Atomic and molecular interaction forces in biology
Outline

• Types of interactions relevant to biology
  • Van der Waals interactions
  • H-bond interactions
Types of interactions

• Interactions between different types of particles are responsible for assembly, shape and dynamical evolution of living matter.

• Main interactions are:
  – Covalent bonds, including disulphide bonds (attractive)
  – Electrostatic interactions (attractive/repulsive)
  – Van der Waals interactions (attractive)
  – Hydrogen bonds (attractive)
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Van der Waals interactions

Attractive interaction between molecules going as $\sim 1/r^6$

- Due to interactions between permanent and induced dipoles
  - Composed of three terms:
    1. (Permanent) dipole-dipole (a.k.a. Keesom) interactions
    2. Dipole-induced dipole interactions
    3. Induced dipole-induced dipole interactions, a.k.a. London or dispersion interactions
Keesom interactions

Occur only between polar molecules

Potential energy of interaction between two dipoles $\mu_1$ and $\mu_2$:

$$ V = \frac{\mu_1 \mu_2 f(\theta)}{4 \pi \varepsilon_0 r^3}, \quad f(\theta) = 1 - 3 \cos^2 \theta $$

If dipoles (molecules) were freely rotating, then:

$$ \langle f(\theta) \rangle = 0 \rightarrow \langle V \rangle = \frac{\mu_1 \mu_2 \langle f(\theta) \rangle}{4 \pi \varepsilon_0 r^3} = 0 $$

However, potential energy depends on mutual orientation.

Molecules do not rotate freely, low-energy orientations slightly favored:

$$ \langle V \rangle = -\frac{C}{r^6}, \quad C = \frac{2 \mu_1^2 \mu_2^2}{3 (4 \pi \varepsilon_0)^2 kT} $$

Keesom interaction
Keesom interactions

\[ \langle V \rangle = -\frac{C}{r^6}, \quad C = \frac{2\mu_1^2\mu_2^2}{3(4\pi\varepsilon_0)^2kT} \]

- Derived assuming \( V \ll kT \)
- Goes as \( r^6 \), thus is a van der Waals interaction
  - Inversely proportional to temperature
    (higher \( T \) ↔ lower barrier to rotation)
  - Inversely proportional to square of permittivity \( \varepsilon_0 \).
Dipole-induced dipole interactions

- Polar molecule with dipole $\mu_1$ can induce dipole $\mu^*_2$ in neighboring polarizable molecule.

- Induced dipole interacts with permanent one giving net attraction.

\[
\langle V \rangle = -\frac{C}{r^6}, \quad C = \frac{\mu_1^2 \alpha'_2}{4\pi \varepsilon_0}, \quad \alpha'_2 \approx \frac{1}{4\pi \varepsilon_0} \frac{2e^2 R^2}{\Delta E_{\text{LUMO-HOMO}}}
\]

Dipole-induced dipole interaction

- Goes as $r^6$, thus is a van der Waals interaction
- $\alpha'_2 \rightarrow$ polarizability volume of molecule 2
- Independent of $T$
London (dispersion) interactions

Some evidences for interactions between non-polar molecules

• Formation of liquid phases of non-polar substances (H, Ar) at low T
  • Benzene liquid at normal T
  • ...

PLEASE NOTE! This material is meant just as a guide, it does not substitute the books suggested for the Course.
London (dispersion) interactions

Weak interactions caused by momentary changes in electron density in a molecule.

Two electrically neutral, closed-shell atoms in proximity

Temporary dipole resulting from quantum fluctuation

\( \delta^- \quad \delta^+ \)

\( \delta^- \quad \delta^+ \)

\( \delta^- \quad \delta^+ \)

\( \delta^- \quad \delta^+ \)

Gives net attraction

Induced dipole, due to presence of other dipole
London (dispersion) interactions

- As two dipoles attract each other, potential energy of pair lowers.
- When size and direction of instantaneous dipole of first molecule changes, electron distribution of second molecule will follow.

\[ \delta^- + \delta^+ \]

Two dipoles correlated in direction, so that attraction between two instantaneous dipoles does not average to zero!

Temporary dipole resulting from quantum fluctuation

\[ \delta^- \quad \bullet \quad \delta^+ \]

Gives net attraction

Induced dipole, due to presence of other dipole
London (dispersion) interactions

\[ \langle V \rangle = -\frac{C}{r^6}, \quad C = \frac{3}{2} \alpha_1' \alpha_2' \frac{I_1 I_2}{I_1 + I_2} \]

**London formula: dispersion potential**

- Precise formulation involved, but London formula good approximation to true interaction energy.
- Proportional to polarizabilities of both molecules.
- Proportional to ionization energies of both molecules.
- All (macro)molecules interact through dispersion forces.
- Only attractive forces present in nonpolar compounds!
London (dispersion) interactions

The larger the surface area, the larger the attractive force between two molecules, the stronger the intermolecular forces (due to relation between radius and polarizability).
London (dispersion) interactions

Indeed (beginning of whole history)...

Boiling point of liquids formed by H bound to elements of Periods 3, 4, 5 and Groups 15, 16, 17

Increase in boiling point across same Period of Table of elements...

- Molecules get larger (contain more electrons) across Period
- Dispersion forces become greater
London (dispersion) interactions

Force proportional to polarizabilities.

small, less polarizable atoms

weaker force of attraction

large polarizable atoms

stronger force of attraction
Van der Waals interactions

\[
\langle V \rangle = -\frac{1}{r^6} \left( \frac{2 \mu_1^2 \mu_2^2}{3(4\pi\varepsilon_0)^2 kT} + \frac{\mu_1^2 \alpha'_2}{4\pi\varepsilon_0} + \frac{3}{2} \alpha'_1 \alpha'_2 \frac{I_1 I_2}{I_1 + I_2} \right)
\]

Van der Waals interaction energy

<table>
<thead>
<tr>
<th>Interaction type</th>
<th>Typical energy (kcal/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keesom</td>
<td>~0.4 (at ~3 Å)</td>
</tr>
<tr>
<td>Dipole-induced dipole</td>
<td>~0.2 (at ~3 Å)</td>
</tr>
<tr>
<td>London (dispersion)</td>
<td>~0.5 (at ~3 Å)</td>
</tr>
</tbody>
</table>

London dispersion forces usually dominate interactions between molecules having no H-bonding groups.
Limitations of vdw theory

- Van der Waals equation has limited validity!
  - Do not include higher-order multi-pole interactions, important if molecules do not have permanent electric dipole moments (although dipolar interactions dominant when average separation of molecules is large).
  - Expressions derived by assuming that molecules can rotate freely. Not true in rigid media, where interaction goes as $1/r^3$ (Boltzmann averaging irrelevant when molecules are trapped in fixed orientation).
Limitations of vdw theory

Van der Waals equation has limited validity!

• Summing up only pairwise interaction energies not correct.

• Total dispersion energy of three closed-shell atoms, for instance, given approximately by Axilrod–Teller formula:

\[
\langle V \rangle = - \frac{C}{r_{AB}^6} - \frac{C}{r_{BC}^6} - \frac{C}{r_{CA}^6} + \frac{C'}{(r_{AB}r_{BC}r_{CA})^3}, \quad C' = a(3 \cos \theta_A \cos \theta_B \cos \theta_C + 1)
\]

Non-additive three-body term

• Three-body term contributes up to 10% of interaction energy in liquid argon.
Van der Waals example in life

Geckos climb over glass thanks to London dispersion forces!
Types of interactions

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H-bonds

• How it is an H-bond defined?

• Term used in literature for nearly a century.

• Importance realized by physicists, chemists, biologists, and material scientists, however…complex phenomenon and continual debate about what this term means…

New (short) definition adopted by IUPAC in 2011:

“The hydrogen bond is an attractive interaction between a hydrogen atom from a molecule or a molecular fragment D–H in which D is more electronegative than H, and an atom or a group of atoms in the same or a different molecule, in which there is evidence of bond formation.”
H-bonds

Involves three atoms:

D–H ⋯ A

• Hydrogen H bound to donor D

• Donor atom D, which must be more electronegative than H
  (nitrogen, oxygen and less frequently fluorine in biomolecules)

• Acceptor electronegative atom (A) in close proximity
H-bonds

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

\[ \text{D-H} \quad \cdots \quad \text{A} \]

D more electronegative than H

\[ \Downarrow \]

Electron withdrawal from H to D

\[ \Downarrow \]

Polarization of D-H bond:
D and H bear partial negative and positive charges

- Proximity of acceptor A induces further polarization

\[ \Downarrow \]

- Close approach of A to H

- Higher interaction energy than simple van der Waals
H-bonds

Six criteria indicated to have evidence of bond formation:


2. Nature of physical forces involved in H-bond:
   I. No single physical force ascribed to H-bonds, but interaction should not be primarily due to dispersion force, which is not highly directional.
   II. Electrostatic forces play significant role in directionality of H-bonding (connected with requirement that D and A are more electronegative than H).

4. Based on spectroscopy:
   I. Red-shift in D–H vibrational frequency observed in IR.
   II. De-shielding of H in D-H observed in NMR.
H-bonds

Six criteria indicated to have evidence of bond formation:

6. Energetic:
   
   I. Energetic limit for binding energy not specified and very subjective.

   II. However, thermal vibrational energy along all coordinates that can break H-bond should be less than potential barriers for breaking H-bond along those coordinates.
H-bonds

Six typical characteristics observed in H-bonded systems:

2. Proton transfer as intermediate between D–H⋯A and D⋯H–A.
3. Directionality and the resultant influence in crystal packing.
4. Correlation between extent of charge transfer and H-bond strength.
5. (3,−1) bond critical point between H and A in electron density topological analysis (see Bader’s AIM theory).
6. Strong correlation between pK\textsubscript{a} of D–H and pK\textsubscript{b} of A–Z with energy of H-bond formed between them.
**H-bond forming liquids**

- Boiling point of compounds containing first element in each group abnormally high (particularly true for water).
- Electronegativity decreases monotonically from top to bottom in periodic table.
- Some additional intermolecular forces of attraction must be significant in addition to induced dipole (van der Waals) forces \( \rightarrow \) H-bonds due to permanent dipoles!
H-bond forming liquids

Why HF boils at higher T than NH$_3$?

- F significantly more electronegative than N.
- H-F bond more polar than N-H. NH$_3$ has dipole moment $\sim$1.4 D, HF $\sim$1.9D.
- Very strong H-bonding occurs between HF molecules leading to higher boiling point.
H-bond forming liquids

Why $\text{H}_2\text{O}$ boils at higher $T$ than $\text{HF}$?

• Despite F is more electronegative than O, H-bond interactions in HF are so strong that HF exists as H-bonded dimers (and even larger clusters) in vapour, whereas $\text{H}_2\text{O}$ is only H-bonded when liquid or ice.

• Not all H-bonds need to break to boil HF → lower boiling point than $\text{H}_2\text{O}$.
H-bond forming liquids

Why $\text{H}_2\text{O}$ boils at higher $T$ than $\text{HF}$ and $\text{NH}_3$?

- Each $\text{H}_2\text{O}$ molecule has two $\text{H}$ atoms and the $\text{O}$ atom has two lone pairs
  $\rightarrow$ when $N_{\text{mol}} \gg 1$, each couple of water molecules can make two H-bonds.

- $\text{HF}$ has only 1 $\text{H}$ and $\text{NH}_3$ has only one lone pair on $\text{N}$
  $\rightarrow$ when $N_{\text{mol}} \gg 1$, both can only make only one H bond.

* NB: These pictures are only meant to show the H-bond possibilities of each molecule!
References

• Books, journals, etc…
  • Atkins, Physical Chemistry 9th ed., chap. 18
  • Arunan et al., Pure Appl. Chem. 83, 1619 (2011)
  • Arunan et al., Pure Appl. Chem. 83, 1637 (2011)

• Online resources
  • http://www.wiley.com/legacy/wileychi/ecc/samples/sample02.pdf
  • http://www.cryst.bbk.ac.uk/PPS2/projects/loesel/chap03c.htm