

Chemical Foundations of Physiology I: Chemical Energy and Intermolecular Forces

1.4

Learning Objectives

- List the chemical elements that make up the organic part of the body
- List the major chemical elements found as electrolytes in the body
- List the chemical elements found in trace quantities and used as cofactors for enzymes
- Explain why single CC bonds rotate easily whereas double CC bonds do not
- Define and give examples of structural isomerism, geometric isomerism, and optical isomerism
- Write correct estimates of bond length and energy (within a factor of 2) for covalent bonds
- Define electronegativity
- Describe what is meant by a polar bond
- Distinguish between covalent and ionic bonds
- Define dipole moment and be able to calculate the energy of dipole–dipole interactions
- Describe the hydrogen bond and recognize its typical energy
- Describe what is meant by London dispersion forces
- Draw the Lennard-Jones Potential and label the axes

ATOMS CONTAIN DISTRIBUTED ELECTRICAL CHARGES

In ordinary chemical reactions, atoms are the fundamental particles. The word *atom* derives from the Greek *atomos*, which means *indivisible*. The atoms themselves are composed of simpler subatomic particles, the **neutrons**, **protons**, and **electrons**. These particles are characterized by their rest mass and electrical charge, as shown in [Table 1.4.1](#).

Ernest Rutherford showed that all of the positive charges in an atom are concentrated within a very small volume, called the **nucleus**, and was awarded the 1908 Nobel Prize in Chemistry for the work. The nucleus has dimensions on the order of 10^{-15} m! This requires some new thinking: if positive charges repel each other according to Coulomb's law, how can they be concentrated in the nucleus? The answer is that there are other fundamental forces at work here, the strong nuclear force and weak nuclear force, that have effects

only over very short distances ($<10^{-14}$ m) and account for the stability of atomic nuclei.

Each atom has a definite number of neutrons, protons, and electrons. The number of protons in the nucleus is called the **atomic number**, *Z*, and this number defines the chemical element that describes the atom. In a neutral atom, the number of electrons is equal to *Z*, and these orbit the nucleus. The behavior of the electrons defines the chemical reactivities of the elements, and the concentrated positive charge of the nucleus, in turn, determines the behavior of the surrounding electrons.

ELECTRON ORBITALS HAVE SPECIFIC, QUANTIZED ENERGIES

Although we refer to electrons as *particles*, in fact they have wave-like characteristics such as constructive and destructive interference. The structure of the atom cannot be explained using classical physics. Instead, it requires quantum mechanics. Quantum mechanics posits that the "orbit" of electrons around the nucleus is described by a wave function, which has been interpreted as being related to the probability of finding the electron in some volume. The wave function has quantum numbers in that it allows electron orbitals to have only specific energy levels, and transitions between them can occur only when the exchange of energy is exactly equal to the difference in the two energy levels. A set of quantum numbers uniquely describes the energy state of each individual electron in an atom. One quantum number describes the electron "shell," a second describes the "orbital" within that shell, and a third describes the spin of the electron. The Pauli exclusion principle states that no two electrons can share the same set of quantum numbers within an atom. These orbitals are generally described as "clouds," indicating the distributed nature of the orbital electrons.

TABLE 1.4.1 Mass and Charge of Subatomic Particles

Particle	Rest Mass (g)	Electrical Charge (C)
Neutron	1.6747×10^{-24}	0
Proton	1.6726×10^{-24}	$+1.602176 \times 10^{-19}$
Electron	9.132×10^{-28}	$-1.602176 \times 10^{-19}$

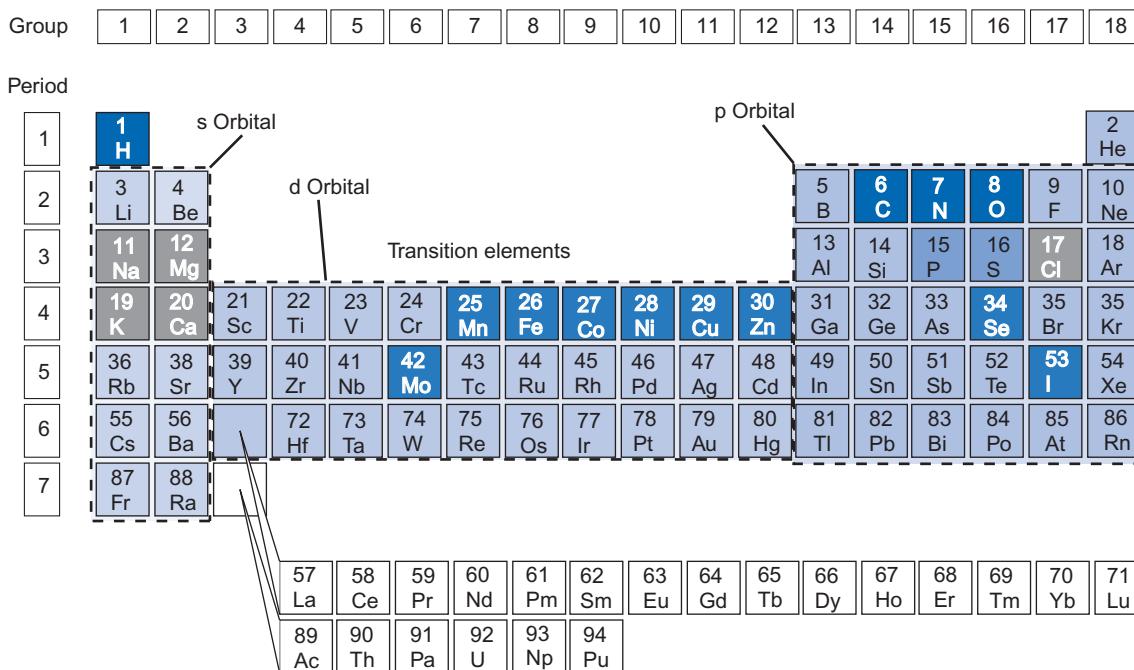


FIGURE 1.4.1 Periodic table of the elements. Each element is distinguished by the atomic number, the number of protons in the nucleus of each atom. Each chemical element is symbolized by a one or two letter abbreviation, as indicated in the figure. Some elements have special biological significance. C, H, O, and N (carbon, hydrogen, oxygen, and nitrogen, respectively) form the basic organic structures of the body. Phosphorus and sulfur (P and S, respectively) are less common parts of the organic substance. Sodium (Na), potassium (K), magnesium (Mg), calcium (Ca), and chlorine (Cl) highlighted in gray make up the electrolytes of the body fluids and are necessary in large amounts. Other elements, particularly transition elements, bind to organic structures and enable their activities. These are required in trace amounts and include iron (Fe), manganese (Mn), cobalt (Co), nickel (Ni), copper, (Cu), zinc (Zn), selenium (Se), molybdenum (Mo), and iodine (I).

HUMAN LIFE REQUIRES RELATIVELY FEW OF THE CHEMICAL ELEMENTS

As noted above, each chemical element consists of atoms whose nuclei contain a definite number of protons and some number of neutrons, which typically is about the same as the number of protons, and an equal number of electrons distributed among the atomic orbitals. There are 94 naturally occurring elements, but relatively few of these are essential to human life, as illustrated in Figure 1.4.1.

ATOMIC ORBITALS EXPLAIN THE PERIODICITY OF CHEMICAL REACTIVITIES

There are eight main “shells,” referring to the principal quantum number, $n = (1, 2, 3, 4, 5, 6, 7, 8)$ that describes atomic orbitals. There are four major subshells: s, p, d, and f, whose names derive from spectroscopic descriptions of *sharp*, *principal*, *diffuse*, and *fundamental*. These orbitals are described by the azimuthal quantum number, $l = (0, 1, 2, 3)$ for (s,p,d,f), respectively. Each subshell has a structure and a capacity for electrons that is described by the magnetic quantum number, m , and the spin quantum number, s . The s subshell is spherically symmetrical and holds only 2 electrons; each set of p orbitals holds 6 electrons, the d orbitals hold 10, and the f orbitals hold 14. The sequential filling of these

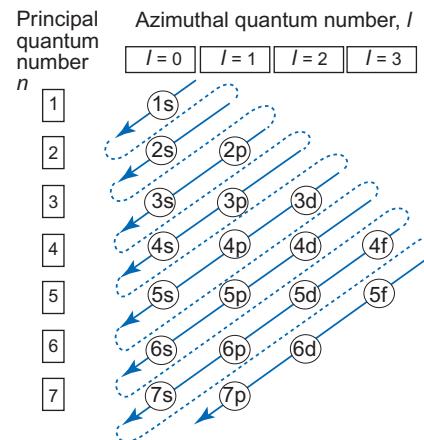


FIGURE 1.4.2 Order of filling of atomic orbitals. Electronic orbits are characterized by a principal quantum number that determines the main shell, an azimuthal quantum number that determines the subshell, a magnetic quantum number that determines the orbital, and the spin quantum number that determines the spin of the electron. There are four subshells: s, p, d, and f. These have 1, 3, 5, and 7 orbitals that each can hold up to two electrons of opposite spin. The order of filling with increasing number of electrons follows the blue diagonal arrows in the diagram: 1s fills first, followed by 2s and 2p; next is 3s followed by 3p and 3s, followed by 3d, 4p, and 4s; next is 4d, 5p, and 6s; then 4f, 5d, 6p, and 7s.

orbitals accounts for the periodic chemical behavior of the elements with their atomic number. This order of filling is shown in Figure 1.4.2. Each subshell (s, p, d, f) is typically filled with the requisite number of electrons

before filling the remaining subshells. Each electron has a spin quantum number, s, that is represented as "up" or "down." The orbitals in the subshells are typically filled singly with electrons of parallel spin before double occupancy begins. This is the so-called "bus seat rule," analogous to the filling of a bus where double seats tend to fill with single individuals before double occupancy occurs.

Full orbitals are inherently stable, because they have low energy, and atoms having full orbitals are chemically unreactive. These correspond to the noble gases, helium (He), neon (Ne), argon (Ar), krypton (Kr), xenon (Xe), and radon (Rn). The electronic structure of some of these stable atoms is shown in Figure 1.4.3. All of the other elements can react with other atoms, in order to become more stable by attempting to fill their orbitals. They do this by sharing electrons, a process that constitutes chemical bonding. This sharing can be equal or very unequal, corresponding to the extremes of covalent bonding and ionic bonding.

ATOMS BIND TOGETHER IN DEFINITE PROPORTIONS TO FORM MOLECULES

Two or more elements can combine to form a compound, and the resulting character of the compound

is entirely different from the two elements themselves. A classic example is water. Two volumes of hydrogen gas will combine with one volume of oxygen gas to produce water, which at the same temperature is a liquid and behaves altogether differently from either the hydrogen or oxygen gas. Such combinations of elements are called **compounds**, and the fundamental unit of them is the **molecule**. Molecules consist of atoms that are bonded together through the sharing of electrons in their outer atomic orbitals. The electrostatic shielding and energy involved in the orbital electrons overcome the repulsive forces between the positively charged nuclei. The resulting molecule is generally more stable than the starting materials. In order to break apart the molecule, energy must be supplied. This energy is called the **bond energy**, and its magnitude depends on the compound.

COMPOUNDS HAVE CHARACTERISTIC GEOMETRIES AND SURFACES

Carbon has an atomic number of 6. Its electronic structure is $1s^2 2s^2 2p^2$: there are two electrons in the 1s orbital, two in the 2s orbital, and two in the 2p orbitals, as shown in Figure 1.4.4. Carbon can achieve the stable neon configuration of $1s^2 2s^2 2p^6$ by sharing electrons with four hydrogen atoms. The resulting

Helium (2) $1s^2$	Neon (10) $1s^2 2s^2 2p^6$	Argon (18) $1s^2 2s^2 2p^6 3s^2 3p^6$	Krypton (36) $1s^2 2s^2 2p^6 3s^2 3p^6 4s^2 3d^10 4p^6$	Xenon (54) $1s^2 2s^2 2p^6 3s^2 3p^6 4s^2 3d^10 4p^6 5s^2 4d^{10} 5p^6$
s	s p	s p d	s p d	s p d
1 ↑↓	1 ↑↓	1 ↑↓	1 ↑↓	1 ↑↓
2	2 ↑↓↑↑↑↑	2 ↑↓↑↑↑↑	2 ↑↓↑↑↑↑	2 ↑↓↑↑↑↑
3	3	3 ↑↓↑↑↑↑	3 ↑↓↑↑↑↑	3 ↑↓↑↑↑↑
4	4	4	4 ↑↓↑↑↑↑	4 ↑↓↑↑↑↑
				5 ↑↓↑↑↑↑
				6

FIGURE 1.4.3 Electronic structure of the inert gases. These inert gases are chemically unreactive because their orbitals are already filled. Helium, with $n = 2$ protons in its nucleus, fills the 1s orbital with 2 electrons of opposite spin. Spin is indicated in the drawing by an arrow pointed upward or downward. Neon ($n = 10$) fills the 2s and 2p orbitals with a total of 8 electrons. Each orbital in the subshells carries at most two electrons. The order of filling of the orbitals corresponds to that shown in Figure 1.4.2.

Carbon (6) $1s^2 2s^2 2p^2$
s p
1 ↑↓
2 ↑↓↓↓
3
4

FIGURE 1.4.4 Electronic structure of carbon. Carbon has 6 protons in its nucleus and 6 electrons that occupy the orbitals, 2 in the 1s orbital, 2 in the 2s orbital, and 2 more in the p orbitals. Only two of the three p orbitals are occupied by electrons. Carbon requires four more electrons to reach the stable configuration of Neon.

compound is methane, written as CH₄ to convey the definite and fixed proportion of 1C for 4H atoms. All molecules in methane have this compositional **stoichiometry**. The close approach of the H nuclei and C nucleus alters the electronic structure of both the carbon and hydrogen. In molecular orbital theory, both the 2s and 2p orbitals of carbon participate in bonding by forming four hybrid molecular orbitals, termed sp³, meaning the hybrid of the 2s orbital with 3p orbitals (see Figure 1.4.5). The angle between the neighboring CH bonds is 109°28'. The shape-filling model of methane shows the edges of the carbon and hydrogen atoms as if they were hard spheres, but really the orbitals do not have such definite boundaries. The electron orbitals define these soft edges. All compounds are defined by the relative locations of their atomic nuclei and the three-dimensional distribution of their electronic charges. These make up a three-dimensional surface that can interact with other three-dimensional surfaces.

The bedrock of all of chemistry and physiology is the interaction of these surfaces.

SINGLE CC BONDS CAN FREELY ROTATE

Carbon can also form bonds with other carbon atoms. Ethane has the compositional stoichiometry of C₂H₆ (see Figure 1.4.6). It is two methane molecules in which two CH bonds are replaced by a single CC bond. In the single CC bond, the sp³ hybrid orbitals overlap along their axis and form a circularly symmetric sigma bond. There is relatively free rotation around the axis of symmetry of this single bond, with three dips of about 12 kJ mol⁻¹ for each rotation when the H atom from one methyl group aligns with the space between the H atoms of the opposite methyl group. These ideas are shown schematically in Figure 1.4.6.

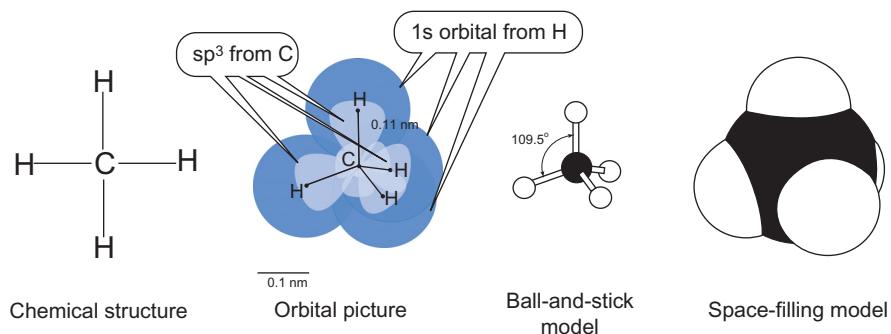


FIGURE 1.4.5 Structure of methane. The compositional stoichiometry of methane is CH₄—one carbon atom bonded to four hydrogen atoms. It arises from the sharing of the 1s electron of H with the 2s and 2p electrons of carbon. The bonding arises from overlap of the 1s H electron with electrons with hybrid C orbitals called sp³—formed from one s orbital and three p orbitals.

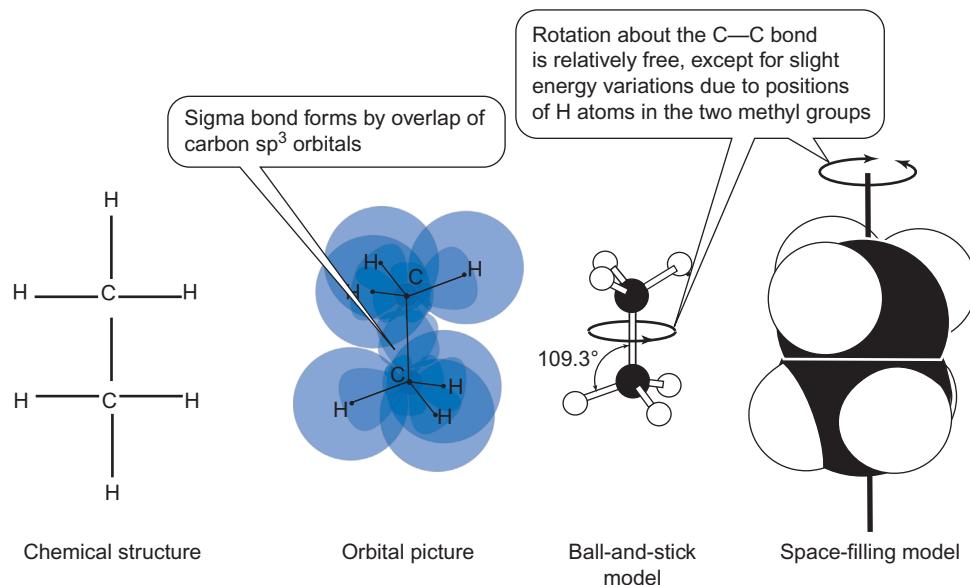


FIGURE 1.4.6 Structure of ethane. Here 1C atom binds to another C and 3H atoms. The CC bond forms by overlap of the sp³ orbital along its axis to form a sigma bond that has circular symmetry. This bond can rotate about its axis, with some resulting configurations having just a little more stability than others. The most stable arrangement is shown, with the H atom of one methyl group aligned with the space between the H atoms in the opposing methyl group.

DOUBLE CC BONDS PROHIBIT FREE ROTATION

Carbon can form double bonds by altering its molecular orbitals. Ethylene is ethane in which another pair of CH bonds converts to a second CC bond (see Figure 1.4.7). Instead of combining $2s^2$ with $2px^1$, $2py^0$, and $2pz^1$ to form the $4sp^3$ orbitals, it can arrange the electrons in a planar trigonal geometry by hybridizing the $2s^2$ with the $2px^1$ and $2py^0$ orbitals to form three sp^2 orbitals with one electron each, and another pz^1 orbital that can form a second bond, a pi bond, out of the plane of the sp^2 orbitals. This bond resists twisting and a 90° twist breaks the overlap of the p orbitals, and hence breaks the second bond. Thus double bonds such as that in ethylene, shown in Figure 1.4.7, produce a somewhat rigid plane in any molecule in which they are found.

CHEMICAL BONDS HAVE BOND ENERGIES, BOND LENGTHS, AND BOND ANGLES

So far we have discussed CH bonds, CC single bonds, and CC double bonds. There are a host of other kinds

of bonds that connect atoms together to make molecules, and each of these bonds has definite average bond lengths, bond angles, and bond energies. Table 1.4.2 summarizes approximate values for some of these bonds. These are approximate because atoms bound to other parts of the molecule can influence the molecular orbitals some distance away, thereby altering the angle, or length, or energy of any particular bond.

BOND ENERGY IS EXPRESSED AS ENTHALPY CHANGES

Earlier we wrote the conservation of energy theorem as

$$[1.3.6] \quad dE = dq - dW$$

where dE was the incremental change in the energy of a system, dq is defined as the heat absorbed *by* the system from its surroundings, and dW is defined as the work performed *by* the system on its surroundings. The total energy content of the system, E , does not depend on the path taken to get to its configuration. It is a state variable. If we conduct a change of state at constant pressure, then Eqn [1.3.6] can be written as

$$[1.4.1] \quad dE = dq_p - P dV$$

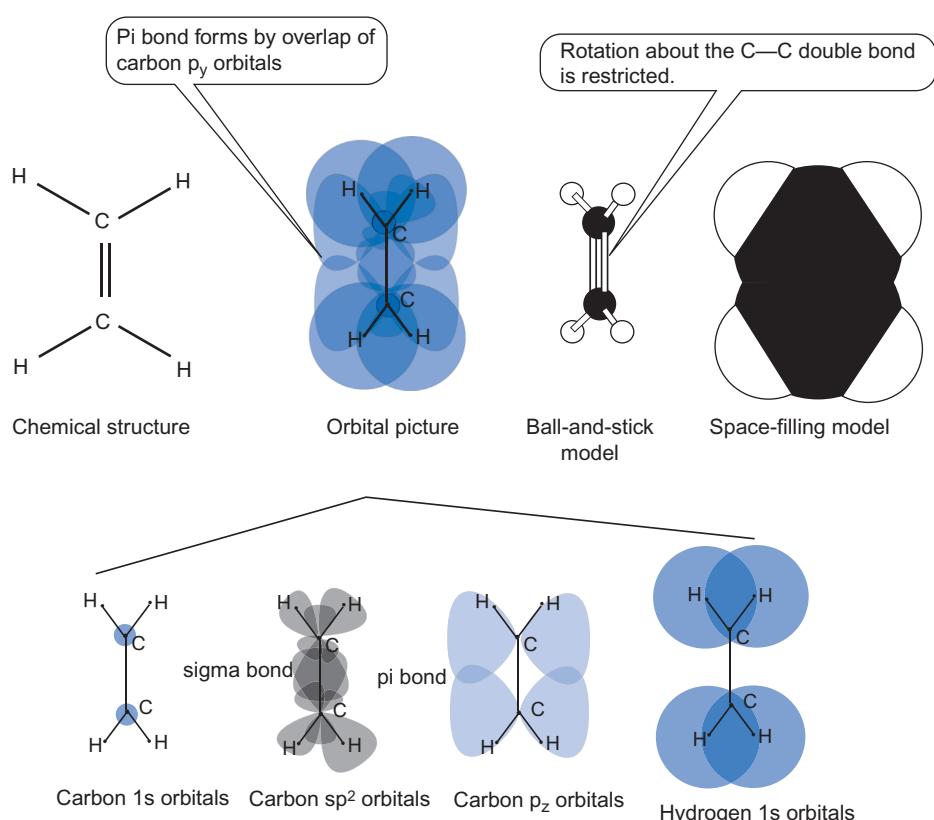


FIGURE 1.4.7 Structure of ethylene. The double CC bond is stronger than the single bond (it requires more energy to break) and locks the C atoms and all of the bonded groups into a single plane. This plane resists twisting because twist along the CC axis rotates the p orbitals away from overlap, breaking the pi bond. The space-filling model is not oriented the same way as the ball-and-stick model; the plane of the space-filling model is parallel to the plane of the paper. The lower part of the diagram shows the component orbitals. The 1s orbitals from carbon do not participate in molecular bonding. The sp^2 orbitals bond to the H 1s orbitals through sigma bonds and form the C–C sigma bond. The p_z orbitals perpendicular to the plane of the sp^2 orbitals form a second C–C bond, a pi bond.

TABLE 1.4.2 Typical Bond Length and Bond Energy for Some Bonds Important in Physiology

Bond	Length (pm)	Energy (kJ mol ⁻¹)	Bond	Length (pm)	Energy (kJ mol ⁻¹)	Bond	Length (pm)	Energy (kJ mol ⁻¹)
CC	154	346	CC	134	602	CC	120	835
CN	147	308						
CO	143	360	CO	120	799			
CS	182	272						
HC	109	411						
HN	101	386						
HO	96	459						
HvS	134	363						
PO	163	335	PO	150	544			
SS	205	226						

Bond lengths are given in pm ($=10^{-12}$ m) and bond energy is reported in kilojoule per mole (kJ mol⁻¹). Many tables of bond energies report them in kcal mol⁻¹. The calorie is defined as the amount of heat energy required to raise the temperature of 1 g of water from 14.5°C to 15.5°C. The calorie is readily converted to the joule using the conversion factor 1 cal = 4.184 J. Calorie derives from the Latin *calor*, meaning to heat.

if the only work is pressure–volume work. Note here that

$$[1.4.2] \quad F dx = \frac{F}{A} A dx = P dV$$

clarifies that a pressure moving a volume has the same work units as a force moving through a distance. Integrating Eqn [1.4.1] between two states, we obtain

$$\begin{aligned} \int_i^f dE &= \int_i^f dq_p - \int_{V_i}^{V_f} P dV \\ E_f - E_i &= q_p - P(V_f - V_i) \\ [1.4.3] \quad (E_f + PV_f) - (E_i + PV_i) &= q_p \\ H_f - H_i &= q_p \\ \Delta H &= q_p \end{aligned}$$

Here we make the definition

$$[1.4.4] \quad H = E + PV$$

where H is the **enthalpy**. Since E , P , and V are all state variables, depending only on the state and not the path taken to that state, enthalpy is also a state variable. The **bond energies** are differences in the enthalpy of formation of the products and reactants in any chemical reaction.

THE MULTIPLICITY OF CX BONDS PRODUCES ISOMERISM

Some chemical compounds with identical compositional stoichiometry behave differently. Their different behaviors can be obvious and large, or quite subtle, depending on how the compounds differ. These compounds with identical composition differ in the way the atoms are arranged in the molecule. They are called **isomers**, meaning *same weight*. There are three major classes of isomers, structural, geometric, and optical,

which are described below and shown schematically in Figures 1.4.8–1.4.10:

- **Structural isomers** differ in the connectivity of the atoms in the molecule.
- **Stereoisomers** have identical connectivity but the atoms are arranged differently in space. These consist of two classes:
 - **Geometric isomers**, involving a double CC bond that does not allow free rotation
 - **Optical isomers**, existing in two types.
- **Enantiomers** are mirror images of each other. They have identical physical characteristics such as melting point and density but are not superimposable. This requires an asymmetric carbon atom in which four nonidentical groups are bonded. They differ in their ability to rotate the plane of polarized light.
- **Diastereomers** are optical isomers that are not enantiomers. They typically differ in the spatial distribution about one or more asymmetric carbons, while not being mirror images.

UNEQUAL SHARING MAKES POLAR COVALENT BONDS

The electrons that are shared in covalent bonds distribute themselves according to the charges on the nuclei within the molecule and the other electrons in the unshared orbitals that shield that charge from the electron. In almost all cases, the electrons are not shared equally but tend to spend more time near one or the other of the nuclei involved in the bond. The ability of an atom in a molecule to attract shared electrons is called its **electronegativity**. It generally increases going up the periodic table and going to the right, so that F has the highest electronegativity and Fr has the lowest. The electronegativity of some common elements is shown in Table 1.4.3 in arbitrary *Pauling units* scaled to F at 4.0.

Structural isomerism: same formula, different connectivity

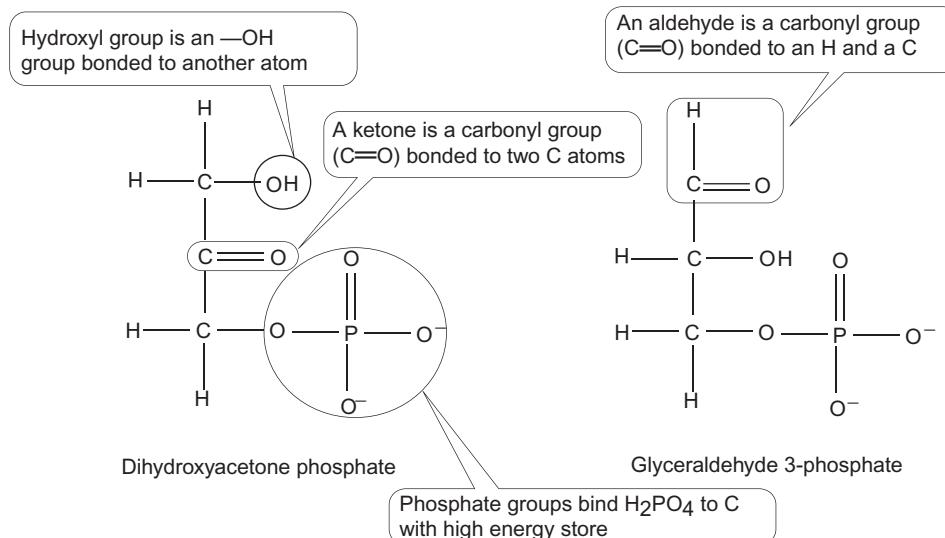


FIGURE 1.4.8 An example of structural isomerism. Both glyceraldehyde 3-phosphate and dihydroxyacetone phosphate contain the same number of each type of atom. However, the connectivity of the atoms differs. Glyceraldehyde 3-phosphate contains an aldehyde group, which is defined as a C atom with a double bond to O and a single bond to H. Dihydroxyacetone phosphate contains a ketone group, which is a C atom with a double bond to O and the remaining bonds to C atoms. Conversion of the two chemicals requires breaking and reforming chemical bonds.

Geometric isomerism: same connectivity but different spatial distribution

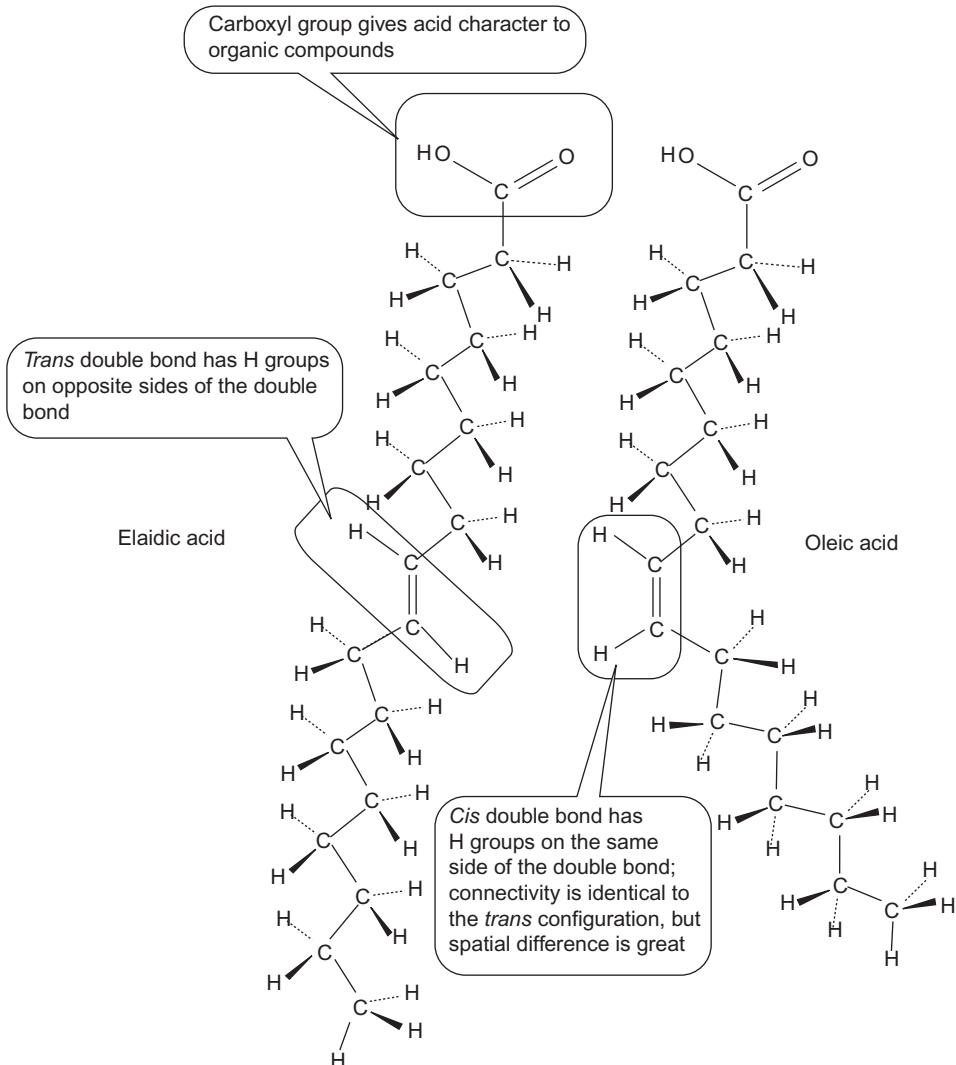


FIGURE 1.4.9 An example of geometric isomerism. Both elaidic acid and oleic acid belong to a class of organic compounds called fatty acids, characterized by a carboxyl group at one end of an unbranched hydrocarbon chain. In these molecules, the chains are 18 carbons long. Both have one double bond beginning at the ninth carbon from the carboxyl end or the ninth carbon from the terminal methyl end. The spatial arrangement of the carbon chain and hydrogens at the double bond can be achieved in two ways: either *cis* or *trans*. In the *cis* arrangement, found in oleic acid, the two hydrogens are on the same side of the double bond, meaning that the hydrocarbon chain toward the carboxyl end and the hydrocarbon chain toward the methyl end are also on the same side, opposite to the hydrogens. This produces a kink in the hydrocarbon chain. In the *trans* arrangement, in the case of elaidic acid, the two H atoms on the doubly bonded C atoms are on opposite sides of the double bond. This has the effect of keeping the hydrocarbon chain straighter. Both compounds have the same composition but different physical properties due to this geometric isomerism.

Optical isomerism: same connectivity, not superimposable

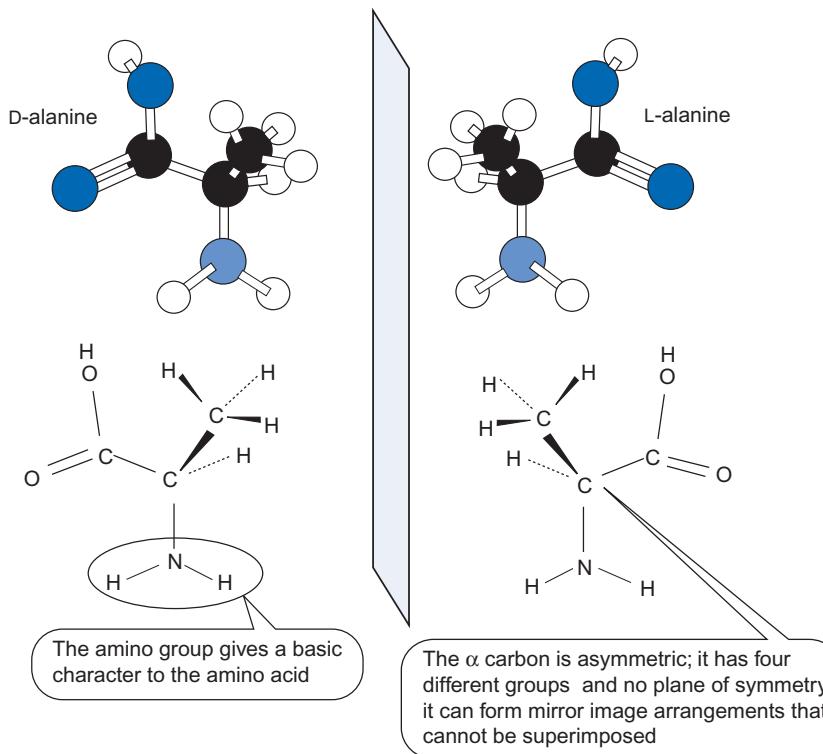


FIGURE 1.4.10 An example of optical isomerism. Amino acids consist of a backbone of a carboxyl group bonded to a central C atom, called the α carbon, and an amino group bonded to the other side of the α carbon. Typically the α carbon has two more bonds, one to an H atom and the other to a variable group, called R for residue, whose composition determines the kind of amino acid. There are 20 different R groups and 20 different amino acids. The R group for alanine, shown here, is a methyl group. Because the α C atom is asymmetric—there is no plane of symmetry—the four groups can be arranged in two nonequivalent ways. Our bodies use only the L-amino acids. In the L-amino acids, starting from the carboxyl group and moving toward the amino group, the R group is to the left. This is very important, as D-amino acids in proteins would have their R groups pointing the wrong way.

TABLE 1.4.3 Electronegativity of Common Atoms

Atoms	H	C	N	O	F	Na	Mg	P	S	Cl
Electronegativity	2.2	2.5	3.0	3.5	4.0	0.9	1.2	2.1	2.5	3.0

Source: L. Pauling, *The Nature of the Chemical Bond*. Cornell University Press, 1960.

Atoms with similar electronegativities will share bonding electrons equally and will produce nonpolar bonds. Examples include the CC bond, CH bond, and HS bond. Bonds such as OH will be polar bonds.

IONIC BONDS RESULT FROM ATOMS WITH HIGHLY UNEQUAL ELECTRONEGATIVITIES

If the difference in electronegativity is too great, an ionic bond will form in which the strongly electronegative atom strips an electron from the weakly electronegative atom. Examples include NaCl, KCl, CaCl₂, MgCl₂, and a host of other physiologically relevant compounds. These are noted for their dissociation in water to form ions, Na⁺, Cl⁻, K⁺, Ca²⁺, and Mg²⁺, for example. These isolated ions are stabilized by their interaction with the polar water molecule, which presents a negative side towards the positive ions (**cations**) and a positive side towards the negative ions (**anions**).

WATER PROVIDES AN EXAMPLE OF A POLAR BOND

The bond angle defined by HOH is 104.5°, which is close to the tetrahedral angle. In this case, O forms 3 orbitals by hybridization of the 2s² orbitals with the 2px and 2py orbitals. This leaves 2 O electrons in an sp² orbital that are unshared and 2 electrons in a p_z² orbital that are also unshared. These form the **lone electron pairs** of water that participate in yet another kind of bonding, the **hydrogen bond**, discussed later. The electronegative O atom attracts the electrons away from the H nuclei, forming a partial separation of charge in the molecule itself. Thus the bond is said to be **polar** (see Figure 1.4.11).

The estimated charge separation is about -0.67 on the O atom and about +0.33 on each of the H atoms. The **dipole moment** is defined as

$$[1.4.5] \quad \mathbf{p} = q\mathbf{d}$$

where **p** is a vector, the dipole moment, **q**, is the charge divided into equal q_- and q_+ , and **d** is the vector pointing from q_- to q_+ . The dipole moment of a single water molecule is 1.855 debye (1 debye = 3.33564×10^{-30} C m), but the dipole moment of water varies with the size of the water cluster, because nearby water molecules rearrange themselves in the presence of an electric field. Dipoles themselves produce an electric field and therefore interact with electric charges in its vicinity. These electrostatic interactions are part of the forces that govern the interaction of surfaces. In an electric field, the dipole experiences a torque given by

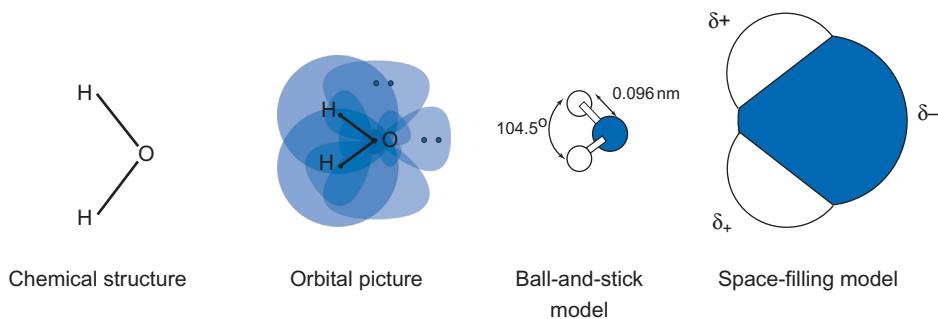


FIGURE 1.4.11 Structure of water. The HOH angle is 104.5° and the bond length is about 96 pm. The O atom is far more electronegative than the H atoms, thereby causing an asymmetric redistribution of the electrical charges away from the H atoms and surrounding the O atom. These partial separations of charges produce a polar compound and a net dipole moment.

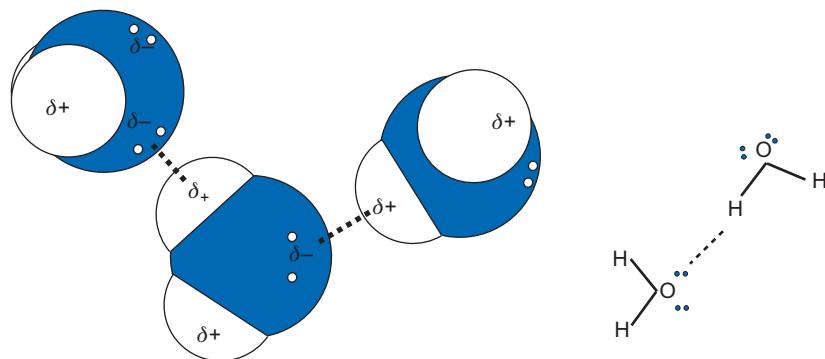


FIGURE 1.4.12 The hydrogen bond in water. The polar OH bond involves a separation of charge. The partial positive charge on the H atom in water is attracted to the lone electron pairs on the opposite side of the molecule on adjacent molecules. This forms a weak bond that is easy to form and easy to break. In many situations, the number of hydrogen bonds significantly stabilizes large structures. In water, there are many hydrogen bonds because each water molecule has the potential of participating in four of them: two because of the H atoms and two more because of the two lone electron pairs.

$$[1.4.6] \quad \tau = p \times E$$

where τ is the torque, p is the dipole moment, and E is the electric field strength.

INTERMOLECULAR FORCES ARISE FROM ELECTROSTATIC INTERACTIONS

Chemical bonds join atoms together to form molecules. Molecules can also be attracted to each other through a variety of intermolecular forces that include:

- Hydrogen bonding
- Dipole–dipole interactions
- London dispersion forces.

HYDROGEN BONDING OCCURS BETWEEN TWO ELECTRONEGATIVE CENTERS

The hydrogen bond involves the sharing of the positive charge of hydrogen between two electronegative centers such as oxygen and nitrogen. It requires proximity and proper orientation of the two electronegative centers. In the case of water, the bond is strongest when the OH bond on one water molecule aligns with the lone electron pair orbital of the adjacent water molecule, as shown in Figure 1.4.12. The hydrogen bond

requires only $8\text{--}40 \text{ kJ mol}^{-1}$ to break, compared to much higher values for covalent bonds such as CC (346 kJ mol^{-1}) or CH (411 kJ mol^{-1}). This low bond energy makes it useful, because it means that the bond can form and break under the influence of normal thermal agitation. At the same time, a large number of hydrogen bonds can stabilize structures such as proteins and DNA.

DIPOLE–DIPOLE INTERACTIONS ARE EFFECTIVE ONLY OVER SHORT DISTANCES

By virtue of their spatial separation of charges, dipoles produce an electric field surrounding them whose magnitude is given by

$$[1.4.7] \quad U(r, \theta) = \frac{p \cos \theta}{4\pi\epsilon_0\kappa r^2}$$

An elementary proof of this result is given in Appendix 1.4.A1. The angle θ is defined as the angle between the point at which potential is given and the midpoint between the two separated charges within the dipole. Note that this is a potential, not the force. In Coulomb's law, the potential varied with $1/r$ (see Eqn [1.3.5]) but here it varies with $1/r^2$. Replacing one ion with a dipole causes the interaction to be shorter range. At short range,

a nearby charge “sees” both charges; at longer range the charge “sees” two opposing dipole charges that tend to neutralize each other; the interaction becomes weaker at longer distances.

Because they both produce an electric field, pairs of dipoles interact with each other. The energy of interaction is given by

$$[1.4.8] \quad U(r) = -\frac{2}{3kT} \left(\frac{p_A p_B}{4\pi\epsilon_0 \kappa} \right)^2 \frac{1}{r^6}$$

where k is a new physical constant, Boltzmann’s constant, which is the gas constant per molecule. Its value is $1.38 \times 10^{-23} \text{ J K}^{-1}$; T is the temperature in K, p_A and p_B are the dipole moments of the two dipoles, ϵ_0 is the electrical permittivity of space, given earlier as $8.85 \times 10^{-12} \text{ C}^2 \text{ N}^{-1} \text{ m}^{-2}$, and r is the separation of the centers of the dipoles.

LONDON DISPERSION FORCES INVOLVE INDUCED DIPOLES

Water has a permanent dipole moment. Symmetrical compounds such as methane and H_2 have no permanent dipole moment, but these can be induced to form a dipole by the presence of an externally applied electric field. A **polarizable** atom redistributes its internal charge in response to an electric field to form a dipole moment aligned with the applied field. For small electric field strength, the induced dipole is approximately proportional to the applied field:

$$[1.4.9] \quad p_{\text{ind}} = \alpha E$$

where p_{ind} is the **induced dipole moment**, E is the electric field, and α is the **polarizability**. The SI unit for α is $\text{C m}^2 \text{ V}^{-1}$, but it is often converted to units of volume, cm^3 , by multiplying by $1/4\pi\epsilon_0 \times 10^{-6}$, where ϵ_0 is the electrical permittivity of space. This effect, shown in Figure 1.4.13, results in the attraction of a neutral molecule to a charged molecule.

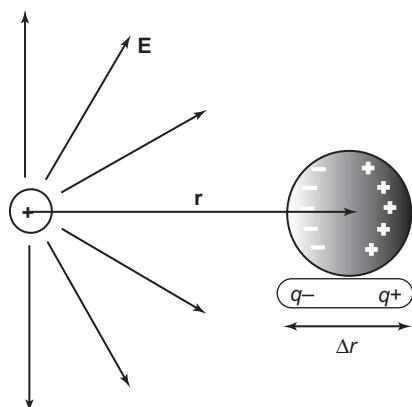


FIGURE 1.4.13 Electrical polarizability. The presence of a charge establishes a local electrical field. Electrons within nearby molecules can respond to this field by redistribution of charge, causing an induced dipole. Because of the separation of charge, the induced dipole experiences unequal forces from the fixed charge. The result is a net movement of the induced dipole.

Even molecules that do not have a permanent dipole moment can transiently produce dipole moments that result in their attraction. We imagine that electrons orbit their nucleus in an “electron cloud” but this picture is an average distribution. At any instant the electrons are separated from their nucleus, producing a transient dipole. When nearby atoms synchronize the distribution of electrons in their clouds, they can produce attractive forces first described by F. London in 1937 and called London dispersion forces.

The totality of forces between atoms or molecules due to dipole–dipole, dipole-induced dipole, and instantaneously induced dipoles (London dispersion force) is called the **van der Waals force**. It excludes the interaction due to covalent bonds or electrostatic interactions.

CLOSE APPROACH OF MOLECULES RESULTS IN A REPULSIVE FORCE THAT COMBINES WITH THE VAN DER WAALS FORCES IN THE LENNARD–JONES POTENTIAL

Imagine two atoms or molecules separated by a large distance. Because of the large distance, their interaction is very small—there is little force between them. Even if they have very little dipole moment, as they approach one another they will experience attractive forces due to London dispersion forces, and these are attractive. As the distance between their atomic nuclei shortens, they begin to experience repulsive forces due to the interpenetration of their atomic or molecular orbitals. This repulsive force varies quite steeply with separation. The overall potential energy for the interaction of nonbonding particles has been mathematically approximated by the **Lennard–Jones potential**. It is given as

$$U(r) = 4\epsilon \left[\left(\frac{\sigma}{r} \right)^{12} - \left(\frac{\sigma}{r} \right)^6 \right] = \epsilon \left[\left(\frac{r_m}{r} \right)^{12} - 2 \left(\frac{r_m}{r} \right)^6 \right]$$

$$[1.4.10]$$

where $U(r)$ is the potential energy of the interaction, ϵ is depth of the potential well (a measure of the strength of the attractive forces), and σ is the distance at which the intermolecular potential is zero; r_m is the distance of separation when the potential is $-\epsilon$ (see Figure 1.4.14).

ATOMS WITHIN MOLECULES WIGGLE AND JIGGLE, AND BONDS STRETCH AND BEND

The bond lengths, angles, and energies listed in Table 1.4.2 are averages. Two atoms involved in a bond actually oscillate back and forth around the average bond length. In addition, the angles defined by, say, HCH are not fixed, but the three atoms oscillate around the average bond angle. The molecules also translate through the solution or gas, and rotate. Some of these motions affect others, as rapid rotation about an axis perpendicular to a bond tends to

stretch the bond. All of these modes of action within molecules store kinetic and potential energy on a sub-molecular scale. When a moving body stops because of friction, the kinetic energy does not disappear; it is converted from the macromolecular to the molecular scale—the kinetic energy appears as heat and the temperature of the surfaces increases. This conversion is a one-way street: we can never fully recover that molecular energy back into macromolecular action. The temperature is, in one sense, a measure of this dynamic motion. These various modes of thermal motion are shown in [Figure 1.4.15](#).

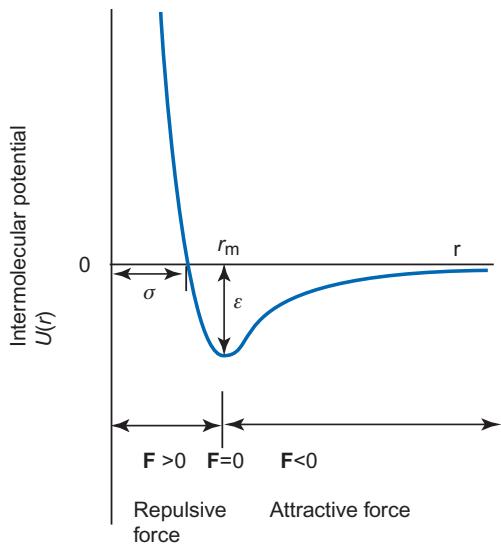


FIGURE 1.4.14 The Lennard-Jones potential. At far separation, there is little force and no potential. Because of the inverse 6th power dependence on the separation, this force becomes larger as particles approach one another, reaching a minimum at $U(r) = \varepsilon$ and $r = r_m$. The separation at which $U(r) = 0$ is $r = \sigma$. The equilibrium for the particles occurs at the minimum potential.

SUMMARY

Atoms are the fundamental units of the elements and are defined by the number of protons in the atomic nucleus. Only relatively few of the chemical elements have active roles in the body. The electrons orbit the nucleus in electron orbitals that have definite energy levels. These electron orbitals describe the distributed nature of the electrons within their atoms. Electrons populate the orbitals in a defined sequence that gives rise to the periodic behavior of the chemical elements within the periodic table.

The chemical elements can combine to form compounds in fixed ratios to each other, often by sharing the outer orbital electrons. These bonds form by combination of their atomic orbitals or by the formation of molecular orbitals in which the electrons are distributed among the nuclei that make up the molecule. Most organic compounds form covalent bonds in which the electrons are shared approximately equally among the nuclei. These bonds have energies in the range 200–500 kJ mol^{-1} and have bond lengths on the order of 0.1–0.2 nm. The bond angles are determined by the kind of bonds that form. Many of the biochemicals within the human body are organic compounds that have CC, CC, CN, COH, CO, and CH bonds. The single bonds typically freely rotate about the axis connecting the two nuclei. Double bonds do not permit free rotation because the rotation would break the second bond and this requires energy.

The rigid form of the CC bond gives rise to geometric isomerism. The different arrangement of the same nuclei around the CC bond can cause large differences in the overall shape of molecules. Isomerism also arises from the different spatial arrangement of chemical groups around an asymmetric C atom. Such isomers can be mirror images of each other (enantiomers) or not. All of the amino acids (except glycine) exist in enantiomeric forms, but only the L-type of amino acids are used to make proteins.

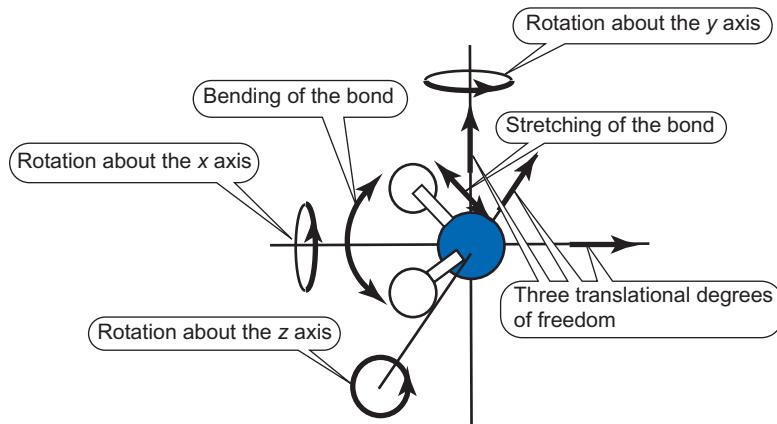


FIGURE 1.4.15 Degrees of freedom of motion in water. The HOH bond can bend, changing its angle; the OH bond can oscillate, stretch, and compress its bond length; the entire molecule can rotate around several independent axes; the molecule can translate in three independent directions. Each of these modes of movement is independent and each carries some kinetic energy. The energy distributed amongst the various modes of motion increases with increase in temperature.

Polar bonds involve unequal sharing of bonding electrons between the two nuclei involved in the bond. A good example is the OH bond in which the oxygen atom is more electronegative. Electronegativity refers to the ability of a nucleus to attract shared electrons. Because O is more electronegative than H, the resulting OH bond is polar, with more negative charge around the O atom than the H atom. This partial separation of charge produces a dipole which is described by its dipole moment, equal to the charge times its separation directed from the $-$ to the $+$ charge. The dipole moment produces an electric field that can interact with other nearby atoms. The OH group is very important because it forms hydrogen bonds with other electronegative atoms. This low energy bond is easy to form and easy to break and can stabilize biological structures.

Ionic bonds occur when two atoms or chemical groups differ greatly in their electronegativities. The more electronegative atom or group effectively “steals” an electron from the less electronegative atom. When dissolved in water, these types of compounds typically dissociate into a cation and anion.

Molecules can interact with each other through ion–ion interactions, described by Coulomb’s law, hydrogen bonding, dipole–dipole interactions, and London dispersion forces. The London dispersion forces arise from transient dipoles in atoms that induce transient dipoles in nearby atoms, producing an attractive force. The Lennard–Jones potential describes the overall interaction between nonbonded particles.

Atoms and molecules form surfaces that interact with other surfaces. Almost all of physiology is about how these surfaces interact to produce catalysis or tight binding or loose binding or specificity of binding.

REVIEW QUESTIONS

- What is the fundamental unit of an element? What is the fundamental unit of a chemical compound?
- Why do atoms form compounds in definite and fixed proportions?
- What forms the surfaces of atoms and molecules?
- Why are the CH bonds in methane arranged to point toward the vertices of a tetrahedron?
- What is the tetrahedral angle?
- What are typical energies for CH and CC bonds?
- What are typical bond distances for CH and CC bonds?
- What is meant by structural isomerism?
- What is meant by geometric isomerism?
- What is optical isomerism?
- Why does water form polar covalent bonds?
- What is hydrogen bonding? How much energy is in a hydrogen bond?
- What is an electric dipole?
- What are dipole–dipole interactions?
- What are London dispersion forces?

APPENDIX 1.4.A1 DIPOLE MOMENT

A DIPOLE CONSISTS OF TWO EQUAL CHARGES SEPARATED BY A DISTANCE, D, AND IS DESCRIBED BY ITS ELECTRIC DIPOLE MOMENT

An electric dipole consists of two equal charges, q_+ and q_- , separated by a distance d , as shown in Figure 1.4.A1.1. These are typically molecules whose separation distance is small compared to the distance at which electrical effects are noted. As we shall see, cardiomyocytes can also act as electric dipoles. The electric dipole moment is *defined* as

$$[1.4.A1.1] \quad \mathbf{p} = q_+ \mathbf{d}$$

where \mathbf{d} is a vector pointing from q_- to q_+ , as shown in Figure 1.4.A1.1. The net force on a unit positive test charge at any point surrounding the dipole can be determined by the vectorial sum of the component forces from q_+ and q_- , as shown in Figure 1.4.A1.1. We can determine a set of points surrounding the dipole that has the same magnitude of force, but in varying directions. This set forms a curve. The family of lines for a set of force magnitudes, shown in Figure 1.4.A1.2, represents the electric field surrounding the dipole. Moving a positive unit charge from a large distance away (∞) to any point within the electric field entails

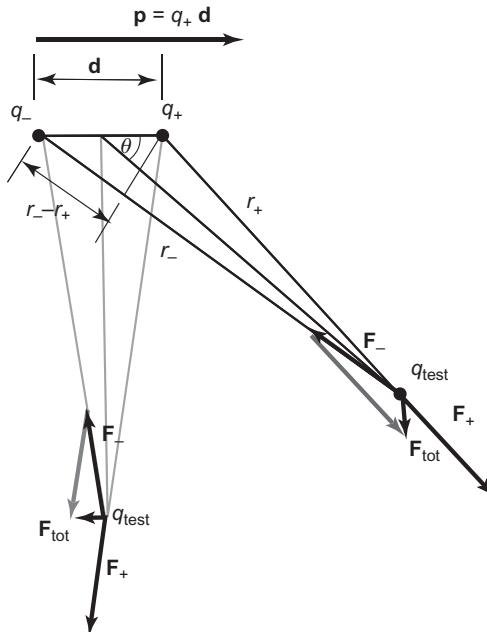


FIGURE 1.4.A1.1 Origin of the electrical forces near an electric dipole determined at two different locations. The electric dipole consists of two equal charges (q_+ and q_-) separated by a distance, d . Charges placed nearby experience a force as a result of the electric dipole. The net force is the vector sum of the forces exerted by the two charges, as shown for two different positions. Because the force declines as $1/r^2$, the direction of the force changes with distance and angle, θ , made between the line joining the center of the dipole and the test charge, and the electric dipole moment.

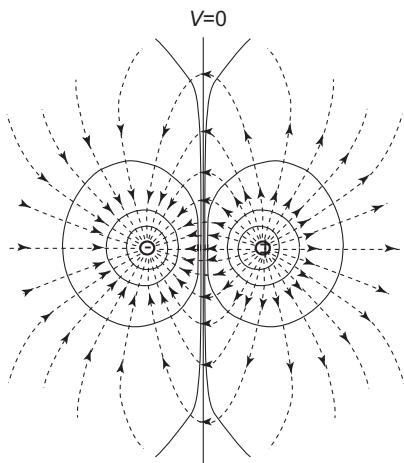


FIGURE 1.4.A1.2 Electric field and electrical potential surrounding a dipole. The electric field lines are shown in *dashed lines with arrows*. They represent the lines of equal force that would be felt by a positive unit test charge as it approaches the dipole. The electric field is a vector which, when magnified by the size of a charge, gives the magnitude and direction of the force. The electric potential contour lines are shown in *solid*. The negative gradient of these contour lines are the electric field lines. Thus the electric field is the steepest slope down the potential surface. The lines of equal potential intersect the electric field lines at right angles, much like the steepest descent off a hill intersects its altitude contour lines at right angles.

expending energy that is stored as potential energy, which is identified as the electrical potential. The potential at any point is the scalar sum of the potential energy associated with each charge. That is, the potential at any point is just the sum of the potential energy of q_+ and that of q_- . Contour lines of equal potential are shown

in [Figure 1.4.A1.2](#). These lines intersect the lines of electric force at right angles.

The electric potential surrounding a dipole is just the sum of the potentials associated with each charge. Thus we write:

$$\begin{aligned}
 V_{\text{total}} &= V_+ + V_- \\
 &= \frac{q_+}{4\pi\epsilon_0 r_+} + \frac{q_-}{4\pi\epsilon_0 r_-} \\
 &= \frac{q_+}{4\pi\epsilon_0} \left[\frac{1}{r_+} - \frac{1}{r_-} \right] \\
 &= \frac{q_+}{4\pi\epsilon_0} \left[\frac{r_- - r_+}{r_+ r_-} \right] \\
 &\approx \frac{q_+ \mathbf{d} \cos \theta}{4\pi\epsilon_0 r^2} = \frac{\mathbf{p} \cos \theta}{4\pi\epsilon_0 r^2}
 \end{aligned} \tag{1.4.A1.2}$$

where the quantity $q_+ \mathbf{d}$ appears. We have identified this as the electric dipole moment, $\mathbf{p} = q_+ \mathbf{d}$. Here $\mathbf{d} \cos \theta$ enters the equation as an approximation of $r_- - r_+$, as suggested by the geometry of [Figure 1.4.A1.1](#). This assumption is generally made when $r \gg d$. Thus the voltage at any point is inversely proportional to the square of the distance and varies with the relative position of the point with respect to \mathbf{p} , the electric dipole moment. The point of these calculations is to show that the electric dipole creates an electric field and a potential field that can be measured some distance away. The value of the potential depends on the distance and the relative position compared to the dipole.