BCH210H:

Biochemistry I: Proteins, Lipids and Metabolism

Fall 2021

Week 0-1

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FUNDAMENTALS

INTERMOLECULEAR FORCE

Inter-molecular forces are forces between molecules. All following inter-molecular interactions can be considered as **electrostatic interaction** with increasing strength.

1. Van der Waals Force
    - Van der Waals force includes **London dispersion**, **Induction force** and **Dipole-dipole** interactions.

2. Hydrogen Bond
    - The H-bond is similar to the dipole-dipole interaction.
    - H is directly attached to Oxygen (O) or Nitrogen (N) usually.
    - **Lone pairs can act as H-bond acceptor, and H that is attached to N or O can act as H-bond donor.**

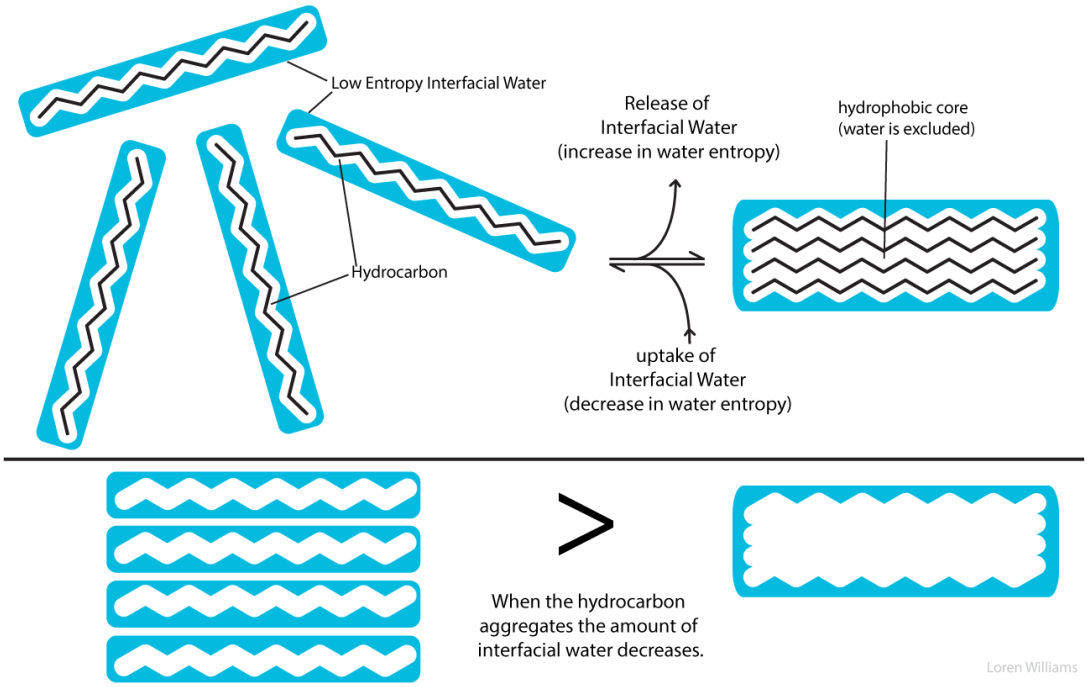
3. Ionic
    - The electrostatic interaction between two ions with opposite charge.

4. Hydrophobic Effect

HYDROPHOBIC EFFECT

Definition: The tendency of hydrocarbons (or of lipophilic hydrocarbon-like groups in solutes) to form intermolecular aggregates in an aqueous medium, and analogous intramolecular interactions.

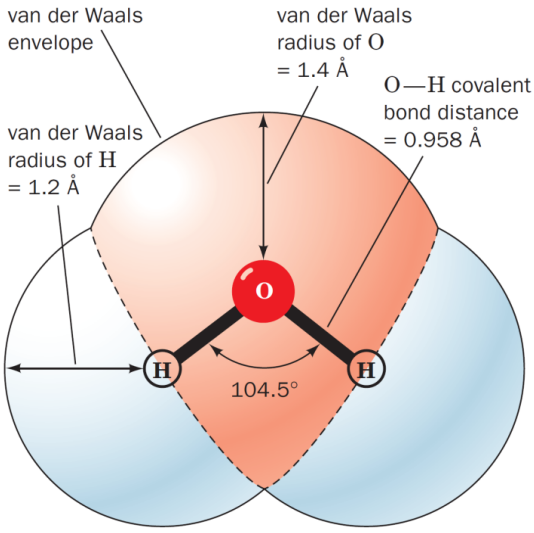
- Entropy explanation



WATER

Water is the fundamental solvent in human body.

STRCUTURE



Properties of water:

1. Oxygen atom in water is **sp^3-hybridized** and O is more electronegative than H.
2. Water is a **polar molecule** with a non-zero dipole moment.
3. Water is able to form **H-bond network** (act as both donor and acceptor).
4. 1 H_2O molecule can potentially form 4 H-bonds.

PROTEIN BIOCHEMISTRY

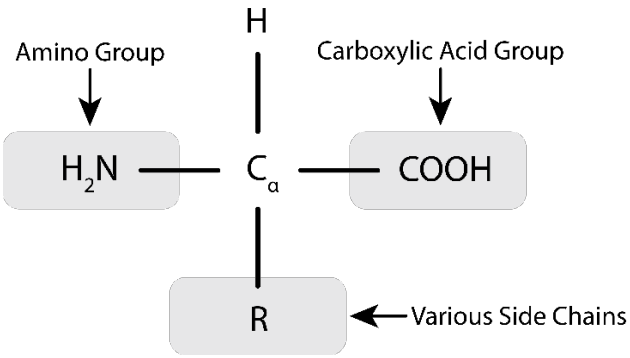
- Proteins are made of **amino acids** that are linked by peptide bond.
- Proteins are the fundamental agents that exert biological functions.
- The protein sequences are encoded by genes and mutations could cause alternation of peptide sequence which leads to protein malfunction and inherited diseases.

AMINO ACIDS

Amino acids are building blocks of proteins.

- Different amino acids have different properties.
- The sequence and the property of the amino acid can affect the structure and function of the protein.

STRUCTURE

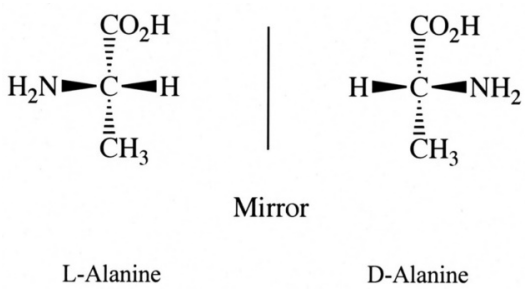


Properties of amino acids:

1. The amino group and carboxylic acid are attached to the same carbon.
2. The properties of amino acids are mainly determined by the side chains.
3. They are **zwitterions**.
4. They can be linked by peptide bond (Amide bond) through condensation reaction.

STEREOCHEMISTRY & PEPTIDE BOND

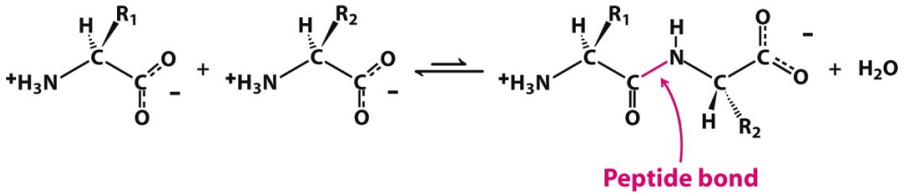
1. L-, D- Stereochemistry



> 1. Most amino acids are chiral with optical activity except for Glycine.
> 2. The L- and D- conformation depends on the position of amino group in the Fischer projection.

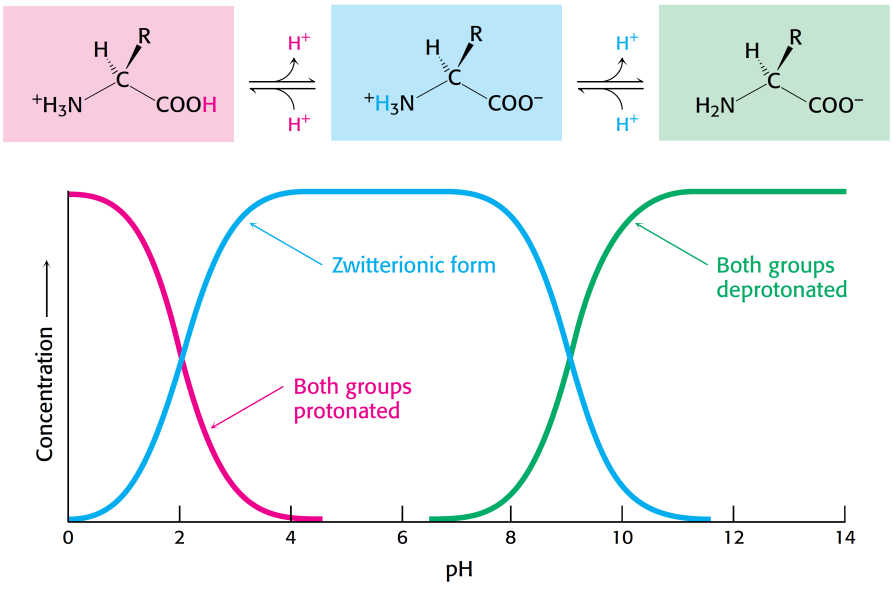
   a. **Only L-amino acid can be incorporated into proteins.**
   b. D-amino acid can be found in bacterial cell wall.

2. Covalent peptide bond formation (Condensation reaction)
   a. Happening at the ribosome in the cells.
   b. Peptide bond is an amide bond and has double bond property.



ZWITTERIONIC FORM

Zwitterion is a neutral molecule with both positive and negative charges.



1. Acid dissociation constant

$$HA(aq) + H_2O(l) \rightleftharpoons A^-(aq) + H_3O^+(aq)$$

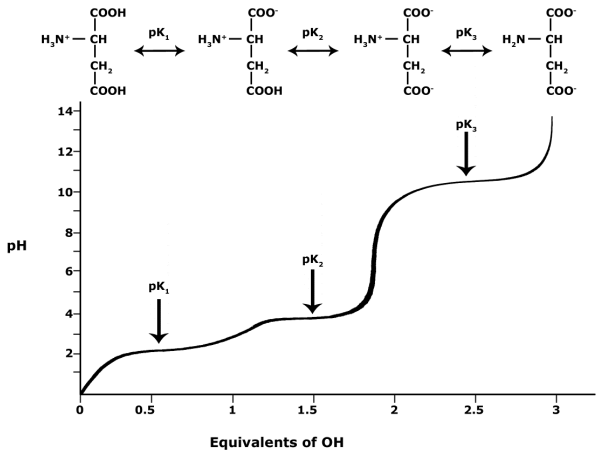
a. Expression

$$K_a = \frac{[A^-][H_3O^+]}{[HA]}$$

K_a: Acid dissociation constant.

[ ]: Concentrations.

b. Titration curve of an amino acid



Henderson-HasselbaLch Equation:

$$\mathbf{pH = pK_a + \log\left(\frac{[A^-]}{[HA]}\right)}$$

pH: pH value of the solution.

pK_a: pK_a of a particular acid.

$[A^-]$: Concentration of the conjugate base at equilibrium.

[HA]: Concentration of the acid at equilibrium.

2. Isoelectric point (pI)
   a. Definition: The pH at which the net charge of an amino acid is 0 and it does not migrate in an electric field.
   b. Calculation:

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

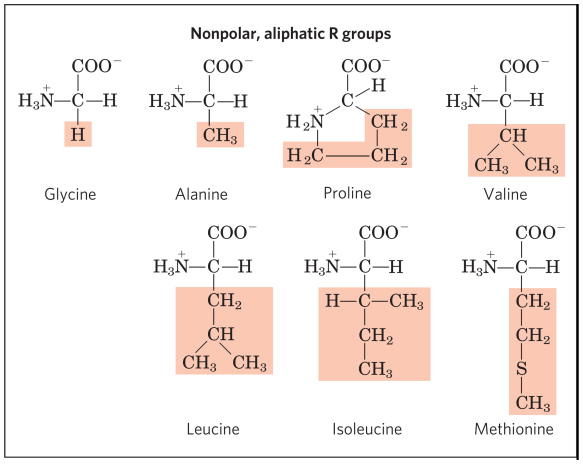
pI: Isoelectric point.

pK_1, pK_2: pHs beside the zwitterion.

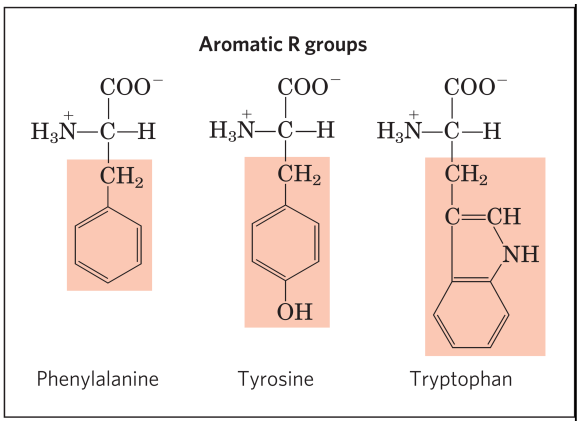
PROPERTY OF 20 AMINO ACIDS

Property of 20 amino acids is determined by their side chains.

1. Nonpolar, aliphatic side chain

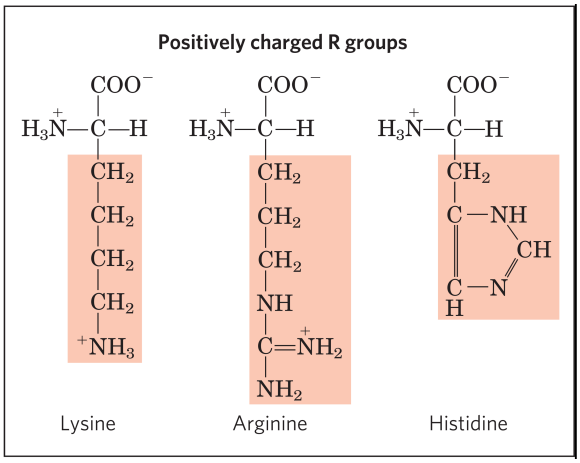


2. Aromatic side chain

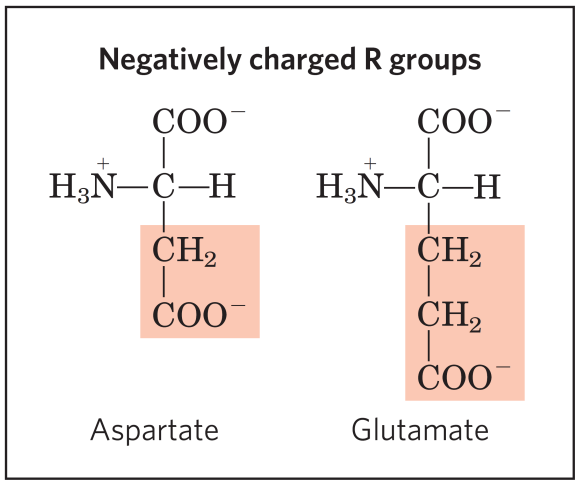


1. Aromatic side chains primarily absorb UV light at wavelength of 280 nm.
2. Spectroscopic property can be used to determine protein concentration

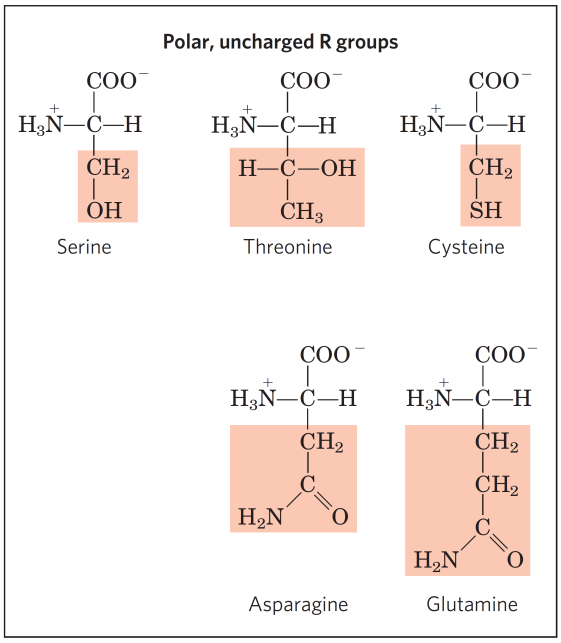
3. Positively charged (Basic) side chain



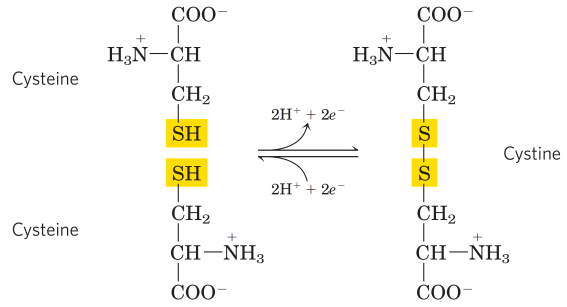
4. Negatively charged (Acidic) side chain



5. Polar uncharged side chain

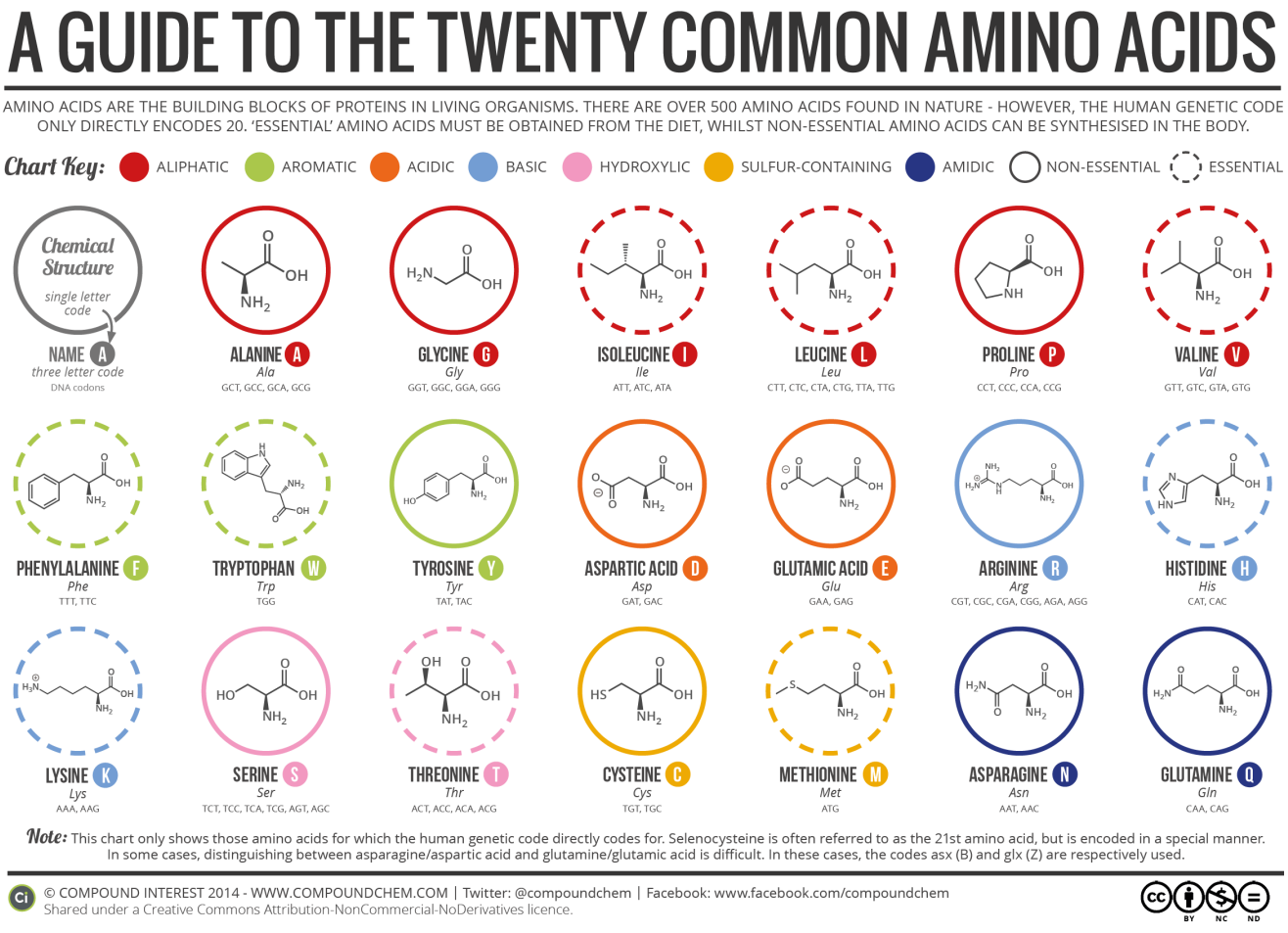


1. Two cysteine can form disulfide bond.



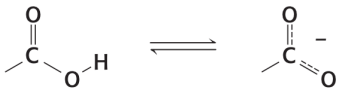
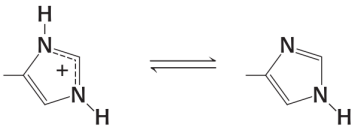
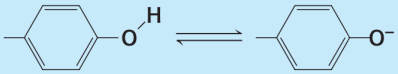
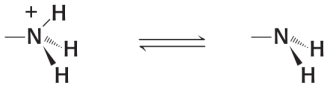
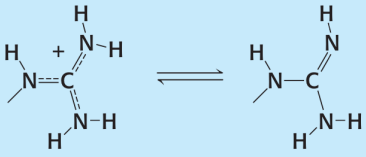
2. Disulfide bond can be reduced.
   - β-mercaptoethanol (BME)
   - Dithiothreitol (DTT)
   - Alkylation of -SH prevents disulfide bond formation.

20 AMINO ACIDS & PROPERTIES



- There are 2 additional amino acids can be incorporated into proteins: selenocysteine and pyrrolysine and they are encoded by **stop codon**.
- There are other amino acids that cannot be incorporated into proteins, but they are found in metabolic pathways.

PKA VALUES OF IONIZABLE GROUPS

Group	Acid ⇌ Base	Typical pK_a
Terminal α-carboxyl group		3.1
Aspartic acid Glutamic acid		4.1
Histidine		6.0
Terminal α-amino group		8.0
Cysteine		8.3
Tyrosine		10.9
Lysine		10.8
Arginine		12.5

POST-TRANSLATIONAL MODIFICATIONS

After proteins are synthesized in the ribosomes, amino acid in the protein can be further modified transiently or permanently.

1. Common modification
    a. Acetylation
    b. Methylation
    c. Hydroxylation
    d. Carboxylation
    e. Glycosylation → Important for cell signaling and adhesion.
    f. Ubiquitination → Target proteins for degradation in proteasome.
    g. Phosphorylation → Activate or deactivate enzymes.
2. Formation of disulfide bond.

FUNCTION OF PROTEINS

Proteins are the fundamental working molecule in a living organism.

1. Common function
    a. Signaling
    b. Transporting
    c. Structural
    d. Motility
    e. Etc.
2. Cofactors & Coenzyme
    a. Cofactors are usually non-protein molecules and metal ions that assist with their structure and/or function.
    b. Coenzyme is usually a partner of a protein serving as a shuttle for common functional groups.