

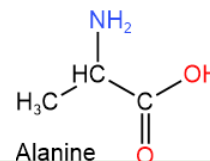
7.2: Amino acids

Learning Objectives

- Define and distinguish amino acids, α -amino acids, and proteinogenic amino acids.
- Draw Fisher projections and assign D/L or R/S stereodescriptors to proteinogenic amino acids.
- Understand the classification of proteinogenic amino acids based on the characteristics of the side chain.
- Define isoelectric point and understand the ionization states of amino acids under physiological conditions.
- Define essential amino acids and their sources.

What are amino acids?

Amino acids are the building blocks of proteins, i.e., they are the monomers of proteins. Amino acids are organic compounds that contain both an amine ($-\text{NH}_2$) and a carboxylic acid ($-\text{COOH}$) group in the same molecule. For example, alanine, shown on the right, is an amino acid. Proteins contain a subclass of amino acids called α -Amino acids.



Alpha (α)-amino acids

α -Amino acids have an amine ($-\text{NH}_2$) on the α C to $-\text{COOH}$ group, i.e., both the amine ($-\text{NH}_2$) group and the carboxylic acid ($-\text{COOH}$) group are attached to the same C. For example, alanine is an α -amino acid.

Proteinogenic amino acids

Proteinogenic amino acids are a subclass of α -amino acids incorporated into proteins during biosynthesis. Twenty proteinogenic amino acids are usually present in proteins, and two additional are included in exceptional cases. This chapter's word "amino acid" refers to the 20 standard proteinogenic amino acids.

Configuration of α C of an α -amino acids

the α C of α -amino acid have four different groups attached to it: amine ($-\text{NH}_2$), carboxylic acid ($-\text{COOH}$), hydrogen ($-\text{H}$), and alkyl side chain ($-\text{R}$, as shown in Figure 7.2.1. There is one exception "glycine" that has two H's at the α C

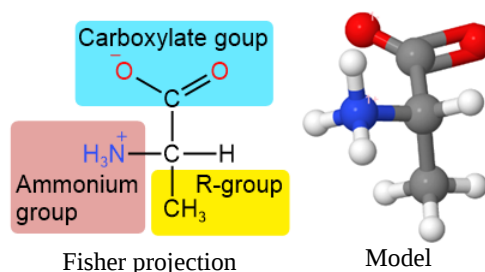


Figure 7.2.1: Fisher projection and model of an amino acid shown using alanine as an example. (Copyright; Public domain)

Three groups, i.e., $-\text{NH}_2$, $-\text{COOH}$, and $-\text{H}$ are present in all α -amino acids, and the fourth group, i.e., the side chain ($-\text{R}$) varies in different α -amino acids.

The $-\text{COOH}$ is acidic (pK_a 2-5) and the $-\text{NH}_2$ is basic (pK_a ~10). The $-\text{COOH}$ loses its proton and exists as a carboxylate ion ($-\text{COO}^-$); the $-\text{NH}_2$ gains a proton and exists as ammonium ion ($-\text{NH}_3^+$) at physiological pH of 7.4. These groups ionize the same way if present in the side chain in addition to the α C.

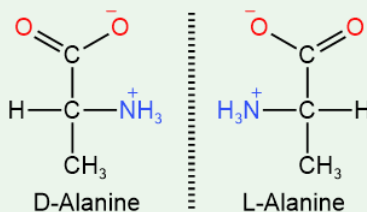
Zwitterions

Compounds that have a positive charge on one atom and a negative charge on another atom in the same molecule are called **zwitterions**. Most of the α -amino acids usually exist as zwitterions at physiological pH, as shown in Figure 7.2.1.

A C with four different groups is a chiral center. α C of α -amino acids is a chiral center at α C, with one exception, "glycine" that has two H's at the α C. α -Amino acids are presented in Fisher projections with the C-chain placed vertically and the $-\text{NH}_2$ and $-\text{H}$ bonds shown horizontally, as shown in Figure 7.2.1.

D- and L-configurations of α -amino acids

The α -amino acids that have their $-\text{NH}_2$ group placed to the left side of their Fisher projections are called D-amino acids, and those having $-\text{NH}_2$ group placed to the right side are called L-amino acids. The D- and the corresponding L-amino acids are enantiomers, as shown in the figure below for the case of alanine.



Proteinogenic amino acids are L-amino acids, with the exception of glycine, which is not chiral. In the R/S system, proteinogenic amino acids are (S) at the α C, with the exception of "cysteine" being (R) and glycine not chiral.

The α -amino acids are known by their common names, which are also abbreviated in three letters and one letter, as shown in Figure 7.2.2. For example, Alanine is abbreviated as Ala in three letters or as A in one letter form. The proteinogenic amino acids are classified based on the nature of the side chain.

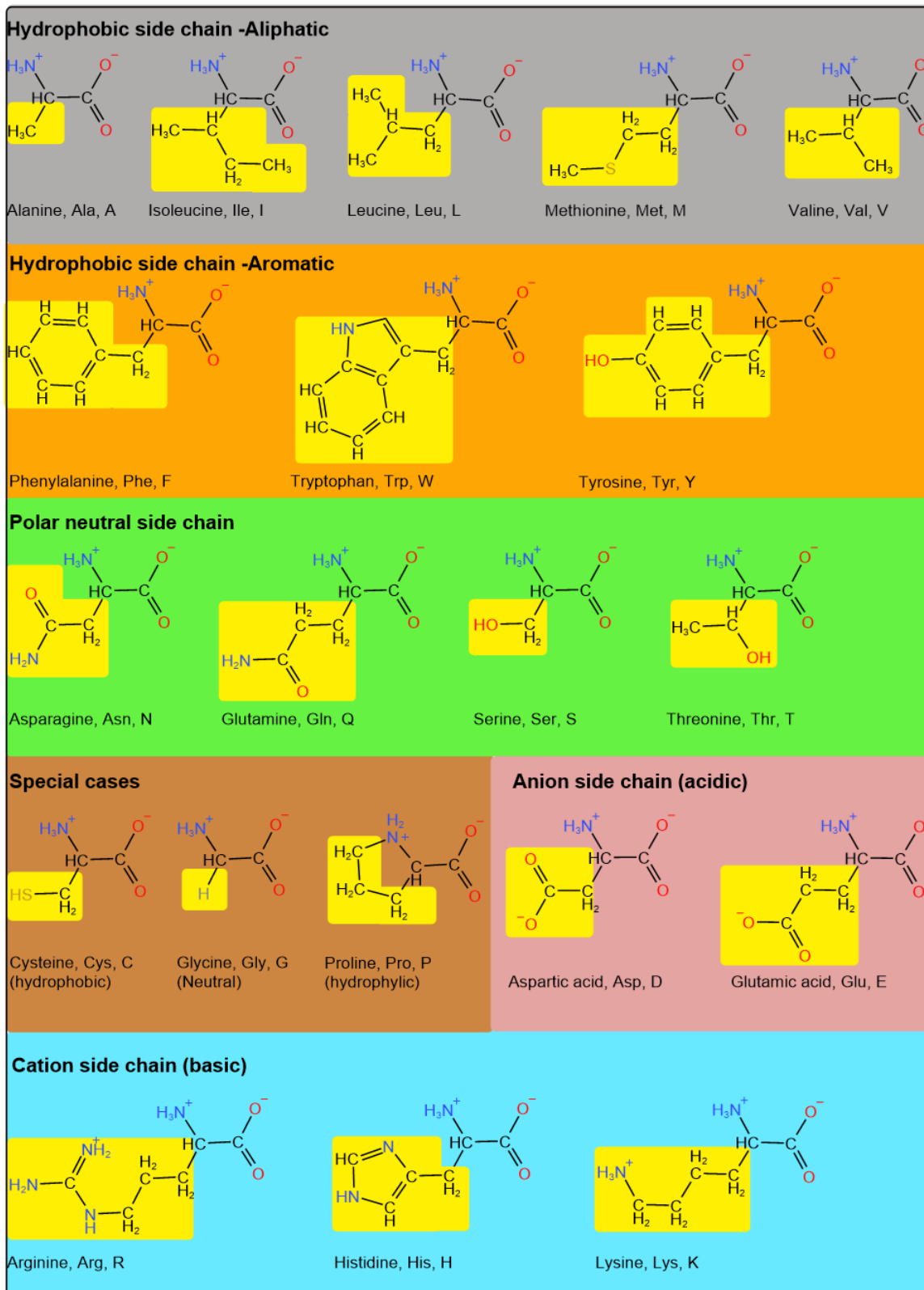


Figure 7.2.2: Structures of proteinogenic amino acids are shown in their zwitterionic forms with side chain protonation states determined at physiological pH of 7.4. Names, three-letters, and one-letter abbreviations are also shown. The alkyl side chains are highlighted in yellow color boxes. (Copyright; Public domain)

Classification of proteinogenic amino acids

α -Amino acids are classified based on the hydrophobicity of their side chain.

Hydrophobic and hydrophilic

Hydrophobic means "water fearing", i.e., molecules or entities that tend to repel water, not dissolve, or not wetted by water.

Hydrophilic means "water-loving", i.e., molecules or entities that tend to mix with, dissolve, or be wetted by water.

Hydrocarbons and other non-polar compounds are hydrophobic compounds that do not dissolve in water. Polar or ionic compounds are usually soluble in water. Based on these criteria, amino acids are classified into the following classes, shown in Figure 7.2.2.

- Nonpolar amino acids with an **aliphatic side chain** are hydrophobic. Methionine having a thioether group in the side chain is non-polar and placed in this group.
- Nonpolar amino acids with an **aromatic side chain** are hydrophobic. Tyrosine has phenol as part of its side chain, but it is hydrophobic and placed in this group.
- Polar neutral amino acids with a **polar neutral side chain** are hydrophilic. This class of side chain contains alcohol ($-\text{OH}$) or amide $-\text{CONH}_2$ groups in their side chain that hydrogen bond with water but do not ionize.
- Amino acids in a special class include cysteine, glycine, and proline.
 - Speciality of cysteine is that its thiol $\{ce-SH$ group is easily oxidized forming a disulfide ($\text{S}-\text{S}$ bond, which is the only covalent bond in protein besides the amide bonds. Cysteine is classified as nonpolar and hydrophobic because $\{ce-SH$ is a nonpolar group.
 - Glycine is the only proteinogenic acid that has no chiral center. The $-\text{H}$ side chain places it at a borderline between hydrophilic and hydrophobic categories, it is considered neutral.
 - Proline is the only amino acid with a secondary α -amine group. The side chain is a five member ring with N of α -amine as part of the ring. It is classified as a hydrophilic. The ring structure puts restrictions on the allowed configurations when it is incorporated in proteins. It creates a bent or kink in the protein backbone structure.
- Acidic amino acids with an **acidic side chain** are hydrophilic. These amino acids have carboxylic acid ($-\text{COOH}$) group in their side chain that ionize to anion $-\text{COO}^-$ under physiological conditions.
- Basic amino acids with a **basic side chain** are hydrophilic. These amino acids have basic primary or secondary amine groups in their side chain that ionize to cation $-\text{NH}_3^+$ or $-\text{NRH}_2^+$. Histidine has an amine group that has pK_a 6.04 and is not ionized at pH 7.4, but it is placed in this group as it ionizes at pH below 6.0.

Acid-base nature of α -amino acids

The pK_a is a measure of the strength of an acid, i.e., the lower the pK_a stronger the acid. Amino acids have $-\text{COOH}$ group that is acidic with pK_a 2-3 and $-\text{NH}_2$ on adjacent C that is basic with $\text{pK}_a \sim 4$. Conjugate acid of $-\text{NH}_2$, i.e., $-\text{NH}_3^+$ has $\text{pK}_a \sim 10$. Acids lose their proton when they are in a medium with a pH higher than the pK_a of the acid. For example $-\text{COOH}$ exist as $-\text{COO}^-$ in physiological medium with pH ~ 7.4 . Bases gain protons in a medium with a pH lower than the pK_a of their conjugate acid. For example, $-\text{NH}_2$ exist as $-\text{NH}_3^+$ in physiological medium with pH ~ 7.4 . Amino acids exist as zwitterions, i.e., have both cation $-\text{NH}_3^+$ and anion $-\text{COO}^-$ in the same molecule. Some amino acids have an additional acid or base group in their side chain that also ionizes depending on the pH of the medium.

The gain or loss of protons is an equilibrium process. In a strongly acidic medium, basic groups gain more protons than the protons lost by their acid groups. So, the amino acids have an overall positive charge in a strong acid medium. In a strongly basic medium basic groups gain fewer protons than those lost by their acid groups. So, the amino acids have an overall negative charge in a strongly basic medium. At a certain pH in the middle, an amino acid has an equal positive and negative charge and is neutral overall.

Isoelectric point (pI)

An amino acid's **isoelectric point (pI)** is the pH at which it has equal positive and negative charges and carries no net charge, i.e., it is neutral overall.

The pK_a value of $-\text{COOH}$ and $-\text{NH}_3^+$ on the $\alpha\text{-C}$, pK_a values of acidic or basic groups in the side chain, and pI values of 20 α -amino acids found in proteins are listed in Table 1 below.

Table 1: Names, three-letters, and one-letter abbreviations, pK_a values of alpha-carboxylic acid and ammonium groups, pK_a values of acid groups in the side chain, and isoelectric point (pI) of 20 amino acids found in proteins. (Reference: D.R. Lide, *Handbook of Chemistry and Physics*, 72nd Edition, CRC Press, Boca Raton, FL, 1991)

Amino acid	Three letters abbreviations	One letter abbreviations	pK_a of $\alpha\text{-COOH}$	pK_a of $\alpha\text{-NH}_3^+$	pK_a of side chain group	Isoelectric point (pI)
Alanine	Ala	A	2.34	9.69	–	6.00
Arginine	Arg	R	2.17	9.04	12.48	10.76
Asparagine	Asn	N	2.02	8.80	–	5.41
Aspartic acid	Asp	D	1.88	9.60	3.65	2.77
Cysteine	Cys	C	1.96	10.28	8.18	5.07
Glutamic acid	Glu	E	2.19	9.67	4.25	3.22
Glutamine	Gln	Q	2.17	9.13	–	5.65
Glycine	Gly	G	2.34	9.60	–	5.97
Histidine	His	H	1.82	9.17	6.00	7.59
Isoleucine	Ile	I	2.36	9.60	–	6.02
Leucine	Leu	L	2.36	9.60	–	5.98
Lysine	Lys	K	2.18	8.95	10.53	9.74
Methionine	Met	M	2.28	9.21	–	5.74
Phenylalanine	Phe	F	1.83	9.13	–	5.48
Proline	Pro	P	1.99	10.60	–	6.30
Serine	Ser	S	2.21	9.15	–	5.68
Threonine	Thr	T	2.09	9.10	–	5.60
Tryptophan	Trp	W	2.83	9.39	–	5.89
Tyrosine	Tyr	Y	2.20	9.11	10.07	5.66
Valine	Val	V	2.32	9.62	–	5.96

Essential amino acids

Nine amino acids are essential because humans can not synthesize them fast enough to meet their demands.

The **essential amino acids** are valine, isoleucine, leucine, methionine, phenylalanine, tryptophan, threonine, histidine, and lysine.

The essential amino acids are obtained from foods. Foods from animal sources, e.g., eggs, milk, fish, meat, etc., are complete foods with all the essential amino acids. Foods from plant sources, e.g., wheat, rice, corn, etc., are usually deficient in one or more essential amino acids. So, vegetarians have to eat various vegetarian foods to obtain all the essential amino acids.

Deficiency of essential amino acids in different foods

- Wheat, rice, and oats are deficient in lysine.
- Corn is deficient in lysine and tryptophan.
- Soy is deficient in methionine.
- Beans are deficient in methionine and tryptophan.
- Peas and peanuts are deficient in methionine
- Almonds and walnuts are deficient in lysine, tryptophan
- Foods from animal sources, e.g., milk, eggs, meat, fish, etc., have all the essential amino acids.

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