This document contains two sets of notes.

Amino Acids and Proteins

- **What is an amino acid?**
  - A molecule which contains an amino group (NH₂) and a carboxyl group (COOH).
  
  ![Amino Acid Structure](image)
  
  - How is amino acid different from α-amino acid?
    - α-amino acid contains an amino group (NH₂) and a carboxyl group (COOH), which is bonded to the same carbon. This carbon is called the "α-carbon."
    
    ![α-carbon Diagram](image)
    
    - α describes the location of amino group and carboxyl group. Different from the "α" used to describe the stereoelectronic configuration at an aromatic carbon in carbohydrates.

- α-amino acids combine to form polypeptides. Polypeptides are polymers of α-amino acids. (Thinkback)

- Naturally occurring α-amino acids have the following characteristics:
  1. They have the same stereoelectronic configuration at α-carbon (Thinkback)
  2. Most of them are primary amines (RCH₂NH₂). Proline is the only exception, for it is a secondary amine (R₂NH).
    * None of them are tertiary amines (R₃N) because then the nitrogen will not have a lone pair - therefore no π character, hence rotation around the C-N bond would be possible and this can hinder the rigidity of the protein and we might have a "flappy" protein.

  - General structures of amines:
    
    ![Amine Structures](image)
    
    - Geometry is roughly trigonal pyramidal.
- The configuration of an amino acid: "amine group is on the left, carboxyl group is on right, and the side chain is coming out toward the viewer." (thinkbook). Side chain always start with \( \text{CH}_3 \).

- Based on the nature of side chain, amino acid are further classified as:
  1. Hydrophilic: side chain which is polar (or "water loving")
  2. Hydrophobic: side chain is non polar ("water hating")
  3. Acidic: side chain contains acidic group which can donate \( \text{H}^+ \).
  4. Basic: side chain contains basic groups which can accept \( \text{H}^+ \).

- The most important feature that helps in preserving the rigidity of a protein is a peptide bond: a bond between a nitrogen atom of one amino acid and the carbonyl group of another amino acid." (thinkbook). and is formed when \( \text{NH}_2 \) and \( \text{CO}^- \) are activated when \( \text{H}_2\text{O} \) is released.

- Why is it important that a peptide bond is rigid and how is it able to maintain its rigidity?

  - RESONANCE (answer to every question in the universe!)

  - Lone pair on the nitrogen is in resonance, which suggests that the amide bond has partial \( \pi \) character. (thinkbook). Because of this \( \pi \) bond character, rotation around the bond is restricted, resulting in maximum overlap of the \( p_z \) orbital of the carbonyl carbon and nitrogen’s lone pair (which are in parallel orientation).

- The peptide bond helps in maintaining the shape of the protein because of the rigid amide linkage.

  - If the linkage was not rigid then the "enzymes could not maintain well defined active sides necessary for efficient and selective chemistry, and the structural proteins would collapse." (thinkbook)

- The peptide bond also contains sites available for hydrogen bonding and this is very important in the secondary structure of the protein because it’s the hydrogen bonding which links these amino acids.
There are 4 levels of protein structure:

1. **Primary structure**: "is an amino acid sequence" (thinkbook)
   - Amino acids → polypeptide (linear sequence of amino acids bound by peptide bonds).

2. **Secondary structure**:
   - consists of "α helices, β-sheets, or coils" (thinkbook)

3. **Tertiary structure**: "response to environment" → R group is either in or out — depends on whether the surrounding is hydrophilic or hydrophobic.
   - Disulphide bridges → make up the structure → "bonds formed between two SH amino acid chains" (thinkbook)

4. **Quaternary structure**: consists of "two or more non-covalently associated subunits." (thinkbook)
- The structure of the polypeptide, SPD, indicates which atoms lie in the same plane by being drawn tightly.

- Identify the plane of the polypeptide.
- The plane starts from one C of one amino acid to the α-C of another amino acid, and includes all atoms except which are the substituents on the α-carbon (i.e., R). (i.e., R)

How does polymerization of an amino acid occur?

- Loss of H₂O.

Example:

- Alanine + Serine

- Amino acids are always in L configuration.

Note: Carbohydrates are natural when they have D configuration, but this is different for amino acids. Amino acids are natural when they have L configuration.
AMINO ACIDS & PROTEINS

*Lecture Supplement Page 51*

Proteins →

- biopolymer of amino acids (aa) that are held together by amides
- made from carboxylic acid fragment of one aa and an amine
  group of another aa
- repeated units ⇒ polyamides

Amino Acids →

- Stereochemistry observed for all aas
- *Called an α-Amino Acid because it contains HN-C-CO₂H

α-Carbon
(because adjacent to two functional groups)

\[
\begin{array}{c}
\text{H}_2\text{N} \\
\text{CO}_2\text{H}
\end{array}
\]

\[
\begin{array}{c}
\text{R} \\
\text{H}
\end{array}
\]

*Zwitterionic form

- Lecture supplement (s1) & 21 naturally occurring amino acids
- all primary amines (NH₂) except proline (R₂NH)
- 4 types of side chains:
  1. Hydrophobic = "water hating" (mostly C-C or C-H bonds)
    - Isoleucine, side-chain = sec-butyl group
  2. Hydrophillic = "water loving"
**Amino Acids (continued)**

- Hydrophilic side chains
  - **ex.** Serine, side-chain = CH$_2$OH
- Further divided into acidic, basic, or neither
  - (3) Acidic **ex.** Aspartic Acid, side-chain = CH$_2$CO$_2$H
  - (4) Basic **ex.** Histidine, side-chain = CH$_2$-imidazole

**Amino Acid → Peptide →**

- Carboxylic Acid and amine group come together to make peptide

\[
\begin{align*}
\text{Alanine} & \quad \text{Serine} & \quad \text{Valine} \\
\text{removed as H}_2\text{O} & \quad \text{removed as H}_2\text{O}
\end{align*}
\]

\[
\text{N-terminus} \quad \text{Ala-Ser-Val} \quad \text{C-terminus}
\]

**Primary Structure**

- Amino acid sequence (simplest)

**ex.** (Gly)$_{14}$ → 14-mer

- All bonds have own set of rotations
- $3^1$ for each $\alpha$-carbon add to that rotation about amide and rotation around $R$ group
Primary Structure (continued)

- With so much rotation (as mentioned on previous page) how does it stay rigid and useful?
  - Amide portion

\[
\begin{align*}
\text{Trans} & \quad \leftrightarrow \quad \text{Cis} \\
\text{likes to be planar}
\end{align*}
\]

- Suggests conjugation because torsional strain ignored
- \(\text{is conjugated}\)
- Carbonyl parallel to N lone pair, so max. \(\pi\) orbital overlap
- So parallel \(\text{cis}\) or \(\text{trans}\) \(\rightarrow\) \(\text{trans}\) more stable conformation, because \(\text{R}\) group wants to be next to \(\text{H}\) rather than \(\text{R}\) group
- Allows for barrier to rotation around above circled bond
- Important in maintenance of protein shape, because if protein "floppy", then active sites of enzymes wouldn't be well-defined, eliminating their trait of being highly specific; also structural proteins would break apart

Secondary Structure

*Thinkbook p. 52

(1) \(\alpha\)-helix
- Characterized by helical shape
- Held together by H-bond between carbonyl above to amide below (ie adjacent turns of coils)
Secondary Structure (continued)

(2) β-Sheet
- Amino acid chains parallel, carbonyl of 1 strand H-bonded to NH of other strand
- Not flat, but pleated/folded (Pg. 53 of Thinkbook expanded version)
- R-groups on ridges, so some stick up others stick down
- Antiparallel polypeptide chains (as drawn here) or parallel

(3) Coil
- Arrangement of aa that is not like helix or sheet
  (ie: not symmetrical, more "random" but folds up in same way)
  (every time and is influenced by amide planarity and H-bonds)

Tertiary Structure
- Causes: (1) Disulfide Bridges
  - S-S bond between 2 cysteine SH groups
  \[
  \begin{array}{c}
  \text{HS} \\
  \text{SH}
  \end{array}
  \xrightarrow{\text{Fe/S bond}}
  \begin{array}{c}
  \text{S} \\
  \text{S}
  \end{array}
  \]
  - Not very strong; weak covalent
  - Common in keratin (protein of hair)

(2) Response to environment
  - Side chains either towards or away from environment
    - If polar R groups and in H₂O then stick out
    - If nonpolar R groups and in H₂O then fold in/away
Quaternary Structure →

· Subunits of proteins that form together into larger structures via noncovalent association
  · many enzymes are comprised of multiple subunits

Lecture Examples →

(1) Myoglobin
  · in muscles to capture/store O₂
  · coils/helices
    · "holes" where heme goes

(2) Retinol Binding Protein
  · in eyes to capture retinol
    · "hole" in middle where retinol bound
  · mostly β-sheet

(3) Lactate Dehydrogenase
  · α-helices, β-sheet, coil
  · 4 subunits → quaternary structure through noncovalent interactions

END NOTES