

1. Molecules can have more than one buffering region. Alanine, for example has both an amine group and a carboxyl group that can gain/lose protons (hydrogen ions). It will thus have two pKas, one for the carboxyl group and one for the amine group.
2. A buffer system will be at maximum capacity when the concentration of the undissociated acid (HA) equals that of the salt ( $A^-$ ) (Acid = Salt). The Henderson Hasselbalch equation further reveals that when this is true,  $pH = pKa$ .

Please see the extra problems on the schedule page for practice.

3. Amine systems (also in amino acids) have two forms:

$NH_3^+$  and  $NH_2$ . Note that the  $NH_3^+$  is the acid and  $NH_2$  is the salt in my nomenclature.

Carboxyl systems have two forms too.  $COOH$  has no charge and when it loses its proton,  $COO^-$  has a negative one charge.

4. Students make mistakes calling things acids and bases. Carboxyl groups are acidic and most think of amine groups as basic. Consequently, they get confused when they think of an amine like  $NH_3^+$  donating protons (acting like an acid). The same students usually aren't confused, however, about  $COO^-$  accepting protons (acting like a base). That is why I avoid calling amine groups "bases".
5. The Henderson Hasselbalch equation tells us we can predict the ratio of salt to acid as a function of pH if we know the pKa. Consequently, we can predict the charge on amino acids in a protein as the pH changes. Subtle changes in pH in the body can have drastic changes in protein structure and function. We'll see soon how hemoglobin undergoes drastic changes between the lungs (relatively high pH) and actively respiring tissue (relatively low pH). The pH changes are not very large, so it is important to recognize that very small pH changes can make a big difference.
6. It is important for you to be able to use the Henderson-Hasselbalch equation to make predictions relating to pH, pKa, and/or salt/acid.
7. The value of the Henderson Hasselbalch equation is that by knowing the pH and the pKa of a molecule, the approximate charge of it in solution can be determined. For this class, we will assume that if the pH is more than one unit below the pKa of a group, that the proton is ON it. If the pH is more than one unit above the pKa of the group, the proton is OFF it. This is only useful for estimating charge. Determination of the pI (pH at which a molecule has a charge of exactly zero) requires calculation (described in class).

## Highlights Protein Structure I

1. Protein structure dictates protein function. The structure of a protein is a function of the sequence of amino acids comprising it.
2. Amino acids are the monomeric (building block) units of proteins. They are covalently joined together in peptide bonds to make proteins (polypeptides).
3. There are 20 amino acids commonly found in proteins and of these 20, 19 have a chiral center and thus can

exist in two stereoisomeric forms. The only one that doesn't have a chiral center is glycine. Almost all biologically made amino acids are in the same stereoisomeric form - the 'L' form. The 'D' form occurs only in very rare peptides, such as in the cell wall of bacteria (discussed later in the course).

4. Amino acids are grouped into several structural categories based on the composition of their R groups - we will use the designations of your book, as I described in the outline. You will need to know the names of the 20 amino acids of proteins, which of the groups above each one belongs to and will need to be able to predict ionization at given pH values if you are supplied pKa values. The problem solving videos I've posted illustrate this. Of these amino acids, the ones we will be concerned with have R groups that can ionize. These include the aminos, the carboxyls, the sulfhydryl (cysteine) and the hydroxyl or tyrosine.

5. I mentioned briefly some of the properties of individual amino acids in the lecture. You should know those general properties (such as hydrophobic, hydrophilic, sulfhydryl, and ionizing side chains.) Though I didn't mention it, you should know that glycine is the simplest amino acid because it only has a hydrogen as its R-group. It is the only amino acid that doesn't have D and L forms. Another important one structurally is proline. I'll say more about it later.

6. Molecules, such as amino acids, that are capable of gaining/losing more than one proton, have pKa's that correspond to each functional group that can lose a proton. For example, a simple amino acid, such as alanine, has an amino group (pKa about 9.5) and a carboxyl group (pKa about 2.5).

7. A titration plot for a simple amino acid (no R groups that can lose protons) has two flattened regions - each one occurring at the respective pKa. You will not need to memorize any pKa values for the exam, but you should know how to use a pKa table to predict charge if I give you one on the exam. See the problem solving video I posted for more information.

8. A zwitterion is a molecule whose net charge is zero.

9. The pI of a molecule is the point at which its charge is exactly zero. The assumptions above about protons on/off cannot be used to find the pI. It must be calculated. The pI of a molecule is the average of the pKa values around the point on the titration curve where the charge is zero

10. The sequence of amino acids in a protein is ultimately responsible for all of the properties a protein has. The sequence of amino acids of a protein is referred to as its primary structure.

11. Bonds holding amino acids together in a protein are called peptide bonds and they occur between the alpha amino group of one amino acid and the alpha carboxyl group of the next one.