Amino Acids and Proteins

Proteins functions

- Most abundant and functionally diverse group of molecules
- Indispensable for life
- Have several diverse functions:
    - Catalytic functions [enzymes]
    - Receptor [insulin receptor]
    - Structural function [collagen]
    - Transport [haemoglobin, myoglobin]
    - Protective functions [immunoglobulins]
    - Hemostasis [clotting factors]
    - Hormonal functions [insulin, glucagon, GH]
    - Control of gene expression [transcription factors]
    - DNA packing [histones]
    - Act as buffers

Amino Acids - Proteins

Amino acids are the building blocks of proteins. Proteins are natural polymers of successive amino acids

There are 20 different amino acids that make up human proteins

Two common amino acids found in proteins

Amino Acid Functions

1. Amino acids are the building blocks of proteins
2. Some amino acids and their derivatives function as neurotransmitters hormones and other regulators

Examples Include

L-dopamine

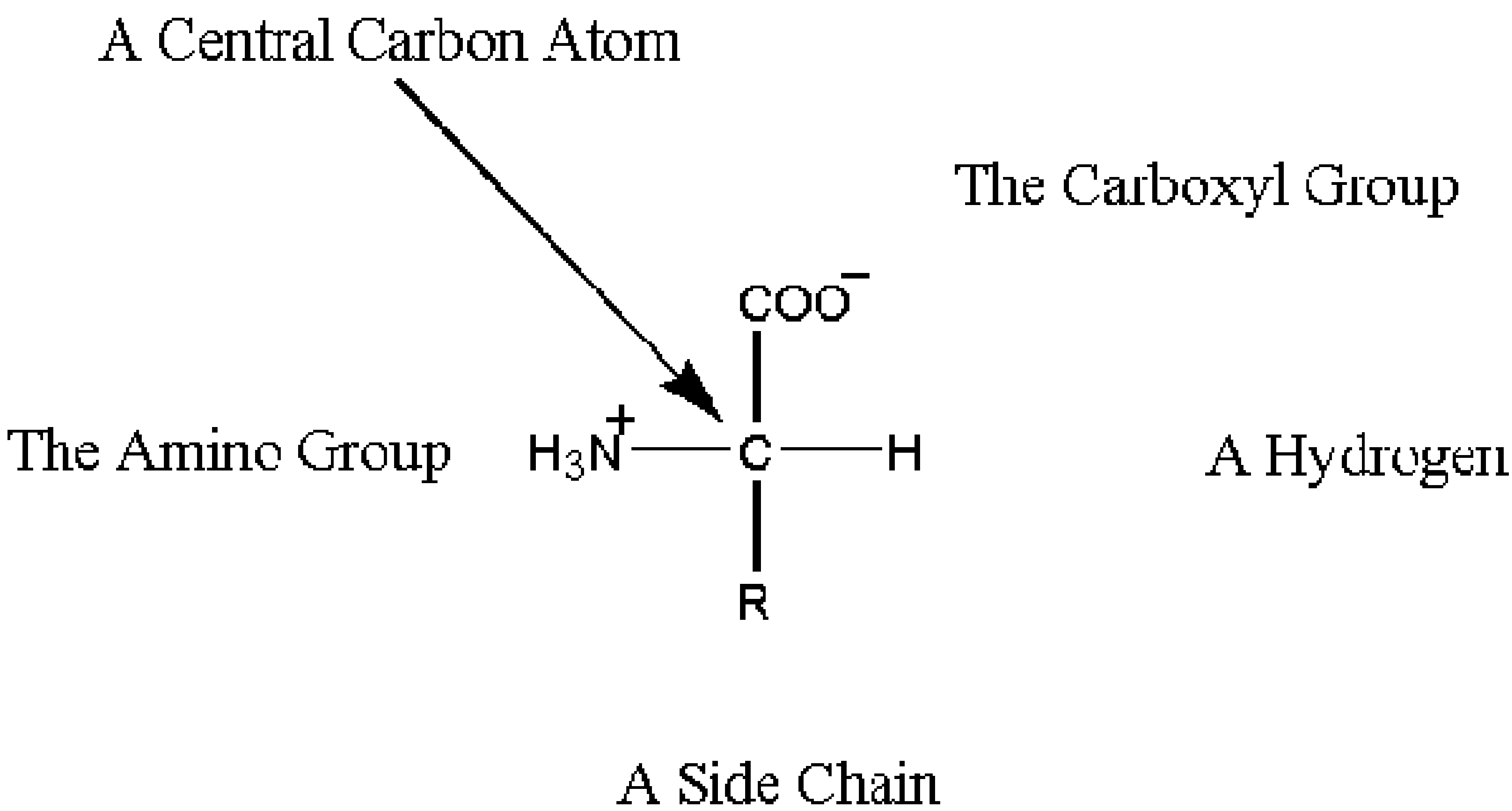
Epinephrine

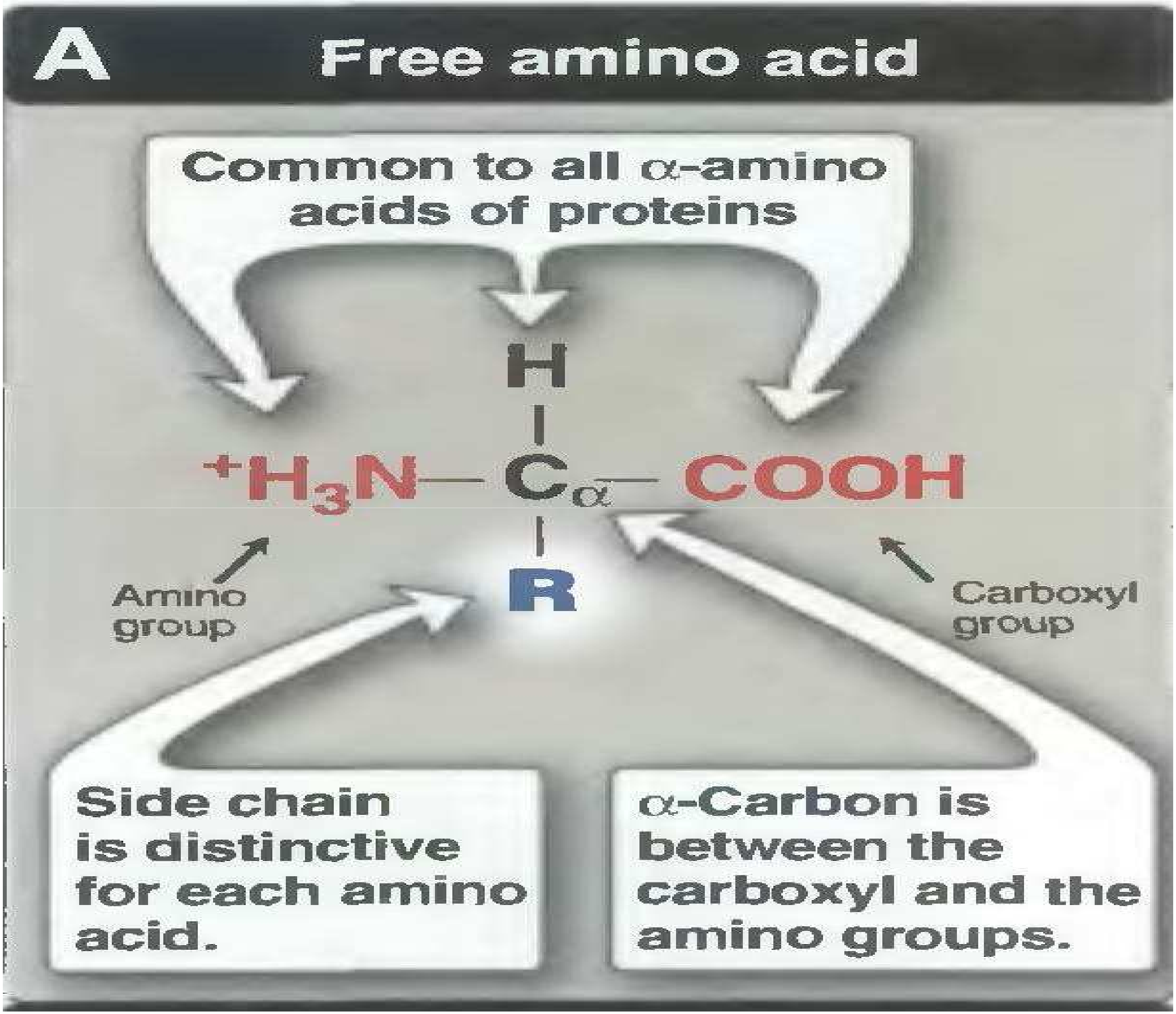
Thyroxine

Amino Acids

- 20 naturally occurring amino acids
- 10 can be synthesized in the body
- 10 ‘essential’ amino acids have to be obtained from food
- amino acid polymers form proteins
- The properties of each amino acid are determined by its specific side chain (R –groups)
- R-groups vary in structure , size , electric charge and solubility in water from one amino acid to other.
- Amino acids names are often abbreviated as either 3 letters or single letters .

Proteins are made of Amino Acid




A
Free amino acid
Common to all α-amino acids of proteins
H
⁺H3N — Cα — COOH
R
Amino group
Carboxyl group
Side chain is distinctive for each amino acid.
α-Carbon is between the carboxyl and the amino groups.

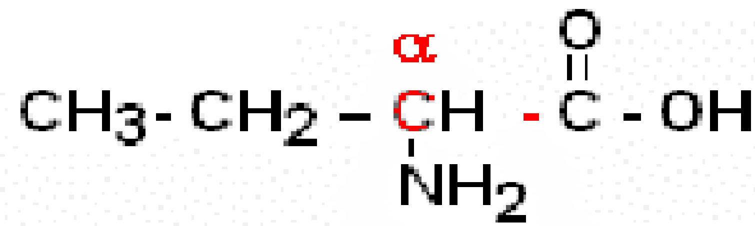
Amino Acid Structure

Amino acids may be characterized as α, β , or γ amino acids depending on the location of the amino group in the carbon chain.

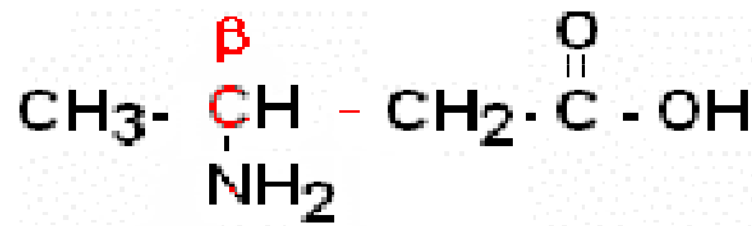
α are on the carbon adjacent to the carboxyl group.

β are on the 2nd carbon

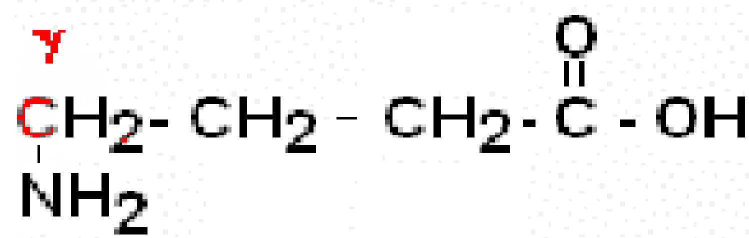
γ on the 3rd carbon from the carboxyl group



α– aminobutanoic acid



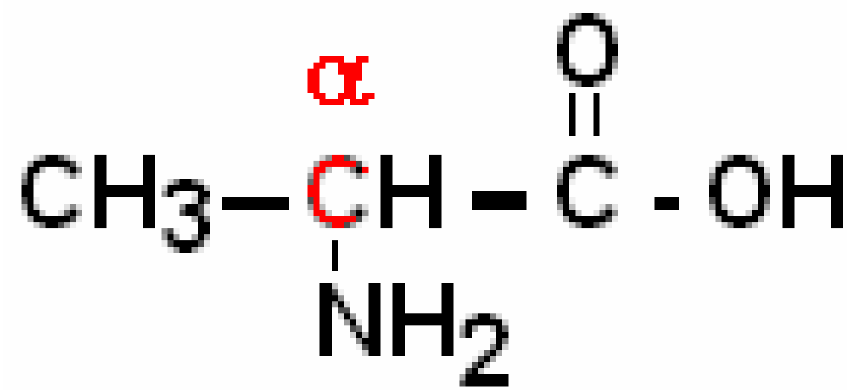
β – aminobutanoic acid



γ – aminobutanoic acid

α– amino acids

Amino acids found in proteins are α– amino acids. The amino group is always found on the carbon adjacent to the carboxyl group



Alanine is an α amino acid

Classification of Amino Acids

- As the properties of the amino acids and their role in proteins are determined by the side chain , therefore amino acids are classified according:

1-Polarity of the side chain.

-Acid

-Basic

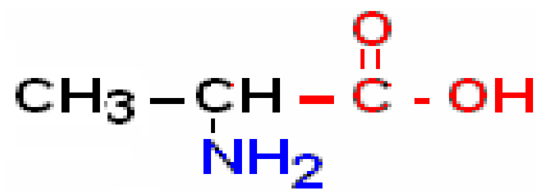
-Neutral

2- Structure of side chain

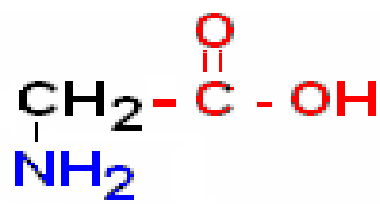
- Aliphatic
- Aromatic

Neutral Amino Acids

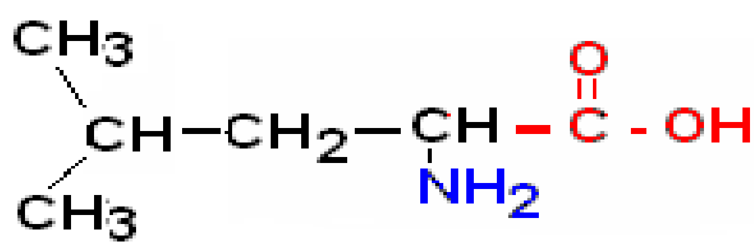
These amino Acids are considered neutral. There is one carboxyl group per amino group



Alanine



Glycine

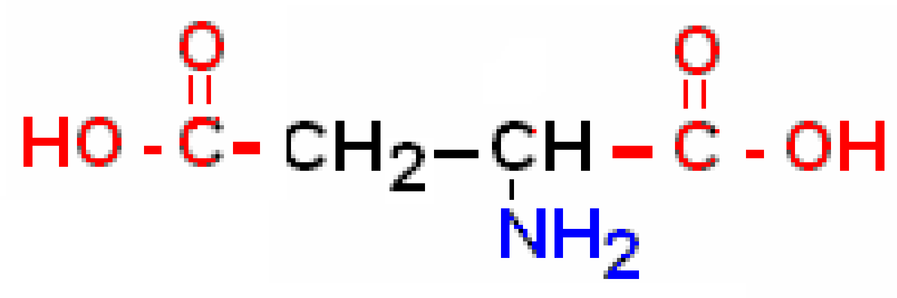


Leucine (

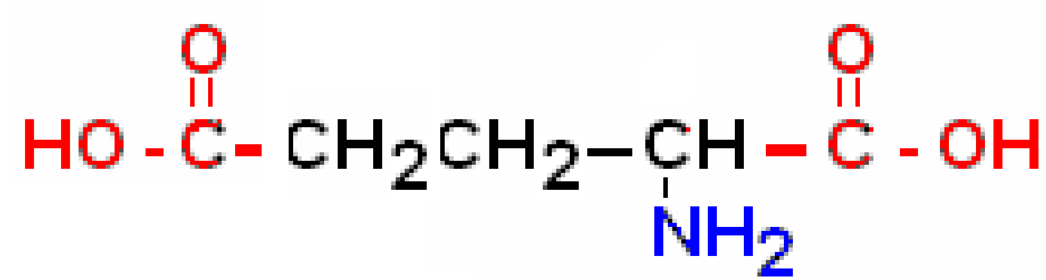
Acidic Amino Acids

There are two acidic amino acids.

There are two carboxyl groups and only one amino group per molecule



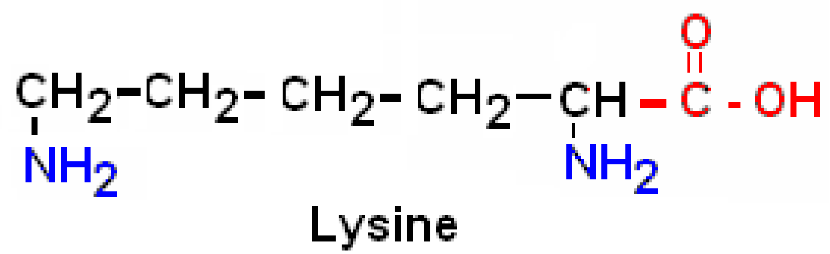
Aspartic Acid

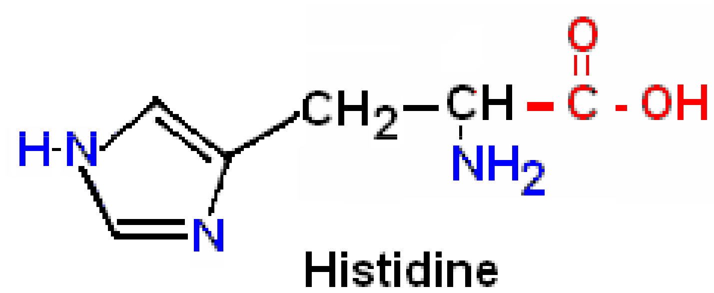


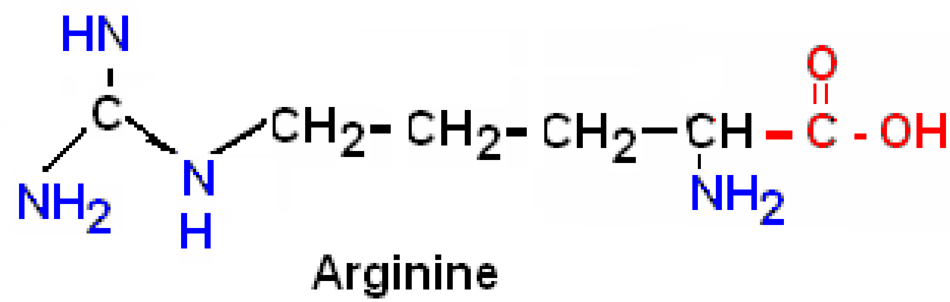
Glutamic Acid

Basic Amino Acids

These amino acids are basic. They have more amino groups than carboxyl groups

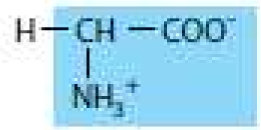
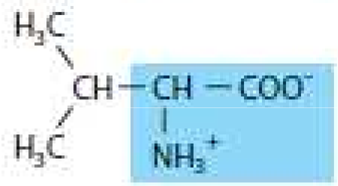
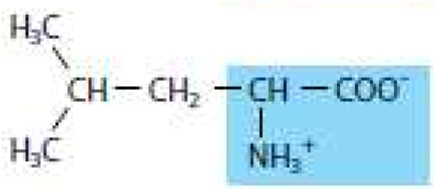
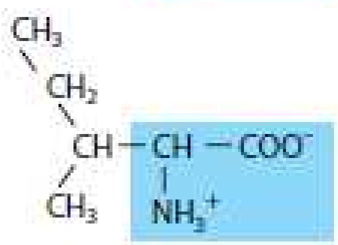


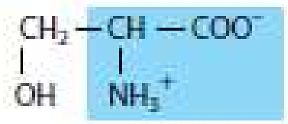
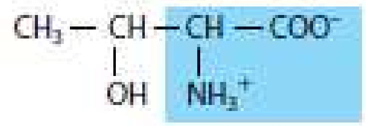
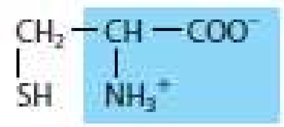
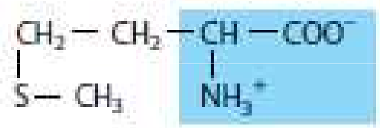
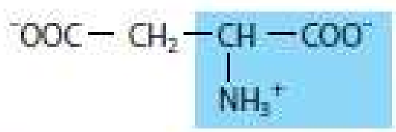
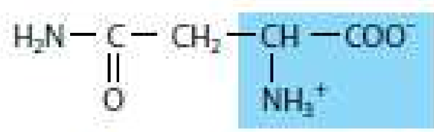
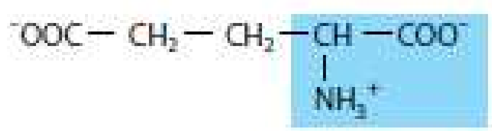
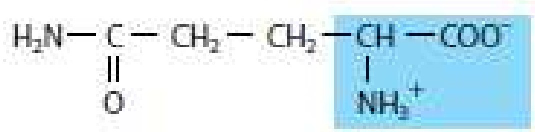


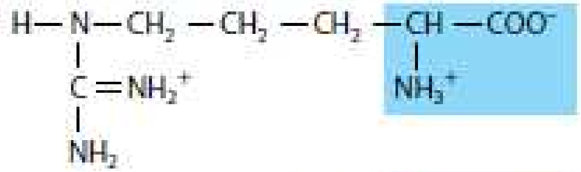
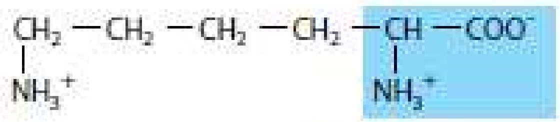
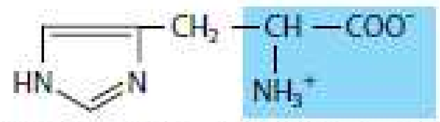
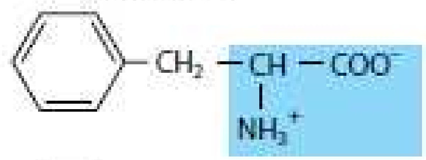
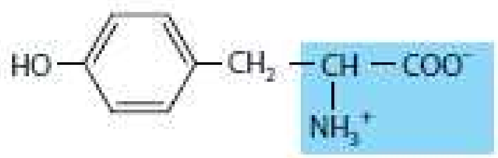
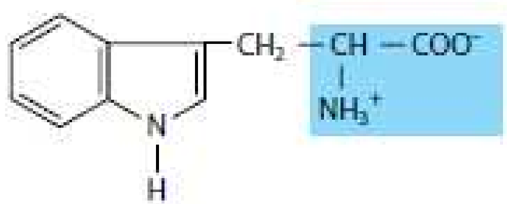
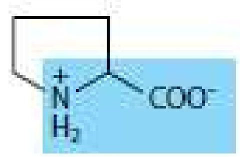


AMINO ACID CLASSIFICATION
Depending on side chain structure

- Aliphatic side chain
- aromatic side chain
- Sulphur – containing side chain
- Acidic side chain
- Basic side chain
- Amide side chain
- Hydroxylic side chain
- Imino Side Chain

Name	Symbol	Structural Formula	pK_1	pK_2	pK_3
With Aliphatic Side Chains			α-COOH	α-NH_3^+	R Group
Glycine	Gly [G]		2.4	9.8	
Alanine	Ala [A]		2.4	9.9	
Valine	Val [V]		2.2	9.7	
Leucine	Leu [L]		2.3	9.7	
Isoleucine	Ile [I]		2.3	9.8	

With Side Chains Containing Hydroxylic (OH) Groups					
Serine	Ser [S]		2.2	9.2	about 13
Threonine	Thr [T]		2.1	9.1	about 13
Tyrosine	Tyr [Y]	See below.			
With Side Chains Containing Sulfur Atoms					
Cysteine	Cys [C]		1.9	10.8	8.3
Methionine	Met [M]		2.1	9.3	
With Side Chains Containing Acidic Groups or Their Amides					
Aspartic acid	Asp [D]		2.0	9.9	3.9
Asparagine	Asn [N]		2.1	8.8	
Glutamic acid	Glu [E]		2.1	9.5	4.1
Glutamine	Gln [Q]		2.2	9.1	

Name	Symbol	Structural Formula	pK_1	pK_2	pK_3
With Side Chains Containing Basic Groups			α-COOH	α-NH_3^+	R Group
Arginine	Arg [R]		1.8	9.0	12.5
Lysine	Lys [K]		2.2	9.2	10.8
Histidine	His [H]		1.8	9.3	6.0
Containing Aromatic Rings					
Histidine	His [H]	See above.			
Phenylalanine	Phe [F]		2.2	9.2	
Tyrosine	Tyr [Y]		2.2	9.1	10.1
Tryptophan	Trp [W]		2.4	9.4	
Imino Acid					
Proline	Pro [P]		2.0	10.6	

With Side Chains Containing Hydroxylic (OH) Groups					
Serine	Ser [S]	$CH_2(OH)-CH(NH_3^+)-COO^-$	2.2	9.2	about 13
Threonine	Thr [T]	$CH_3-CH(OH)-CH(NH_3^+)-COO^-$	2.1	9.1	about 13
Tyrosine	Tyr [Y]	See below.			
With Side Chains Containing Sulfur Atoms					
Cysteine	Cys [C]	$CH_2(SH)-CH(NH_3^+)-COO^-$	1.9	10.8	8.3
Methionine	Met [M]	$CH_3-S-CH_2-CH_2-CH(NH_3^+)-COO^-$	2.1	9.3	
With Side Chains Containing Acidic Groups or Their Amides					
Aspartic acid	Asp [D]	$^-OOC-CH_2-CH(NH_3^+)-COO^-$	2.0	9.9	3.9
Asparagine	Asn [N]	$H_2N-C(=O)-CH_2-CH(NH_3^+)-COO^-$	2.1	8.8	
Glutamic acid	Glu [E]	$^-OOC-CH_2-CH_2-CH(NH_3^+)-COO^-$	2.1	9.5	4.1
Glutamine	Gln [Q]	$H_2N-C(=O)-CH_2-CH_2-CH(NH_3^+)-COO^-$	2.2	9.1	

ALIPHATIC AMINO ACIDS

Monoamino-monocarboxylic acids

- Glycine [Gly; G]
- Alanine [Ala; A]
- Isoleucine [Ile; I]
- Valine [Val; V]
- Leucine [Leu; L]

- **Hydroxy-monoamino-monocarboxylic acids**
- Serine [Ser; S]
- Threonine [Thr; T]

- **Monoamino-dicarboxylic acids**
- Aspartic acid [Asp; D]
- Glutamic acid [Glu; E]

- **Monoamino-dicarboxyl-co-amides**
- Asparagine [Asn; N]
- Glutamine [Gln; Q]

- **Diamino-monocarboxylic acids**
- Arginine [Arg; R]
- Lysine [Lys; K] - Hydroxylysine
- Ornithine

- **Sulphur-containing amino acids**
- Cysteine [Cys; C] - Cystine
- Methionine [Met; M]

- **Heterocyclic amino acids**
- Tryptophan [Trp; W]
- Histidine [His; H]
- Proline [Pro; P] - Hydroxyproline

AROMATIC AMINO ACIDS

- Phenylalanine [Phe; F]
- Tyrosine [Tyr; Y]
- Tryptophan [Trp; W]

A. Amino acids with nonpolar side chains

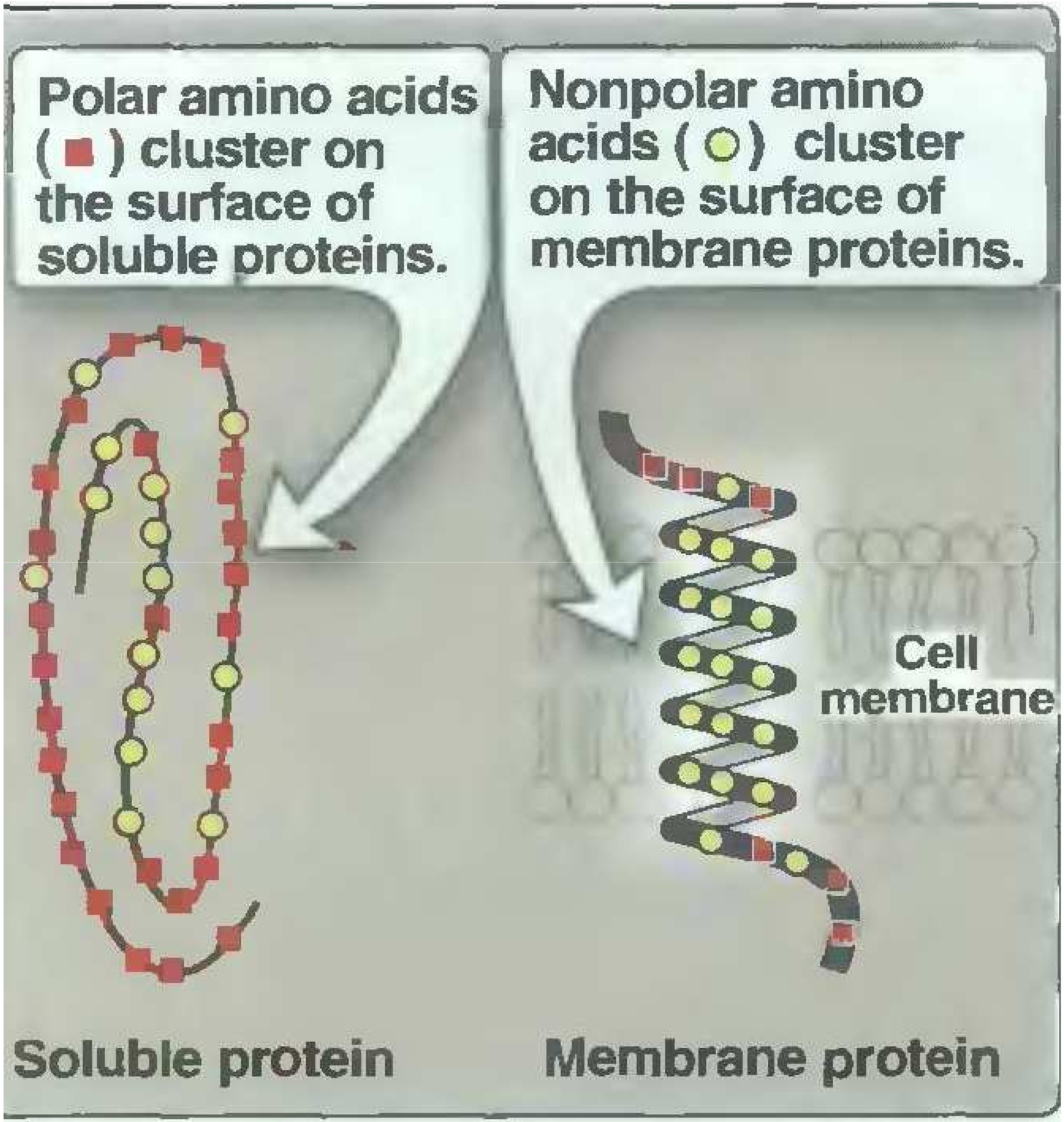
Each of these amino acids has a nonpolar side chain that does not bind or give off protons or participate in hydrogen or ionic bonds .

The side chains of these amino acids can be thought of as “oily” or lipid-like, a property that promotes hydrophobic interactions .

1-Location of nonpolar amino acids in proteins:

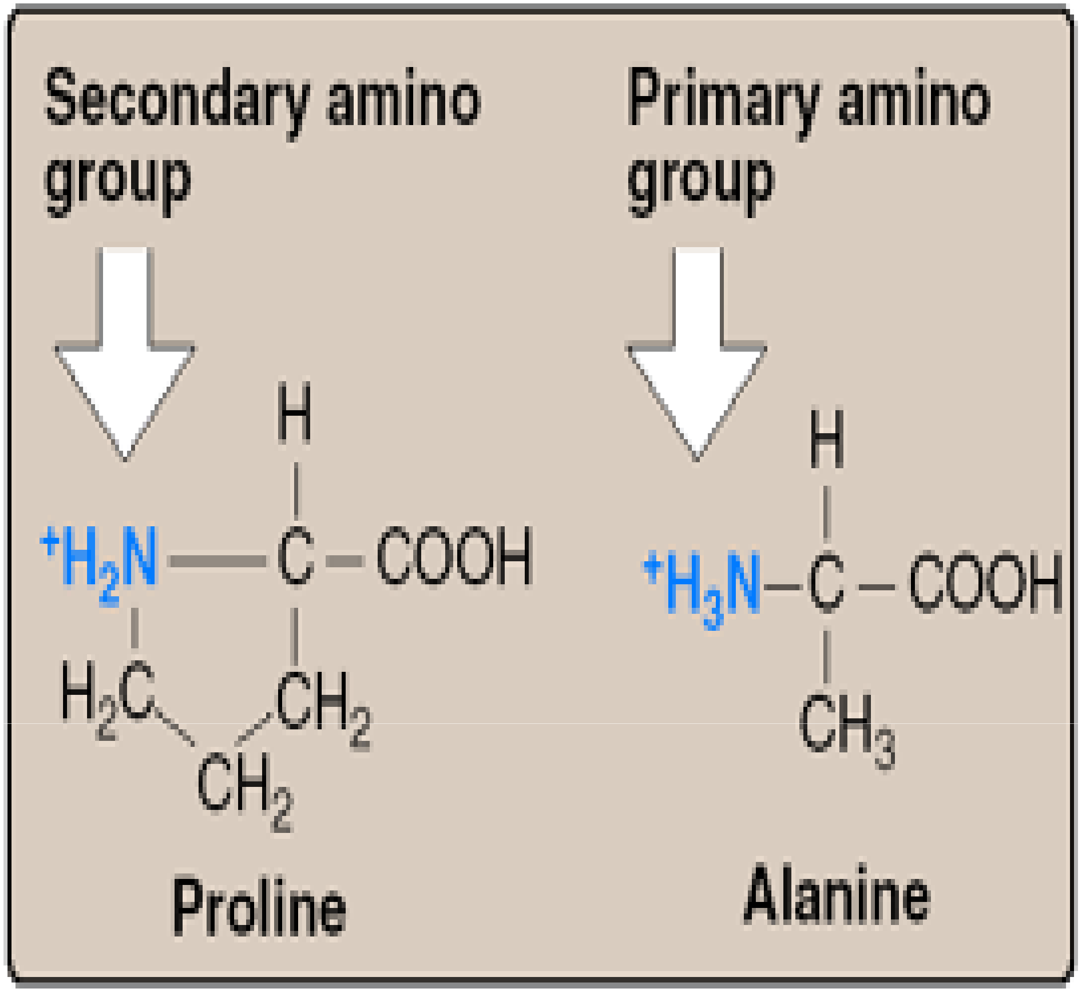
In proteins found in aqueous solutions—a polar environment—the side chains of the nonpolar amino acids tend to cluster together in the interior of the protein . This phenomenon is the result of the hydrophobicity of the nonpolar R-groups, which act much like droplets of oil that coalesce in an aqueous environment.

The nonpolar R-groups thus fill up the interior of the folded protein and help give it its three-dimensional shape. However, for proteins that are located in a hydrophobic environment, such as a membrane, the nonpolar R-groups are found on the outside surface of the protein, interacting with the lipid environment . The importance of these hydrophobic interactions is stabilization of protein structure



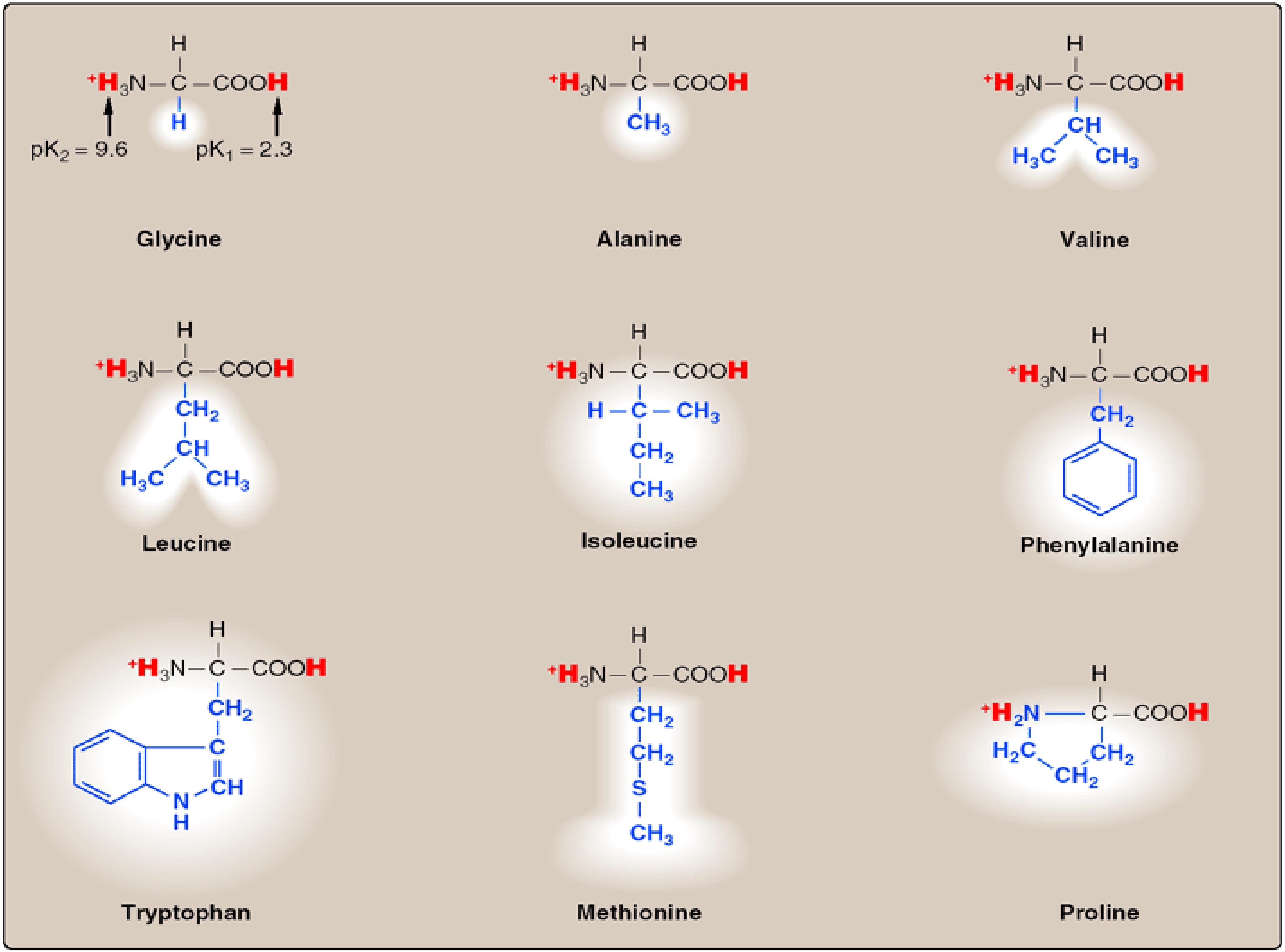
Polar amino acids (■) cluster on the surface of soluble proteins.
Nonpolar amino acids (○) cluster on the surface of membrane proteins.
Cell membrane
Soluble protein
Membrane protein

2- Proline: Proline differs from other amino acids in that proline's side chain and α-amino N form a rigid, five-membered ring structure . Proline, then, has a secondary (rather than a primary) amino group. It is frequently referred to as an imino acid. The unique geometry of proline contributes to the formation of the fibrous structure of collagen , and often interrupts the α-helices found in globular proteins .



Comparison of the secondary amino group found in proline with the primary amino group found in other amino acids, such as alanine.

NONPOLAR SIDE CHAINS

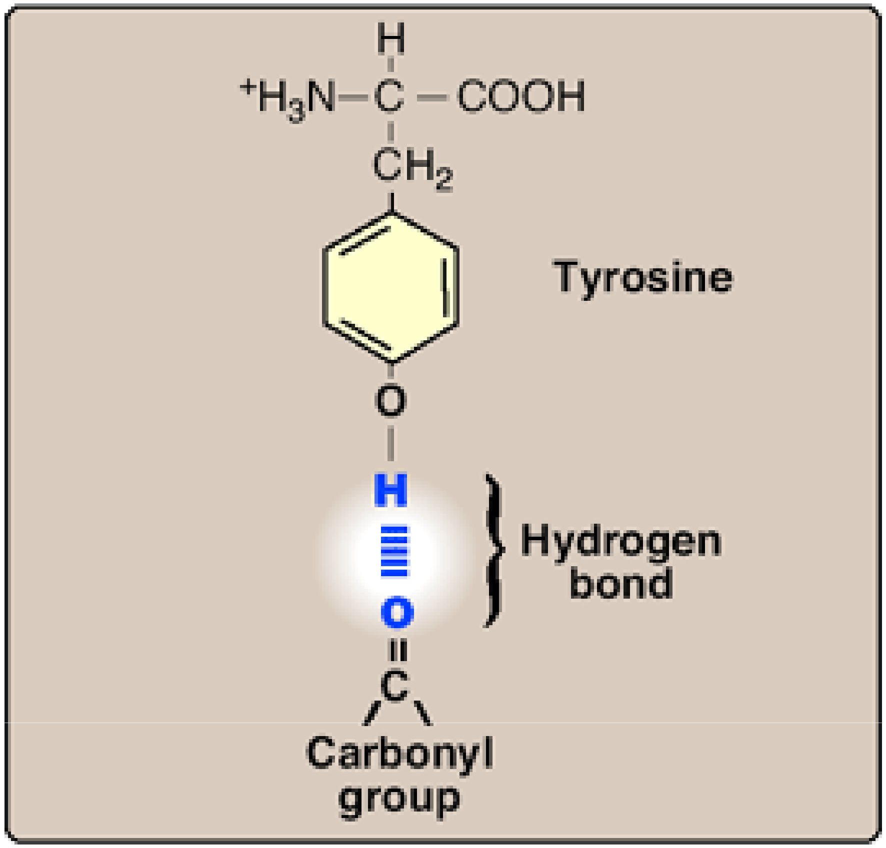


B. with uncharged polar side chains

These amino acids have zero net charge at neutral pH, although the side chains of cysteine and tyrosine can lose a proton at an alkaline pH .

Serine, threonine, and tyrosine each contain a polar hydroxyl group that can participate in hydrogen bond formation .

The side chains of asparagine and glutamine each contain a carbonyl group and an amide group, both of which can also participate in hydrogen bonds. Amino acids



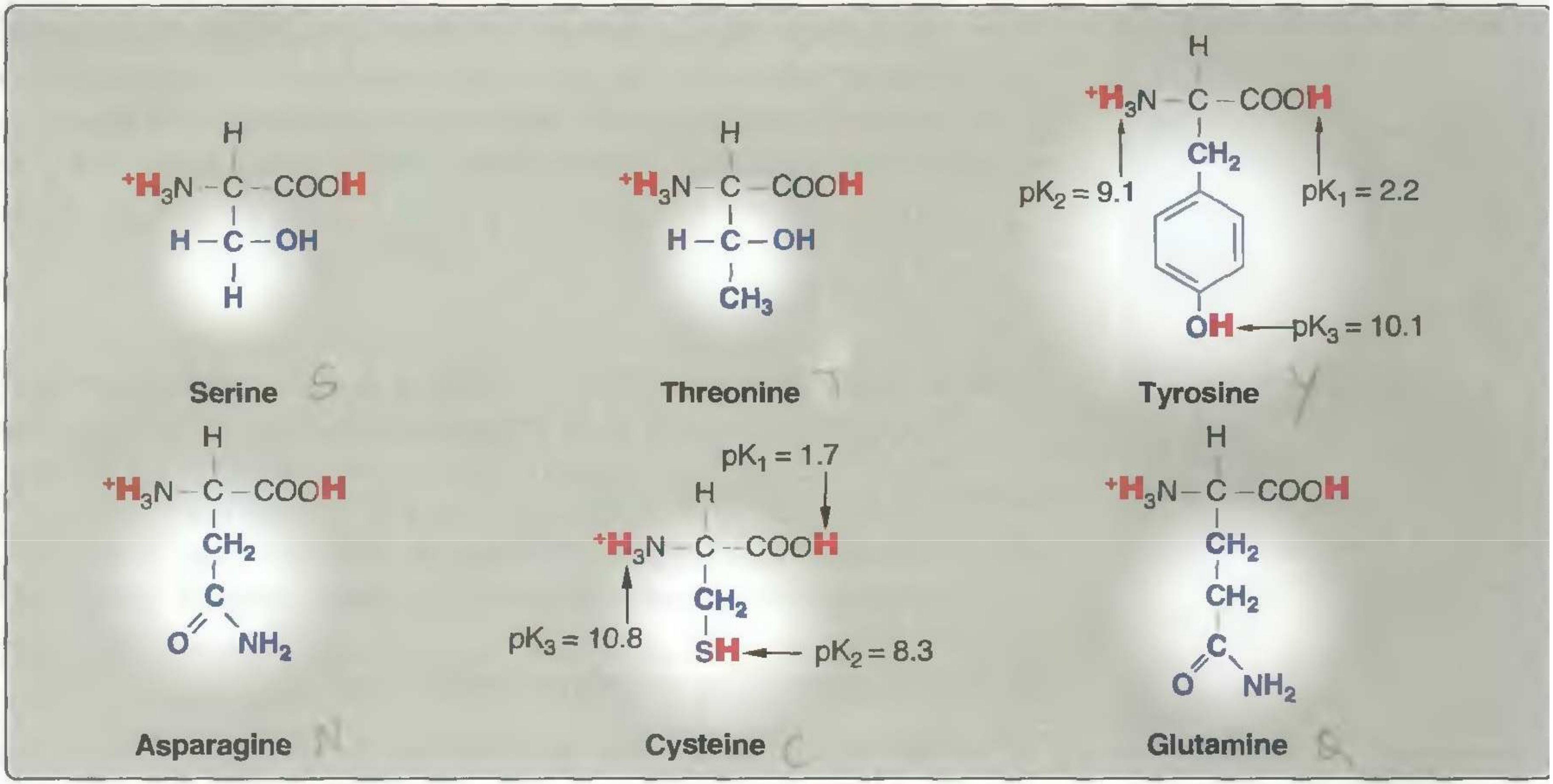
Hydrogen bond between the phenolic hydroxyl group of tyrosine and another molecule containing a carbonyl group.

1- Disulfide bond: The side chain of cysteine contains a sulfhydryl group (–SH), which is an important component of the active site of many enzymes. In proteins, the –SH groups of two cysteines can become oxidized to form a dimer, cystine, which contains a covalent cross-link called a disulfide bond (–S–S–).

2- Side chains as sites of attachment for other compounds: The polar hydroxyl group of serine, threonine, and, rarely, tyrosine, can serve as a site of attachment for structures such as a phosphate group. In addition, the amide group of asparagine, as well as the hydroxyl group of serine or threonine, can serve as a site of attachment for oligosaccharide chains in glycoproteins (see p. 158).

Many extracellular proteins are stabilized by disulfide bonds. Albumin, a blood plasma protein that functions as a transporter for a variety of molecules, is an example.

UNCHARGED POLAR SIDE CHAINS



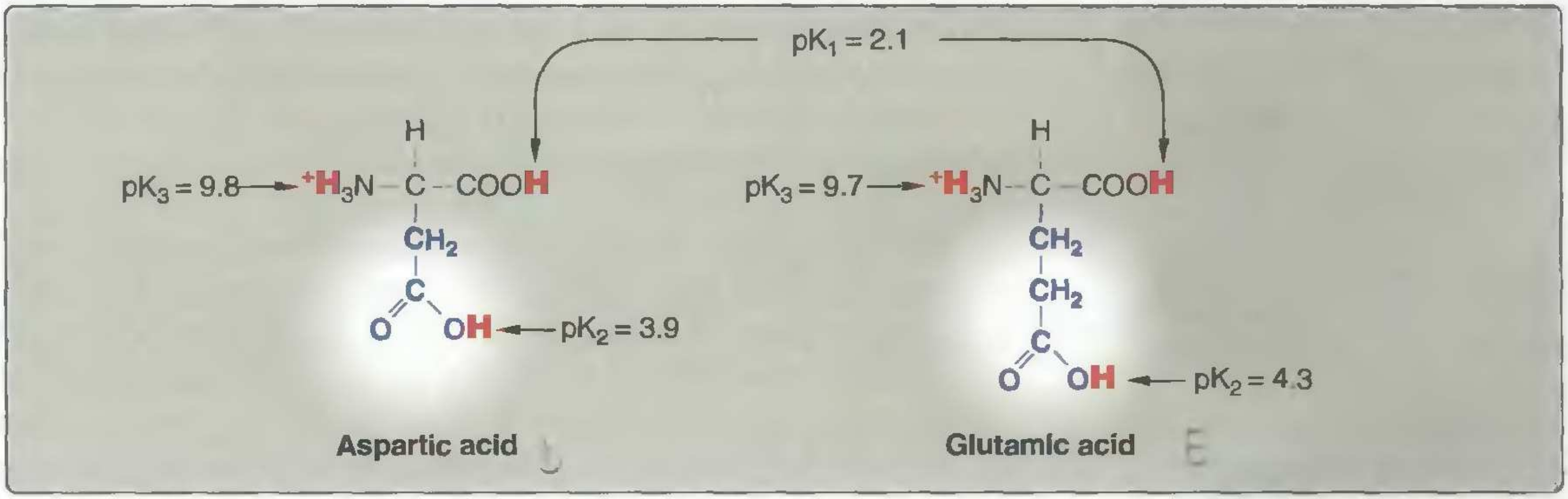
C. Amino acids with acidic side chains

The amino acids aspartic and glutamic acid are proton donors. At physiologic pH, the side chains of these amino acids are fully ionized, containing a negatively charged carboxylate group ($–COO^-$). They are, therefore, called aspartate or glutamate to emphasize that these amino acids are negatively charged at physiologic pH .

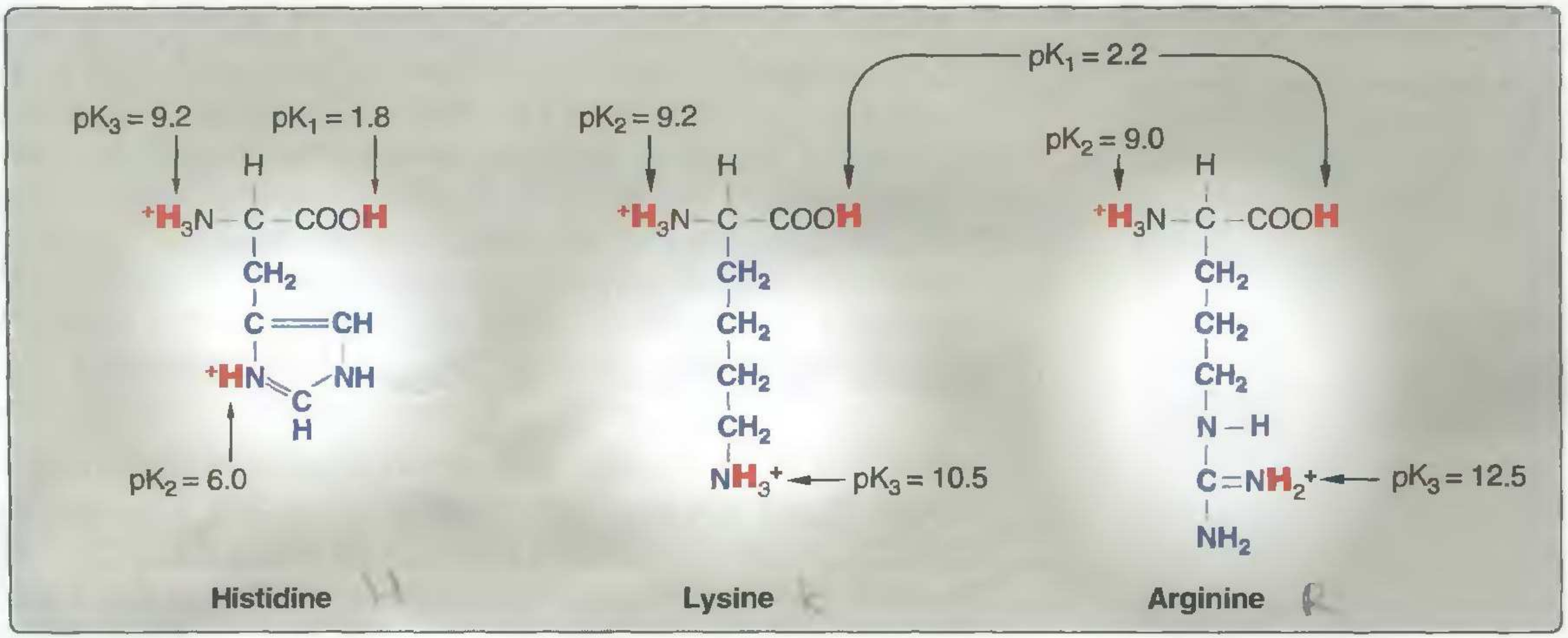
D. Amino acids with basic side chains

The side chains of the basic amino acids accept protons . At physiologic pH the side chains of lysine and arginine are fully ionized and positively charged. In contrast, histidine is weakly basic, and the free amino acid is largely uncharged at physiologic pH. However, when histidine is incorporated into a protein, its side chain can be either positively charged or neutral, depending on the ionic environment provided by the polypeptide chains of the protein. This is an important property of histidine that contributes to the role it plays in the functioning of proteins such as hemoglobin .

ACIDIC SIDE CHAINS

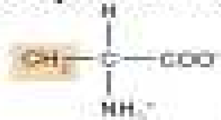


BASIC SIDE CHAINS



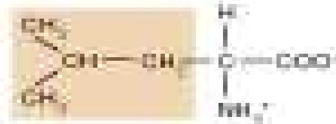
Amino acids with nonpolar R groups

Alanine (Ala)



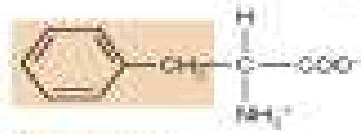
Isoleucine (Ile)

Leucine (Leu)



Methionine (Met)

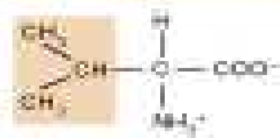
Phenylalanine (Phe)



Proline (Pro)

Tryptophan (Trp)

Valine (Val)



Amino acids with negatively charged R groups

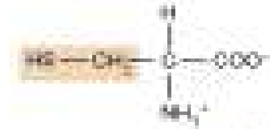
Aspartic acid (Asp)

Glutamic acid (Glu)

Amino acids with uncharged polar R groups

Asparagine (Asn)

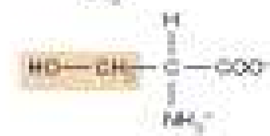
Cysteine (Cys)



Glutamine (Gln)

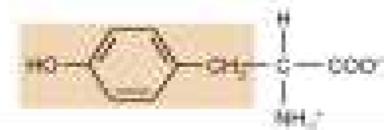
Glycine (Gly)

Serine (Ser)



Threonine (Thr)

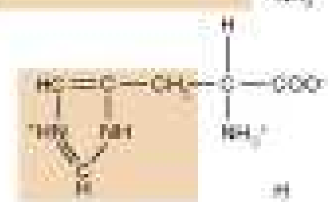
Tyrosine (Tyr)



Amino acids with positively charged R groups

Arginine (Arg)

Histidine (His)



Lysine (Lys)

Sickle cell disease is a pathology that results from the substitution of polar glutamate by nonpolar valine in the β subunit of hemoglobin

Metabolic Classification of the Amino Acids

- Essential and Non-essential
- Glucogenic and Ketogenic

Essential Amino Acids

- Of the 20 amino acids that make up proteins 10 of them can be synthesized by the human body
- The other 10 amino acids **must be acquired from food** sources. These amino acids are known as **essential amino acids**

Essential Amino Acids

Complete protein

- Contains all 10 essential amino acids
- Proteins derived from animal sources are complete proteins
- Beans contain some complete protein as well

Incomplete protein

- Lack one of more of the essential amino acids
- Most vegetable proteins are incomplete proteins
- Beans are an exception to this generalizations

Essential Amino Acids in Humans

- Required in diet
- Humans incapable of forming requisite carbon skeleton

- Arginine*
- Histidine*
- Isoleucine
- Leucine
- Valine
- Lysine
- Methionine
- Threonine
- Phenylalanine
- Tryptophan

* Essential in children, not in adults

Non-Essential Amino Acids in Humans

- **Not required in diet**
- **Can be formed from α-keto acids by transamination and subsequent reactions**

  - Alanine
  - Asparagine
  - Aspartate
  - Glutamate
  - Glutamine
  - Glycine
  - Proline
  - Serine
  - Cysteine (from Met*)
  - Tyrosine (from Phe*)

* Essential amino acids

Essential and Nonessential Amino Acids

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

Amino acids are classified as glucogenic or ketogenic

Glucogenic amino acids are degraded to compounds that can be used as carbon skeletons for glucose synthesis via gluconeogenesis

Ketogenic amino acids are degraded to compounds that can only be used to generate the ketone bodies

Both Glucogenic and ketogenic amino acids:
Several amino acids are classified as both glucogenic and ketogenic because of their degradation products

Glucogenic Amino Acids

- **Metabolized to α-ketoglutarate, pyruvate, oxaloacetate, fumarate, or succinyl CoA**

  → Phosphoenolpyruvate → Glucose

- Aspartate
- Asparagine
- Arginine
- Phenylalanine
- Tyrosine
- Isoleucine
- Methionine
- Valine
- Glutamine
- Glutamate
- Proline
- Histidine
- Alanine
- Serine
- Cysteine
- Glycine
- Threonine
- Tryptophan

Ketogenic Amino Acids

- Metabolized to acetyl CoA or acetoacetyl CoA

Animals cannot convert acetyl CoA or acetoacetyl CoA to pyruvate

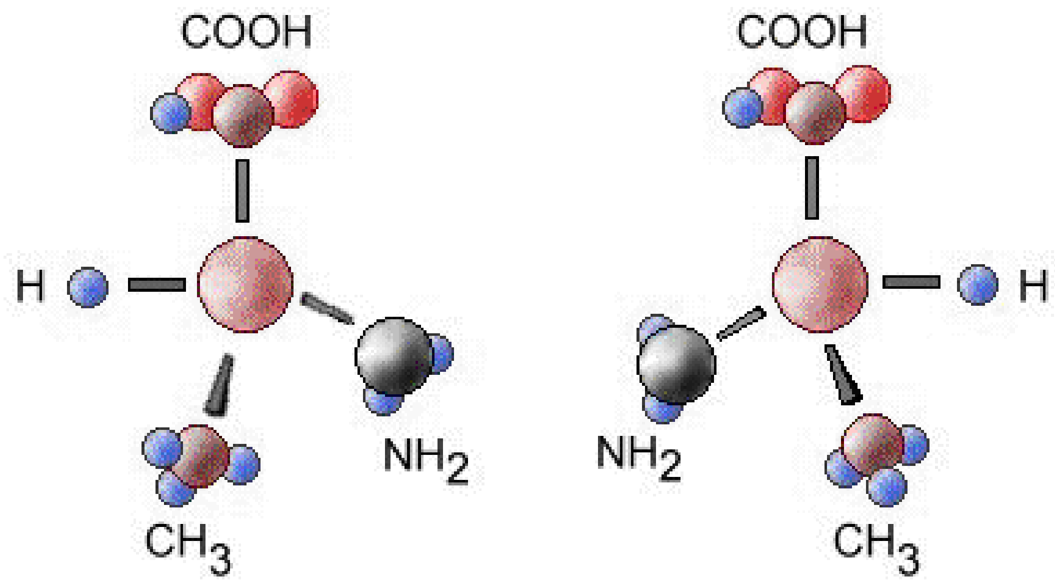
- Leucine *
- Lysine *

- Tryptophan
- Phenylalanine
- Tyrosine
- Isoleucine
- Threonine

*** Leucine and lysine are only ketogenic**

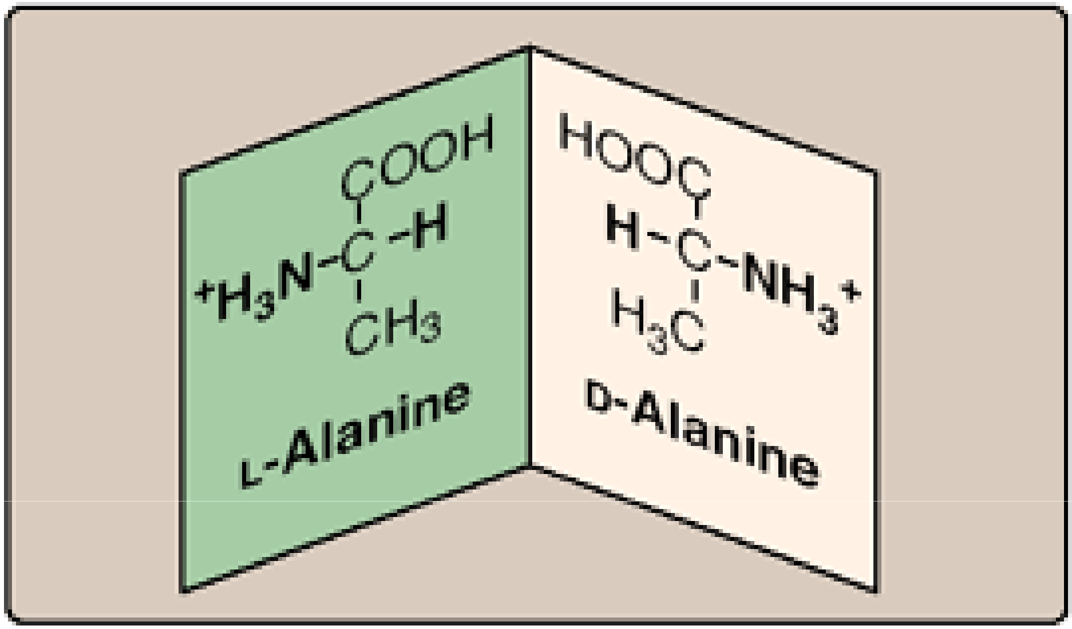
Amino Acids and Optical Isomers

- Except for glycine, all amino acids have a chiral carbon atom. Therefore they can have optical isomers
- The amino acids found in proteins are all levarotatory or L forms.



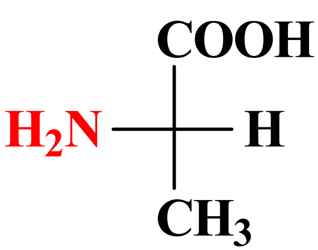
Optical properties of amino acids

The α-carbon of each amino acid is attached to four different chemical groups and is, therefore, a chiral or optically active carbon atom.
Glycine is the exception because its α-carbon has two hydrogen substituents and, therefore, is optically inactive.
Amino acids that have an asymmetric center at the α-carbon can exist in two forms, designated D and L, that are mirror images of each other. The two forms in each pair are termed stereoisomers, optical isomers, or enantiomers.
All amino acids found in proteins are of the L-configuration. However, D-amino acids are found in some antibiotics and in plant and bacterial cell walls.

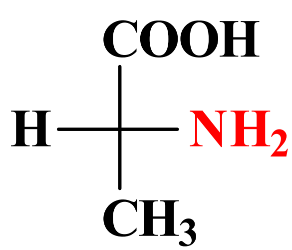


D and L forms of alanine are mirror images.

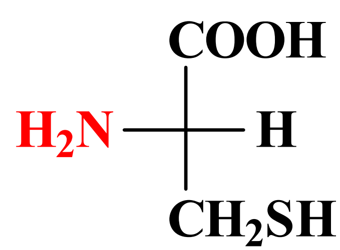
- All amino acids except glycine are chiral.
- Amino acids have stereoisomers.
- In biological systems, only L amino acids are used in proteins.



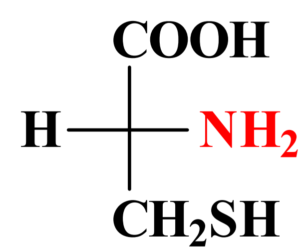
L-Alanine



D-Alanine



L-Cysteine



D-Cysteine