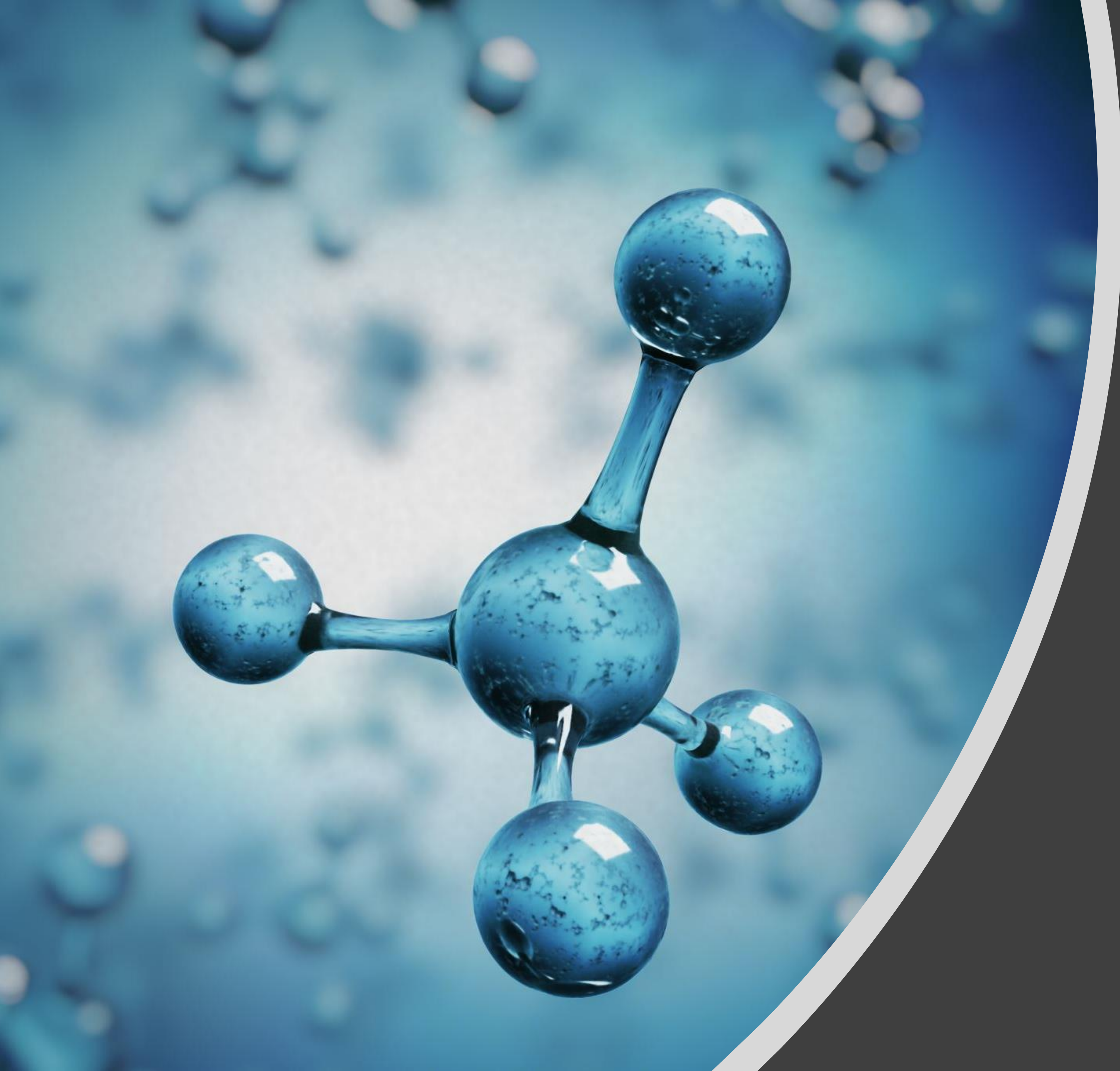

Amino Acids, Classification, Chemical Nature, Physical Properties

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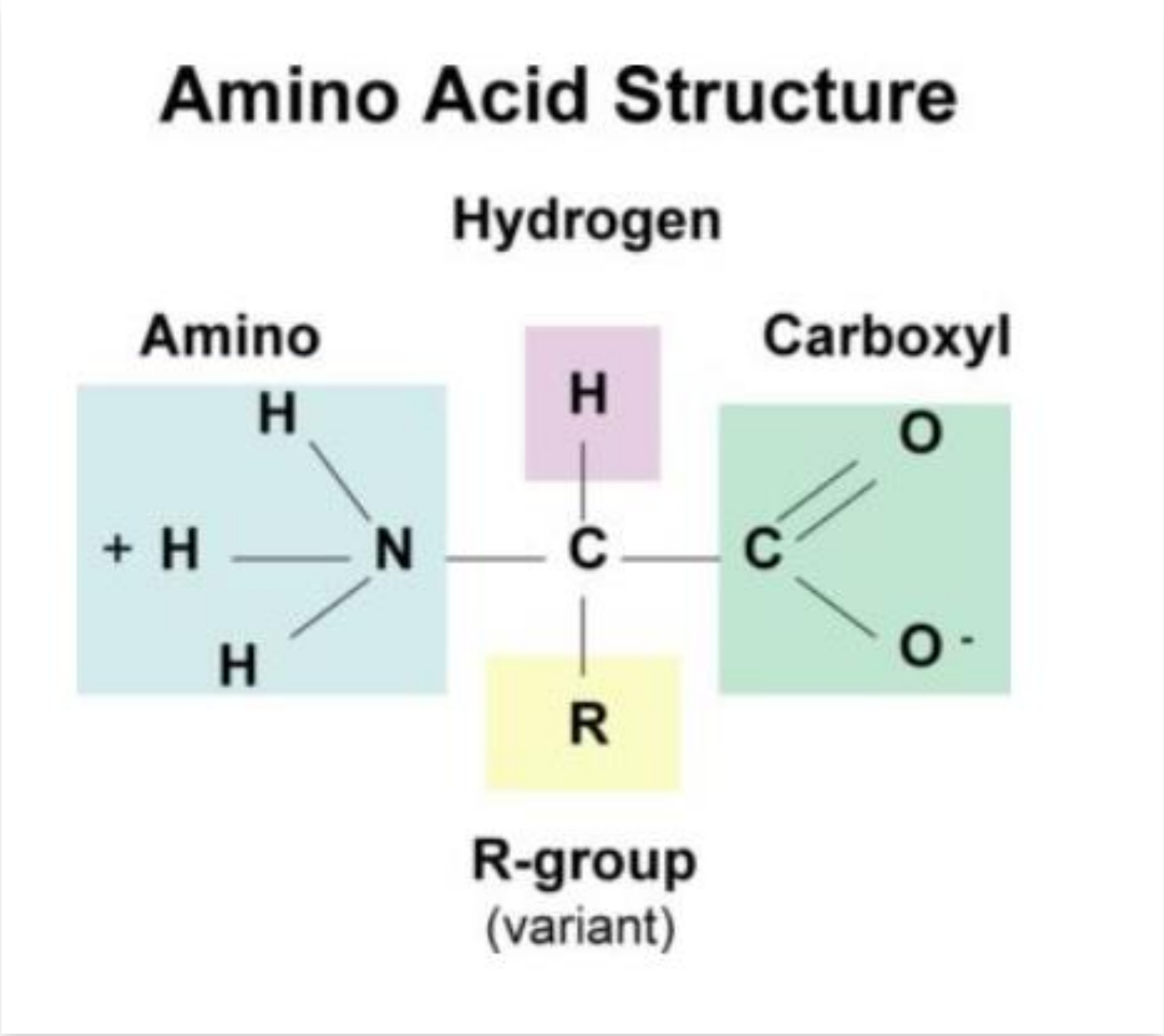
Amino acids

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 of Amino Acids



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 two **selenocysteine** and **pyrrolysine** are incorporated into proteins by unique synthetic mechanisms.

Selenocysteine is incorporated when the mRNA being translated includes SECIS.

Nomenclature of Amino Acids

- All amino acids have trivial names
- E.g. **NH2CH2COOH** is better known as **glycine** rather then **α-amino acetic acid** or **2-amino ethanoic acid.**
- These **trivial names usually reflects 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 elimination of water molecule is called a peptide bond
- The product formed by linking amino acid molecules through peptide linkages,-CO-NH-, is called a peptide

Classification

Amino acids are classified into different ways on **polarity, structure, nutritional requirements, metabolic fate etc.**

Generally used classification is based on polarity.

Classification on Polarity basis

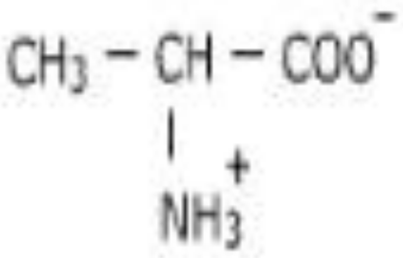
- Based on polarity, amino acids are classified into four groups as follows
- **Non-polar amino acids**
- **Polar amino acids with no charge**
- **Polar amino acids with positive charge**
- **Polar amino acids with negative charge**

Non-Polar Amino Acids

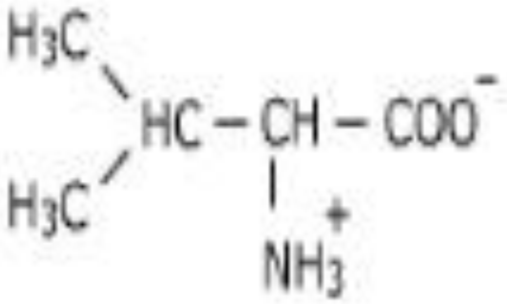
Non-Polar Amino acids have equal number of amino and carboxyl groups and are neutral.

These amino acids are **hydrophobic** and have **no charge on the "R" group.**

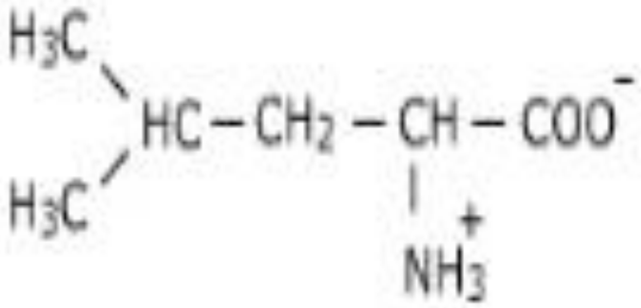
The amino acids in this group are **alanine, valine, leucine, isoleucine, phenyl alanine, glycine, tryptophan, methionine** and **proline.**



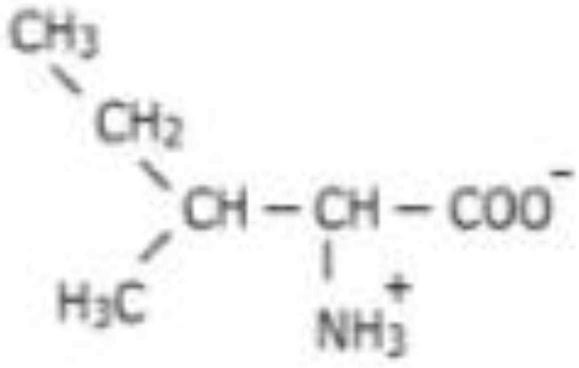
Alanine



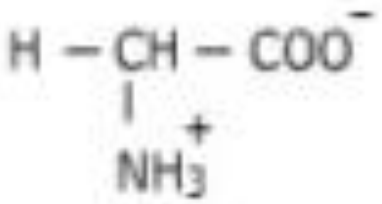
Valine



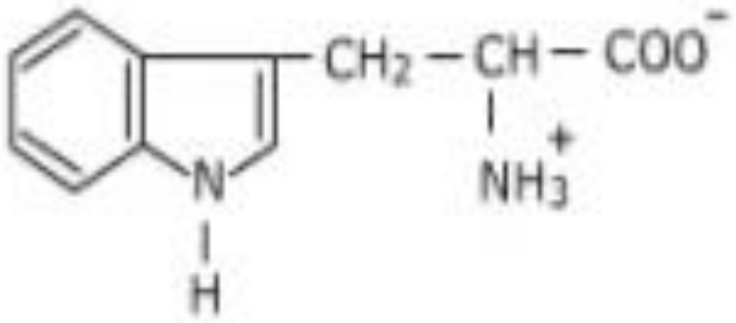
Leucine



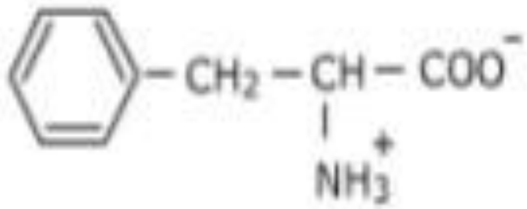
Isoleucine



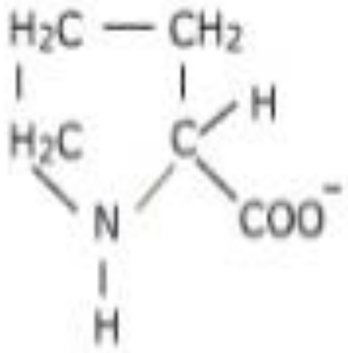
Glycine



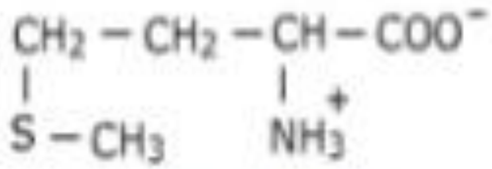
Tryptophan



Phenyl alanine



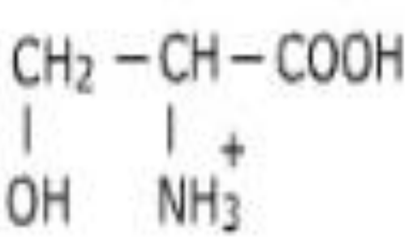
Proline



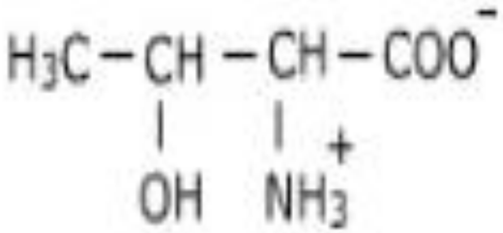
Methionine

Polar Amino Acids with no Charge

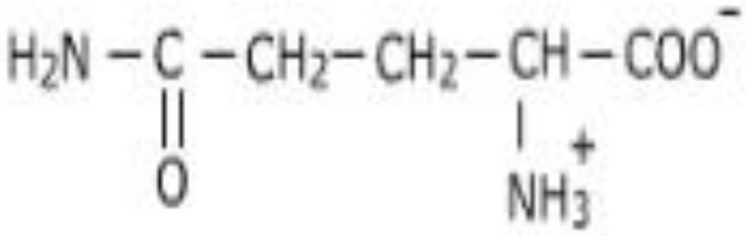
- These amino acids **do not have any charge on the "R" group**.
- These amino acids **participate in hydrogen bonding of protein** structure.
- The amino acids in this group are **serine, threonine, tyrosine, cysteine, glutamine** and **aspargine.**



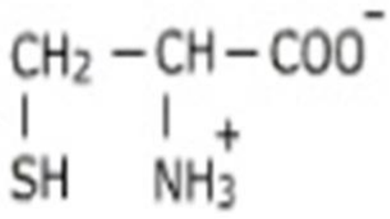
Serine



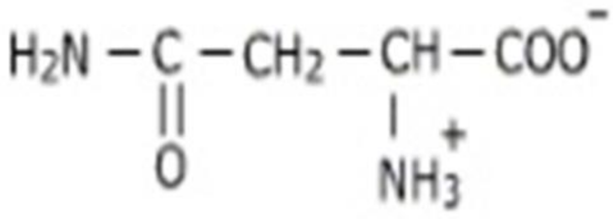
Threonine



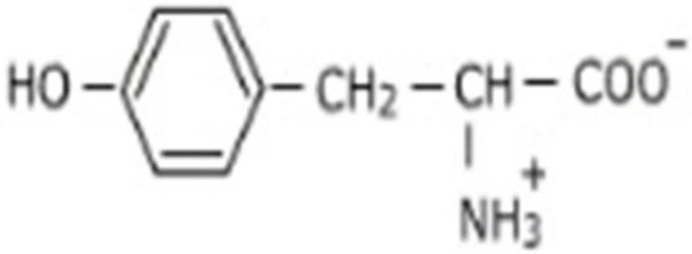
Gultamine



Cysteine



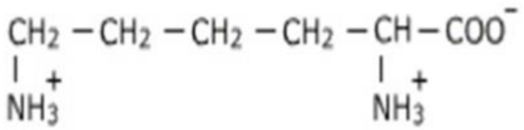
Aspargine



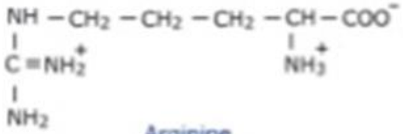
Tyrosine

Polar Amino Acids with Positive Charge

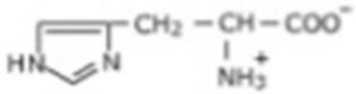
- Polar amino acids with **positive charge have more amino groups as compared to carboxyl group making it basic**.
- The amino acids, which have **positive charge** on the **“R”** group are placed in this category.
- They are **lysine, arginine** and **histidine.**



Lysine



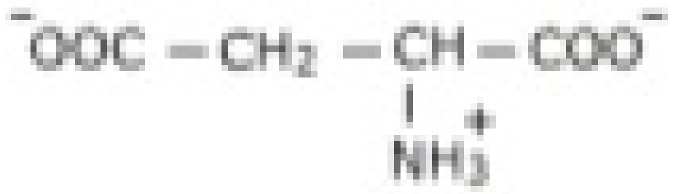
Arginine



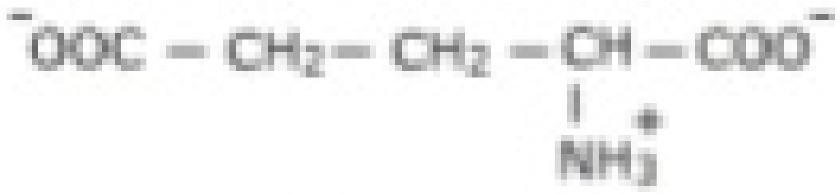
Histidine

Polar Amino Acids with Negative Charge

- Polar amino acids with **negative charge have more carbon 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.**



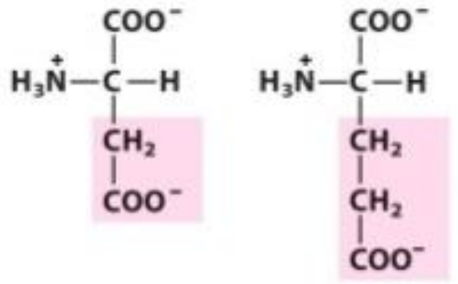
Aspartic acid



Glutamic acid

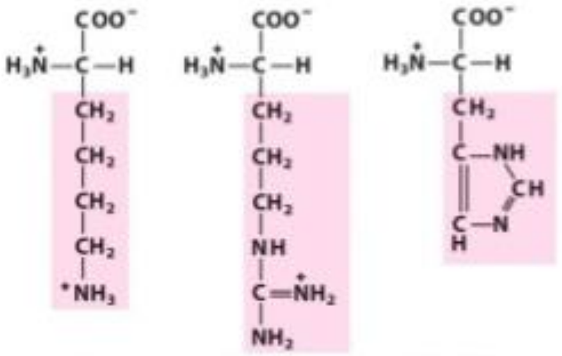
Acidic and Basic Amino Acids

- 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

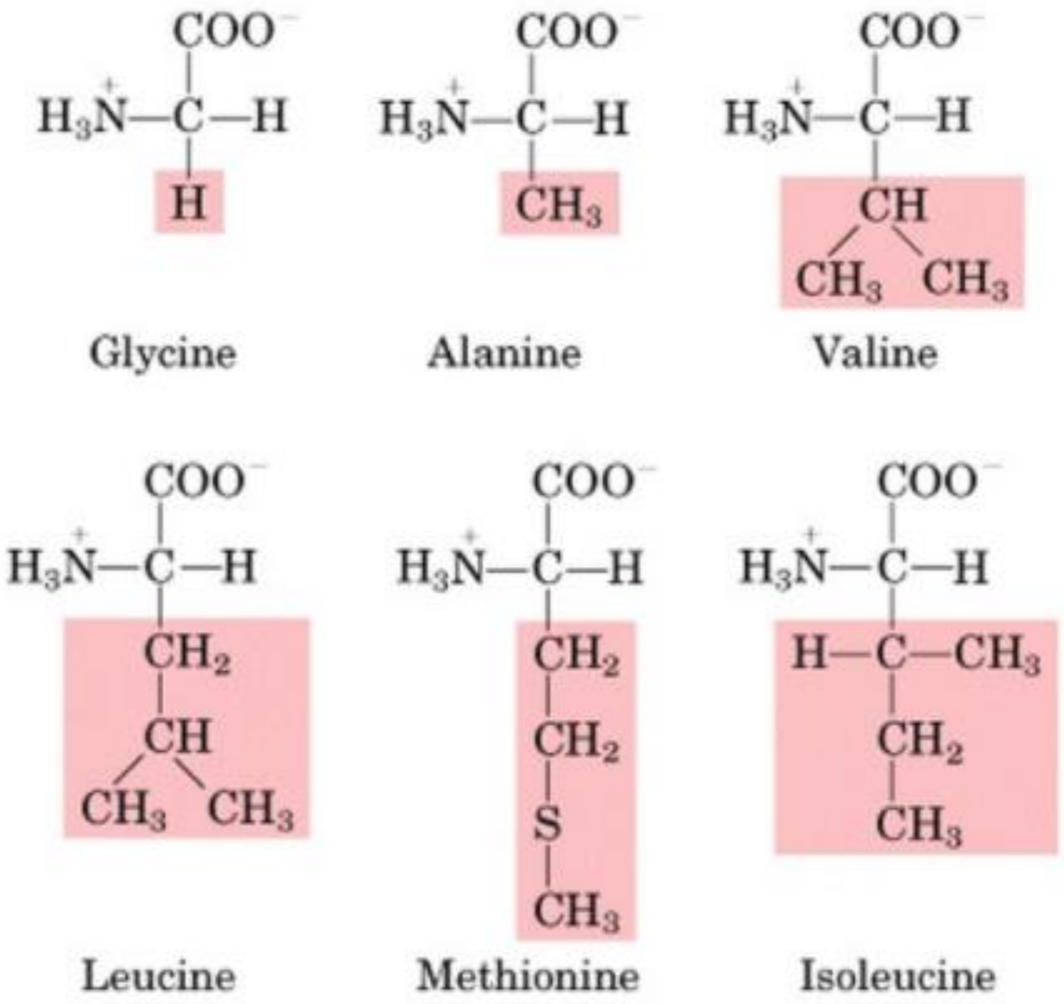
Classification on side chain basis

- 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

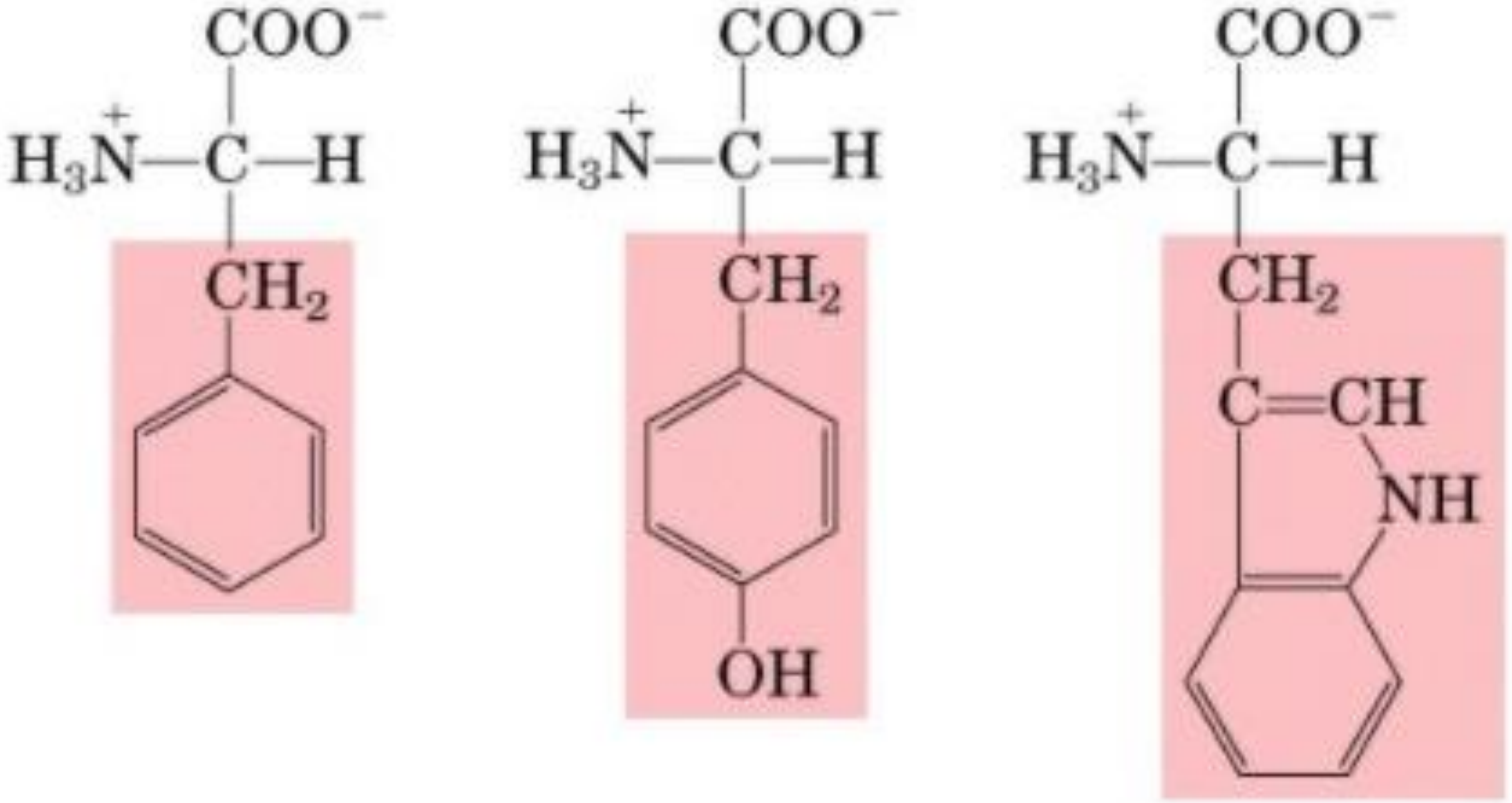
Classification of amino acids based on R-group

- **Nonpolar, Aliphatic amino acids**: The R groups in this class of amino acids are nonpolar and hydrophobic. **Glycine, Alanine, Valine, leucine, Isoleucine, Methionine, Proline.**
- **Aromatic amino acids: Phenylalanine, tyrosine,** and **tryptophan,** with their aromatic side chains, are relatively nonpolar (hydrophobic). All can participate in hydrophobic interactions.
- **Polar, Uncharged amino acids:** The R groups of these amino acids are more soluble in water, or more hydrophilic, than those of the nonpolar amino acids, because they contain functional groups that form hydrogen bonds with water. This class of amino acids includes **serine, threonine, cysteine, asparagine,** and **glutamine.**
- **Acidic amino acids**: Amino acids in which R-group is acidic or negatively charged. **Glutamic acid** and **Aspartic acid**
- **Basic amino acids**: Amino acids in which R-group is basic or positively charged. **Lysine, Arginine, Histidine**

Nonpolar, aliphatic R groups

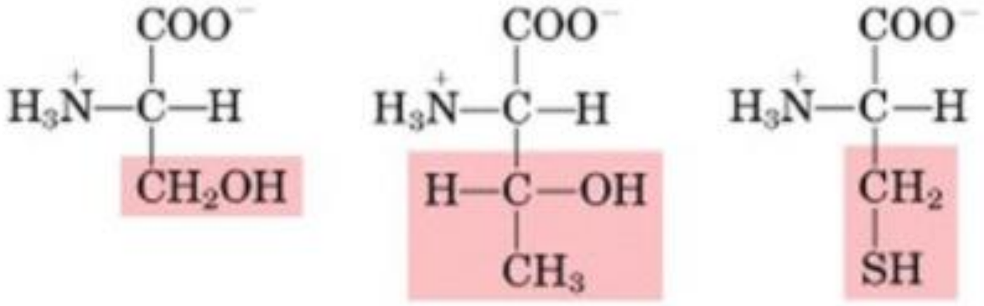


Aromatic R groups

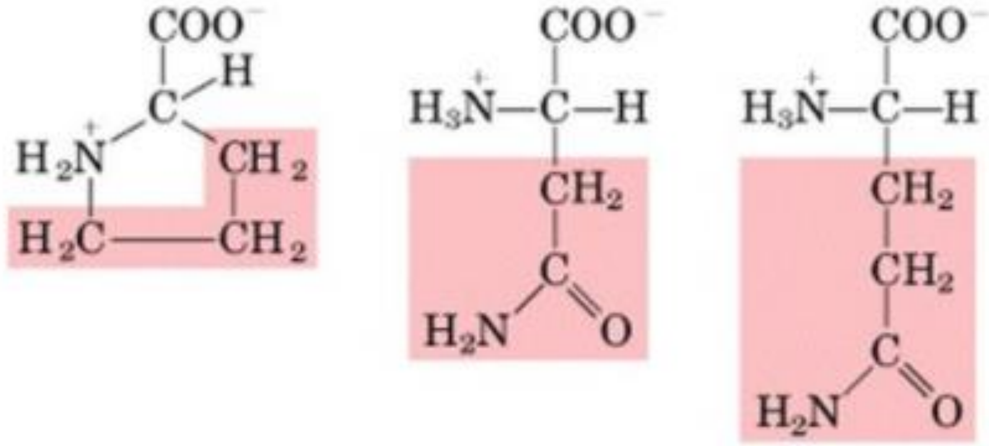


Phenylalanine Tyrosine Tryptophan

Polar, uncharged R groups

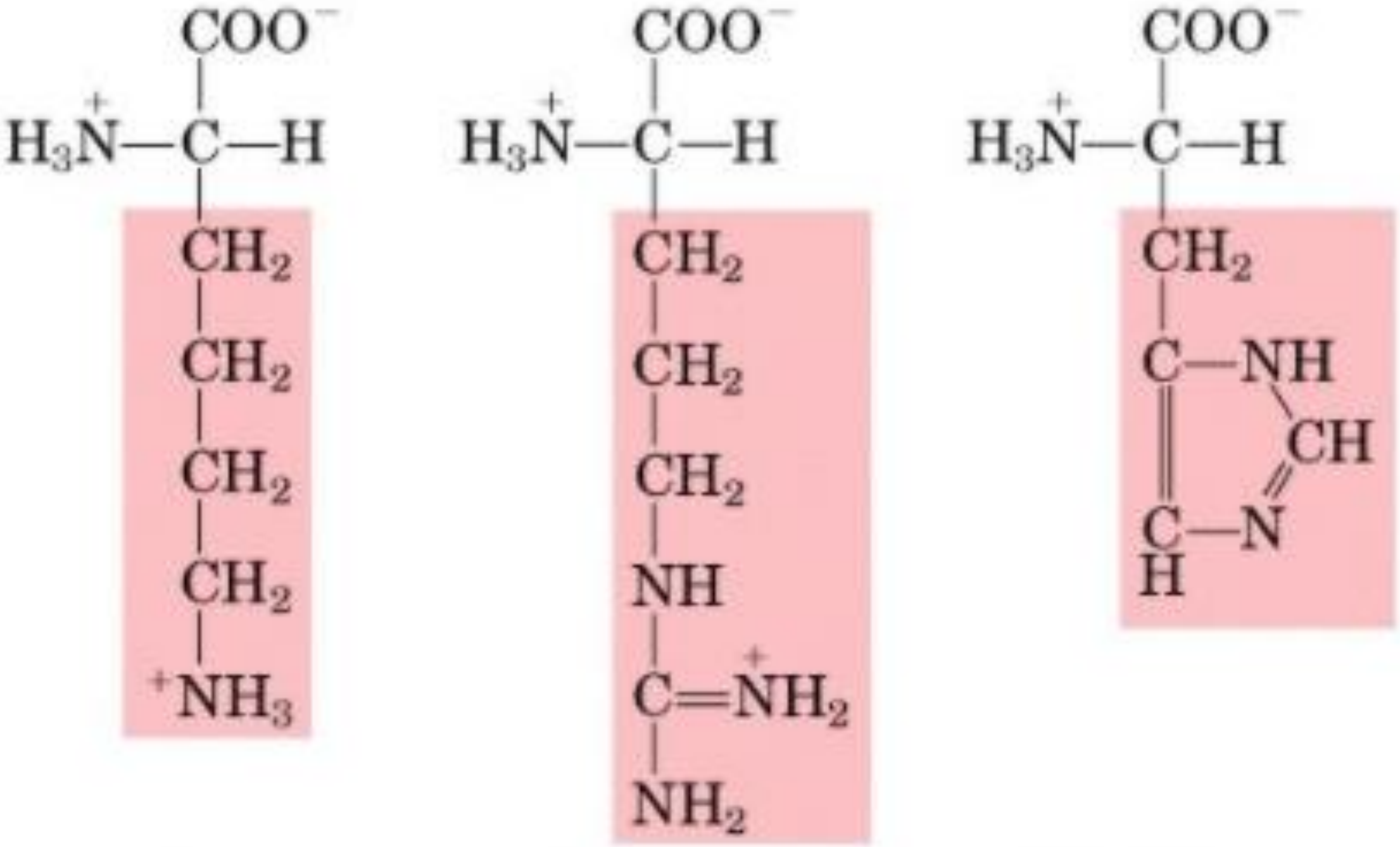


Serine | Threonine | Cysteine



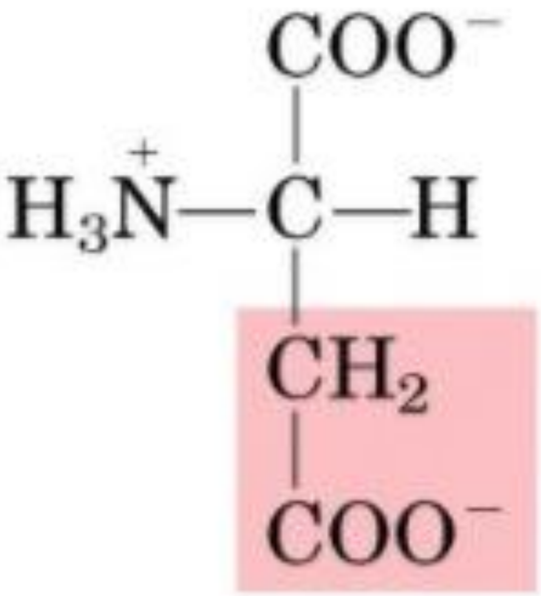
Proline | Asparagine | Glutamine

Positively charged R groups

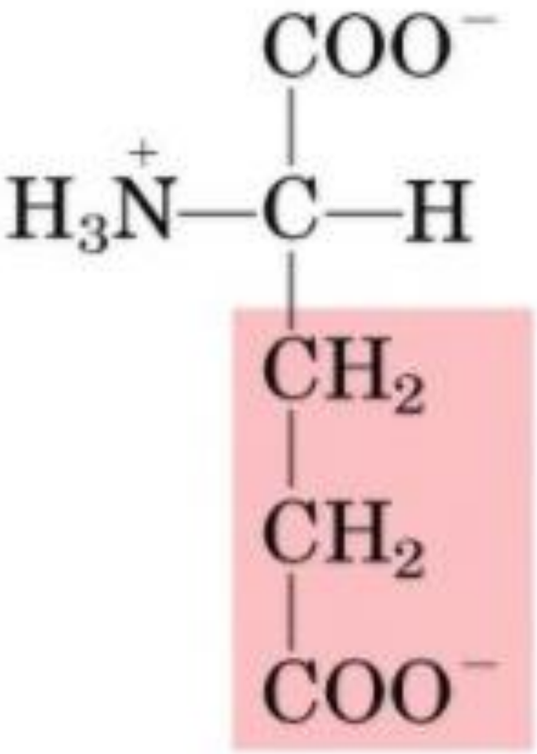


Lysine Arginine Histidine

Negatively charged R groups



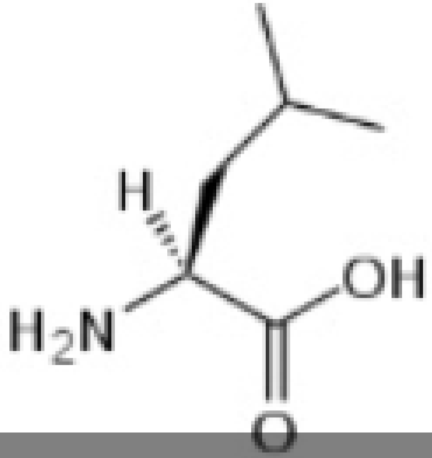
Aspartate



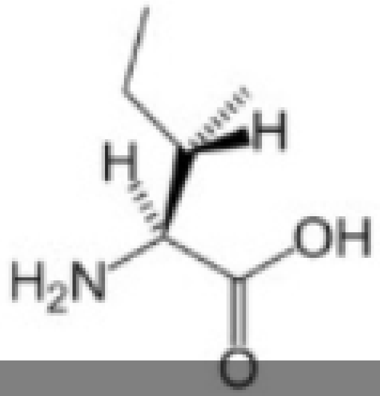
Glutamate

Branched Chain Amino Acid (BCAA)

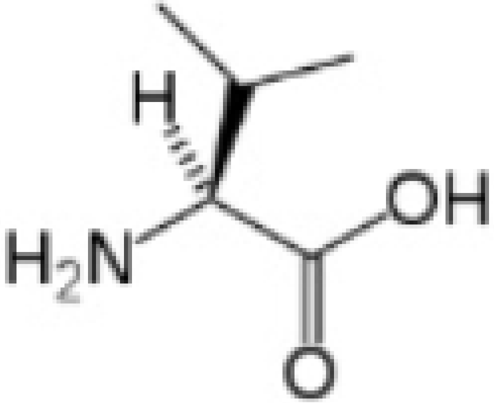
- A branched chain amino acid (BCAA) is an **amino acid having aliphatic side chains with a branch** i.e. carbon atom bound to more than two other carbon atoms. Among the proteinogenic amino acids, there are three BCAAs: **Leucine, isoleucine** and **valine**.



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 performed 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 other 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

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	Conditionally Non-Essential	Non-Essential
Histidine	Arginine	Alanine
Isoleucine	Cystine	Asparagine
Leucine	Glutamine	Aspartate
Lysine	Glycine	Glutamate
Methionine	Proline	Serine
Phenylalanine	Tyrosine	
Threonine		
Tryptophan		
Valine		

Classification of amino acids based on the metabolic fate

- **Glucogenic amino acids**: These amino acids serve as precursors gluconeogenesis for glucose formation. Glycine, alanine, serine, aspartic acid, asparagine, glutamic acid, glutamine, proline, valine, methionine, cysteine, histidine, and arginine.
- **Ketogenic amino acids**: These amino acids breakdown to form ketone bodies. Leucine and Lysine.
- **Both glucogenic and ketogenic amino acids**: These amino acids breakdown to form precursors for both ketone bodies and glucose. Isoleucine, Phenylalanine, Tryptophan, and tyrosine.

Glucogenic amino acids	Glucogenic and ketogenic	Ketogenic amino acids
Alanine, Arginine, Asparagine, Aspartate Asparagine, Cysteine, Methionine Glutamate, Glutamine, Glycine, Histidine Proline, Serine, Threonine,Valine	Tyrosine Isoleucine Phenylalanine Tryptophan	Leucine Lysine

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, phenyalanine, threonine and tryptophan.

Non-essential Amino Acids

- The amino acids that **can be synthesize by the body** are called non-essential amino acids.
- They are: **Glycine, alanine, serine, cysteine, aspartic acid, glutamic acid, aspargine, 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	Alanine	N.A.
Arginine	Arg	R	aRginine	~12
Aspartate	Asp*	D	asparDic acid	~4
Asparagine	Asn*	N	asparagiNe	N.A.
Cysteine	Cys	C	Cysteine	~8.5
Glutamate	Glu**	E	gluEtamic acid	~4
Glutamine	Gln**	Q	Q-tamine	N.A.
Glycine	Gly	G	Glycine	N.A.
Histidine	His	H	Histidine	~6.5
Isoleucine	Ile	I	Isoleucine	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 n**on-proteinogenic** or **non-standard** . Those either **are not found in protein** (for example **caritine**, 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.**

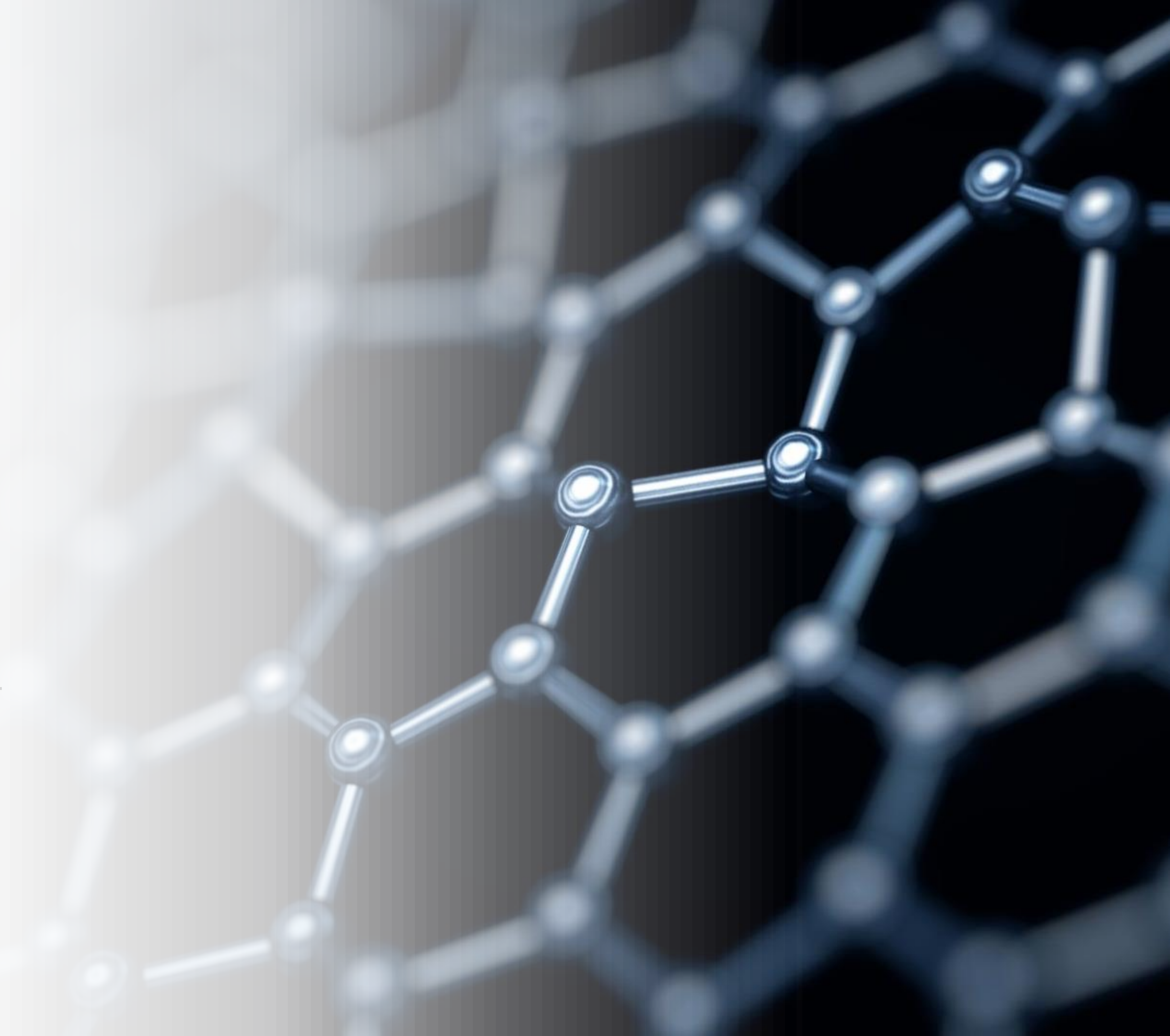
- **Some nonstandard amino acids are not found in proteins.** Examples include **lanthionine, 2-aminoisobutaric acid** and the neurotransmitter **gamma-aminobutaric acid.**
- Non-standard amino acids occur as **intermediates in the metabolic pathways** for standard amino acids-for example, **ornithine** 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-amino propanoic acid)**, which is used in plants and microorganisms in the **synthesis of pantothenic acid (Vitamin B5), a component of coenzyme A**

Example of Non-standard Amino Acids

- Citrulline
- Ornithine
- Arginosuccinic acid
- Beta alanine
- Panthothenic acid
- GABA
- DOPA
- Homocysteine
- Iodinated amino acids: MIT,DIT,T3 &T4

PROPERTIES OF AMINO ACIDS

Physical properties



Physical properties of Amino Acids

- Amino acids are colorless, crystalline solid.
- All amino acids have a high melting point greater than 200˚C
- **Solubility:** They are soluble in water, slightly soluble in alcohol and dissolve with difficulty in methanol, ethanol, and propanol. R-group of amino acids and pH of the solvent play important role in solubility.
- On heating to high temperatures, they decompose.
- All amino acids (except glycine) are optically active.
- **Peptide bond formation:** Amino acids can connect with a peptide bond involving their amino and carboxylate groups. A covalent bond formed between the alpha-amino group of one amino acid and an alpha-carboxyl group of other forming -CO-NH-linkage. Peptide bonds are planar and partially ionic.

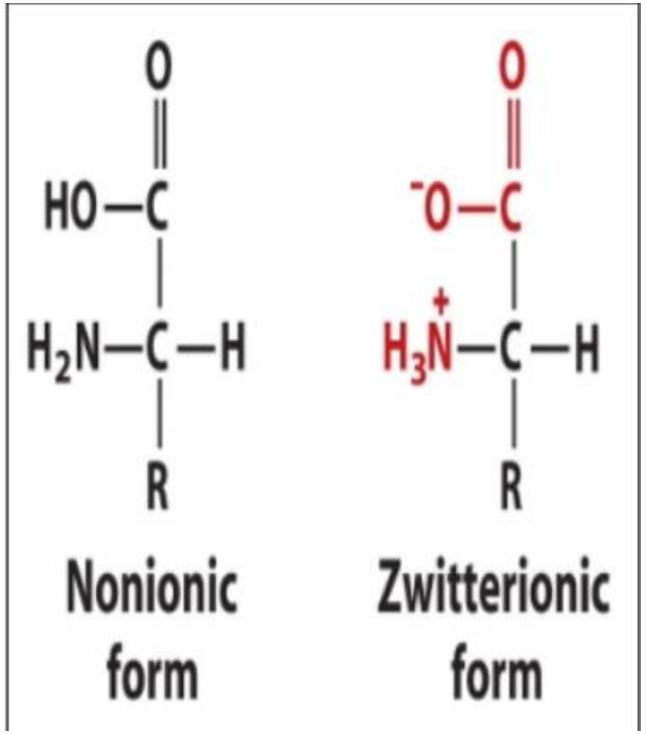
Chemical Properties

Amphoteric nature and Zwitterion formation

Since Amino acids contain both carboxyl and an amino group they can react with acids and bases to form salts.

Such compounds are called **amphoteric compounds** or **ampholites**

Zwitterions



- Carboxylic acid groups(-COOH) can be **deprotonated to become negative carboxylates (COO-)** and **α-amino groups (NH2) can be protonated to become positive α-ammonium groups (+NH3)**
- Both the –NH2 and the –COOH groups in an amino acid **undergo ionization in water.**
- At **physiological pH(7.4) a Zwitterion forms** i.e.

  Both + and – charges

  Overall neutral

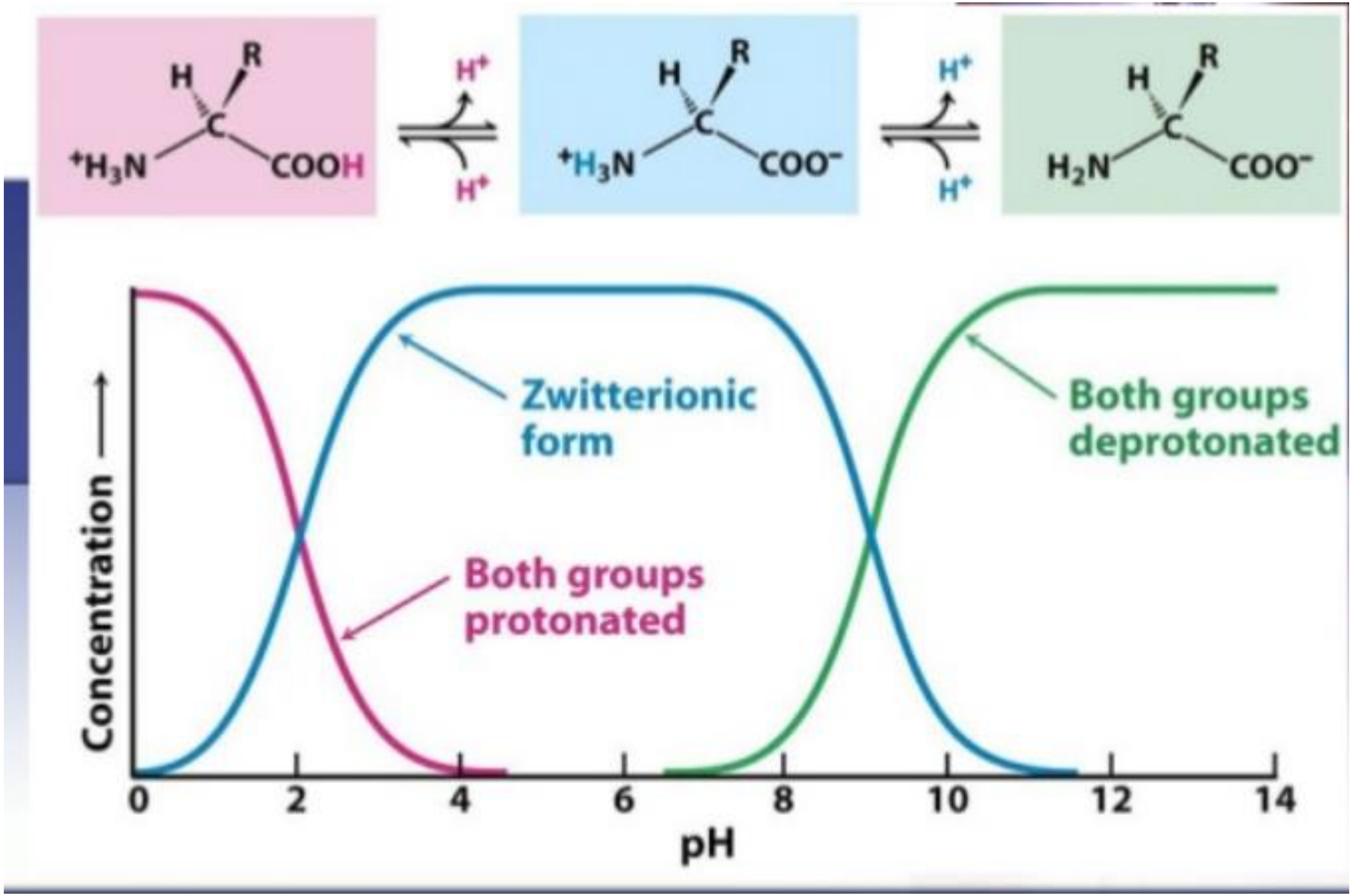
  Amphoteric

  ***Amino group is protonated**

  ***Carboxyl group is deprotonated**
- Soluble in polar solvents due to ionic character
- Structure of R also influence solubility

Acid-base Properties

- Amino acids have multiple pKa’ s due to multiple ionizable
- At **pH value greater than the pKa** of the carboxylic acid group the **negative carboxylate ion predominates**.
- At **pH values lower than the pKa**, 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-amino group, so has net zero charge.** This molecular state is known as **a Zwitterion**, (German, ion of both kind) or dipolar ion)



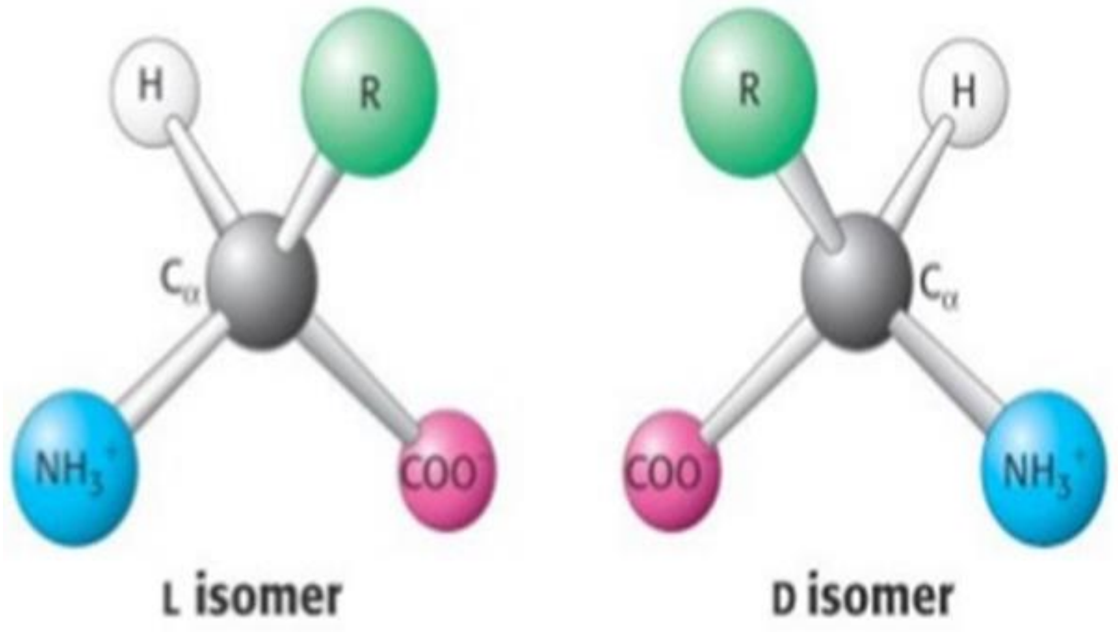
H
R
C
+H3N
COOH
H+
H+
H
R
C
+H3N
COO−
H+
H+
H
R
C
H2N
COO−
Zwitterionic
form
Both groups
deprotonated
Both groups
protonated
Concentration
0
2
4
6
8
10
12
14
pH

Isomerism

- Of the standard α- amino acids, all but **glycine** can exist in **either two optical isomers,** called **L or D amino acids, which are mirror image 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.

Sterioisomerism

- 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 atom in space.**
- This contrast 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 super imposable



Isoelectric Point

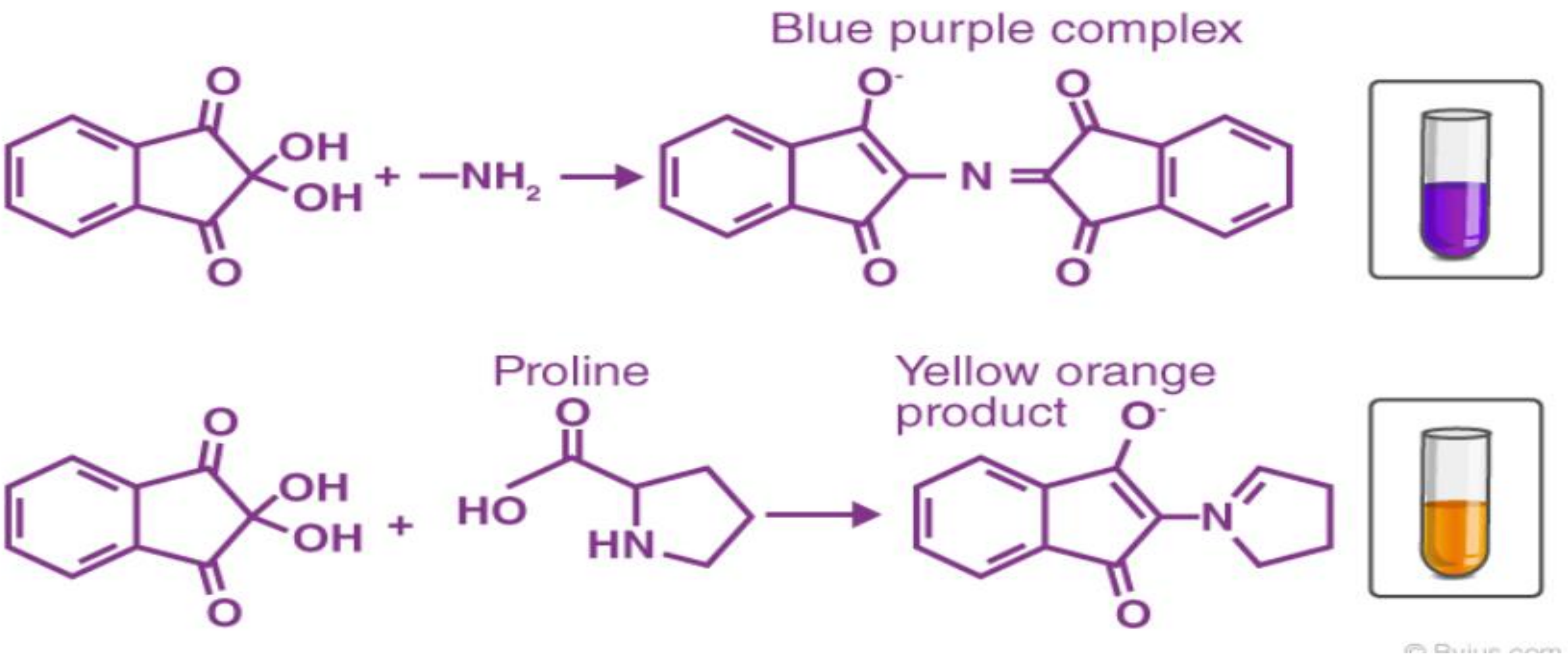
At **pH value** between the two pKa values the **zwitterion pre-dominates but coexists in dynamic equilibrium with small amount of net negative and net positive ions.**

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.**

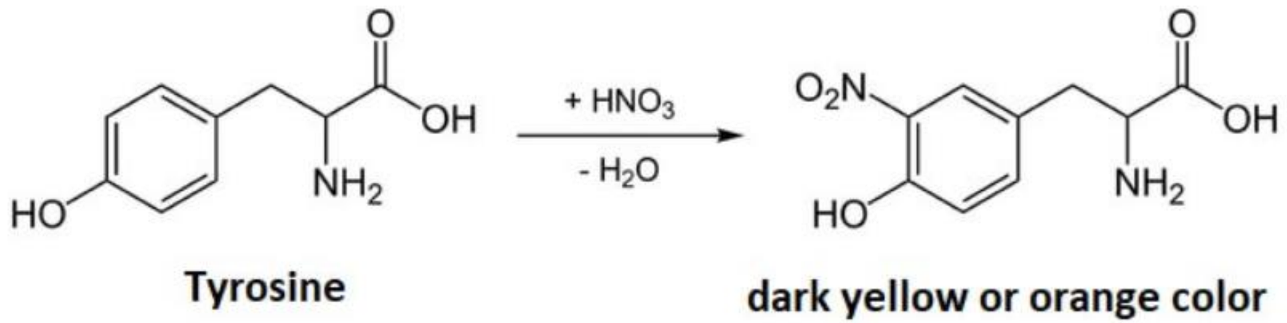
Ninhydrin test

- When 1 ml of Ninhydrin solution is added to a 1 ml protein solution and heated, the formation of a violet color indicates the presence of α-amino acids.



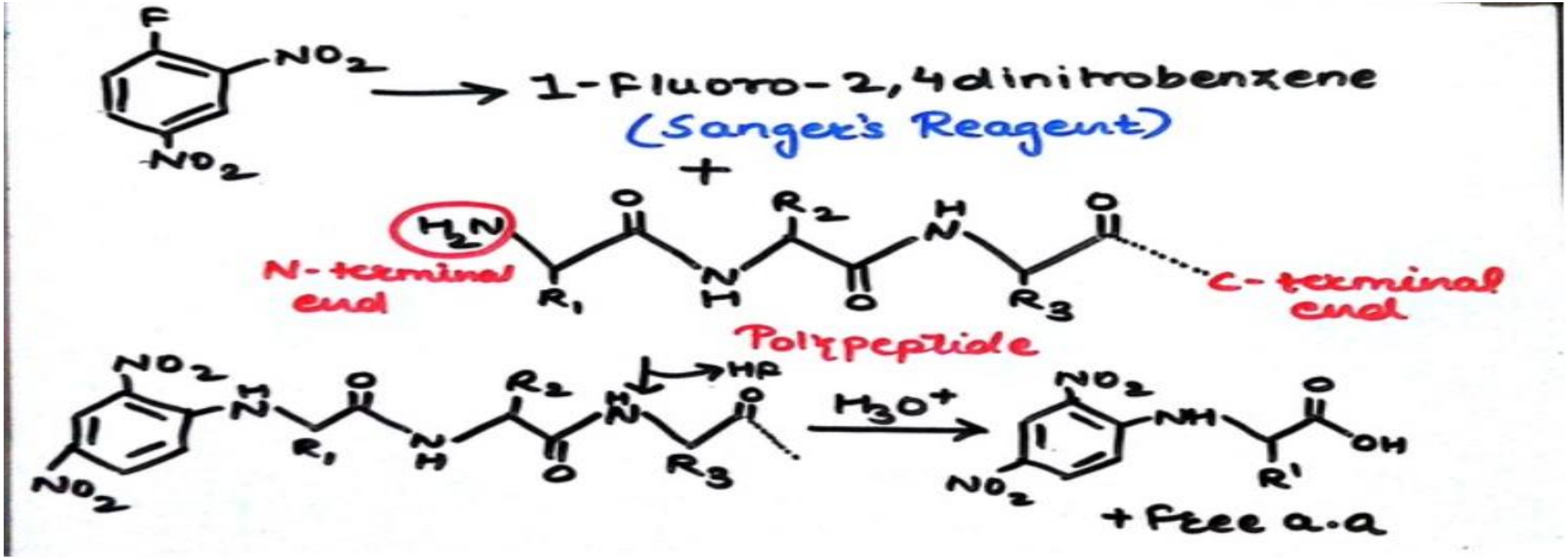
Xanthoproteic test

- The xanthoproteic test is performed for the **detection of aromatic amino acids** (**tyrosine, tryptophan,** and **phenylalanine**) in a protein solution. The nitration of benzoic radicals present in the amino acid chain occurs due to reaction with nitric acid, giving the solution **yellow coloration.**



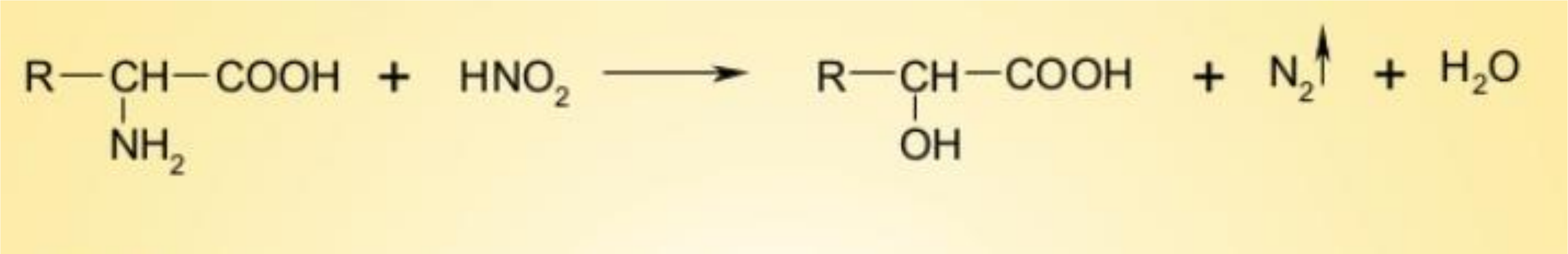
Reaction with Sanger's reagent

- **Sanger's reagent (1-fluoro-2, 4-dinitrobenzene**) reacts with a **free amino group** in the peptide chain in a mild alkaline medium under cold conditions. Sanger's reagent is a simple chemical that reacts with N-terminal amino acid of a polypeptide chain and thus, **helps in protein sequencing**.



Reaction with nitrous acid

- Nitrous acid reacts with the amino group to liberate nitrogen and form the corresponding hydroxyl.



Function of Amino Acids

- In particular, **20 very important amino acids** are **crucial for life** as they contain peptides and proteins and are known to be the **building blocks for all living things.**
- The linear sequence of amino acid residues in a polypeptide chain determines the three-dimensional configuration of a protein, and the structure of a protein determines its function.
- Amino acids are imperative for sustaining the health of the human body. They largely promote the: **Production of hormones, Structure of muscles, Human nervous system's healthy functioning , The health of vital organs, Normal cellular structure**
- The amino acids are used by various tissues to **synthesize proteins** and to produce nitrogen-containing compounds (e.g., purines, heme, creatine, epinephrine), or they are **oxidized to produce energy.**
- The breakdown of both dietary and tissue proteins yields **nitrogen-containing substrates and carbon skeletons.**
- The nitrogen-containing substrates are used in the **biosynthesis of purines, pyrimidines, neurotransmitters, hormones, porphyrins, and nonessential amino acids.**
- The carbon skeletons are used as a fuel source in the citric acid cycle, used for **gluconeogenesis, or used in fatty acid synthesis**.

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THANK YOU