Amino Acids, Peptides, and Proteins

- Amino acids are carboxylic acids that also have an amine group
- Two amino acids can react in such a way as to form an amide
- This amide linkage is known as a peptide bond
- Two amino acids form a dipeptide, three a tripeptide, and so on
- When many amino acids are bonded together, a polymer or polypeptide is formed
- Proteins are polypeptides that contain more than 50 amino acids
- Skin, hair, muscle, and most enzymes are proteins

Structure and Stereochemistry

- Glycine is the simplest and only amino acid that is not chiral
- All others have a chiral or $\alpha$ carbon
- Nearly all naturally occurring amino acids have the S configuration at this carbon, the exception is cysteine
- This is the same configuration that is found in L-(-)-Glyceraldehyde
- The D and L convention was adopted for carbohydrates
- Since all naturally occurring amino acids have S configuration, they are known as L-amino acids
Essential Amino Acids

- Although more than 700 amino acids are known to occur naturally, only 20 are present in proteins.
- Humans can only synthesize about half of these.
- These 10 amino acids are called essential amino acids.
- Essential amino acids:
  - Arginine
  - Valine
  - Methionine
  - Leucine
  - Threonine
  - Phenylalanine
  - Histidine
  - Isoleucine
  - Lysine
  - Tryptophan
Essential Amino Acids

Acid-Base Properties

- Amino acids are referred to as dipolar or zwitterionic molecules
- Why?
- Amino acids have high mps, like salts
- Amino acids are soluble in water, like salts
- Amino acids have large dipole moments
- Amino acids are amphoteric, can act as either acid or base
- Neural amino acids have pK\(_a\)\(_1\) for the \(-\text{COOH}\) which are smaller than acetic acid and pK\(_a\)\(_2\) for the \(-\text{NH}_3^+\) which are smaller than CH\(_3\)NH\(_3^+\)
Titration of Glycine

- There are three important regions in the titration curve for glycine:
  - $\text{pK}_a_1$, $\text{pK}_a_2$, and the point where the zwitterion exists which is called the isoelectric point, $\text{pI}$

Isoelectric Points and Amino Acid Structure

- The isoelectric point is roughly half the sum of $\text{pK}_a_1$ and $\text{pK}_a_2$
- Neutral amino acids have an isoelectric point around pH=6
- However, depending on the side chain attached to the $\alpha$ carbon, this value could be above or below pH= 6
- Acidic amino acids:
  - Aspartic acid, $\text{pI}=2.77$  Tyrosine, $\text{pI}=5.66$
  - Glutamic acid, $\text{pI}=3.22$  Cysteine, $\text{pI}=5.07$
- Basic amino acids:
  - Lysine, $\text{pI}=9.74$  Histidine, $\text{pI}=7.59$
  - Arginine, $\text{pI}=10.76$
Acidic and Basic Amino Acids

Structure and pKa Values
- For Glycine, the pKa for the ~COOH is lower (2.3) than ordinary carboxylic acids (acetic acid, pKa = 4.76)
- This is due to the stabilization of the carboxylate by the nearby ~NH₃⁺ group
- Similarly, the ~NH₃⁺ has a pKa = 9.6, which is lower than aliphatic amines (10.7)
- This is due to the electron withdrawing effect of the nearby carboxylate ion
- For Lysine, the pKa of the side chain is similar to the pKa of aliphatic amines
- In the case of Aspartic Acid, the side chain carboxylic acid has a pKa which is somewhere between that of Glycine and acetic acid

Electrophoresis
- A mixture of amino acids or proteins can be separated based on their isoelectric points
- This technique is called electrophoresis
- In this procedure, the solution containing the amino acids or proteins is placed near the center of a strip of filter paper or acrylamide gel
- The paper or gel is moistened with an aqueous buffer with a specific pH
- The pH is chosen such that some species will be neutral, some cationic, and some anionic
- A voltage is applied to the paper or gel
- The cationic species will migrate toward the cathode, the anionic species toward the anode, and the neutral will stay in the center
Electrophoresis

Paper strip at pH = 5.97

Lysine  \( pI = 9.74 \)
Glycine  \( pI = 6.97 \)
Aspartic acid  \( pI = 2.77 \)

Bonding in Peptides

- Amino acids are unique in that they contain both an amine group and a carboxylic acid group.
- We have already seen that when these two groups react, they form amides.
- Amides are the most stable of all acid derivatives.
- Recall that this is due to resonance.

\[ \text{R-N=O} \leftrightarrow \text{R-CONR}_2 \]
**Bonding in Peptides**

- Because of the resonance structure that exists which has a C=\(\text{N}\) bond, there is restricted rotation
- This causes the peptide chain to adopt this “cis/trans” configuration

**Nomenclature**

- By agreement, peptide structures are written such that the amino group \(\sim \text{NH}_3^+\) or \(\sim \text{NH}_2\) is at the left of the structure
- The Carboxyl group \(\sim \text{CO}_2^-\) or \(\sim \text{COOH}\) is at the right
- The left end of the peptide is known as the N-terminus or amino terminus
- The right end of the peptide is known as the C-terminus or carboxyl terminus
- The order of bonding in a peptide is known as the sequence
- When naming a peptide, the N-terminus comes first and the C-terminus comes last

**Example**

- Alanine
- Serine
- Ala-Ser
Sulfide Bonds

- A second type of bonding which occurs in peptides is a disulfide bond, RS-SR
- These are formed between two cysteine residues
- This occurs because thiols are easily oxidized under mild conditions
- The disulfide bond is easily cleaved by mild reduction to reform the two thiols
- These disulfide bonds can link two peptide chains together or cause a loop in a single peptide chain

Oxytocin
Protein Classification

- Proteins can be classified by their composition
  - Simple Proteins are comprised of amino acids
  - Conjugated Proteins are comprised of both amino acids and a non-amino acid portion called a prosthetic group
    - For example, the prosthetic group in hemoglobin is a hemin also known as a porphyrin
- Proteins can also be classified by their solubility in H₂O
  - Fibrous Proteins are insoluble in water
  - Globular Proteins are water soluble

Fibrous vs. Globular Proteins

- Fibrous Proteins
  - Long and thread-like
  - Tend to lie side by side to form fibers
  - Held together at many points by hydrogen bonding
  - Tough and insoluble in water
- Globular Proteins
  - Fold into compact units that are sphere-like
  - Folding takes place in such a way that hydrophobic parts turn inward, away from water
  - Hydrogen bonding is an intramolecular force, intermolecular attractive forces are weaker

Protein Structure

- Primary structure: the way amino acids are bonded together
- Secondary structure: the way in which chain segments are arranged in space, such as coils, sheets, or compact spheres
- Tertiary structure: the way in which the entire protein molecule is arranged spatially
- Quaternary structure: the way in which proteins aggregate with each other to yield larger structures