Web site for BCHS 3304:

www.uh.edu/sibs/faculty/cstath/index.htm

Definition of Biochemistry:

Biochemistry is the study of the chemistry of life. Although it overlaps with other disciplines (e.g. cell biology, genetics, immunology, microbiology, pharmacology, and physiology), biochemistry is largely concerned with limited number of issues:

(1) **What are the chemical and three-dimensional structures of biological molecules?**

(2) **How do biological molecules interact with each other?**

(3) **How does the cell synthesize and degrade biological molecules?**

(4) **How is energy conserved and used in the cell?**

(5) **What are the mechanisms for organizing biological molecules and coordinating their activities?**

(6) **How is genetic information stored, transmitted, and expressed?**

[redacted]

BIOCHEMISTRY IS THE STUDY OF MOLECULAR BASIS OF LIFE

There is much excitement and ferment in biochemistry throughout the world for several reasons:

(1) The chemical mechanisms of many central processes of life are now understood:

- **The discovery of double- helical structure of DNA**
- **The elucidation of the flow of genetic information**
- **The determination of the 3D structure and mechanism of action of many proteins**
- **The unraveling of central metabolic pathways**
- **The development of recombinant DNA technology and the sequencing of the genome**

(2) Common molecular patterns and principles underlie the diverse expressions of life :

- **In bacteria and humans, macromolecules are made by the same building blocks**
- **The flow of genetic information (DNA-->RNA-->Proteins) is essentially the same in all organisms**
- **ATP, the universal currency of energy in biological systems, is generated in similar ways in all forms of life**

(3) Biochemistry is profoundly influencing medicine:

- **The molecular lesions causing many genetic diseases (hemophilia, cystic fibrosis) have been elucidated, opening the door to the discovery and implementation of effective therapies**
- **Biochemistry is contributing richly to clinical diagnostics**
- **Biochemistry makes possible the rational design of new drugs**
- **Agriculture is benefiting from recombinant DNA technology (e.g. engineered plants with greater resistance to insects)**

Biochemistry and Human Biology:

(i) biochemistry is an intrinsically beautiful and fascinating body of knowledge

(ii) biochemistry is greatly influencing medicine and other fields

(iii) advances in biochemistry are enabling researchers to tackle some of the most exciting questions in biology and medicine

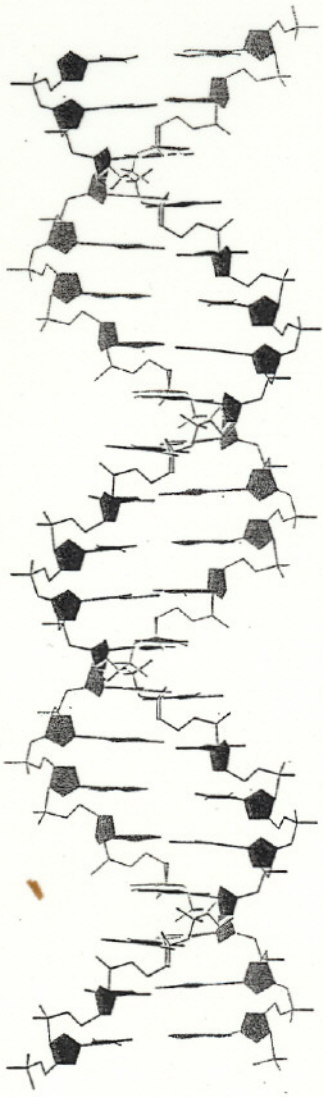


Figure 1-1
Model of the DNA double helix. The diameter of the helix is about 20 Å.

The flow of genetic information:

DNA --------> RNA --------> Proteins

DNA (deoxyribonucleic acid): a linear polymer made up of four different monomers {bases: Adenosine (A), Cytosine (C), Guanine (G), and Thymine (T)}, fixed on a backbone built of repeating sugar-phosphate units.

The structure of DNA was determined by James Watson and Francis Crick in 1953.

RNA (ribonucleic acid): another nucleic acid made up of four different monomers {A, C, G, and Uracil (U)}

mRNA
tRNA
rRNA

Proteins: linear polymers made up of twenty different monomers (amino acids).

Genome Sequencing Projects:

Human Genome Project (HGP): an international effort to determine the complete nucleotide sequence of human DNA and to identify the genes therein. It was launched in 1990, and completed in June 2000.

Other genome sequencing projects: Mouse, rat, zebrafish, mosquito, fly, yeast, several microbes, etc.

MOLECULAR MODELS DEPICT 3D STRUCTURE

Three types of atomic models will be used to depict molecular architecture:

1. **Space-filling**
2. **Ball-and-Stick**
3. **Skeletal**

(1) SPACE-FILLING MODELS:

- **Most realistic**
- **The size and configuration of an atom is determined by its bonding properties and van der Waals radius**
- **Different colors for the model atoms**

(2) BALL-AND-STICK MODELS:

- Not realistic
- The atoms are depicted as spheres of radius smaller than the van der Waals radius
- Bonds are represented by sticks
- Easier to see the bonding arrangement

(3) SKELETAL MODELS:

- Show only the molecular framework
- The position of atoms are implied by the junctions and ends of bonds
- Frequently used to depict large biological macromolecules (e.g. proteins)

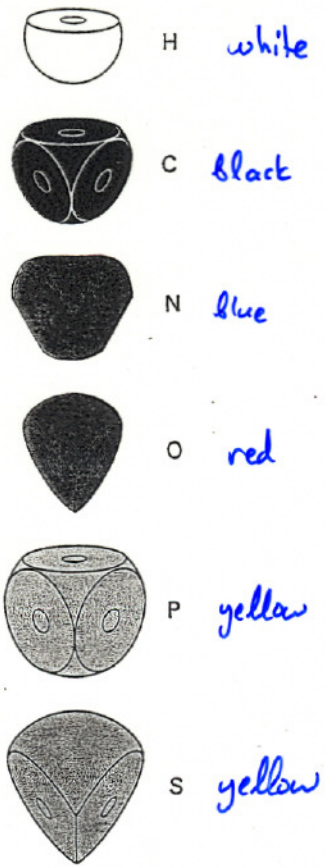


Figure 1-2
Space-filling models of hydrogen, carbon, nitrogen, oxygen, phosphorus, and sulfur atoms.

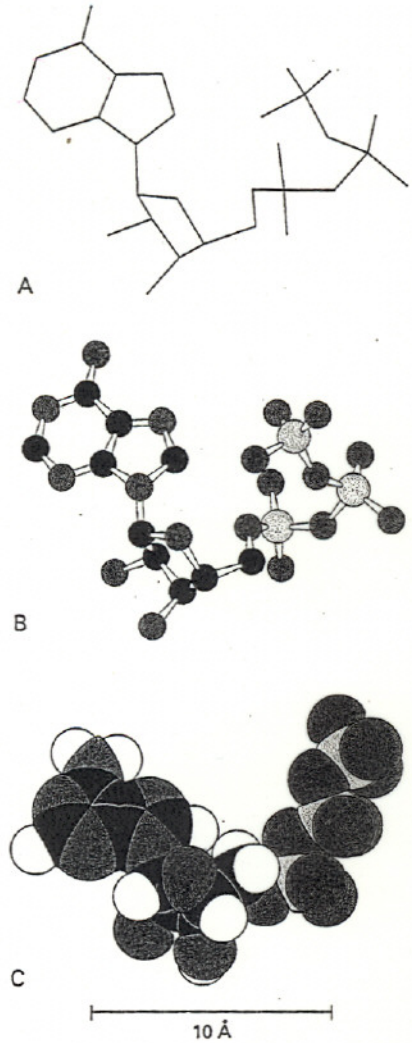


Figure 1-4
Comparison of (A) skeletal, (B) ball-and-stick, and (C) space-filling models of ATP. Hydrogen atoms are not shown in models A and B.

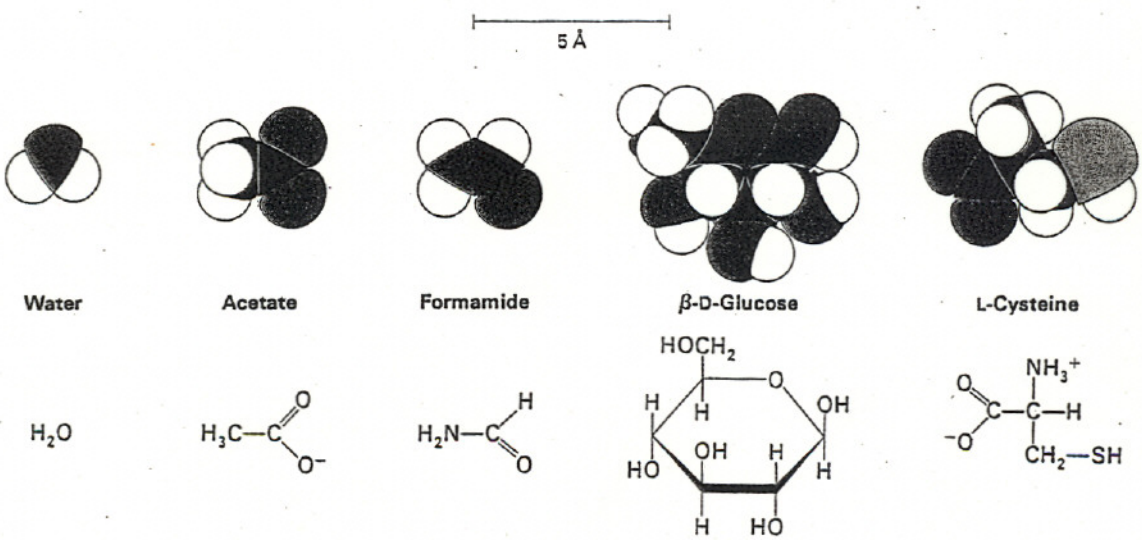


Figure 1-3
Space-filling models of water, acetate, formamide, glucose, and cysteine.

SPACE, TIME, and ENERGY (UNITS)

(1) SPACE:

- **Angstrom (Å) = 10^{-10} m**
- **Nanometer (nm)** = 10^{-9} m
- Millimeter (mm) = 10^{-3} m
- **Micrometer (μm)** = 10^{-6} m
- **The resolution of the light microscope is about 2000 Å (0.2 μm)**

Crystallographers usually use Angstroms as the unit of length, whereas electron microscopists prefer nm or μm

(2) TIME:

- **Millisecond (ms, 10^{-3} s)**
- **Microsecond (μs, 10^{-6} s)**
- **Nanosecond (ns, 10^{-9} s)**
- **Picosecond (ps, 10^{-12} s)**

(3) **ENERGY:**

- **Kilocalories per mole (kcal/ mol)**
- **Joule (J); 1 J = 0.239 calories**

$1\ kcal/mol = 4.184\ kJ/mol$

REVERSIBLE INTERACTIONS OF BIOMOLECULES ARE MEDIATED BY NONCOVALENT BONDS

(1) Electrostatic bonds (ionic bond, salt linkage, salt bridge, or ion pair):

- **A charged group can attract an oppositely charged group.**
- **The force (F) of an electrostatic attraction is given by Coulomb's Law:**

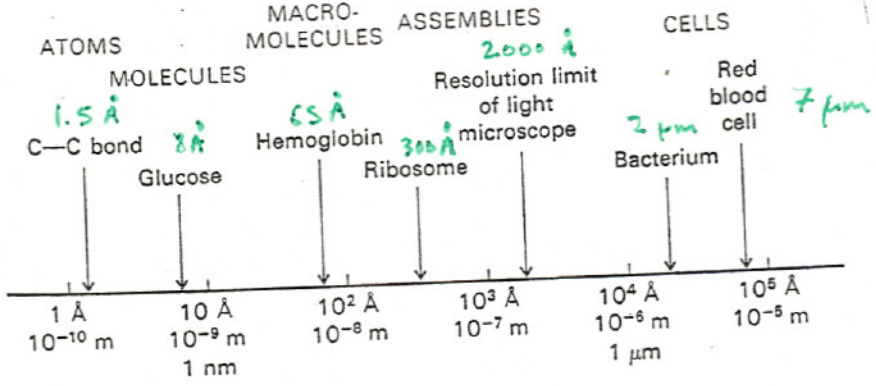


Figure 1-5
Dimensions of some biomolecules, assemblies, and cells.

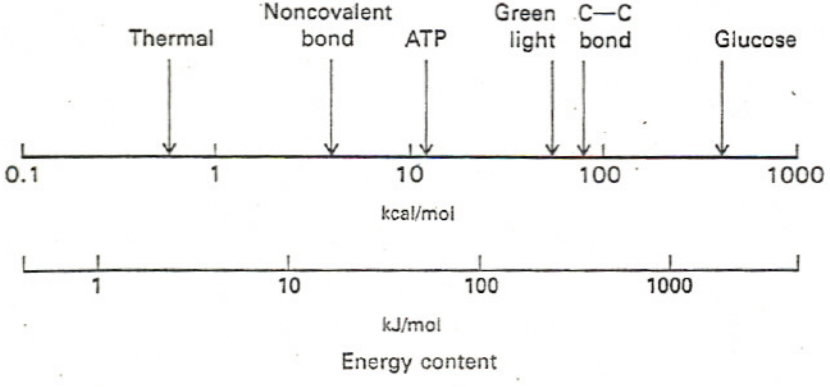


Figure 1-8
Some biologically important energies.

Atom	Number of unpaired electrons (in red)	Number of electrons in complete outer shell
H·	1	2
:Ö·	2	8
:N·	3	8
·C·	4	8
:S·	2	8
:P·	3	8

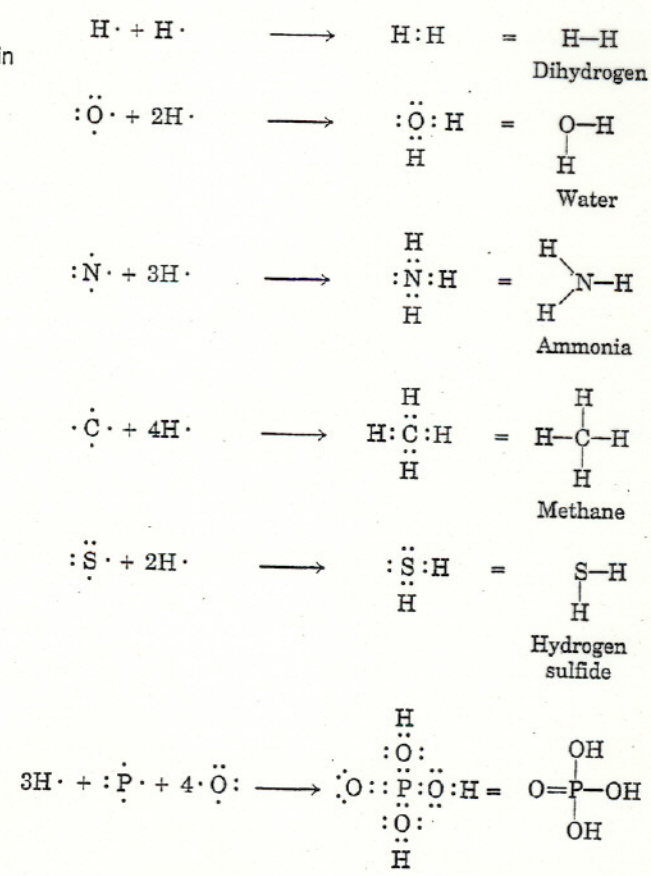


figure 3–2
Covalent bonding. Two atoms with unpaired electrons in their outer shells can form covalent bonds with each other by sharing electron pairs. Atoms participating in covalent bonding tend to fill their outer electron shells.

Covalent bond: a chemical bond that involves sharing of electron pairs.

Bond	*Structure*	*Length (Å)*
C—H	R_2CH_2	1.07
	Aromatic	1.08
	RCH_3	1.10
C—C	Hydrocarbon	1.54
	Aromatic	1.40
C=C	Ethylene	1.33
C≡C	Acetylene	1.20
C—N	RNH_2	1.47
	O=C—N	1.34
C—O	Alcohol	1.43
	Ester	1.36
C=O	Aldehyde	1.22
	Amide	1.24
C—S	R_2S	1.82
N—H	Amide	0.99
O—H	Alcohol	0.97
O—O	O_2	1.21
P—O	Ester	1.56
S—H	Thiol	1.33
S—S	Disulfide	2.05

$$F = \frac{q_1 q_2}{r^2 D}$$

q_1, q_2—the charges of the two groups

R-- the distance between the two groups

D-- the dielectric constant of the medium

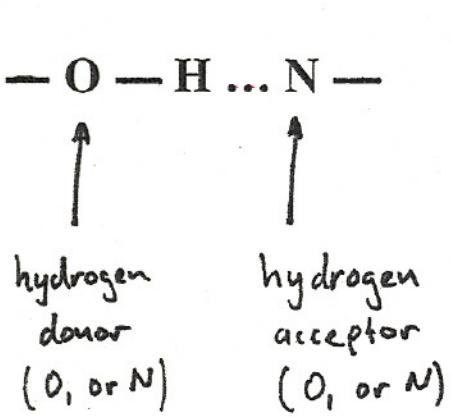
- The attraction is strongest in a vacuum (where D=1) and is weakest in a medium in such as water (where D= 80)

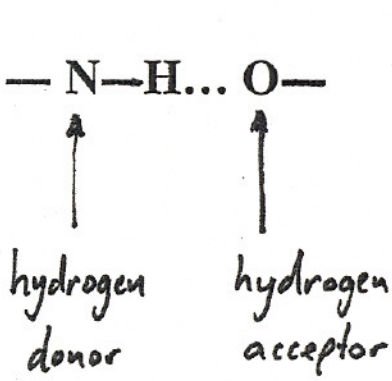
The distance between oppositely charged atoms in an optimal electrostatic attraction is about 2.8 Å

(2) HYDROGEN BONDS:

- **In hydrogen bonds, a hydrogen atom is shared by two other atoms**

The atom to which the hydrogen atom is more tightly linked is called the hydrogen donor, the other atom is the hydrogen acceptor





length of Bond:
2.6 - 3.1 Å

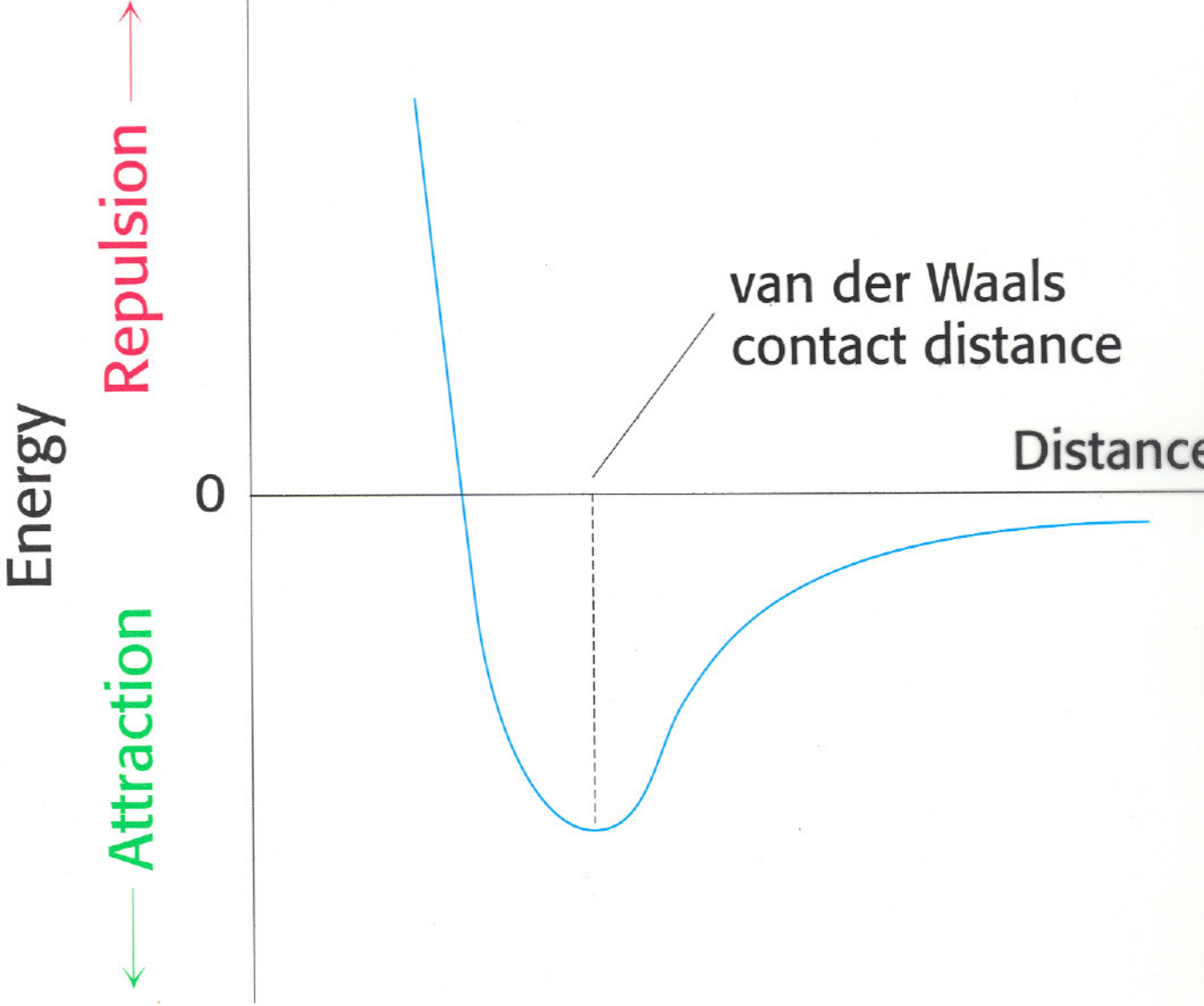
- **The strongest hydrogen bonds are those in which the donor, hydrogen, and acceptor atoms are colinear**

- **Hydrogen bonds are stronger than van der Waals bonds but are much weaker than covalent bonds**

- **Hydrogen bonds play an important role in the structure of proteins and DNA**

(4) Van der Waals bonds:

- A nonspecific attractive force, come into play when any two atoms are 3 to 4 Å apart
- The basis of these bonds is that the distribution of electronic charge around an atom changes with time, at any instant, the charge distribution is not perfectly symmetric
- Because van der Waals bonds are relatively weak, their importance arises when there is a large number of van der Waals bonds simultaneously
- Effective van der Waals interactions depend on steric complementarity



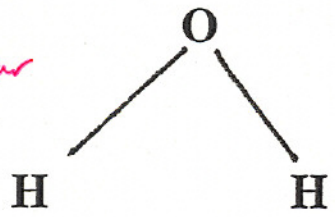
Energy of a van der Waals interaction as two atoms approach one another. The energy is most favorable at the van der Waals contact distance.

Figure 1-10
Stryer, Tymoczko, & Berg, BIOCHEMISTRY, Fifth Edition.

THE BIOLOGICALLY IMPORTANT PROPERTIES OF WATER

(1) POLARITY: Water is a polar molecule

triangular



(net positive charge)

(2) COHESIVENESS: Water is highly cohesive

- Neighboring water molecules have a high affinity for each other
- A positively charged region in one water molecule tends to orient itself towards a negatively charged region in one of its neighbors

ICE: Highly regular crystalline structure in which all potential hydrogen bonds are made 4 hydrogen bonds/molecule

LIQUID WATER: Partly ordered structure in which hydrogen bonded clusters of molecules are continually forming and breaking up 3.4 hydrogen bonds/molecule

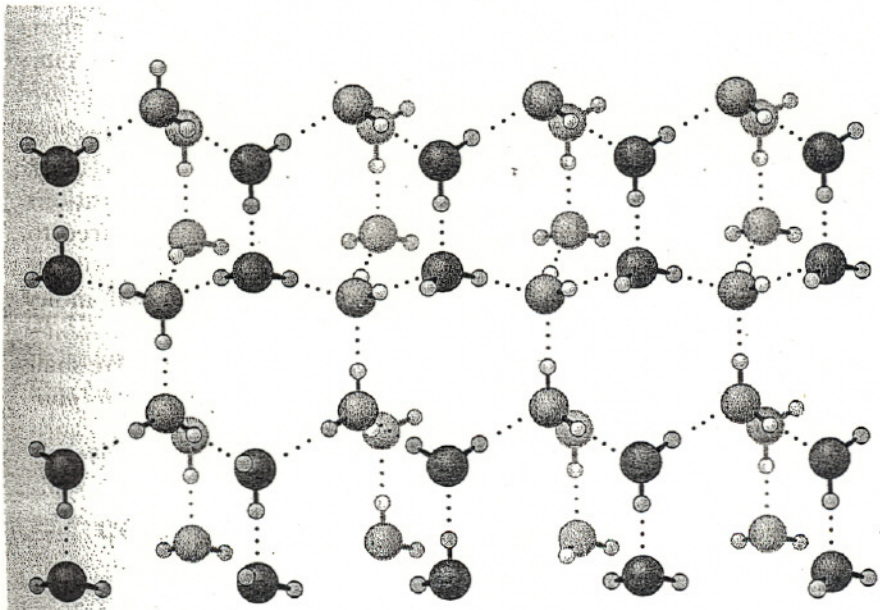


Figure 1-11
Structure of a form of ice. [After L. Pauling and P. Pauling. *Chemistry* (W.H. Freeman, 1975), p. 289.]

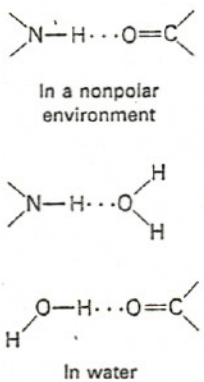


Figure 1-12
Water competes for hydrogen bonds.

Table 1-3
Dielectric constants of some solvents at 20°C

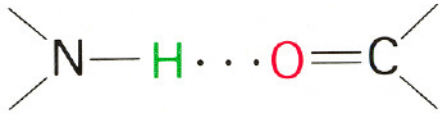
Substance	*Dielectric constant*
Hexane	1.9
Benzene	2.3
Diethyl ether	4.3
Chloroform	5.1
Acetone	21.4
Ethanol	24
Methanol	33
Water	80
Hydrogen cyanide	116

WATER SOLVATES POLAR MOLECULES AND HENCE WEAKENS IONIC AND HYDROGEN BONDS

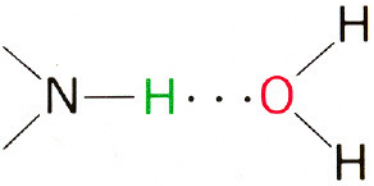
- Water is an excellent solvent for polar molecules
- Water weakens electrostatic forces and hydrogen bonds by competing for their interactions
- The existence of life on earth depends critically on the capacity of water to dissolve a remarkable array of polar molecules that serves as fuels, building blocks, catalysts, and information carriers
- The existence of water as a solvent poses a problem, for it also weakens interactions between polar molecules (water-free microenvironments)

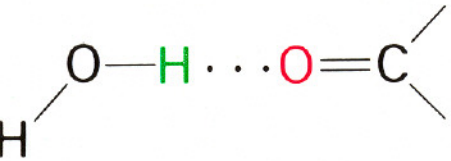
HYDROPHOBIC ATTRACTIONS

- Non-polar molecules or groups tend to cluster together in water; these interactions are called HYDROPHOBIC INTERACTIONS
- Non- polar solute molecules are driven together in water not primarily because they have a high affinity for each other but because water bonds strongly to itself.

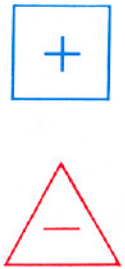


In a nonpolar environment

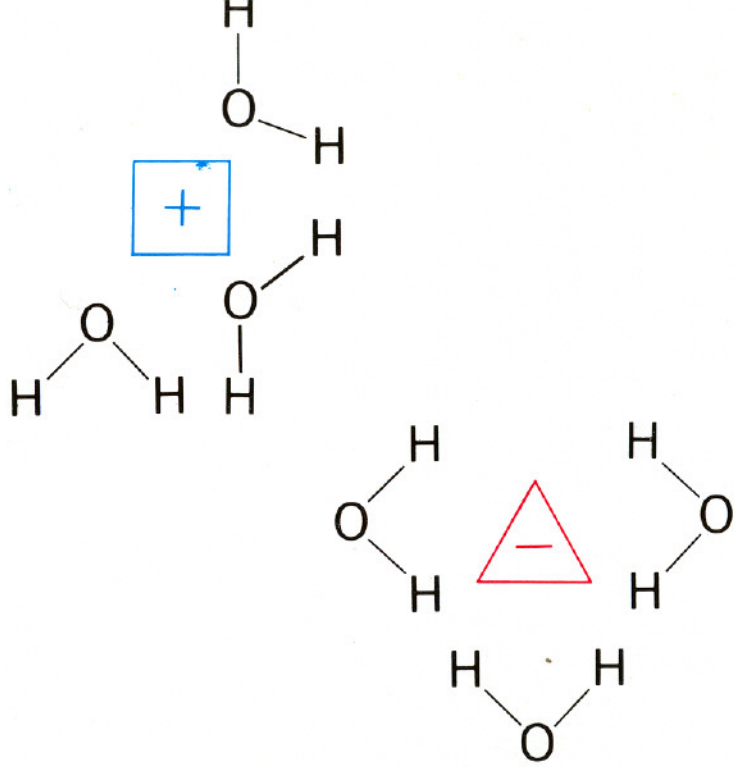




In water



Electrostatic interaction in a nonpolar environment



Water surrounds the charged groups and attenuates their interaction

Stryer: *Biochemistry,* Fourth Edition

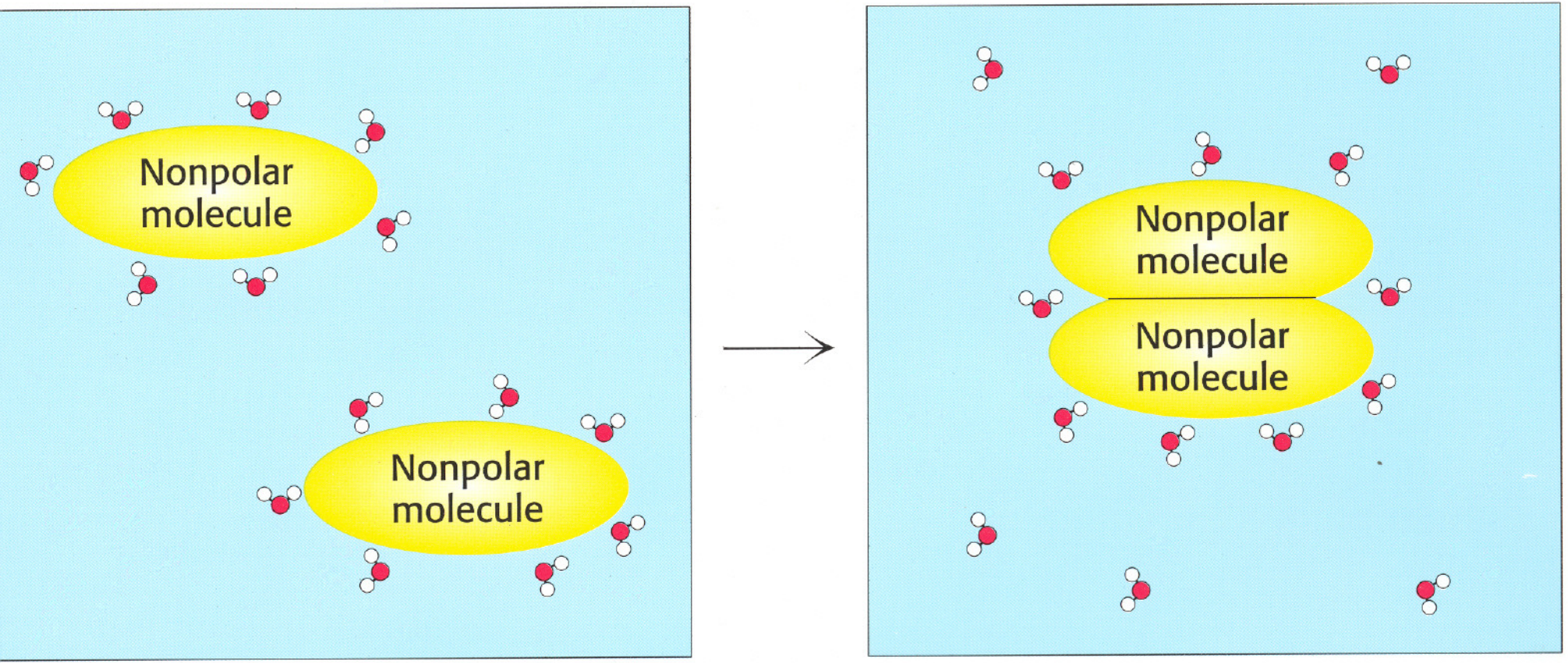


Figure 1-15
Stryer, Tymoczko, & Berg, BIOCHEMISTRY, Fifth Edition.