CHAPTER

2

Chemical Level of Organization

Introduction to the Chapter

The incredibly small scale of atoms and molecules makes them difficult for many students to visualize. This is understandable since, in a sense, atomic and molecular events are unseen in daily life. Yet, physiologists and clinicians see all of the body's activities as the end result of interactions between chemicals. All thoughts, movements, and memories rely on ions interacting with protein molecules suspended in a boundless sea of fluid phospholipids. The enzymatic breakdown of sugars and fats yields the energy that powers our bodies and enables the addition of new molecules to the body during growth, development, and repair. Pharmaceutical researchers scrutinize the chemical properties of their drugs to ensure they are properly transported, processed, and recognized by our bodies once they are injected or ingested. Numerous biotechnologies and genetic tests hold great potential to diagnose or treat disorders passed down through changes in nucleotides in our DNA. Thinking like a doctor or a physiologist requires such comfort with the chemical basis of life, it is almost deceiving to separate out chemistry into its own distinct chapter. Students will find that chemistry reappears in some way in every chapter to follow. Because of that fact, many instructors take this as a chance to very briefly introduce some common terms and concepts, with much more detailed examinations of specific molecules put off until those molecules are applied to physiological processes in the following chapters. Real-world applications, diagramming exercises, and the use of larger-scale models or role-playing activities will help students gain comfort with this tiniest level of organization that is central to the work of all health scientists.

Chapter Learning Outcomes

2.1 Define an atom, and describe the properties of its subatomic particles.

2.2 Describe an atom and how atomic structure affects the mass number and atomic weight of the various chemical elements.

2.3 Explain the relationship between electrons and energy levels.

2.4 Compare the ways in which atoms combine to form molecules and compounds.

2.5 Describe the three states of matter and the importance of hydrogen bonds in liquid water.

2.6 Define metabolism and distinguish between work, kinetic energy, and potential energy.

2.7 Use chemical notation to symbolize chemical reactions.

2.8 Distinguish among the major types of chemical reactions that are important for studying physiology.

2.9 Describe the crucial role of enzymes in metabolism.

2.10 Describe four important properties of water and their significance in the body.

2.11 Explain how the chemical properties of water affect the solubility of inorganic and organic molecules.

2.12 Discuss the importance of pH and the role of buffers in body fluids.

2.13 Describe the common elements of organic compounds and how functional groups modify the properties of organic compounds.

2.14 Discuss the structures and functions of carbohydrates.

2.15 Discuss the structures and functions of lipids.

2.16 Discuss the structures and diverse functions of eicosanoids, steroids, phospholipids, and glycolipids.

2.17 Discuss protein structure and the essential functions of proteins within the body.

2.18 Explain how enzymes function within the body.

2.19 Discuss the structure and function of high-energy compounds.

2.20 Compare and contrast the structures and functions of DNA and RNA.

Teaching Strategies

1. Encouraging Student Talk

a. Show students a picture of someone doing a belly flop in a calm swimming pool (numerous such open-access pictures can be found online). Ask students to think about why this is not an ideal method for getting into a pool full of water. Instruct students to work in pairs to create a labeled diagram of the water molecules on the surface of the pool just before the belly flop. Tell students to label the names of any chemical bonds or charges in their drawing. Select a few random pairs to share/describe their diagrams, resisting the chance to immediately correct any inaccuracies in the diagrams. Numerous misconceptions (see Misconceptions section to follow) might be present in the diagrams that you can address as the topics arise during lectures on chemical annotation and molecular bonds. Have students return to this exercise after instruction, looking to see whether water molecules are appropriately drawn, covalent and hydrogen bonds are labeled, and partial charges on oxygen and hydrogen atoms are indicated.

2. Lecture Ideas & Points to Emphasize

a. In support of the crucial roles that careful observation and inference play in science, you can point out that Mendeleev, the author of the best-accepted periodic table in the 1860s, lacked a comprehensive structural model of the atom, commonplace today, but still saw and ordered the periodicities.

b. Even though a single hydrogen bond possesses only about 1/100 of the bonding energy of a covalent bond, the total energy of all the hydrogen bonds within a single molecule or between molecules can be quite significant. H bonds maintain the 3-D shape of large molecules and supramolecular ensembles such as proteins and nucleic acids. It is the H bonds that are disrupted when pH drops or temperature rises during denaturation reactions.

c. It is important to illustrate that H bonds occur between separate molecules (or distant regions of a large molecule) whose atoms are joined by covalent bonds. A board

drawing of several water molecules, with both the polar covalent bonds and the H bonds clearly labeled, will emphasize this point.

d. The information in Module 2.7 is not necessarily obvious or intuitive for students. However, chemical annotation will become an important part of the communication skills students apply throughout A&P courses. Further, students will need to understand chemical annotation for applied purposes in health science fields. The new figure in Module 2.7 translated a text-only table regarding chemical annotation into visual representations. This makes it much easier to look at the written annotations and directly compare them to the appearance of the chemicals themselves.

e. It is hard to overemphasize the significance of enzymes. In the first case, it is the first form of molecular recognition they will encounter in the course. The lock-and-key fit between enzyme and substrate molecule is what confers specificity on the catalyzed reaction. Later examples include hormone receptors, channels, carriers, pumps, 2nd messengers, cell adhesion molecules, and neurotransmission. Enzymes make life possible, exploiting a chemical trick to accelerate chemical reactions at mild temperature. Living things would not survive in the chemist's boiling cauldron!

f. When presenting the different classes of reactions, anticipate their roles in metabolism (catabolic vs. anabolic). Also, link each with an important physiological example such as dissociation/association applied to the chemistry of carbonic acid dissociation/association. This connects to buffering reactions as well.

3. Making Learning Active

a. You might perform a "jigsaw" activity on organic molecules to use peer teaching, rather than a traditional lecture, for this subject. A couple of days prior to class, randomly assign each student either carbohydrates, lipids, proteins, or nucleic acids. Instruct students to perform some research on the monomers, polymers, physiological functions, and common examples/variations for their organic molecule. To extend the content, you could also ask students to identify and describe a disease directly related to their type of molecule. On the class day, students would check in briefly with other students who had their same type of molecule and then divide into heterogeneous groups to sit with students assigned different types of molecules. Even in large classrooms, these logistics are relatively easy to arrange. Sheets of paper taped to the walls can tell students where to congregate to start class, and then heterogeneous groups can be formed by counting off students in the homogeneous groups. In the heterogeneous "jigsaw" groups, students share the information they researched and take notes on the molecules presented by their peers. The instructor can then administer some brief discussion/quiz questions to enforce student accountability for learning the material and address any misconceptions that arose.

4. Analogies

a. Anthropomorphize molecules by describing them as both "greedy" and "lazy." They want their outer energy level complete and will look around for someone else's excess electrons. However, they are lazy; they won't take on more than half the number of electrons required to fill the level. In those cases, they would just as soon give up the electrons in the outer energy level but will be left with one less energy level. A few molecules are lucky enough to come equipped with completed outer energy levels, and so can be standoffish. The noble gases do not interact with anyone!

Likewise, if atoms can't agree on who is going to give up an electron to make an ionic bond, they may form even stronger covalent bonds by simply sharing the electron in their outer shells. Some atoms express electronegativity when in a compound. This means that bonding electrons spend more time in their neighborhood, conferring a par-

tial negative on them. This induces a corresponding electropositivity on other atoms within a compound. "Hydrogen bonds" form between the partly charged oxygen atom and a hydrogen atom of two neighboring water molecules and confer many of water's unusual properties.

b. Compare the primary structure of a protein to a toy train made up of many types of cars (amino acids). When hooking the cars together, there is a definite front and back, just like the C- and N-terminus of a polypeptide chain. The chain of cars may be made as long as you wish and of very different forms and functions by assembling boxcars, passenger cars, club cars, baggage cars, tank cars, and so on. The hydrolytic digestive enzymes can be analogized to railroad workers that separate the cars at their couplings, thus making the cars available to form new trains.

c. Enzymes will work at their optimum rate as long as there is plenty of substrate and other conditions are favorable. Think of a roofer fixing a roof. He pounds in nails to hold down shingles (combining two substrates to produce a product), and can use the same hammer again and again (enzymes are catalysts not consumed in the reaction). This process can continue as long as there are nails and shingles and as long as the environmental conditions on the roof don't become so harsh as to harm the roofer (denaturing).

d. Compare one strand of DNA to a spiral staircase: The alternating sugar and phosphate groups make up the helical supports, while the bases are analogous to the steps. Of course, DNA is made of two antiparallel helices, which would be a very confusing stairway!

e. Enzymes can be thought to work like helpers getting a car from down in one valley, over the hill, and down into a lower valley. The enzyme "lowers the hill," making it easier to get from one side to the other with much less kinetic (heat) energy. Enzymes don't change where you start or where you finish but just make it easier (and thus faster) to get over the hill. Refer to the artwork in Module 2.9 during this analogy.

5. Demonstrations

a. Compare the different levels of protein structure with ribbon used to wrap a package. A ribbon can be stretched out straight (primary), coiled in a spiral (secondary), crimped (secondary), or stripped with a scissors so that it develops many overlapping curls (tertiary). You can even bunch several of the curly ribbons together to make a wreath (quaternary).

b. The instructor can easily use student role-players to demonstrate the components of atoms and the interactions between atoms to form bonds. Students can be selected randomly and given roles such as electron, hydrogen nucleus, oxygen nucleus, and so forth. The roles can be made clear by providing students with sheets of paper showing their roles and electrical charges in a large font size. Using these role-players, the instructor can have students hold hands or link arms to demonstrate the formation of atoms and ionic, covalent, and hydrogen bonds (e.g., showing how the oxygen atom in a water molecule is "greedy" with the electrons—holding them close and leaving the hydrogen atoms relatively positive). The exercise can be simplified by only modeling reactive electrons in the atoms.

6. Applications

a. Consider bringing up free radicals when discussing the roles of electrons and reactivity. Mention the strong evidence that eating plentiful amounts of fruits and vegetables high in antioxidants (and thus, presumably better able to quench free radicals) protects against cancer, heart disease, and possibly other grave illnesses. Oddly, little benefit, and sometimes harm, results when the antioxidant nutrients are consumed in pure form, away from the foods in which they naturally occur.

b. Explain the role of cholesterol, both as a membrane component and as starting material for steroid hormones.

c. Explain the structural and functional roles of phospholipids and glycolipids. You can use the diagram in Module 2.16 to anticipate the phospholipid bilayer by asking the students to imagine what would result if a spherical micelle were flattened.

d. Most students have probably heard of "transfats," and have read nutritional information about saturated vs. unsaturated fats in food products. This provides an excellent opportunity to discuss the chemical differences between those molecules, their sources, and their uses in the body.

e. Solutions are very important in biology and medicine. Be sure students are clear about how a solution forms. Make sure they understand which is the solute and which is the solvent. The cell cytoplasm and the blood plasma are good examples of complex biological solutions. Use some general examples of pH balance or imbalance to show the special importance of hydrogen and hydroxide ions in the body.

f. Issues of polarity and water solubility are highly relevant to pharmaceutical drug makers. As will become clearer when cell membranes are studied in the next chapter, large polar molecules often require special techniques to get in and out of cells. Hence, drugs made mostly of large polar molecules may have difficulty getting to their sites of action. On the other hand, drugs composed of hydrophobic molecules tend to easily gain access to even those places heavily protected by membrane layers, like the nervous systems, and can also sometimes lead to dependency. Take time to ensure that students understand the nature and implications of polarity, so they can begin to apply those concepts when studying cell membrane physiology.

7. Common Student Misconceptions & Problems

a. Even if students have had an introductory chemistry course in the past, it is not unusual for students to struggle with chemical notation. Surprisingly, many students will draw a water (H_2O) molecule with two oxygen atoms and one hydrogen atom, with the idea that the "2" refers to "two Os." You may need to provide students with some practice by showing a number of sample molecule names/symbols and asking them how many of each type of atom are present.

b. Students frequently consider any covalent bond involving a hydrogen atom to be a "hydrogen bond." Create opportunities to confront students directly with this misconception. Point to covalent bonds involving hydrogen atoms and ask students whether you're pointing to a hydrogen bond. If not, why? If possible, have individual students create drawings to practice their annotation of covalent vs. hydrogen bonds (see Encouraging Student Talk section). Remind students how scientists use solid lines for electron-sharing covalent bonds, and dashed or dotted lines for the weaker attractions of hydrogen bonds.

c. The subject of acids vs. bases vs. salts is often difficult for students. Try to provide plenty of applied examples of each, so that students see the similarities and differences between those substances when dissolved in water. Students generally know that acidity relates to pH, but they frequently guess that more acidic solutions have a higher pH. Contrary to what students might guess, the lower the pH value, the higher the concentration of hydrogen ions. Other students may confuse pH with an actual substance found in water (e.g., "This solution has more pH."). Demonstrate that each integer change in pH value represents a tenfold change in the concentration of hydrogen ions. If the blood pH is 7.3, although an alkaline pH, it is in fact more acidic than the normal pH of blood (7.35–7.45). Hydrogen ions affect the pH only if they are in solution. A buffer acts like an ion sponge, binding or releasing hydrogen ions, and so limits changes in pH if hydrogen ions are added or removed from solution.

d. Students might confuse the very similar-sounding chemical names for "nucleic acids" and "amino acids." You might address this directly by asking students if they agree or disagree with the statement, "Proteins are made up of chains of nucleic acids." While they should certainly disagree with this statement, it could also lead to a conversation about the ways nucleic acids do influence the structures of proteins.

e. Anticipate the possible confusion between the alpha helix in the secondary structure of proteins and the double helix of the two complementary antiparallel strands in DNA.

f. Clarify that "cholesterol" is not merely a "bad" thing but is actually an important body chemical. It is a component of many cell membranes, plasma lipoproteins, and the source of steroid hormones. Only certain cholesterol compounds in an unbalanced state promote cardiovascular disease.

8. Terminology Aids

a. For mnemonics for cation vs. anion (that is, positive ion vs. negative ion), let the "t" in cation remind you of a "+": ca+ion. Also, let ANion remind you of A Negative ion.

b. To distinguish hydrophilic from hydrophobic, remember that "phobia" is a fear, in this case, molecules that "fear" or "dislike" water. Also, hydrophilic ends with "lic," which resembles "like"; that is, water-liking molecules.

c. Regarding charged atoms and molecules, remind students that "opposites attract" (i.e., positively charged ions will be attracted to negatively charged ions). However, this rule does not apply when comparing hydrophobic and hydrophilic substances. Hydrophobic and hydrophilic substances, which could seem like another type of "opposite," do not mix well together. That situation can be compared to "oil and water," which students know do not mix.

d. Describe to students that carbohydrates are literally "hydrated water" or "carbo-" + "-hydrate"; that is, their chemical formula is an integral number of "C–H_2O". Thus glucose, galactose, and fructose are all $C_6H_{12}O_6$; that is, 6 x C•H_2O. Disaccharides, of any class, are all $C_{12}H_{22}O_{11}$.

9. Incorporating Diversity & the Human Side of A&P

a. Marie Maynard Daly was a biochemist who performed research on the roles of nucleic acids, proteins, and cholesterol in the human body. She was also the first African American woman in the United States to earn a PhD in chemistry, which she received in 1947. Her father loved science and aspired to be a chemist, but was forced to drop out of college for financial reasons. This inspired Marie Daly to persist in the sciences and fulfill her father's dream. Marie Daly's work and personal story could help to introduce the chapter or frame the content in Section 4.

References/Additional Information:

http://www.chemheritage.org/discover/online-resources/chemistry-in-history/themes/biomolecules/proteins-and-sugars/daly.aspx

Additional Chapter Integration Scenario

In 1982, Stanley Prusiner, a biomedical researcher at the University of California–San Francisco, dropped a bombshell by proposing in a research paper that proteins can cause disease. Dr. Prusiner was initially skeptical of his own results, as his initial hypotheses revolved around a new type of virus—not a protein—as the cause of the neurological disease he studied. The disease, called scrapie, is similar to mad cow disease and its equivalent in humans, Creutzfeldt–Jakob disease. These diseases are not curable and result in death of cells

in the brain. Dr. Prusiner's proposition was so controversial, since most biologists believed *all* pathogens used DNA or RNA, not protein, as the basis for reproducing and spreading.

Though Dr. Prusiner received intense criticism and personal attacks, his lab eventually isolated the protein that nearly all biologists now agree is the causative agent of scrapie and other similar brain diseases. The characterization of this protein, called a prion, resulted in Dr. Prusiner being awarded the Nobel Prize in medicine. Prions cause disease due to their misfolded structures. Inside the body, prions create abnormal clumps in the brain characterized by pleated sheets. Since infectious prions may be transmitted by food, careful regulations have been put in place to make sure the nervous systems of cows and other livestock are not used for food. Infectious prions may also be sterilized in tissue through protein hydrolysis and the application of strong acids or bases.

Questions

1. Describe the chemical makeup of prions: What types of monomers are found in a prion? What level of protein structure is described by the pleated sheets that prions form? What types of chemical bonds form the "backbone" of the prion vs. the folding pattern of the prion?
2. Propose chemical explanations for how the sterilization techniques might neutralize infectious prions. For example, how would hydrolysis affect the chemical bonds of the prion? How would this compare to the application of acids or bases?
3. What other types of sterilization techniques might you suggest for eliminating harmful prions?

Suggested Answers

1. Prions are proteins made of amino acid monomers. Pleated sheets are a type of secondary structure, and the entire three-dimensional shape of the prion would result from its tertiary structure. Covalent bonds (peptide bonds) link the amino acids in the backbone of the prion, and hydrogen bonds are largely responsible for the folding pattern.
2. Strong acids and bases might tug at the hydrogen bonds of the prion, which would disrupt its harmful shape. Hydrolysis would break the peptide bonds in the prion backbone, while using up a molecule of water.
3. Heat is another way to denature proteins. Similar to acids/bases, heat can disrupt hydrogen bonds, changing the protein shape.