Med Learn

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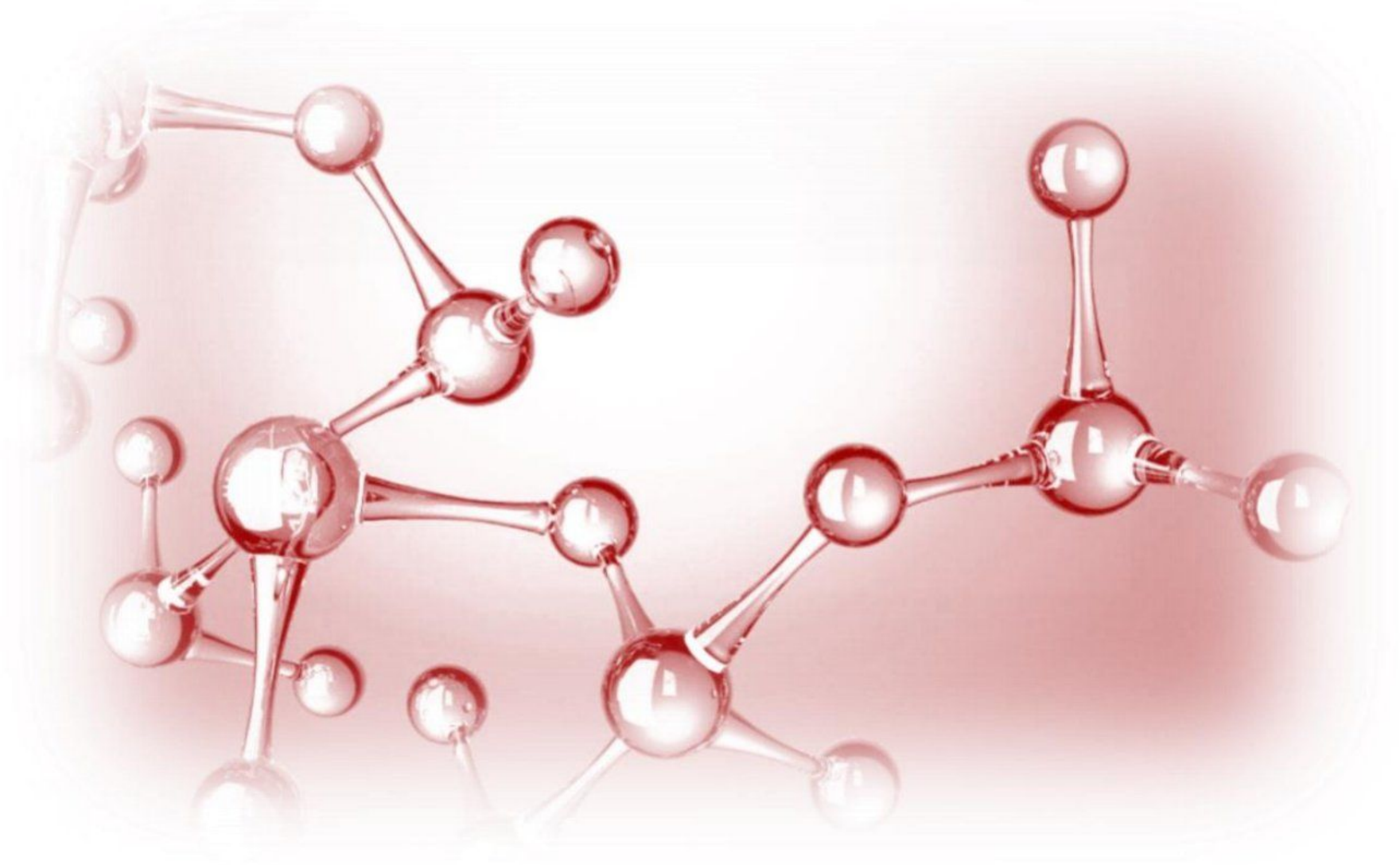
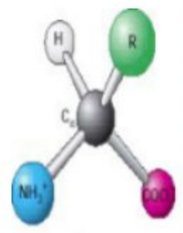
# Biochemistry

## *Amino acids*



## ❖ Amino acids

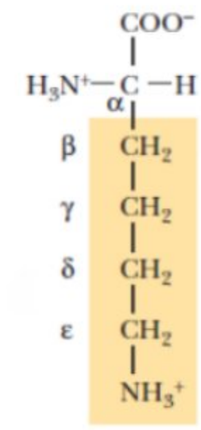
- They are the <u>building blocks of proteins</u>
- They are composed of **α- carbon** bound to:
  - **Amino group ($NH_3^+$)**
  - **Carboxyl group ($COO^-$)**
  - **H atom**
  - **R-group (side chain)** → varies between different amino acids



- R group determines the identity of the A.A.

- All amino acids are **chiral except Glycine**
- Amino acids has **L & D stereoisomers:**
  - <u>Amino group right</u> → D (dexter)
  - <u>Amino group left</u> → L (laevus)
- Amino acids are **not super imposable on their mirror images** <u>except Glycine</u>
  - Because it is achiral
- L, D amino acids are stereoisomer (**optical** isomers) → **enantiomers**

- Both D & L isomers present in nature, but:
  - **Only L-isomers present in proteins naturally**
  - **D**-isomers occur naturally in **bacterial cell walls & some antibiotics** (<u>not in proteins</u>)



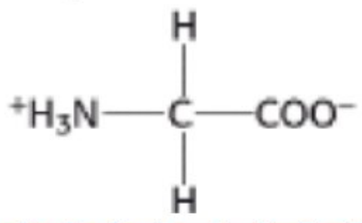
- Side-chain carbon atoms are designated with letters of the Greek alphabet
  - Counting from the **α**-carbon → These carbon atoms are **β, γ, δ and ε** carbons
  - If the side chain is **terminated by a carbon** → it will be **ω-carbon**

- There are a lot of amino acids only 20 amino acids are used in making our proteins
- These amino acids are classified according to properties of their side chains:
  - **Size, shape, charge, Hydrogen bonding capacity, Hydrophobic character, chemical reactivity of their functional groups**

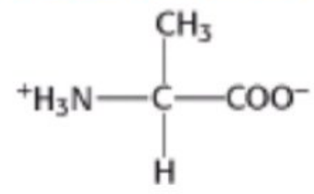
- **Amino acids classified according the polarity of their R groups into:**

### 1) Non-Polar amino acids:

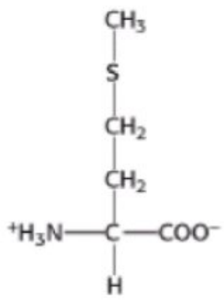
- **Glycine (Gly , G)**
  - Derivative of **acetic acid** or **ethylamine**
  - The **simplest amino acid**
  - R group = <u>H atom</u>



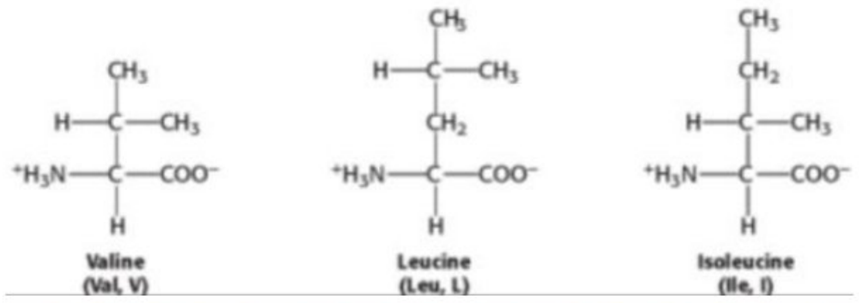
- **Alanine (Ala , A)**
  - R group = <u>$CH_3$ (methyl)</u>



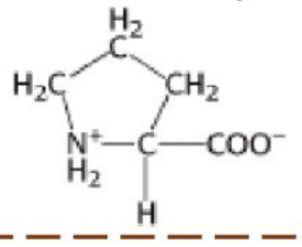
- **Methionine (Met , M)**
  - R group = <u>$CH_2CH_2S\text{-}CH_3$</u>
  - Used to Form S-Adenosyl-L-Methionine **(SAM)** by reacting with Adenine
  - Acts as **methyl donor** in reactions
- S is a very polar atom but it is surrounded by 2 methyls making the A.A. non-polar



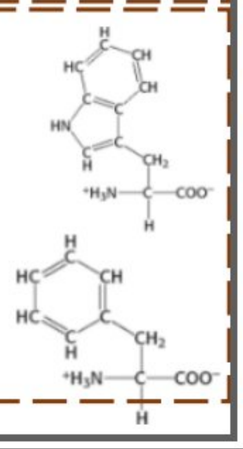
- **Valine (Val , V)**
- **Leucine (Leu , L)**
- **Isoleucine (Ile , I)**
  - **Branched amino acids**
  - Essential amino acids
    - Obtained from diet only → can't be synthesized in the body




- **Proline (Pro , P)**
  - The only amino acid that has a connect between the R chain and the back bone by the amino group forming a **secondary amine group** → so it is **imino acid**



- **Phenylalanine (Phe , F)**
- **Tryptophan (Trp , W)**
  - **Aromatic amino acids**
- ✓ **Trp → Indole ring (2 fused rings)**
- ✓ **Phe → Benzene ring**

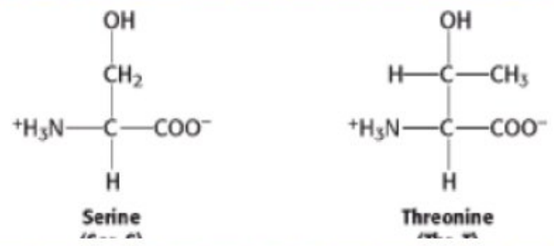


## 2) Polar Amino Acids

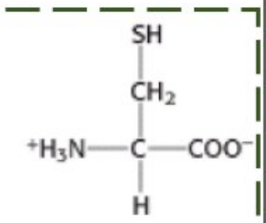
➢ Can be Neutral, Positively or Negatively charged amino acids

### A) Polar Amino acids (Neutral, Uncharged)

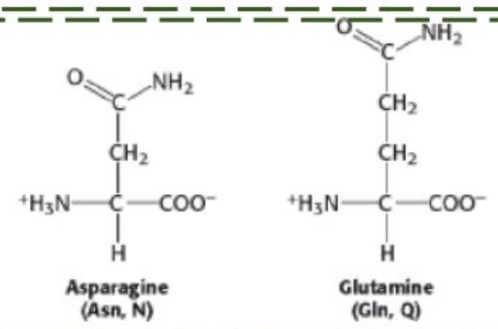
- **Serine (Ser , S)**
- **Threonine (Thr , T)**
  - Have **OH group**



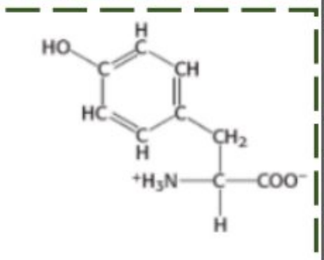

- **Cysteine (Cys , C)**
  - Has a **Thiol group** (SH)
  - Thiol group in Cys form **disulfide bridges** when reacting with another Cys



- **Asparagine (Asn , N)**
- **Glutamine (Gln , Q)**
  - Have Amide group (**$CONH_2$**)

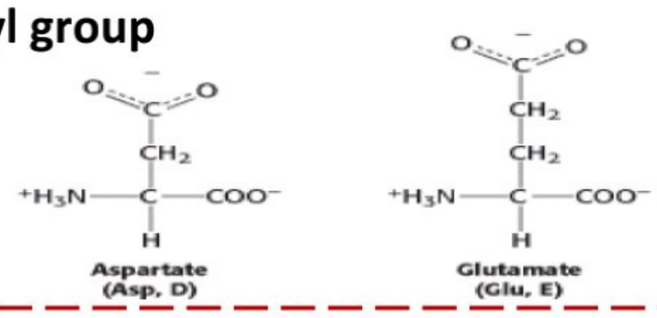



- **Tyrosine (Tyr , Y)**
  - **Benzene ring** with **OH group** (Aromatic + polar)



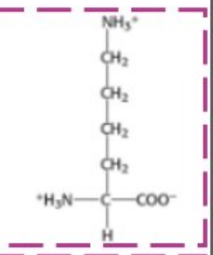
### B) Negatively charged (Acidic, Polar)

- **Aspartic acid (Asp , D)**
- **Glutamic acid (Glu , E)**
  - Have **Carboxyl group** ($COO^-$)

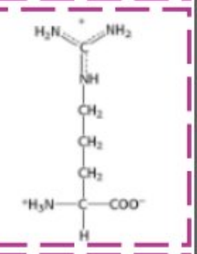



### C) Positively charged (Basic, Polar)

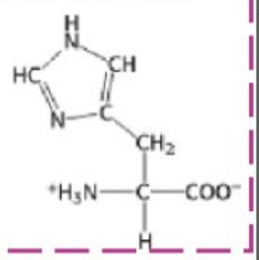
- **Lysine (Lys , K)**
  - Has 4 carbons + **Amino group**



- **Arginine (Arg , R)**
  - Has **3 carbons + Amino group + <u>Guanidino group</u>**



- **Histidine (His , H)**
  - Has an aromatic ring with 2 N atoms called **imidazole**
  - Act as a **buffer** (pKa very close to physiological pH)



- **<u>Notes:</u>**
  - ➢ **Guanidino:** is a complex basic group specific for Arginine
  - ➢ All amino acids have <u>Aliphatic</u> side chains **<u>except</u>** 4 amino acids **(Phe, Tyr, Trp & His) which are aromatic (rings)**
  - ➢ Methionine coded in the **starting codon** → in the beginning of all proteins
  - ➢ The largest amino acid is **Tryptophan**

- **<u>Biological significance of amino acids:</u>**
- We Have a lot of amino acids in our body (amino acid pool)
- <u>Most</u> amino acids are used to make (synthesis) **proteins**
- They can also be <u>converted into other molecules</u> such as (glucose, glycogen, Ketone bodies FAs, steroids & $CO_2$)
- Also **α -nitrogen atom** of amino acids is a <u>primary source for Nitrogen</u> in our bodies so they affect the nitrogen balance in the body
  - ➢ Nitrogen is a precursor of **amonia (NH3) which is very toxic** → so instead of forming ammonia amino acids are used to produce many useful nitrogenous compound, such as:
    - ✓ Hormones, creatine, porphyrins, Neurotransmitters, Purines, pyrimidines & Biological active peptides

- **<u>Uncommon & specialized amino acids (different forms of amino acids):</u>**

❖ **Tyrosine**

- It is converted into **catecholamine (neurotransmitters)** → <u>Dopamine, Norepinephrine & Epinephrine</u> which are used in <u>flight or fight</u> conditions
  - ➢ **Catechol = Benzene ring and 2 OH groups**

- Tyrosine is converted into **Melanin (skin color)**, **Thyroxine (hormone)**
  - **Thyroxine:** It has 4 Iodide atoms, produced by thyroid gland, and it **regulates metabolism**
- **Cheese contain high amounts of tyramine**, which mimics (similar to) epinephrine → for many people a cheese omelet in the morning is a favorite way to start the day
  - **Tyrosine** is converted by **Tyrosine decarboxylase** into **Tyramine**

### ❖ Tryptophan

- Tryptophan serves as the precursor for the synthesis of **Neurotransmitters (Serotonin & Melatonin)**
  - **Melatonin:** produced by pineal gland → it is the sleep hormone (regulated **day-night cycle**)
  - **Serotonin: Sedative-neurotransmitter**

### ❖ Histamine

- **Histidine decarboxylase** removes the carboxyl group of **Histidine → producing Histamine**
- Released by **Basophilic & Mast cells** (types of blood cells have granules filled with histamine)
- **Histamine has many functions:**
  - **Allergic mediator** → acts as vasodilator causing → more leakage of fluid → **redness & swelling**
  - Regulate physiological function in the **gut**
  - Acts as a **neurotransmitter**
  - Contributes into **inflammatory response**
  - Causes **constriction of smooth muscles** → causing asthma & dyspnea (shortness of breathing)

### ❖ Glutamate

- It is a precursor of **GABA & Gla**
  - **GABA (γ-aminobutyric acid)**
    - ✓ Synthesized in the **CNS (the brain)** → can't cross the BBB (blood brain barrier)
    - ✓ Produced by **decarboxylation of glutamate**
    - ✓ It is an **inhibitory neurotransmitter** → reduces neuronal excitability → so it has relaxing, anti-anxiety & anti-convulsive effects
  - **Gla (γ-Carboxyglutamate)**
    - ✓ Synthesized by the carboxylation of glutamate in some **clotting factors** (with the aid of **vitamin K**)
    - ✓ This carboxylation process is important for clotting process → because that gives it an **extra negative charge** → more attraction with calcium ions → more clotting

### ❖ Arginine

- L-arginine is the precursor of **nitric oxide (NO)**, which a signaling molecule causes:
  - **Vasodilation, Inhibition of platelet adhesion, inhibition of leukocyte adhesion, anti-proliferative action, scavenging superoxide anion (anti-inflammatory)**
  - It is a gas → diffuse easily through the membrane

### ❖ Lysine & proline

- They are **hydroxylated and then become parts of collagen → it is a supportive (structural protein)**
- Post-translational modifications (hydroxylation) of lysine & proline gives collagen more strength

## ❖ Mono-sodium glutamate (MSG)

- **Glutamic acid** derivative
- Flavor enhancer → used in **Asian food**
- It can cause physiological rections in some people (**chills, headaches & dizziness**)
- Can cause **Chinese restaurant syndrome**

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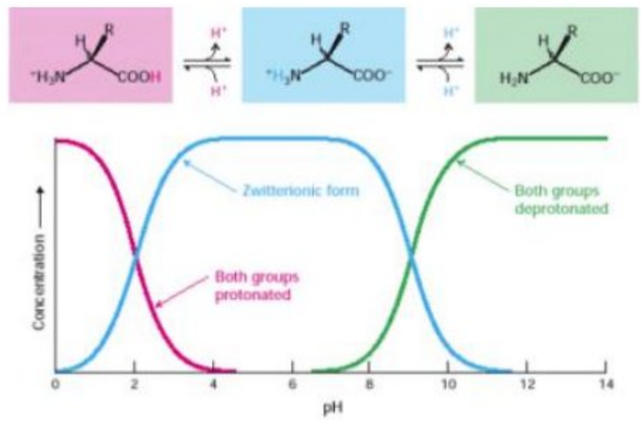
## ❖ Ionization of amino acids




- Amino acids have:
  - ➢ Carboxyl group → pKa = about 2
  - ➢ Amino group → pKa = about 9
- These groups can be protonated or deprotonated depending on the pH
- **At the <u>physiological pH</u> (about 7.4):**
  - ➢ **Carboxyl** ➔ pH > pKa → deprotonated ($COO^-$) ➔ **Negatively charged**
  - ➢ **Amino** ➔ pH < pKa → protonated ($NH_3^+$) ➔ **positively charged**

✓ So, At physiological pH → amino acids (<u>without</u> ionizable R group) have **+1,-1 → 0 net charge (Neutral)**

- ➢ **Zwitterion (isoelectric):** A molecule with <u>opposite charges</u> & the **net charge is Zero**

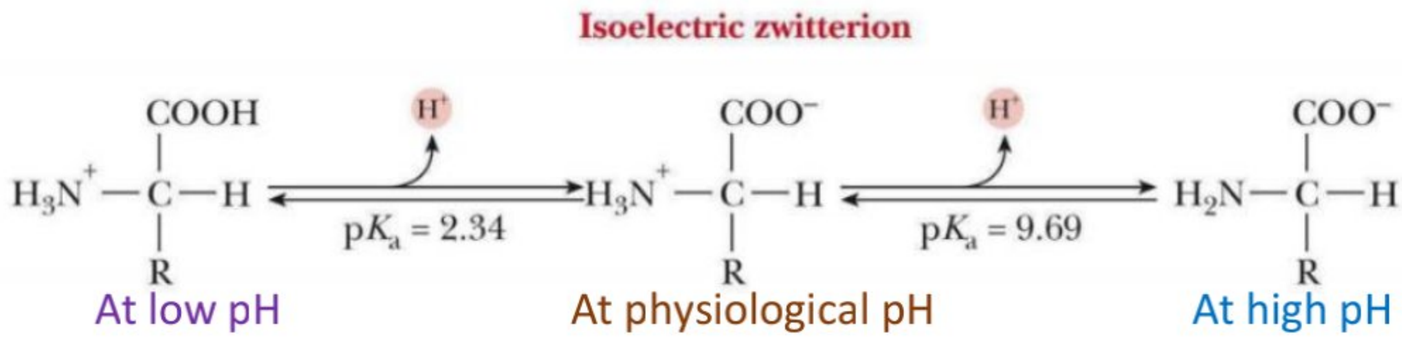
- At very low pH values (for example pH = 1):
  - ➢ **Carboxyl** ➔ pH < pKa → Protonated (COOH) → **Uncharged**
  - ➢ **Amino** ➔ pH < pKa → protonated ($NH_3^+$) → **Positively charged**

✓ The net charge = **+1**

- At high pH values (such as pH = 12):
  - ➢ **Carboxyl** ➔ pH > pKa → deprotonated ($COO^-$) → **Negatively charged**
  - ➢ **Amino** ➔ pH > pKa → deprotonated ($NH_2$) → **Uncharged**

✓ The net charge = **-1**

- **If pH = pKa of carboxyl → 50% protonated (COOH) & 50% deprotonated ($COO^-$)**
- **If pH = pKa of Amine → 50% protonated ($NH_3^+$) & 50% deprotonated ($NH_2$)**




### Note:

- R groups can be either ionizable or non-ionizable

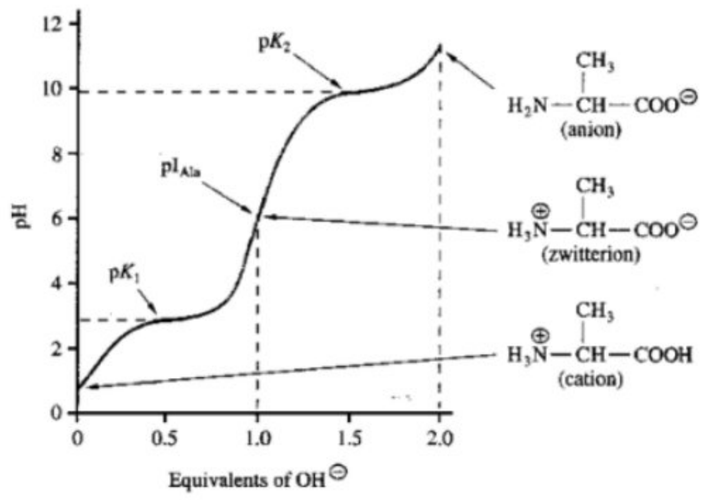
1) **Non-ionizable** → these R groups can't ionize (non-polar & some polar) → these amino acids have **only 2 pKa values** (of carboxyl & Amine groups of the backbone)

2) **Ionizable** → can **ionize affecting the pH and the total charge of the amino acid** → they have their own pKa values, such as the groups of these amino acids:
   - ➢ **Aspartic & glutamic acids**, **Lysine, Arginine & Histidine**, **Tyrosine, Serine & Threonine, Cysteine**

- **Isoelectric (Zwitterion) point (pI):** It is <u>pH where the net charge of a molecule is zero</u>
- It is calculated (for amino acids **without ionizable R groups**) by taking the <u>average of the carboxyl pKa & Amine pKa</u>

$$pI = \frac{pK_{a1} + pK_{a2}}{2}$$

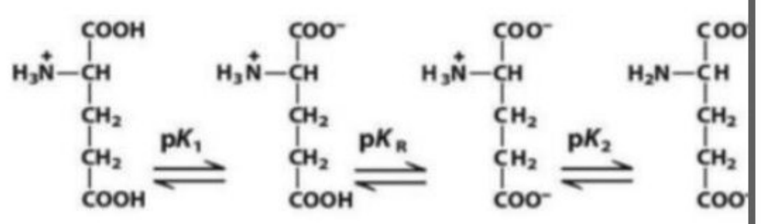
- **<u>Example:</u>**
- Alanine is a non-polar amino acid → so it has only 2 pKa values that determine the pI:
  - ➢ pI = (2.34 + 9.69)/2 = 6
  - ➢ At pH = $pKa_1$ (pka of carboxyl)
    - 50% of alanine molecules are Neutral (Zwitterion) & 50% are positively charged (cation)
  - ➢ At pH = $pKa_2$ (pKa of Amine group)
    - 50% of alanine molecules are Neutral (Zwitterion) & 50% are Negatively charged (anion)

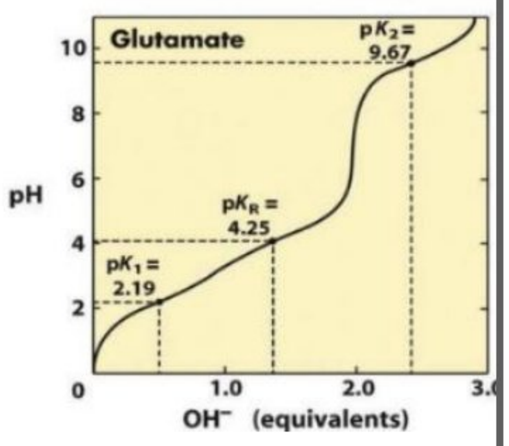



- pI is calculated for amino acids **with ionizable R groups** by taking the <u>average of 2 pKa values that surround the Zwitterion state</u>
- **<u>Examples:</u>** (don't memorize pKa values)

**1) Glutamate:**

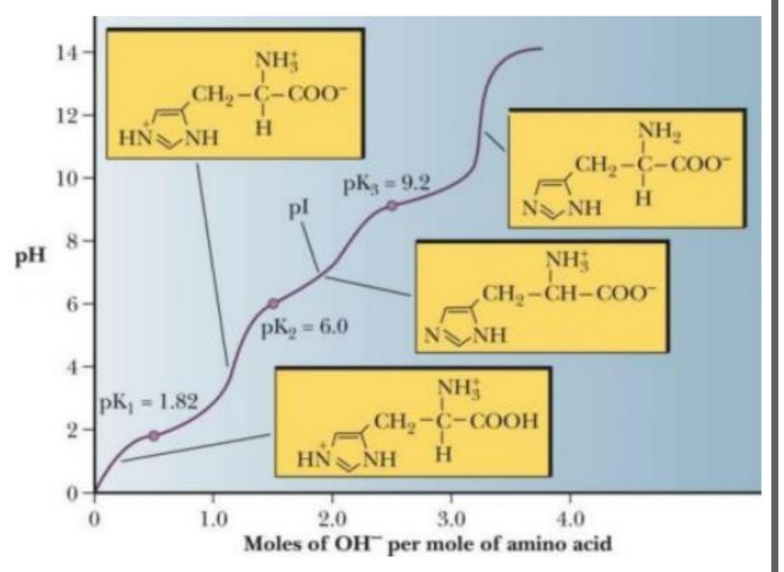
- Pka of R group (which contains carboxyl) = 4.25
  - ➢ At low pH
    - All groups are protonated (COOH, $NH_3^+$, COOH)
    - So it is positively charged (cation)
  - ➢ At pH between pKa of carboxyl & R group
    - pH > $pKa_1$ → deprotonated → $COO^-$
    - pH < $pKa_R$ & $pKa_2$ → protonated → $NH_3^+$ & COOH
    - So net charge = 0 (Zwitterion)
  - ➢ **So Zwitterion state is between $pKa_1$ & $pKa_R$** → pI = (2.19 + 4.25)/2 = 3.22

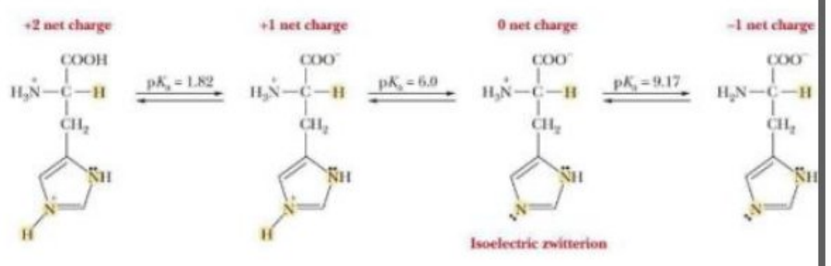



**2) Histidine:**

- pKa of R group (imidazole → contains 2 N atoms) = 6
  - ➢ At low pH
    - All groups are protonated (COOH, $NH_3^+$, $NH^+$)
    - So it is positively charged (cation)
  - ➢ At pH between pKa of carboxyl & R group
    - pH > $pKa_1$ → deprotonated → $COO^-$
    - pH < $pKa_R$ & $pKa_2$ → protonated → $NH_3^+$ & $NH^+$
    - So, the net charge +1 → positively charged (cation)
  - ➢ At pH between pKa of R group & amine group
    - pH > $pKa_1$ & $pKa_R$ → deprotonated → $COO^-$ & N
    - pH < $pKa_2$ → protonated → $NH_3^+$
    - So net charge = 0 (Zwitterion)
  - ➢ pI = (9.2 + 6)/2 = 7.6




- **<u>Questions:</u>**
  - ➢ **What is the pH of conjugate base/acid of glutamate at pH 4.5 (pKa = 4.25):**

    ➔ pH = pKa + log ($A^-$/HA) ➔ log ($A^-$/HA) = 0.25 ➔ ($A^-$/HA) = **1.78**

  - ➢ **What is the total charge of lysine at pH 7 (pka = 11):**

    ➔ **+1**