Lecture 1

Amino acids and the Peptide Bond-I

Introduction

The word protein is believed to originate from the from Greek *prōteios* meaning primary. This is perhaps a perfect way to describe what these molecules actually are – without them we do not exist. Proteins provide the structural framework of cells and tissues. All life processes involve proteins. They are required for transport of nutrients and are essential to make us function. Proteins are required in your diet to help your body to repair cells and make new ones. When proteins are digested we are left with amino acids – the building blocks of proteins.

A dictionary definition for 'protein' is as follows**:** any of various naturally occurring extremely complex substances that consist of amino-acid residues joined by peptide bonds, contain the elements carbon, hydrogen, nitrogen, oxygen, usually sulfur, and occasionally other elements (as phosphorus or iron), and include many essential biological compounds (as enzymes, hormones, or antibodies)

It appears to be quite a complicated matter indeed and before we go deeper into the intricacies of the subject we will understand the basic building blocks of proteins

So we realize that

- proteins are essential for life
- the body requires protein to repair and maintain itself
- the basic structure of proteins is a chain of amino acids that are linked together

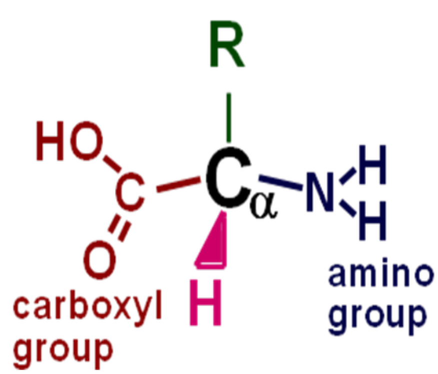
Amino Acids – The Building Blocks

Amino acids are compounds form the building blocks of proteins.

Each amino acid consists of:

- a central carbon atom referred to as the C_α (C-alpha) atom
- an amino group ($-NH_2$)
- a carboxyl group (-COOH) and.
- a side chain (-R)

Differences in the side chains distinguish the various amino acids.



What do we know about compounds that have four different substituents to the carbon atom? We know that these molecules are chiral. A chiral molecule is a type of molecule that has a non-superposable mirror image. The presence of an asymmetric carbon atom is normally the reason a molecule is chiral and this property is also referred to as asymmetry.

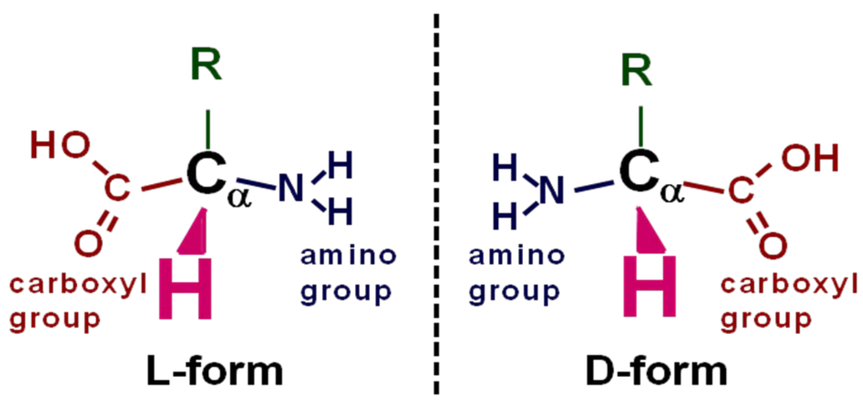
The most common example of chiral objects are our hands – our hands are mirror images of one another and we cannot superimpose them on each other. So in whichever way we orient our hands it will be impossible to make all features coincide.

We see right away that the amino acids are also chiral since the central carbon atom meets the criteria for chirality. Are all the amino acids chiral?

After we learn about the different types of amino acids, we will see that only one amino acid is achiral – meaning that the four atoms attached to the central C_α are not all different.

The R-group represents what is called a side chain which varies from one amino acid to another. This R-group is what makes each amino acid unique in nature. This group of atoms may have just carbon and hydrogen or in addition to these atoms may contain heteroatoms such as nitrogen, oxygen and/or sulfur. This specific combination of atoms will give rise to a particular side chain with specific properties that will define the characteristics of the amino acid.

An important feature of amino acid structure that is not apparent from the above representation is the stereochemistry. Shown below are the two enantiomers of the amino acid alanine, L-alanine and D-alanine. Each of these molecules are mirror images of one another. This means that even if you rotate the molecules in any way, it is impossible put these two molecules in the exact same position. The L-form is the isomer mostly seen in organisms.



This means that all amino acids found in proteins usually occur in the L-configuration about the central chiral carbon atom. D-amino acids are not found in proteins naturally and they are by and large not a part of the metabolic pathways in higher organisms. D- amino acids are, however, sometimes the components of certain bacterial cell walls.

The origin of the term *chirality* is from the Greek word for hand, *kheir*. In chemistry, chirality refers to molecules – the two mirror images of a chiral molecule are referred to as enantiomers. They are also called optical isomers.

The normal practice by chemists is to use what is called an R, S system to distinguish between enatiomers of molecules. However, many biochemical systems – mostly amino acids and sugars – use the D and L system based on the earliest method for identifying enantiomers from glyceraldehyde.

The glyceraldehyde molecule contains three carbon atoms with one form referred to as D and the other as L based on their ability to rotate polarized light either to the right (dexter) or left (laevus). The enantiomers of the amino acids are designated on the basis of their similarity to the D and L forms of glyceraldehyde.

To determine whether a specific amino acid is of the L or D form, orient the molecule either visually or using paper and pencil so that the hydrogen is directly behind the central carbon atom. Since the central carbon atom has four groups that are arranged in a tetrahedron about it, the remaining three substituents will form a triangle if we view it the way it has been oriented. The next step is to trace the direction of rotation from the **–CO**OH to **–R** to –**N**H_2, or **CORN**. If the direction traced is anticlockwise, then the amino acid is an L-isomer and if it is clockwise then it is the D-isomer.

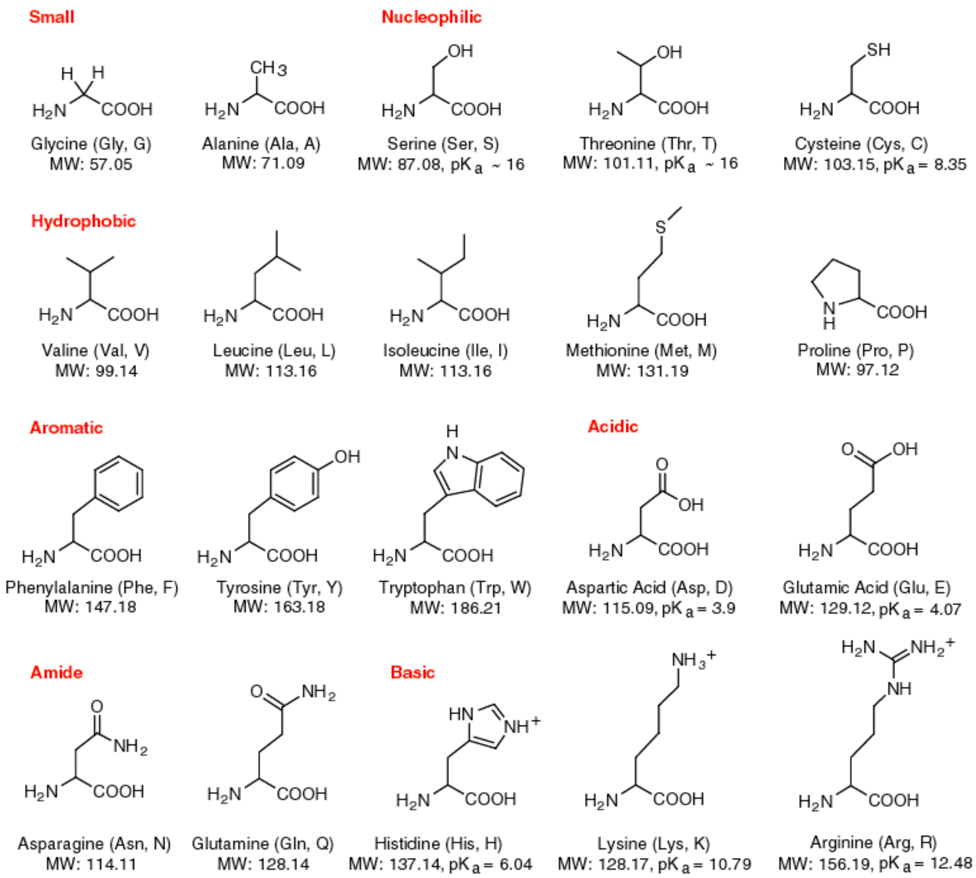
The amino acids are usually grouped based on the properties of their side chains, that is the –R group. Even though it is possible to have many different types of R groups nature has chosen 20 specific types of R groups that form the essential amino acids.

The groupings of the amino acids have been done in different ways – the major groups are hydrophobic and hydrophilic. Aliphatic and aromatic amino acids exist as do sulfur containing amino acids. There also polar amino acids that may be charged or uncharged. The acidic and basic amino acids remain charged at physiological pH.

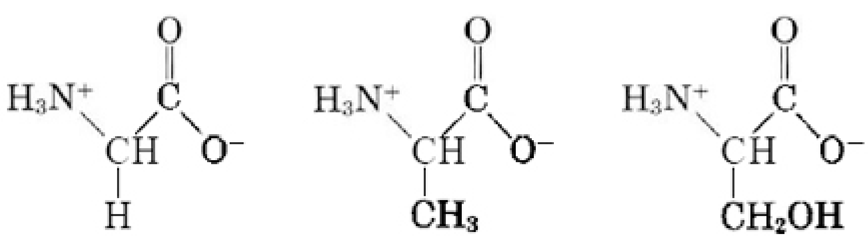
The polar side chains that are hydrophilic in nature can form hydrogen bonds.

Each amino acid has a unique three-letter and one-letter code for identification which is useful in their representation.

These are listed below:



In practice the amino acids exist as zwitterions and they should be written as



Zwitterionic forms of 3 amino acids.

Amino acids are also classified as Essential and Nonessential amino acids. Essential amino acids cannot be made by the body, and must be supplied by food. Nonessential amino acids are synthesized by the body from essential amino acids or obtained from the normal breakdown of proteins.

The nine essential amino acids are:

- Histidine
- Isoleucine
- Leucine
- Lysine

- Methionine
- Phenylalanine
- Threonine
- Tryptophan
- Valine

Proteins also contain several amino acid derivatives. An amino acid derivative is one where the original amino acid has an additional chemical moiety or lacks a specific moiety. One such example is the neurotransmitter, epinephrine which is made from tyrosine, in a synthetic pathway that involves several enzymes and intermediate molecules. In the first step, an additional -OH group is added to the tyrosine residue.

Other examples are 4-hydroxyproline and 5-hydroxylysine that are important structural constituents of collagen, a fibrous protein present in mammals.

These specific modifications of the residues occur after the polypeptide chain of the protein is formed. We will learn about the polypeptide chain in the next lecture.

The amino acids therefore possess novel acid-base properties, are of varied structure and functionality and have the capacity to polymerize.