Student Study Guide/ Solutions Manual to accompany Biochemistry: An Introduction Second Edition

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to accompany

Biochemistry: An Introduction

Second Edition

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The chemistry of living organisms is immensely complex. Every day, scientists are making strides in understanding how chemical reactions are organized and regulated. Despite the seemingly limitless amount of biochemical information which exists today, there are some fundamental concepts and principles which this study guide will highlight.

General Study Tips

A combination of approaches is necessary to effectively learn biochemistry. Memorization of basic concepts and structures, for example, is important. But memorization alone will only take you so far. Biochemistry is akin to learning a foreign language: you must first learn the vocabulary and grammar before you will be able to communicate. Biochemists have developed their own "vocabulary," such as the names and structures of amino acids, nucleic acids, sugars, and lipids. Biochemical "grammar," so to speak, involves chemical reactions which transform one molecule into another. The immensity of biochemical pathways, reactions, and compounds makes it unreasonable for anyone to memorize everything.

One important commonality in basic biochemistry is that there is often a function or purpose for every metabolic pathway which occurs. Although some of these functions may not be immediately obvious or understood, it is nonetheless critically important to learn and remember them. In studying biochemistry, be sure to think about the function of reactions. Why do they occur? What is their significance? In asking questions, however, be mindful that biochemistry is a dynamic and constantly changing discipline which does not have all the answers. The excitement of biochemical research comes in pursuing and finding answers to many challenging questions.

Special Thanks

I must acknowledge and thank all of my former instructors for their excitement and enthusiasm about science, which in turn stimulated my interest in biochemistry. These individuals include UCLA professors Steven Clarke, Richard Weiss, Charles West, and, most importantly, my Ph.D. advisor Daniel Atkinson. I would also like to thank Mike Fester, my introductory biochemistry teaching assistant, for his encouragement in my entering the world of academia, my wife Joy for her tireless support, and Joel Dirksen, who assisted me in compiling information for this study guide.

Best wishes in your studies of biochemistry!

Bruce H. Morimoto
March 1998

Contents

1 Biochemistry: An Introduction

Objectives

1. What principles are central to our understanding of living organisms?

   The following principles have been established by biochemists to be central to our understanding of living organisms:

   a. Cells, the basic structural units of all living organisms, are highly organized. A constant source of energy is required for the maintenance of a cell's ordered state.

   b. Living processes consist of thousands of chemical reactions. Precise regulation and integration of these reactions are required for maintenance of life.

   c. Certain fundamental reaction pathways, such as the energy-generating conversion of glucose to pyruvic acid, known as glycolysis, are found in all organisms.

   d. All organisms utilize the same types of molecules. Examples of such biomolecules include carbohydrates, lipids, proteins, and nucleic acids.

   e. Encoded in each organism's nucleic acid are instructions for growth, development, and reproduction.

2. What characteristics distinguish prokaryotes from eukaryotes?

   Prokaryotes lack a true nucleus, unlike eukaryotes which contain a complex membrane-bound structure of genetic information. Along with well-formed nuclei, eukaryotic cells contain a number of subcellular structures called organelles. Given the simplicity of prokaryotic cells, biochemical diversity has allowed various species to occupy not only all temperate environments, but also harsh and seemingly lifeless ones. One of the most noticeable differences between the two cells is that eukaryotic cells are much larger than prokaryotic cells.

3. What are the four major types of small biomolecules found in cells?

   Cells contain four families of small biomolecules: amino acids, sugars, fatty acids, and nucleotides.

4. What are the primary functions of metabolism in living organisms?

   Metabolism – the total chemical reactions in a cell – performs the primary function of acquisition and utilization of energy, synthesis of molecules needed for cell structure and functioning, and removal of waste.

5. What are the most common types of chemical reactions in living organisms?

   Among the more frequent reactions encountered in biochemical processes are the following: nucleophilic substitution reactions, elimination, isomerization, oxidation-reduction, and hydrolysis.

6. How do cells maintain a high degree of internal order?

   The complex structure of cells requires a high degree of internal order. This is accomplished in four ways: synthesis of biomolecules, transport of ions and molecules across membranes, production of force and movement, and the removal of metabolic waste products and other potentially toxic substances.

General Principles

Biochemistry is the study of how living cells form and break apart molecules. The function of the cell is: 1) to live, which requires energy (light for plants, and chemical for animals) and, 2) to grow, which requires synthesis of new biomolecules.

How do cells satisfy these requirements?

Plants convert light energy into chemical energy (**photosynthesis**). Animals then consume plants as a source of chemical energy in which they convert larger molecules into smaller ones (**catabolism**), and in the process generate energy (in the form of ATP, the energy currency of the cell). Using this energy, the smaller molecules can be converted into larger molecules (**anabolism**).

Catabolism

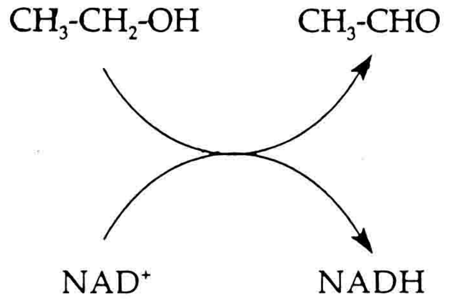
Living cells extract chemical energy by breaking down molecules. Energy is in the form of electrons. The removal of electrons from a molecule is called **oxidation**.

$$C_6H_{12}O_6 \longrightarrow CO_2 + H_2O + \text{electrons}$$

The carbon in sugar loses electrons and is therefore oxidized. The reverse of oxidation is called **reduction**.

$$CO_2 \longrightarrow C_6H_{12}O_6$$

In order for something to be oxidized, another molecule must be simultaneously reduced.



Ethanol, for example, loses electrons and is therefore oxidized. NAD^+ accepts electrons and is therefore reduced.

Catabolism can be either:
- Aerobic (with air, or oxygen) or
- Anaerobic (without air), sometimes referred to as fermentation

Plants, animals, and bacteria catabolize sugars to produce energy. Six-carbon sugars are broken down into three-carbon molecules, thereby generating some energy and electrons. Without oxygen, the electrons have no where to go, and the molecules which carry or transfer electrons cannot be recycled.

In yeast and some bacteria, the electrons are donated back to a three-carbon molecule to form ethanol and carbon dioxide. This is called **fermentation** and is the basis by which yeast are used to make beer and wine (ethanol), or make breads rise (production of CO_2).

For animals, in the absence of oxygen, a three-carbon molecule accepts the electrons and is converted into lactic acid. As the name denotes, lactic acid is an acid and is responsible for muscle cramps. When we exercise vigorously, for example, our muscles become starved for oxygen. The electron-carrying intermediates recycle and form lactic acid. This results in a drop in muscle pH, which in turn results in a muscle cramp.

What does oxygen do?

It allows three-carbon molecules to be oxidized to CO_2, because the electrons are transferred to oxygen, converting oxygen into water. Oxygen functions as a terminal electron acceptor.

2 Living Cells

Objectives

1. How are prokaryotes and eukaryotes alike and how are they different?

   Similarities

   Both cells are self-contained units surrounded by a membrane that separates them from their environment.

   The two cells are composed of the same type of molecules.

   Differences

   The most obvious difference between the two cells is their size: the eukaryotic cell is much larger than the prokaryotic cell.

   Another distinct difference is that the eukaryotic cell has a complex internal structure with a variety of membrane-bound organelles, whereas the prokaryotic cell has simple structures.

2. Which organelles carry out the processes required to maintain a living state in eukaryotic cells?

   A eukaryotic cell is composed of seven basic organelles which maintain its living state:

   Plasma membrane: Performs selective permeability in which certain substances are prevented from entering the cell and others from leaking out.

   Nucleus: Contains the cell's information; exerts a profound influence over all cellular metabolic activities; plays a major role in the synthesis of the RNA components of ribosomes.

   Endoplasmic reticulum: Primarily involved in protein synthesis, lipid synthesis, and biotransformation.

   Cytoplasmic ribosomes: Involved in the biosynthesis of proteins.

   Peroxisomes: Noted for their involvement in the generation and breakdown of peroxides.

   Mitochondria: Involved in the biosynthesis of ATP through aerobic respiration.

   Cytoskeleton: Involved in the maintenance of cell shape, facilitation of cellular movement, and the intracellular transport of organelles.

3. How might eukaryotic cells have evolved from prokaryotic cells?

According to the endosymbiotic hypothesis, eukaryotic cells began as large anaerobic organisms. Mitochondria arose when small aerobic bacteria were ingested by the larger cells. In exchange for the benefits of protection and a constant nutrient supply, the smaller cell provided its host with energy generated by a process known as **aerobic respiration.** As time passed, the bacteria lost their independence because of the transfer of several genes to the nucleus. Similarly, chloroplasts are believed to have descended from cells which were similar to modern cyanobacteria, while cilia and flagella were derived from ancient spiral prokaryotes.

4. What technologies have aided scientists in discovering how cells function?

Much of the current knowledge of biochemical processes is due directly to technological innovations. There are several technologies which have had an enormous impact on biochemistry, such as cell fractionation, the electron microscope, and autoradiography. Cell fractionation techniques allow the study of cell organelles in a relatively intact form outside of cells. The electron microscope provides a view of cellular ultrastructure that is not possible with the use of the more commonly available light microscope. Autoradiography is a technique that is used to study the intracellular location and behavior of cellular components.

General Principles

Chemical reactions do not occur randomly in the cell; there exists quite a bit of organization. This biological organization forms two major classifications of organisms:

Prokaryotic (meaning, before the nucleus)
Eukaryotic (meaning, true nucleus)

Bacteria are the best example of prokaryotes. They are single-celled organisms and perhaps the most adaptable creatures on earth. They are found almost everywhere and in extreme temperatures ranging from glaciers in Antarctica to undersea volcanoes in the Pacific Ocean. Bacteria can perform nearly any chemical reaction; from consuming oils, for instance, to producing pharmaceuticals.

Eukaryotes differ from prokaryotes in that eukaryotes have organelles.

Organelles are compartments within the cell that have specialized functions. The compartments are separated from the rest of the cell by membranes which function as barriers.

3 Water: The Medium of Life

Objectives

1. How is the molecular structure of water related to its chemical behavior?

   Water is composed of two atoms of hydrogen and one atom of oxygen. Each hydrogen atom is linked to the oxygen atom by a single covalent bond. Water molecules have a bent geometry with a bond angle of 104.5°. Because the oxygen atom is more electronegative than the hydrogen atom, the unequal electron distribution results in a bent geometry and polarity of the molecule. The chemical behavior of water is largely dependent upon its polarity and the intermolecular interactions which can occur.

2. How does non-covalent bonding affect the chemical and biological properties of water?

   There are four basic non-covalent bonding interactions which determine the capacity of water to interact with other types of molecules. These are hydrogen bonding, electrostatic interactions, van der Waal's forces, and hydrophobic interactions. These interactions are especially important because biological reactions take place in a water medium and determine the shape and function of biomolecules.

   Hydrogen bonds: One consequence of the large difference in electronegativity between hydrogen and oxygen is that the hydrogen of one water molecule is attracted to the unshared pairs of electrons of another water molecule, thereby forming a hydrogen bond. The hydrogen bond is largely responsible for the thermal properties of water.

   Electrostatic interactions: These interactions occur between oppositely charged atoms or groups. This is an important aspect because electrostatic interactions are responsible for the hydration of ions. The polar water molecules form shells of water molecules when they are attracted to the charged ions. As ions become hydrated, the attractive force between them is reduced and the charged species dissolve in the water.

   Van der Waal's forces: This is a class of weak, transient electrostatic interactions which occur between permanent and/or induced dipoles. They may be attractive or repulsive, depending on the distance between the atoms or groups involved.

Hydrophobic interactions: Hydrophobic interactions occur when small amounts of non-polar substances are observed to coalesce into droplets when mixed with water. Hydrophobic interactions have a profound effect on living cells. For example, they are responsible for the structure of membranes and the stability of proteins.

3. What is pH and how does it affect living cells?

   pH is defined as the negative logarithm of the concentration of hydrogen ions.

   The concentration of hydrogen ions affects most cellular and organismal processes. For example, the structure and function of proteins and the rates of most biochemical reactions are strongly affected by hydrogen ion concentration. Additionally, hydrogen ions play a major role in processes such as energy generation and endocytosis.

4. What is a buffer? What role do buffers play in living cells?

   A buffer is a solution which contains a weak acid and its salt, and is resistant to large pH changes upon addition of stronger acids or bases. The three most important buffers in the body are: bicarbonate, phosphate, and protein buffers. Bicarbonate controls the pH in the blood; phosphate buffer controls the pH of the intracellular fluids; and protein buffer controls the pH of the blood and many other fluids.

5. What are the colligative properties of water solutions?

   Colligative properties (vapor pressure depression, boiling point elevation, freezing point depression, and osmotic pressure) are grouped together because they depend on the number of dissolved particles in a given mass solvent rather than the identity of the particles.

General Principles

Approximately 70-80% of our body weight is water. Water is essential for life as we know it. Water has unique chemical properties, some of which allow biomolecules to function

What makes water unique?

The chemical nature of water confers some of these special properties:

A **covalent bond** is formed between two atoms when those atoms share electrons between each other. When the atoms share the electrons equally, the electron spends the same amount of time around each atom. This gives rise to a **non-polar** bond.

Some atoms are more attractive to electrons than others. This property is called **electronegativity**. The electronegativity of common biological atoms is $H \approx C < N < O$ (order of increasing electronegativity in which oxygen is the most electronegative atom of the series).

For a C-O bond, the electrons will spend more time around oxygen than carbon. When hydrogen is bonded to either nitrogen or oxygen, the electrons will be more attracted to oxygen or nitrogen.

Electrons are negatively charged, which gives rise to partial charges denoted as δ (Greek lowercase delta). The unequally shared electrons give rise to a **polar** bond.

While a particular bond can be polar, overall molecules can still be non-polar. This is because geometry also influences the polarity of a molecule.

<u>Example</u>: CO_2

$$O{=}C{=}O$$

Each C=O bond is polar, but since CO_2 is linear, the polar bond of each half cancels out the other, and the molecule CO_2 is therefore non-polar.

Since water is bent at an 105° angle, the direction of the polar bonds cannot cancel one another out. This gives rise to a **dipole**, which means that one end has a δ^- and the other has a δ^+.

The polar nature of water allows it to interact with a variety of other molecules. For example, table salt (NaCl) dissolves completely in water because of ion-dipole interactions. Alcohol dissolves in water via dipole-dipole interactions.

This gives rise to two terms:

<u>Hydrophilic:</u> meaning water-loving, such as polar and ionic molecules,

and

<u>Hydrophobic</u>: meaning water-fearing, such as non-polar molecules

Molecules can have both polar and non-polar ends; these molecules are termed **amphiphilic**. For example, salts of fatty acids are soaps. Soap was first produced by boiling animal fat with lye (NaOH). Sodium lauryl sulfate, a synthetic soap, is found in many household products such as toothpaste.

Why are soaps effective at getting rid of grease?

The hydrophobic tail interacts with the non-polar "grease" molecule. This allows the polar end of the soap to interact with water. Water is then able to completely surround the grease molecule, allowing the grease/detergent micelle to become water-soluble.

Study Tips

Important Concepts

- polarity of chemical bonds
- non-covalent bonds
- pH
- acids/bases

How to solve acid-base problems

All problems use the Henderson-Hasselbalch equation:

$$pH = pK_a + \log \frac{[\text{base}]}{[\text{acid}]}$$

The single greatest hurdle in solving acid-base problems is identifying the weak acid and its conjugate base.

Remember that an acid is a proton donor and a base is a proton acceptor; the weak acid will therefore have an extra proton when compared to its conjugate base.

Example:

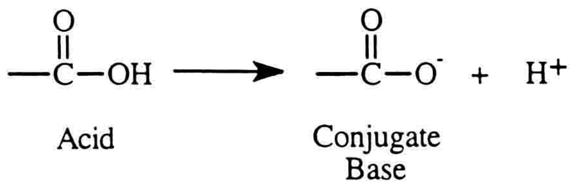
HCO_3^- acid	CO_3^{2-} conjugate base
$H_2PO_4^-$ acid	HPO_4^{2-} conjugate base

When asked, "What is the pH of...?" you will want to solve for pH. You will therefore need to have the pK_a and the [acid] and [base].

When asked, "What is the charge of...?" you will want to solve for the ratio:

$$\frac{[\text{base}]}{[\text{acid}]}$$

Remember that the acid HA, and the base A^-, will differ by **one** charge. For example, if a molecule has a carboxyl group as the weak acid,



When the ratio $\frac{[A^-]}{[HA]}$ is small, the molecule will be uncharged.

When the ratio $\frac{[A^-]}{[HA]}$ is large, the molecule will be negatively charged.

Examples:

1. What is the pH of a phosphate buffer when the $[H_2PO_4^-]$ = 10 mM and the $[HPO_4^{2-}]$ = 1 mM? The pK_a = 6.7

   First identify the acid and the conjugate base.

   $$H_2PO_4^- \longrightarrow HPO_4^{2-} + H^+$$

   Since $H_2PO_4^-$ donates a protein, it is the acid and HPO_4^{2-} is the conjugate base.

   The Henderson-Hasselbalch equation, $pH = pK_a + \log \frac{[base]}{[acid]}$ is then used to determine the pH of the buffer solution.

   $$pH = 6.7 + \log \frac{[HPO_4^{2-}]}{[H_2PO_4^-]} = 6.7 + \log \frac{1\ mM}{10\ mM} = 6.7 + \log 0.1 = 5.7$$

2. Calculate the ratio of $\frac{[HPO_4^{2-}]}{[H_2PO_4^-]}$ at pH 5.7, 6.7, and 7.7. The pK_a is 6.7.

   Again, first identify the acid and the conjugate base.

   $$H_2PO_4^- \longrightarrow HPO_4^{2-} + H^+$$

   As before, $H_2PO_4^-$ is the acid and HPO_4^{2-} is the conjugate base.

   The Henderson-Hasselbalch equation, $pH = pKa + \log \frac{[base]}{[acid]}$ is then rearranged to solve for the ratio, $\frac{[base]}{[acid]}$.

   $$\log \frac{[base]}{[acid]} = pH - pK_a$$

$$\frac{[\text{base}]}{[\text{acid}]} = 10^{(\text{pH} - \text{p}K_a)}$$

$$\text{At pH 5.7, } \frac{[\text{base}]}{[\text{acid}]} = 10^{(5.7 - 6.7)} = 10^{-1} = 0.1 \text{ or } \frac{1}{10}$$

$$\text{At pH 6.7, } \frac{[\text{base}]}{[\text{acid}]} = 10^{(6.7 - 6.7)} = 10^{0} = 1 \text{ or } \frac{1}{1}$$

$$\text{At pH 7.7, } \frac{[\text{base}]}{[\text{acid}]} = 10^{(7.7 - 6.7)} = 10^{1} = 10 \text{ or } \frac{10}{1}$$

3. What is the concentration of CO_2 in blood when the pH of blood is 7.1 and the concentration of HCO_3^- is 8 mM? The pK_a is 6.1.

First identify the acid and the conjugate base.

$$CO_2 + H_2O \longrightarrow H_2CO_3 \longrightarrow HCO_3^- + H^+$$

CO_2 is the acid and HCO_3^- is the conjugate base. Let us now rearrange the Henderson-Hasselbalch equation to solve for the concentration of acid (CO_2).

$$\text{pH} = \text{pKa} + \log \frac{[\text{base}]}{[\text{acid}]}$$

$$\log \frac{[\text{base}]}{[\text{acid}]} = \text{pH} - \text{p}K_a$$

$$\frac{[\text{base}]}{[\text{acid}]} = 10^{(\text{pH} - \text{p}K_a)}$$

$$[\text{acid}] = \frac{[\text{base}]}{10^{(\text{pH} - \text{p}K_a)}}$$

$$[CO_2] = \frac{[HCO_3^-]}{10^{(\text{pH} - \text{p}K_a)}}$$

$$[CO_2] = \frac{8 \text{ mM}}{10^{(7.1 - 6.1)}} = 0.8 \text{ mM}$$

4. What is the concentration of HCO_3^- and CO_2 at pH 7.4 when the concentration of the buffer is 25.2 mM?

From the previous example we know that CO_2 is the acid and HCO_3^- is the conjugate base, and the pK_a is 6.1.

$$\frac{[HCO_3^-]}{[CO_2]} = 10^{(pH - pK_a)} = 10^{(7.4 - 6.1)} = 10^{1.3} = 20$$

The concentration of buffer means, $[CO_2] + [HCO_3^-] = 25.2$ mM, and since the Henderson-Hasselbalch equation told us that $[HCO_3^-] = 20\ [CO_2]$

$$[CO_2] + 20\ [CO_2] = 25.2 \text{ mM}$$

$$21\ [CO_2] = 25.2 \text{ mM}$$

$$[CO_2] = 1.2 \text{ mM}$$

$$[HCO_3^-] = 25.2 \text{ mM} - 1.2 \text{ mM} = 24 \text{ mM}$$