Intermolecular Forces

**Intermolecular forces** are attractive forces *between* molecules.

**Intramolecular forces** hold atoms together in a molecule.

**Intermolecular vs Intramolecular**

- 41 kJ to vaporize 1 mole of water (*inter*)
- 930 kJ to break all O-H bonds in 1 mole of water (*intra*)

Generally, *inter*molecular forces are much weaker than *intra*molecular forces.

"Measure" of intermolecular force

- boiling point
- melting point
- $\Delta H_{\text{vap}}$
- $\Delta H_{\text{fus}}$
- $\Delta H_{\text{sub}}$
Intermolecular Forces

**Ion-Dipole Forces**

Attractive forces between an ion and a polar molecule

[Diagram showing Ion-Dipole Interaction with Na\(^{+}\) and I\(^{-}\) ions]
Ion-Dipole Forces

Directional forces

Can be attractive or repulsive

Medium range \((1/r^2)\)

Significantly weaker than ion-ion interactions
Intermolecular Forces

Dipole-Dipole Forces

Attractive forces between polar molecules

Orientation of Polar Molecules in a Solid
Dipole-Dipole Forces

Directional forces

Can be attractive or repulsive

Short range \( (1/r^3) \)

Significantly weaker than ion-dipole interactions
Intermolecular Forces

Dispersion Forces

Attractive forces that arise as a result of *temporary dipoles induced* in atoms or molecules

![Diagram of ion-induced dipole interaction](image)

ion-induced dipole interaction

![Diagram of dipole-induced dipole interaction](image)
dipole-induced dipole interaction
**Polarizability** is the ease with which the electron distribution in the atom or molecule can be distorted.

Polarizability increases with:

- greater number of electrons
- more diffuse electron cloud

Dispersion forces usually increase with molar mass.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Melting Point (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₄</td>
<td>-182.5</td>
</tr>
<tr>
<td>CF₄</td>
<td>-150.0</td>
</tr>
<tr>
<td>CCl₄</td>
<td>-23.0</td>
</tr>
<tr>
<td>CBr₄</td>
<td>90.0</td>
</tr>
<tr>
<td>Cl₄</td>
<td>171.0</td>
</tr>
</tbody>
</table>

**Table 11.2 Melting Points of Similar Nonpolar Compounds**
Intermolecular Forces

**Hydrogen Bond**

The *hydrogen bond* is a special dipole-dipole interaction between the hydrogen atom in a polar N-H, O-H, or F-H bond and an electronegative O, N, or F atom.

\[
A \rightarrow H \cdots B \quad \text{or} \quad A \rightarrow H \cdots A
\]

A & B are N, O, or F

![Diagram showing examples of hydrogen bonds between N-H, O-H, and F-H bonds and electronegative atoms O, N, and F.](image)
HYDROGEN BONDS: THE STATE-OF-THE-ART

Hydrogen bond definition

Pauling’s definition (1963):

Ch. 12-1. THE NATURE OF THE HYDROGEN BOND
It was recognized some decades ago that under certain conditions an atom of hydrogen is attracted by rather strong forces to two atoms, instead of only one, so that it may be considered to be acting as a bond between them. This is called the hydrogen bond.


He also proposed a symbol for it: 

He associated its stability to electrostatics

First mention:

Recognition of its relevance and widespread occurrence:

First specific book:
A hydrogen bond is said to exist when (1) there is evidence of a bond, and (2) there is evidence that this bond sterically involves a hydrogen atom already bonded to another atom.

Pimentel and McClellan (1960)

Any cohesive interaction where H carries a positive charge and A a negative charge (partial or full) and the charge on H is more positive than on X.

Steiner and Saenger (1993)
Hydrogen bond (~20-60 kJ/mol)

supramolecular synthons are structural units within supermolecules which can be formed and/or assembled by known or conceivable synthetic operations involving intermolecular interactions,
General rule: donor strength is increased by neighboring electron-withdrawing groups and decreased by electron donating groups

O–H > N–H > S–H > C–H

oxygen subclass

H₃O⁺ > O=CH > PhOH > Cₛᵖ₃–OH > H₂O > OH⁻

nitrogen subclass

I⁻N–H > R₃N⁺–H > R₂NH⁺–H > Cₛᵖ₂N–H > Cₛᵖ₃NH > N–NH₂

carbon subclass

Cl₃CH > C≡–H > (RN₂)₂Cₛᵖ₂ –H > (Cl, C)C–sp₃ –H > R₂C –H > R₃C –H > O –CH₃ > CH₃CH₂ –H

Donor/Acceptor Strengths

- Relative acceptor strengths

**General rule:** acceptor strength is increased by neighboring electron-donating groups and decreased by electron withdrawing groups

**oxygen subclass**

\[
\text{OH}^- > \text{COO}^- > \text{H}_2\text{O} > \text{C}_{sp3}^-\text{OH} \geq \text{Ph}^-\text{OH} > \text{C}^\text{--NO}_2 \geq \text{M}^-\text{CO}
\]

**nitrogen subclass**

\[
\text{C}_{sp3}^-\text{NH}_2 > \text{R}_2\text{N}^-\text{H} \geq \text{R}_3\text{N}^-\text{H} > \text{CN} > \text{C}_{sp2}^-\text{NH}_2 > \text{C}^\text{=N}^-\text{S}
\]

**halogen subclass**

\[
\text{F}^- > \text{C}^-\text{F} > \text{Cl}^- > \text{Br}^- > \text{I}^-
\]

- These trends are highly dependent on acceptor/donor pairings

Other interesting characteristics

- Cooperativity

\[ \delta^- \quad \delta^+ \quad X - H \quad \delta^- \quad \delta^+ \quad \delta^- \quad \delta^+ \]

\[ X - H - \quad X - H - \quad Y - H - \quad X - H \]

- Charges flow through the X–H sigma bonds.
- This effect drives the clustering of polar groups (e.g. carbohydrates)
- Anticooperativity

Hydrogen bonds may not only enhance, but also reduce the strengths of each other.
Evidence of H-bonding by X-ray and Neutron Diffraction Studies

- \( r, d \) and \( \alpha \) are the main parameters to characterise an \( A-H-B \) hydrogen bond. For X-ray data \( R \) is often used as \( r \) and \( d \) cannot be determined accurately.

- In order to claim an \( A-H-B \) hydrogen bond, \( \alpha \) must be close to linearity and \( d \) has to be smaller than the sum of the van der Waals radii of \( B \) and \( H \) minus an arbitrary value in the range of 0.1-0.2 Å.
The categories of Hydrogen Bonds (HB)

Classification such as weak, strong, and........................ possibly also in between.

Hydrogen bonds can be considerate **moderate** if they resemble those between water molecules or in carbohydrates (also call **normal**), with energies in the range 4 — 15 kcal/mol

Hydrogen bonds with energies above and below this are termed **strong** and **weak**, respectively.
The categories of Hydrogen Bonds (HB)

<table>
<thead>
<tr>
<th>Interaction Type</th>
<th>Strong</th>
<th>Moderate</th>
<th>Weak</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bond Lengths (Å)</td>
<td>1.2–1.5</td>
<td>1.5–2.2</td>
<td>2.2–3.3</td>
</tr>
<tr>
<td>X–H vs. H- - -A</td>
<td>X–H ≈ H- - -A</td>
<td>X–H&lt;H- - -A</td>
<td>X–H &lt;&lt; H- - -A</td>
</tr>
<tr>
<td>X- - -A (Å)</td>
<td>2.2–2.5</td>
<td>2.5–3.2</td>
<td>&gt;3.2</td>
</tr>
<tr>
<td>Directionality</td>
<td>Strong</td>
<td>Moderate</td>
<td>Weak</td>
</tr>
<tr>
<td>Bond Angles (°)</td>
<td>170–180</td>
<td>&gt;130</td>
<td>&gt;90</td>
</tr>
<tr>
<td>$^1$H Downfield Shift</td>
<td>14–22</td>
<td>&lt;14</td>
<td>&lt;4</td>
</tr>
<tr>
<td>Bond Energy (kcal/mol)</td>
<td>15–40</td>
<td>4–15</td>
<td>&lt;4</td>
</tr>
</tbody>
</table>

The "normal" H-bond

The categories of HB

**strong hydrogen bonds** exist when the pK\(_a\) of the hydrogen bond donor is similar to the pK\(_a\) of the conjugate acid of the acceptor

Very strong hydrogen bonds are formed only if the pK\(_a\) values of the partners are suitably matching.
Qualitative properties of HB lengths

- Strong hydrogen bonds

Strong hydrogen bonds can be grouped into several classes
- combination of acids with their conjugate base

\[
\begin{align*}
\text{X--H--X} & \rightleftharpoons \text{X--H--X}^- \\
\text{X--H--X}^+ & \rightleftharpoons \text{X--H--X}
\end{align*}
\]

similarly

\[
\begin{align*}
\text{X--H--X}^- & \rightleftharpoons \text{X--H--X}^+ \\
\text{X--H--X} & \rightleftharpoons \text{X--H--X}^-
\end{align*}
\]

pKa \(X \approx \) pKa \(A\)

proton transfer leads to a chemically equivalent situation

pKa \( \sim 4.76\)

pKa \( \sim -1.7\)
Qualitative properties of HB lengths

Strong hydrogen bonds

Strong hydrogen bonds can be grouped into several classes

- Chemically unrelated partners can form strong hydrogen bonds only, if their pKa values match at least roughly. Interesting examples are hydrogen bonds between carboxylic acids and N-oxides.
The categories of HB

\[
\begin{array}{c}
\text{pKa values very different: moderate } X-H---Y^+ \\
\text{or ionic } X^{-}---H-Y \text{ hydrogen bond is formed}
\end{array}
\]

<table>
<thead>
<tr>
<th></th>
<th>H\cdots\cdot B</th>
<th>A\cdots\cdot B</th>
<th>A\cdash H\cdots\cdot B</th>
<th>bond energy kcal/mole</th>
</tr>
</thead>
<tbody>
<tr>
<td>medium</td>
<td>1.5-2.2Å</td>
<td>2.5-3.2Å</td>
<td>130-180°</td>
<td>4-14</td>
</tr>
</tbody>
</table>
The categories of HB

<table>
<thead>
<tr>
<th>H---B</th>
<th>A---B</th>
<th>A---H---B</th>
<th>bond energy kcal/mole</th>
</tr>
</thead>
<tbody>
<tr>
<td>medium</td>
<td>1.5-2.2 Å</td>
<td>2.5-3.2 Å</td>
<td>130-180°</td>
</tr>
</tbody>
</table>

1.011 Å (neutron diffraction)

1.642 Å (X-ray crystal structure)
The categories of HB

<table>
<thead>
<tr>
<th>Medium</th>
<th>Bond Length</th>
<th>Bond Angle</th>
<th>Bond Energy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5-2.2 Å</td>
<td>2.5-3.2 Å</td>
<td>130-180°</td>
<td>4-14 kcal/mole</td>
</tr>
</tbody>
</table>

**Diagram:**

- Medium
  - Bond Length: 1.5-2.2 Å
  - Bond Angle: 130-180°
  - Bond Energy: 4-14 kcal/mole

- Gas phase
  - Bond Length: 1.04 Å
  - Bond Energy: 2.629 Å

- Crystal structure
  - Bond Length: 1.66 Å
The categories of HB

<table>
<thead>
<tr>
<th></th>
<th>bond energy kcal/mole</th>
</tr>
</thead>
<tbody>
<tr>
<td>medium</td>
<td></td>
</tr>
<tr>
<td>H ..... B</td>
<td>1.5-2.2Å</td>
</tr>
<tr>
<td>A ..... B</td>
<td>2.5-3.2Å</td>
</tr>
<tr>
<td>A − H ..... B</td>
<td>130-180°</td>
</tr>
</tbody>
</table>

Diagram:

- The distance between H and B is 2.820 Å.
Qualitative properties of HB lengths

Moderate hydrogen bonds

\[ \text{X--H--A} \]

\[ d_1 < d_2, \text{ X–H is long compared to weak bonds} \]

- moderate bonds have both weak and strong characteristics and tends to be blurred depending upon the experimental treatment
- generally regarded as electrostatic
Qualitative properties of HB lengths

- C–H donor groups are most widely studied, includes the H-bond pi interaction
- generally regarded as electrostatic/dispersed
- ability to form bifurcated and trifurcated structures

\[
\begin{align*}
\delta^- & \quad d_1 \quad d_1 \quad \delta^+ \\
X & \quad H^- \quad - \quad -A
\end{align*}
\]

\(d_1 < d_2\), \(X–H\) is shorter than in moderate H bonds

O/N–H bonded species are 2–4 kcal/mol higher with neutral species and 15 kcal/mol higher in charged species

- A reasonable way of thinking about the H-Bond is as a frozen proton transfer event
- Currently no widely accepted theoretical method for predicting H bonds exists
Geometries of H-bond

Donor Directionally

The main structural feature distinguishing the hydrogen bond from the van der Waals interaction is preference for linearity.

To obtain the more relevant frequencies per solid angle, one must weight the absolute values with $1/\sin \theta$ (cone correction $\int$).

Directionality of OH...O hydrogen bonds in carbohydrates

The probability that the angle is $180^\circ$ is proportional to $\sin \theta$: conic factor or correction.
Geometries of HB

Donor Directionally
Geometries of H-bond

Donor Directionally

The degree of directionality depends on the polarity of the donor

Decrease gradually from (a) to (d) and interaction (e)

1) donors

2) Van der Waals

X-H···Y angle/°
**Geometries of H-bond**

- **Two centered hydrogen bonds**
  - most understood and researched
  - ![Diagram](image)

- **Three centered hydrogen bonds or bifurcated H bond**
  - most examples are found in biology, carbohydrates (~25%) and amino acids (over 25%)
  - ![Diagram](image)
  - ![Diagram](image)
Geometries of H-bond

- Four centered hydrogen bonds or trifurcated H bond
  - Rare
  - Also found in biology

Close pairs of carboxylates: a possibility of multicenter hydrogen bonds in proteins

Ivan Y. Torshin, Robert W. Harrison, and Irene T. Weber

Protein Engineering vol.16 no.3 pp.201–207, 2003
DOI: 10.1093/proeng/gzg027

Fig. 1. A model of hydrogen bonding between a pair of carboxylates. (a) Maximal O–H distance; (b) maximal O–O distance.