Chapter 2 - Chemical Foundations

I. Introduction

By weight, cells are about 70% water, about 1% ions, about 6% small organic molecules (including amino acids, sugars, nucleotides), and about 23% macromolecules.
What do we mean by organic molecules? These molecules are made up of a carbon backbone with a combination of accessory hydrogen, nitrogen, phosphorous, oxygen, or sulfur atoms attached.
(C,H,N,O,P,S)
Macromolecules are composed of the small organic molecules. For example, proteins are made of amino acids, complex carbohydrates such as starch are made up of repeating sugar units, DNA and RNA are made of nucleotides, and fats or lipids are comprised of, among other things which we'll discuss, fatty acids.

II. Bonds

A. Intro to Atoms

- Atoms are comprised of a nucleus containing one or more positively charged protons and uncharged neutrons (except hydrogen), and a surrounding shell of negatively charged electrons.
- Usually, but not always, the number of electrons equals the number of protons. Atomic number is the number of protons in the nucleus; atomic mass is equal to the sum of the mass of protons and neutrons and is written as a superscript that precedes the letter abbreviation. Often the number of protons equals the number of neutrons but not always.
- Electrons move around the nucleus of an atom in clouds called orbitals. An atom is most stable when its outer most orbital is completely filled.
- The first orbital is filled when it contains two electrons, the second and third are filled when they contain eight electrons, and the fourth and fifth shells can hold 18 each. Since an unfilled shell is less stable than a filled shell, atoms with unfilled outer shells tend to interact with one another in ways so that they can either gain or lose electrons to have filled outer shells; these interactions are chemical bonds.

B. Covalent Bonds

- In a covalent bond two atoms share one or more pairs of electrons. In one covalent bond one pair is shared and in a double covalent bond, two pairs are shared. Triple bonds are relatively rare in biology.
- Covalent bonds are very stable because the energy required to break them is much greater than the thermal energy available at room or body temperature.
- Covalent bonds have characteristic geometries. Atoms can generally rotate freely around single bonds but not double bonds. Double bonds introduce a rigid planarity to molecules.
- Sometimes in covalent bonds electrons are not quite shared equally as different atoms have different abilities to attract the shared electrons. Water is an excellent example of this type of polar covalent bond.
- **All covalent N-H and O-H bonds are polar.**
- **All CH bonds are non-polar.**
- **Polar molecules are hydrophilic whereas non-polar molecules are hydrophobic.**

- One final feature of covalent bonds is the concept of asymmetry. In biological systems, we’ll discuss this in the context of an asymmetric carbon atom. A carbon atom with four dissimilar groups is said to by asymmetric, or a chiral carbon. For example, amino acids exist as either L- or D- isomers. These isomers can not be interconverted. Although the D- and L- isomers have the same chemical properties, their biological activities are distinct. We only find the L-form of amino acids in proteins.

- A similar situation exists for carbohydrates. Carbohydrates are hydrates of carbon **$(CH_2O)n$**. For glucose, n equals 6 and carbons 2, 3, 4 and 5 are asymmetric. When the hydroxyl group of carbon 2 points down, we have glucose; when it points up we have mannose. These sugars have different biological roles.
- These simple sugars and can be linked together to form polymers in condensation reactions and are referred to as polysaccharides. These linkages are made by forming bonds between the number 1 carbon on one sugar with the hydroxyl group of another. For these simple sugars the hydroxyl group of the number one is designated as alpha when it points downward and beta when it points upward. In glycogen, a large branched polymer of glucose, the glucose monomers are linked primarily by **alpha 1-4 bonds**. In plants, the primary storage form of carbohydrate is starch. **Starch** comes in both branched and unbranched forms but the glucose units are linked primarily by **alpha 1-4 bonds**. Plants also make another polymer of glucose known as **cellulose** which is a major constituent of cell walls. Cellulose is the most abundant organic molecule on earth. In cellulose, the glucose units of the unbranched polymer are linked by **beta 1-4 bonds**. The human digestive system can hydrolyze alpha 1-4 bonds but not beta 1-4 bonds.

C. Noncovalent Bonds

Non-covalent bonds are equally important in biological systems and are critical in maintaining the three dimensional structure of large molecules. Because the energy released in the formation of a **noncovalent bond is only 1-5 kcal/mol**, there is sufficient kinetic energy at room or body temp that these bonds can be broken. Sometimes these bonds are referred to as interactions.

Hydrogen Bonds

- Hydrogen bonds form between two polar molecules such as water. In the case of water molecules, the hydrogen atom of one molecule is attracted to a pair of electrons in the outer shell of an oxygen atom of an adjacent molecule. The presence of hydroxyl or amino groups makes many molecules soluble in water.

Ionic Interactions

- In ionic bonds, electrons are never shared. They are "**transferred**". Unlike covalent or hydrogen bonds, ionic bonds **do not have specific geometries**, although crystals of salts do have very regular structures that represent the most energetically favorable way of packing together positive and negative ions.

Van der Waals Interactions

- These interactions result from random fluctuations in the distribution of ions around two atoms as they approach each other. These interactions involving either transient or permanent dipoles occur in all types of molecules, polar and non-polar. Van der Waals as well as other non-covalent interactions mediate the binding of many enzymes with their substrates.

Hydrophobic Bonds.

Hydrophobic molecules have a strong tendency to interact with one another. The force that causes hydrophobic molecules or non-polar portion of molecules to associate with one another rather than to dissolve in water is referred to as a hydrophobic bond**.** Most textbooks will refer to these as **hydrophobic interactions**. Molecules that have one domain that interacts with water and one that doesn't are referred to as **amphipathic**.

III. Chemical Equilibrium

At any given time hundreds of chemical reactions are taking place in cells. The extent to which a reaction can proceed and the rate at which it actually proceeds determines which reactions take place.

A. Equilibrium Constants

- When reactants come together the rate of their reaction is determined in part by their initial concentrations. As the reaction proceeds and products form, the concentration of reactants decreases. But, as the concentration of products increases, the reactants slowly begin to reform. When the rates of the forward and reverse reactions are equal so that the concentrations of the products and reactants stop changing, the mixture is **in chemical equilibrium.**

- The equilibrium constant is the ratio of products to reactants at equilibrium and is independent of the reaction rate. At standard conditions **the Keq of a reaction is the same whether a catalyst is present or not**.

- In cells, the products of one reaction are commonly used immediately as substrates for another reaction. In this case, reactants and products are generally in **steady state** but not equilibrium.

- Many reactions involve the binding of one molecule to another by non covalent interactions, such as a protein associating with DNA or a ligand binding to a receptor. For these reactions, we often refer to K_D or **dissociation constant** which is **the inverse of Keq.** K_D is a term that we often use to describe the affinity of a ligand for a receptor. **The lower the K_D, the higher the affinity for the receptor**.

B. pH

- Protons, or hydrogen ions, and hydroxyl ions are the dissociation products of water. In pure water the concentration of each is approximately 10^{-7} molar. The concentration of hydrogen ions in solution is referred to as pH. pH is the negative log of the [H].
- Solutions with a pH greater than 7 are considered basic and less than 7 are considered acidic.
- In general any molecule or ion that tends to release a proton is called an acid, and any molecule that readily combines with a proton is called a base.
- In cells it is very important to maintain constant pH even though many acids are produced as by-products of metabolism. Cells maintain pH by having a reservoir of weak acids and weak bases that soak up extra protons or hydroxyl ions when added to solution. The overall pH of a solution will not change substantially when additional protons or hydroxyl ions are present. All biological systems contain one or more buffers.

IV. Biochemical Energetics

A. Types of Energy

Kinetic Energy - Kinetic energy is the energy of motion.

- Heat or **thermal energy** is a form of kinetic energy but cells usually maintain a constant temperature.
- **Radiant energy** is the kinetic energy of photons or waves of light. This type of energy is critical to photosynthetic organisms. Radiant energy can be converted to thermal energy. In photosynthesis, light energy is absorbed by chlorophyll and ultimately converted to energy stored in the covalent bonds of sugars.
- One form of **electrical energy** is also kinetic which includes the energy of moving electrons or charged particles.

Potential Energy - Stored Energy

- Several forms of potential energy are of biological significance. Potential energy is stored in the bonds connecting atoms in molecules. For example, cell break down glucose and capture the energy released from those bonds and harness it to do work.
- Potential energy is also stored in concentration gradients.
- Electrical potential is also a form of potential energy. This is the energy of charge separation.

B. Free Energy

- **One measure of potential energy, called free energy or G**, can be used to predict the direction of a chemical reaction. The free energy change or **delta G is the G of the products minus the G of the reactants**. Like Keq, deltaG is independent of the reaction mechanism or rate.
- **If delta G is negative, the forward reaction will proceed spontaneously.**
- **If delta G is positive, the reverse reaction will proceed spontaneously.**
- **If delta G is 0, the reaction is at equilibrium.**
- The change in free energy of a reaction is influenced by temperature, pressure, and the concentration of reactants and products. In biological systems, temperature and pressure are generally constant. The **standard free energy change** is the free energy change of a reaction at standard conditions of temperature and pressure where the initial concentration of reactants and products are all 1M. For biological reactions you will most often find the standard free energy change reported.
- Reactions that have a positive delta G requires the input of cellular chemical energy in order to proceed.

C. Oxidation - Reduction Reactions

- Many chemical reactions result in the transfer of electrons from one atom or molecule to another, which may or may not accompany the formation of new chemical bonds. **Loss of electrons is referred to as oxidation and the gain of electrons is referred to as reduction**. For any atom that is oxidized another is reduced.
- The readiness with which an atom or molecule gains an electron is its redox potential and it is measured in volts. Molecules with a **negative redox potential make good electron donors**. Molecules with **positive redox potential make good electron acceptors**.
- What is the relationship between changes in free energy and reduction potentials? In oxidation reduction reactions the total **voltage change is the sum of the reduction potential of the individual steps**. There is a formula for the conversion of delta E to delta G but I won't ask you learn that formula. What I would like you to know is that generally, reactions that have a **positive delta E will have a negative delta G** and will proceed from left to right.

D. Coupling Unfavorable Chemical Reactions with Energetically Favorable Reactions

- Many chemical reactions in cells have positive delta G and are therefore energetically unfavorable. Cells are able to carry out these reactions by coupling them to reactions with a negative delta G of larger magnitude.
- In cells, energetically unfavorable reactions are often coupled to the hydrolysis of adenosine triphosphate or **ATP**. In almost all organisms, ATP is the most important molecule for capturing and transferring free energy. The useful free energy in an ATP molecule is stored in the **phosphoanhydride bonds.**
- Cells use ATP in many cellular processes including synthesis of molecules and macromolecules, cell movement, generation of electrical gradients and transport of substances against a concentration gradient.
- Cells need a constant source of ATP, which they derive from the breakdown of certain molecules during cellular respiration. The byproducts of respiration plus energy captured from sunlight are used

to generate sugars and oxygen needed for respiration. Therefore, light energy captured in photosynthesis is the source of chemical energy for almost all cells.

E. Activation Energy

- All chemical reactions proceed through one or more transition-state intermediates whose content of free energy is greater than that of either the reactants or products. The overall reaction rate depends on the **activation energy, the difference in free energy between the transition state intermediate and the reactants.**
- **Enzymes, like other catalysts, accelerate specific reactions by decreasing the activation energy**. A particular enzyme generally only facilitates one possible transformation that its substrate can undergo.