Amino Acids

Amino Acids are the building units of proteins. Proteins are polymers of amino acids linked together by what is called " Peptide bond" (see latter).

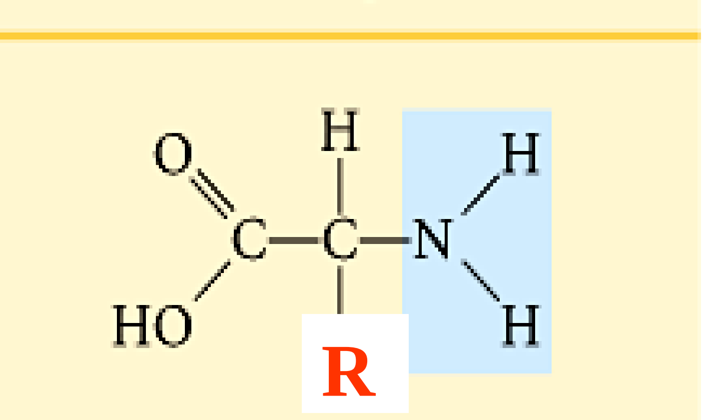
- **There are about 300 amino acids occur in nature. Only 20 of them occur in proteins.**

Structure of amino acids:

Each amino acid has 4 different groups attached to α- carbon (which is C-atom next to COOH). These 4 groups are : amino group, COOH gp,

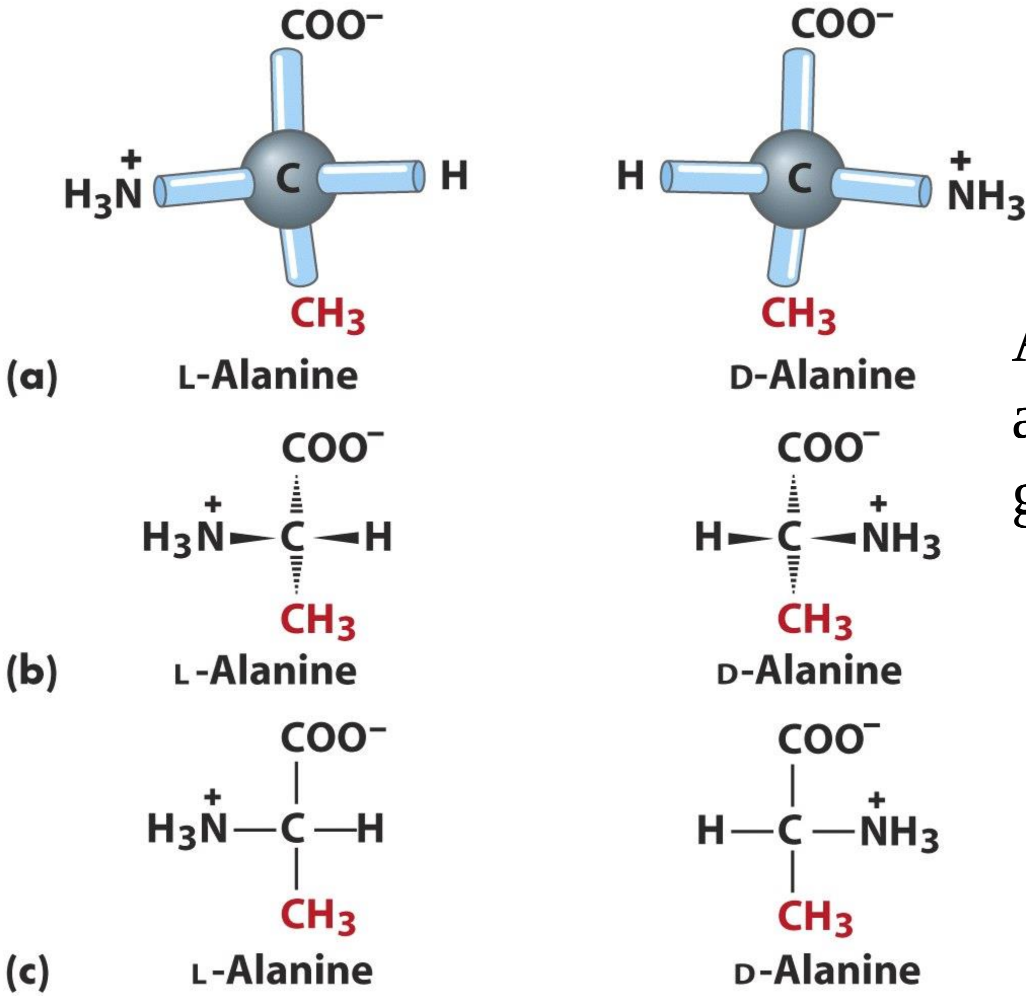
Hydrogen atom and side

Chain (R)



- **At physiological PH (7.4), -COOH gp is dissociated forming a negatively charged carboxylate ion (COO^-) and amino gp is protonated forming positively charged ion (NH_3^+) forming Zwitter ion**
- **N.B. Proline is an imino acid not amino acid (see latter)**

Stereoisomers of α-amino acids

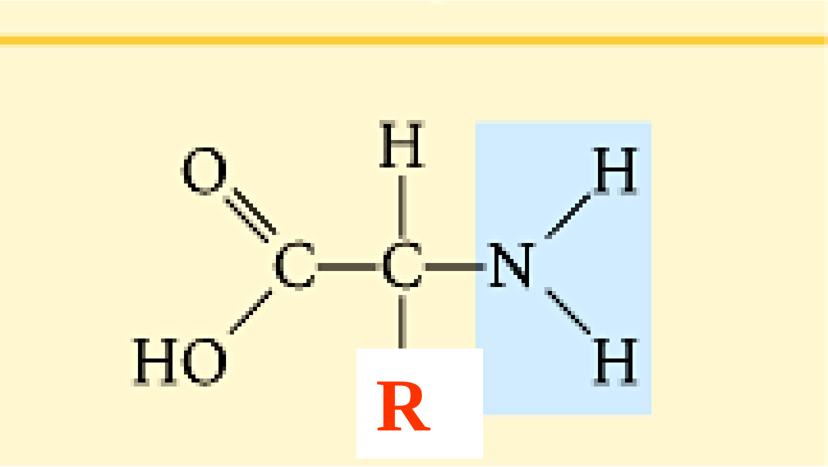


All amino acids in proteins are L-amino acids, except for glycine, which is achiral.

Classification of amino acids

I- Chemical classification: According to number of COOH and NH_2 groups i.e. according to net charge on amino acid.

A- **Monobasic, monocarboxylic amino acids i.e. neutral or uncharged:**



Subclassification of neutral amino acids:

All structures are required (See structures in hand out)

1- **Glycine** R= H

2- **Alanine** R= CH_3

3- **Branched chain amino acids:** R is branched such as in:

a - **Valine** R= isopropyl gp

b- **Leucine** R= isobutyl gp

c- **Isoleucine** R = is isobutyl

R is isobutyl in both leucine and isoleucine but branching is different: in leucine → branching occurs on γ carbon

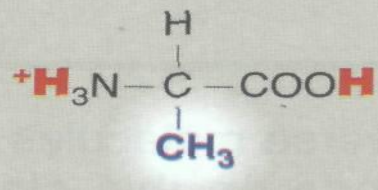
in isoleucine→ branching occurs on β- carbon

4- Neutral Sulfur containing amino acids:

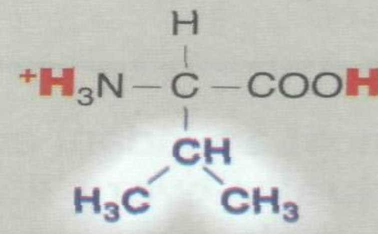
e.g. Cysteine and Methionine.

5- Neutral, hydroxy amino acids:

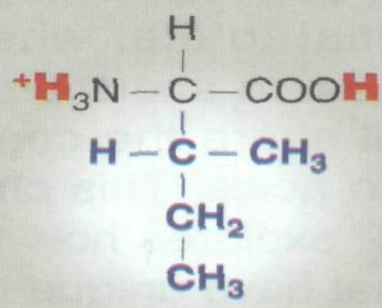
e.g. Serine and Threonine



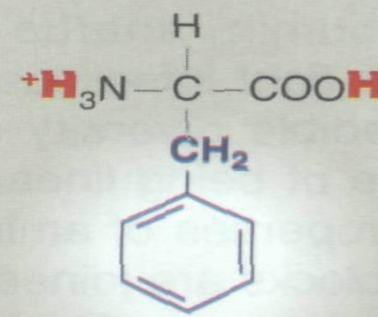
Alanine



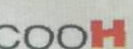
Valine

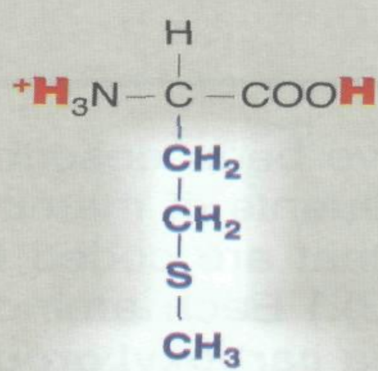


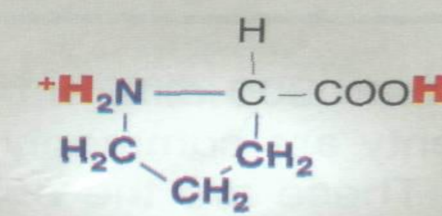
Isoleucine



Phenylalanine







6- Neutral aromatic amino acids:

a- Phenyl alanine : It's alanine in which one hydrogen of CH_3 is substituted with phenyl group. So it's called phenyl alanine

b- Tyrosine: - it is P- hydroxy phenyl alanine

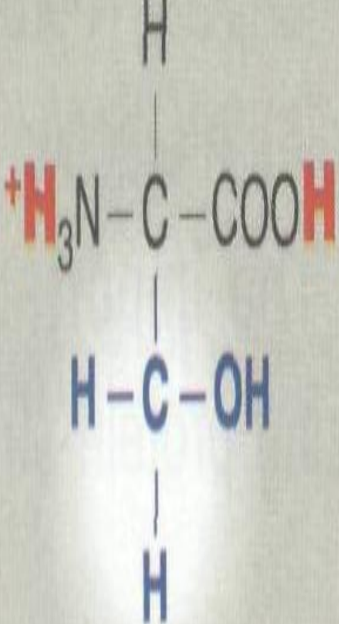
- it is classified as **phenolic amino acid**

c- Tryptophan: as it contains indole ring so it is classified as **heterocyclic amino acid**

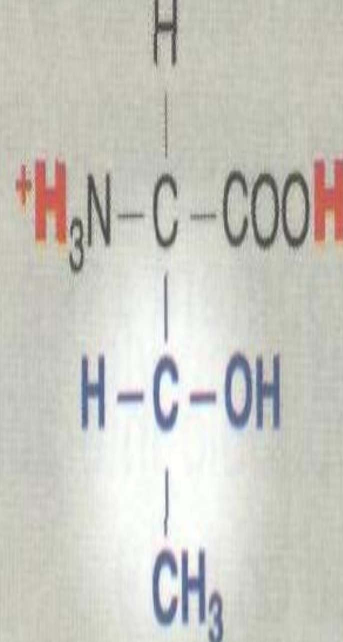
7- Neutral heterocyclic amino acids:

a- Tryptophan: contains indole ring

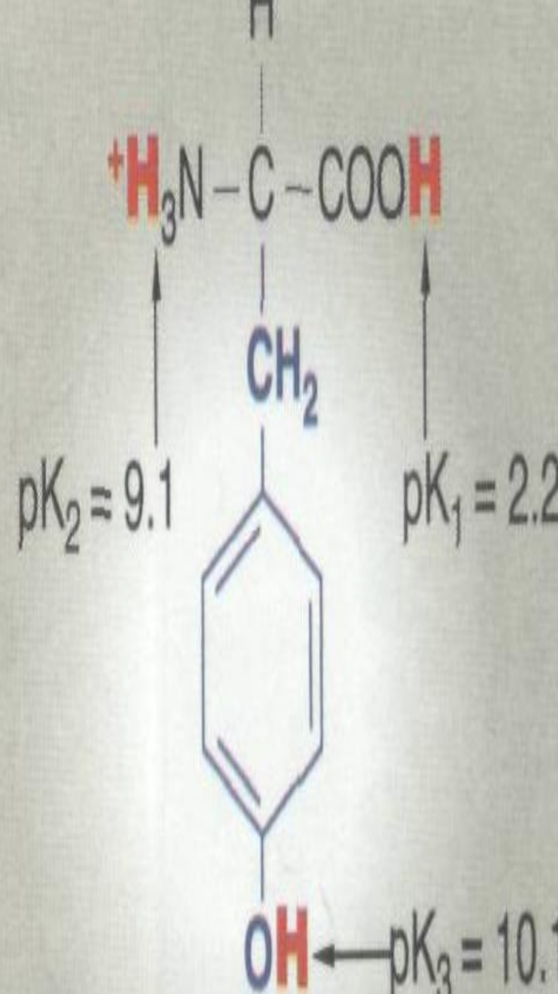
b- Proline: In proline, amino group enters in the ring formation being α-imino gp so proline is an α-imino acid rather than α-amino acid



Serine S



Threonine T



Tyrosine Y

B- Basic amino acids: Contain two or more NH_2 groups or nitrogen atoms that act as base i.e. can bind proton.

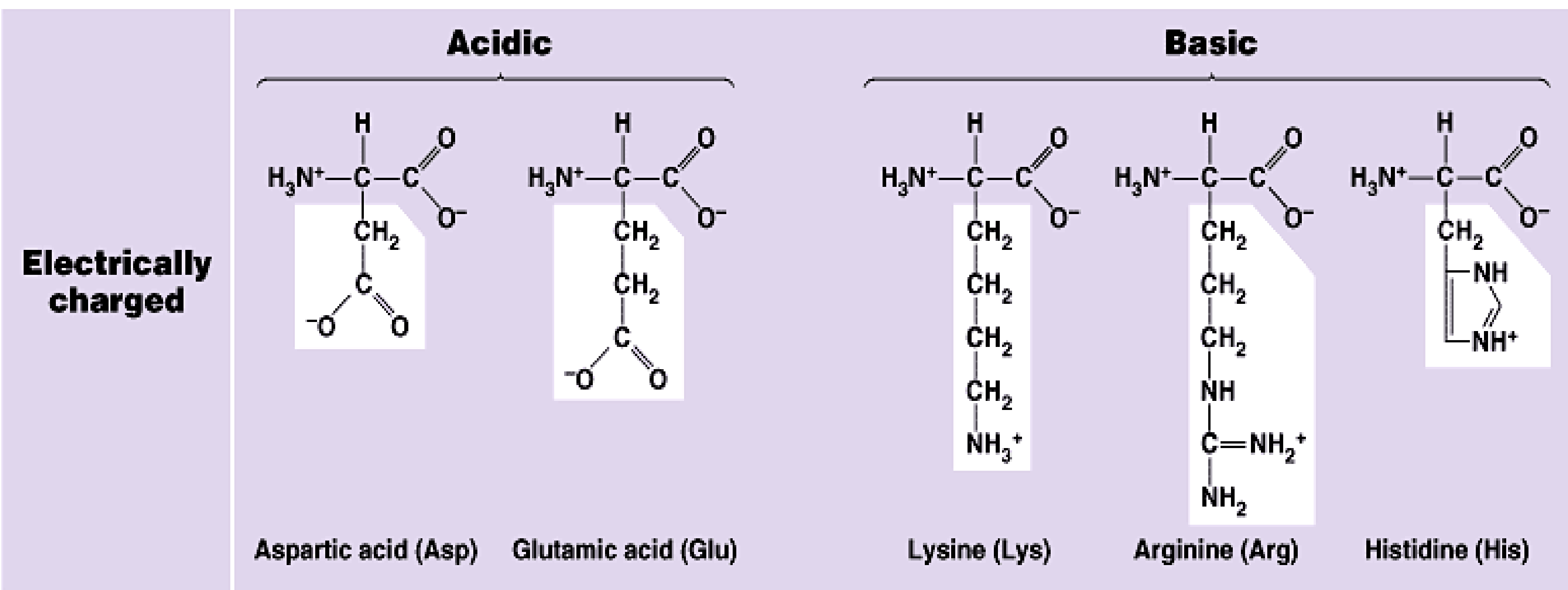
At physiological pH, basic amino acids will be **positively charged**.

e.g.

a- Lysine

b- Arginine: contains guanido group

c- Histidine: is an example on basic heterocyclic amino acids



C- Acidic Amino acids: at physiological pH will carry negative charge.

e.g. Aspartic acid (aspartate) and Glutamic acid (glutamate). see structures in hand out.

Aspargine and Glutamine: They are amide forms of aspartate and glutamate in which side chain COOH groups are amidated.
They are classified as neutral amino acids.

II- Classification according to polarity of side chain (R):

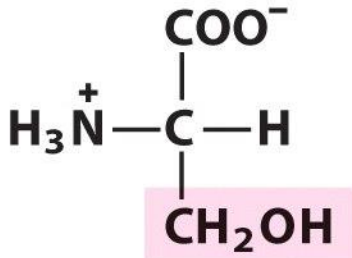
A- Polar amino acids: in which R contains polar hydrophilic group so can forms hydrogen bond with H_2O. In those amino acids, R may contain:

1- OH group : as in serine, threonine and tyrosine
2- SH group : as in cysteine
3- amide group: as in glutamine and aspargine
4- NH_2 group or nitrogen act as a base (basic amino acids): as lysine, arginine and histidine
5- COOH group (acidic amino acids): as aspartic and glutamic .

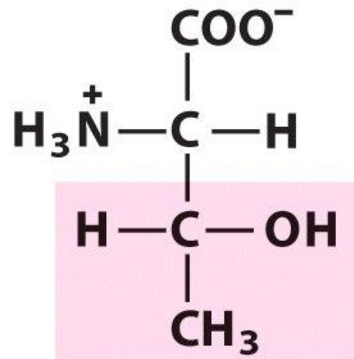
B- Non polar amino acids:

R is alkyl hydrophobic group which can't enter in hydrogen bond formation. 9 amino acids are non polar (glycine, alanine, valine, leucine, isoleucine, phenyl alanine, tryptophan, proline and methionine)

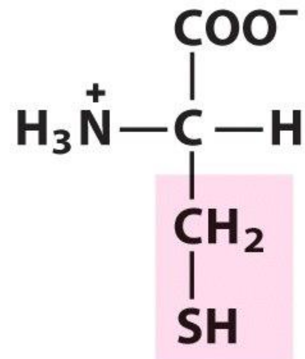
Polar, uncharged R groups



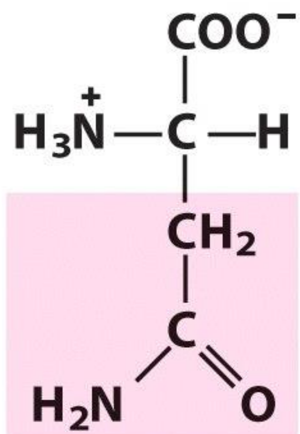
Serine



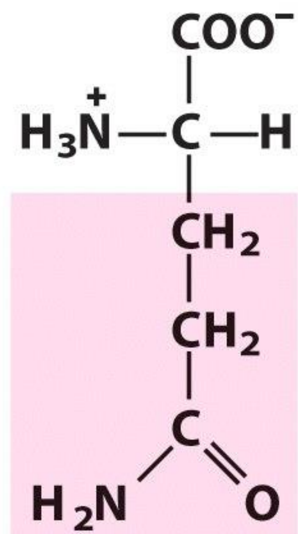
Threonine



Cysteine

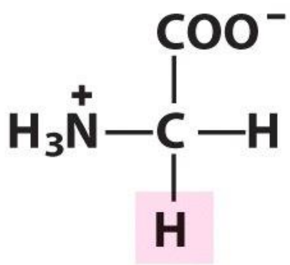


Asparagine

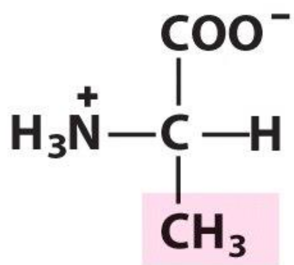


Glutamine

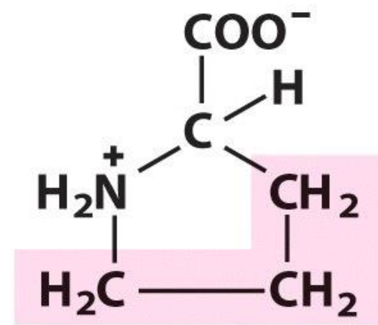
Nonpolar, aliphatic R groups



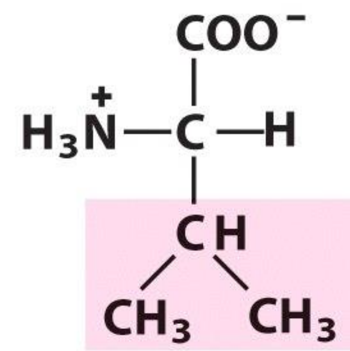
Glycine



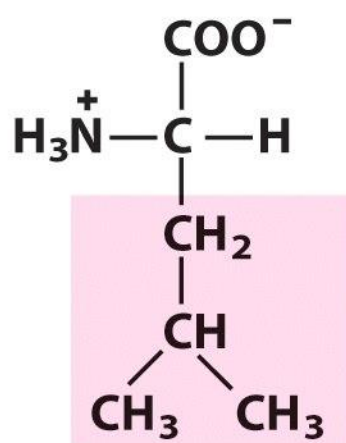
Alanine



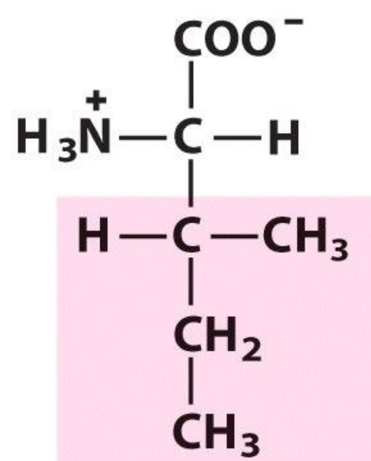
Proline



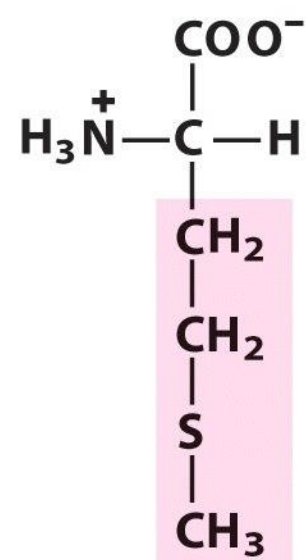
Valine



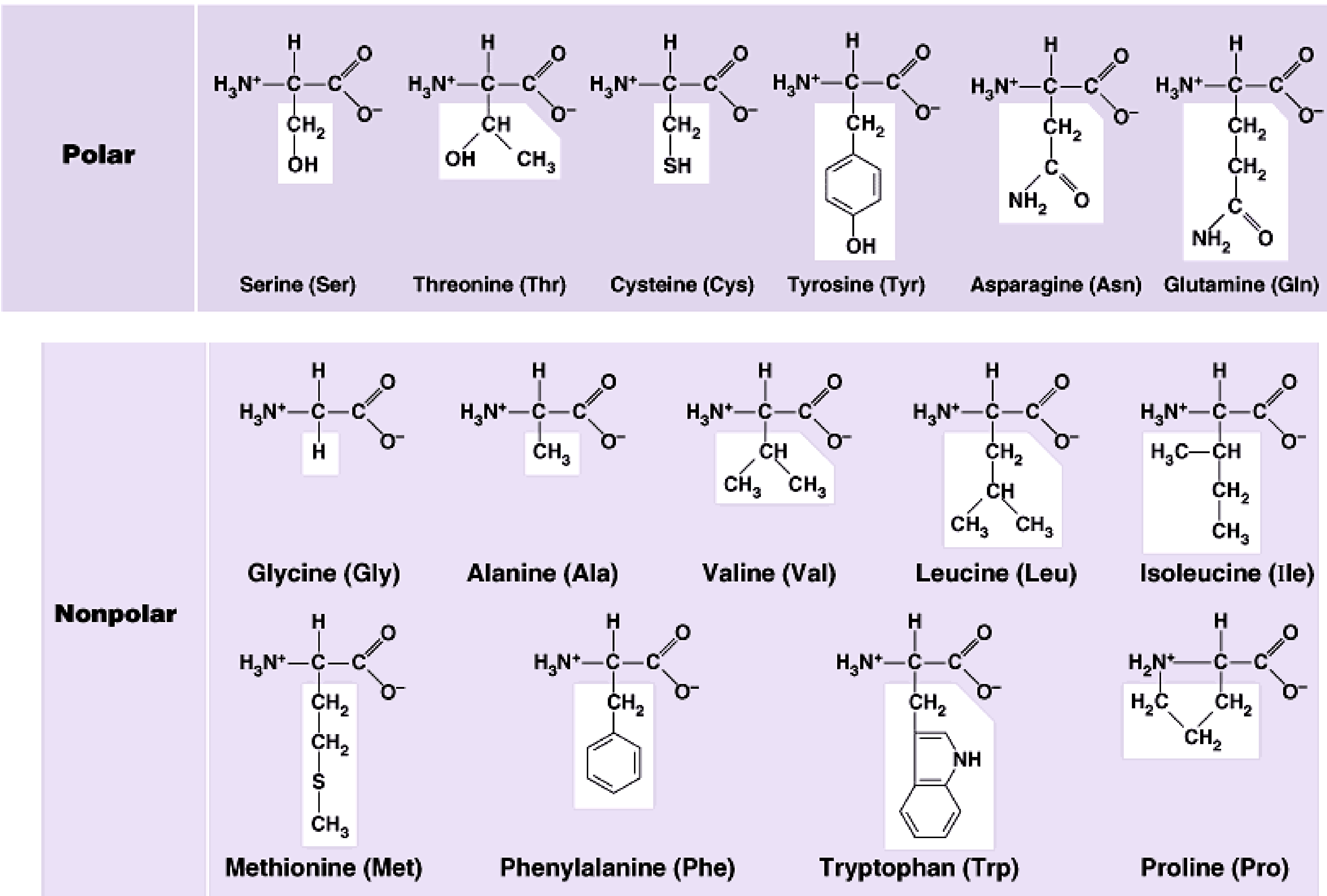
Leucine



Isoleucine



Methionine


Polar
Serine (Ser)
Threonine (Thr)
Cysteine (Cys)
Tyrosine (Tyr)
Asparagine (Asn)
Glutamine (Gln)
Nonpolar
Glycine (Gly)
Alanine (Ala)
Valine (Val)
Leucine (Leu)
Isoleucine (Ile)
Methionine (Met)
Phenylalanine (Phe)
Tryptophan (Trp)
Proline (Pro)

III- Nutritional classification:

1- Essential amino acids: These amino acids can't be formed in the body and so, it is essential to be taken in diet. Their deficiency affects growth, health and protein synthesis.

2- Semiessential amino acids: These are formed in the body but not in sufficient amount for body requirements especially in children.

Summary of essential and semiessential amino acids:

V= valine i= isoleucine l= lysine l= leucine

A = arginine* H= histidine* M= methionine

T= tryptophan Th= threonine P= phenyl alanine

*= arginine and histidine are semiessential

3- Non essential amino acids: These are the rest of amino acids that are formed in the body in amount enough for adults and children. They are the remaining 10 amino acids.

IV- Metabolic classification: according to metabolic or degradation products of amino acids they may be:

1- Ketogenic amino acids: which give ketone bodies . **Lysine** and **Leucine** are the only pure ketogenic amino acids.

2- Mixed ketogenic and glucogenic amino acids: which give both ketonbodies and glucose.These are: isoleucine, phenyl alanine, tyrosine and tryptophan.

3- Glucogenic amino acids: Which give glucose. They include the rest of amino acids. These amino acids by catabolism yields products that enter in glycogen and glucose formation.

Amphoteric properties of amino acids: that is they have both basic and acidic groups and so can act as base or acid.

Neutral amino acids (monobasic, monocarboxylic) exist in aqueous solution as " Zwitter ion" i.e. contain both positive and negative charge. Zwitter ion is electrically neutral and can't migrate into electric field.

Isoelectric point (IEP) = is the pH at which the zwitter ion is formed. e.g IEP of alanine is 6

Chemical properties of amino acids:

1- Reactions due to COOH group:

-Salt formation with alkalis, ester formation with alcohols, amide formation with amines and decarboxylation

-**2- Reactions due toNH2 group:** deamination and reaction with ninhydrin reagent.

-Ninhydrin reagent reacts with amino group of amino acid yielding blue colored product. The intensity of blue color indicates quantity of amino acids present.

Ninhydrine can react with imino acids as proline and hydroxy proline but gives **yellow color.**

3- Reactions due to side chain (R):

1- Millon reaction: for tyrosine gives red colored mass

2- Rosenheim reaction: for trptophan and gives violet ring.

3- Pauly reaction: for imidazole ring of histidine: gives yellow to reddish product

4- **Sakagushi test:** for guanido group of arginine and gives red color.

5- Lead sulfide test (sulfur test): for sulfur containing amino acids as cysteine give brown color.

Peptides and Proteins

20 amino acids are commonly found in protein.

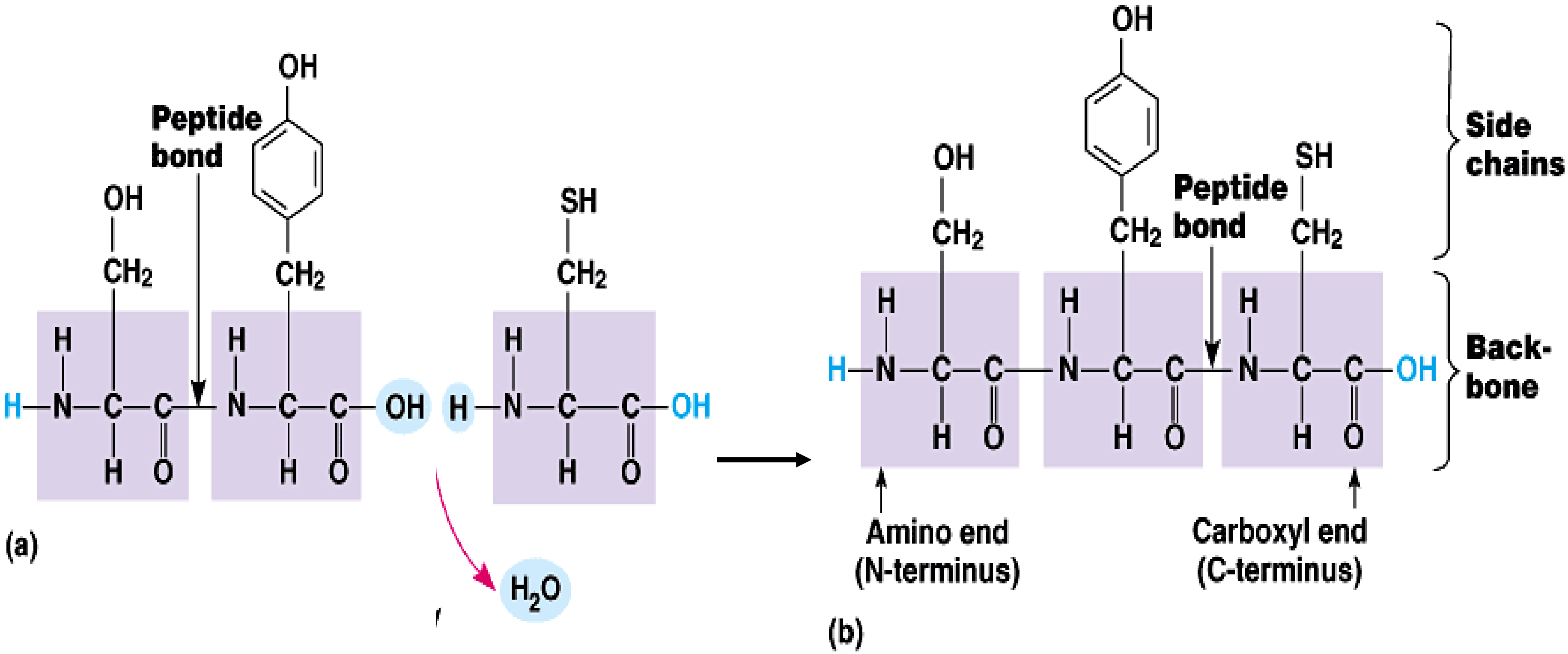
These 20 amino acids are linked together through "peptide bond forming peptides and proteins (what's the difference?).

- The chains containing less than 50 amino acids are called **"peptides",** while those containing greater than 50 amino acids are called **"proteins".**

Peptide bond formation:

α-carboxyl group of one amino acid (with side chain R1) forms a covalent peptide bond with α-amino group of another amino acid (with the side chain R2) by removal of a molecule of water. The result is : **Dipeptide** (i.e. Two amino acids linked by one peptide bond). By the same way, the dipeptide can then forms a second peptide bond with a third amino acid (with side chain R3) to give **Tripeptide.** Repetition of this process generates a polypeptide or protein of specific amino acid sequence.

Peptide bond formation:



- Each polypeptide chain starts on the left side by free amino group of the first amino acid enter in chain formation . It is termed (N- terminus).
- Each polypeptide chain ends on the right side by free COOH group of the last amino acid and termed (C-terminus).

Examples on Peptides:

1- Dipeptide **(tow amino acids joined by one peptide bond):**

Example: **Aspartame** which acts as sweetening agent being used in replacement of cane sugar. It is composed of aspartic acid and phenyl alanine.

2- Tripeptides (3 amino acids linked by two peptide bonds).

Example: **GSH** which is formed from 3 amino acids: glutamic acid, cysteine and glycine. It helps in absorption of amino acids, protects against hemolysis of RBC by breaking H_2O_2 which causes cell damage.

3- octapeptides: (8 amino acids)

Examples: Two hormones; oxytocine and vasopressin (ADH).

4- polypeptides: 10- 50 amino acids: e.g. Insulin hormone

Protein structure:

There are four levels of protein structure (primary, secondary, tertiary and quaternary)

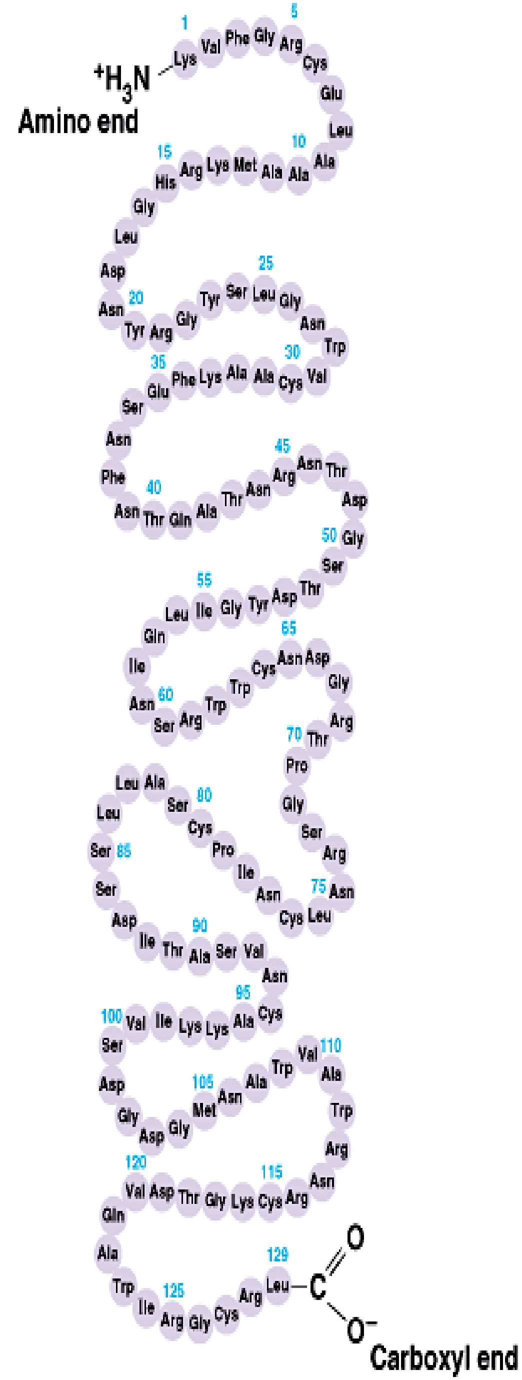
Primary structure:

The primary structure of a protein is defined by the linear sequences of amino acid residues. Protein contain between 50 and 2000 amino acid residues.

The mean molecular mass of an amino acid residue is bout 110 Dalton units (Da).

Therefore the molecular mass of most proteins is between 5500 and 220,000 Da.

The amino acid composition of a peptide chain has a profound effect on its physical and chemical properties of proteins.



Protein rich in polar amino acids are more water soluble. Proteins rich in aliphatic or aromatic amino groups are relatively insoluble in water and more soluble in cell membranes (can easily cross the cell membrane).

- Lysozyme, an enzyme that attacks bacteria, consists of a polypeptide chain of 129 amino acids.
- The precise primary structure of a protein is determined by inherited genetic information.
- At one end is an amino acid with a free amino group the (the N-terminus) and at the other is an amino acid with a free carboxyl group the (the C-terminus).

High orders of Protein structure

- **A functional protein** is **not just** a polypeptide chain, but **one or more** polypeptides precisely **twisted, folded and coiled** into a molecule of unique shape (**conformation).** This conformation is essential for some protein function e.g. Enables a protein to recognize and bind specifically to another molecule e.g. hormone/receptor; enzyme/substrate and antibody/antigen.
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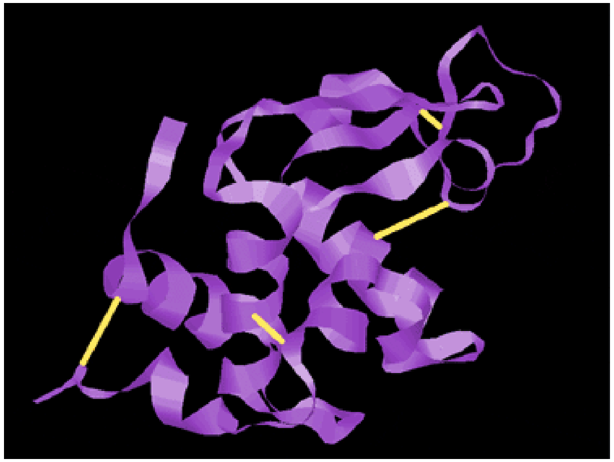
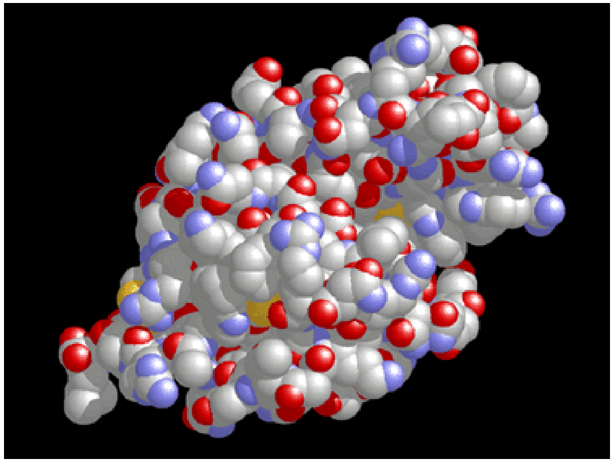


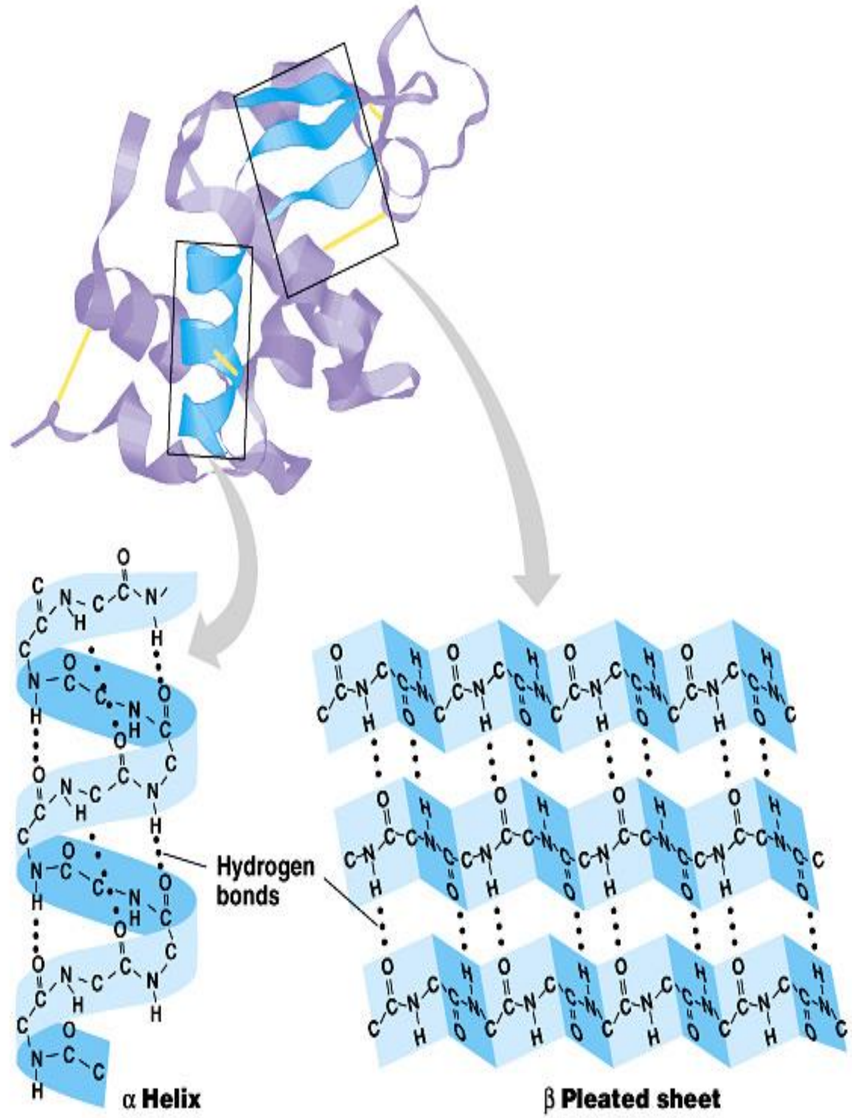


2- Secondary structure:

Results from hydrogen bond formation between hydrogen of –NH group of peptide bond and the carbonyl oxygen of another peptide bond. According to H-bonding there are two main forms of secondary structure:

α-helix: It is a spiral structure resulting from hydrogen bonding between one peptide bond and the fourth one

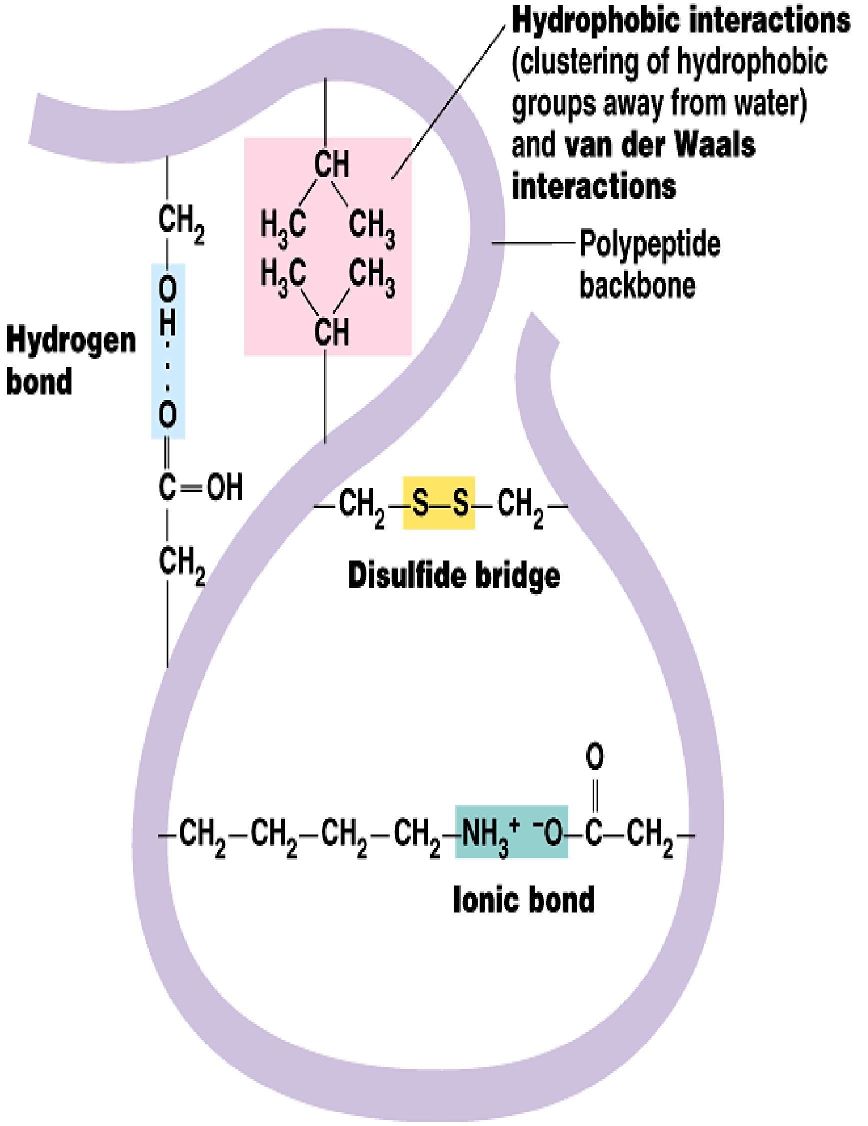
β-sheets: is another form of secondary structure in which two or more polypeptides (or segments of the same peptide chain) are linked together by hydrogen bond between H- of NH- of one chain and carbonyl oxygen of adjacent chain (or segment).



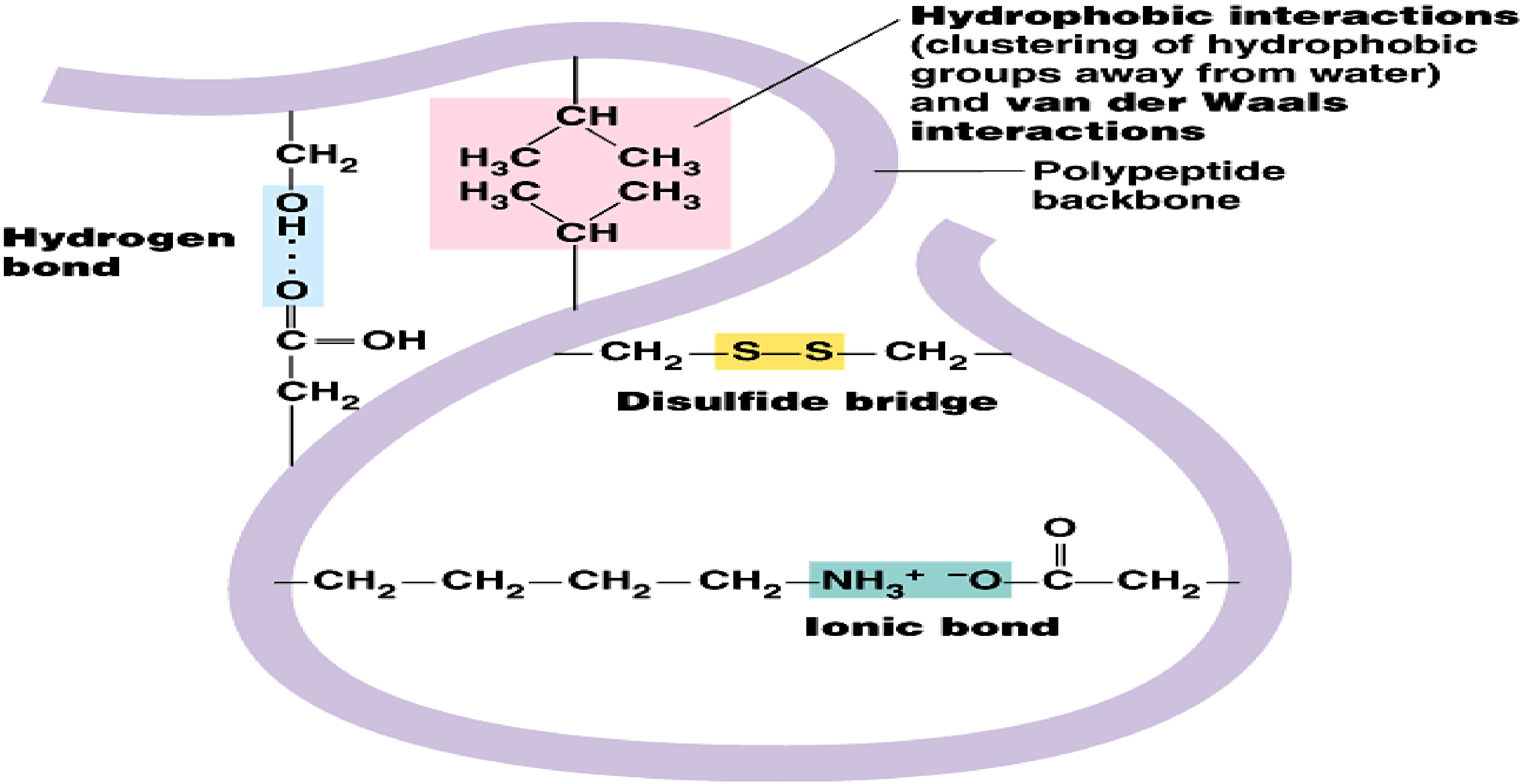
- **Tertiary structure** is determined by a variety of interactions (bond formation) among R groups and between R groups and the polypeptide backbone.

a. **The weak interactions** include:

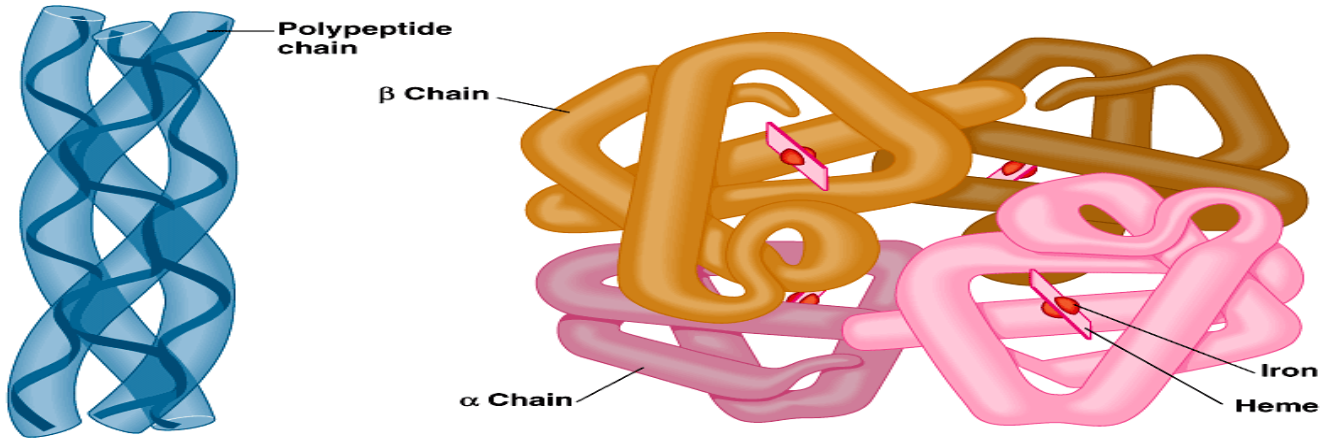
- **Hydrogen bonds** among polar side chains
- **Ionic bonds** between charged R groups (basic and acidic amino acids)
- **Hydrophobic interactions** among hydrophobic (non polar) R groups.



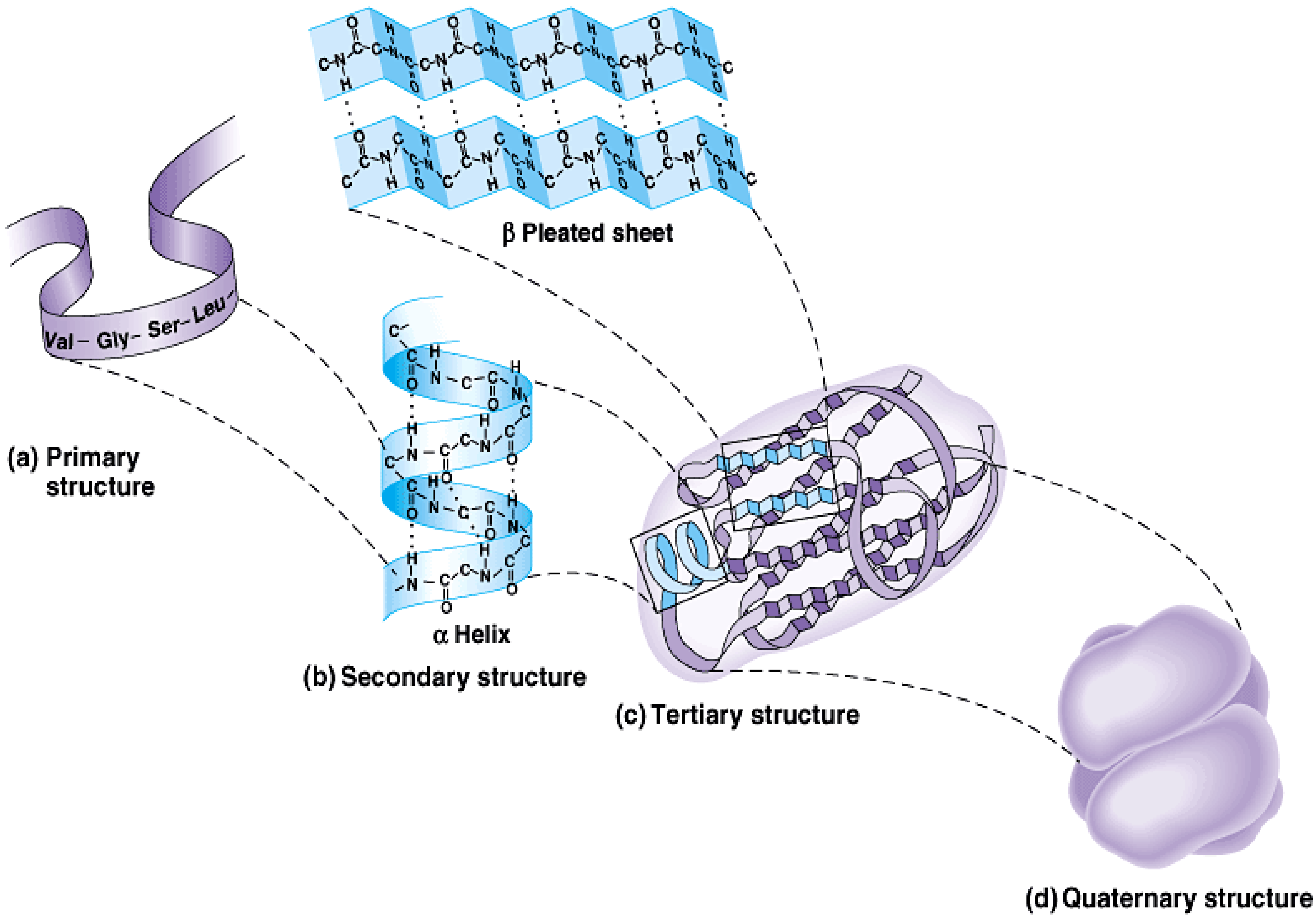
b. **<u>Strong covalent bonds</u>** include **disulfide bridges**, that form between the sulfhydryl groups (SH) of cysteine monomers, stabilize the structure.



- **Quaternary structure:** results from the aggregation (combination) of two or more polypeptide subunits held together by non-covalent interaction like H-bonds, ionic or hydrophobic interactions.
- Examples on protein having quaternary structure:
  - **Collagen** is a fibrous protein of three polypeptides (trimeric) that are supercoiled like a rope.
  - This provides the structural strength for their role in connective tissue.
  - **Hemoglobin** is a globular protein with four polypeptide chains (tetrameric)
  - **Insulin** : two polypeptide chains (dimeric)



(a) Collagen (b) Hemoglobin


β Pleated sheet
Val – Gly – Ser – Leu –
(a) Primary structure
α Helix
(b) Secondary structure
(c) Tertiary structure
(d) Quaternary structure

Classification of proteins

I- Simple proteins:

i.e. on hydrolysis gives only amino acids

Examples:

1- Albumin and globulins: present in egg, milk and blood

They are proteins of high biological value i.e. contain all essential amino acids and easily digested.

Types of globulins:

α1 globulin: e.g. antitrypsin: see later

α2 globulin: e.g. hepatoglobin: protein that binds hemoglobin to prevent its excretion by the kidney

β-globulin: e.g. transferrin: protein that transport iron

γ-globulins = **Immunoglobulins** (antibodies) : responsible for immunity.

2- Globins (Histones): They are basic proteins rich in histidine amino acid.

They are present in : a - combined with DNA
b - combined with heme to form hemoglobin of RBCs.

3- Gliadines are the proteins present in cereals.

4- Scleroproteins: They are structural proteins, not digested. include: keratin, collagen and elastin.

a- α-keratin: protein found in hair, nails, enamel of teeth and outer layer of skin.

- It is α-helical polypeptide chain, rich in cysteine and hydrophobic (non polar) amino acids so it is water insoluble.

b- collagens: protein of connective tissues found in bone, teeth, cartilage, tendons, skin and blood vessels.

- Collagen may be present as gel e.g. in extracellular matrix or in vitreous humor of the eye.
- Collagens are the most important protein in mammals. They form about 30% of total body proteins.
- There are more than 20 types of collagens, the most common type is **collagen I** which constitutes about 90% of cell collagens.

- **Structure of collagen:** three helical polypeptide chains (trimeric) twisted around each other forming triplet-helix molecule.
- ⅓ of structure is glycine, 10% proline, 10% hydroxyproline and 1% hydroxylysine. Glycine is found in every third position of the chain. The repeating sequence –Gly-X-Y-, where X is frequently proline and Y is often hydroxyproline and can be hydroxylysine.

Solubility: collagen is insoluble in all solvents and not digested.

- When collagen is heated with water or dil. HCl it will be converted into **gelatin** which is soluble , digestible and used as diet (as jelly). Gelatin is classified as derived protein.

Some collagen diseases:

1- Scurvy: disease due to deficiency of vitamin C which is important coenzyme for conversion of proline into hydroxyproline and lysine into hydroxylysine. Thus, synthesis of collagen is decreased leading to abnormal bone development, bleeding, loosing of teeth and swollen gum.

2- Osteogenesis Imperfecta (OI): Inherited disease resulting from genetic deficiency or mutation in gene that synthesizes collagen type I leading to abnormal bone formation in babies and frequent bone fracture in children. It may be lethal.

C- Elastin: present in walls of large blood vessels (such as aorta). It is very important in lungs, elastic ligaments, skin, cartilage, ..

It is elastic fiber that can be stretched to several times as its normal length.

Structure: composed of 4 polypeptide chains (tetramer), similar to collagen being having 33% glycine and rich in proline but in that it has low hydroxyproline and absence of hydroxy lysine.

Emphysema: is a chronic obstructive lung disease (obstruction of air ways) resulting from deficiency of α1-antitrypsin particularly in cigarette smokers.

Role of α1-antitrypsin: Elastin is a lung protein. Smoke stimulate enzyme called elastase to be secreted form neutrophils (in lung). Elastase cause destruction of elastin of lung.

α1-antitrypsin is an enzyme (secreted from liver) and inhibit elastase and prevent destruction of elastin. So deficiency of α1-antitrypsin especially in smokers leads to degradation of lung and destruction of lung (loss of elasticity of lung, a disease called emphysema.

Conjugated proteins

i.e. On hydrolysis, give protein part and non protein part and subclassified into:

1- Phosphoproteins: These are proteins conjugated with phosphate group. Phosphorus is attached to oH group of serine or threonine.
e.g. Casein of milk and vitellin of yolk.

2- Lipoproteins:

These are proteins conjugated with lipids.

Functions: a- help lipids to transport in blood

b- Enter in cell membrane structure helping lipid soluble substances to pass through cell membranes.

3- Glycoproteins:

proteins conjugated with sugar (carbohydrate)

e.g. – Mucin

- Some hormones such as erythropoeitin
- present in cell membrane structure
- blood groups.

4- Nucleoproteins: These are basic proteins (e.g. histones) conjugated with nucleic acid (DNA or RNA).

e.g. a- chromosomes: are proteins conjugated with DNA

b- Ribosomes: are proteins conjugated with RNA

5- Metalloproteins: These are proteins conjugated with metal like iron, copper, zinc, ……

a- Iron-containing proteins: Iron may present in heme such as in

- hemoglobin (Hb)
- myoglobin (protein of skeletal muscles and cardiacmuscle),
- cytochromes,

Iron may be present in free state (not in heme) as in:

- Ferritin: Main store of iron in the body. ferritin is present in liver, spleen and bone marrow.
- Hemosidrin: another iron store.
- Transferrin: is the iron carrier protein in plasma.

b- Copper containing proteins:

e.g. - Ceruloplasmin which oxidizes ferrous ions into ferric ions.

- Oxidase enzymes such as cytochrome oxidase.

c- Zn containing proteins: e.g. Insulin and carbonic anhydrase

d- Mg containing proteins: e.g. Kinases and phosphatases.

6-Chromoproteins: These are proteins conjugated with pigment. e.g.

- All proteins containing heme (Hb, myoglobin, ………..)
- Melanoprotein:e.g proteins of hair or iris which contain melanin.

Derived proteins

Produced from hydrolysis of simple proteins.

e.g. - Gelatin: from hydrolysis of collagen

- Peptone: from hydrolysis of albumin