The pK_a value of a particular group is not the same in all molecules; it is often significantly different.

For example, the pK_a values of α- carboxyl groups in the amino acids exhibit small differences (1.8 to 2.5) as shown in Table 4-2.

Likewise, the pK_a values of the α-amino groups exhibit significant differences (8.7 to 10.7).

The pK_a of the secondary amino group in proline is different from that in hydroxyproline, a modified form of proline-

The amino group in proline is a stronger base than in hydroxyproline.

Also observe that the pK_a values of the α, β and χ carboxylic acid groups differ significantly from each other and that of acetic acid-

Some of these differences can be explained in terms of the effects of neighboring groups in the molecule.

For example, the inductive effect of the -OH group makes hydroxyproline a weaker base than proline-

The protonated form of hydroxyproline is less stable and therefore a stronger acid than the protonated form of proline.

The pK_a values for the α,β and χ-carboxylic acid groups increase as the distance from the α-amino group increases.

This appears to be due to the electrostatic effect of the α-amino group that is protonated in the pH range where the carboxylic acid groups ionize-

The protonated amino group has the effect of increasing the acidity of the carboxylic acid group by stabilizing the conjugate base (carboxylate) form.

The electrostatic effect also accounts for differences in the pK_a values for the α-NH_2 and α-CO_2H groups in glycine and the dipeptide glycylglycine-

We observe then that the pK_a value of a group is in part dependent on the environment of the group in a molecule.

Let's define another quantity characteristic of ionizing molecules.

The isoelectric point (pI) is the pH at which the average net charge on a molecule is zero.

Consider what the pI would be for the dipeptide gly-asp

In practice we could determine the pI experimentally by observing the migration (mobility) of the molecule in an electric field at different pH values.

To do this we might spot a solution of the dipeptide in the center of a piece of filter paper, then place the paper on a tray with the ends dipped into a buffer solution at a chosen pH as shown in Fig 5-20.

If we apply an electrical potential difference between the electrodes with an external power supply, the dipeptide will migrate toward the cathode if it is a cation at the chosen pH.

If the dipeptide is an anion at the chosen pH, it will migrate toward the anode.

The mobility μ defined by $\mu = v/E$ will be zero at a pH for which q is zero.

The pI corresponds to this pH.

In practice one could determine the μ at various pHs and plot the results to determine the pI-

The pI is a useful characteristic of a molecule, particularly for one of unknown structure.

The pI tells us whether the molecule will be positively or negatively charged at a given pH.

At pH values greater than the pI, the molecule will have a negative charge.

At pH values less than the pI, the molecule will have a positive charge.

We can estimate the pI of a molecule of known structure by considering what the net charge would be on the molecule during a pH titration-