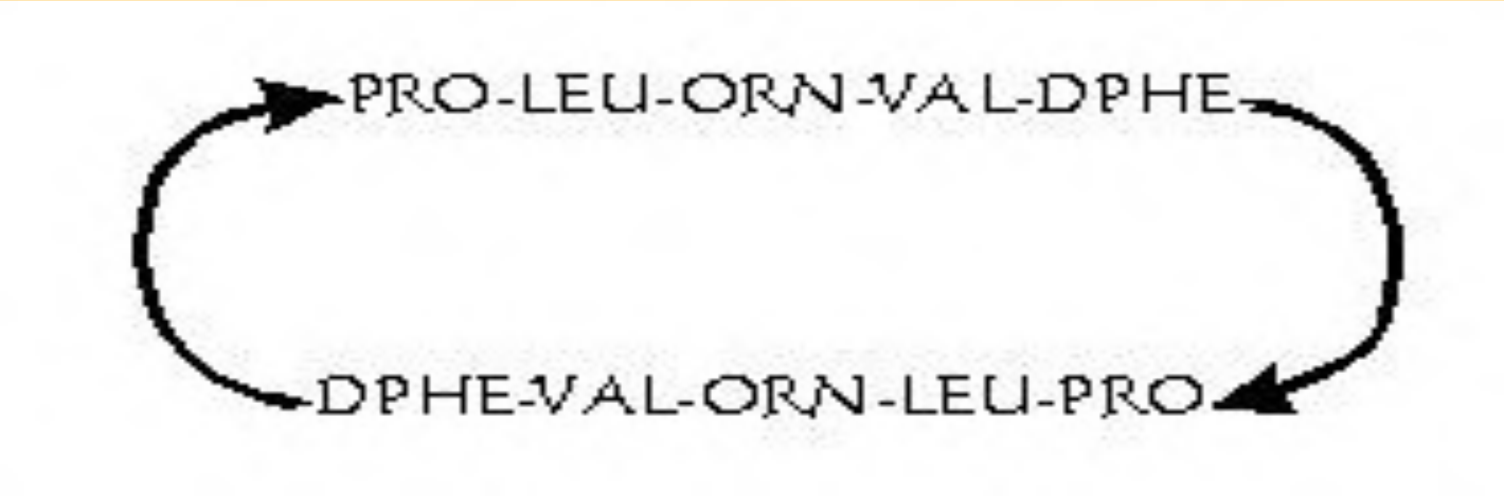
Vasopressin

- Vasopressin is also called ADH (antidiuretic hormone)
- Vasopressin increases blood pressure and inhibits diuresis.
- It constricts blood vessels rising the blood pressure and affecting water and electrolyte balance

Vassopressin

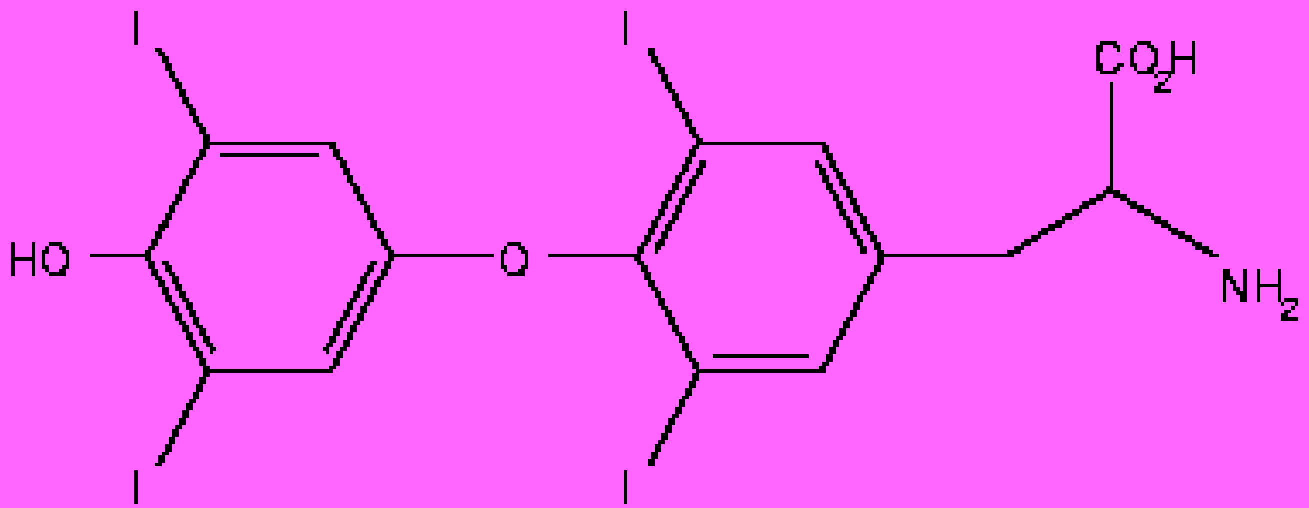


Gramicidin S



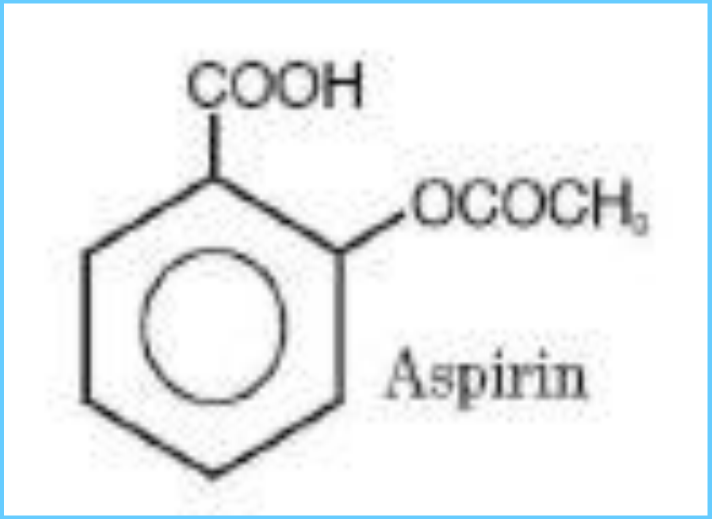
Gramicidin S is an antibiotic for topical use and effective for gram-positive bacterial infection.

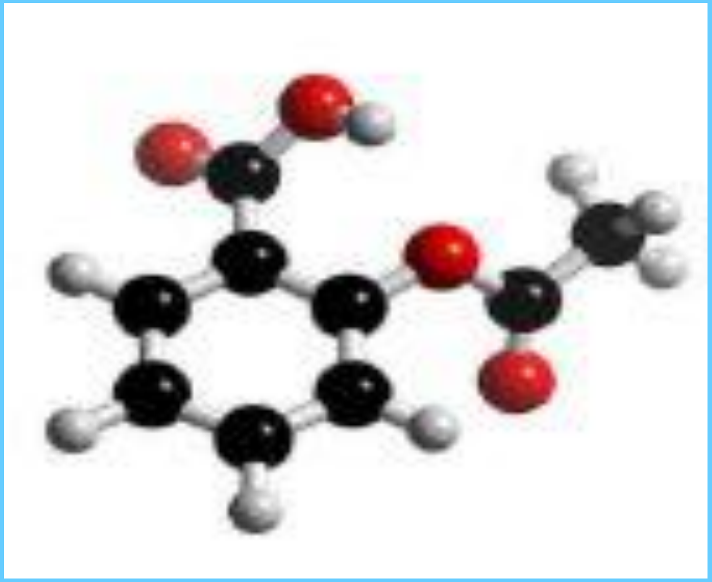
Thyroxine



- **Thyroxine (T4) and Triiodothyronine (T3) represents 2 iodonated tyrosine residues on the same polypeptide chain.**
- **The synthesis of these hormones involves iodination of the tyrosine ring, which concentrates iodide ion from the blood serum .**

Aspirin





The anti-inflammatory and analgesic properties of aspirin derive from the inhibition of PGHS-2 or prostaglandin H synthetase-2.

Chemical test for Proteins

Separation of Amino Acids and Proteins

1. **Chromatography** – the method of separating amino acids on the basis of differences in absorption, ionic charges, size and solubility of molecules
2. **Electrophoresis** – effects separation in an electric field on the basis of differences in charges carried by amino acids and proteins under specific condition
3. **Ultracentrifugation** – effects separation on the basis of molecular weight when large gravitational forces are applied in the ultracentrifuge.
4. **Precipitation Methods** – salts as sodium sulfate, ammonium sulfate, cadmium nitrate, silver nitrate and mercuric chloride at specific conc. precipitate some proteins while others remain in solution
5. **Dialysis** – is for the removal of small, crystalloidal molecules from protein solution.

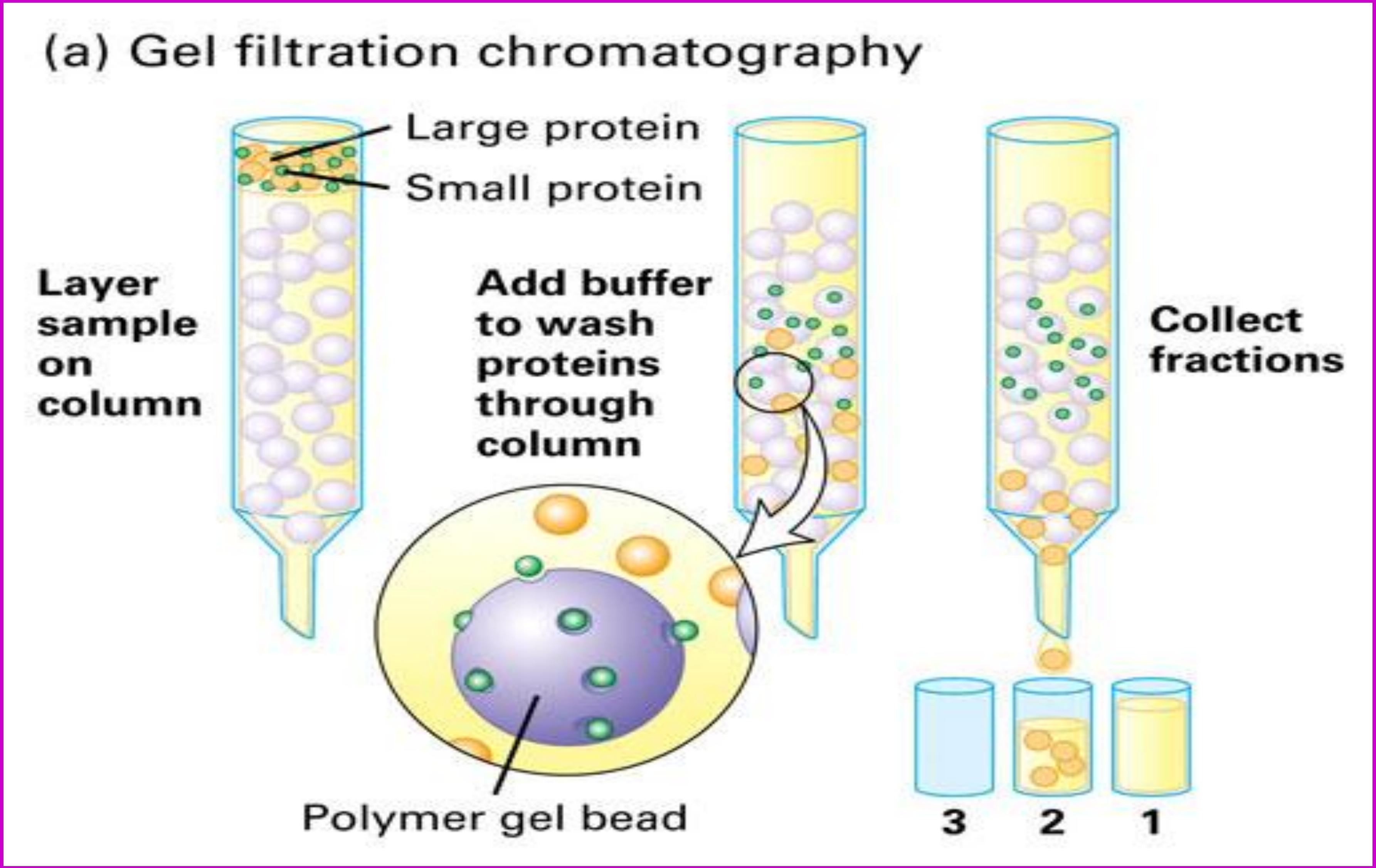
Chromatography

- Much of modern biochemistry depends on the use of column chromatographic methods to separate molecules.
- Chromatographic methods involve passing a solution (the mobile phase) through a medium (the immobile phase) that shows selective solute components.
- The important methods of chromatography are:

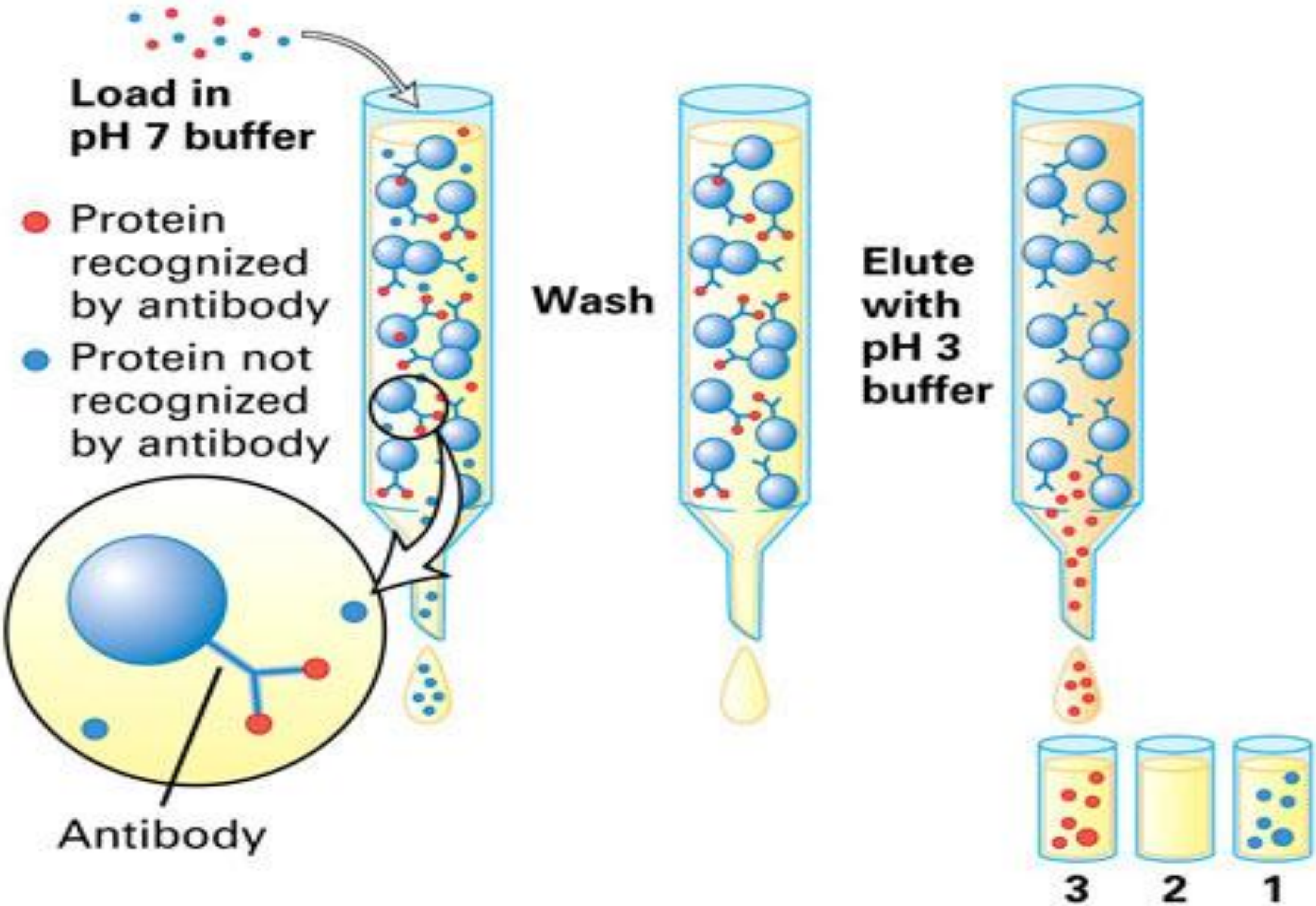
1. Ion-Exchange Chromatography
2. Antibody Affinity Chromatography
3. Gel Filtration Chromatography
4. HPLC (High Performance Liquid Chromatography)

HPLC

Gel Filtration Chromatography

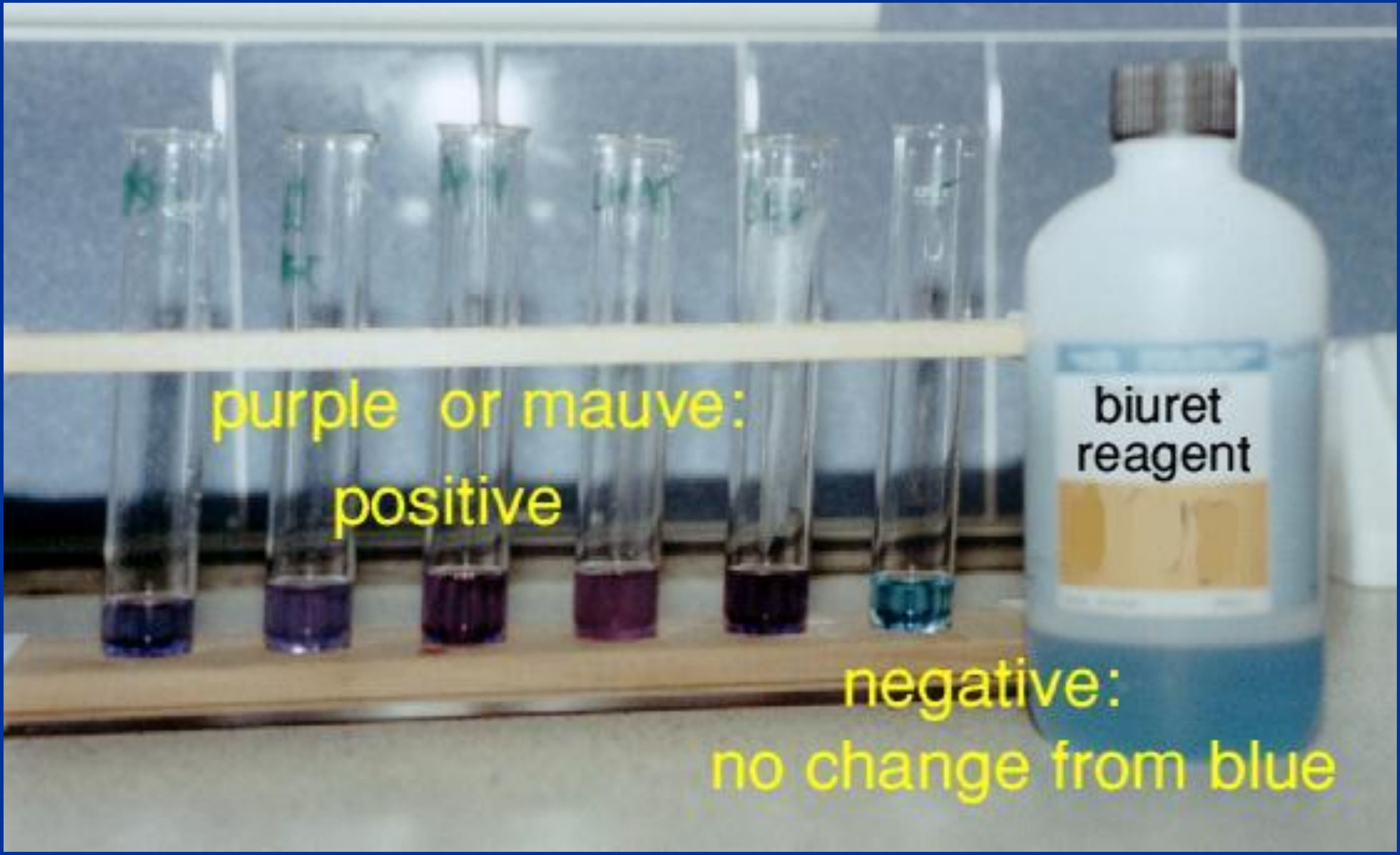


(c) Antibody-affinity chromatography

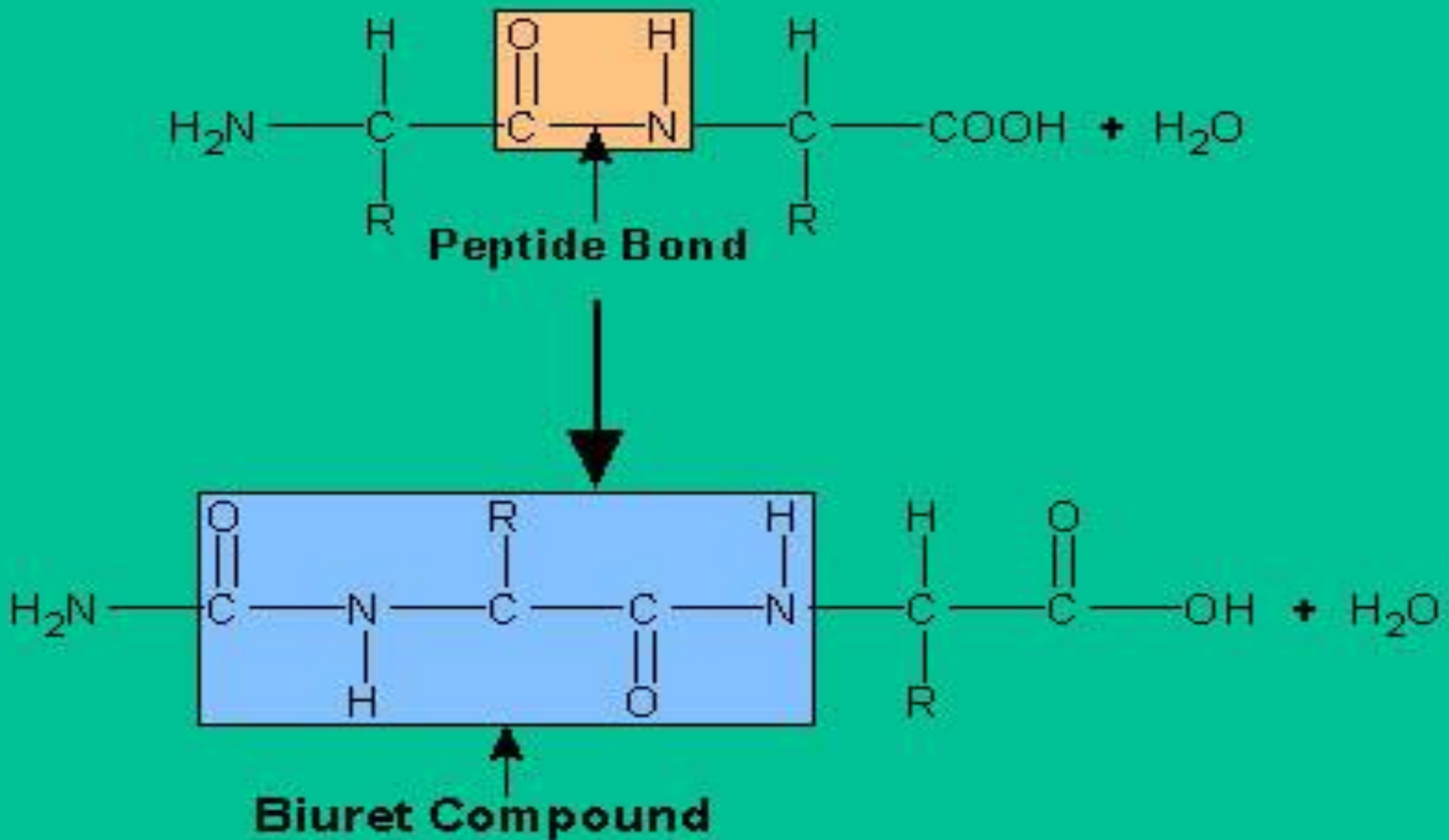


Precipitation of proteins

Biuret Test


purple or mauve:
positive
biuret
reagent
negative:
no change from blue

Chemical Reaction in the Biuret test



Proteomics

- Proteomics is the science of protein expression of all the proteins made by a cell
- Proteome pertain to all proteins being made according to the transcriptome (RNA profile). It is often visualized by a system interaction map as seen in the proteogram.

Procedures of the Proteomics

- Commonly used procedures by Proteomics are:
- Mass Spectrophotometry – detects exact mass of small peptides (molecular weight).
- X-ray Crystallography – determines 3D shape of molecules mathematically
- NMR Spectroscopy – magnetic signal indicates distances between atoms

Summary

- Proteins are polymers of α-amino acids. Twenty different amino acids are coded for in genes and incorporated into proteins. Other non-protein amino acids exist, and there are also modifications of amino acids found in proteins.
- The variety of side chains – hydrophilic, hydrophobic, acidic, basic, neutral – allows much functional complexity in proteins.
- Additional variation is made possible by modification of some amino acids after they have been incorporated into proteins. The presence of both positive and negative charges on side chains makes proteins polyampholytes.







Next meeting

- Quiz on Proteins
- Discussion on Chemistry of Nucleoproteins