Appendix D

Acids and Bases

Charges are essential for the stability and function of many proteins. To understand the effect of the environment, particularly its pH on stability and function, a few concepts are needed.

D.1 Acids and Bases

An acid is a proton donor, a base a proton acceptor; they are always occur in conjugated pairs :

$$\mathrm{acid} \leftrightarrow \mathrm{base} + \mathrm{H}^{+}. \tag{D.1}$$

Examples are

NH_4^+	$\leftrightarrow$	NH_3	+ H^+
H_2SO_4	$\leftrightarrow$	HSO_4^-	+ H^+
H_3O^+	$\leftrightarrow$	H_2O	+ H^+
H_2O	$\leftrightarrow$	OH^-	+ H^+

Some compounds can act as either base or acid.

Physicists often believe that the H^+ indeed appears as a proton. In reality, however, protons have the tendency to sneak into the electron shell of neighboring molecules. In aqueous solution, protons appear in the form of *hydronium ions*, H_3O^+. The dissociation of an acid, Eq.D.1, thus occurs as shown in Fig.D.1.

The acid transfers its proton directly onto a neighboring water molecule. The correct way to describe the acid-base equilibrium hence is

$$\mathrm{AH} + \mathrm{H_2O} \leftrightarrow \mathrm{A}^{-} + \mathrm{H_3O}^{+}. \tag{D.2}$$

For “similplicity” (and to confuse physicists), the reaction is usually written in the form of Eq. (D.1).

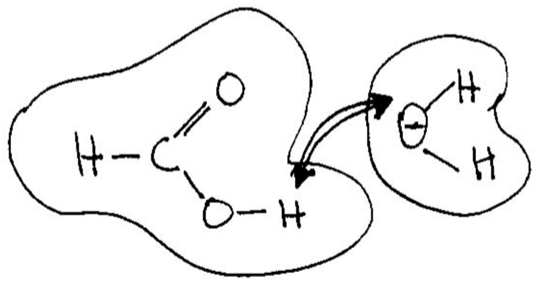

Figure D.1: Acid-base equilibrium.

D.2 The pH Scale

In water, Eq. (D.2) becomes

$$\mathrm{H_2O} + \mathrm{H_2O} \leftrightarrow \mathrm{HO}^- + \mathrm{H_3O}^3, \tag{D.3}$$

or

$$\mathrm{H_2O} \leftrightarrow \mathrm{OH}^- + \mathrm{H}^+. \tag{D.4}$$

The equilibrium coefficient of this reaction is given by

$$K = [\mathrm{H}^+][\mathrm{OH}^-]/[\mathrm{H_2O}] \tag{D.5}$$

Usually, the concentration [H_2O] of water is very large, about 55 M, and the concentrations of the H^+ and OH^- ions very small, [H_2O] is essentially constant during the reaction (D.5). A new coefficient K_{eq} is consequently introduce through the definition

$$[\mathrm{H}^+][\mathrm{OH}^-] = K_{eq}. \tag{D.6}$$

The coefficient K_{eq} is called the ion product of water. Its value at $25°C$ is $1.0 \times 10^{-14} M^2$. In an acid solution, the concentration [H^+] is relatively high; in a basic solution, [OH^-] is relatively high.

Equation (D.6) is the basis for the *pH scale*. Since K_{eq} can change over many orders of magnitude, it is more convenient to use logarithms than powers. The term pH is defined as[2]

$$\mathrm{pH} = -\log[\mathrm{H}^+]. \tag{D.7}$$

Table D.1:

Blood plasma	pH 7.4
Intracellular fluids	
muscle	pH 6.1
liver	pH 6.9
Intestitial fluid	pH 7.4

In pure water, Eq. (D.5) tells us that [H$^-$] = [OH$^+$] = $10^{-7}M$ and hence pH (pure water) = 7. The pH of some solutions is given in Table **??**.

D.3 The Henderson-Hasselbalch Equation

Consider a conjugate acid-base pair, AH $\leftrightarrow$ A$^-$ + H$^+$. The equilibrium coefficient K for this reaction is called the dissociation coefficient.

$$K = \frac{[\mathrm{A}][\mathrm{H}^+]}{[\mathrm{AH}]} \tag{D.8}$$

Again it is customary to use its negative logarithm,

$$\mathrm{p}K = -\log K. \tag{D.9}$$

Equation (D.9) then can be written as

$$\mathrm{pH} = \mathrm{pK} - \log\{[\mathrm{AH}]/[\mathrm{A}^-]\}. \tag{D.10}$$

In this form, it is called the Henderson-Hasselbalch equation. At a fixed pH, it gives the ratio of protonated (AH) to deprotonated (A$^-$) form of the acid AH.

D.4 Amino Acids

The charges on amino acids are crucial for the function of proteins. Amino acids with neutral side chains can assume three charge states, A$^+$, A^0, and A$^-$. For the reactions A$^+$ $\leftrightarrow$ A^0 + H$^+$ and A^0 $\leftrightarrow$ A$^-$ + H$^+$, two equilibrium coefficients K_1 and K_2 can be defined in analogy to Eq.(D.4). At low pH (pH $<$ pK$_1$) the amino acid will be predominantly positive; at pH $>$ pK$_2$, it will be predominantly negative. At pH = pK$_1$, the probabilities of finding A$^+$ or A^0 are equal. For amino acids with charged side chains pK$_R$ similarly indicates the pH at which charged and neutral sidechains have equal probabilities. Some values are given in the following Table D.2. pI is the pH of an aqueous solution such that the net charge on the molecule is zero[3].

Table D.2: Values of pK's for some amino acids.

Amino acid	pK_1 COOH	pK_2 NH_3	pK_R Residue	pI
ASP	2.10	9.82	3.89	2.98
GLU	2.1	9.47	4.07	3.08
GLY	2.35	9.78	—	6.06
HIS	1.77	.9.18	6.10	7.64
LYS	2.18	8.95	10.53	9.47
TYR	2.20	9.11	10.07	5.63

Bibliography

[1] G. Adam, P. Läuger, and G. Stark, *Physikalische Chemie und Biophysik*, Springer, Berlin, 1977.

[2] The correct definition ofo pH involves the concept of activity (I. M. Klotz and R. M. Rosenberg, *Chemical Thermodynamics*, Addison-Wesley, 1972). For details see for instance R. G. Bates, *Determination of pH: theory and practice*, Wiley, New York, 1973.

[3] C. Tanford, *Physical Chemistry of Macromolecules*, Wiley, 1961.