

# CHEM 153A Week 2

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## Ionization Constants

- The tendency for any acid (HA) to lose a proton and form its conjugate base ( $A^-$ ) is defined by the equilibrium constant ( $K_{eq}$ ) for the reversible reaction



for which

$$K_{eq} = \frac{[H^+][A^-]}{[HA]} = K_a$$

## Acid Strength Comparison: $K_a$ and $pK_a$ Values of Common Acids

No.	Acid	$K_a$	$pK_a$
1	Hydroiodic acid (HI)	$3.16 \times 10^9$	-9.5
2	Hydrobromic acid (HBr)	$1.0 \times 10^9$	-9
3	Hydrochloric acid (HCl)	$1.0 \times 10^6$	-6
4	Sulfuric acid ( $H_2SO_4$ )	$1.0 \times 10^3$	-3
5	Hydronium ion ( $H_3O^+$ )	55	-1.74
6	Nitric acid ( $HNO_3$ )	28.2	-1.45
7	Trifluoroacetic acid ( $CF_3COOH$ )	$5.62 \times 10^{-1}$	0.25
8	Oxalic acid ( $HOOC-COOH$ )	$5.37 \times 10^{-2}$	1.27
9	Acetic acid ( $CH_3COOH$ )	$1.75 \times 10^{-5}$	4.76

## $pK_a$

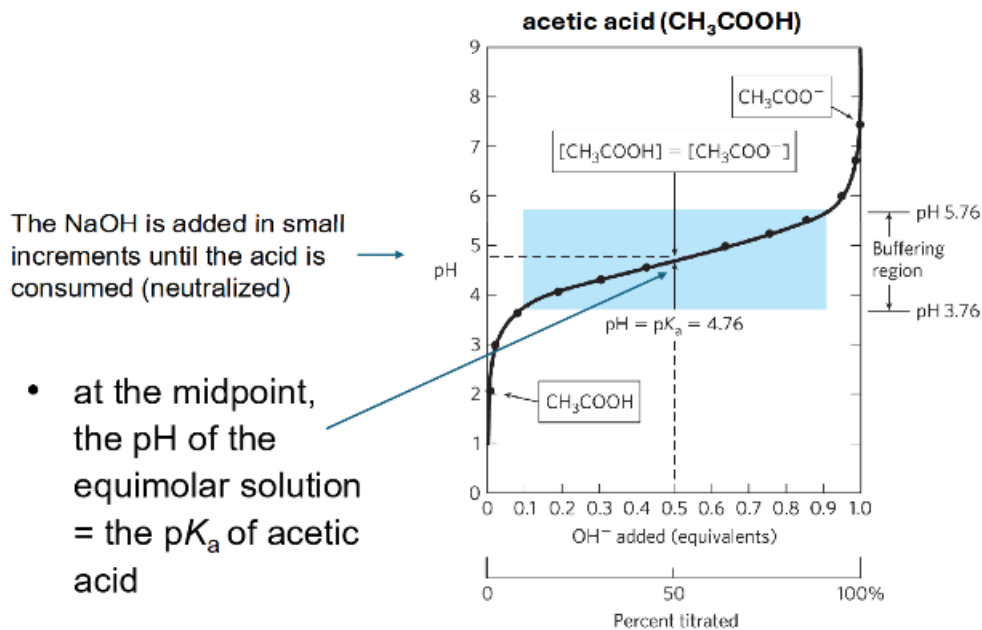
- $pK_a$  = analogous to pH and defined by the equation

$$pK_a = \log \frac{1}{K_a} = -\log K_a$$

- the stronger the tendency to dissociate a proton, the stronger the acid and the lower its  $pK_a$
- $pK_a$  can be determined experimentally

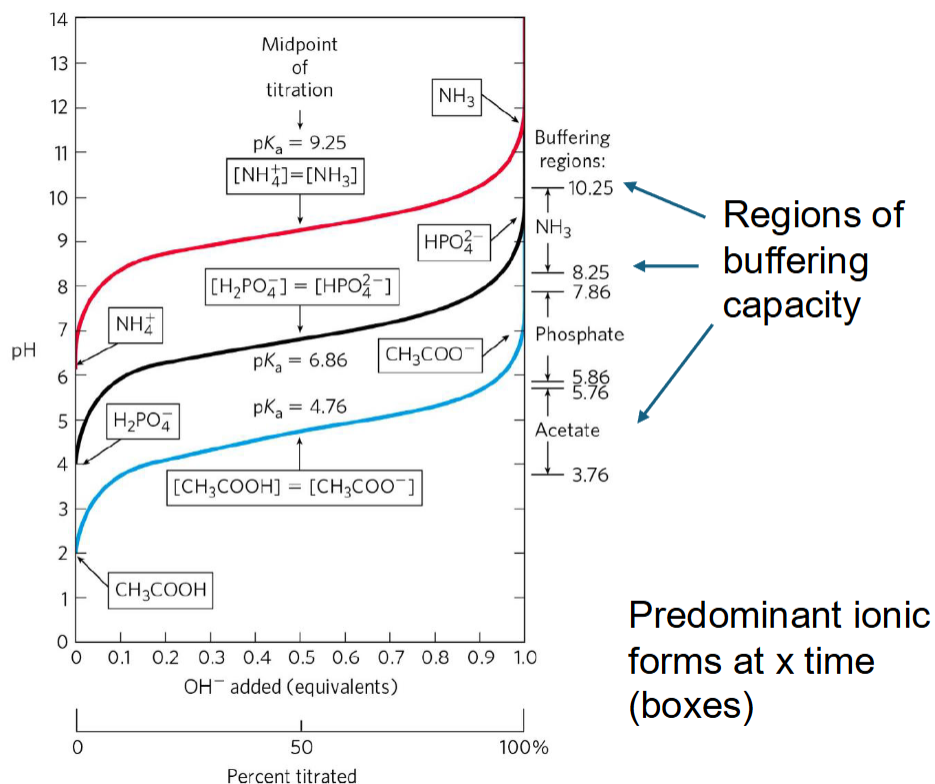
## Titration Curves Reveal the $pK_a$ of Weak Acids

- titration curve = a plot of pH against the amount of OH equivalents added



### Comparison of the Titration Curves of Three Weak Acids

- a weak acid and its anion - a conjugate acid-base pair - can act as a **buffer**
- Titration curves for acetic acid, dihydrogen phosphate, and ammonium are shown below
- Conjugate acid-base pairs are effective buffers between approximately 10% and 90% neutralization of the proton donor species



## Buffers are Mixtures of Weak Acids and Their Conjugate Bases

- buffers = aqueous systems that tend to resist changes in pH when small amounts of acid ( $\text{H}^+$ ) or base ( $\text{OH}^-$ ) are added
- a buffer system consists of a weak acid (the proton donor) and its conjugate acid (the proton acceptor)
- The **buffering region** is the flat zone of a titration curve (see above)
  - the boundaries of a buffer system are  $\text{pH} = \text{p}K_a \pm 1$  (so acetic acid buffer range is 3.76-5.76)

The buffering capacity is strongest when the ration of  $[\text{HA}]$  to  $[\text{A}^-]$  is close to 1:1. This occurs at the  $\text{p}K_a$  of the weak acid, where half of the weak acid is dissociated.

**If the ratio of acid to base (or base to acid) becomes too large** - greater than 10:1 or less than 1:10 - the buffer's capacity to neutralize added acids or bases weakens significantly

## The Henderson-Hasselbalch Equation Relates pH, $\text{p}K_a$ , and Buffer Concentration

- **Henderson-Hasselbalch equation** = describes the shape of the titration curve of any weak acid

$$\text{pH} = \text{p}K_a + \log \frac{[\text{A}^-]}{[\text{HA}]}$$

- Equation only works within the buffer region, outside of this it starts becoming inaccurate

### Primary Uses of the Henderson-Hasselbalch Equation

1. Calculating pH of Buffers
  - Predicts pH based on acid/base ratios
2. Designing Buffers
  - Helps create buffers with a desired pH by adjusting the acid-base ratio.
3. Estimating  $\text{p}K_a$ 
  - Can determine the  $\text{p}K_a$  of weak acids and bases experimentally

## Deriving the Henderson-Hasselbalch Equation (not needed for exam)

$$\begin{aligned}K_a &= \frac{[\text{H}^+][\text{A}^-]}{[\text{HA}]} \\[\text{H}^+] &= K_a \cdot \frac{[\text{HA}]}{[\text{A}^-]} \\-\log[\text{H}^+] &= -\log K_a - \log \frac{[\text{HA}]}{[\text{A}^-]} \\ \text{pH} &= \text{p}K_a - \log \frac{[\text{HA}]}{[\text{A}^-]} \\ \text{pH} &= \text{p}K_a + \log \frac{[\text{A}^-]}{[\text{HA}]}\end{aligned}$$

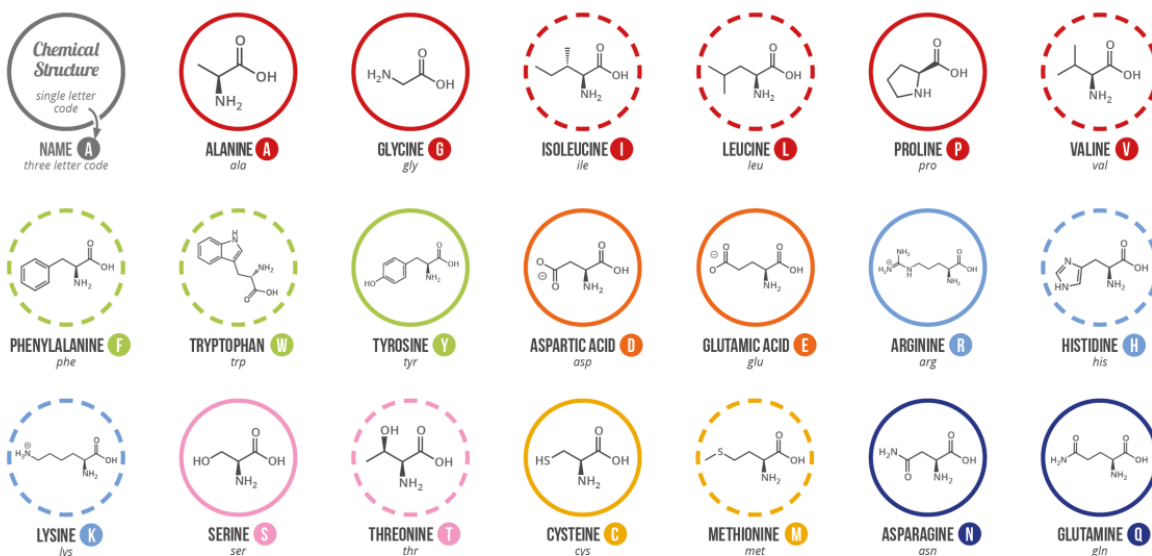
## Amino Acids

- In every living organism, proteins are constructed from a common set of 20 amino acids\*
- Each amino acid has a side chain with distinctive chemical properties. Amino acids may be regarded as the alphabet in which the language of protein structure is written.

# A GUIDE TO THE TWENTY COMMON AMINO ACIDS

AMINO ACIDS ARE THE BUILDING BLOCKS OF PROTEINS IN LIVING ORGANISMS. THERE ARE OVER 500 AMINO ACIDS FOUND IN NATURE - HOWEVER, THE HUMAN GENETIC CODE ONLY DIRECTLY ENCODES 20. 'ESSENTIAL' AMINO ACIDS MUST BE OBTAINED FROM THE DIET, WHILST NON-ESSENTIAL AMINO ACIDS CAN BE SYNTHESISED IN THE BODY.

**Chart Key:** ● ALIPHATIC ● AROMATIC ● ACIDIC ● BASIC ● HYDROXYLIC ● SULFUR-CONTAINING ● AMIDIC ○ NON-ESSENTIAL ○ ESSENTIAL



**Note:** This chart only shows those amino acids for which the human genetic code directly codes for. Selenocysteine is often referred to as the 21st amino acid, but is encoded in a special manner. In some cases, distinguishing between asparagine/aspartic acid and glutamine/glutamic acid is difficult. In these cases, the codes asx (B) and glx (Z) are respectively used.

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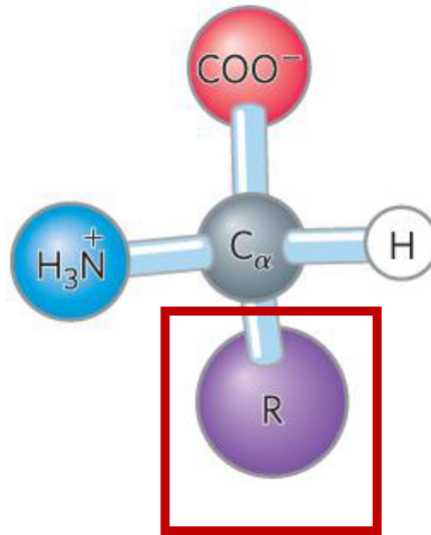


## Amino Acids Share Common Structural Features

- $\alpha$  carbon and four substituents
- $\alpha$  carbon is the **chiral center** (except in Glycine, which is not chiral)
- Tetrahedral

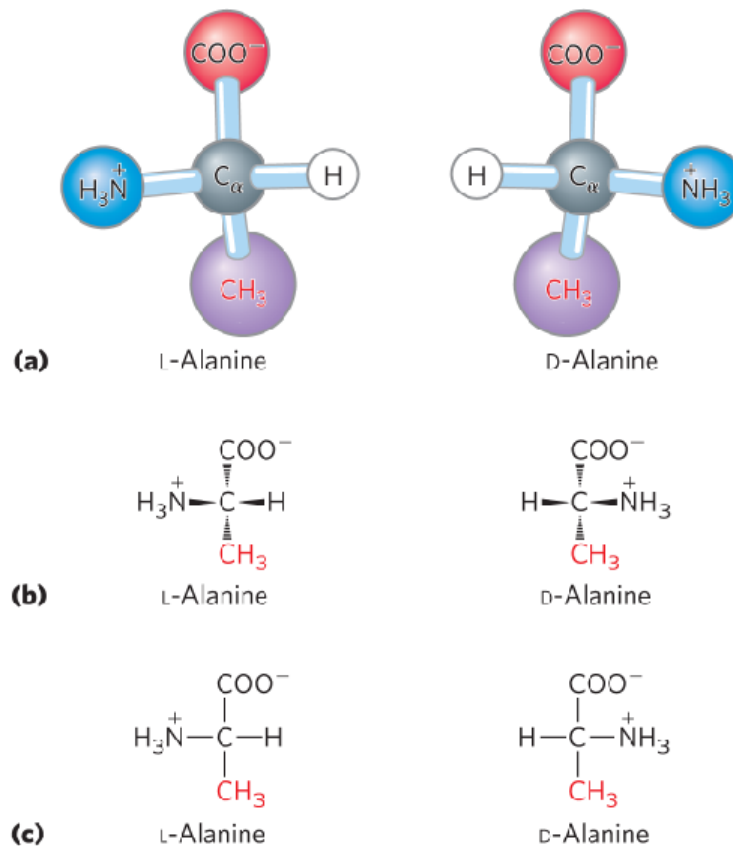
The four substituents are:

- a carboxyl group
- an amino group
- a hydrogen atom
- an **R group** (a side chain unique to each amino acid)
  - **Glycine** has a second hydrogen atom instead of an R group.



### The Amino Acid Residues in Proteins are L Stereoisomers

- Two possible stereoisomers = **enantiomers**
- **optically active** = polarize light is rotated in different directions by enantiomers (Glycine is the exception)
- D, L system specifies **absolute configuration**



## Amino Acids can be classified by the R Group

There are five main classes:

- Nonpolar, aliphatic (7)
- Aromatic (3)
- Polar, uncharged (5)
- Positively charged, Basic (3)
- Negatively charged, Acidic (2)

### Nonpolar, Aliphatic R Groups

The **hydrophobic effect** stabilizes protein structure

- Glycine
- Alanine
- Proline
- Valine
- Leucine
- Isoleucine
- Methionine

### Aromatic R Groups

R groups absorb UV light at 270-280 nm, and can contribute to the hydrophobic effect.

- Phenylalanine
- Tyrosine
- Tryptophan

### Polar, Uncharged R Groups

R groups can **form hydrogen bonds**, and Cysteine can **form disulfide bonds**

- Serine
- Threonine
- Cysteine
- Asparagine
- Glutamine

### Positively Charged R Groups

Have significant positive charge at pH 7.0.

- Lysine
- Arginine
- Histidine

## Negatively Charged R Groups

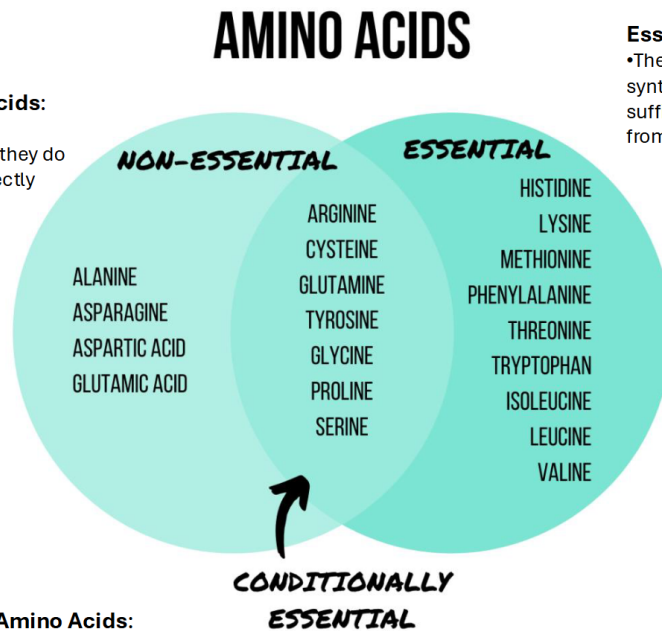
Have net negative charge at pH 7.0.

- Aspartate
- Glutamate

## Essential Amino Acids

### Non-Essential Amino Acids:

•These amino acids can be synthesized by the body, so they do not need to be obtained directly through the diet



### Essential Amino Acids:

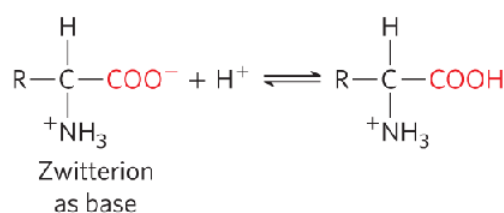
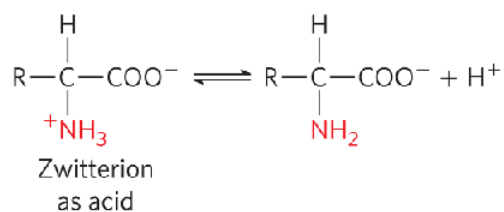
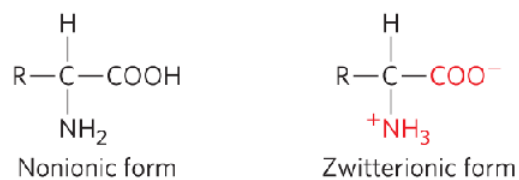
•These amino acids cannot be synthesized by the human body in sufficient amounts and must be obtained from the diet

### Conditionally Essential Amino Acids:

•Under normal conditions, these amino acids are synthesized by the body, but during periods of illness, stress, or growth, their production might not meet the body's demands, and they must be supplemented through the diet

## Amino Acids can act as Acids or Bases

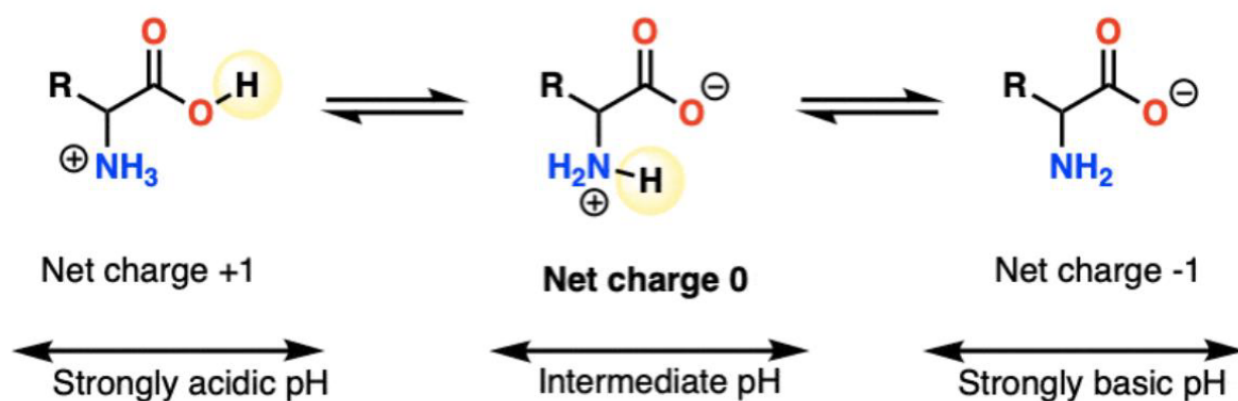
- Amino acids are **acids**. They are also **bases** containing an amino group.
- The term **amphoteric** is often used to describe amino acids, meaning that they are capable of acting as both acids and bases
- **zwitterion** occurs at neutral pH.



### The pH-dependent structures of a typical amino acid

For a typical amino acid with a neutral sidechain **R**:

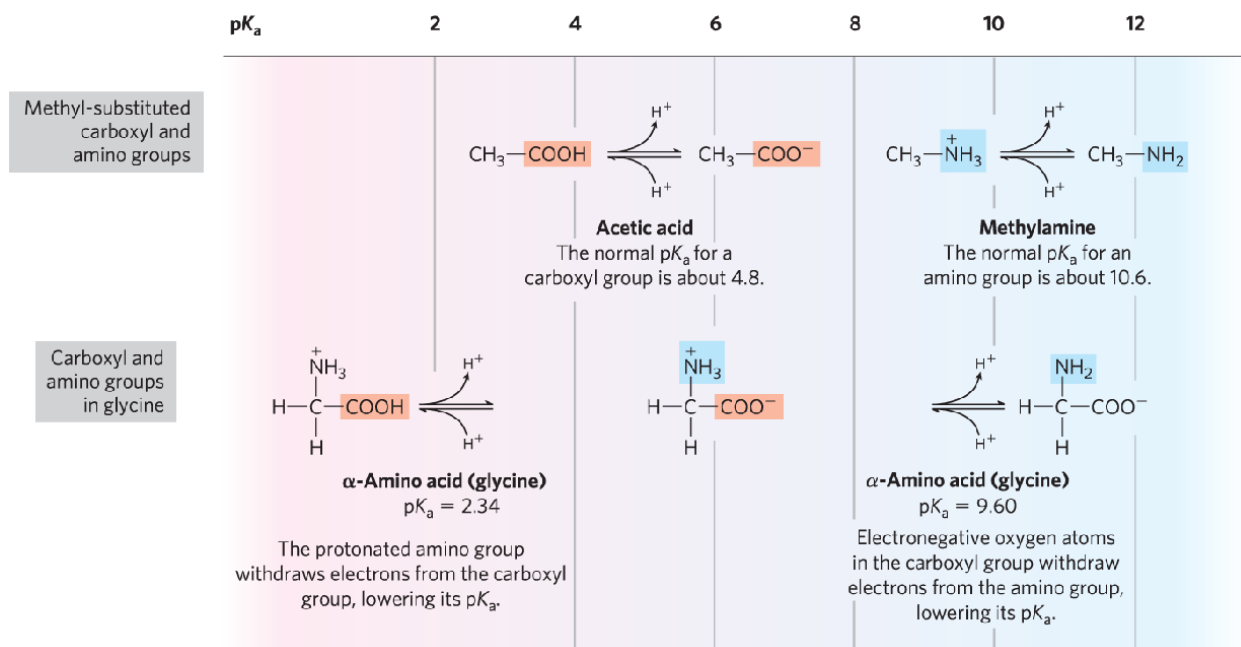
- the positively charged form (+1) dominates at low pH.
- the zwitterionic (neutral) form dominates at intermediate pH, and
- the negatively charged form (-1) dominates at high pH.



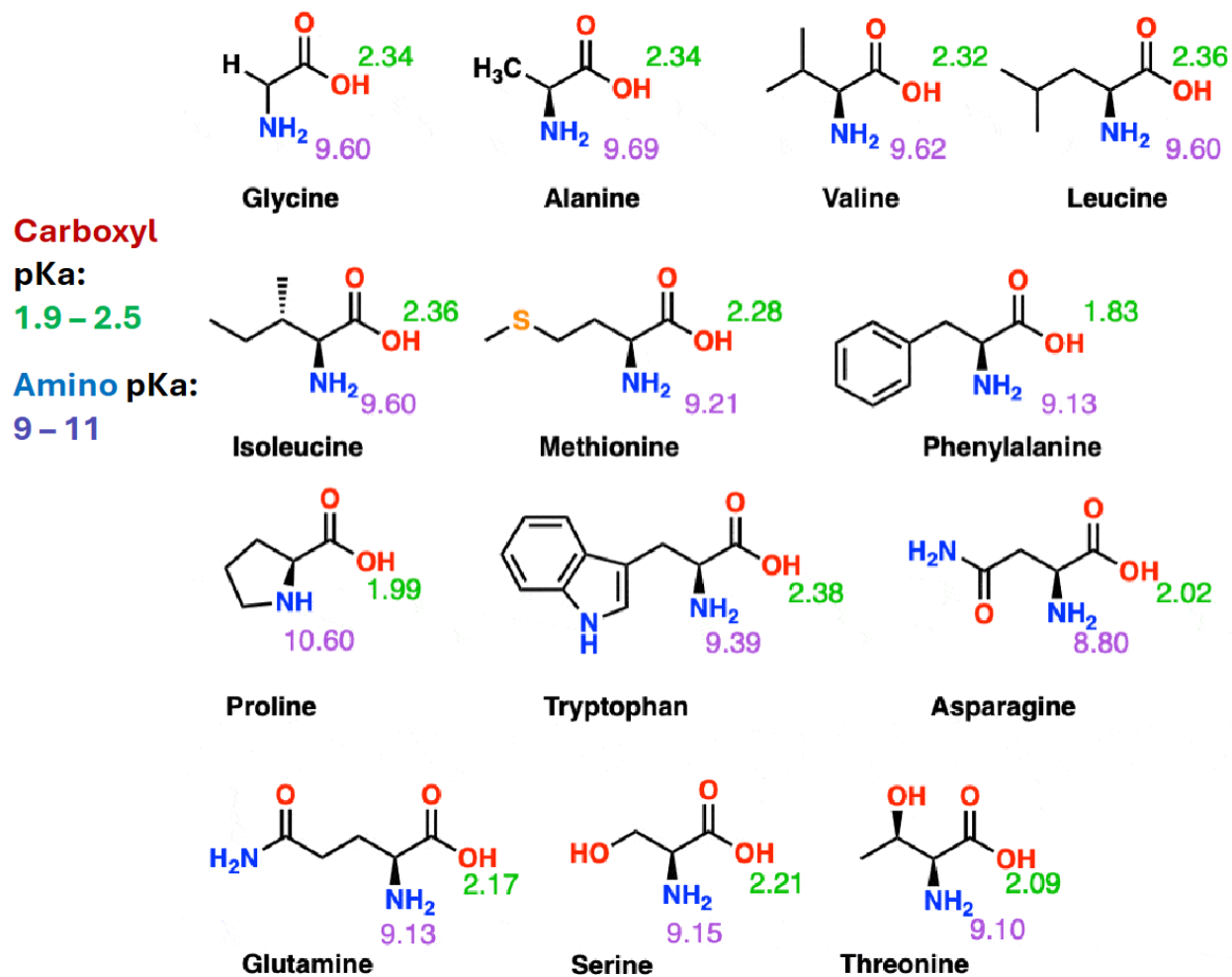
### Effect of the Chemical Environment on $pK_a$

- $\alpha$ -carboxyl group is more acidic than in carboxylic acids
- $\alpha$ -amino group is less basic than in amines





## Structures (and $pK_a$ ) values of selected amino acids



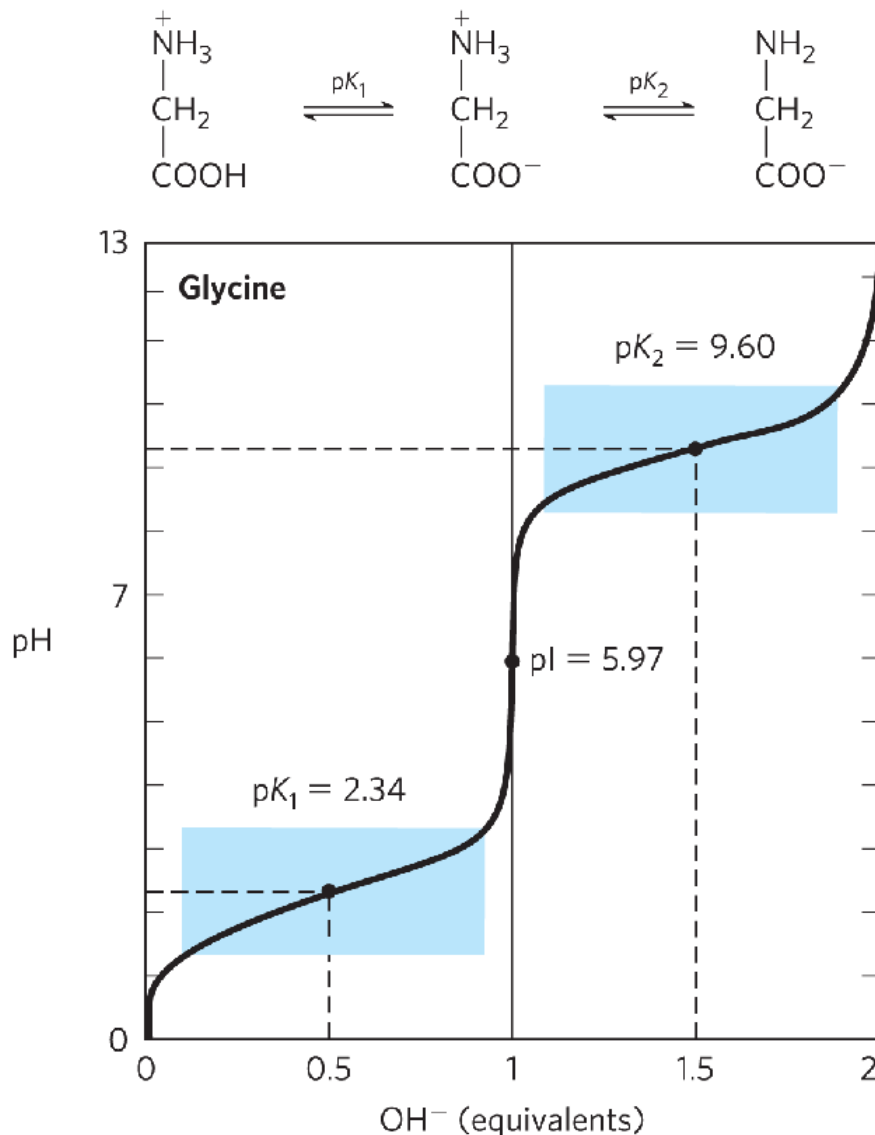
## Table of Amino Acid $pK_a$ s

Functional Group	$pK_a$
COO <sup>-</sup> -terminus	3.5
<sup>+</sup> NH <sub>3</sub> -terminus	8.5
$\alpha$ -COO <sup>-</sup> (free amino acid)	2
$\alpha$ - <sup>+</sup> NH <sub>3</sub> (free amino acid)	9.5
Aspartate R group	3.9
Glutamate R group	4.3
Histidine R group	6
Cysteine R group	8.3
Tyrosine R group	10
Lysine R group	10.8
Arginine R group	12.5

## Titration of Amino Acids

- Cation  $\rightleftharpoons$  zwitterion  $\rightleftharpoons$  anion
- -COOH (carboxyl) has an acidic  $pK_a$  ( $pK_1$ )

- $\text{-NH}_3^+$  (amino) has a basic  $\text{p}K_a$  ( $\text{p}K_2$ )
- the pH at which the net electric charge is zero is the **isoelectric point (pI)**



This titration curve is a qualitative measure of the  $\text{p}K_a$  of each ionizing group.

- shows buffering power
  - flat regions are buffer regions. Glycine has two, one centered at  $\text{p}K_1 = 2.34$ , the other at  $\text{p}K_2 = 9.6$
  - Buffer regions are highlighted in blue.
- shows relationship between its net charge and the pH of the solution
  - isoelectric point, or pI, can be calculated
- In the above image, glycine is present predominantly as its dipolar form, fully ionized with no net electric charge. At the point (pH = 5.97, 1eq base), glycine has an equal number of positive and negative charges.

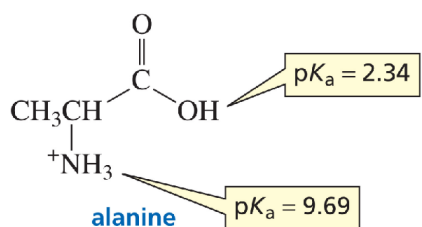
## The Isoelectric Point

- The **isoelectric point (pI)** determines the pH at which a molecule carries no net electric charge
- This occurs when the positive and negative charges on the molecule are balanced. For amino acids, the pI is determined by the  $pK_a$  values of its ionizable groups, such as the amino ( $-\text{NH}_3^+$ ) and carboxyl ( $-\text{COOH}$ ) groups, and sometimes the side chain, if it is ionizable.
- for amino acids without ionizable side chains, the **isoelectric point (pI)** is:

$$pI = \frac{pK_1 + pK_2}{2}$$

- $pH = pI$  = net charge is zero (amino acid least soluble in water, does not migrate in electric field)
- $pH > pI$  = net negative charge
- $pH < pI$  = net positive charge

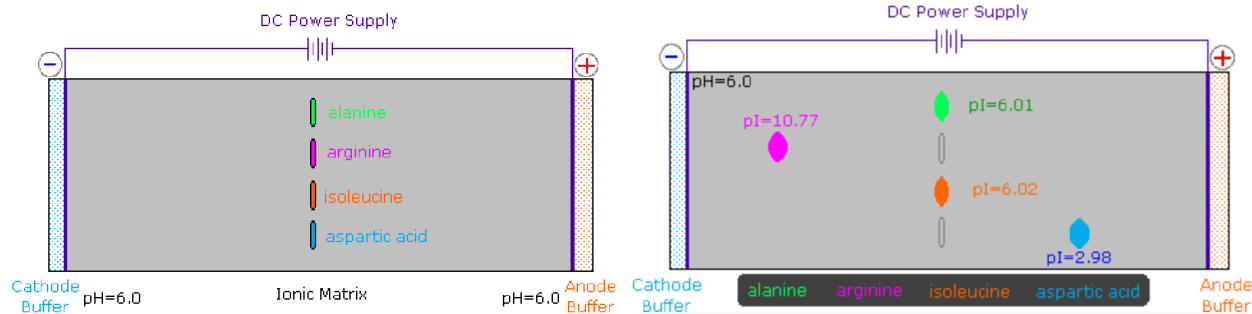
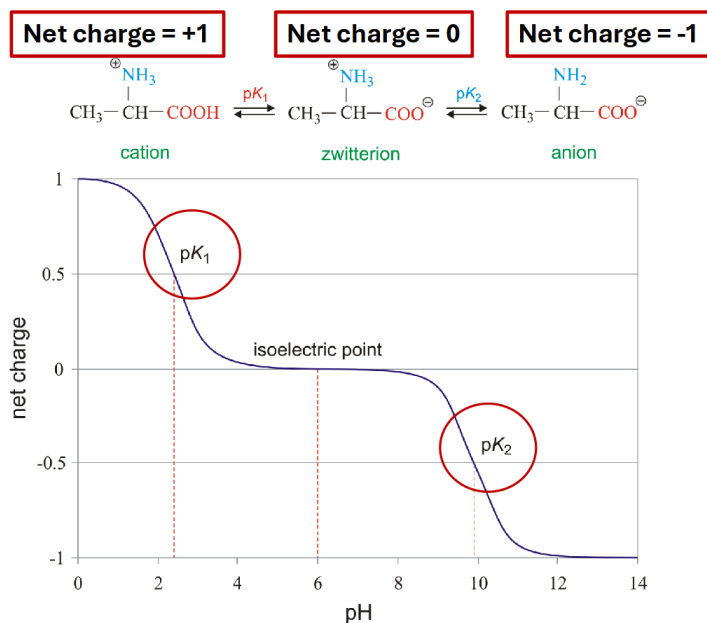
## Isoelectric point - Alanine



$$pI = \frac{2.34 + 9.69}{2}$$

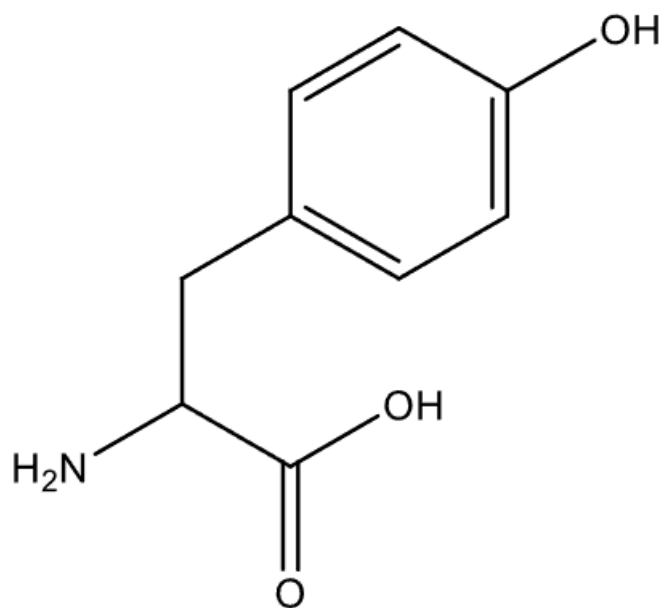
$$pI = 6.015$$

- Not a range, we average the two  $pK_a$ s around the point to get one number



## Tyrosine at different pH

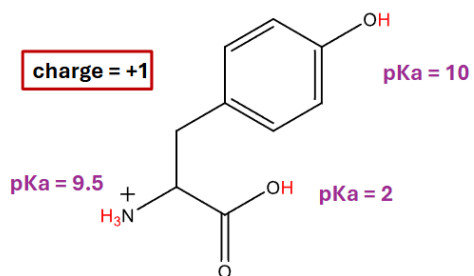
### Standard Representation



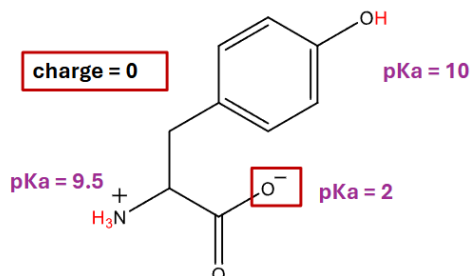
- This is the standard representation of Tyrosine, found in many online sources and textbooks
- It is important to note that **this structure does not exist at any pH!**
- The molecule is made neutral just because, to display its structure.

## Representations at different pH

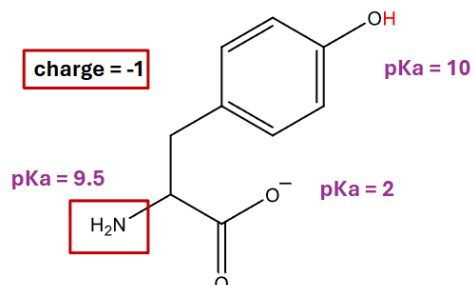
**Predominant tyrosine species at pH = 1  
(or any pH < 2)**



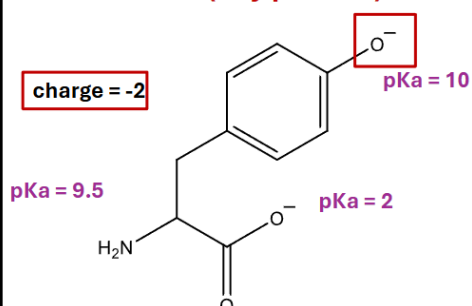
**Predominant tyrosine species at pH = 7  
(in range 2 < pH < 9.5)**



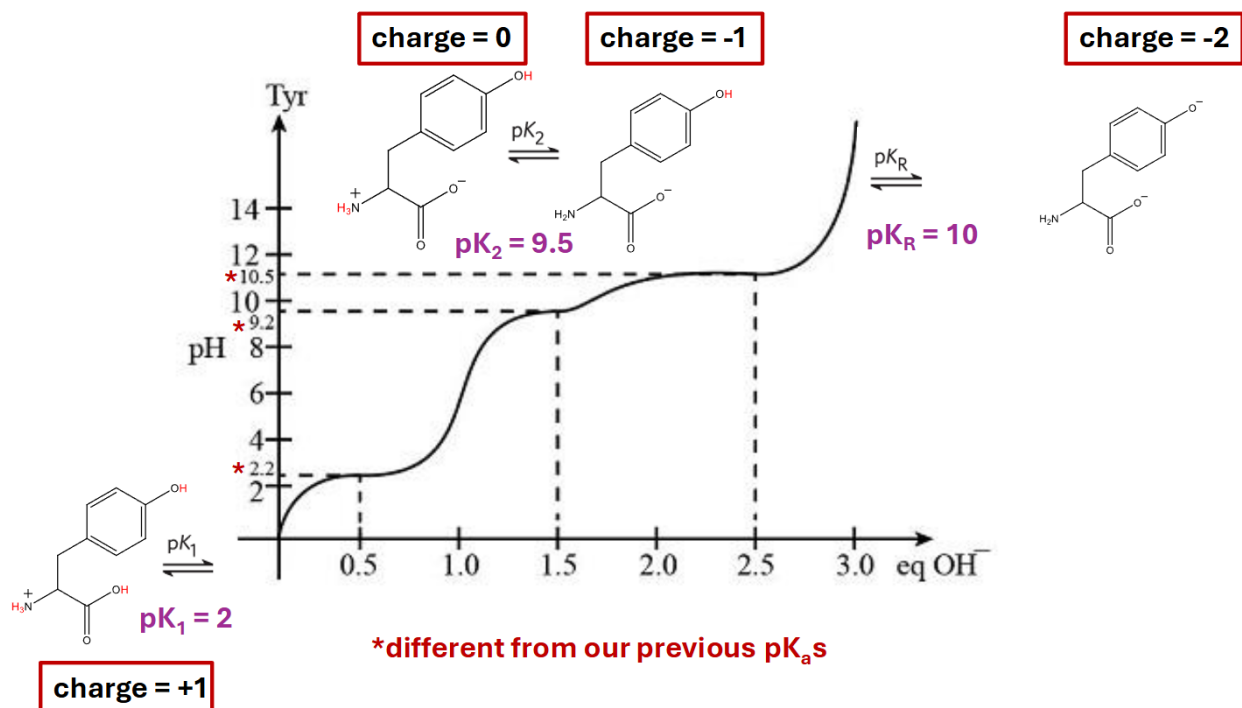
**Predominant tyrosine species at pH = 9.75  
(in range 9.5 < pH < 10)**



**Predominant tyrosine species at pH = 12  
(any pH > 10)**

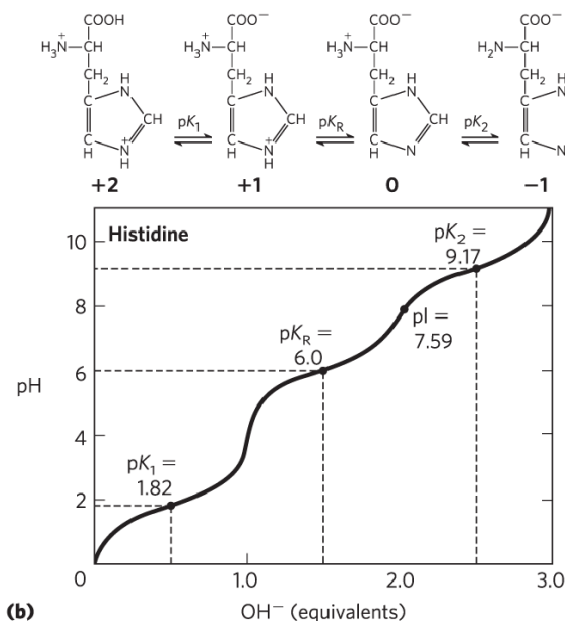
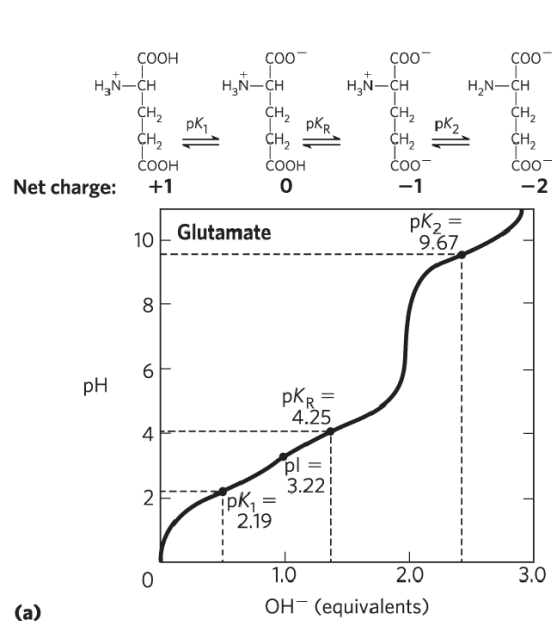


## Titration of Tyrosine



- Notice there is a buffer region around each pK<sub>a</sub>

## Titration of Amino Acids with an Ionizable R Group



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## Peptides and Proteins

In proteins, amino acids are joined in characteristic linear sequences through a common amide linkage, the **peptide bond**. The amino acid sequence of a protein constitutes its primary structure.

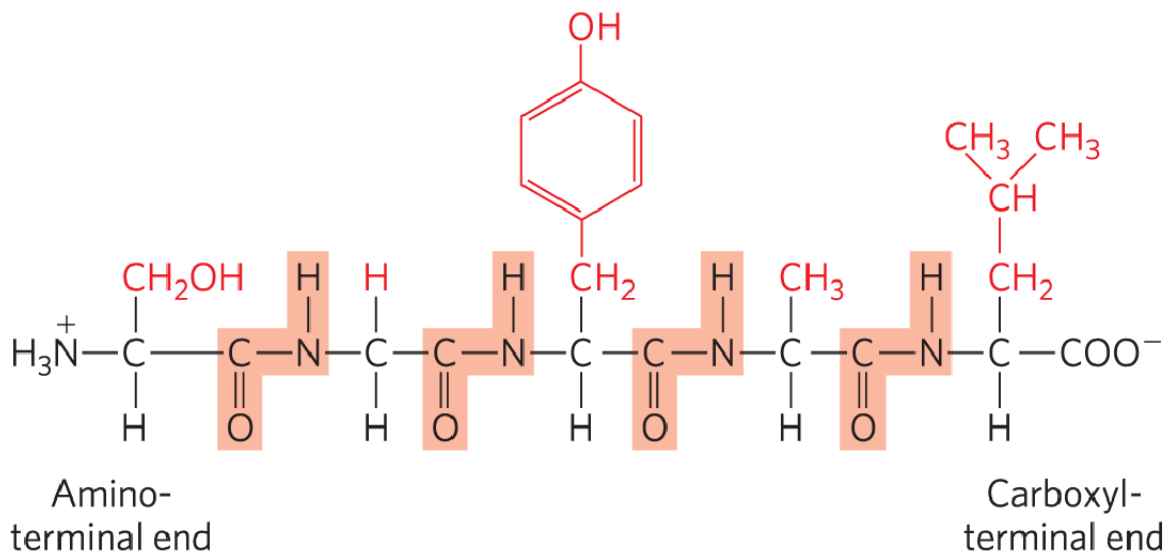
- Peptides are chains of amino acids
- Peptide bond:
  - Covalent
  - formed through **condensation**
  - broken through **hydrolysis**
- The **carboxyl group** of one amino acid loses a hydroxyl group (-OH)
- The **amino group** of the second amino acid loses a hydrogen atom (-H)





## Peptide Terminals

Convention: numbering (and naming) starts from the **amino-terminal residue** (*N*-terminal)



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**N-terminal**

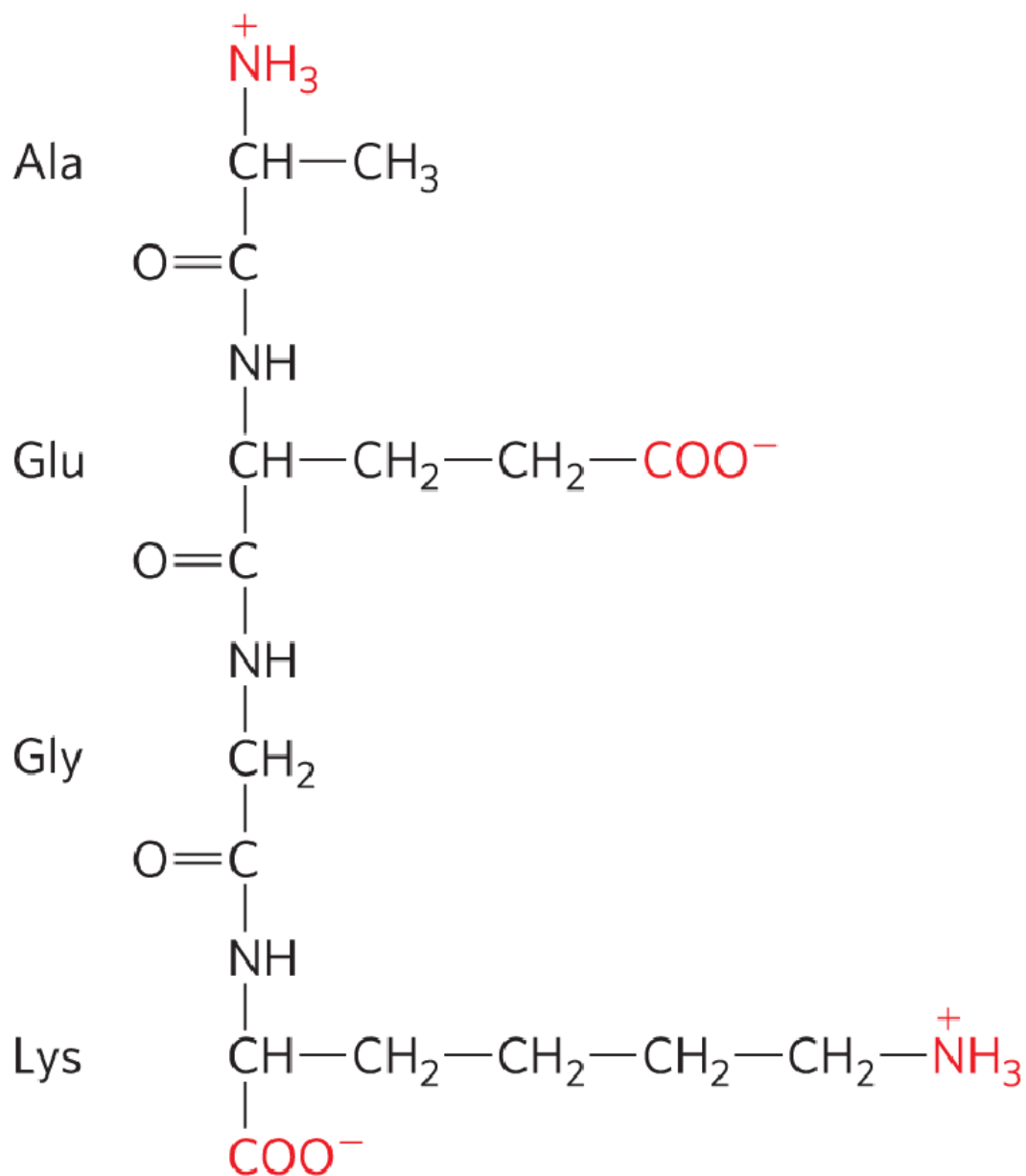
**C-terminal**

## Naming Peptides

- Full amino acid names: serylglycyltyrosylalanylleucine
- Three letter code abbreviations: Ser-Gly-Tyr-Ala-Leu
- One letter code abbreviation: SGYAL

## Peptides can be distinguished by their ionization behavior

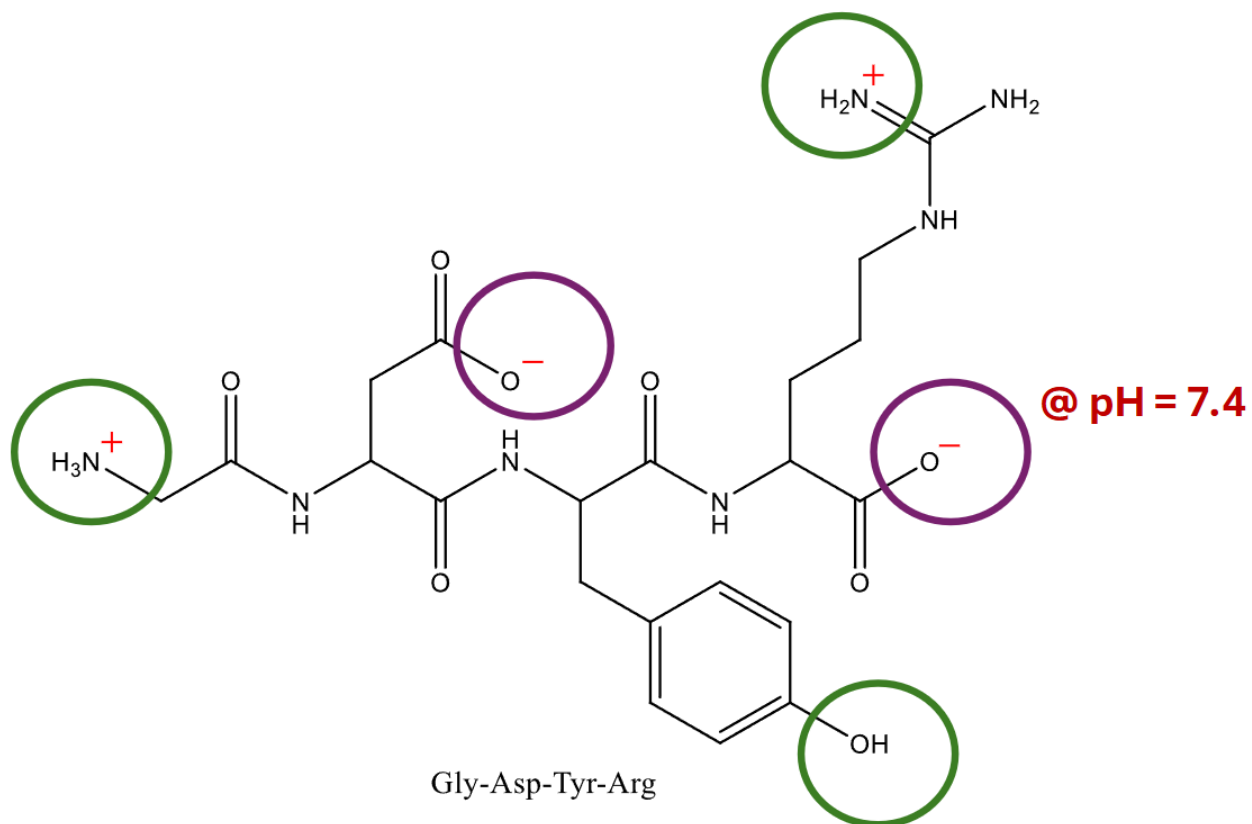
- Ionizable groups in peptides:
  - one free  $\alpha$ -amino group
  - one free  $\alpha$ -carboxyl group
  - some R groups



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### Drawing oligopeptides

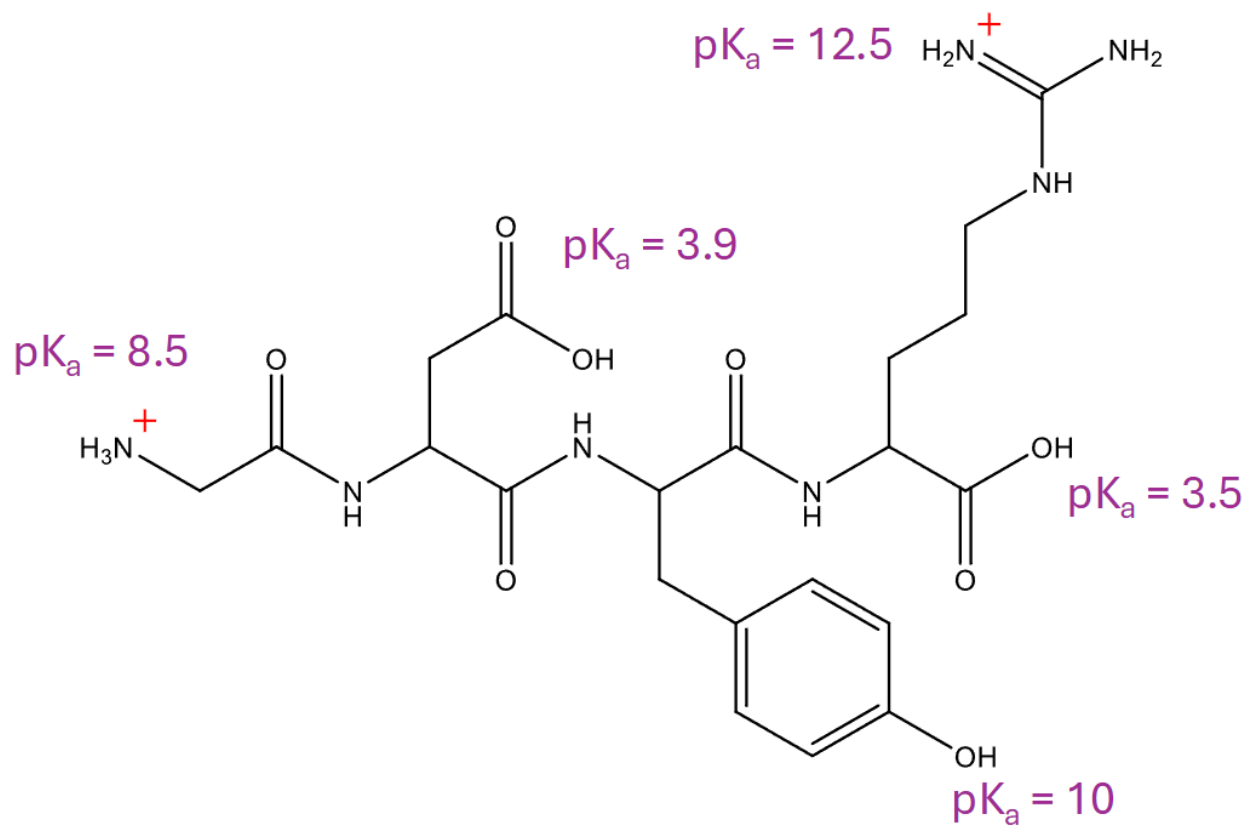
Draw the oligopeptide Gly-Asp-Tyr-Arg at physiological pH



- Refer to the functional group pH table earlier in this document.
- $\text{pH} < \text{pK}_a$ : The molecule is protonated (it holds onto its protons)
- $\text{pH} > \text{pK}_a$ : The molecule is deprotonated (it loses its protons)

### Determining pI of peptide

1. Draw the peptide at its most protonated form (low pH)
2. Calculate overall charge
3. Calculate the change in charge as pH rises (noting  $\text{pK}_a$ s)
4. Use the 2  $\text{pK}_a$ s surrounding peptide at 0 charge  $\rightarrow$  average



pH range	<3.5	3.5 - 3.9	3.9 - 8.5	8.5 - 10	10 - 12.5	>12.5
~net charge	+2	+1	0	-1	-2	-3

$$\text{pI} = \frac{8.5 + 3.9}{2} = 6.2$$