Biochemistry:
an Introduction

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Introduction and Scope of Biochemistry

- Biochemistry is the branch of life science which deals with the study of chemical reactions occurring in living cells and organisms.
- The term “Biochemistry” was first introduced by the German Chemist **Carl Neuberg** in 1903.
- It studies the nature of the chemical constituents of living matter, their transformations in biological systems and the energy changes associated with these transformations.
- Biochemistry is a discipline in which biological phenomena are analyzed in terms of chemistry. Biochemistry for the same reason, has been variously named as “Biological Chemistry or Chemical Biology.

Carl Neuberg

Subject of biochemistry

Biological chemistry is the science of the molecular/chemical essence of life.

It studies:

- **the chemical nature of the substances that make up living organisms,**
- **their transformations, as well as**
- **the relationship of these transformations with the activity of cells, organs and tissues and the whole body**.

- In other words, **biochemistry studies the processes** of **development and functioning** of organisms in the language of molecules, the structure and chemical processes that provide a life to single and multicellular creatures that inhabit the Earth.

The **objects** of biochemistry are various living organisms:

- viruses
- bacteria
- plants,
- Animals, and
- human organism.

Biochemistry consists of several **sections**

1. **Static biochemistry** studies the chemical composition of organisms and the structure of their constituent molecules: (proteins, amino acids, nucleic acids, nucleotides, carbohydrates and their derivatives, lipids, vitamins, hormones).
2. **Dynamic biochemistry** studies the chemical reactions that represent the metabolism (metabolism), namely the pathways of the transformation of molecules and the mechanisms of the reactions between them.

Simple molecules and their derivatives (monosaccharides, fatty acids, amino acids, nucleotides, etc.) formed during the metabolism are called ***metabolites***.

3. **Functional biochemistry** studies the biochemical reactions that underlie physiological functions.

It studies the biochemical basis of digestion of nutrients in the gastrointestinal tract; mechanisms of muscle contraction, nerve impulse conduction, blood respiratory function, regulation of acid-base balance, liver and kidney function, immune system, etc.

Following sections of biochemistry are also distinguished by the areas of research:

- **Technical biochemistry** (molecular basis of baking, cheese making, winemaking, etc.);
- **Medical/clinical biochemistry** or human biochemistry (biochemical processes in the human body are normal and with pathology),
- **Evolutionary biochemistry** (evolution of metabolism in the framework of the evolution of living organisms);
- **Enzymology** (structure, properties and mechanism of action of enzymes), etc.

Outcomes of the “Biochemistry” Course

As a result of studying the discipline, the student will be able to:

1. demonstrate knowledge of the main classes of biological substances (their structure, properties);
2. demonstrate an understanding of the relationship between biological function and molecular structure;
3. to systematize and generalize knowledge about the Chemical Composition of cells / tissues, the structure of substances that make up living organisms;
4. Understand metabolic reactions, energy transformation processes in living organisms;
5. To apply the basic methods of biochemical research;
6. Conduct a qualitative and quantitative analysis of biological material;
7. Work with biochemical equipment and apparatus;

9. Demonstrate experimental research skills.

Proteins

- Almost all processes in living organisms are associated with the functioning of proteins and nucleic acids.
- Proteins are molecular machines, building blocks, and living cell weapons.
- Proteins account for **at least half the dry weight** of a living cell.
- In living organisms, they perform a wide variety of functions (building, catalytic, storage, transport, motor, energy, regulatory, protective) and serve as those molecular tools by which genetic information is realized.

- Each organism is characterized by a unique set of proteins.
- The human body contains about 50,000 individual proteins. Each individual protein differs from all other proteins in structure and function. The total protein content in an adult is approximately 15 kg.
- And the *E.coli* cell contains about 3,000 different proteins.

Proteins Are Built from a set of 20 Amino Acids

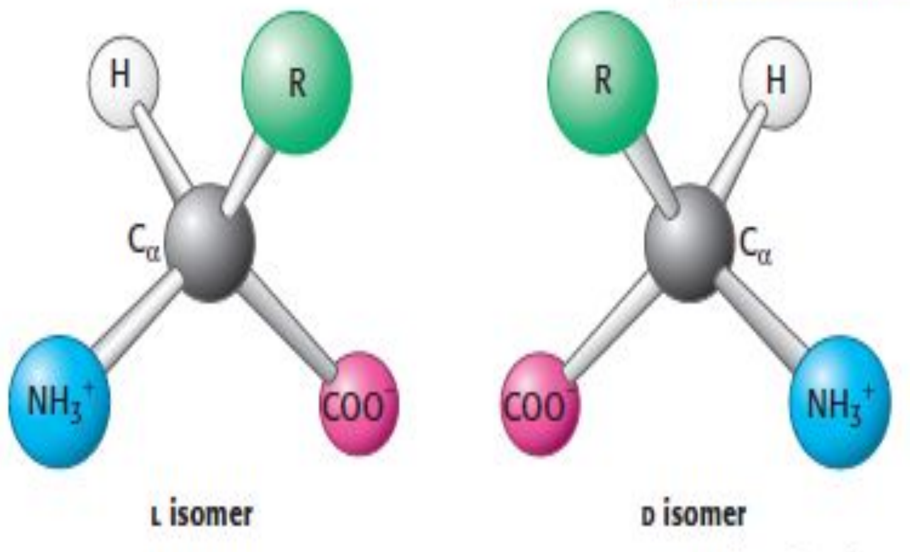
- Amino acids are the building blocks of proteins.
- An ***α-amino acid*** consists of a central **carbon atom**, called the a *carbon,* which is bonded to an amino group, a carboxylic acid group, a hydrogen atom, and a *side chain,* called the R group.
- Each kind of amino acid has a different R group.

- The common amino acids of proteins have been assigned **three-letter abbreviations** and **one-letter sy**mbols (Table 3-1), which are used as shorthand to indicate the composition and sequence of amino acids polymerized in proteins.

- The three-letter code is transparent, the abbreviations generally consisting of the first three letters of the amino acid name. The one-letter code was devised by **Margaret Oakley Dayhoff**, considered by many to be the founder of the field of bioinformatics. The one-letter code reflects an attempt to reduce the size of the data files (in an era of punch-card computing) used to describe amino acid sequences.

Amino acid	Abbreviation/symbol
Nonpolar, aliphatic R groups	
Glycine	Gly G
Alanine	Ala A
Proline	Pro P
Valine	Val V
Leucine	Leu L
Isoleucine	Ile I
Methionine	Met M
Aromatic R groups	
Phenylalanine	Phe F
Tyrosine	Tyr Y
Tryptophan	Trp W
Polar, uncharged R groups	
Serine	Ser S
Threonine	Thr T
Cysteine[e]	Cys C
Asparagine	Asn N
Glutamine	Gln Q
Positively charged R groups	
Lysine	Lys K
Histidine	His H
Arginine	Arg R
Negatively charged R groups	
Aspartate	Asp D
Glutamate	Glu E

Most Amino Acids Exist in Two Mirror-Image Forms



- With four different groups connected to the tetrahedral α-carbon atom, α-amino acids are *chiral:* they may exist in one or the other of two mirror-image forms, called the **l** isomer and the **d** isomer (**Figure 1**).

- *Only* **l** *amino acids are constituents of proteins (*some fungi are able to utilize d amino acids*)*.

All Amino Acids Have at Least Two Charged Groups

- Free amino acids in solution at neutral pH exist predominantly as *dipolar ions* (also called *zwitterions*). In the dipolar form, the amino group is protonated (NH3+) and the carboxyl group is deprotonated (COO^-). The ionization state of an amino acid varies with pH (**Figure 2**).
- In acid solution (e.g., pH 1), the amino group is protonated (NH_3^+) and the carboxyl group is **not** dissociated (−COOH).
- As the pH is raised, the carboxylic acid is the first group to give up a proton.
- The dipolar form persists until the pH approaches 9, when the protonated amino group loses a proton.
- Under physiological conditions (near pH 7.0), amino acids exist in the dipolar form.

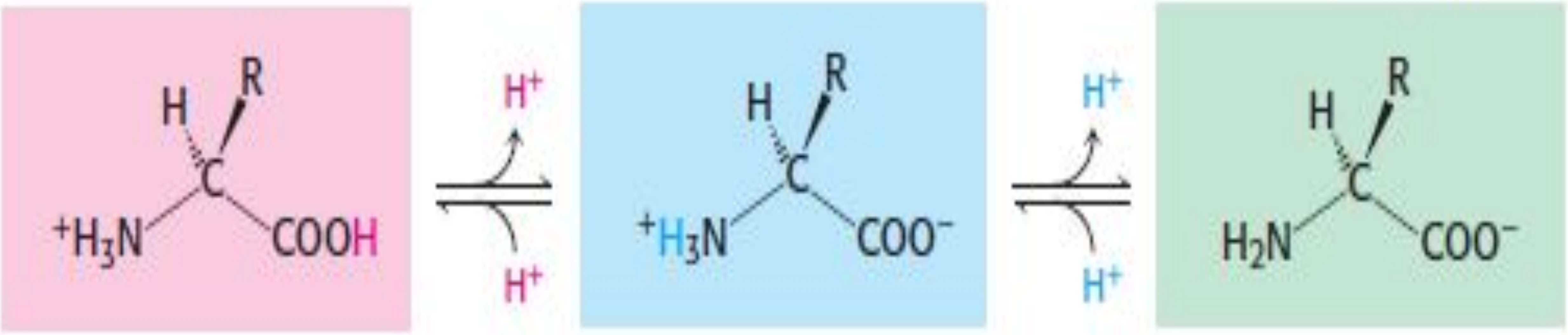


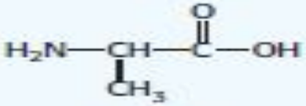
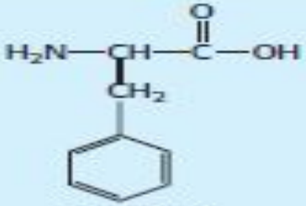
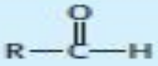
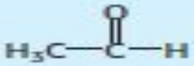
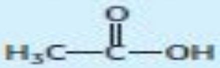
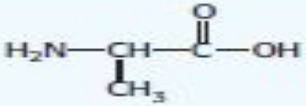
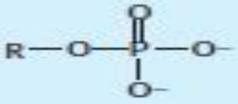
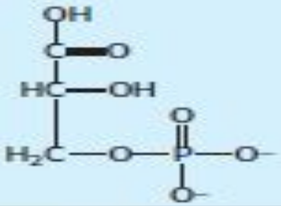
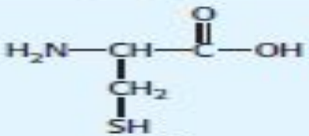
Figure 2. Ionization state as a function of pH. The ionization state of amino acids is altered by a change in pH

In acid solution (e.g., pH 1), the amino group is protonated (NH_3^+) and the carboxyl group is **not** dissociated (−COOH).
As the pH is raised, the carboxylic group gives up a proton.
The dipolar form persists until the pH approaches 9, when the protonated amino group loses a proton.
Under physiological conditions (near pH 7.0), amino acids exist in the dipolar form.

Amino Acids Contain a Wide Array of Functional Groups

- Twenty **types of side chains** varying in *size, shape, charge, hydrogen-bonding capacity, hydrophobic character,* and *chemical reactivity* are commonly **found in proteins**. Many of these properties are conferred by functional groups (Table).
- The amino acid functional groups include alcohols, thiols, thioethers, carboxylic acids, carboxamides, and a variety of basic groups. Most of these groups are chemically reactive.
- **All proteins** in all species – bacterial, archaeal, and eukaryotic – are **constructed from the same set of 20 amino acids** with only a few exceptions.
- The remarkable range of functions mediated by proteins results from the diversity and versatility of these 20 building blocks.

Table 2.1 Some key functional groups in biochemistry

Functional group	Class of compounds	Structural formula	Example
Hydrophobic	Hydrocarbon chains (aliphatic)	R—CH_3	 Alanine
	Aromatic (hydrocarbons in a ring structure with multiple double bonds)		 Phenylalanine
Hydroxyl	Alcohol	R—OH	H_3C—CH_2—OH Ethanol
Aldehyde	Aldehydes		 Acetaldehyde
Keto	Ketones		 Acetone
Carboxyl	Carboxylic acid		 Acetic acid
Amino	Amines	R—NH_2	 Alanine
Phosphate	Organic phosphates		
Sulfhydryl	Thiols	R—SH	

Classification of amino acids

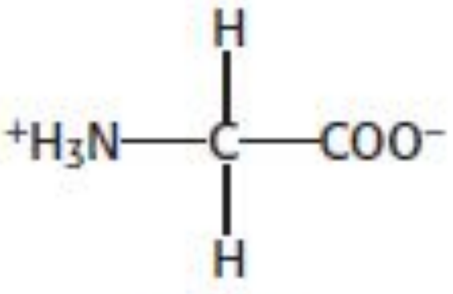
Although **there are many ways to classify** amino acids, we will assort these molecules into **four groups, on the basis of the** general **chemical characteristics of their R groups**:

1. Hydrophobic amino acids with nonpolar R groups;
2. Polar amino acids with neutral R groups but the charge is not evenly distributed;
3. Positively charged amino acids with R groups that have a positive charge at physiological pH (pH ≈ 7.4);
4. Negatively charged amino acids with R groups that have a negative charge at physiological pH.

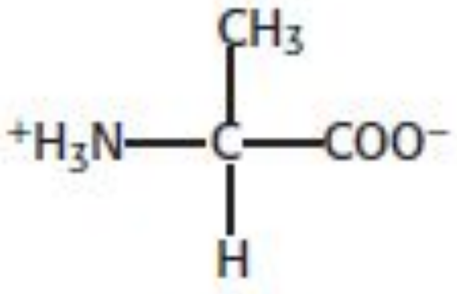
1. Hydrophobic amino acids with nonpolar R groups

Hydrophobic amino acids **have mainly Hydrocarbon Side Chains**.

- The amino acids having side chains consisting only of hydrogen and carbon are hydrophobic.
- The simplest amino acid is ***glycine***, which has a single hydrogen atom as its side chain. With two hydrogen atoms bonded to the α-atom, glycine is unique in being achiral.
- ***Alanine***, the next simplest amino acid, has a methyl group (−CH3) as its side chain.
- The three-letter abbreviations and one-letter symbols under the names of the amino acids depicted in Figures.

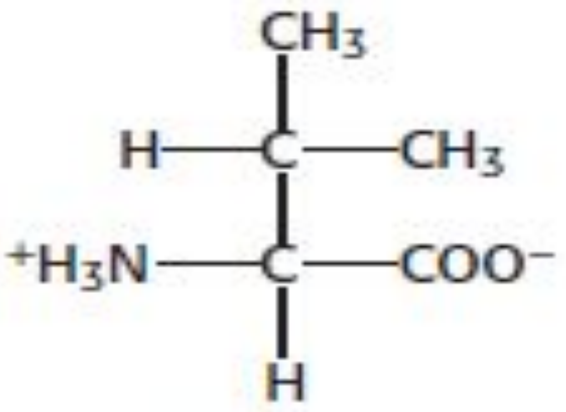


Glycine
(Gly, G)

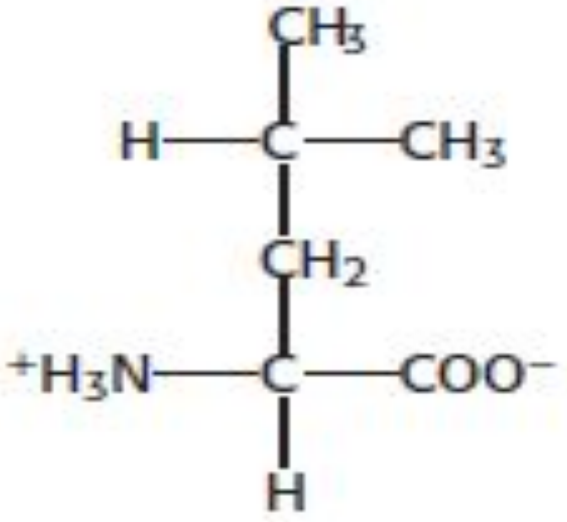


Alanine
(Ala, A)

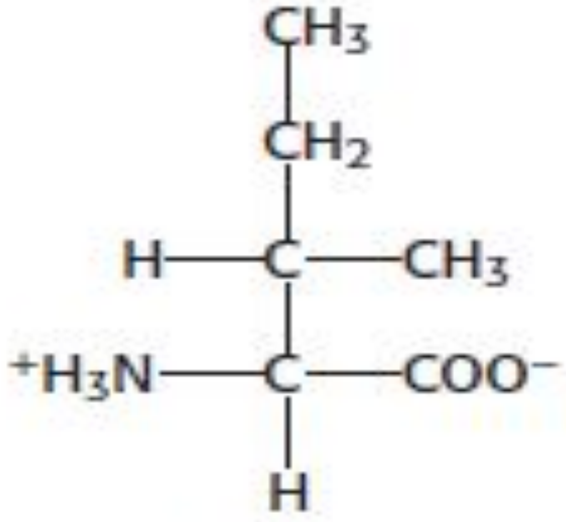
- Larger aliphatic side chains are found in the branched-chain amino acids ***valine, leucine***, and ***isoleucine***. ***Methionine*** contains a largely aliphatic side chain that includes a *thioether* (−S−) group.
- The different sizes and shapes of these hydrocarbon side chains enable them to pack together to form compact structures with little empty space.



Valine
(Val, V)

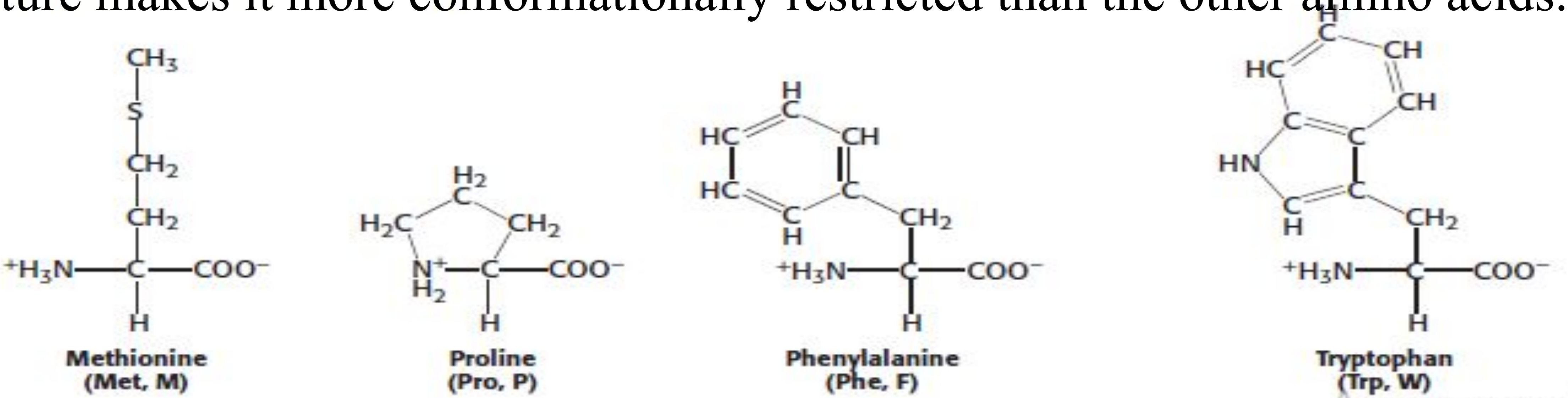


Leucine
(Leu, L)



Isoleucine
(Ile, I)

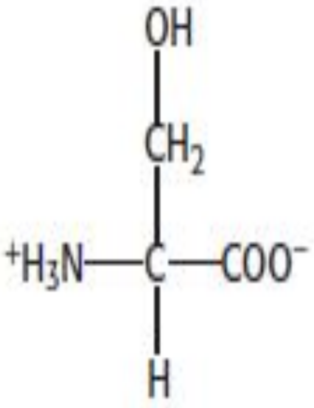
•***Proline*** also has an aliphatic side chain, but it differs from other members of the set of 20 in that its side chain is bonded to both the a-carbon and the nitrogen atom. Proline markedly influences protein architecture because its ring structure makes it more conformationally restricted than the other amino acids.



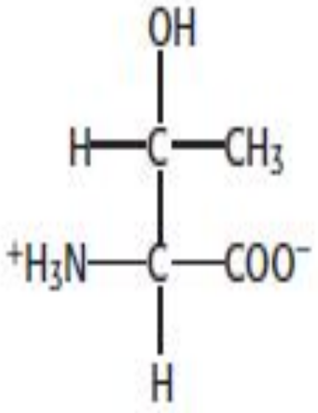
Two amino acids with simple ***aromatic side chains*** are also classified as hydrophobic. ***Phenylalanine,*** as its name indicates, contains a phenyl ring attached in place of one of the methyl hydrogen atoms of alanine.
Tryptophan has an indole ring joined to a methylene (−CH2−) group; the indole group comprises two fused rings and an NH group.

2. Polar Amino acids

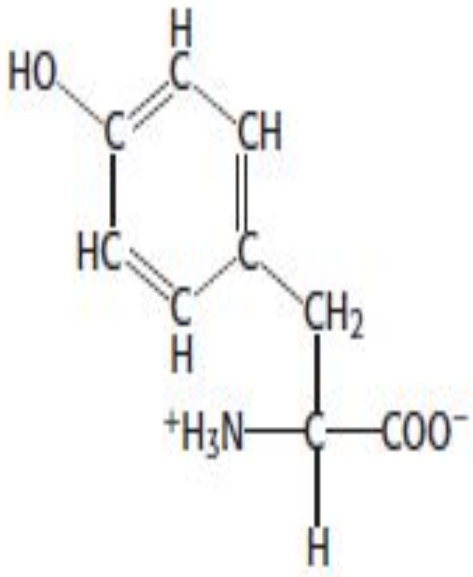
- The next group of amino acids that we will consider are those that are neutral overall, yet they are polar because the R group contains an electronegative atom that hoards electrons. Three amino acids, *serine*, *threonine,* and *tyrosine,* contain hydroxyl (−OH) groups (**Figure 3.4**). The electrons in the O−H bond are attracted to the oxygen atom, making it partly negative, which in turn makes the hydrogen partly positive.
- ***Serine*** can be thought of as a version of alanine with a hydroxyl group attached to the methyl group, whereas ***threonine*** resembles valine with a hydroxyl group in place of one of the valine methyl groups.
- ***Tyrosine*** is similar to phenylalanine but contains a hydrophilic hydroxyl group attached to the large aromatic ring.
- The hydroxyl groups on **serine, threonine, and tyrosine make them more *hydrophilic*** (water soluble) and ***reactive*** than their respective nonpolar counterparts.



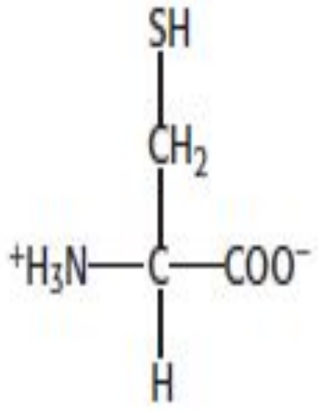
Serine
(Ser, S)



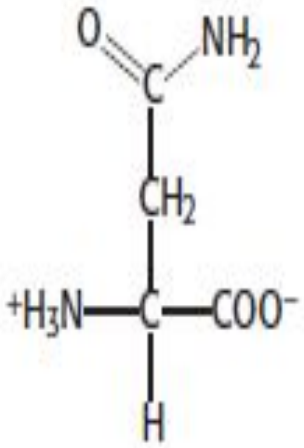
Threonine
(Thr, T)



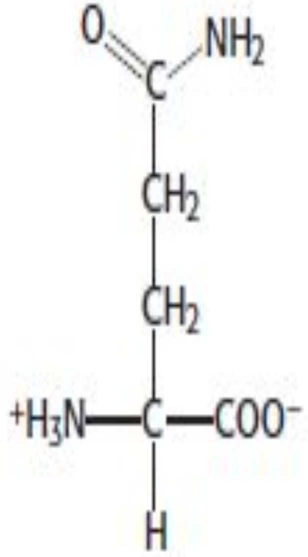
Tyrosine
(Tyr, Y)



Cysteine
(Cys, C)



Asparagine
(Asn, N)



Glutamine
(Gln, Q)

Polar amino acids

3. Positively Charged Amino Acids are hydrophilic

Amino acids having positively charged side chains that render these amino acids highly hydrophilic (**Figure 3.5**).

- *Lysine* and *arginine* have long side chains that terminate with groups that are *positively charged* at neutral pH.
- ***Lysine*** is topped by an amino group and ***arginine*** by a guanidinium group.

- The R groups of **lysine and arginine** have dual properties – the carbon chains constitute a hydrocarbon backbone, similar to the amino acid leucine, but the chain is terminated with a positive charge.

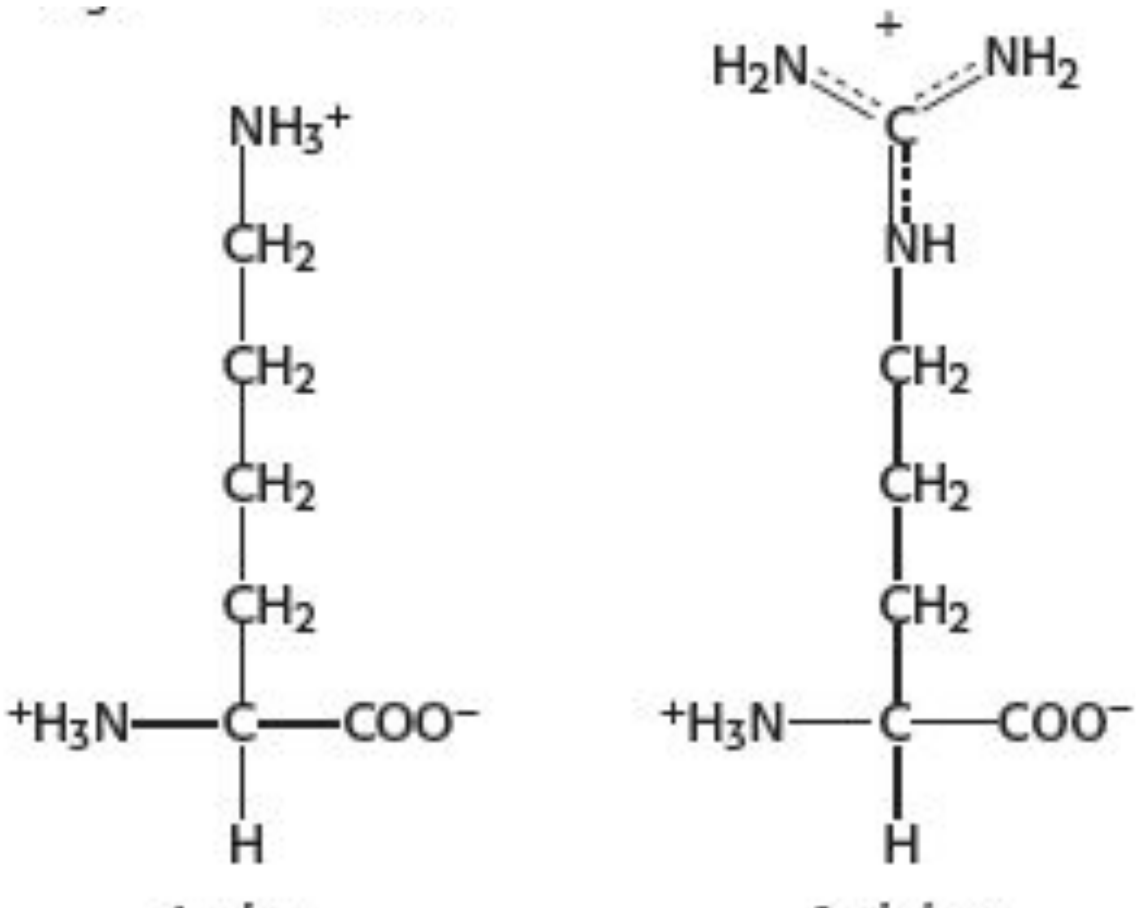
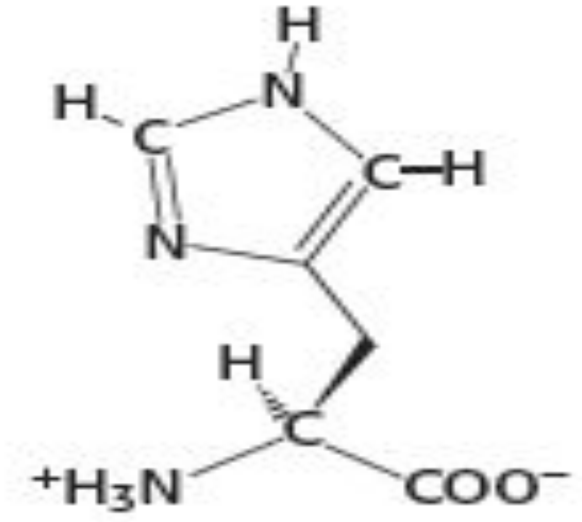
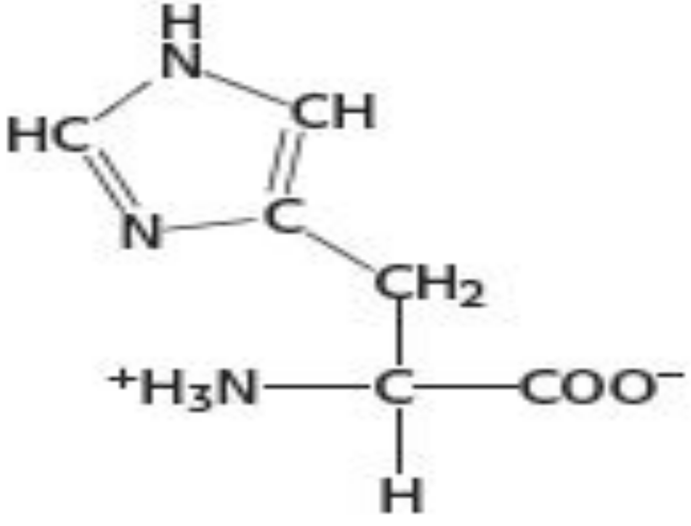


Figure 3.5 Positively charged amino acids.

Histidine contains an imidazole group, an aromatic ring that also can be positively charged.

The imidazole group of histidine is unique in that it can be uncharged or positively charged near neutral pH, depending on its local environment.





Histidine (His, H)

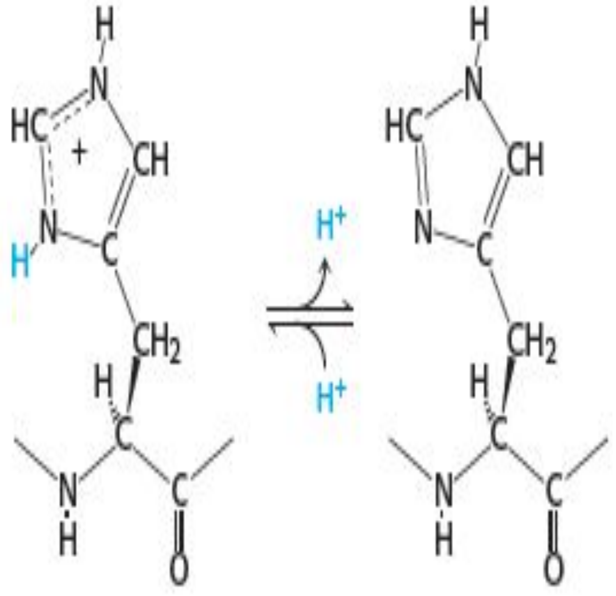


Figure 3.6 Histidine ionization. Histidine can bind or release protons near physiological pH.

4. Negatively Charged Amino acids have Acidic Side Chains

- The two amino acids in this group, *aspartic acid* and *glutamic acid,* have *acidic side chains* that are usually negatively charged under intracellular conditions (**Figure 3.7**).
- These amino acids are often called *aspartate* and *glutamate.*
- In some proteins, these side chains accept protons, which neutralize the negative charge.
- This ability is often functionally important.

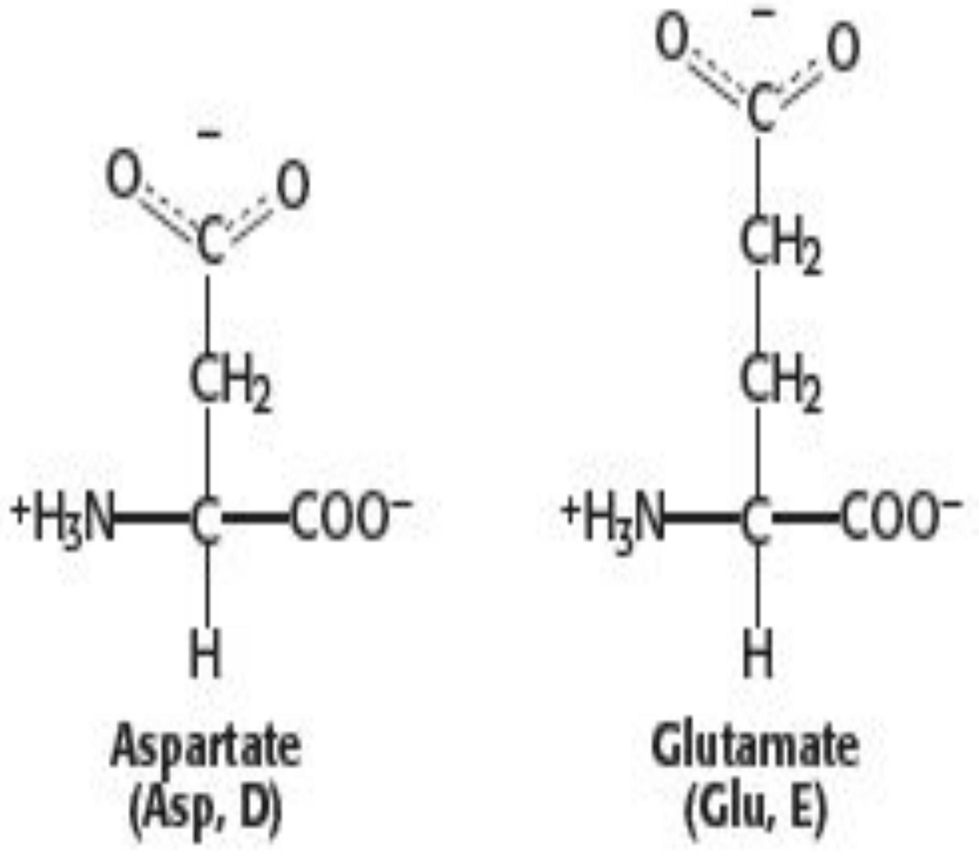


Figure 3.7 Negatively charged amino acids.

Essential Amino Acids must Be obtained from the Diet

- Most microorganisms can synthesize the entire basic set of 20 amino acids, whereas **human beings can make only 11 of them**.
- Amino acids that cannot be generated in the body must be supplied by the diet and are termed ***essential*** *amino acids*.

The others are called **nonessential amino acids** (**Table 3.2**).

These designations refer to an organism under a particular set of conditions.

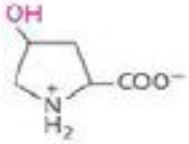
For example, a human adult can synthesize enough arginine to meet his or her needs, but a growing child requires more arginine than the body can provide to meet the protein-synthesis needs of rapid growth.

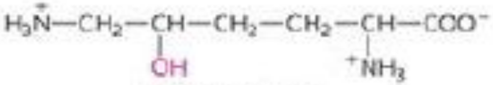
Table 3.2 Basic set of 20 amino acids

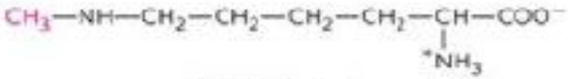
Nonessential	Essential
Alanine	Histidine
Arginine	Isoleucine
Asparagine	Leucine
Aspartate	Lysine
Cysteine	Methionine
Glutamate	Phenylalanine
Glutamine	Threonine
Glycine	Tryptophan
Proline	Valine
Serine	
Tyrosine	

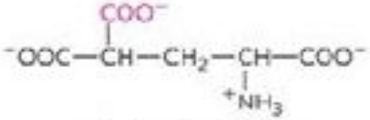
Uncommon Amino Acids also have important Functions

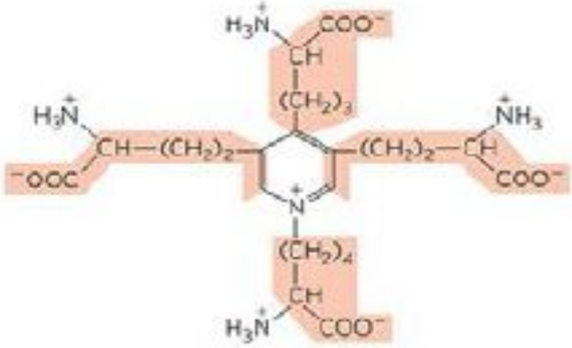
- In addition to the 20 common amino acids, proteins may contain residues created by modification of common residues already incorporated into a polypeptide – that is, through postsynthetic modification **(Fig. 3-8a)**.
- Among these uncommon amino acids are **4-hydroxyproline**, a derivative of proline, and **5-hydroxylysine**, derived from lysine. The former is found in plant cell wall proteins, and both are found in collagen, a fibrous protein of connective tissues.
- **6-*N*-Methyllysine** is a constituent of myosin, a contractile protein of muscle.
- Another important uncommon amino acid is ***γ*-carboxyglutamate**, found in the blood-clotting protein *prothrombin* and in certain other proteins that bind Ca2+ as part of their biological function.
- More complex is **desmosine**, a derivative of four Lys residues, which is found in the fibrous protein elastin.
- **Selenocysteine** and **pyrrolysine** are special cases. Selenocysteine contains selenium rather than the sulfur of cysteine.

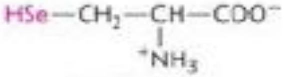

4-Hydroxyproline

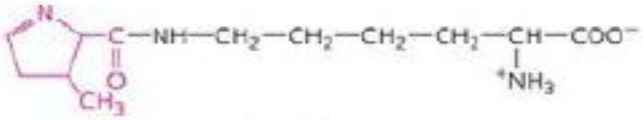

5-Hydroxylysine


6-*N*-Methyllysine

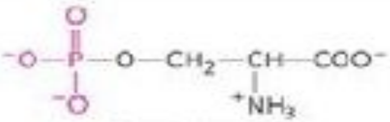

γ-Carboxyglutamate

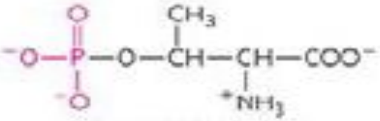

Desmosine

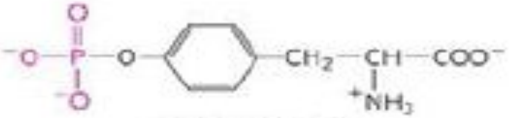

Selenocysteine

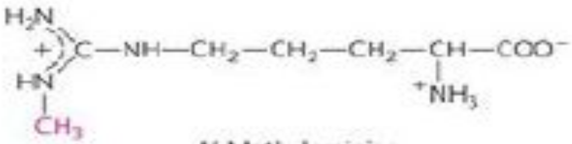

Pyrrolysine

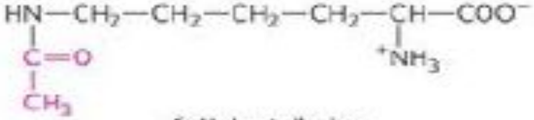
(a)

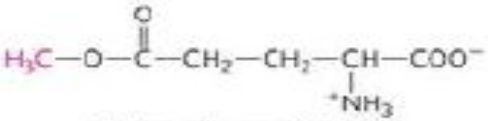

Phosphoserine

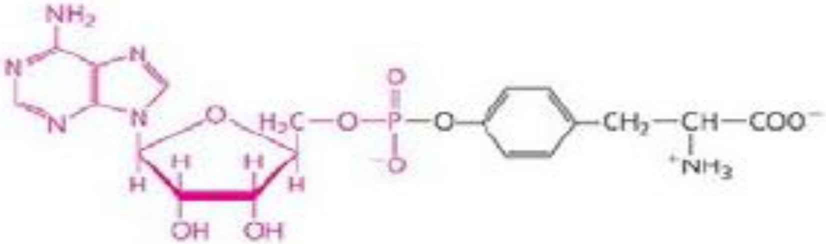

Phosphothreonine


Phosphotyrosine


ω-*N*-Methylarginine


6-*N*-Acetyllysine


Glutamate γ-methyl ester


Adenylyltyrosine

(b)

Summary

1. **Proteins Are Built from a set of 20 Amino Acids**.

Proteins are linear polymers of amino acids.

Each amino acid consists of a central tetrahedral carbon atom that is bonded to an amino group, a carboxylic acid group, a distinctive side chain, and a hydrogen atom.

Only the ***l isomer*** exists in natural proteins.

All natural proteins are constructed from the same set of 20 amino acids.

2. Amino Acids Contain a Wide Array of Functional Groups.

The side chains of these 20 building blocks vary tremendously in size, shape, and the presence of functional groups. **AA** can be grouped as follows on the basis of the chemical properties of the side chains:

(1) **hydrophobic side chains**: glycine, alanine, valine, leucine, isoleucine, methionine, proline, and the aromatic amino acids phenylalanine and tryptophan;

(2) **polar amino acids** – serine, threonine, tyrosine, asparagine, and glutamine;

(3) **positively charged amino acids –** lysine, arginine, and histidine; and

(4) **negatively charged amino acids** – aspartic acid and glutamic acid.

3. Essential Amino Acids Must Be Obtained from the Diet.

Most microorganisms are capable of making all 20 of the amino acids from simpler molecules.

Although human beings can make 11 amino acids, 9 must be acquired from the diet. These 9 amino acids are called essential amino acids because they are required for healthy growth and development.