

AMINO ACIDS





AMINO ACID

- An amino acid is bi functional organic molecule that contains both a carboxyl group, $-\text{COOH}$ as well as an amine group, $-\text{NH}_2$. Amino acids derived from proteins have the amino group on the alpha (α) carbon i.e; the carbon atom next to the carboxyl group.



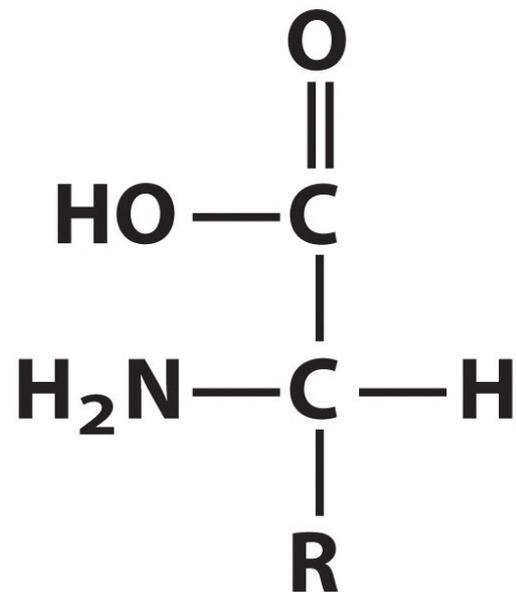
- **Amino acids** are the building blocks of proteins. There are 300 amino acids that occur in nature. Among these only 22 are known as **standard amino acids** that commonly occur in proteins.



- The amino acids differ in the nature of R-group attached to α carbon atom. The nature of R-group determines the properties of proteins.



General formula





- Amino acids are the structural units that make up proteins. They join together to form short **polymer** chains called **peptides** or longer chains called either **polypeptides** or **proteins**. These polymers are linear and unbranched, with each amino acid within the chain attached to two neighboring amino acids.



- The process of making proteins is called *translation* and involves the step-by-step addition of amino acids to a growing protein chain by a **ribozyme** that is called a **ribosome**. The order in which the amino acids are added is read through the **genetic code** from a **mRNA** template, which is a **RNA** copy of one of the organism's **genes**.



- Twenty-two amino acids are naturally incorporated into polypeptides and are called **proteinogenic** or natural amino acids. Of these, 20 are encoded by the universal **genetic code**. The remaining 2, **selenocysteine** and **pyrrolysine**, are incorporated into proteins by unique synthetic mechanisms. **Selenocysteine** is incorporated when the mRNA being translated includes a **SECIS**.



Nomenclature of Amino Acids

- All **amino acids** have trivial names.
- e.g; $\text{NH}_2\text{CH}_2\text{COOH}$ is better known as glycine rather than α -amino acetic acid or 2-amino ethanoic acid.
- These trivial names usually reflect the property of that compound or its source.
Example: Glycine is so named since it has sweet taste (in Greek glykos means sweet) and tyrosine was first obtained from cheese (in Greek, tyros means cheese).



Peptide Bond Formation

- Proteins are formed by joining the carboxyl group of one amino acid to the α -amino group of another amino acid. The bond formed between two amino acids by the elimination of a water molecule is called a peptide linkage or bond.

The product formed by linking amino acid molecules through peptide linkages, $-\text{CO}-\text{NH}-$, is called a peptide.



- Peptides are further designated as di, tri, tetra or penta peptides accordingly as they contain two, three, four or five amino acid molecules, same or different, joined together.



Classification

- Amino acids are classified into different ways based on polarity, structure, nutritional requirement, metabolic fate, etc. Generally used classification is based on polarity. Amino acid polarity chart shows the polarity of amino acids.



Classification on polarity basis

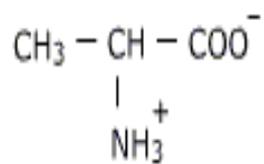
Based on polarity, amino acids are classified into four groups as follows,

- Non-polar amino acids.
- Polar amino acids with no charge.
- Polar amino acids with positive charge.
- Polar amino acids with negative charge.

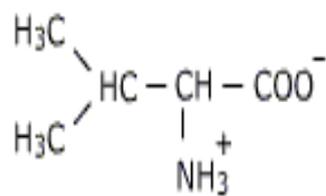


Non Polar Amino Acids

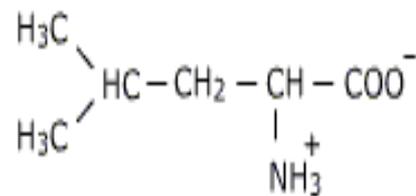
Non Polar Amino Acids have equal number of amino and carboxyl groups and are neutral. These amino acids are hydrophobic and have no charge on the 'R' group. The amino acids in this group are alanine, valine, leucine, isoleucine, phenyl alanine, glycine, tryptophan, methionine and proline.



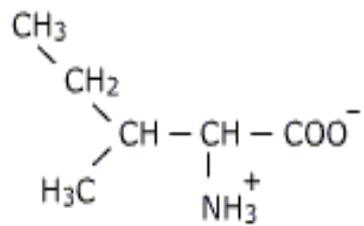
Alanine



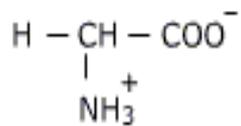
Valine



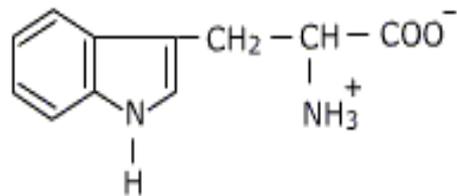
Leucine



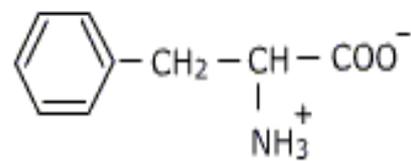
Isoleucine



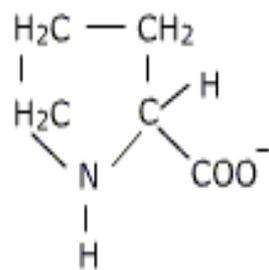
Glycine



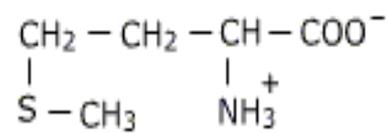
Tryptophan



Phenyl alanine



Proline

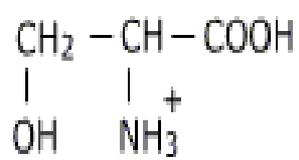


Methionine

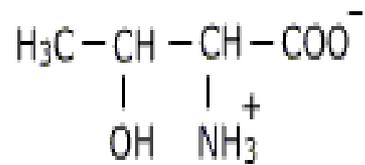


Polar Amino Acids with no Charge

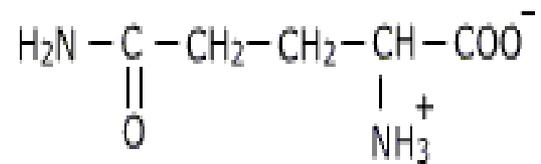
These amino acids do not have any charge on the 'R' group. These amino acids participate in hydrogen bonding of protein structure. The amino acids in this group are serine, threonine, tyrosine, cysteine, glutamine and asparagine.



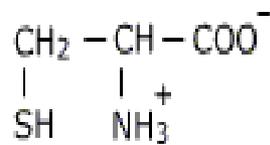
Serine



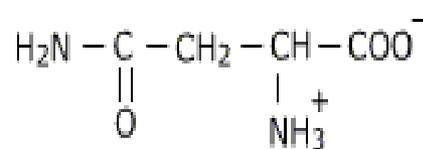
Threonine



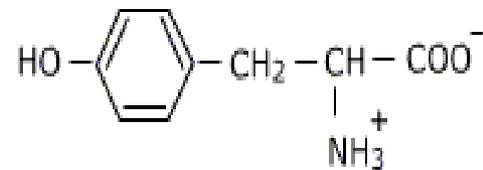
Gultamine



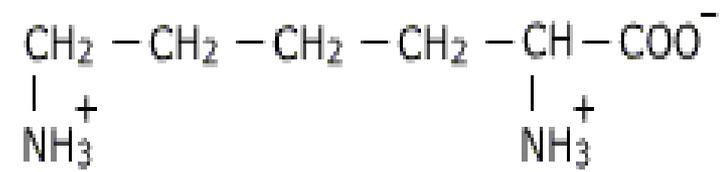
Cysteine



Asparagine



Tyrosine

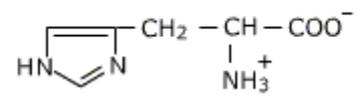


Lysine

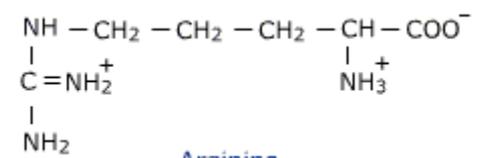


Polar Amino Acids with Positive Charge

Polar amino acids with positive charge have more amino groups as compared to carboxyl groups making it basic. The amino acids, which have positive charge on the 'R' group are placed in this category. They are lysine, arginine and histidine.



Histidine

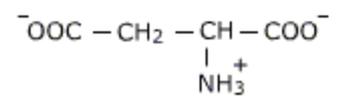


Arginine

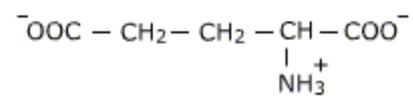


Polar Amino Acids with Negative Charge

Polar amino acids with negative charge have more carboxyl groups than amino groups making them acidic. The amino acids, which have negative charge on the 'R' group are placed in this category. They are called as dicarboxylic mono-amino acids. They are aspartic acid and glutamic acid.



Aspartic acid



Glutamic acid



Classification on side chain basis

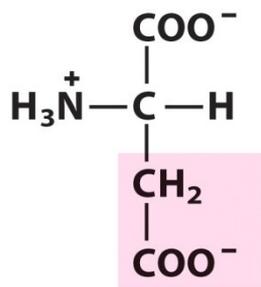
- Aliphatic side chains
- Aromatic side chains
- Hydroxyl-containing side chains
- Sulfur-containing side chains
- Basic side chains
- Acidic side chains
- Amide side chains
- Imino acids



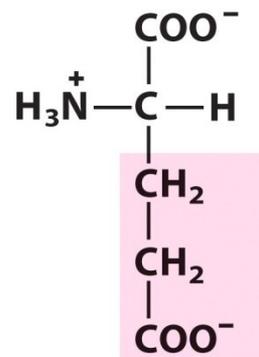
Acidic and Basic Amino Acids

■ Acidic

- R group = carboxylic acid
- Donates H⁺
- Negatively charged



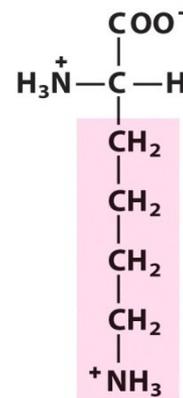
Aspartate



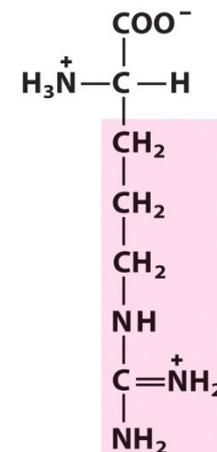
Glutamate

■ Basic

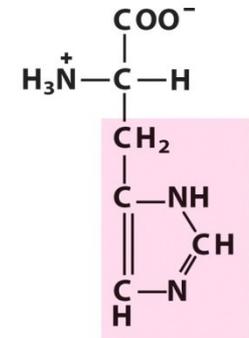
- R group = amine
- Accepts H⁺
- Positively charged
- Its ionizes at pH 6.0



Lysine



Arginine



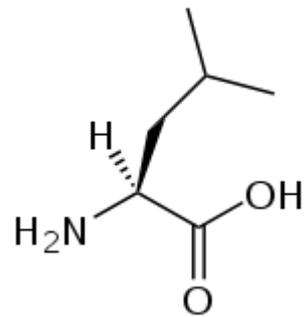
Histidine



Branched-chain amino acid (BCAA)

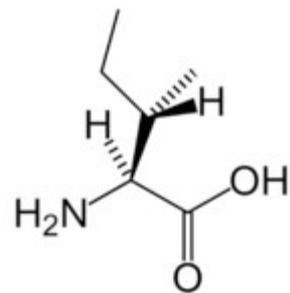
- A **branched-chain amino acid (BCAA)** is an amino acid having **aliphatic side-chains** with a branch i.e; a **carbon** atom bound to more than two other carbon atoms. Among the **proteinogenic amino acids**, there are three BCAAs: **leucine**, **isoleucine** and **valine**.

Leucine



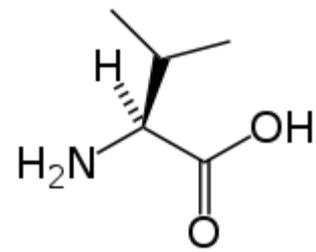


Isoleucine





Valine





- The BCAAs are among the essential amino acids for humans, accounting for 35% of the essential amino acids in muscle proteins and 40% of the preformed amino acids required by mammals. BCAA's have been used clinically to aid in the recovery of burn victims. They are also used in the treatment in some cases of **hepatic encephalopathy**.



MAPLE SYRUP URINE DISEASE

- Degradation of branched-chain amino acids involves the **branched-chain alpha-keto acid dehydrogenase (BCKDH)**. A deficiency of this complex leads to a buildup of the branched-chain amino acid (**leucine**, **isoleucine**, and **valine**) and their toxic by products in the blood and urine, giving the condition the name **maple syrup urine disease**.



STANDARD AMINO ACIDS

- >300 amino acids.
- Only 22 form all proteins in plants as well as animals. Humans can produce 10 of the 20 amino acids. The others must be supplied in the food. Failure to obtain enough of even 1 of the essential amino acids, those that we cannot make, results in degradation of the body's proteins.



Nutritional Classification

- According to the classification based on nutrition, they are divided into 3 types:
- They are:
- 1-Essential amino acids, those that we cannot make, results in degradation of the body's proteins.
- 2- Conditional amino acids.
- 3- Non essential amino acids.



Essential Amino Acids

The amino acids that are to be supplied through diet are called as essential amino acids. They cannot be produced by the body. The essential amino acids are valine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine and tryptophan.



Non-essential Amino Acids

The amino acids that can be synthesized by the body are called non essential amino acids. They are: Glycine, alanine, serine, cysteine, aspartic acid, glutamic acid, asparagine, glutamine and proline.



Conditionally Essential

- Essential only in certain cases.
- Some amino acids like arginine and histidine are growth promoting factors. They are not synthesized in sufficient amount during growth, so essential in growing children, pregnancy and lactation.
- Tyrosine is produced from phenylalanine, so if the diet is deficient in phenylalanine, tyrosine will be required as well.



Amino acid (or residue)	3-letter symbol	1-letter symbol	Mnemonic help for 1-letter symbol	Approximate pK_a of R group (if it's ionizable) in peptides and proteins
Alanine	Ala	A	A lanine	N.A.
Arginine	Arg	R	aR ginine	~ 12
Aspartate	Asp*	D	aspar D ic acid	~ 4
Asparagine	Asn*	N	asparagi N e	N.A.
Cysteine	Cys	C	C ysteine	~ 8.5
Glutamate	Glu**	E	glu E tamic acid	~ 4
Glutamine	Gln**	Q	Q -tamine	N.A.
Glycine	Gly	G	G lycine	N.A.
Histidine	His	H	H istidine	~ 6.5
Isoleucine	Ile	I	I soleucine	N.A.



Leucine	Leu	L	Leucine	N.A.
Lysine	Lys	K	(before L)	~ 10
Methionine	Met	M	Methionine	N.A.
Proline	Pro	P	Proline	N.A.
Phenylalanine	Phe	F	Fenylalanine	N.A.
Serine	Ser	S	Serine	N.A.
Threonine	Thr	T	Threonine	N.A.
Tryptophan	Trp	W	tWo rings (or tWyptophan)	N.A.
Tyrosine	Tyr	Y	tYrosine	~ 10
Valine	Val	V	Valine	N.A.



Non-standard amino acids

- Aside from the 22 standard amino acids, there are many other amino acids that are called *non-proteinogenic* or *non-standard*. Those either are not found in proteins (for example **carnitine**, **GABA**, or are not produced directly and in isolation by standard cellular machinery e.g; **hydroxyproline** and selenomethionine.



- Non-standard amino acids that are found in proteins are formed by **post-translational modification**, which is modification after translation during protein synthesis. These modifications are often essential for the function or regulation of a protein e.g; the **carboxylation** of **glutamate** allows for better binding of **calcium cations**, and the **hydroxylation** of **proline** is critical for maintaining **connective tissues**.



Some nonstandard amino acids are not found in proteins. Examples include **lanthionine**, **2-aminoisobutyric acid**, **dehydroalanine**, and the neurotransmitter **gamma-aminobutyric acid**. Nonstandard amino acids often occur as intermediates in the **metabolic pathways** for standard amino acids — for example, **ornithine** and **citrulline** occur in the **urea cycle**, part of amino acid catabolism.



- A rare exception to the dominance of α -amino acids in biology is the β -amino acid **beta alanine** (3-aminopropanoic acid), which is used in plants and microorganisms in the synthesis of **pantothenic acid** (vitamin B₅), a component of **coenzyme A**.



- 1. Citrulline.
- 2. Ornithine.
- 3. Arginosuccinic acid.
- 4. beta alaninne.
- 5. Pantothenic acid.
- 6. GABA.
- 7. DOPA.
- 8. Homocysteine.



- 9. Iodinated amino acids:
MIT, DIT, T3 & T4.



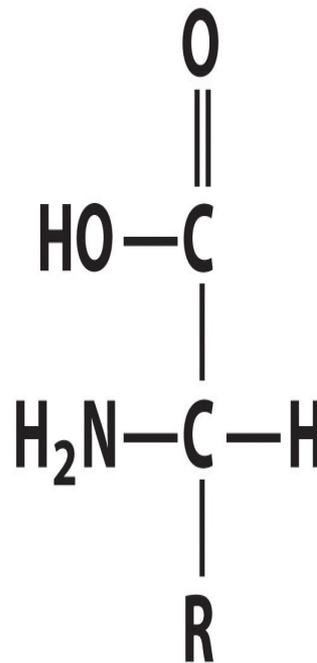
Zwitterions

- The amine and carboxylic acid functional groups found in amino acids allow them to have **amphiprotic** properties. Carboxylic acid groups ($-\text{CO}_2\text{H}$) can be deprotonated to become negative carboxylates ($-\text{CO}_2^-$), and α -amino groups (NH_2-) can be protonated to become positive α -ammonium groups ($^+\text{NH}_3$).

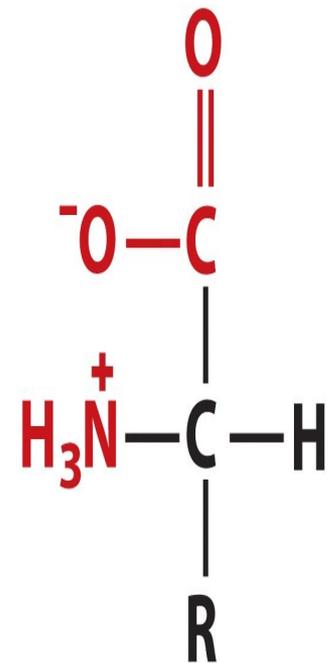


zwitterion

- Both the -NH_2 and the -COOH groups in an amino acid undergo ionization in water.
- At physiological pH (7.4), a **zwitterion** forms
 - Both + and - charges
 - Overall neutral
 - Amphoteric
 - Amino group is protonated
 - Carboxyl group is deprotonated
- Soluble in polar solvents due to ionic character
- Structure of R also influence solubility



**Nonionic
form**

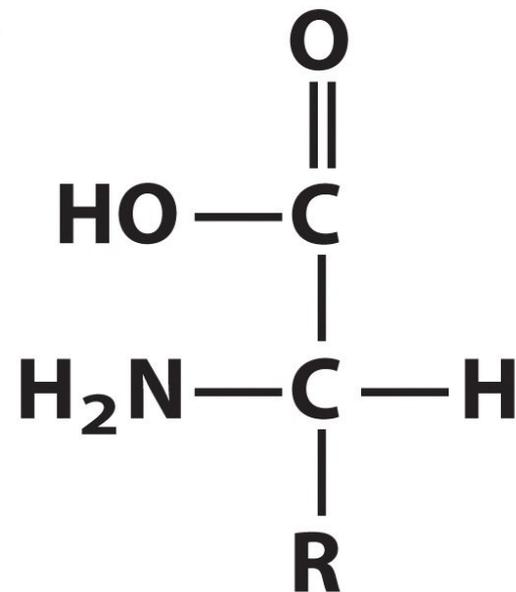


**Zwitterionic
form**



Acid-base Properties

- Amino acids have multiple pK_a 's due to multiple ionizable groups.

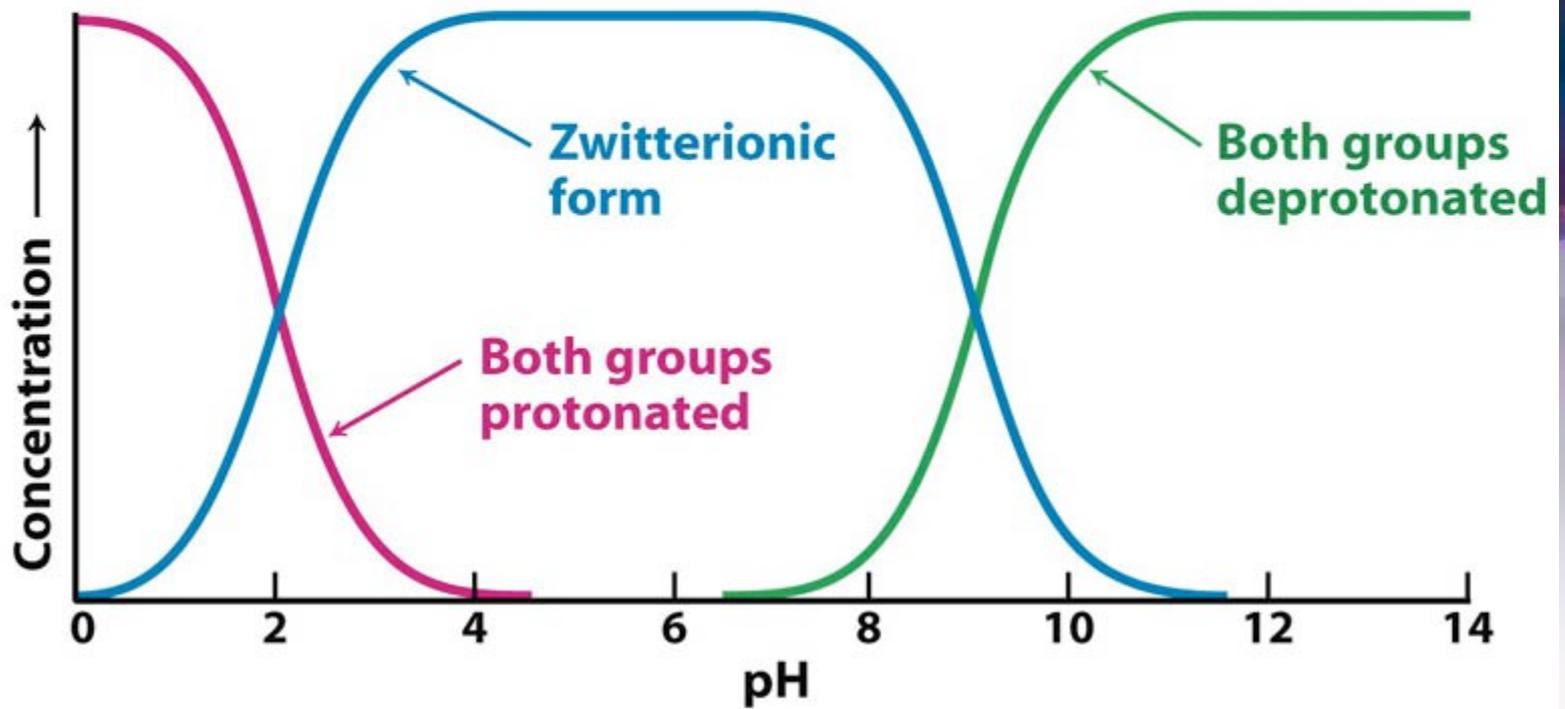
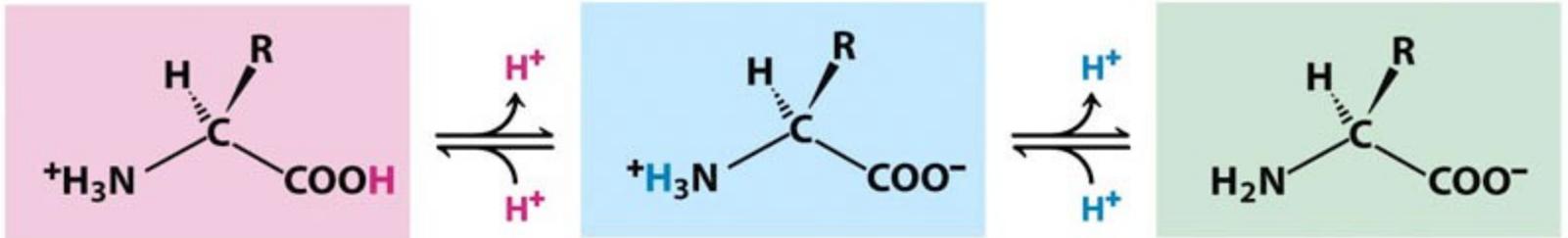




- At pH values greater than the **pKa** of the carboxylic acid group (mean for the 20 common amino acids is about 2.2)the negative carboxylate ion predominates. At pH values lower than the pKa (mean for the 20 common α -amino acids is about 9.4), the nitrogen is predominantly protonated as a positively charged α -ammonium group. Below pH 2.2, the predominant form will have a neutral carboxylic acid group and a positive α -ammonium ion (net charge +1), and above pH 9.4, a negative carboxylate and neutral α -amino group (net charge -1).



- Thus, at pH between 2.2 and 9.4, the predominant form adopted by α -amino acids contains a negative carboxylate and a positive α -ammonium group, so has net zero charge. This molecular state is known as a **zwitterion**, from the German **Zwitter** meaning *hermaphrodite* or *hybrid*.





Isomerism

- Of the standard α -amino acids, all but **glycine** can exist in either of two **optical isomers**, called L or D amino acids, which are mirror images of each other. While L-amino acids represent all of the amino acids found in **proteins** during translation in the ribosome, D-amino acids are found in some proteins produced by **post translational modifications**. They are also abundant components of the **peptidoglycan cell walls** of **bacteria**, and D-serine may act as a **neurotransmitter** in the **brain**.

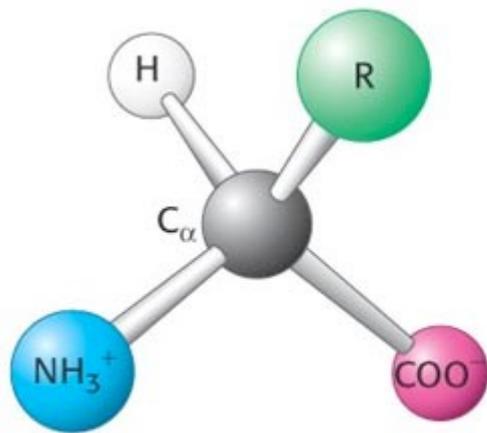


STEREISOMERISM:

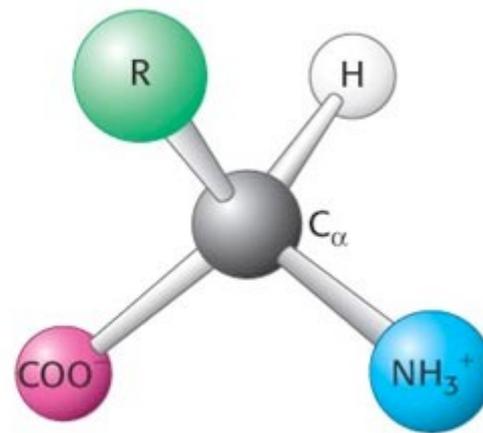
- **Stereoisomers** are **isomeric molecules** that have the same molecular formula and sequence of bonded atoms (constitution), but that differ *only* in the three-dimensional orientations of their atoms in space. This contrasts with **structural isomers**, which share the same **molecular formula**, but the bond connections and/or their order differ(s) between different atoms/groups.



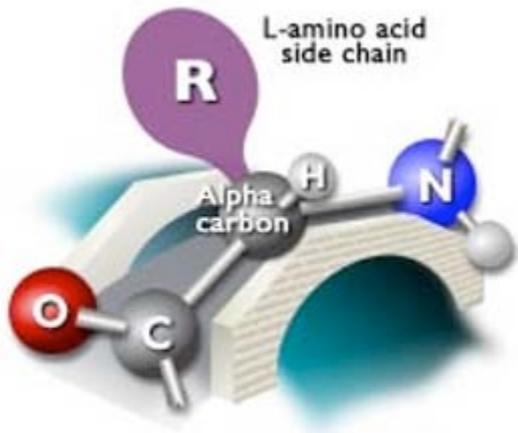
- Enantiomers are stereoisomers that are related to each other by a reflection.
- Mirror image but not superimposeable.



L isomer



D isomer





Isoelectric point

- At pH values between the two pKa values, the zwitterion predominates, but coexists in **dynamic equilibrium** with small amounts of net negative and net positive ions. At the exact midpoint between the two pKa values, the trace amount of net negative and trace of net positive ions exactly balance, so that average net charge of all forms present is zero. This pH is known as the **isoelectric point**.



- The individual amino acids all have slightly different pKa values, so have different isoelectric points. For amino acids with charged side-chains, the pKa of the side-chain is involved.



- Amino acids have zero mobility in electrophoresis at their isoelectric point, although this behaviour is more usually exploited for peptides and proteins than single amino acids. Zwitterions have minimum solubility at their isoelectric point and some amino acids (in particular, with non-polar side-chains) can be isolated by precipitation from water by adjusting the pH to the required isoelectric point.



FUNCTIONS

- **Non-protein functions**
- In humans, non-protein amino acids also have important roles as **metabolic intermediates**, such as in the biosynthesis of the **neurotransmitter gamma-aminobutyric acid**. Many amino acids are used to synthesize other molecules, for example:
 - **Tryptophan** is a precursor of the neurotransmitter **serotonin**.
 - **Tyrosine** is a precursor of the **neurotransmitter dopamine**.
 - **Glycine** is a precursor of porphyrins such as heme.



- Arginine is a precursor of nitric oxide.
- Ornithine and S-adenosylmethionine are precursors of polyamines.
- Aspartate, glycine, and glutamine are precursors of nucleotides.
- Phenylalanine is a precursor of various phenylpropanoids, which are important in plant metabolism



Protein functions

- Enzymes (catalytic proteins) *Lactase, ribonuclease, pyruvate dehydrogenase, fumarase, proteinase*
- Structural proteins *Collagen, elastin, keratin*
- Regulatory or hormonal proteins *Insulin, adrenaline*
- Transport proteins *Hemoglobin, myoglobin*
- Genetic proteins *Nucleoproteins, histones*
- Immune Proteins *Gamma Globulin, Ig's, (Ab's)*
- Contractile Proteins *Actin, myosin*
- Storage Proteins *Zein, ovalbumin, casein*