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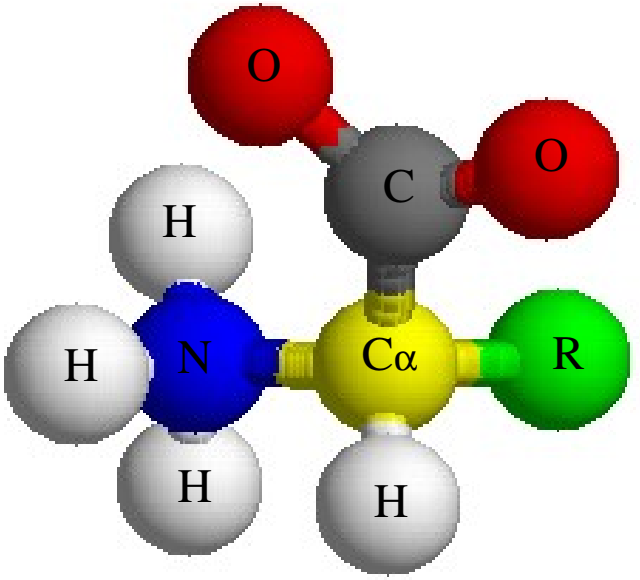
# Chapter 4: Amino Acids




## Voet & Voet: Pages 67 - 81

**Any introductory Biochemistry textbook will have a chapter on amino acids and their properties**

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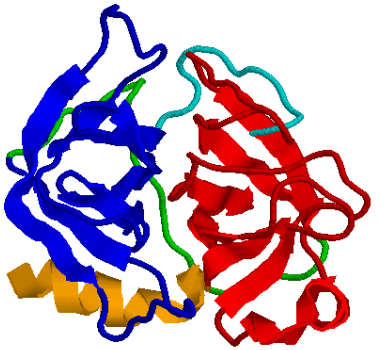
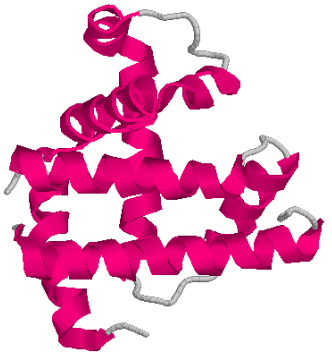
# Proteins

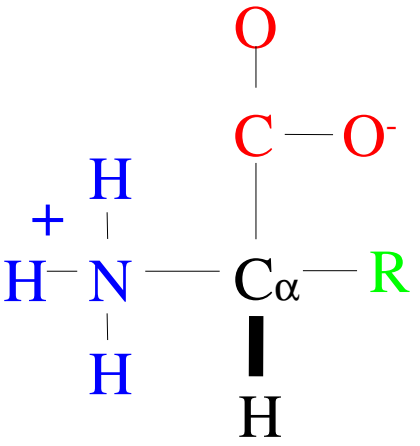


- Most abundant macromolecules in cells
- Variable size and physical properties
  - Accounts for diversity of structure and biological function
- Final product of most genes
  - Means of expressing of genetic information
- Linear, heteropolymers of amino acids

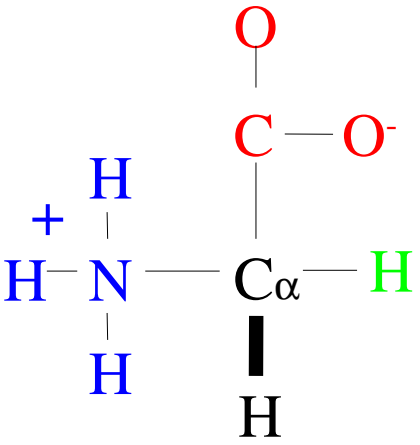


# Amino Acids

- **Building blocks of proteins**
  - **20 common amino acids used by all organisms**
- **All have an amino group and a carboxylate group covalently attached to a tetrahedral α carbon (Cα)**
- **Only differ at R group (side chain)**
  - **Amino acids can be classified based upon the physiochemical properties of the R group**
    - ***eg* non polar, polar uncharged, polar charged**



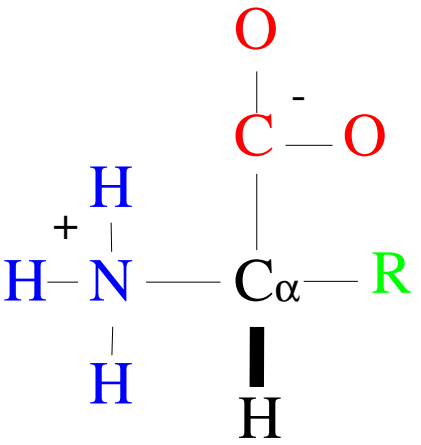

**Generic amino acid at neutral pH**




**Glycine – a common amino acid at neutral pH**

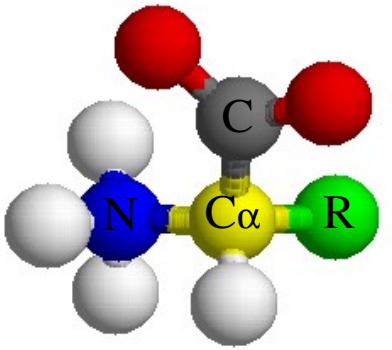
# Amino Acids are zwitterions

***In the physiological pH range (5-8), the α-carboxyl and α-amino groups of amino acids are completely ionized***



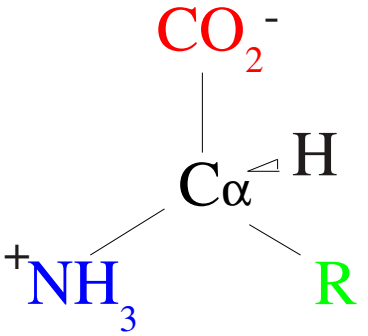

- **Compounds with this property are referred to as zwitterions (or dipolar ions or ampholytes)**
- **Zwitterions can act as either an acid or a base**

**α-carboxyl groups have $pK_a$s near 2.2 while α-amino groups have a $pK_a$s near 9.4**

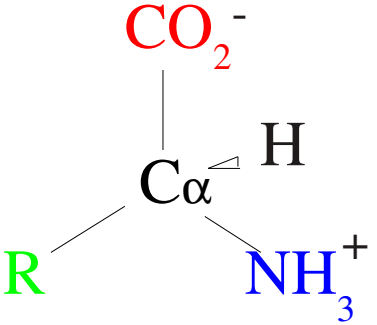


# Chirality

- **Amino acids (except glycine) have a tetrahedral Cα bonded to four different chemical groups**
  - **Consequently, amino acids are optically active or chiral**
- **Common amino acids are all L stereoisomers**
  - **Amino acid configuration uses the D,L system while synthetic chemistry generally uses the R,S system**
- **"CO-R-N" mnemonic useful for distinguishing L and D stereoisomers**
  - **Looking down the H – C bond, CO-R-N spelled clockwise indicates the L stereoisomer**



L-amino acid



D-amino acid

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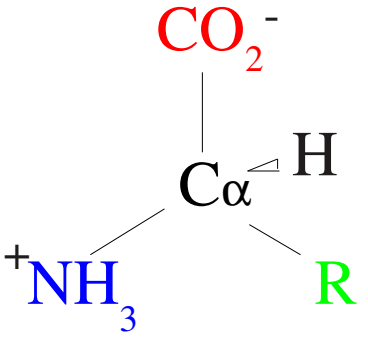
# Why the L isomer?

## No definitive answer

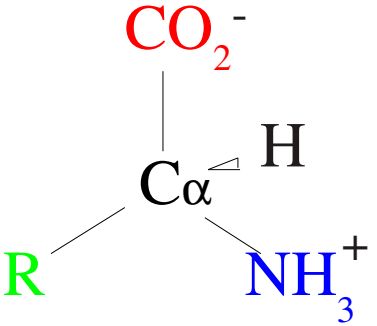
- **D and L isomers have identical energies**

***Repetitive substructure in proteins (helices, sheets, turns) require all amino acids have the same configuration.***



L-amino acid

- **Apparently, living systems evolved from L amino acids based upon an initial random choice.**



D-amino acid

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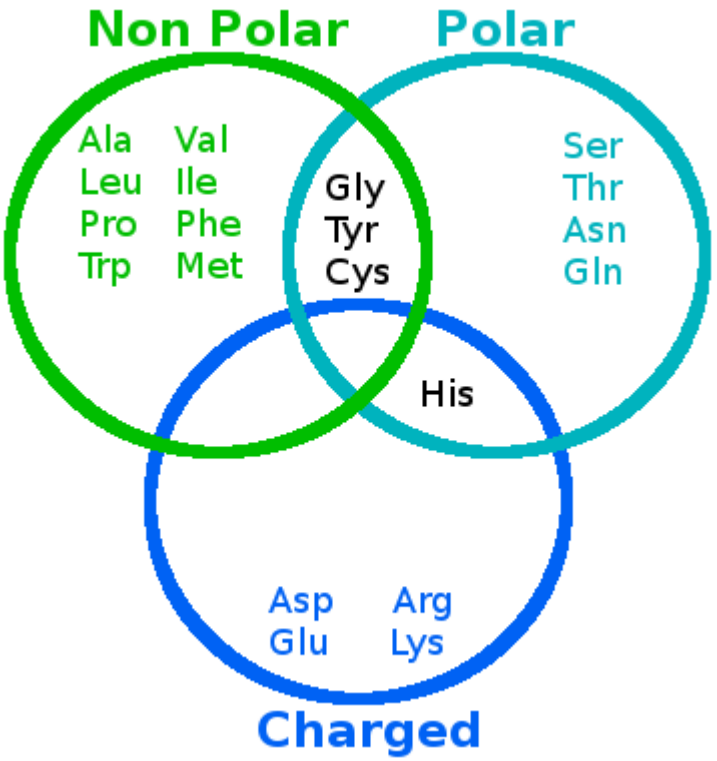
# Classification of Amino Acids

- **Amino Acids are classified or grouped according the physiochemical properties of their R-group**
  - **Voet & Voet presents one common classification scheme based upon polarity**

- **Polarity is defined as *the magnitude of the dipole induced in the presence of an external electromagnetic field.***




**Amino acids grouped by Polarity (at neutral pH).**

**Classification schemes are an aid to recalling structure and properties of amino acids**

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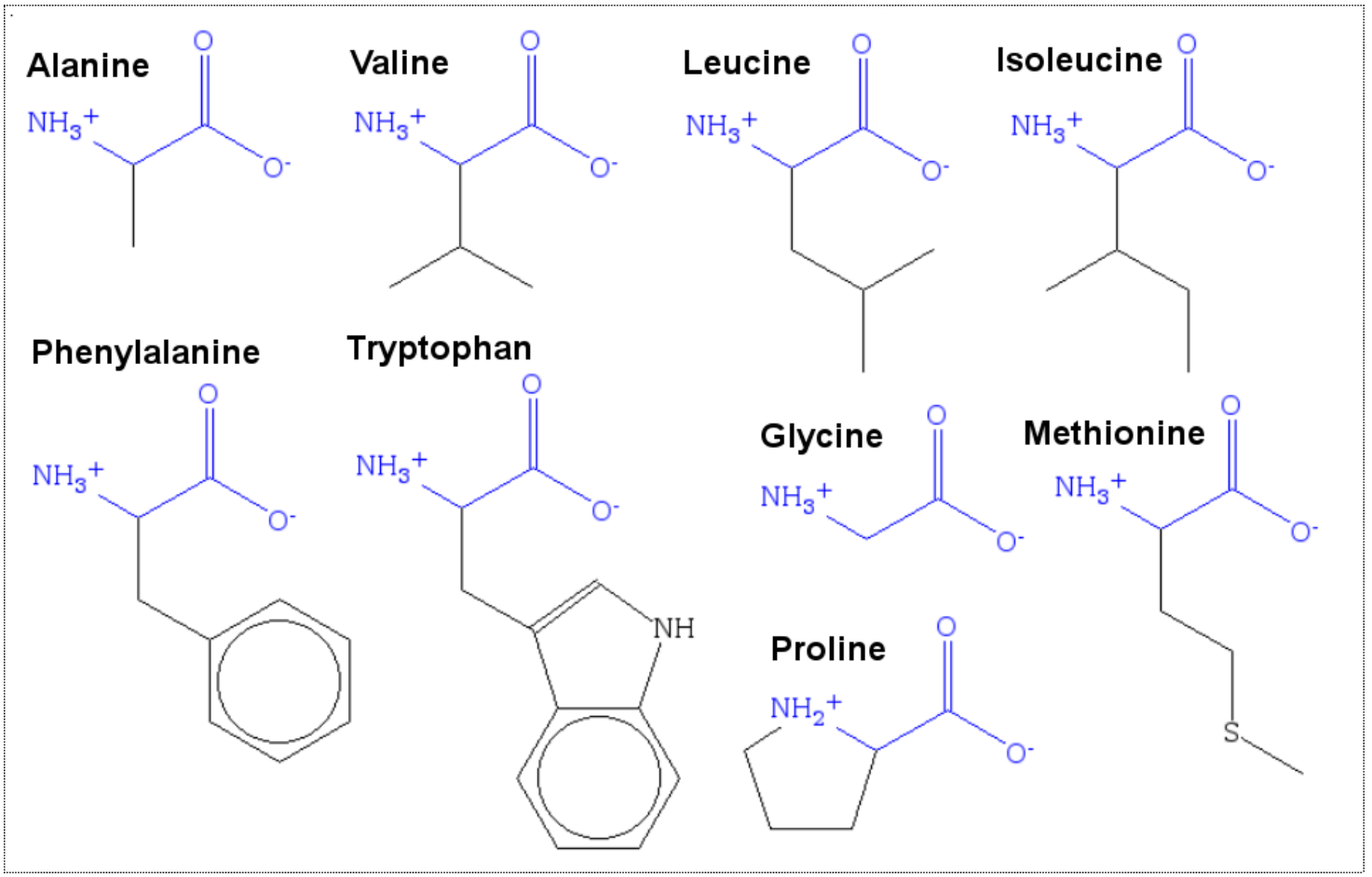
# Non Polar Amino Acids

## R-group is a hydrocarbon (also includes Trp & Met)




**Aromatic amino acids absorb UV light**

**Proline R-group is covalently bonded to α-amine**

**Glycine can also be classified as polar uncharged**

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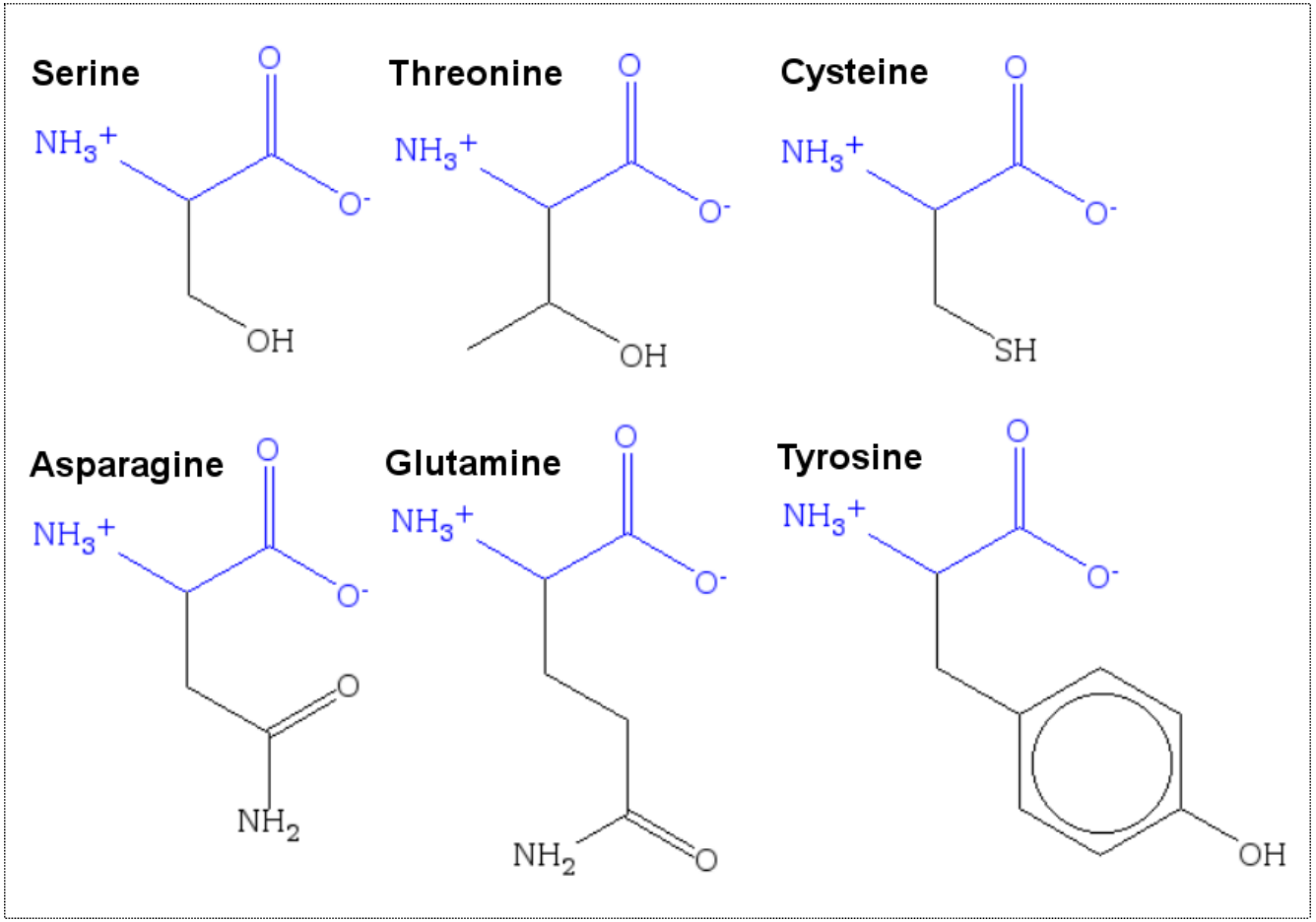
# Polar (uncharged) Amino Acids

**R-group contains polar (hydroxyl, thiol or carboxyamide) functional group and has neutral charge at pH 7**

**Ser, Thr and Cys are often involved in enzymatic reactions**

**Cys can form disulfide bridges (cystine)**

**Tyr and Cys can also be classified as non polar.**

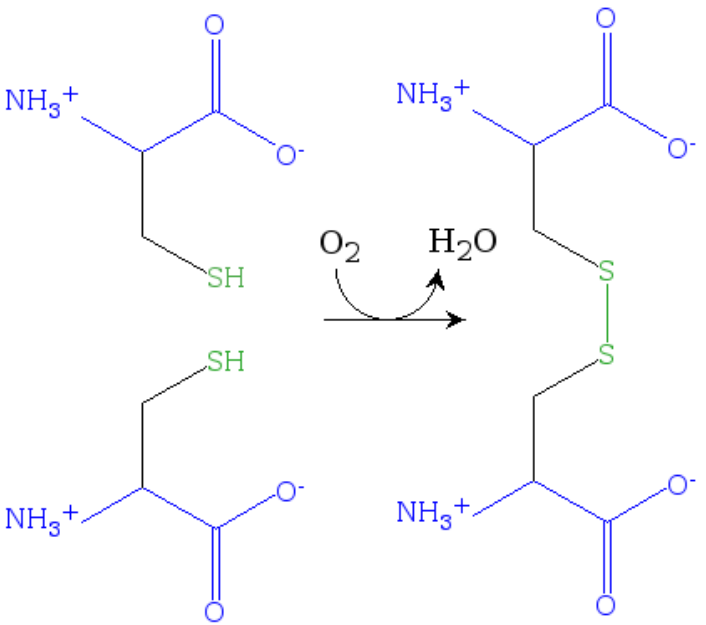


# Cysteine

- **Polar uncharged amino acid due to it thiol group**
- **Cysteines spontaneously form a covalent bond (disulfide bridge) between their thiol groups in the presence of oxidizing agents**

**Disulfide bonded cysteine residues are referred to as cystine.**

**Cysteine is polar (uncharged) …**




**… and Cystine is (very) non-polar**

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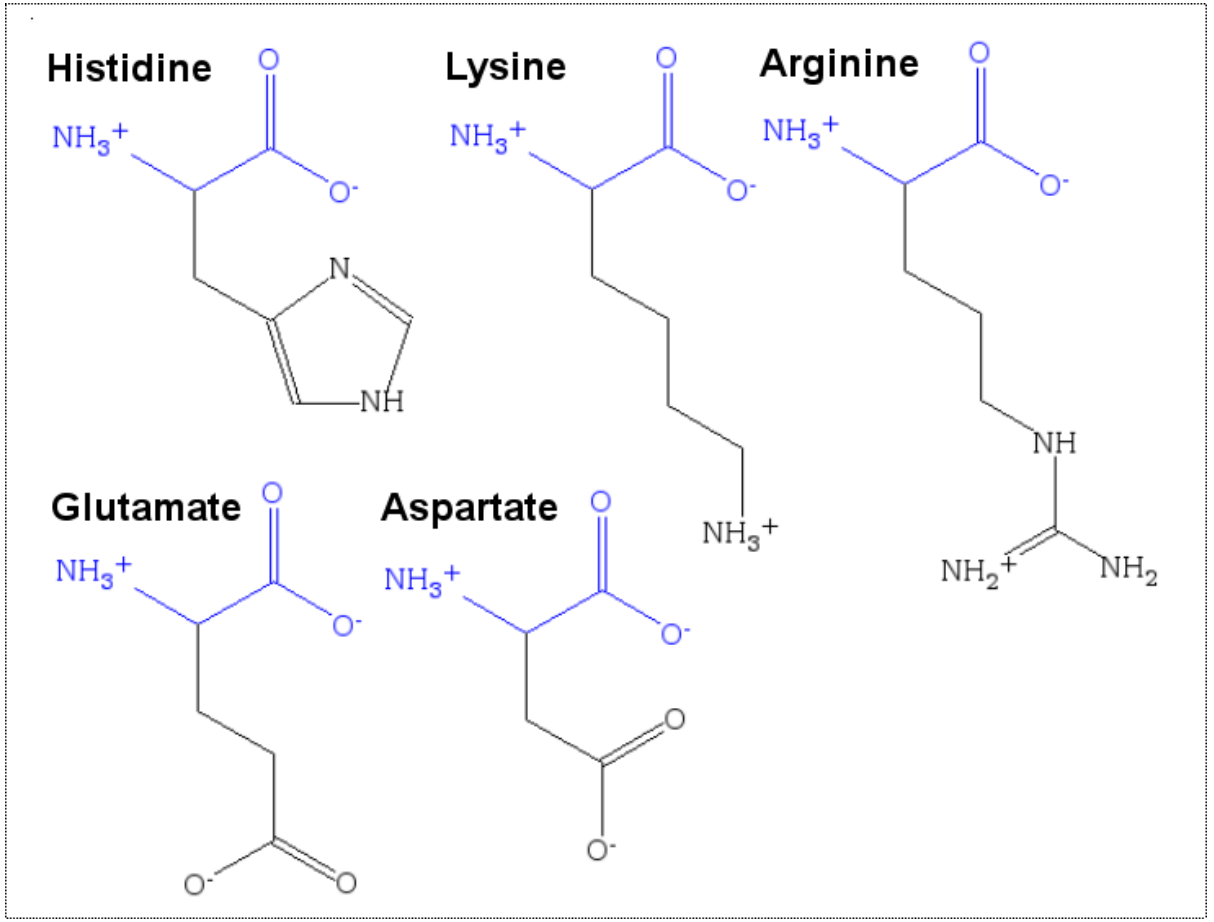
# Polar (charged) Amino Acids

**R group contains (carboxylate or amine) functional group that is partially or fully ionized at neutral pH**




**His** has a $pK_a$ near neutral

Amines are neutral or positively charged

Carboxylates are neutral or negatively charged

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# Names, Abbreviations, and more

Residues are named by replacing the **-ine** suffix of amino acids with **-yl**

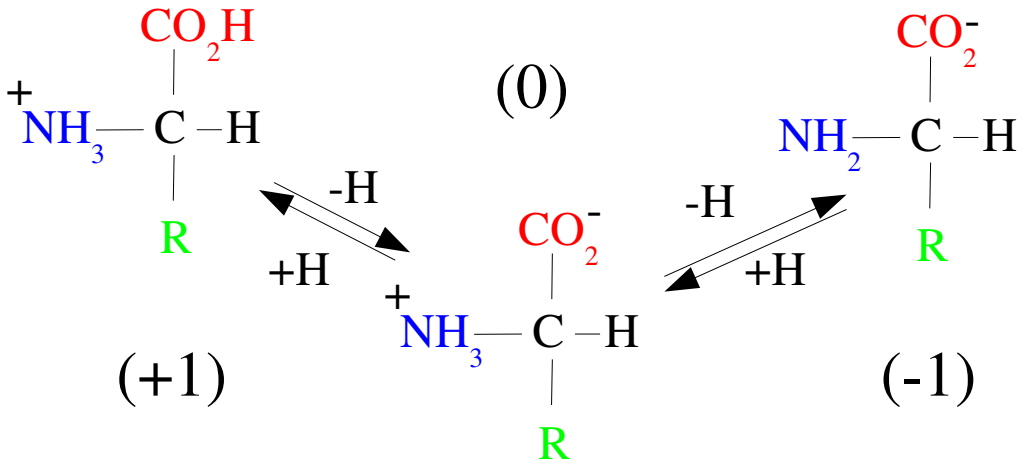
- Need to know amino acid names, 3 letter code, R-group $pK_a$s and residue names

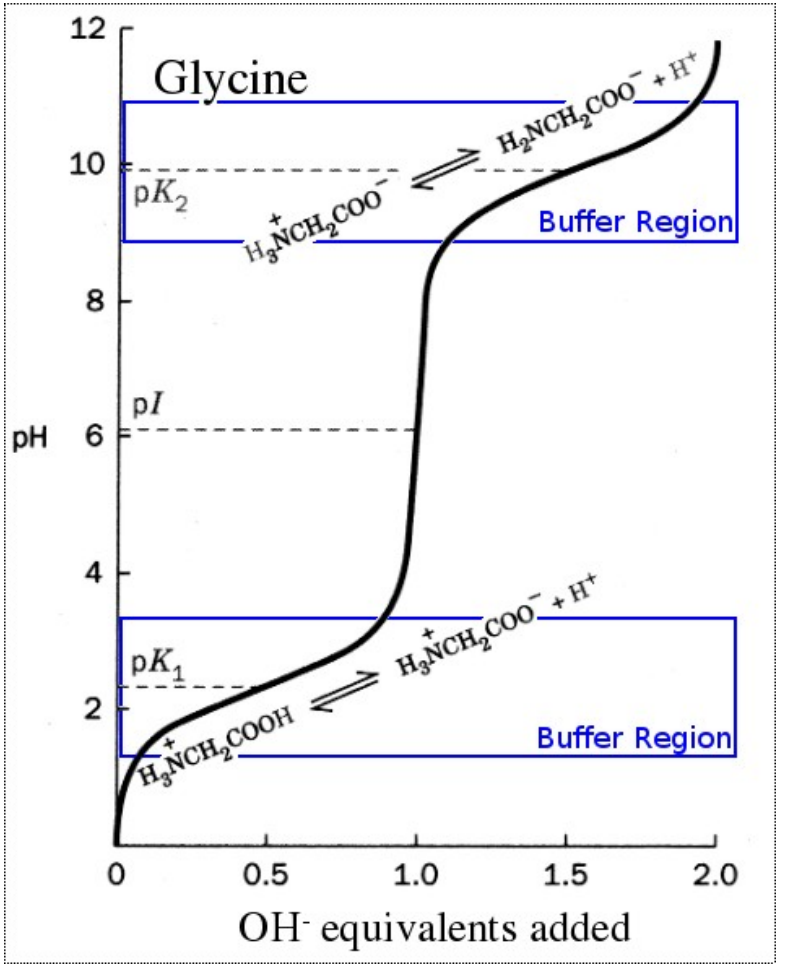
| Amino Acid | Residue | 3-letter Code | 1-letter Code | R-group $pK_a$ | Frequency (%) |
|---|---|---|---|---|---|
| **Nonpolar** | | | | | 50.1 |
| Glycine | Glycyl | Gly | G | | 7.1 |
| Alanine | Alanyl | Ala | A | | 8.3 |
| Proline | Prolyl | Pro | P | | 4.7 |
| Valine | Valyl | Val | V | | 6.9 |
| Leucine | Leucyl | Leu | L | | 9.7 |
| Isoleucine | Isoleucyl | Ile | I | | 6.0 |
| Tryptophan | Tryptophanyl | Trp | W | | 1.1 |
| Phenylalanine | Phenylalanyl | Phe | F | | 3.9 |
| Methionine | Methionyl | Met | M | | 2.4 |
| **Polar uncharged** | | | | | 24.0 |
| Serine | Seryl | Ser | S | | 6.5 |
| Threonine | Threonyl | Thr | T | | 5.3 |
| Cysteine | Cystyl | Cys | C | 8.4 | 1.4 |
| Asparagine | Asparagyl | Asn | N | | 4.0 |
| Glutamine | Glutaminyl | Gln | Q | | 3.9 |
| Tyrosine | Tyrosyl | Tyr | Y | 10.5 | 2.9 |
| **Polar charged** | | | | | 25.9 |
| Histidine | Histidyl | His | H | 6.0 | 2.3 |
| Lysine | Lysyl | Lys | K | 10.5 | 5.9 |
| Arginine | Arginyl | Arg | R | 12.5 | 5.5 |
| Aspartate | Aspartyl | Asp | D | 3.9 | 5.4 |
| Glutamate | Glutamyl | Glu | E | 4.1 | 6.8 |

# Ionization States of Free Amino Acids

**Free amino acids** have 2 (or more) acid/base groups and produce **complex acid/base titration curves**

***eg.*** amino acid <u>without ionizable</u> R group



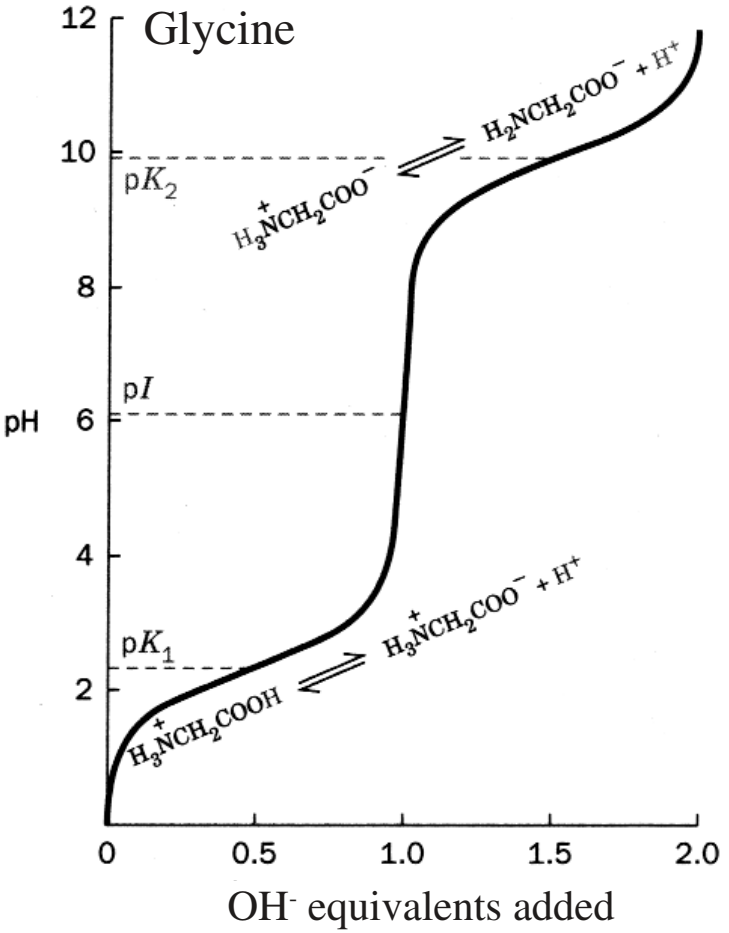



# Isoelectric Point

- **Isoelectric point is the pH at which the total charge of the amino acid (peptide or protein) is zero**
  - **For amino acids without ionizable R groups, the pI is the average of the $pK_a$s**

$$pH = pK + \log \frac{[A^-]}{[HA]}$$

$$pI = \frac{1}{2}(pK_i + pK_j)$$



# More Ionization States (complex case)

A) +2 B) +1 C) 0 D) -1

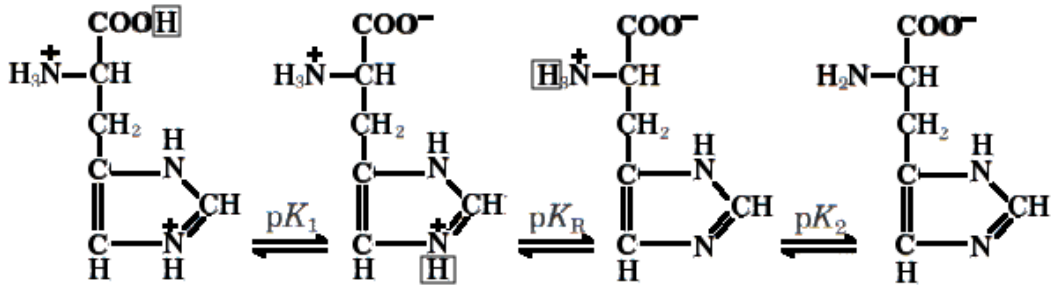
## Free amino acid with ionizable R group

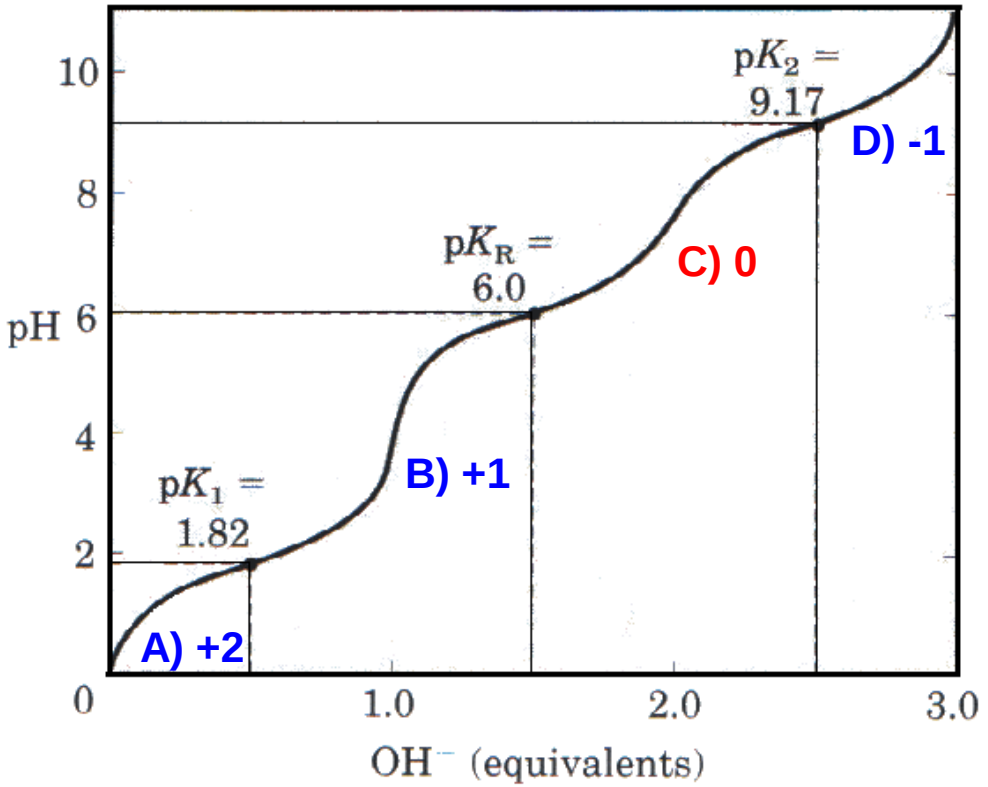
- *eg.* Histidine titration curve is more complex

## So what is the pI?

- Average of the $pK_a$s bounding the molecular species with a net charge of zero

  (6.0 + 9.17) / 2 = 7.6



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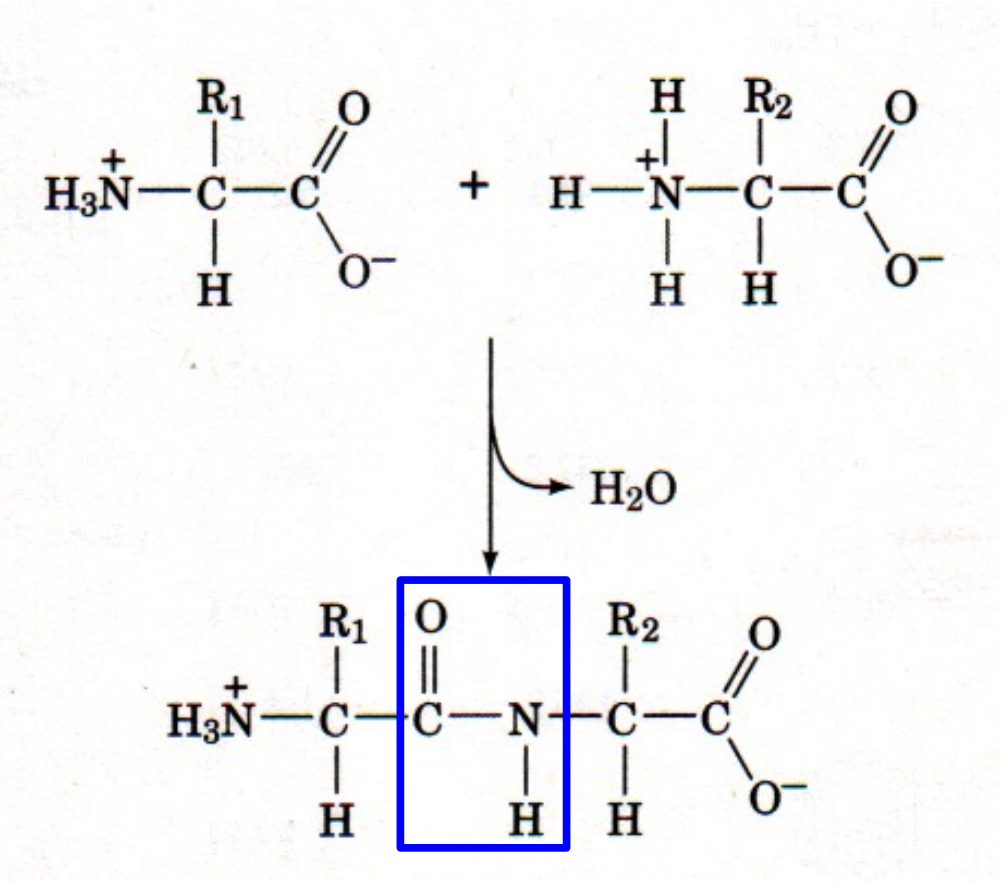
# Peptide Bonds

- Amino acids polymerize via **condensation** reactions
  - Carboxylate group of residue 1 forms a covalent bond with the amine group of residue 2
- Linear polymers of amino acids have an **amino (N)** and **carboxyl (C)** terminus
  - Living organism always synthesize proteins from N to C terminus




Peptide Bond

# Amino Acid Polymers

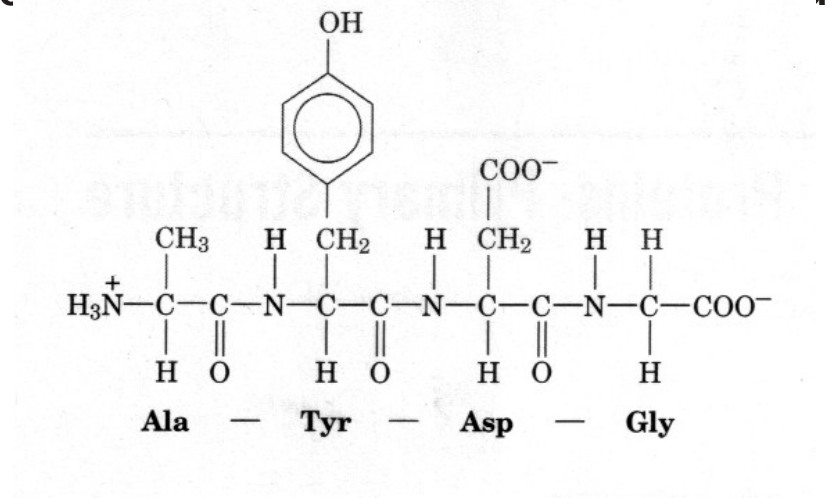
(1) **residue** – an amino acid (or peptide unit) in an oligopeptide, polypeptide or protein

(2) **oligopeptide*** – short polymer of residues linked by peptide bonds; up to 10-20 residues.

(3) **polypeptide*** – longer polymer of residues linked by peptide bonds; larger sizes

(4) **protein*** – one or more polypeptide chains

*biological polymers are associated with biological function

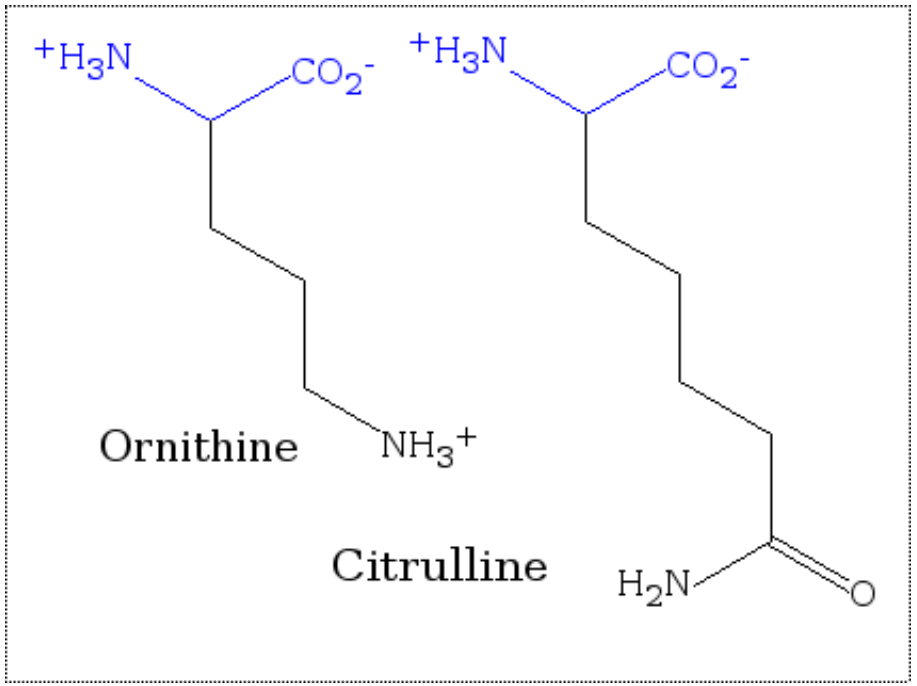



**Full name:**
**Alanyltyrosylaspartylglycine**

# Non Standard Amino Acids

- **> 700 non standard amino acids have been detected in living organisms**
  - **Many are metabolic intermediates**

    ***eg.* ornithine and citrulline are intermediates in urea biosynthesis**




**You are not responsible for drawing the structures of the non standard amino acid structures (Slides 18-20)**

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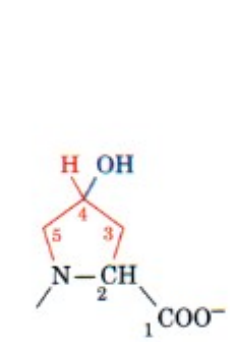
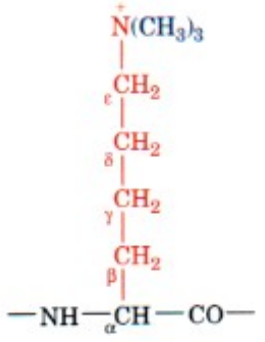
# Non Standard Amino Acids

Non standard amino acids in proteins arise from **post translation modifications**

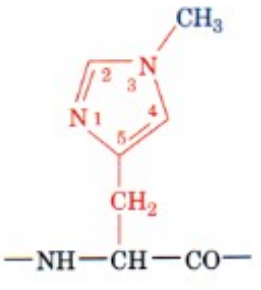
Modification are catalyzed by specific enzymes and target specific residues



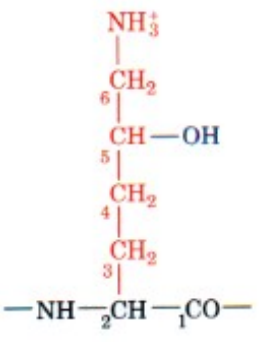
4-Hydroxyproline



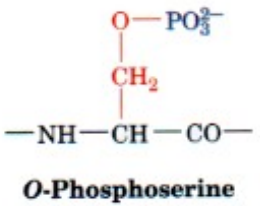
ε-*N,N,N*-Trimethyllysine



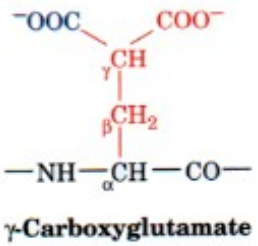
3-Methylhistidine



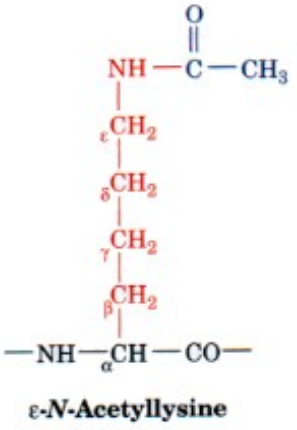
5-Hydroxylysine



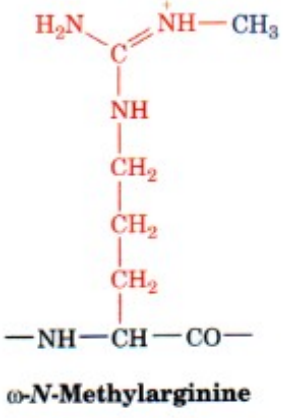
*O*-Phosphoserine



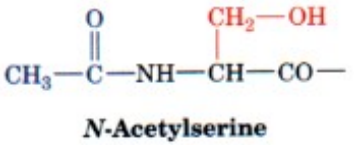
γ-Carboxyglutamate



ε-*N*-Acetyllysine

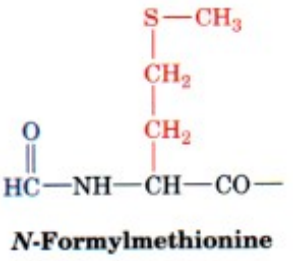


ω-*N*-Methylarginine



*N*-Acetylserine

*N,N,N*-Trimethylalanine

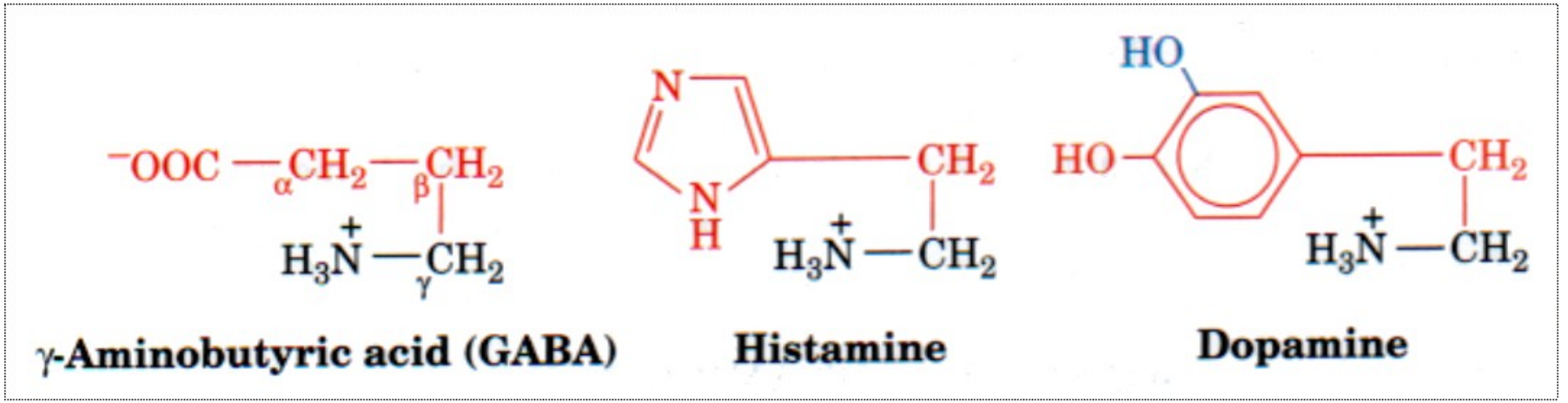


*N*-Formylmethionine

# Amino Acid Derivatives

**Chemical derivatives of amino acids also have important biological functions**

**eg. Catecholamines (below) lack the α-carboxylate of amino acids**




**GABA & Dopamine are neurotransmitters. Histamine mediates parts of the immune response.**