

## Chemical Nature of the Amino Acids

All peptides and polypeptides are polymers of alpha-amino acids. There are 20 amino acids that are relevant to the make-up of mammalian proteins (see below). Several other amino acids are found in the body free or in combined states (i.e. not associated with peptides or proteins). These non-protein associated amino acids perform specialized functions. Several of the amino acids found in proteins also serve functions distinct from the formation of peptides and proteins, e.g., tyrosine in the formation of thyroid hormones or glutamate acting as a neurotransmitter.

The alpha-amino acids in peptides and proteins (excluding proline) consist of a carboxylic acid (-COOH) and an amino (-NH<sub>2</sub>) functional group attached to the same tetrahedral carbon atom. This carbon is the alpha-carbon. Distinct R-groups, that distinguish one amino acid from another, also are attached to the alpha-carbon (except in the case of glycine where the R-group is hydrogen). The fourth substitution on the tetrahedral alpha-carbon of amino acids is hydrogen.

### Table of alpha-Amino Acids Found in Proteins

Amino Acid	Symbol	Structure*	pK <sub>1</sub> (COOH)	pK <sub>2</sub> (NH <sub>2</sub> )	pK R Group
<b>Amino Acids with Aliphatic R-Groups</b>					
Glycine	Gly - G	$\begin{array}{c} \text{H}-\text{CH}-\text{COOH} \\   \\ \text{NH}_2 \end{array}$	2.4	9.8	
Alanine	Ala - A	$\begin{array}{c} \text{CH}_3-\text{CH}-\text{COOH} \\   \\ \text{NH}_2 \end{array}$	2.4	9.9	
Valine	Val - V	$\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{CH} \\ \diagup \\ \text{H}_3\text{C} \end{array} - \text{CH} - \text{CH} - \text{COOH} \\   \\ \text{NH}_2$	2.2	9.7	
Leucine	Leu - L	$\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{CH} \\ \diagup \\ \text{H}_3\text{C} \end{array} - \text{CH} - \text{CH}_2 - \text{CH} - \text{COOH} \\   \\ \text{NH}_2$	2.3	9.7	
Isoleucine	Ile - I	$\begin{array}{c} \text{H}_3\text{C} \\ \diagdown \\ \text{CH}_2 \\ \diagup \\ \text{H}_3\text{C} \end{array} - \text{CH} - \text{CH} - \text{CH} - \text{COOH} \\   \\ \text{NH}_2$	2.3	9.8	
<b>Non-Aromatic Amino Acids with Hydroxyl R-Groups</b>					
Serine	Ser - S	$\text{HO}-\text{CH}_2-\text{CH}-\text{COOH} \\   \\ \text{NH}_2$	2.2	9.2	~13

Threonine	Thr - T	$\begin{array}{c} \text{H}_3\text{C}-\text{CH}-\text{CH}-\text{COOH} \\   \quad   \\ \text{HO} \quad \text{NH}_2 \end{array}$	2.1	9.1	~13
<b>Amino Acids with Sulfur-Containing R-Groups</b>					
Cysteine	Cys - C	$\text{HS}-\text{CH}_2-\text{CH}-\text{COOH}$ $\quad \quad  $ $\quad \quad \text{NH}_2$	1.9	10.8	8.3
Methionine	Met-M	$\text{H}_3\text{C}-\text{S}-(\text{CH}_2)_2-\text{CH}-\text{COOH}$ $\quad \quad \quad \quad  $ $\quad \quad \quad \quad \text{NH}_2$	2.1	9.3	
<b>Acidic Amino Acids and their Amides</b>					
Aspartic Acid	Asp - D	$\text{HOOC}-\text{CH}_2-\text{CH}-\text{COOH}$ $\quad \quad \quad  $ $\quad \quad \quad \text{NH}_2$	2.0	9.9	3.9
Asparagine	Asn - N	$\text{H}_2\text{N}-\text{C}-\text{CH}_2-\text{CH}-\text{COOH}$ $\quad \quad    \quad \quad  $ $\quad \quad \text{O} \quad \quad \text{NH}_2$	2.1	8.8	
Glutamic Acid	Glu - E	$\text{HOOC}-\text{CH}_2-\text{CH}_2-\text{CH}-\text{COOH}$ $\quad \quad \quad \quad  $ $\quad \quad \quad \quad \text{NH}_2$	2.1	9.5	4.1
Glutamine	Gln - Q	$\text{H}_2\text{N}-\text{C}-\text{CH}_2-\text{CH}_2-\text{CH}-\text{COOH}$ $\quad \quad    \quad \quad  $ $\quad \quad \text{O} \quad \quad \text{NH}_2$	2.2	9.1	
<b>Basic Amino Acids</b>					
Arginine	Arg - R	$\begin{array}{c} \text{HN}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}-\text{COOH} \\   \quad \quad \quad   \\ \text{C}=\text{NH} \quad \quad \quad \text{NH}_2 \\   \\ \text{NH}_2 \end{array}$	1.8	9.0	12.5
Lysine	Lys - K	$\text{H}_2\text{N}-(\text{CH}_2)_4-\text{CH}-\text{COOH}$ $\quad \quad \quad  $ $\quad \quad \quad \text{NH}_2$	2.2	9.2	10.8
Histidine	His - H	$\begin{array}{c} \text{CH}_2-\text{CH}-\text{COOH} \\   \quad   \\ \text{HN} \quad \text{N:} \end{array}$	1.8	9.2	6.0
<b>Amino Acids with Aromatic Rings</b>					
Phenylalanine	Phe - F	$\text{C}_6\text{H}_5-\text{CH}_2-\text{CH}-\text{COOH}$ $\quad \quad  $ $\quad \quad \text{NH}_2$	2.2	9.2	

Tyrosine	Tyr - Y		2.2	9.1	10.1
Tryptophan	Trp-W		2.4	9.4	
<b>Imino Acids</b>					
Proline	Pro - P		2.0	10.6	

\* Backbone of the amino acids is red, R-groups are black

## Amino Acid Classifications

Each of the 20  $\alpha$ -amino acids found in proteins can be distinguished by the R-group substitution on the  $\alpha$ -carbon atom. There are two broad classes of amino acids based upon whether the R-group is hydrophobic or hydrophilic.

The hydrophobic amino acids tend to repel the aqueous environment and, therefore, reside predominantly in the interior of proteins. This class of amino acids does not ionize nor participate in the formation of H-bonds. The hydrophilic amino acids tend to interact with the aqueous environment, are often involved in the formation of H-bonds and are predominantly found on the exterior surfaces proteins or in the reactive centers of enzymes.

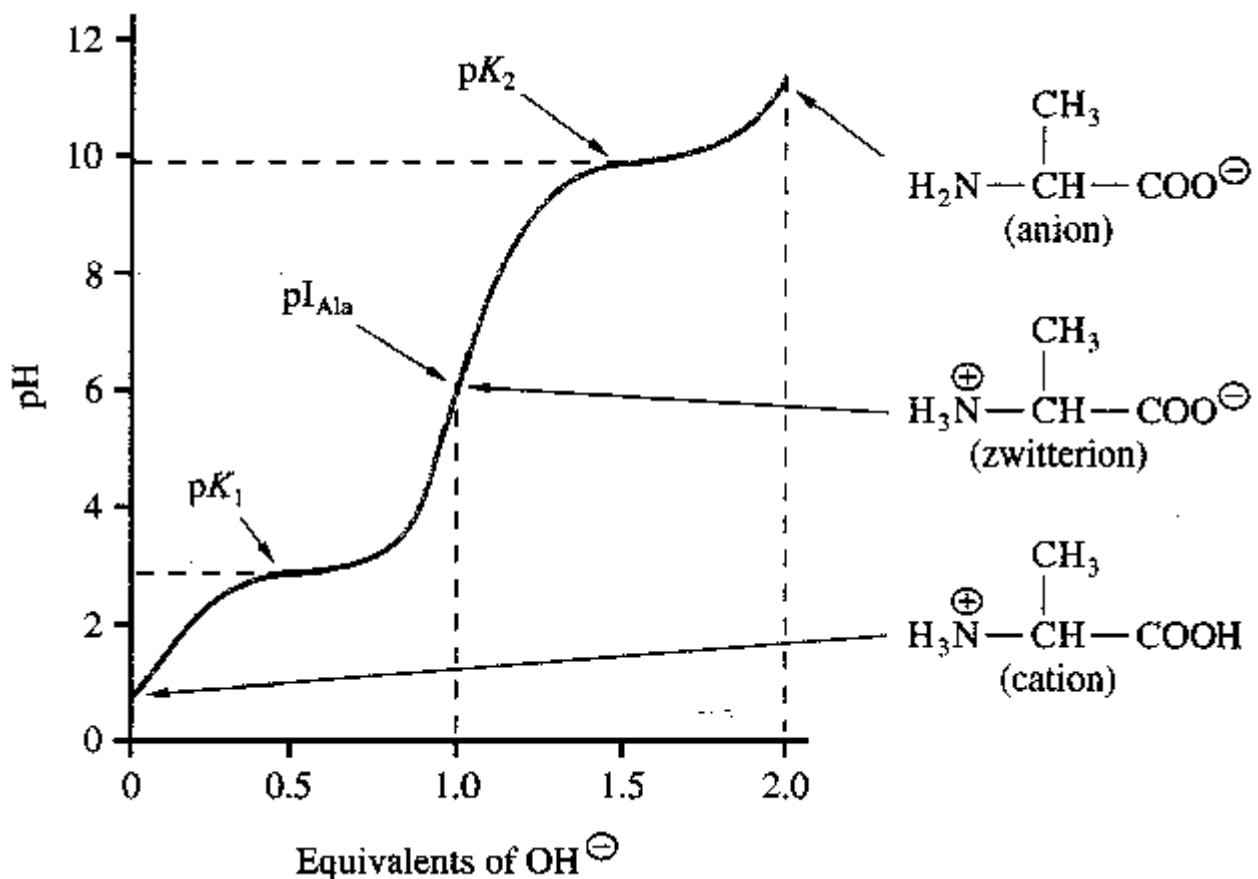
## Acid-Base Properties of the Amino Acids

The  $\alpha$ -COOH and  $\alpha$ -NH<sub>2</sub> groups in amino acids are capable of ionizing (as are the acidic and basic R-groups of the amino acids). As a result of their ionizability the following ionic equilibrium reactions may be written:



The equilibrium reactions, as written, demonstrate that amino acids contain at least two weakly acidic groups. However, the carboxyl group is a far stronger acid than the amino group. At physiological pH (around 7.4) the carboxyl group will be unprotonated and the amino group will be protonated. An amino acid with no ionizable R-group would be electrically neutral at this pH. This species is termed a **zwitterion**.

Like typical organic acids, the acidic strength of the carboxyl, amino and ionizable R-groups in amino acids can be defined by the association constant,  $K_a$  or more commonly the negative logarithm of  $K_a$ , the  $pK_a$ . The net charge (the algebraic sum of all the charged groups present) of any amino acid, peptide or protein, will depend upon the pH of the surrounding aqueous environment. As the pH of a solution of an amino acid or protein changes so too does the net charge. This phenomenon can be observed during the titration of any amino acid or protein. When the net charge of an amino acid or protein is zero the pH will be equivalent to the **isoelectric point: pI**.



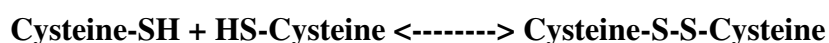
**Titration curve for Alanine**

## Functional Significance of Amino Acid R-Groups

In solution it is the nature of the amino acid R-groups that dictate structure-function relationships of peptides and proteins. The hydrophobic amino acids will generally be encountered in the interior of proteins shielded from direct contact with water. Conversely, the hydrophilic amino acids are generally found on the exterior of proteins as well as in the active centers of enzymatically active proteins. Indeed, it is the very nature of certain amino acid R-groups that allow enzyme reactions to occur.

The imidazole ring of histidine allows it to act as either a proton donor or acceptor at physiological pH. Hence, it is frequently found in the reactive center of enzymes. Equally important is the ability of histidines in hemoglobin to buffer the H<sup>+</sup> ions from carbonic acid ionization in red blood cells. It is this property of hemoglobin that allows it to exchange O<sub>2</sub> and CO<sub>2</sub> at the tissues or lungs, respectively.

The primary alcohol of serine and threonine as well as the thiol (-SH) of cysteine allow these amino acids to act as nucleophiles during enzymatic catalysis. Additionally, the thiol of cysteine is able to form a disulfide bond with other cysteines:



This simple disulfide is identified as cystine. The formation of disulfide bonds between cysteines present within proteins is important to the formation of active structural

domains in a large number of proteins. Disulfide bonding between cysteines in different polypeptide chains of oligomeric proteins plays a crucial role in ordering the structure of complex proteins, e.g. the insulin receptor.

---

## Optical Properties of the Amino Acids

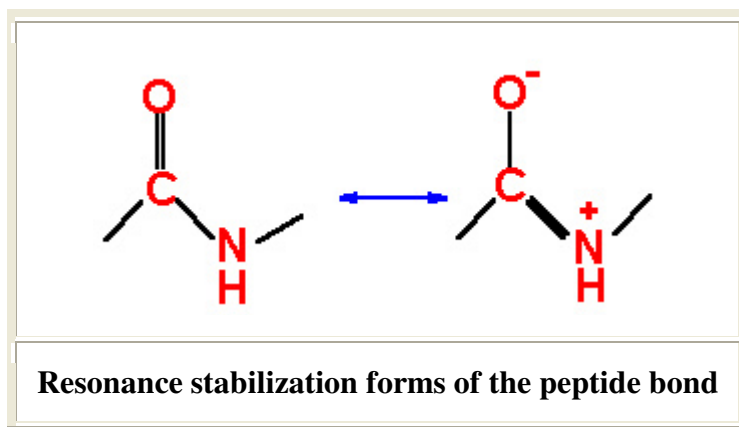
A tetrahedral carbon atom with 4 distinct constituents is said to be chiral. The one amino acid not exhibiting chirality is glycine since its "R-group" is a hydrogen atom. Chirality describes the handedness of a molecule that is observable by the ability of a molecule to rotate the plane of polarized light either to the right (**dextrorotatory**) or to the left (**levorotatory**). All of the amino acids in proteins exhibit the same absolute steric configuration as L-glyceraldehyde. Therefore, they are all L- $\alpha$ -amino acids. D-amino acids are never found in proteins, although they exist in nature. D-amino acids are often found in polypeptide antibiotics.

The aromatic R-groups in amino acids absorb ultraviolet light with an absorbance maximum in the range of 280nm. The ability of proteins to absorb ultraviolet light is predominantly due to the presence of the tryptophan which strongly absorbs ultraviolet light.

---

## The Peptide Bond

Peptide bond formation is a condensation reaction leading to the polymerization of amino acids into peptides and proteins. Peptides are small consisting of few amino acids. A number of hormones and neurotransmitters are peptides. Additionally, several antibiotics and antitumor agents are peptides. Proteins are polypeptides of greatly divergent length. The simplest peptide, a dipeptide, contains a single peptide bond formed by the condensation of the carboxyl group of one amino acid with the amino group of the second with the concomitant elimination of water. The presence of the carbonyl group in a peptide bond allows electron resonance stabilization to occur such that the peptide bond exhibits rigidity not unlike the typical  $\text{-C=C-}$  double bond. The peptide bond is, therefore, said to have partial double-bond character.



<http://www.indstate.edu/thcme/mwking/amino-acids.html>