

Stabilizing Interactions

Weak Chemical Forces and Their Relative Strengths and Distances			
Force	Strength (kJ/mol)	Distance (nm)	Description
Van der Waals interactions	0.4–4.0	0.2	Strength depends on the relative size of the atoms or molecules and the distance between them. The size factor determines the area of contact between two molecules: The greater the area, the stronger the interaction.
Hydrogen bonds	12–30	0.3	Relative strength is proportional to the polarity of the H bond donor and H bond acceptor. More polar atoms form stronger H bonds.
Ionic interactions	20	0.25	Strength also depends on the relative polarity of the interacting charged species. Some ionic interactions are also H bonds: $-\text{NH}_3^+ \dots \text{OOC}-$
Hydrophobic interactions	<40	—	Force is a complex phenomenon determined by the degree to which the structure of water is disordered as discrete hydrophobic molecules or molecular regions coalesce.

Van der Waals Attractive Forces

- ✓ In physical chemistry, the van der Waals force (or van der Waals interaction), named after Dutch scientist Johannes Diderik van der Waals, is the sum of the attractive or repulsive forces between molecules (or between parts of the same molecule) other than those due to covalent bonds, the hydrogen bonds, or the electrostatic interaction of ions with one another or with neutral molecules.
- ✓ Van der Waals forces are the result of induced electrical interactions between closely approaching atoms or molecules as their negatively-charged electron clouds fluctuate instantaneously in time.
- ✓ These fluctuations allow attractions to occur between the positively charged nuclei and the electrons of nearby atoms.
- ✓ At best, van der Waals interactions are weak and individually contribute 0.4 to 4.0 kJ/mol of stabilization energy. However, the sum of many such interactions within a macromolecule or between macromolecules can be substantial.

Van der Waals forces include attractions between atoms, molecules, and surfaces, as well as other intermolecular forces. They differ from covalent and ionic bonding in that they are caused by correlations in the fluctuating polarizations of nearby particles (a consequence of quantum dynamics).

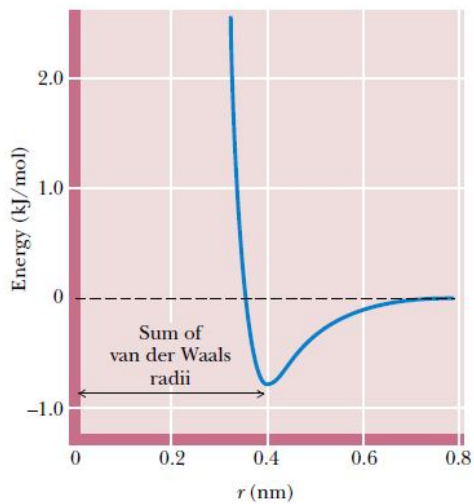
Intermolecular forces have four major contributions:

- A repulsive component resulting from the Pauli exclusion principle that prevents the collapse of molecules.
- Attractive or repulsive electrostatic interactions between permanent charges (in the case of molecular ions), dipoles (in the case of molecules without inversion center), quadrupoles (all molecules with symmetry lower than cubic), and in general between permanent multipoles. The electrostatic interaction is sometimes called the Keesom interaction or Keesom force after Willem Hendrik Keesom.
- Induction (also known as polarization), which is the attractive interaction between a permanent multipole on one molecule with an induced multipole on another. This interaction is sometimes called Debye force after Peter J.W. Debye.
- Dispersion (usually named after Fritz London), which is the attractive interaction between any pair of molecules, including non-polar atoms, arising from the interactions of instantaneous multipoles.

In short

- Force between two permanent dipoles (Keesom force)
- Force between a permanent dipole and a corresponding induced dipole (Debye force)
- Force between two instantaneously induced dipoles (London dispersion force).

The van der Waals interaction energy profile as a function of the distance, r , between the centers of two atoms.

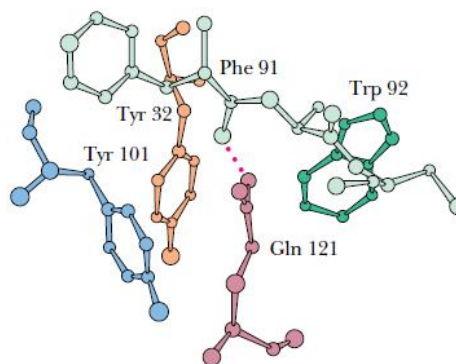
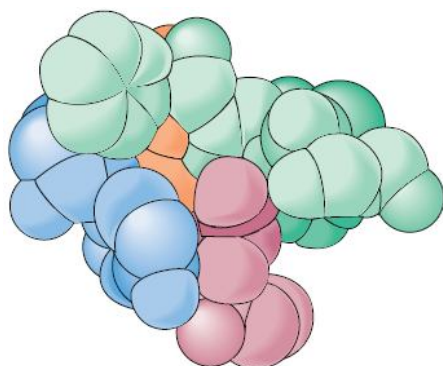


The energy was calculated using the empirical equation $U = B/r^{12} - A/r^6$.

(Values for the parameters $B = 11.5 \times 10^6$ kJnm¹²/mol and $A = 5.96 \times 10^3$ kJnm⁶/mol for the interaction between two carbon (C) atoms are from Levitt, M., 1974, *Journal of Molecular Biology* **82:393–420**.)

Van der Waals attractions operate only over a limited interatomic distance and are an effective bonding interaction at physiological temperatures only when a number of atoms in a molecule can interact with several atoms in a neighboring molecule.







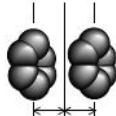
For this to occur, the atoms on interacting molecules must pack together neatly. That is, their molecular surfaces must possess a degree of structural complementarity.



Van der Waals packing is enhanced in molecules that are structurally complementary: Gln¹²¹ represents a surface protuberance on the protein lysozyme. This protuberance fits nicely within a pocket (formed by Tyr¹⁰¹, Tyr³², Phe⁹¹, and Trp⁹²) in the antigen-binding domain of an antibody raised against lysozyme.

- ❑ When two atoms approach each other so closely that their electron clouds interpenetrate, strong repulsion occurs. Such repulsive van der Waals forces follow an inverse 12th power dependence on r ($1/r^{12}$).
- ❑ Between the repulsive and attractive domains lies a low point in the potential curve.
- ❑ This low point defines the distance known as the van der Waals contact distance, which is the interatomic distance that results if only van der Waals forces hold two atoms together. The limit of approach of two atoms is determined by the sum of their van der Waals radii.

Radii of the Common Atoms of Biomolecules

Atom	Van der Waals radius, nm	Covalent radius, nm	Atom represented to scale
H	0.1	0.037	
C	0.17	0.077	
N	0.15	0.070	
O	0.14	0.066	
P	0.19	0.096	
S	0.185	0.104	
Half-thickness of an aromatic ring	0.17	—	

London dispersion force:

London dispersion forces, named after the German-American physicist Fritz London, are weak intermolecular forces that arise from the interactive forces between instantaneous multipoles in molecules without permanent multipole moments. These forces dominate the interaction of non-polar molecules, and also play a less significant role in van der Waals forces than molecules containing permanent dipoles or ionized molecules. London dispersion forces are also known as dispersion forces, London forces, or instantaneous dipole-induced dipole forces. They increase with the molar mass, causing a higher boiling point especially for the halogen group.

Hydrogen Bonds

Hydrogen bonds form between a hydrogen atom covalently bonded to an electronegative atom (such as oxygen or nitrogen) and a second electronegative atom that serves as the hydrogen bond acceptor.

- Hydrogen bonds, at a strength of 12 to 30 kJ/mol, are stronger than van der Waals forces.
- H bonds tend to be highly directional and forming straight bonds between donor hydrogen and acceptor atoms.
- Hydrogen bonds are also more specific than van der Waals interactions because they require the presence of complementary hydrogen donor and acceptor groups.

Bonded atoms	Approximate bond length*
O—H---O	0.27 nm
O—H---O ⁻	0.26 nm
O—H---N	0.29 nm
N—H---O	0.30 nm
N ⁺ —H---O	0.29 nm
N—H---N	0.31 nm

*Lengths given are distances from the atom covalently linked to the H to the atom H-bonded to the hydrogen:

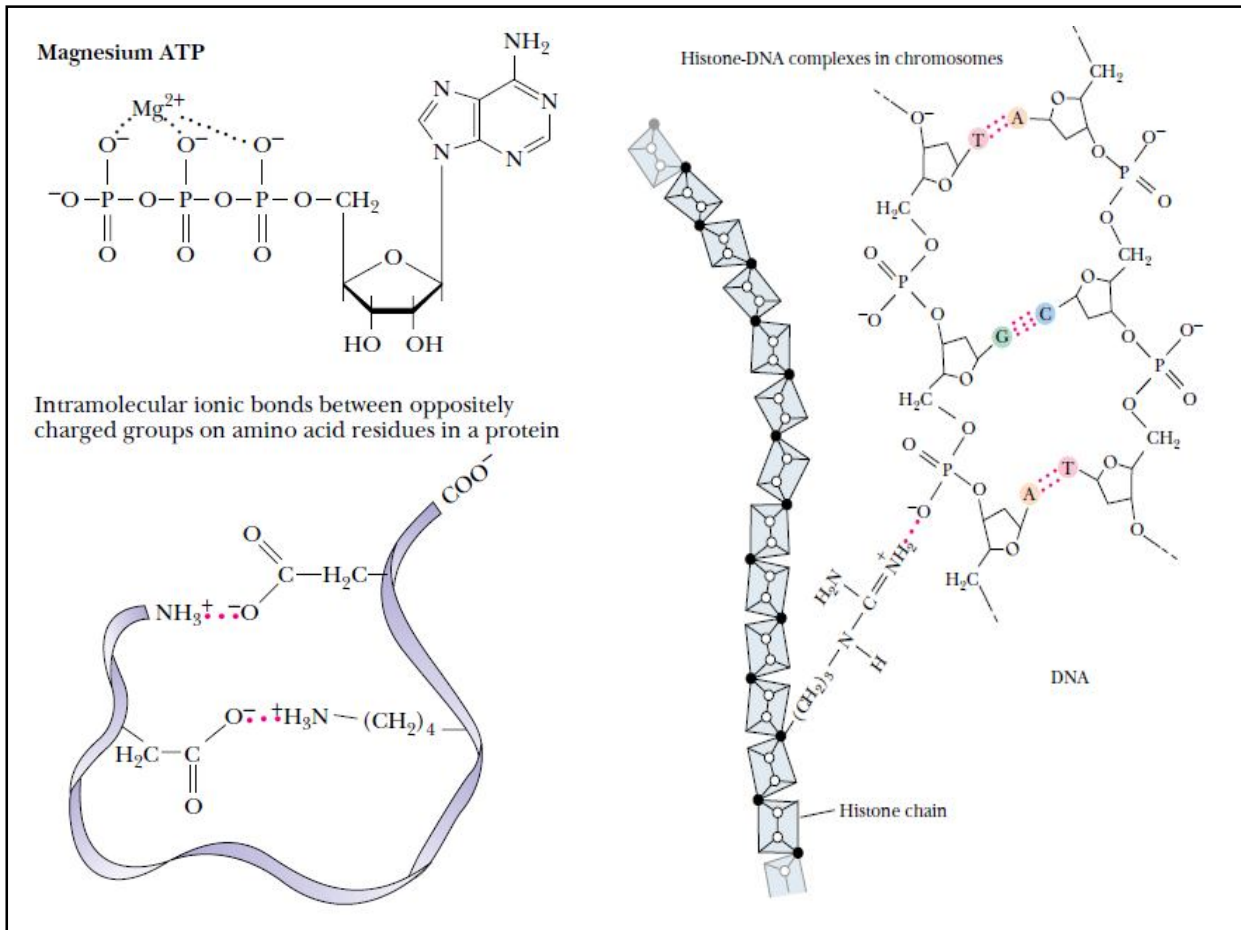
$$\begin{array}{c} \text{O} - \text{H} - \text{---} - \text{O} \\ \left| \text{---} 0.27 \text{ nm} \text{---} \right| \end{array}$$

Functional groups which are important H bond donors and acceptors:

Donors	Acceptors

Ionic interactions

- ✓ Ionic interactions are the result of attractive forces between oppositely charged polar functions, such as negative carboxyl groups and positive amino groups.
- ✓ These electrostatic forces average about 20 kJ/mol in aqueous solutions.
- ✓ Typically, the electrical charge is radially distributed, and so these interactions may lack the directionality of hydrogen bonds or the precise fit of van der Waals interactions.
- ✓ Nevertheless, because the opposite charges are restricted to sterically defined positions, ionic interactions can impart a high degree of structural specificity.
- ✓ The strength of electrostatic interactions is highly dependent on the nature of the interacting species and the distance, r , between them.
- ✓ Electrostatic interactions may involve ions (species possessing discrete charges), permanent dipoles (having a permanent separation of positive and negative charge), and induced dipoles (having a temporary separation of positive and negative charge induced by the environment).
- ✓ Between two ions, the energy falls off as $1/r$. The interaction energy between permanent dipoles falls off as $1/r^3$, whereas the energy between an ion and an induced dipole falls off as $1/r^4$.



Hydrophobic Interactions

- Hydrophobic interactions are due to the strong tendency of water to exclude nonpolar groups or molecules.
- Hydrophobic interactions arise not so much because of any intrinsic affinity of nonpolar substances for one another (although van der Waals forces do promote the weak bonding of nonpolar substances), but because water molecules prefer the stronger interactions that they share with one another, compared to their interaction with nonpolar molecules.
- Hydrogen-bonding interactions between polar water molecules can be more varied and numerous if nonpolar molecules coalesce to form a distinct organic phase.
- This phase separation raises the entropy of water because fewer water molecules are arranged in orderly arrays around individual nonpolar molecules.
- It is these preferential interactions between water molecules that “exclude” hydrophobic substances from aqueous solution and drive the tendency of nonpolar molecules to cluster together.
- Thus, nonpolar regions of biological macromolecules are often buried in the molecule's interior to exclude them from the aqueous milieu.
- The formation of oil droplets as hydrophobic nonpolar lipid molecules coalesce in the presence of water is an approximation of this phenomenon. These tendencies have important consequences in the creation and maintenance of the macromolecular structures and supramolecular assemblies of living cells.