

1.2 The pH scale.

pH is simply a more convenient (if logarithms are convenient!) way of specifying the concentration of H⁺ ions in solution. pH is defined as

$$\text{pH} = -\log [\text{H}^+] = \log (1/[\text{H}^+])$$

By using logarithms, concentrations in the range of 1 M to 10⁻¹⁴ M H⁺ are converted to numbers between 0 and 14. For example, the pH of a neutral solution is

$$\text{pH} = -\log (1 \times 10^{-7}) = 7.0$$

Solutions in which pH = 7.0 are defined as neutral. Solutions with pH < 7.0 are called "acidic," and solutions in which pH > 7.0 are called "basic."

1.2.i. Acid dissociation constants of weak acids.

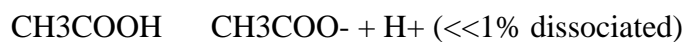
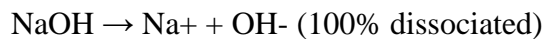
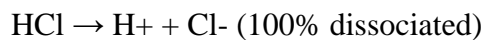
A. Strong and weak acids and bases.

Most reactions are reversible, and equilibrium is achieved when the rate of the forward reaction becomes equal to the rate of the reverse. As in the water ionization example shown above, the equilibrium constant (K_{eq}) for a general reaction is defined as the ratio of products to reactants at equilibrium.



$$K_{eq} = \frac{[\text{C}][\text{D}]}{[\text{A}][\text{B}]}$$

Remember, all reactions have a characteristic K_{eq} at a defined temperature. Many biomolecules (such as amino acids) are weak acids. Unlike strong acids (HCl, H₂SO₄, etc.) which completely dissociate when dissolved in water, weak acids only partially dissociate. Equilibrium reactions for the dissociation of strong acids, strong bases, and the weak acid, acetic acid (CH₃COOH) are shown below.

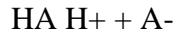


(conj. acid) (conj. base)

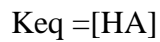
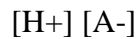
In the case of a weak acid, the two species in solution at equilibrium are called the conjugate acid-conjugate base pair.

Equilibrium constant (K_{eq}) and the pK_a.

The equilibrium constant for dissociation of a weak acid (HA) is



(conj. acid) (conj. base)



The equilibrium constant for acid dissociation is more commonly called the acid dissociation constant, K_a, and K_a = K_{eq}. Note, "the higher the K_a, the stronger the acid." As in the case of pH, biochemists typically use "pK_a" values instead of K_a values for weak acids. pK_a is defined in the same manner as pH,

$$\text{pK}_a = -\log K_a = \log (1/K_a)$$

When comparing pK_as, "the lower the pK_a, the stronger the acid."

1.2.ii.Henderson-Hasselbalch equation.

The Henderson-Hasselbalch equation describes the quantitative relationship between pH and pK_a in buffer solutions. In fact, a titration curve can be plotted using it. The HH equation will be derived in class starting from the equation specifying the equilibrium constant for ionization of a weak acid, K_a = [H⁺][A⁻]/[HA]. The final form of the HH eq is

$$\text{pH} = \text{pK}_a + \log \left(\frac{[\text{A}^-]}{[\text{HA}]} \right)$$

or

$$\text{pH} = \text{pK}_a + \log \left[\frac{\text{[conjugate base]}}{\text{[conjugate acid]}} \right]$$

The equation indicates that the pH of a solution depends on the pK_a and the ratio of conjugate base to conjugate acid components present. The equation can be used to calculate the pH of a solution of a weak acid when the ratio of [A⁻]/[HA] is known, or alternatively, to calculate the ratio of [A⁻]/[HA] when the pH is known.

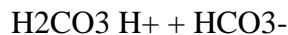
1.2.iii. Buffers:

A buffer is "a solution that tends to resist a change in pH on addition of a small amount of strong acid or base." As shown above for the acetic acid titration curve, the pH of a solution undergoing titration changes minimally near the midpoint of the curve. The optimum buffering power of the solution occurs at the midpoint (where $\text{pH} = \text{pK}_a$, and $[\text{CH}_3\text{COOH}] = [\text{CH}_3\text{COO}^-]$). In practice, the optimum buffering region extends about 1 pH unit on either side of the pK_a . In this pH range, buffering power is best because the concentrations of both buffering species, HA and A^- , are the highest. Buffers are selected based on their pK_a values and the range of pHs to be buffered. For example, acetic acid ($\text{pK}_a = 4.76$) is a good buffer for the range $3.76 < \text{pH} < 5.76$, whereas the compound "Tris" ($\text{pK}_a \sim 8.0$) is a good buffer for the range $7.0 < \text{pH} < 9.0$. The main buffering agent inside cells is phosphate. In this case it is the second dissociation reaction with $\text{pK}_2 = 7.2$



In the blood, the CO_2 -carbonic acid-bicarbonate system is used for buffering. Here the major forms responsible for buffering are carbonic acid and bicarbonate.

While the pK_a for the reaction



is only 6.4, H_2CO_3 readily converts to CO_2 and H_2O which tends to shift the carbonic acid-bicarbonate equilibrium to the left (to a higher pK_a) which is closer to the pH of blood.

1.2.iv. physiological buffers in living systems

Physiological buffers are chemicals used by the body to prevent large changes in the pH of a bodily fluid.

The four physiological buffers are the bicarbonate, phosphate, hemoglobin, and protein systems.

The pH of a buffer is determined by the Henderson-Hasselbalch equation:

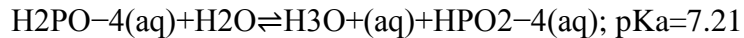
$$\text{pH} = \text{pK}_a + \log\left(\frac{[\text{A}^-]}{[\text{HA}]}\right)$$

The buffer is best able to resist changes in pH when the pH of the buffer is close to the pH of blood (7.37 to 7.42), so the pK_a of the acid should be close to 7.4.

Phosphate Buffer

The phosphate buffer system consists of H_2PO_4^- and HPO_4^{2-} ions.

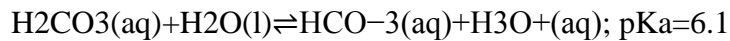
The equilibrium is



The phosphate buffer can easily maintain a pH of 7.4.

Carbonate Buffer

The equilibrium is



This buffer functions in exactly the same way as the phosphate buffer, but it is not ideal because its pK_a is too far from pH 7.4.

Perhaps more importantly, the enzyme *carbonic anhydrase* converts H₂CO₃ into CO₂ that is dissolved in the blood and is then exhaled as CO₂ gas.

Hemoglobin

The general equation is:



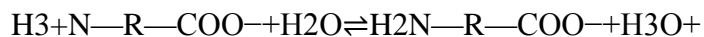
It shows that oxygenation of Hb promotes the formation of H₃O⁺.

This shifts the bicarbonate buffer equilibrium towards CO₂ formation, and CO₂ is released from the red blood cells.

Proteins

A protein is a long chain of amino acid residues, but this long chain still has free carboxylate groups COO⁻ and free amino groups NH₂.

We could write the equation for a protein buffer system as



The protein can then act as a buffer.

1.2.v. Energy in living organism:

Living organisms are highly complicated at the molecular level. A large amount of energy is invested in maintaining the ordered and complicated state of cells and tissues. In humans and animals, energy needed for work and biosynthesis of cellular structures is derived from organic molecules in the diet. Often these come from plant sources, who derived their energy for synthesis of biomolecules from sunlight. In animals, energy is derived from the breakdown of fuel molecules

by processes referred to as catabolism. In turn, the energy released from catabolism is used to drive biosynthetic processes collectively referred to as anabolism.

The flow of energy in biological systems is covered in the discipline known as bioenergetics. Bioenergetics is a sub-discipline of classical thermodynamics, which has been covered in your physics courses. Most of our use of thermodynamics will be concerned with the calculation of free energy changes (ΔG) which can be used to determine the direction of metabolic reactions and their equilibrium constants. ΔG values are determined by the enthalpy (ΔH , heat transfer) and entropy (ΔS , change in randomness) changes associated with a reaction through the equation $\Delta G = \Delta H - T\Delta S$. Negative values of ΔG signify favorable reactions, whereas positive values of ΔG are associated with unfavorable reactions. K_{eq} is based on the ΔG value and gives the ratio of products to reactants once equilibrium is reached. This is important because it will show how a cell can ratio reactions in different directions. Kinetics measures the rate at which a reaction takes place and how the reaction gets from start to finish. So reactions can be thermodynamically favorable but kinetically unfavorable. So cells use enzymes that can only affect the kinetics not the thermodynamics. Bioenergetics is one of the tools used in animal and human nutrition. Weight gain or loss ultimately depend on the difference between caloric intake and expenditure. In this course, we will discuss energy metabolism in different physiological states such as exercise and fasting, and in diseases such as diabetes.