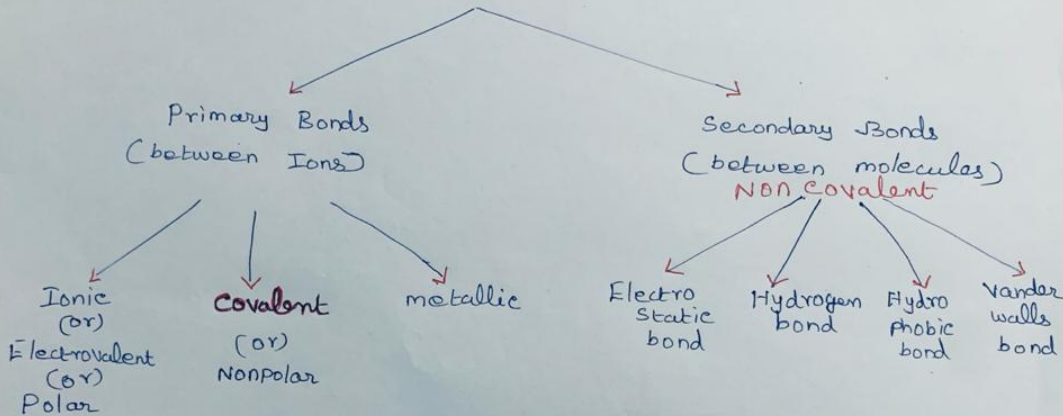


BONDS





Bonds

*Union of the atoms of two or more elements by mutual attraction is called **chemical bonds**.*

A **bond** is an *electrical force* linking atoms.

The bonds are classified into two types. They are *primary bonds* and *secondary bonds*. Primary bonds are *strong bonds*. They hold the atoms together in molecules.

The *secondary bonds* are *weak bonds*. The secondary bonds form between biological molecules.

Primary Bonds

Primary bonds are strong bonds. The formation of breaking of primary bonds need more energy. They bind one atom with another.

The primary bonds are of three types, namely

1. *Ionic bonds*
2. *Covalent bonds*
3. *Metallic bonds*

Secondary bonds

- * Secondary bonds are weak bonds. They are weaker than primary bonds. However they are not secondary with regard to their function.
- * They are formed between molecules or within a molecule.
- * They are very important in joining the *biochemical compounds*.
- * The *three dimensional structure of proteins and nucleic acids* involve several secondary bonds.
- * Generally, weak bonds do not bind one atom with another atom.
- * But they serve as *links* between molecules or within a molecule.
- * The secondary bonds are easily formed and easily broken.
- * They need only *very little energy* for formation or breaking.
- * The important secondary bonds are hydrogen *bonds and Van der Waal's bonds*.

1. Ionic Bonds or Electrovalent Bonds

The bond formed by the transfer of electrons from one atom to another, is called *ionic bonds*.

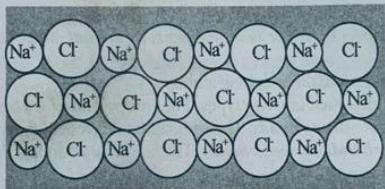


Fig.4.2: Ionic bond of table salt, NaCl.

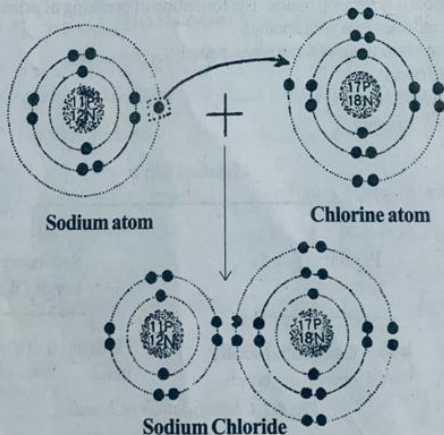


Fig.4.3: Electrovalent bond in sodium chloride.

The term '*electrovalent bond*' was proposed by *Kossel* in 1961. Electrovalent bond links two or more atoms in a molecule or compound. Here the bond is formed by *ionization*. Hence the bond is called *ionic bond* and the compound is called *ionic compound* or *electrovalent compound* or *polar compound*.

Sodium chloride is an ionic compound. Sodium atom (2,8,1) has one electron in the outermost orbit. Chlorine atom (2,8,7) has 7 electrons in the outermost orbit.

The sodium atom transfers one electron to the chlorine atom.

Since sodium loses a negatively charged electron, it becomes *positively charged* or *electropositive*.

As chlorine gains a negatively charged electron, it becomes *negatively charged* or *electronegative*.

The Na^+ ion and Cl^- ion are held together in NaCl by the electrostatic force of attraction.

The *valency of an element is the number of electrons an atom gains or loses in order to become stable*. So the valency of Na is 1 and that of Chlorine is also 1.

Ionic bonds are formed in *crystalline inorganic salts*.

2. Covalent Bonds

In covalent bonds the atoms are linked together by the *sharing of electrons between the atoms*.

The term '*covalent bond*' was proposed by *Lewis* in 1966. This bond is very common in *organic compounds*. Here ionization does not occur. The atoms also neither lose nor gain electrons. These compounds are called *molecular compounds*.

The covalent bonds are also called *homopolar bonds*. They are *strong bonds* compared to ionic bonds. Covalent bonds are *endergonic*, i.e., their formation needs energy.

95% of the chemicals in the cells are bounded covalently.

Both formation and breakdown of covalent bonds occur by *enzyme action* in cells.

Covalent bonds are the properties of *non-metals*.

1. Methane (CH_4)

Carbon combines with 4 hydrogen atoms to form methane. The carbon atom has 4 electrons in the *outer shell*. It requires 4 electrons to complete its outer shell. It completes its outer shell by sharing electrons with 4 hydrogen atoms.

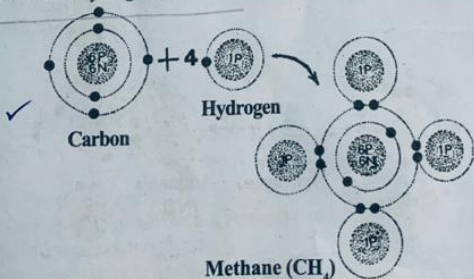


Fig. 4.4: Covalent bond in methane.

2. Carbon Tetra chloride (CCl_4)

Carbon combines with four atoms of chlorine to form carbon tetra chloride. Here also the bond is formed by the sharing of electrons. (4.5)

3. Carbon dioxide (CO_2)

Carbon dioxide is formed by the combination of carbon with 2 oxygen atoms. The carbon atom requires 4 electrons to complete the outer shell and an oxygen atom requires 2 electrons to

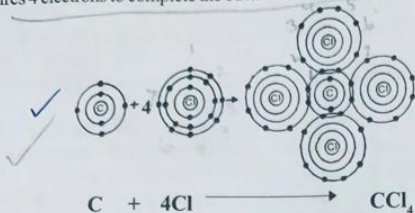


Fig.4.5: Covalent bond in carbon tetrachloride.

complete the outer shell. Both requirements are satisfied by carbon sharing of two pairs of electrons with each of 2 oxygen atoms. Bonds involving two pairs of electrons are known as **double bonds**. (4.6)

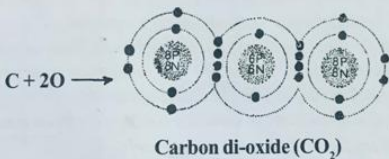


Fig.4.6: Covalent bond in CO_2 .

4. Ammonia (NH_3)

Ammonia is formed by the combination of one nitrogen atom with three hydrogen atoms.

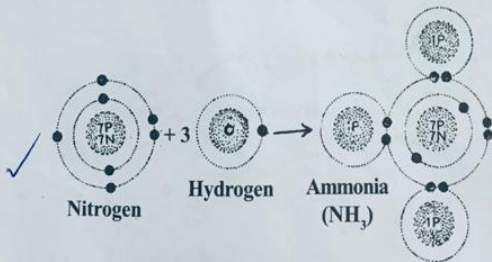


Fig.4.7: Covalent bond in ammonia.

Table 4-5. Bond lengths* of some common covalent bonds

Bond	Bond length (in Å)	Typical compound
C—C	1.54	Ethane, Propane
	1.48	Butadiene
	1.38	Butadiyne
C=C	1.34	Ethylene
	1.28	Butatriene
C≡C	1.20	Acetylene
C—H	1.11	Methane
	1.10	Benzene
	1.08	Acetylene
C—O	1.41	Ethanol
	1.34	Formic acid
C=O	1.20	Formaldehyde
	1.16	Carbon dioxide
C—N	1.47	Methylamine
	1.36	Formamide
C—Cl	1.78	Methyl chloride
C—Br	1.94	Methyl bromide
C—I	2.14	Methyl iodide
O—H	0.96	Methanol
N—H	1.01	Methyl amine

to nitrogen atoms, respectively. In **vitamin B₁₂** also, a Co atom is linked to nitrogen atoms through coordinate bonds. The compound containing coordinate covalent bonds are called **coordinate complexes**.

Noncovalent Bonds or Interactions

In addition to covalent bonding, there are weaker forces of interaction that profoundly influence conformation of biomolecules and their function. These **noncovalent forces**, as they are called, play key roles in the faithful replication of DNA, the folding of proteins into intricate 3-dimensional forms, the specific recognition of substrates by enzymes, and the detection of signal molecules. *Indeed, all biological structures and processes depend on the interplay of noncovalent interactions as well as covalent ones.*

With respect to bonding, weak and strong are used to indicate the amount of energy in a bond. **Strong bonds** such as covalent bonds found in biomolecules require an average of 100 kilocalories/mole or kcal mol⁻¹, to be cleaved and hence are stable and seldom break under physiological conditions.

In contrast, **weak bonds**, such as hydrogen bonds, have energies of 2 to 7 kcal mol⁻¹ and are easily broken. Weak bonds are transient; individually they form and break in small fractions of a second. The transient nature of noncovalent interactions confers flexibility on macromolecules, such as proteins and nucleic acids, that is critical to their function. Furthermore, the large number of noncovalent interactions in a single macromolecule makes it unlikely that at any given moment, all the interactions will be broken; thus macromolecular structures are stable over time. The four fundamental noncovalent bonds are: electrostatic (or ionic) bonds, hydrogen bonds, hydrophobic bonds and van der Waals forces or bonds. They differ in geometry, strength and specificity and are profoundly affected by the presence of water.

A. Electrostatic or ionic bonds

Ionic bonds are formed due to the attraction between atoms or groups, of opposite charges (+ and -). A charged group on a substrate can attract an oppositely-charged group on an enzyme. The force (F) of such an electrostatic attraction is given by Coulomb's law:

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

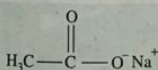
where, q_1 and q_2 = charges of the two atoms or groups,

r = distance between the two atoms or groups, and

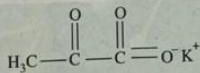
D = dielectric constant of the medium.

The attraction is strongest in a vacuum where D is 1 and is weakest in a medium such as water where D is 80. The distance between oppositely-charged atoms in an optimal electrostatic attraction is about 2.8 Å. The average bond energy of ionic bonds in aqueous solution is about 5 kcal mol⁻¹. This kind of attraction is also called *saline bond, salt linkage, salt bridge or ion pair*.

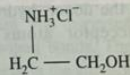
Ionic bonding occurs in crystals and salts that are ionized when dissolved in water. For example, NaCl is a salt composed of Na⁺ (cation) and Cl⁻ (anion). Common examples of the salts of biomolecules are sodium acetate, potassium pyruvate and ethanolamine chloride (Fig. 4-7). This type of interaction even permits the bonding between two different molecules in heteroproteins (for example, in nucleoproteins, between the negatively-charged nucleic acid and the positively-charged basic proteins, esp., the histones).



Sodium acetate



Potassium pyruvate



Ethanolamine chloride

Fig. 4-7. Some salts of biomolecules

Hydrogen Bonds

The term hydrogen bond was suggested by Latimer and Rodenbush.

The attractive force which binds the hydrogen atom of one molecule with the electronegative atom of another molecule is called **hydrogen bond**. It is a secondary bond.

Here the positively charged hydrogen atom approaches an atom with negative charge. The hydrogen bond is also called **proton bond**.

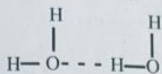


Fig.4.8: Hydrogen bond between water molecules.

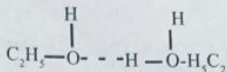


Fig.4.9: Hydrogen bond between ethyl alcohols.

Hydrogen bonding does not involve transfer or sharing of electrons.

When a hydrogen atom carrying positive charge, approaches an atom with negative charge an association is formed. This bonding is the hydrogen bond.

Highlights

Hydrogen Bonds

The weak bond formed between an electronegative atom in one molecule and the electropositive hydrogen atom in another molecule due to the electrostatic force, is called **hydrogen bond**. The term hydrogen bond was introduced by Latimer and Rodenbush. It is also known as **proton bond**.

Hydrogen bond is formed between charged atoms. These are covalently bound to any molecule. It is usually formed between negatively charged oxygen atoms bound to one molecule and positively charged hydrogen atoms. It does not bring about electron transfer or electron sharing between atoms. Hydrogen bond is abbreviated as **H-bond**. In the molecular structures, hydrogen bonds are shown with **dashed lines**.

The length of hydrogen bonds is slightly less than $3A^{\circ}$. The bond energy varies from 2 to 6 Kcal/mole. It is much lower than the lowest bond-energy 36 Kcal for O-O covalent bond.

The following are some examples of hydrogen bonds seen in biological molecules. Hydrogen bonds are indicated by **dashed lines**.

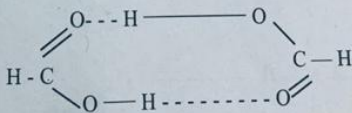


Fig.4.10: Dimer of formic acid.

The macromolecular structure of proteins and nucleic acids are stabilized by hydrogen bonds between amino and keto groups. Hydrogen bonding occurs between hydroxyl groups and between hydroxyl and carboxyl groups.

Hydrogen bonds serve as intermolecular binding forces for the association of molecules formed by primary chemical bonds.

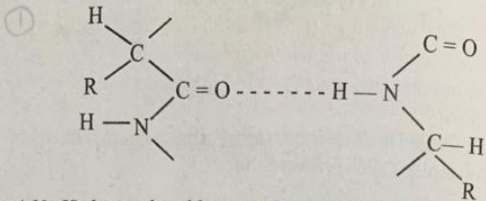


Fig.4.11: Hydrogen bond between keto and imino groups of peptides.

- ◆ They influence the structure and shape of the macromolecules.
- ◆ Hydrogen bonds are predominant in living system. About 70-90% of cytoplasm is made of water where the molecules are linked by means of hydrogen bonds.

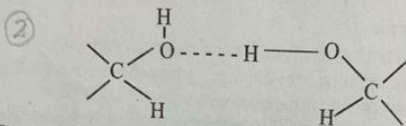


Fig.4.12: Hydrogen bond between hydroxyl groups of peptides.

The mass, structure and electronic configuration of molecules depend upon the number of hydrogen bonds in the molecules. Since molecules are held together by hydrogen bonds, the molecular weight increases simultaneously.

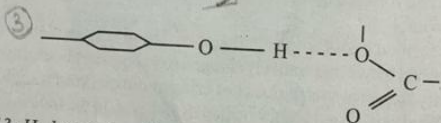


Fig.4.13: Hydrogen bond between hydroxyl group of tyrosine and carboxyl group.

◆ There are also many hydrogen bonds between various groups within a molecule, especially in polypeptides. In such cases, hydrogen bonds do not increase the molecular weight, but increase the number of foldings in the 3-D structure of the molecule.

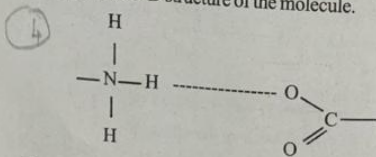


Fig.4.14: Hydrogen bond between amino group and carboxyl group.

◆ In water, H_2O molecules are held together by hydrogen bonding. A water molecule has one oxygen atom and two hydrogen atoms. The oxygen atom forms hydrogen bonds

with two hydrogen atoms of different water molecules. But each hydrogen atom forms a hydrogen bond with an oxygen atom of another water molecule.

Thus, one water molecule is surrounded by 4 water molecules due to hydrogen bonding. The hydrogen bonds determine the **fluidity** of water.

◆ In ice crystal, the H_2O molecules exist in regular **tetrahedrons**. All the H_2O molecules are interconnected by **hydrogen bonds**. Nearly 15% of hydrogen bonds are broken to release the bound water molecules when the ice crystal is melting.

Therefore, water has 15% less hydrogen bonds than in ice crystal. Bond energy of hydrogen bonds in water is measured to be **5 kcal/mole**. It implies that the breaking of hydrogen bond determines the fluidity of water.

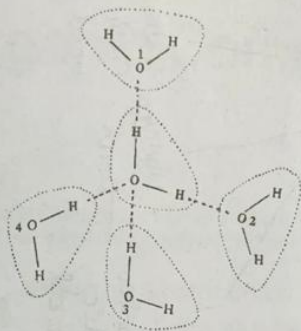


Fig.4.15: Hydrogen bonds in water.

◆ It is observed that about 33% of hydrogen bonds are broken when water is boiling at $100^\circ C$. It reveals the fact that thermal energy is sufficient enough to break hydrogen bonds in water. It is believed that **kinetic energy of thermal motion** breaks the hydrogen bonds in the water.

◆ Experiments have confirmed that the melting point of compounds corresponds to the relative number of hydrogen bonds in them. The melting point increases with the increase in the number of hydrogen bonds in the molecule. As water has the highest proportion of hydrogen bonds, it has the highest melting point.

Table 4.1: Melting points of some chemical compounds.

Compound	Melting Point ($^\circ C$)
H_2O	0
H_2S	-83
H_2Se	-64
H_2Te	-51
HF	-19
HCl	-84
HBr	-67
HI	-36

C. Hydrophobic or nonpolar interactions

The essentiality of hydrophilic (water-loving) properties of biomolecules is obvious. That hydrophobic (water-fearing) characteristics can be valuable may not be as readily apparent. As in the formation of micelles, hydrophobic groups of macromolecules, if in proper spatial relation, will interact (*not bond*) to the exclusion of solvent molecules (water) and thereby reside in a hydrophobic environment. On the contrary, hydrophilic groups usually remain exposed to the aqueous environment where they interact with water molecules. Hydrophobic interactions are a major driving force in the folding of macromolecules, the binding of substrates to enzymes and the formation of membranes that define the boundaries of cells and their internal compartments.

In macromolecules such as proteins, the acceptance or rejection by the aqueous environment of the hydrophilic and hydrophobic moieties respectively exerts a dominant influence on their final conformation. Here the nonpolar side chains of neutral amino acids tend to be closely associated with one another. *The relationship is nonstoichiometric*; hence no true bond may be said to exist. *This clustering together of nonpolar molecules or groups in water is called hydrophobic interaction.* The familiar sight of dispersed oil droplets coming together in water to form a single large oil drop is an analogous process.

To understand the basis of hydrophilic attractions, let us take an example wherein a single nonpolar molecule, such as hexane, is introduced into some water (Fig. 4-11). A cavity in the water is created, which temporarily disrupts some hydrogen bonds between water molecules. The dispersed water molecules then reorient themselves to form a maximum number of hydrogen bonds. The water molecules around the hexane molecule are much more ordered than elsewhere in the solution. Now consider the arrangement of two hexane molecules in water. The two possibilities are: either they sit in two small cavities (Fig. 4-11A) or in a single larger one (Fig. 4-11B). The experimental fact is that

the two hexane molecules come together and occupy a single large cavity. This association releases some of the more ordered water molecules around the separated hexanes. In fact, the basis of a hydrophilic attraction is this enhanced freedom of released water molecules. *Nonpolar 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.*

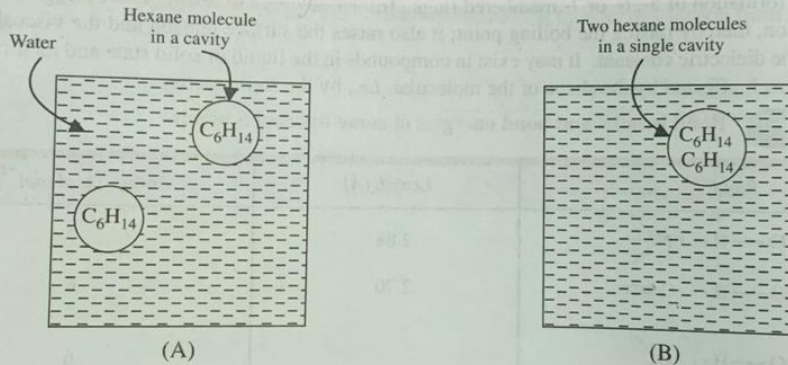


Fig. 4-11. Schematic of two molecules of hexane in a small volume of water

The hexane molecules occupy different cavities in the water structure (A), or they occupy the same cavity, which is energetically more favoured (B).

D. van der Waals interactions

These have already been dealt with in detail in Chapter 2 (*Water: The Solvent of Life*) on pages

F. Van der Waals Interactions

van der Waals interactions (named after J. D. van der Waals) are weak, nonspecific, interatomic attractions and come into play when any two uncharged atoms are 3 to 4 Å apart. Though weaker and less specific than electrostatic and hydrogen bonds, van der Waals interactions are no less important in biological systems. The basis of a van der Waals bond is that the distribution of electronic charge around an atom changes with time.

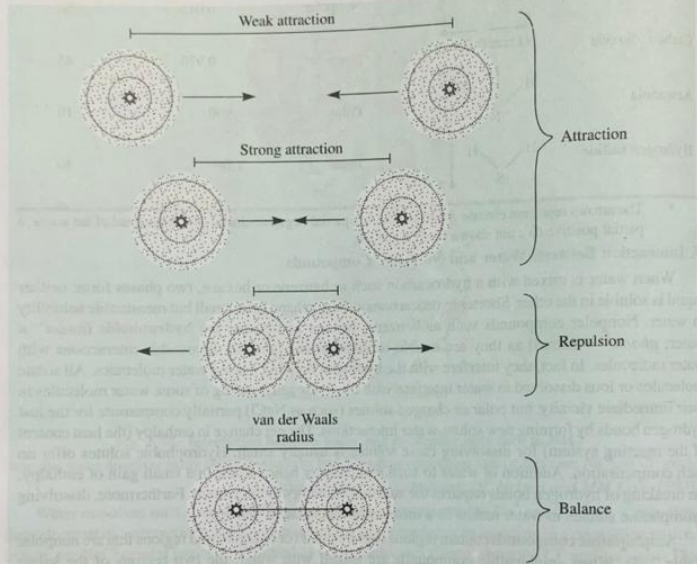


Fig. 2-13. Schematic of van der Waals forces of attraction, repulsion and balance between two atoms

All types of molecules exhibit van der Waals forces which arise from the attraction of the bound electrons of one atom for the nucleus of another. When two atoms are far apart, there is a very weak attraction which becomes stronger as the atoms move closer together (Fig. 2-13). However, if the atoms move close enough for their outer electron shells to overlap, then a force of repulsion occurs. At a certain distance, defined as the *van der Waals contact radius*, there is a balance between the forces of attraction and those of repulsion. Each type of atom has a specific van der Waals contact radius (Table 2-7). At this point of balance, the two atoms are separated by the *van der Waals contact distance* (Fig. 2-14). The contact distance between an oxygen and carbon atom, for example, is 3.4 Å which is obtained by adding 1.4 and 2.0 Å, the contact radii of the O and C atoms, respectively.

Table 2-7. van der Waals contact radii of atoms and group

Atom/Group	Radius (in Å)
H	1.2
O	1.4
N	1.5
S	1.85
P	1.9
C	2.0
CH ₃	2.0

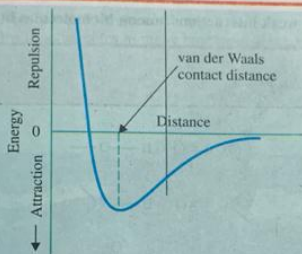


Fig. 2-14. Energy of a van der Waals interaction as a function of the distance between two atoms

The van der Waals bonding energy between two average atoms is very small, *i.e.*, about 1 kcal/mol, which is only slightly greater than the average thermal energy (0.6 kcal/mol) of molecules at room temperature. It is considerably weaker than a hydrogen or electrostatic bond, which is in the range of 3 to 7 kcal/mol. The energy rises rapidly owing to electron-electron repulsion as the atoms move closer together than this distance.

Table 2-8. Strengths of bonds common in biomolecules

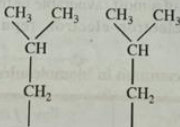
Type of bond	Bond dissociation energy (kJ/mol)	Type of bond	Bond dissociation energy (kJ/mol).
Single bonds		Double bonds	
O—H	461	C = O	712
H—H	435	C = N	615
P—O	419	C = C	611
C—H	414	P = O	502
N—H	389	Triple bonds	
C—O	352	N ≡ N	930
C—C	348	C ≡ C	816
S—H	339	Noncovalent bonds or interactions	
C—N	293	Hydrogen bonds	} 4-20
C—S	260	van der Waals forces	
N—O	222	Hydrophobic bonds	
S—S	214	Ionic interactions	

Since van der Waals interactions are very weak, it is customary to call them as a force rather than a bond. The crystalline compounds possessing these forces are very soft and have low melting points. In fact, the more symmetrical the molecule, the greater are the *van der Waals forces*. These forces are greater for compounds than for atoms and molecules of elements.

ROLE OF NONCOVALENT INTERACTIONS

The noncovalent interactions described above (hydrogen bonds and ionic interactions among charged groups and hydrophobic interactions and van der Waals interactions among nonpolar groups) are much weaker than covalent bonds (Table 2-8). The input of about 350 kJ of energy is required to break a mole (6×10^{23}) of C—C single bonds, and of about 410 kJ to break a mole of C—H bonds, but only 4-8 kJ is sufficient to disrupt a mole of typical van der Waals interactions (Table 2-9).

Table 2-9. Some weak interactions among biomolecules in aqueous solvent

Weak interaction		Stabilization energy (kJ/mol)	
Hydrogen bonds	Between neutral groups	$\text{>C=O} \cdots \text{H—O—}$	8 – 21
	Between peptide bonds	$\text{>C=O} \cdots \text{H—N<}$	8 – 21
Ionic interactions	Attraction	$\text{—}^+\text{NH}_3 \text{—} \leftarrow \text{—} \overset{\text{O}}{\parallel} \text{C—}$	42
	Repulsion	$\text{—}^+\text{NH}_3 \longleftrightarrow \text{H}_3\text{N}^+\text{—}$	≈ -21
Hydrophobic interactions		4 – 8	
van der Waals interactions	Any two atoms in close proximity	4	

Hydrophobic interactions are similarly weak, and ionic interactions and hydrogen bonds are only a little stronger; a typical hydrogen bond can be broken by the input of about 20 kJ/mol. In aqueous solvent at 25°C, the available thermal energy is of the same order as the strength of these weak interactions. Consequently, hydrogen bonds and ionic, hydrophobic and van der Waals interactions are continuously formed and broken.

Although these 4 types of interactions are individually weak relative to covalent bonds, the cumulative effect of many such interactions in a protein or nucleic acid can be very significant. For example, the noncovalent binding of an enzyme to its substrate may involve several hydrogen bonds and one or more ionic interactions, as well as hydrophobic and van der Waals interactions. The formation of each of these weak bonds contributes to a net decrease in free energy; this binding free energy is released as bond formation stabilizes the system.