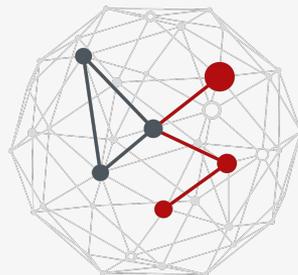


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ACID-BASE THEORY

Master of Science in Data Science

Damiano Piovesan



Arrhenius theory

Arrhenius (second half 1800)

- acid $\text{HA} \rightarrow \text{A}^- + \text{H}^+$ ($\text{H}^+ \rightarrow$ hydrogen ion)
- base $\text{BOH} \rightarrow \text{B}^+ + \text{OH}^-$ ($\text{OH}^- \rightarrow$ oxydril ion)

$$K_a = [\text{A}^-] [\text{H}^+] / [\text{HA}]$$

acid dissociation constant

$$K_b = [\text{B}^+] [\text{OH}^-] / [\text{BOH}]$$

basic dissociation constant

Acid + base \rightarrow salt



Brønsted & Lowry theory

Brønsted & Lowry (1923)

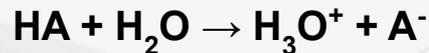
- acid \rightarrow **releases** ions H^+ $\text{HA} + \text{B} \rightarrow \text{A}^- + \text{BH}^+$
- base \rightarrow **accept** / bind H^+ $\text{A}^- + \text{BH}^+ \rightarrow \text{HA} + \text{B}$

In the second reaction **BH⁺** releases H^+ then it is an **acid**, while **A⁻** bins the proton, then it is a **base**

$\text{A}^- \rightarrow$ conjugate base of HA

$\text{BH}^+ \rightarrow$ conjugate acid of B:

Aqueous solution



Acid

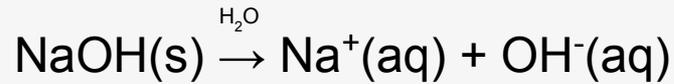


- **React** with water \rightarrow covalent bonds forms and are broken
- It can be an ion +/-, or a neutral compound
- (Brønsted-Lowry) Has to have at least 1 H, but only H bound to a very electronegative atom are exchanged

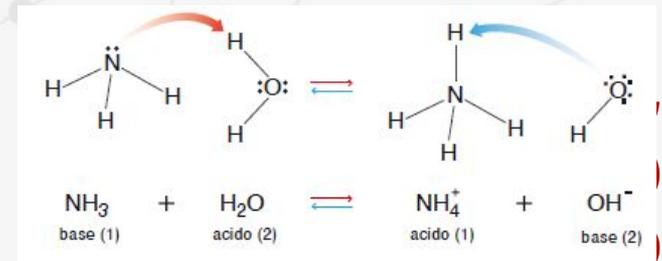
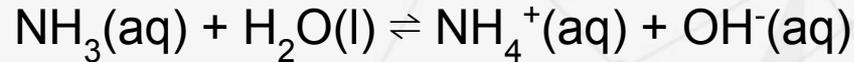


Base

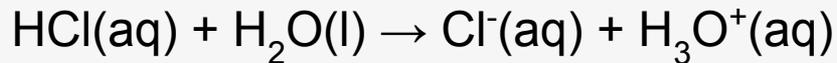
- Only **negative ions** or **neutral** molecules
- Metallic hydroxide → **They dissolve** in water (don't react), ions get solvated



- Other bases → **React** with water



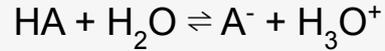
Strong acids and bases



- **React completely** with water to form $\text{H}_3\text{O}^{\text{+}}$
- Complete **dissociation** or **ionization**
- The strength of an acid (or base) **does not depend** on its **concentration**

6 Strong Acids		6 Strong Bases	
HClO_4	perchloric acid	LiOH	lithium hydroxide
HCl	hydrochloric acid	NaOH	sodium hydroxide
HBr	hydrobromic acid	KOH	potassium hydroxide
HI	hydroiodic acid	Ca(OH)_2	calcium hydroxide
HNO_3	nitric acid	Sr(OH)_2	strontium hydroxide
H_2SO_4	sulfuric acid	Ba(OH)_2	barium hydroxide

Acid dissociation constant



$$K = \frac{[\text{A}^-][\text{H}_3\text{O}^+]}{[\text{HA}][\text{H}_2\text{O}]}$$

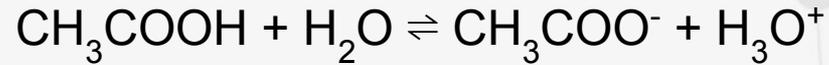
$$K_a = K [\text{H}_2\text{O}] = \frac{[\text{A}^-][\text{H}_3\text{O}^+]}{[\text{HA}]}$$

$$\text{p}K_a = -\log K_a$$

- Water (solvent) concentration stays constant in comparison to the acid (solute)
- Water is removed from the denominator of K and included in K_a



Weak acids



$$K_a = \frac{[\text{H}_3\text{O}^+][\text{CH}_3\text{COO}^-]}{[\text{CH}_3\text{COOH}]} = 1.8 \times 10^{-5}$$

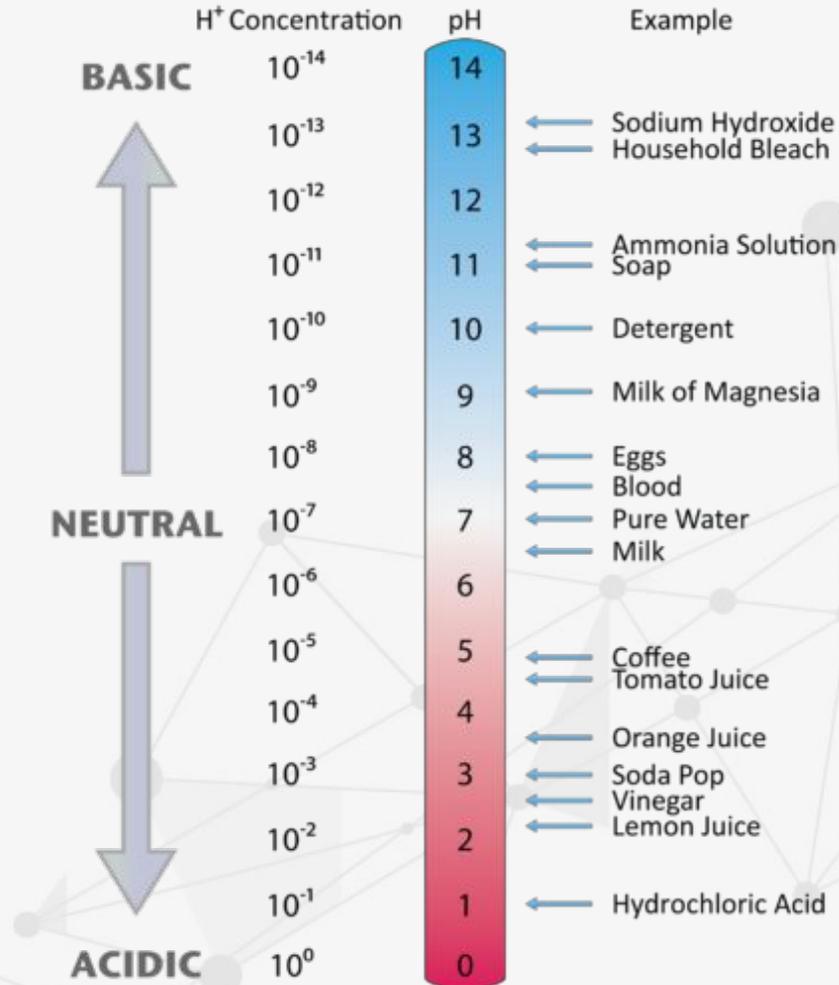
$$\text{p}K_a = ?$$

Given $\text{p}K_a$ how do you calculate the K_a ?

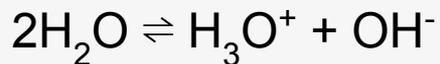
$$K_a = 10^{-\text{p}K_a}$$



pH



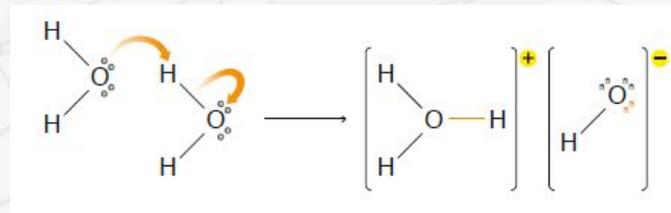
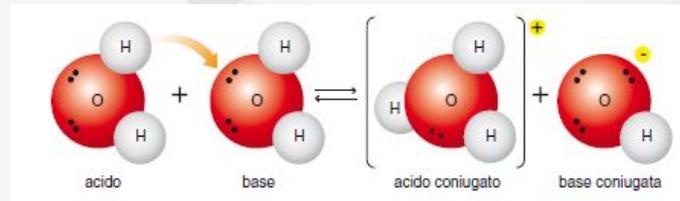
Self-ionization of water



$$K = \frac{[\text{OH}^-] [\text{H}_3\text{O}^+]}{[\text{H}_2\text{O}] [\text{H}_2\text{O}]}$$

$$K_a = K [\text{H}_2\text{O}] = \frac{[\text{OH}^-] [\text{H}_3\text{O}^+]}{[\text{H}_2\text{O}]}$$

$$K_w = K [\text{H}_2\text{O}]^2 = [\text{OH}^-] [\text{H}_3\text{O}^+]$$



Ionic product of water (K_w)

$$K_w = K [\text{H}_2\text{O}]^2 = [\text{H}_3\text{O}^+] [\text{OH}^-] = 10^{-14} \text{ M}^2$$

$$[\text{H}_3\text{O}^+] = [\text{OH}^-] = 10^{-7} \text{ M}$$

$$\text{pH} = -\log [\text{H}_3\text{O}^+] = 7$$

$$\text{p}K_w = \text{pH} + \text{pOH} = 14$$

- K_w is valid for any aqueous solution, not only for water



Exercise

Calculate the concentration of hydroxide ions $[\text{OH}^-]$ of an aqueous solution with a concentration of hydrogen ions of $[\text{H}_3\text{O}^+] = 10^{-5}$

What is the concentration of pure water (you need to know the concept of “concentration” and “molecular weight”)?



Exercise

Calculate the concentration of hydroxide ions $[\text{OH}^-]$ of an aqueous solution with a concentration of “hydrogen ions” of $[\text{H}_3\text{O}^+] 10^{-5}$.

$$[\text{OH}^-] = K_w / [\text{H}_3\text{O}^+] = 10^{-14} / 10^{-5} = 10^{-9}$$

or

$$\text{pH} = -\log([\text{H}_3\text{O}^+]) = -\log(10^{-5}) = 5$$

$$\text{pOH} = 14 - 5 = 9$$

$$[\text{OH}^-] = 10^{-\text{pOH}} = 10^{-9}$$



Exercise

What is the concentration of pure water (you need to know the concept of “concentration” and “molecular weight”)?

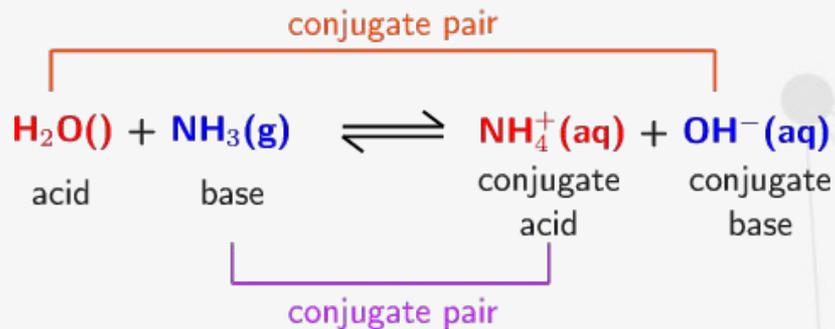
- Concentration \rightarrow Molarity (M) \rightarrow mol \times L⁻¹
- 1 mole = $6.02214076 \times 10^{23}$ particles (Avogadro's Number)

$$\text{Molecular weight}_{\text{H}_2\text{O}} = 16 + 1 + 1 = 18 \text{ g mol}^{-1}$$

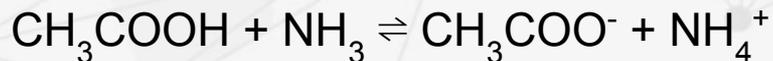
$$\text{Molarity} = 1000 \text{ mL} / 18 \text{ g mol}^{-1} = 55.6 \text{ mol L}^{-1}$$



Conjugate acids and bases (Brønsted-Lowry)



- Molecules or ions pairs are correlated by gaining or losing a proton
- Stronger the acid, weaker the conjugate base
- **Equilibrium is shifted** toward the weakest acid (and base) since strong acids (and bases) react more
- It applies to reactions without water as well:

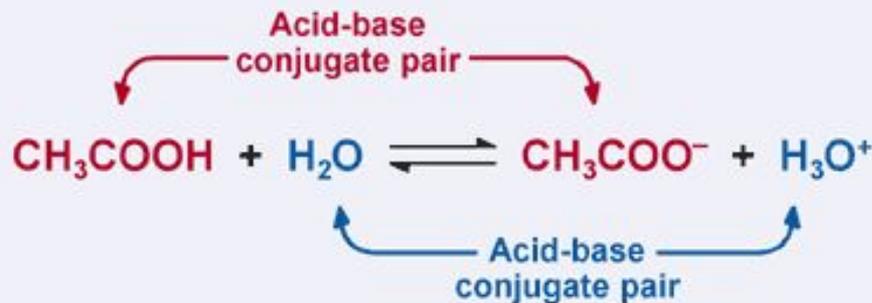


Conjugate acids and bases

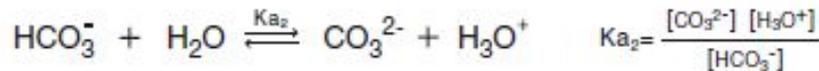
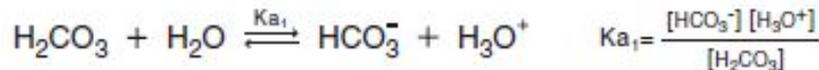
	Acid		Base				
Increasing acid strength ↑	perchloric acid	HClO_4	} Undergo complete acid ionization in water	} Do not undergo base ionization in water	ClO_4^-	perchlorate ion	↓ Increasing base strength
	sulfuric acid	H_2SO_4			HSO_4^-	hydrogen sulfate ion	
	hydrogen iodide	HI			I^-	iodide ion	
	hydrogen bromide	HBr			Br^-	bromide ion	
	hydrogen chloride	HCl			Cl^-	chloride ion	
	nitric acid	HNO_3	NO_3^-	nitrate ion			
	hydronium ion	H_3O^+	H_2O	water			
	hydrogen sulfate ion	HSO_4^-	SO_4^{2-}	sulfate ion			
	phosphoric acid	H_3PO_4	H_2PO_4^-	dihydrogen phosphate ion			
	hydrogen fluoride	HF	F^-	fluoride ion			
	nitrous acid	HNO_2	NO_2^-	nitrite ion			
	acetic acid	$\text{CH}_3\text{CO}_2\text{H}$	CH_3CO_2^-	acetate ion			
	carbonic acid	H_2CO_3	HCO_3^-	hydrogen carbonate ion			
	hydrogen sulfide	H_2S	HS^-	hydrogen sulfide ion			
	ammonium ion	NH_4^+	HN_3	ammonia			
	hydrogen cyanide	HCN	CN^-	cyanide ion			
	hydrogen carbonate ion	HCO_3^-	CO_3^{2-}	carbonate ion			
water	H_2O	OH^-	hydroxide ion				
hydrogen sulfide ion	HS^-	} Do not undergo acid ionization in water	} Undergo complete base ionization in water	S^{2-}	sulfide ion		
ethanol	$\text{C}_2\text{H}_5\text{OH}$			$\text{C}_2\text{H}_5\text{O}^-$	ethoxide ion		
ammonia	NH_3			NH_2^-	amide ion		
hydrogen	H_2			H^-	hydride ion		
methane	CH_4			CH_3^-	methide ion		

Special cases

- **Amphoteric compounds**
 (react both as an acid and as a base)



- **Polyprotic acids**

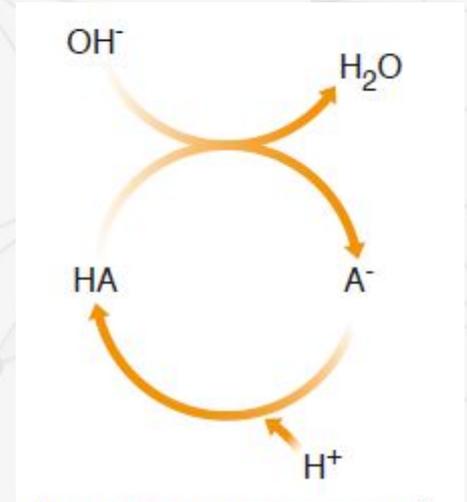


$$K_{a1} = 4,56 \times 10^{-7}$$

$$K_{a2} = 5,61 \times 10^{-11}$$

Buffer solutions

- pH changes very little when a small amount of strong acid or base is added to it (e.g. H_3O^+ or OH^-)
- When H^+ (or OH^-) increases, also the concentration of HA (or A^-) rises but the pH does not change
- The generated HA is a weak acid and does not affect the pH, because it is weak and in low amount

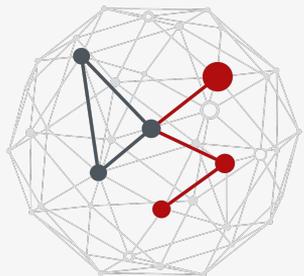


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AMINO ACIDS

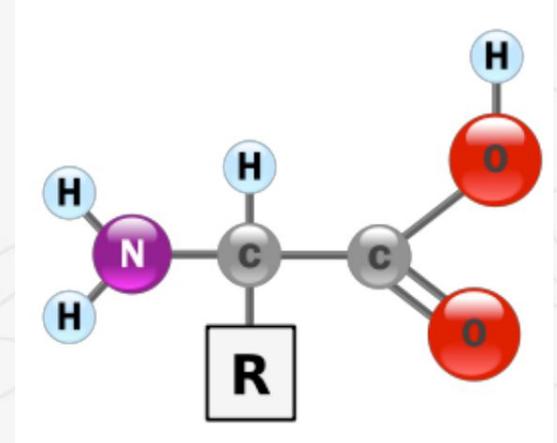
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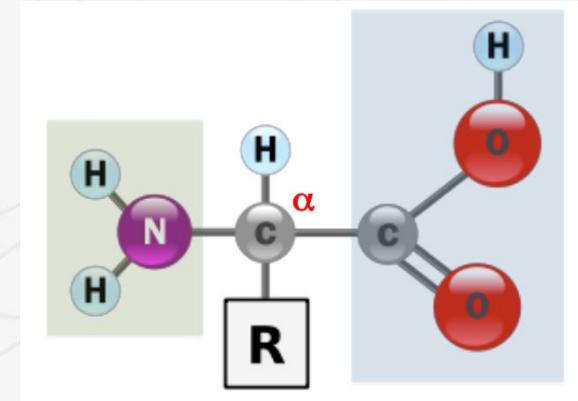
Amino acids

- Amino acids are **monomers** of proteins and other biological macromolecules
- Proteins are **polymers**
- Proteins are **linear chains** of different combinations of 20 different amino acids
- Each amino acid has a specific **chemical behaviour**



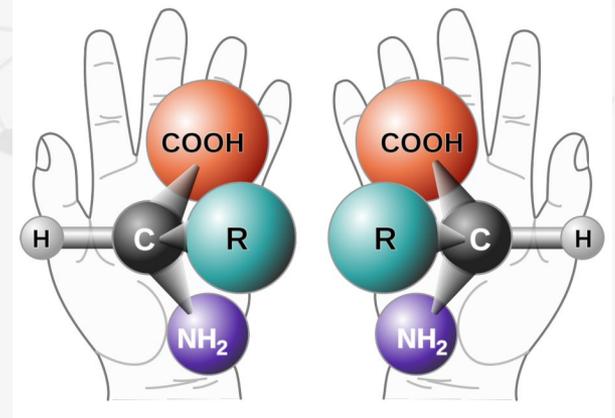
α -amino acids

- Only **20 out of 500** known amino acids appear in proteins
- All α -amino acids have a **carboxyl** (-COOH) and an **amminic** (-NH₂) group bound to the **α carbon**
- They differ for the **side chain** (R)
- Different side chains have different three dimensional **structure** and **charge**
- **Structure, electric charge** and **hydrophobicity** are the principal features



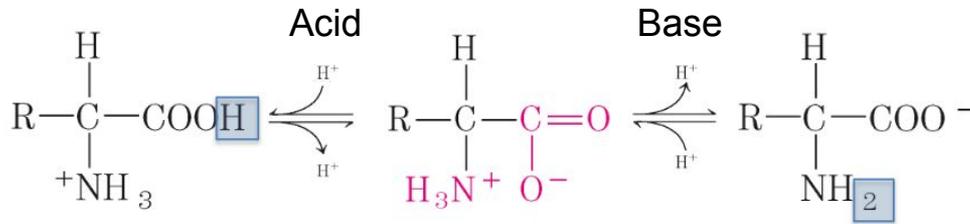
Chirality

- **α -carbon** is always bound to **four different groups** (except Glycine, R \rightarrow H)
- **Chiral molecules** \rightarrow **not superimposable** to mirrored version
- **Translations** and **rotations** not sufficient to superimpose the two versions
- Proteins contain only **L-amino acids**
- Protein **active sites** are asymmetric

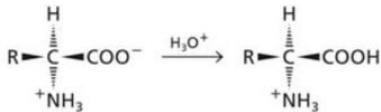


Amino acids as acid-base

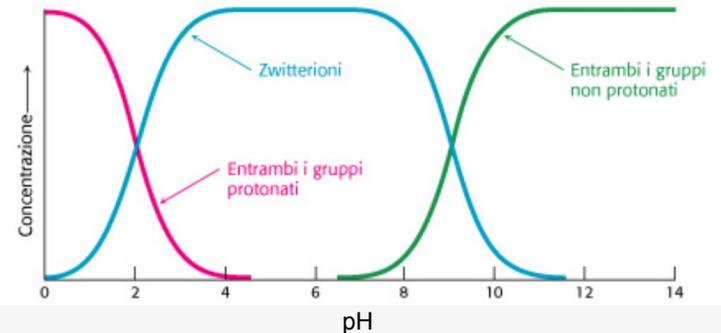
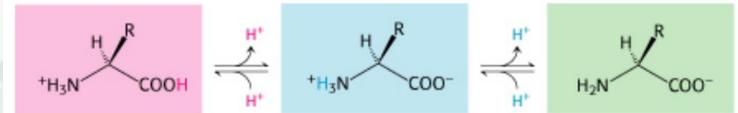
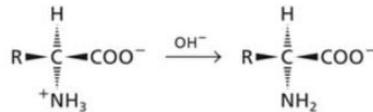
- Amino acid at **physiological pH** (ca. 7.0) exist in the **Zwitterionic** form
- The **isoelectric point (pI)** is the **pH value** at which an amino acid is found as **dipolar ion (Zwitterionic form)** with null net charge



pH 1

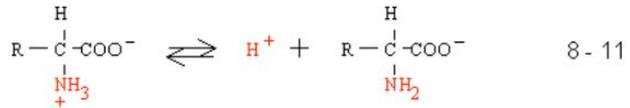
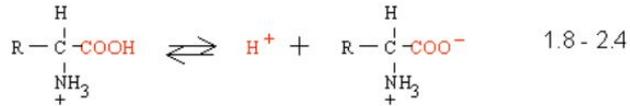


pH 12



Side chains dissociation

Main chain



Acid

Base

Side chain

	$\text{AH} \rightleftharpoons \text{H}^+ + \text{A}^-$	pKa
Aspartate	$\text{HOOC}-\text{CH}_2^- \rightleftharpoons \text{H}^+ + ^-\text{OOC}-\text{CH}_2^-$	3.7
Glutamate	$\text{HOOC}-\text{CH}_2-\text{CH}_2^- \rightleftharpoons \text{H}^+ + ^-\text{OOC}-\text{CH}_2-\text{CH}_2^-$	4.3
Lysine	$^+\text{NH}_3-(\text{CH}_2)_4^- \rightleftharpoons \text{H}^+ + \text{NH}_2-(\text{CH}_2)_4^-$	10.5
Arginine	$\begin{array}{c} \text{H}_2\text{C}-\text{C}-\text{NH}(\text{CH}_2)_3^- \\ \\ \text{NH}_2^+ \end{array} \rightleftharpoons \text{H}^+ + \begin{array}{c} \text{NH}_2-\text{C}-\text{NH}(\text{CH}_2)_3^- \\ \\ \text{NH} \end{array}$	12.5
Histidine	$\begin{array}{c} \text{HC}=\text{C}-\text{CH}_2^- \\ \quad \\ \text{NH}^+ \quad \text{NH} \end{array} \rightleftharpoons \text{H}^+ + \begin{array}{c} \text{HC}=\text{C}-\text{CH}_2^- \\ \quad \\ \text{N} \quad \text{NH} \end{array}$	6.0



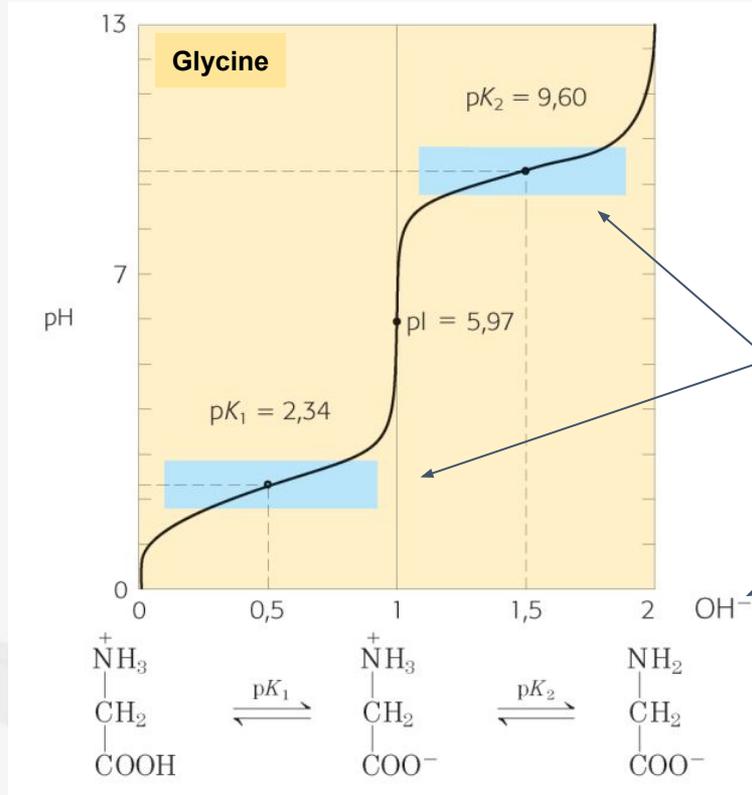
	Amino Acid	pKa Value		
	Name	Alpha Carboxy	+Alpha Amino	Side Chain
Non-Polar Amino Acids	Glycine	2.34	9.60	
	Alanine	2.34	9.69	
	Valine	2.32	9.62	
	Leucine	2.36	9.60	
	Isoleucine	2.36	9.68	
	Methionine	2.28	9.21	
	Phenylalanine	1.83	9.13	
	Tryptophan	2.38	9.39	
	Proline	1.99	10.60	
Polar Amino Acids	Serine	2.21	9.15	
	Threonine	2.63	9.10	
	Cysteine	1.71	10.78	8.33
	Tyrosine	2.2	9.11	10.07
	Asparagine	2.02	8.84	
	Glutamine	2.17	9.13	
Acidic Amino Acids	Aspartic Acid	2.09	9.82	3.86
	Glutamic Acid	2.19	9.67	4.25
Basic Amino acids	Lysine	2.18	8.95	10.79
	Arginine	2.17	9.04	12.48
	Histidine	1.82	9.17	6.04

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Amino Acid Tutorials + Cheat Sheet Leah4sci.com/AminoAcids



How to calculate isoelectric point

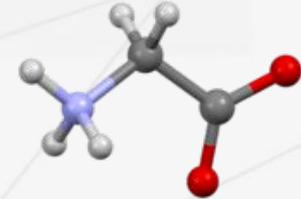
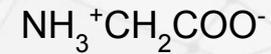


- Two reactions, two pKa

Buffer zones
(pH does not change)
 $pH = pKa$

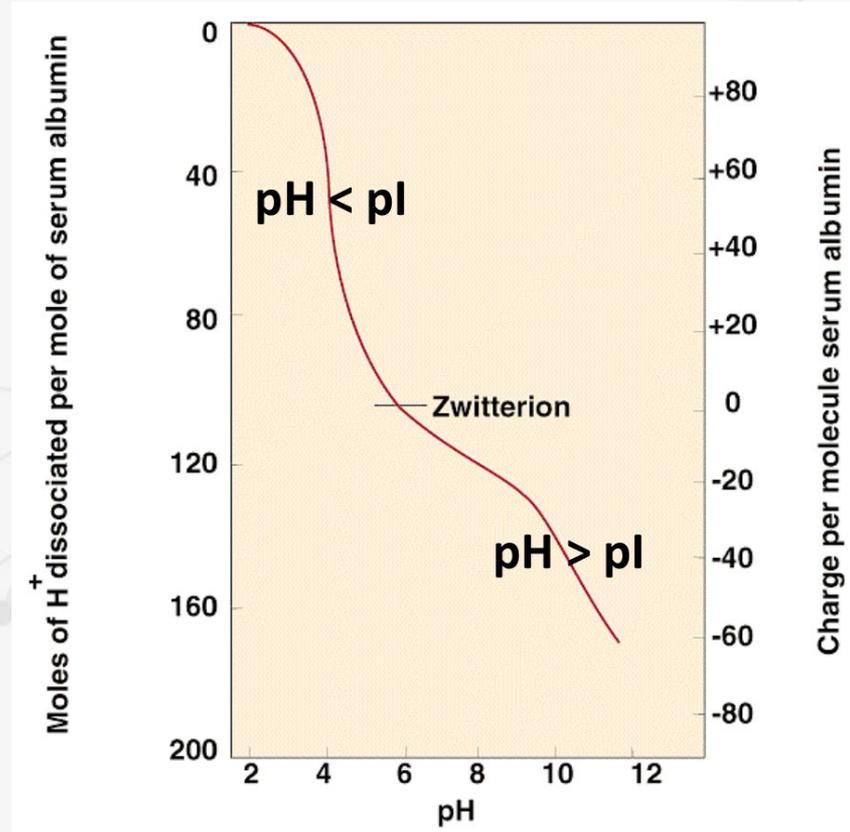
From a strong base
(eg. NaOH)

Zwitterion Glycine



Protein pI

- Proteins have specific pI that correspond to the pH when the protein has a null net charge
- $\text{pH} < \text{pI}$ protein positively charged
- $\text{pH} > \text{pI}$ protein negatively charged

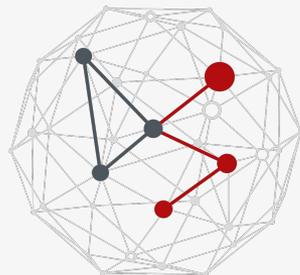


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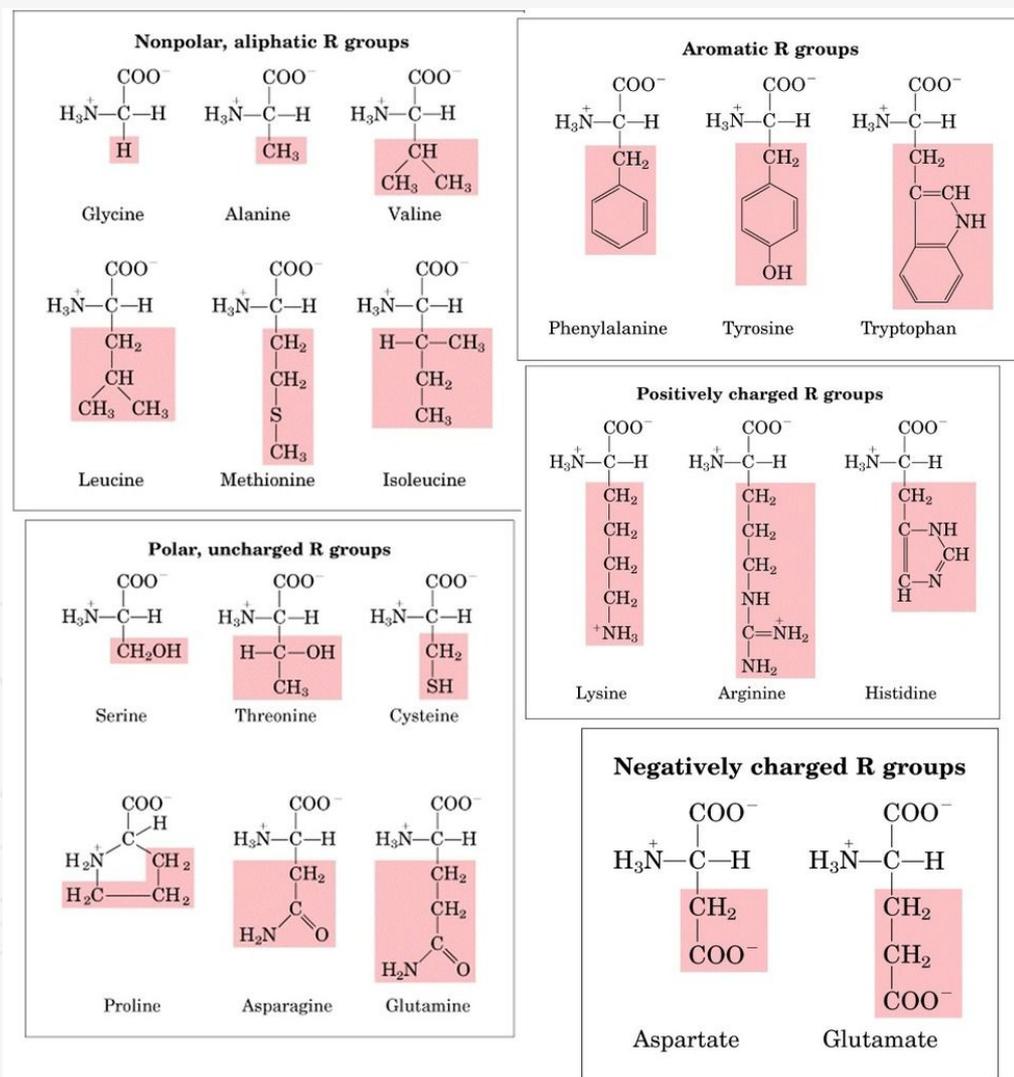
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Classification

- pKa values
- Charges

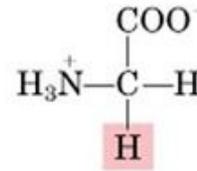
At physiological pH (7.4)



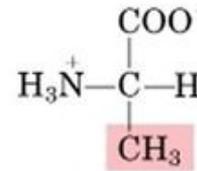
Aliphatic

- Compounds composed solely of **carbon** and **hydrogen**
- **Non polar, hydrophobic**
- Tend to stay within the **protein core** (except Glycine)

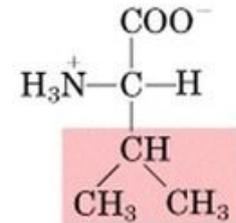
Nonpolar, aliphatic R groups



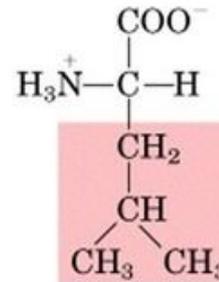
Glycine



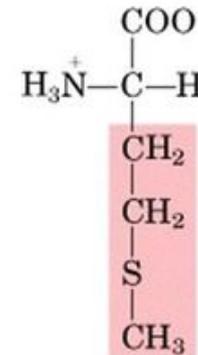
Alanine



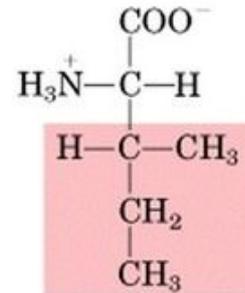
Valine



Leucine



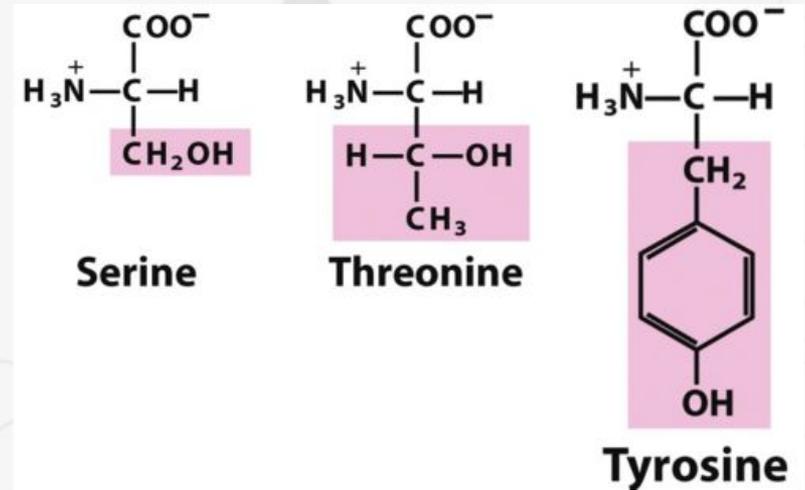
Methionine



Isoleucine

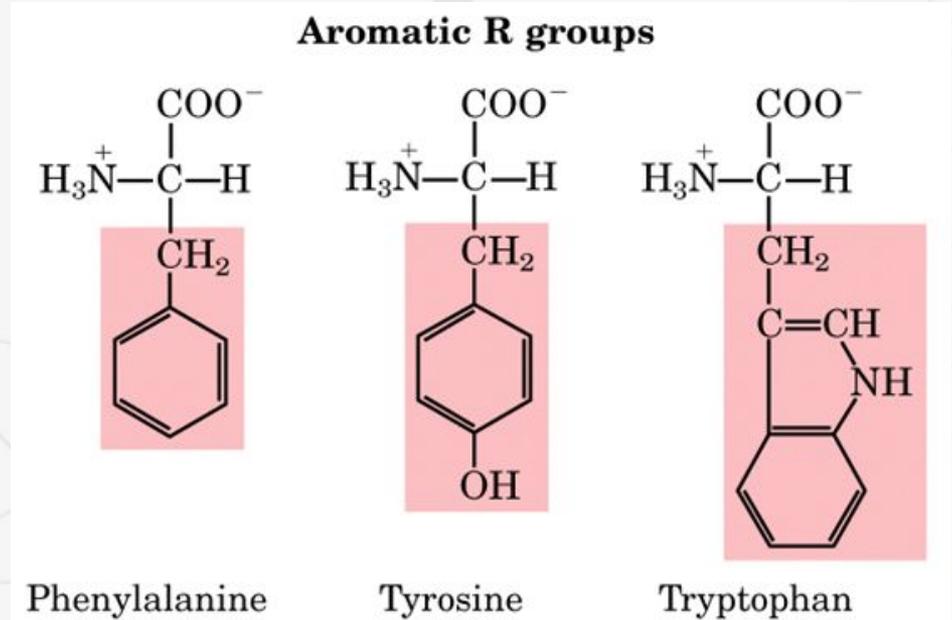
Hydroxyl

- **Polar, uncharged and hydrophilic**
- The phenolic hydroxyl ionizes with a pK_a of 10 and generally regarded as non ionizing
- **Serine** and **Threonine** can be post-translationally modified (phosphorylated)



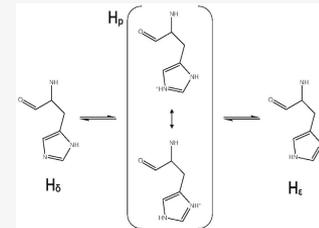
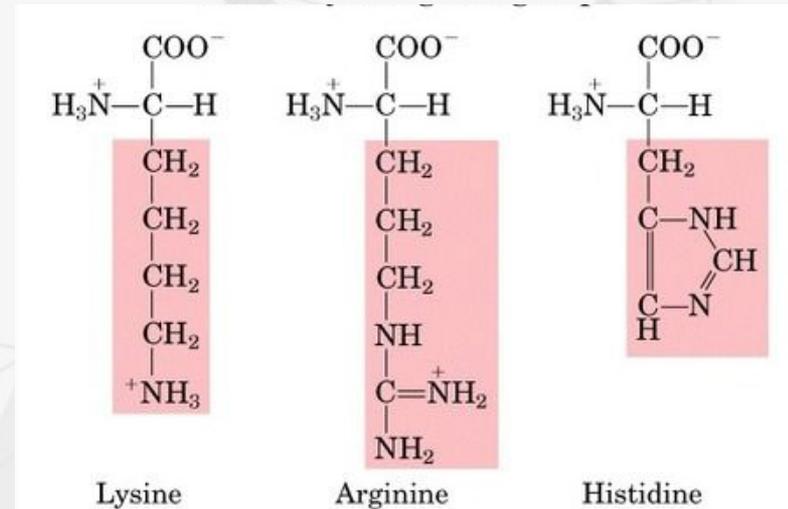
Aromatic

- Relatively **nonpolar**, **hydrophobic**
- **Tyrosine** can form **hydrogen bonds**



Basic

- **Polar and positively charged** (at pH < pKa)
- **Very hydrophilic**
- Almost always in contact with the solvent
- Often **histidine** participates in the **active site** of a protein as **proton donor or acceptor**



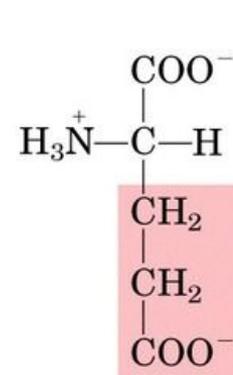
Acidic and their Amides

Acidic

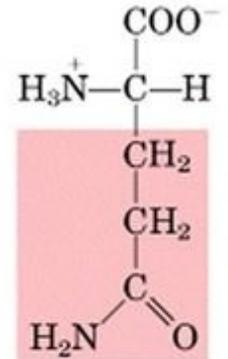
- **Polar and negatively charged**
- Have a **second carboxyl group**

Amides

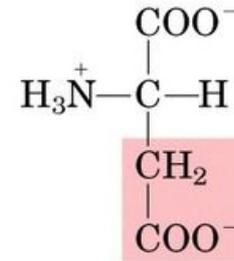
- **Polar and uncharged, and not ionizable**
- **Very hydrophilic**



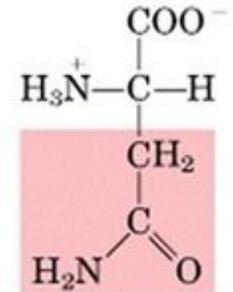
Glutamate



Glutamine



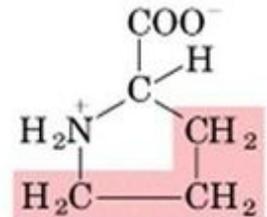
Aspartate



Asparagine

Cyclic

- Proline is the only **cyclic** amino acid
- **Non polar**
- Shares many properties with the **aliphatic** group
- Ambivalent amino acid, it can be **inside** or **outside** of a protein molecule
- Due to its unique structure, proline occurs in proteins frequently **in turns or bends**, which are often on the **surface**

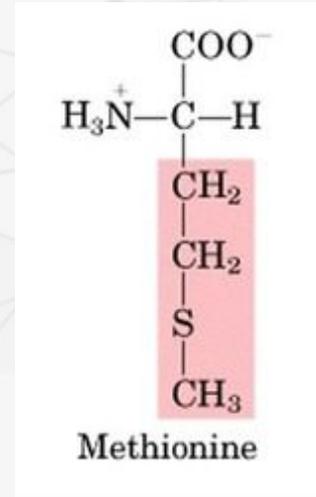
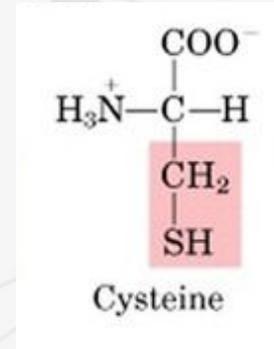


Proline



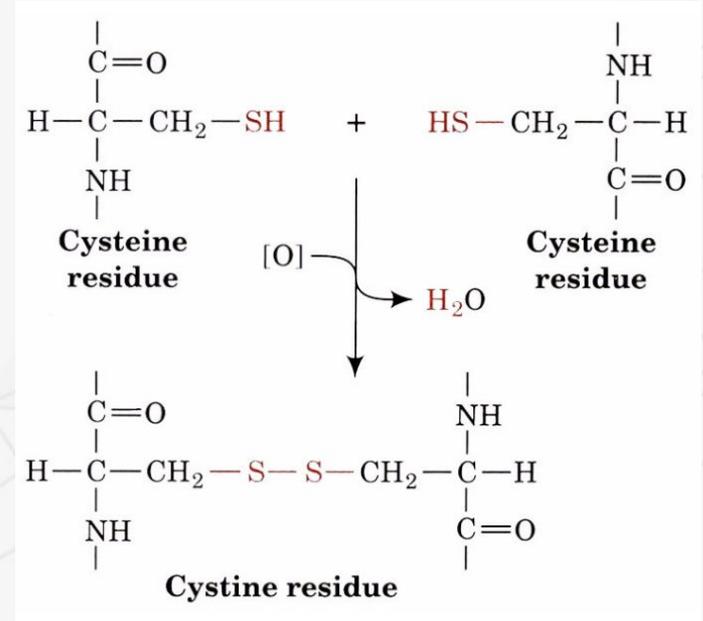
Sulfur-Containing

- **Nonpolar and hydrophobic**
- **Methionine** almost always found on the interior of proteins
- **Cysteine** ionize to yield the thiolate anion
- Sulfur has a **low propensity to hydrogen bond**, unlike oxygen. H_2S is a gas at room temp., H_2O is a liquid
- The **thiol group** of cysteine can react with other thiol groups in an oxidation reaction that yields a **disulfide bond**



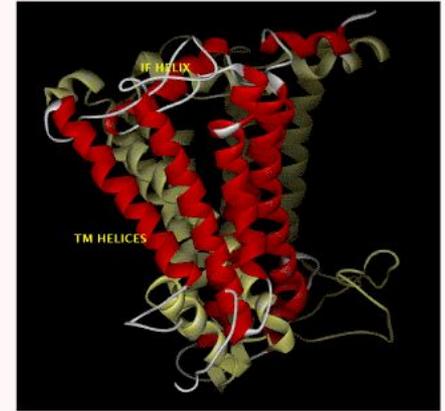
Disulphide bridge

- Two **cysteine** residues can bind by means of an **oxidation** reaction of **-SH** groups
- **S-S** disulfide bridge
- It can connect different regions of a protein, different chains, or stabilize its three dimensional conformation

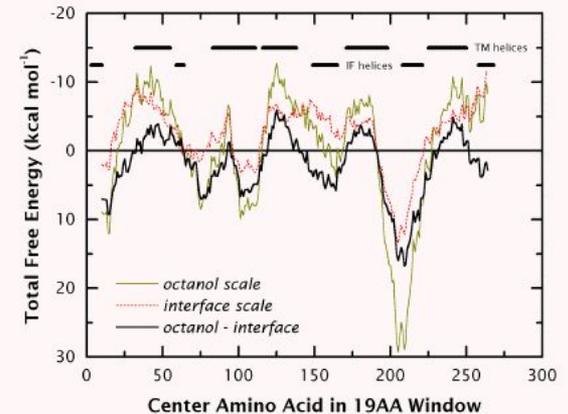


Hydrophobicity

'Volume' classes		'Hydropathy' classes						
	in Å ³	Hydrophobic		Neutral	Hydrophilic			
Very large	189-228	F	W	Y				
Large	162-174	I	L	M		K	R	
Medium	138-154	V			H	E	Q	
Small	108-117		C	P		D	N	
Very small	60-90	A		G	T			
		Aliphatic		Sulfur	Hydroxyl	Basic	Acidic	Amide
		Nonpolar		Uncharged	Charged		Uncharged	
				Polar				

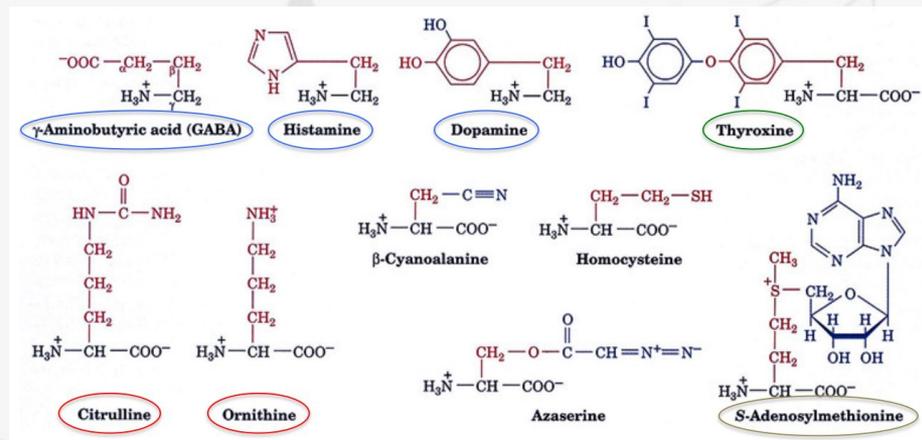


PSRC L-Subunit: *R. sphaeroides*



Non protein amino acids

- Some amino acids does not appear in proteins but are produced by specific metabolic reactions
- They are fundamental components of some biological processes
 - Neurotransmitters (blue), Hormones (green), Urea cycle (red)



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DATA SCIENCE
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PROTEINS

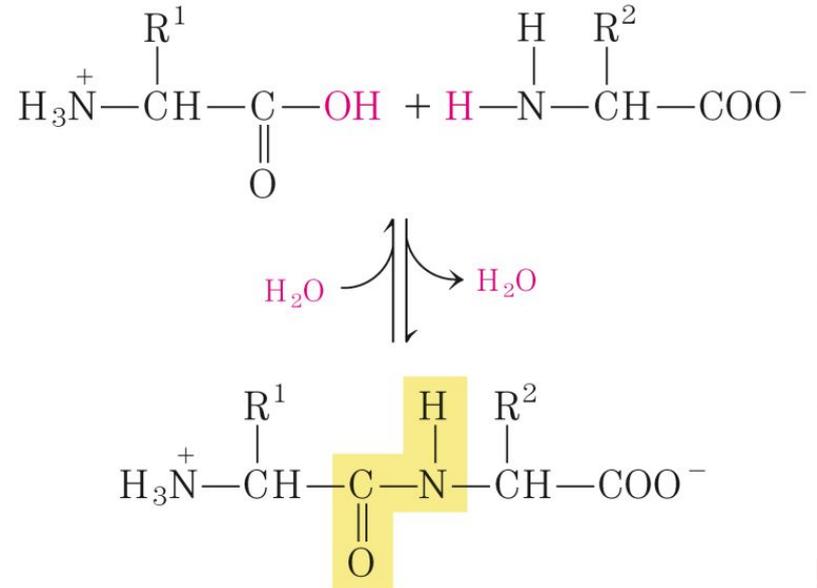
Master of Science in Data Science

Damiano Piovesan



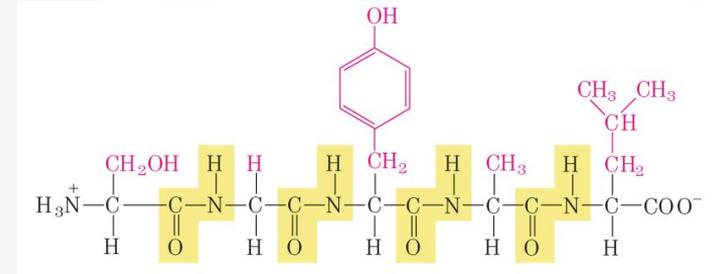
Proteins

- Two amino acids can form covalent bonds (**peptide bond**) through the carboxyl -COOH and the aminic -NH₃ groups
- Proteins are polymers of variable length
- They are made of 20 amino acids covalently bonded with a peptide bond



Peptides and proteins

- **Oligopeptides** are polymers with a low number of amino acids
- **Polypeptides** contains more amino acids than oligopeptides (<10 kDa)
- **Proteins** are even larger (>10 kDa)
- **N-terminal** (left end)
- **C-terminal** (right end)
- Amino acids in the chain are called **residues**



Pentapeptide (Ser--Gly--Tyr--Ala--Leu o SGYAL)

1 Dalton (Da) = 1 Unified Atomic Mass Unit (u)



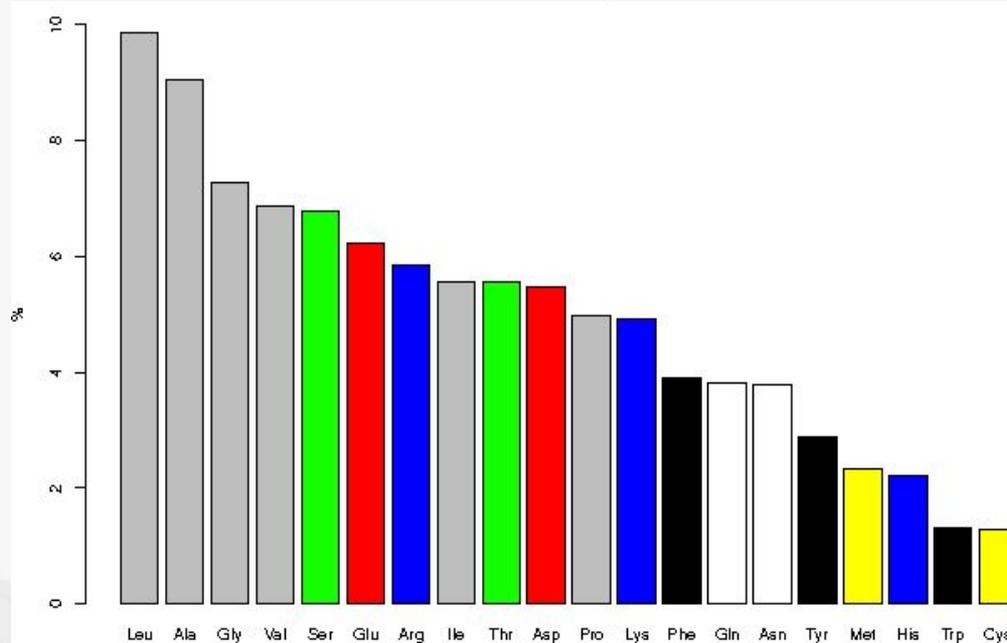
Protein size

- Biologically active peptides and proteins have different size and composition

Protein	Residues	Weight (Da)
Cytochrome C	104	12,400
Ribonuclease A	124	13,700
Albumin	609	66,000
Apolipoprotein B	4,536	513,000
Titin	26,926	2,293,000



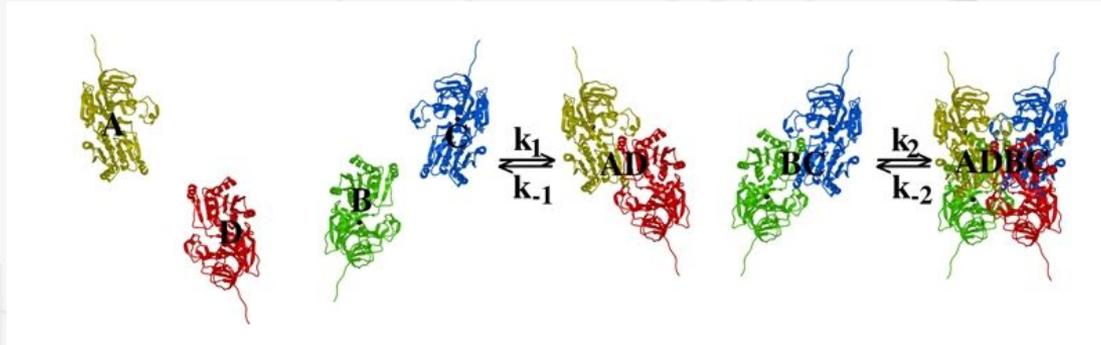
Amino acid composition



gray → aliphatic
 green → small hydroxy
 red → acidic
 blue → basic
 black → aromatic
 white → amide
 yellow → sulfur

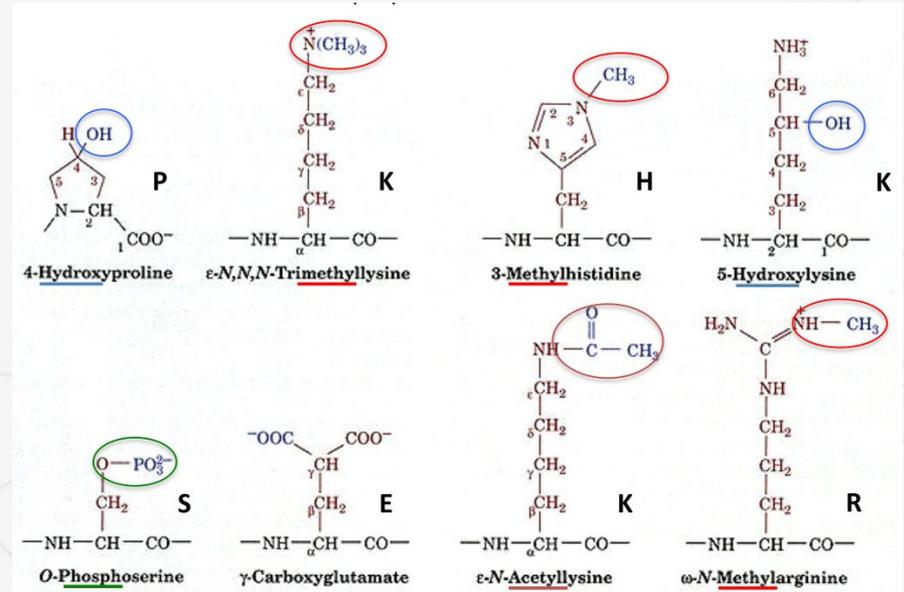
Multi chain proteins

- Functional proteins can have single chains (**monomeric proteins**) or multiple different chains (**multimeric proteins**)
- Chains are not kept together by covalent bonds, but through **intermolecular (weak) interactions**



Post translational modifications

- Amino acids can be modified **after** their **synthesis**
- Chemical **groups** can be **added** to the **side chain** conferring new properties
- The same residue can undergo **multiple** modifications



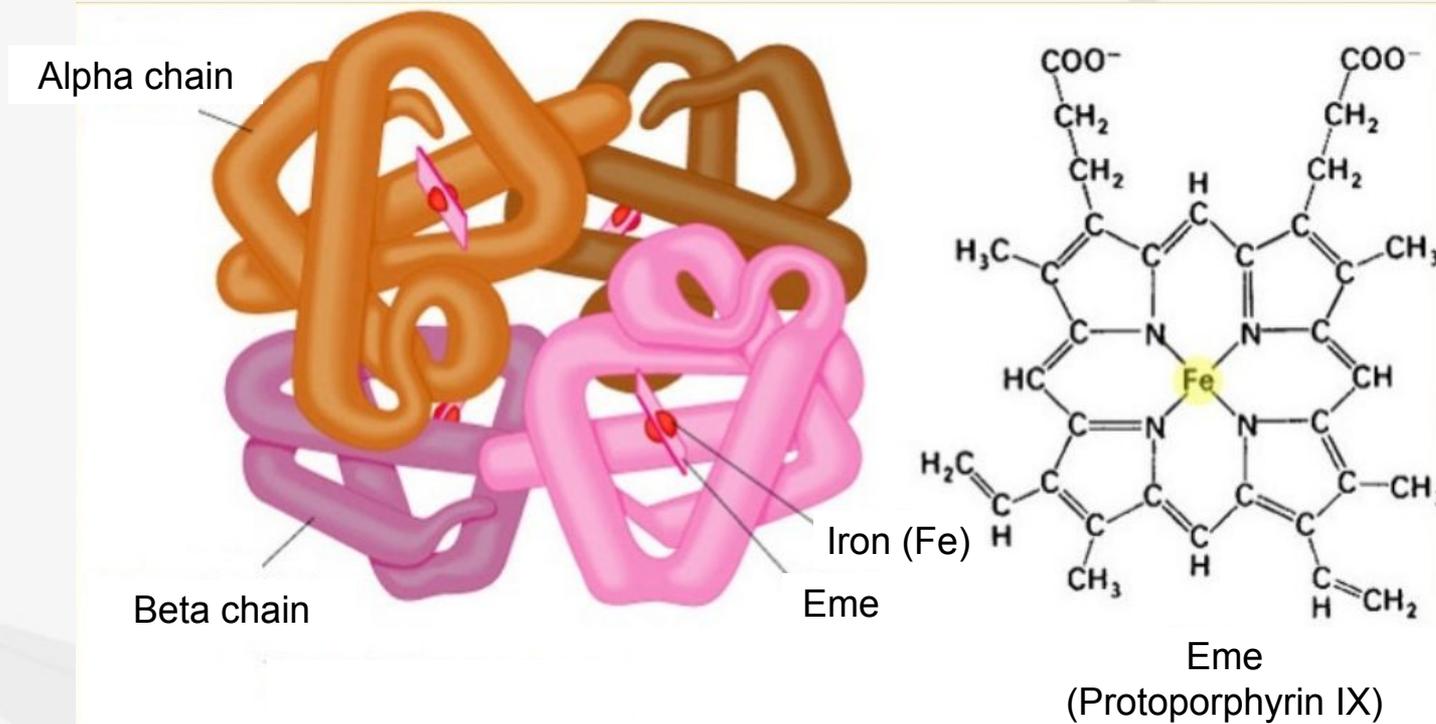
Conjugated proteins

- Some proteins can have **chemical groups** (prosthetic group) different from amino acids

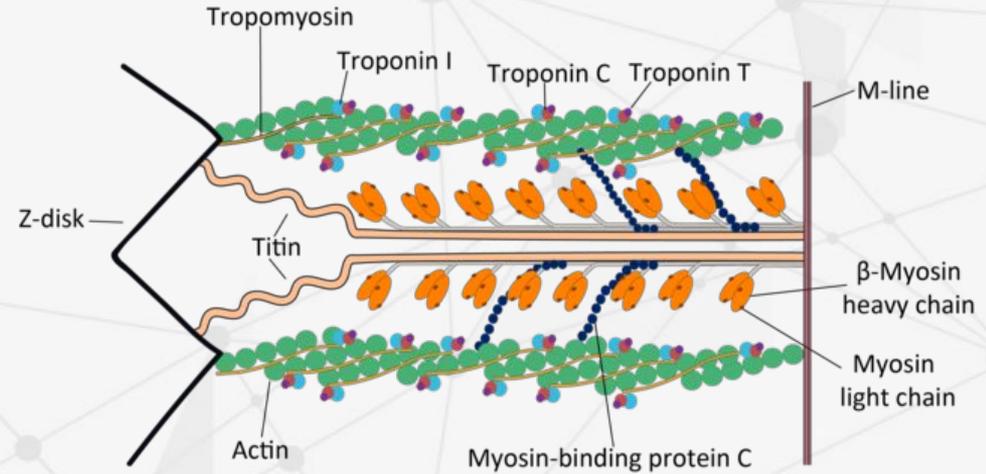
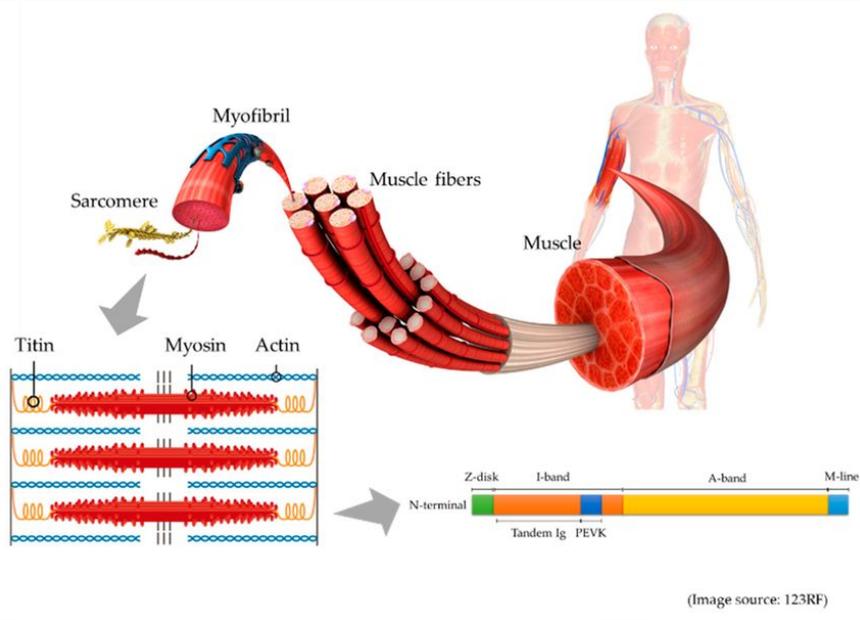
Class	Prosthetic group	
Lipoproteins	Lipids	Blood lipoprotein
Glycoproteins	Carbohydrates	Imunoglobulin
Phosphoproteins	Phosphate	Milk casein
Eme-proteins	Eme	Hemoglobine
Flavoproteins	Nucleotides	Succinate dehydrogenase
Metalloproteins	Iron, Zinc, Calcium, Cupper	Ferritine, Alcohol dehydrogenase, Calmodulin Plastocyanin

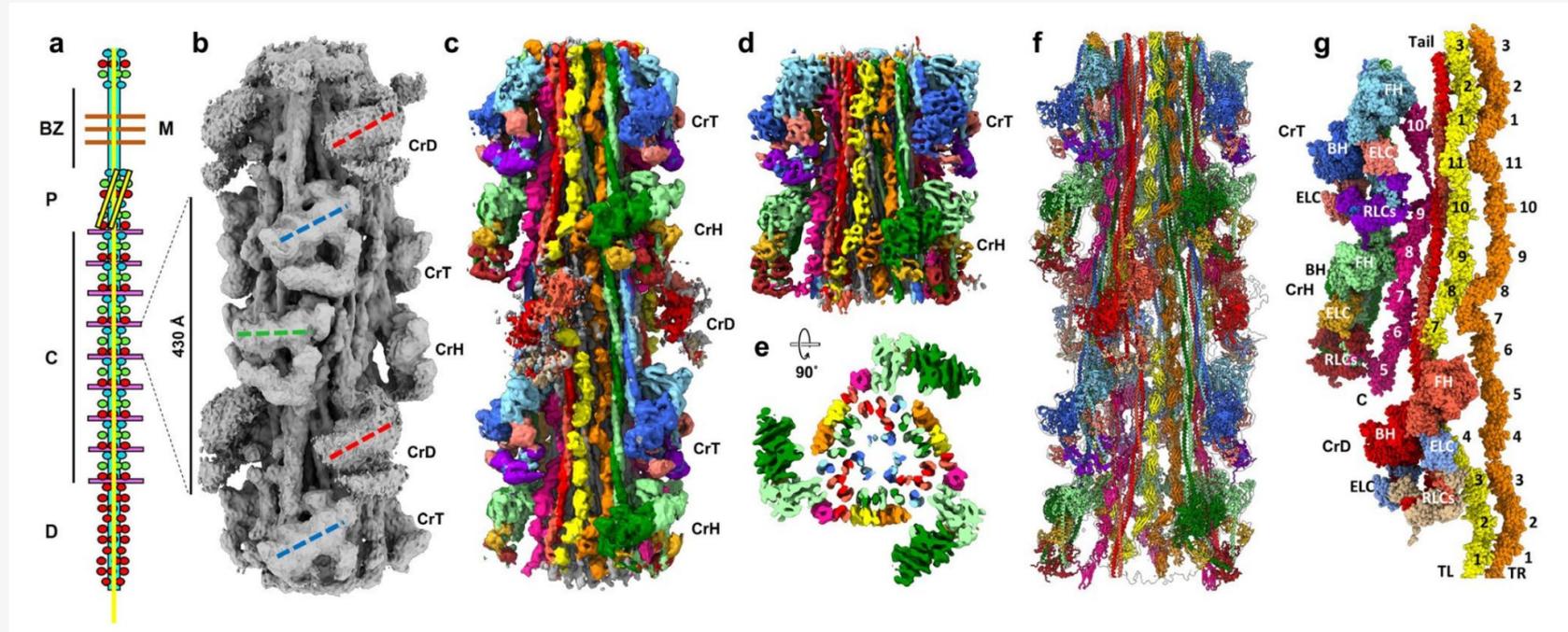


Hemoglobine



Titin





Cryo-EM structure of the human cardiac myosin filament



Kinesin Motor Protein 3D Animation

<https://www.youtube.com/watch?v=ilgdFvit49Y>

