Amino Acids:

Proteins come in several different types: structural (skin, fingernails, silk, cartilage), hormonal (insulin) and enzymatic (DNA polymerase). What is the chemical similarity of the different types of proteins? They are all composed of amino acids linked together by amide bonds or “peptide bonds”. These linkages are formed by effecting a “dehydration” reaction between the amine group of one amino acid and the carboxylic acid group of another amino acid.

![Peptide bond formation](image)

The peptide bond, or formation of an amide functional group, is an extremely strong bond due to the resonance stabilization of the nitrogen lone pair with the pi electrons in the p-orbitals of the carbonyl group. The resonance forms for a peptide bond are shown below and as you can see the C-N bond has double bond character, thus greatly strengthening it. Stabilizing it, and making it highly difficult to break.

![Peptide bond resonance forms](image)

Peptides can be hydrolyzed under aqueous acid conditions. The products of this hydrolysis process are units called amino acids.

![Protein hydrolysis](image)

What are amino acids? Amino acids are a type of organic compound whose common structural feature is the amino group bonded to the carbon alpha to the carbonyl of the carboxylic acid. For this reason, amino acids are sometimes called α-amino carboxylic acids.

A generic amino acid:
With the exception of glycine (R = H), all amino acids contain a chiral center alpha to the carbonyl and thus they are commonly represented as Fischer projections. In similar fashion to the carbohydrates, the amino acid is drawn such that the carboxylic acid group is at the top of the projection and the side chain (R) is at the bottom of the projection. The naturally occurring amino acids belong to the L-series, where the amine group is always found on the left of the Fischer projection (remember – in carbohydrates, the L-series had a hydroxyl group to the left of the projection). Some examples of L-amino acids are shown below.

![Fischer projections of amino acids]

There are twenty amino acids necessary for protein synthesis. All twenty amino acids can be classified as either neutral, acidic or basic depending on what side chain it possesses. Acidic amino acids are those whose side chains possess carboxylic acids. Basic amino acids are those whose side chains contain amino groups. Neutral amino acids are those whose side chains are non-polar alkyl groups or may possess functional groups such as alcohol or thiol groups that would polarize the side chain.  

![Characteristics of Amino Acids]

1. Amino acids have extremely high melting and boiling points, unlike most organic compounds of similar molecular weight
2. Amino acids are soluble in water and polar solvents but not in typical organic, less polar solvents such as diethyl ether.
3. Amino acids have large dipole moments.
4. Amino acids are less acidic than typical organic carboxylic acids (pKa of 10 instead of 5) and less basic than amines (pKb 12 instead of 4).
What causes these characteristics? Why are amino acids so unlike typical organic amines and carboxylic acids? Because the amino acids possess the carboxylic acid and the amine functional group in the same molecule, an internal acid-base reaction is created. This leads to the formation of a dipolar ion (also known as a “zwitterion”).

The internal proton transfer causes the formation of a dipolar ion:

As a result, the compound possesses both a positive charge and a negative charge in the molecule and the compound behaves more like an inorganic salt than an organic compound! The pKₐ value (10) is not due to the carboxylic acid but instead the ammonium cation. The pKₐ value (12) is not due to the amine but instead the carboxylate anion.

**Amphotericism of Amino Acids:**

Because amino acids contain both –CO₂⁻ (carboxylate anion) and –NH₃⁺ (ammonium cation), they are called “amphoteric”. Amphoteric compounds are those that react with both acids and bases.
At low pH levels (acidic solutions):

\[
\begin{align*}
\text{Aspartic Acid} & \\
\text{Isoelectric point} &= 3.0 \\
\end{align*}
\]

must suppress deprotonation of carboxylic acid

Basic side chains have isoelectric points higher to prevent protonation of side chain amine groups, as in lysine. The pH has to be high enough to prevent the amine group from being protonated.

\[
\begin{align*}
\text{Lysine} & \\
\text{Isoelectric point} &= 9.7 \\
\end{align*}
\]

must suppress protonation of amino group

Neutral side chains are neutral but the isoelectric points for these compounds will always be slightly acidic. Why so? If you look at the dipolar ion of an amino acid, you find the ammonium cation and the carboxylate anion. The ammonium cation is a stronger acid than the carboxylate anion is a base. Thus, the dipolar ion donates its proton to the water solvent of the solution, if only to a slight extent. In order to become “neutral” again, the solution must be made slightly acidic to re-protonate the amine group.
Thus the “neutral” amino acids have isoelectric points that are slightly acidic, to maintain the proton on the amine group. An example of this is alanine, whose isoelectric point is a pH of 6.0.

The concept of electrophoresis, a common tool used for separation of amino acids and analysis of proteins, utilizes separation based on a particular pH and the isoelectric points of amino acids. By varying the pH of a system, the charges on the amino acids will vary from positive to neutral to negative and separation can be achieved.

The order in which amino acids are found in a protein molecule determines the relationship of the side chains to one another and consequently determines how the protein interacts with itself and its environment. The presence of side chains with functional groups that may hydrogen bond or the presence of the thiol functional group in the amino acid cysteine create a system that may undergo oxidative coupling to form disulfides that causes cross-linking of protein chains will cause the structure to change.

Consider the different types of amino acid side chains. Hormones and water-soluble proteins must contain amino acids with many polar side chains in order to be soluble. These proteins would orient the polar side chains to the outside of the protein to effect solubility into the system. Muscle proteins, on the other hand, would possess more non-polar side chains on the outside of the protein. One example of the dramatic effect side chains can have in a protein would be the case of sickle-cell anemia, which results from a lack of solubility of the hemoglobin in the blood. This reduces the ability of the hemoglobin to transport oxygen. What causes sickle-cell anemia? Hemoglobin is a protein that contains 146 amino acids linked together. When one valine amino acid is substituted for a glutamic acid, a neutral side chain replaces an acid, polar side chain. The hemoglobin becomes less polar and thus less soluble!
This is the extent to which your understanding of amino acids is required for CHM 332. Further exploration into amino acids and proteins can be found in Biochemistry, thus the lecture ends here.

From this, you should be able to process the following information:

- **You do not have to memorize the structures of the amino acids mentioned here or in the textbook.** You will need to do that for biochem, later in life.
- You should be able to recognize a peptide bond and understand the stability of the peptide bond.
- You should be able to recognize an acidic, a basic or a neutral side chain.
- You should be able to draw the dipolar ion of any amino acid.
- You should understand the concept of amphoterism and what reaction occurs with an amino acid when the solution is acidic or basic.
- You should understand what the isoelectric point is for an amino acid.
- You should understand what effect the side chain plays on the isoelectric point of an amino acid.