INTERNATIONAL COLLEGE OF PHARMACEUTICAL INNOVATION

国际创新药学院

Class	Pharm, BioPharm
Course	Fundamentals of Medicinal & Pharmaceutical Chemistry
Code	FUNCHEM.8
Title	Intermolecular interactions: The medical importance of water in the body.
Lecturer	Prof. Xinchen Teng
Date	2024-10-25

RECOMMENDED READING

- General Chemistry - The Essential Concepts by Chang and Goldsby (7th edition)
  - Section 10.2
  - Section 12.1 – 12.3

Learning outcomes

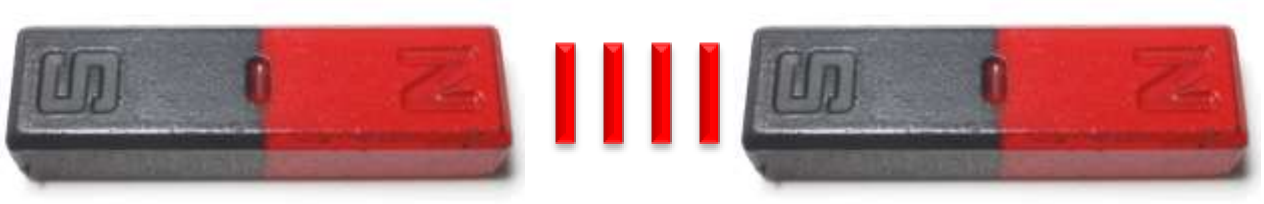
- Recall ‘electronegativity’ and explain how dipoles arise in molecules.
- Recall rules for assigning whether a molecule has a net dipole moment taking into account both polarity and shape.
- Recall and explain ion-dipole, dipole-dipole, dipole-induced dipole and instantaneous dipole-induced dipole forces of attraction.
- Recall and explain hydrogen bonding and how it can account for physical properties such as melting and boiling points.
- Differentiate, in terms of strength of interaction, between different types of intermolecular forces of attraction.
- Discuss medical, biochemical and pharmacological implications associated with intermolecular forces of attraction.

Intermolecular forces

- ***Inter***molecular forces are:
  - attractive forces between molecules.
  - primarily responsible for the bulk properties of matter (for example, melting point and boiling point).
  - are much weaker than ***intra***molecular forces which hold atoms together in a molecule.
    - E.g. 41 kJ will evaporate 1 mole of water at its boiling point. 930 kJ is required to break the two O-H bonds in one mole of water molecules.
  - Boiling points and melting points of substances often reflect the strength of intermolecular interactions.
  - The state of matter is determined by the strength of the intermolecular interactions
    - Solid, Liquid and Gas

The basis of intermolecular interactions

- A magnet demonstrates the fundamental requirements for intermolecular interactions.
- Attraction occurs between oppositely charged regions.



Magnets

Molecules

Dipoles

- In a previous lecture you learned that H-F is a covalent compound with a polar bond.
- When a molecule has a δ+ and a δ- end then the molecule is said to be polarised or possess a dipole.
- Dipoles arise from the unequal sharing of electrons in a covalent bond.
- Electronegativity of atoms determine the sharing of electrons in bonds.
- The greater the electronegativity the greater the dipole.

δ+ H – F δ-

The shift of electron density is symbolized by placing a crossed arrow above the structure to indicate the direction of the e^- shift

δ+ H – F δ-

δ+ H – Cl δ-

δ+ H – Br δ-

δ+ H – I δ-

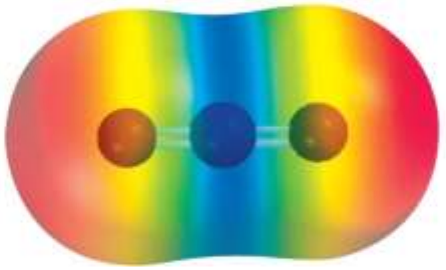
δ (delta) denotes a partial charge

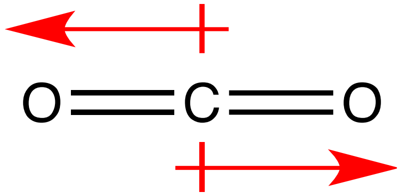
A guide to dipole moments

- The quantitative measure of the degree of polarity in a bond or molecule.
- Diatomic molecules containing the same atoms have no dipole moment
  - e.g. H_2, Cl_2, $O_2 = 0_D$ i.e. NON POLAR
- Diatomic molecules containing different atoms may have dipole moments
  - e.g. HCl, CO, NO $> 0_D$ i.e. POLAR
- The Dipole moment of polyatomic molecules depends on:
  - Polarity of the bonds.
  - Shape of the molecule.

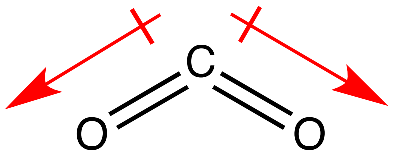
Shape and polarity

- In CO_2 the two dipole moments are equal.
- If CO_2 is a linear molecule, the dipoles are opposite in direction = 0 $_D$
- If CO_2 is a bent the moments are not completely opposite > 0 $_D$





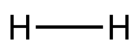
No dipole moment

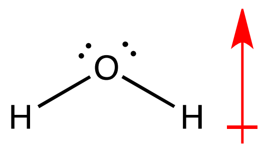


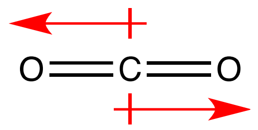
Would have dipole moment

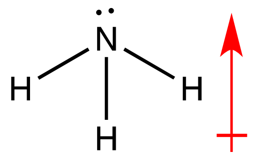
Dipole moments

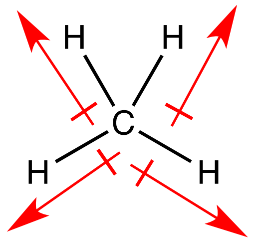
- **Molecule** **Dipole moment**
- H_2 0 D
- H_2O 1.94 D
- CO_2 0 D
- NH_3 1.46 D
- CH_4 0 D







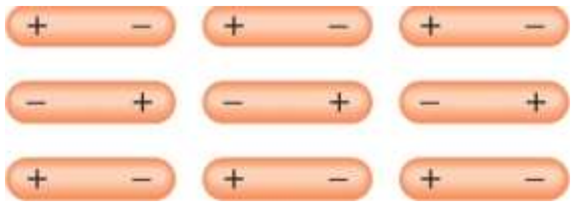


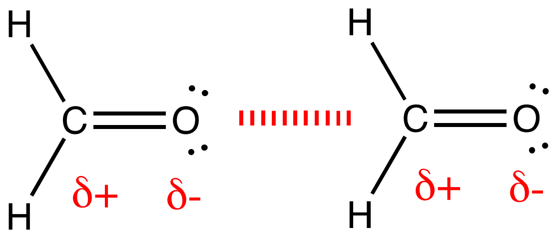


Watch the animation titled 'Polarity of molecules' on the VLE

1. Dipole – dipole forces

- Dipole-dipole interactions occur between polar molecules (i.e. molecules that possess a dipole moment).
- The larger the dipole moment the larger the force.
- To the right is an illustration of alignment of polar molecules in a solid.
- Alignment of polar molecules in a liquid is not a rigid but similar.



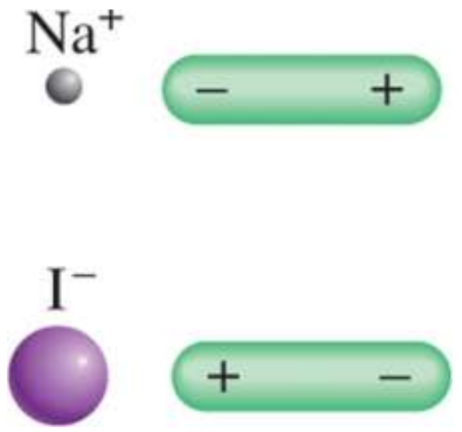


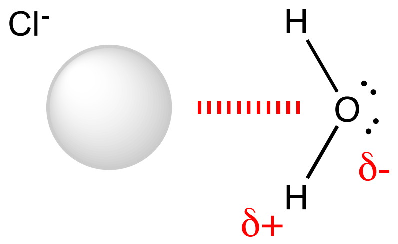
2. Ion – dipole forces

- The attractive forces between an ion and a polar molecule.

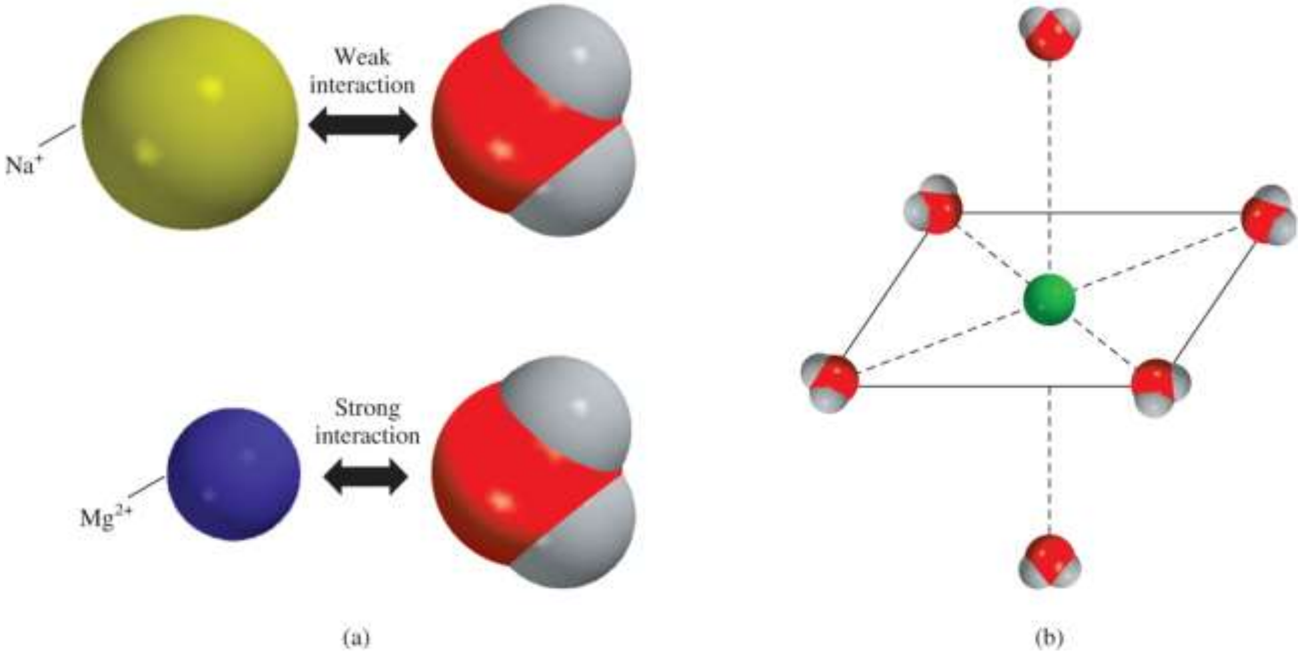
- The strength of the interaction depends on the charge and size of the ion and the magnitude of the dipole moment and size of the molecule.

- Hydration of ions is an example of ion – dipole forces.

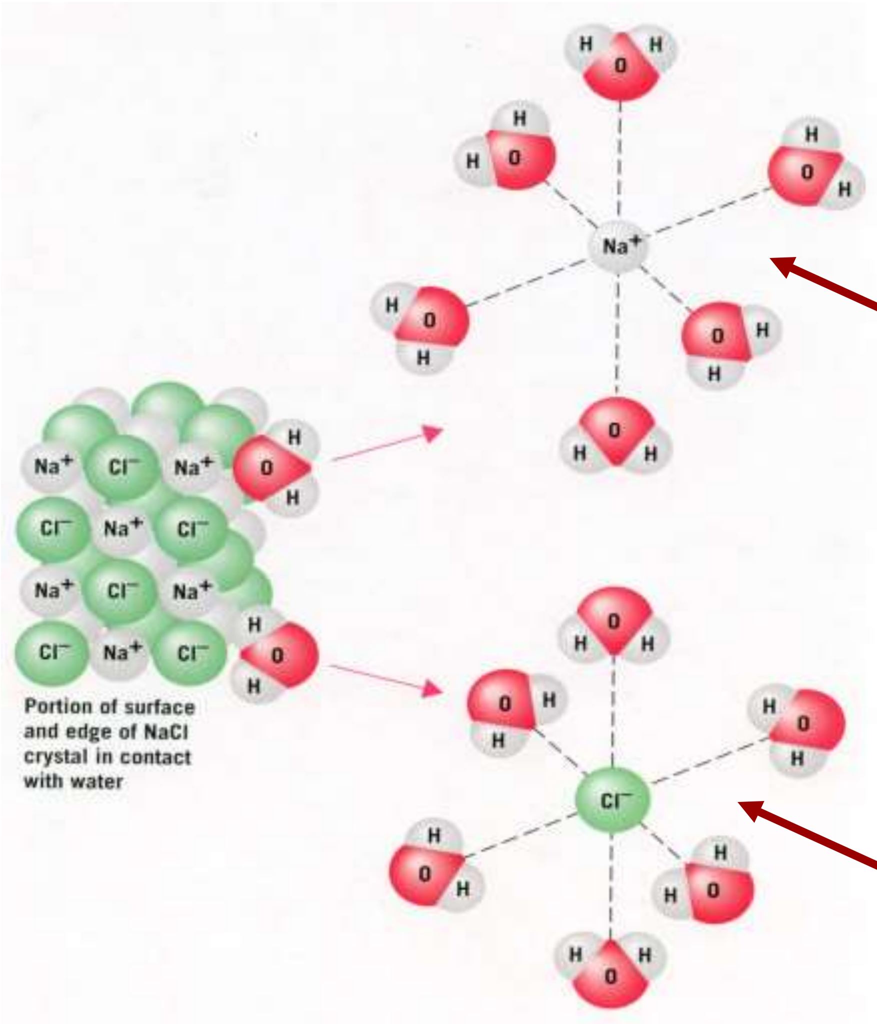




Ion – dipole forces – variable magnitude



Mg^{2+} ion has a higher charge and a smaller ionic radius (78 pm) than that of the Na^{+} ion (98 pm), it interacts more strongly with water molecules

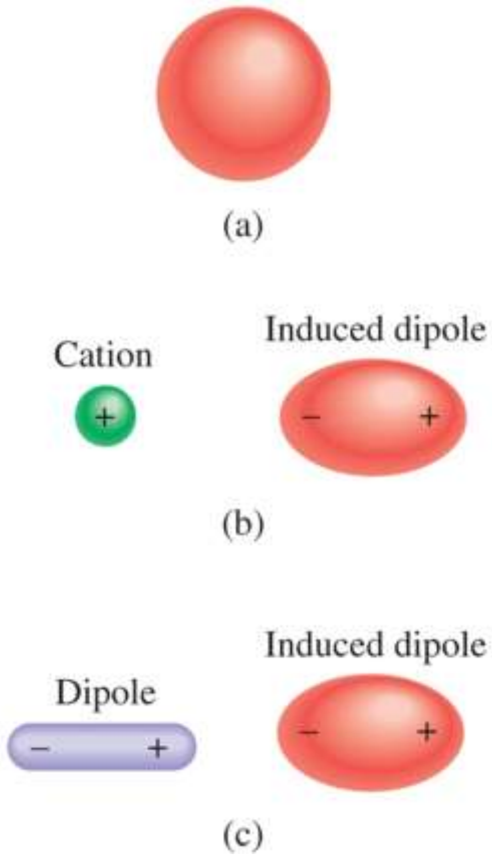


Ion - Dipole

Ion - Dipole

3. Ion – induced dipole forces
4. Dipole – induced dipole forces

- When an ion or polar molecule is placed next to an atom or non-polar molecule, the e- distribution of the atom (or molecule) is distorted by the force of the ion or dipole moment.
- The dipole in the atom or molecule is said to be an induced dipole.
- The extent to which a dipole is induced depends on:
  - Charge on ion or size of dipole moment
  - Polarizability of atom or non-polar molecule



Polarizability is the ease with which the electron distribution in the atom (or molecule) can be distorted. Generally more e- means more polarizable.

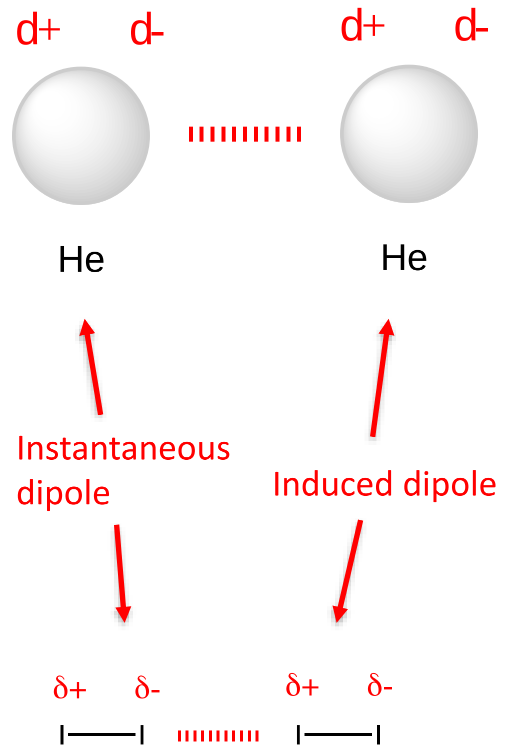
5. Instantaneous dipole – induced dipole forces

- Polarizability enables the creation of instantaneous dipole moments.

- At any instant it is likely that an atom or non-polar molecule will have a dipole moment (instantaneous dipole)

- An instantaneous dipole can induce a dipole in each of its nearest neighbors.

- The magnitude of this attractive interaction is directly proportional to the polarizability of the atom or molecule



5. Instantaneous dipole – induced dipole forces – Also known as dispersion forces

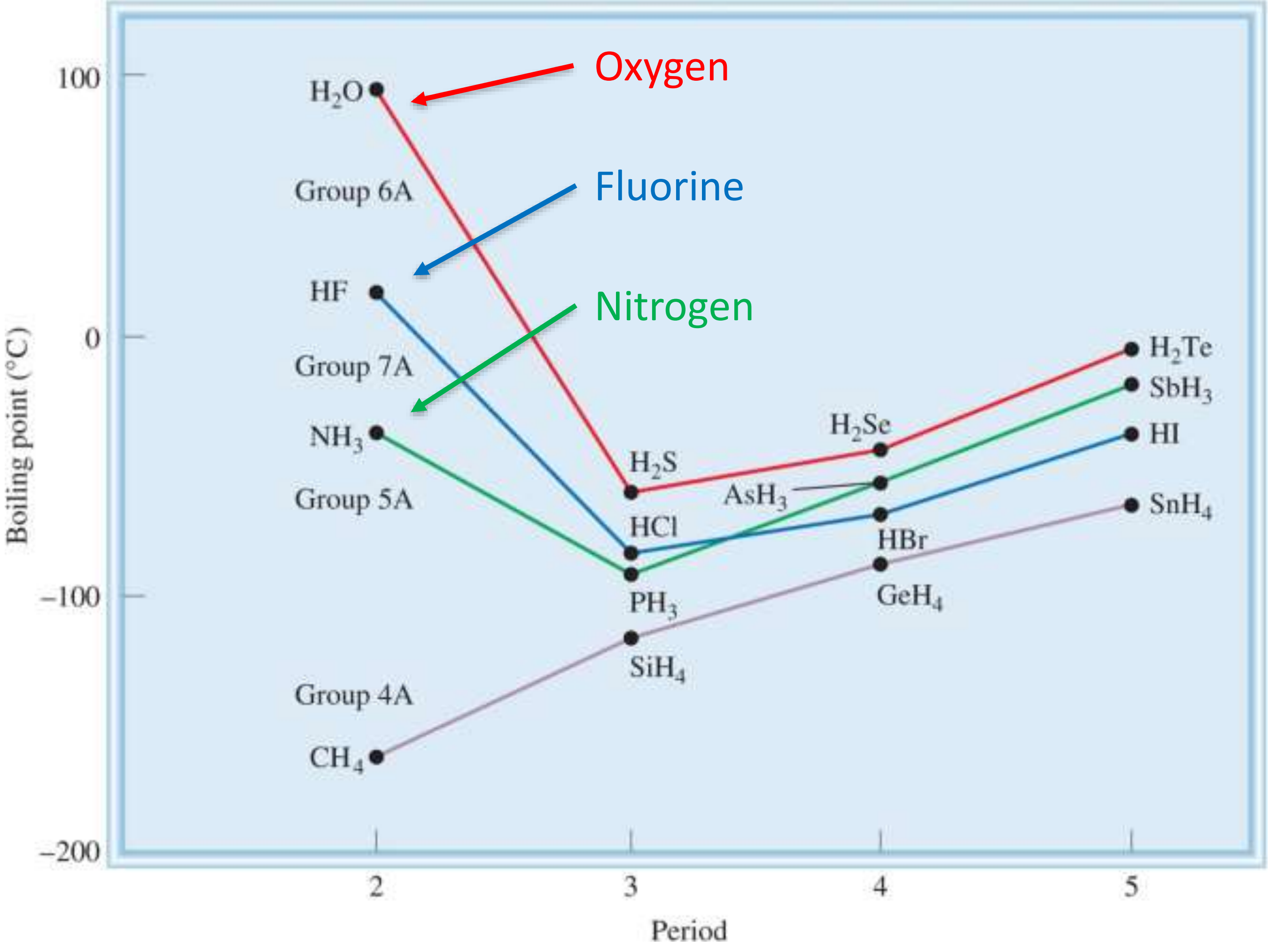
- Usually increase in magnitude with molar mass as dispersion forces increase in strength with the number of electrons present.

- In many cases, dispersion forces are comparable to or even greater than the dipole-dipole forces between polar molecules.

	Melting Point (°C)
CH_4	−182.5
CF_4	−150.0
CCl_4	−23.0
CBr_4	90.0
CI_4	171.0

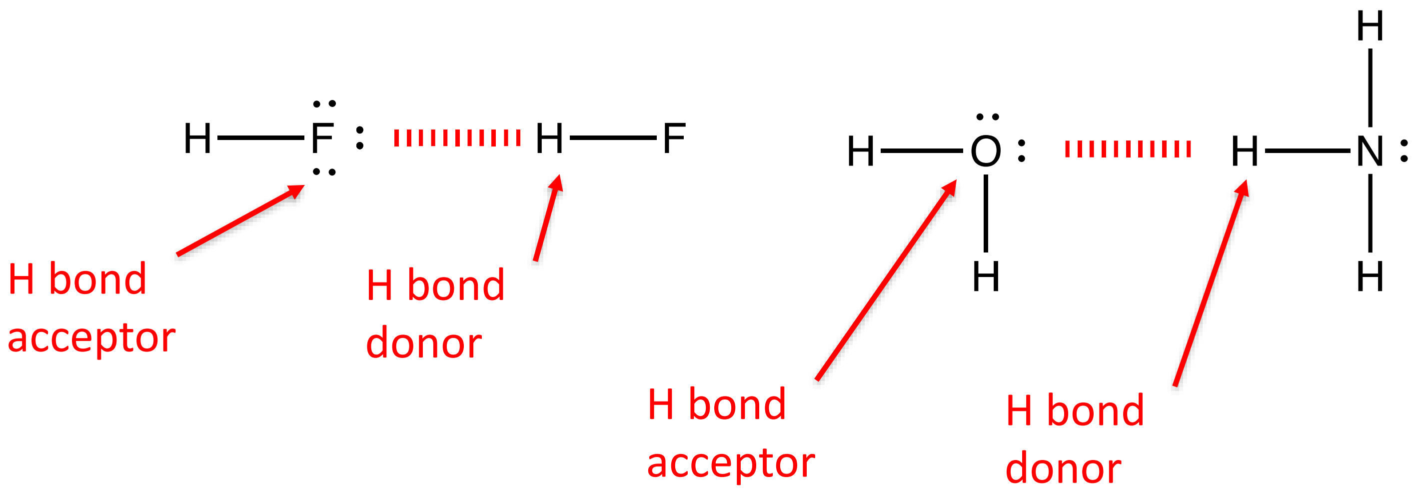
For an illustration of this, you should read pages 406 and 407 in Chang and Goldsby

Evidence for another type of intermolecular interaction



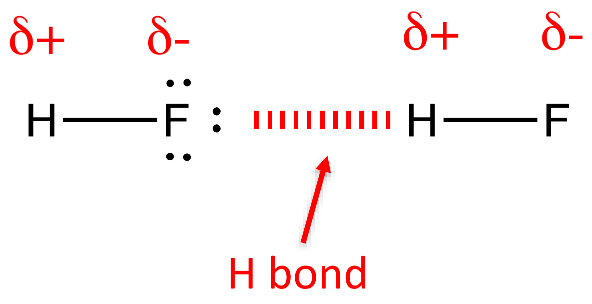
6. Hydrogen bonds

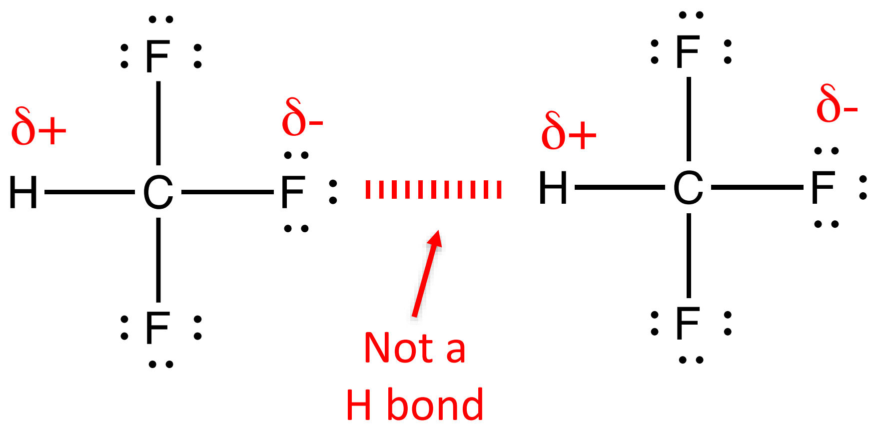
- Particularly strong type of intermolecular force
- A special type of dipole-dipole interaction between the hydrogen atom in a polar bond, such as N—H, O—H, or F—H, and an electronegative O, N, or F atom
- The H atom involved in the bond is known at the H bond donor. The atom whose lone pair is involved in the bond is the H bond acceptor.



Hydrogen bonding rule

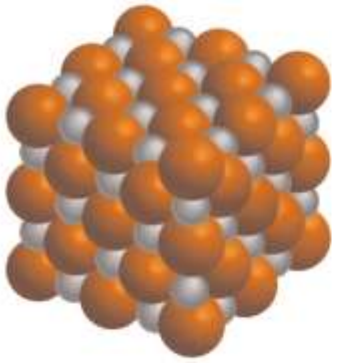
- To be considered a hydrogen bond the H must be attached directly to the electronegative atom (N, O, F)

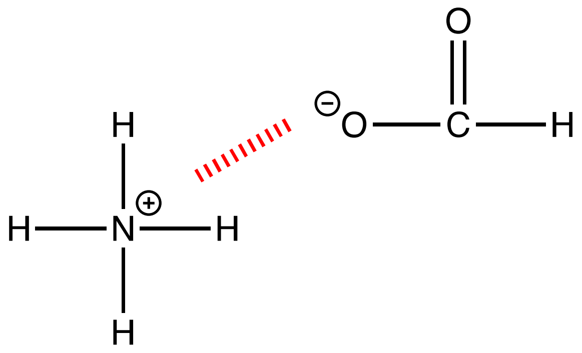




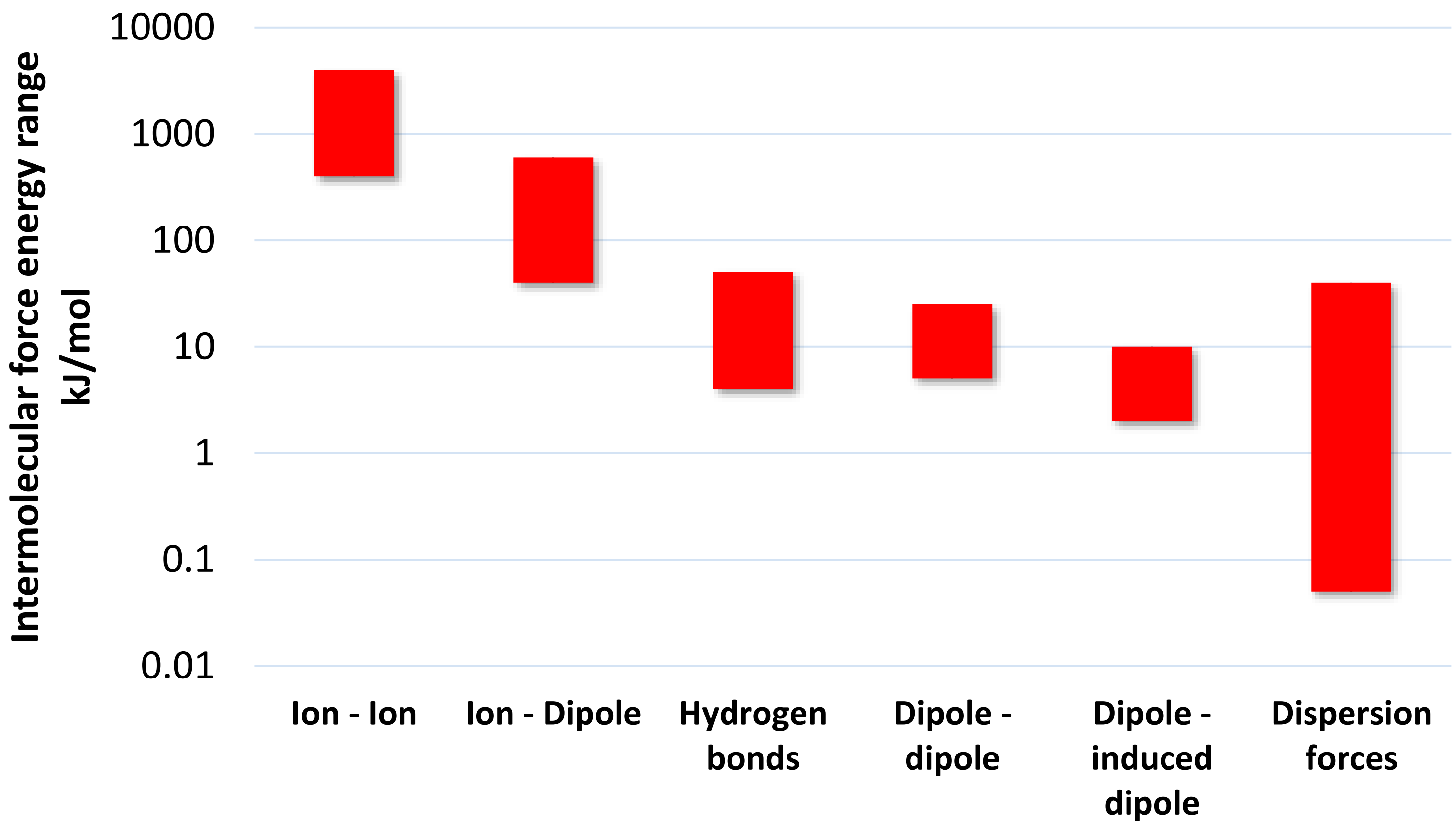
7. Ion – ion forces

- A form of electrostatic force
- Effectively ionic bonding
  - E.g. NaCl, $MgSO_4$
- Form ionic lattice structures using the electrostatic forces of the fully charged ions
  - Ionic interactions take place between many neighbouring ions
- Strong interactions





Intermolecular forces relative strength



Properties of water

- The properties of water and in general other liquids are dictated by the nature of their intermolecular interactions.

- If water did not have the ability to form hydrogen bonds it would be a gas a room temperature.

- Water
  - has a high melting and boiling points ← Due to H bonding
  - has large heat capacity

Heat capacity of water

- Unusually high heat capacity due to the presence of H bonding.
- Specific heat capacity: Energy required to heat 1g of a liquid by 1^{o}C.
  - Specific Heat capacity of water = 4.184 J/g.
  - Specific heat capacity of ethanol = 2.46 J/g.
- The adult body: 60% water.
  - Our bodies can absorb or lose a lot of heat without resulting in the body temp changing by 1^{o}C.

Medical and biological relevance of intermolecular forces.

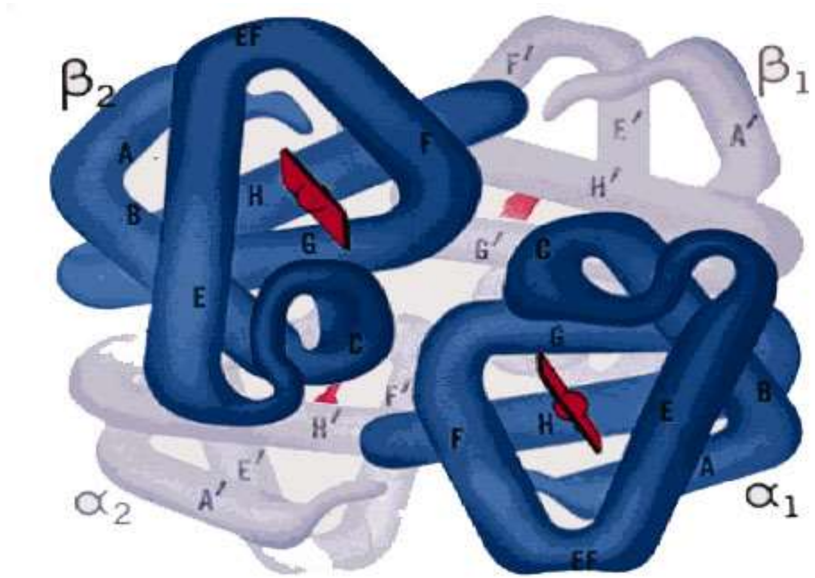
- Sickle cell anaemia

- The symptoms of Sickle Cell Anaemia
  - Narrow capillaries become blocked.
  - The body recognises the sickled cells as abnormal and destroys them faster than they are replace.
  - Anaemia results

Sickle cell anaemia – explained

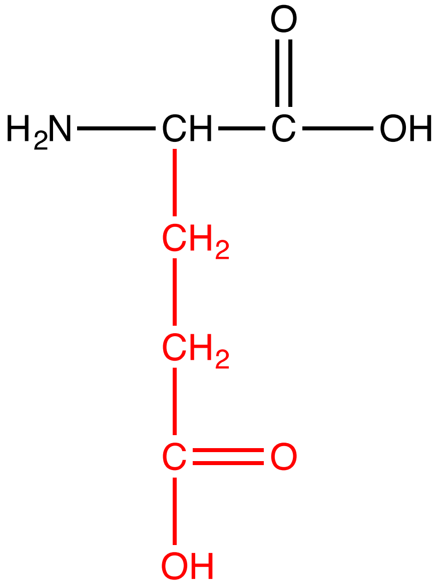
- Sickle cell anemia results from a *single* amino acid substitution (out of 287 amino acids) in the beta-chain of Hb_A.

  The only difference between Hb_A and sickle cell hemoglobin (Hb_S) is the substitution of a negatively charged glutamic acid for a hydrophobic valine.

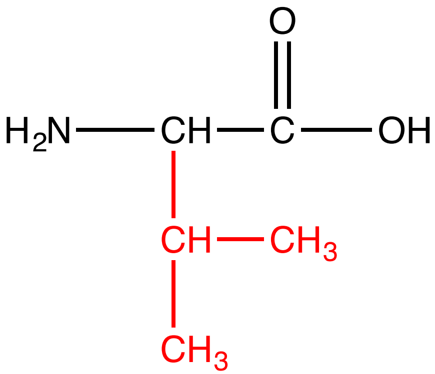


Glutamic acid versus valine

- Valine which is a non-polar a.a. residue replaces polar glutamic acid.
- Valine is exposed in low [O_2] and forms a hydrophobic region.
- The Hb_S molecules aggregate and precipitate.
- Red blood cells become distorted by precipitate and begin to block capiliaries.



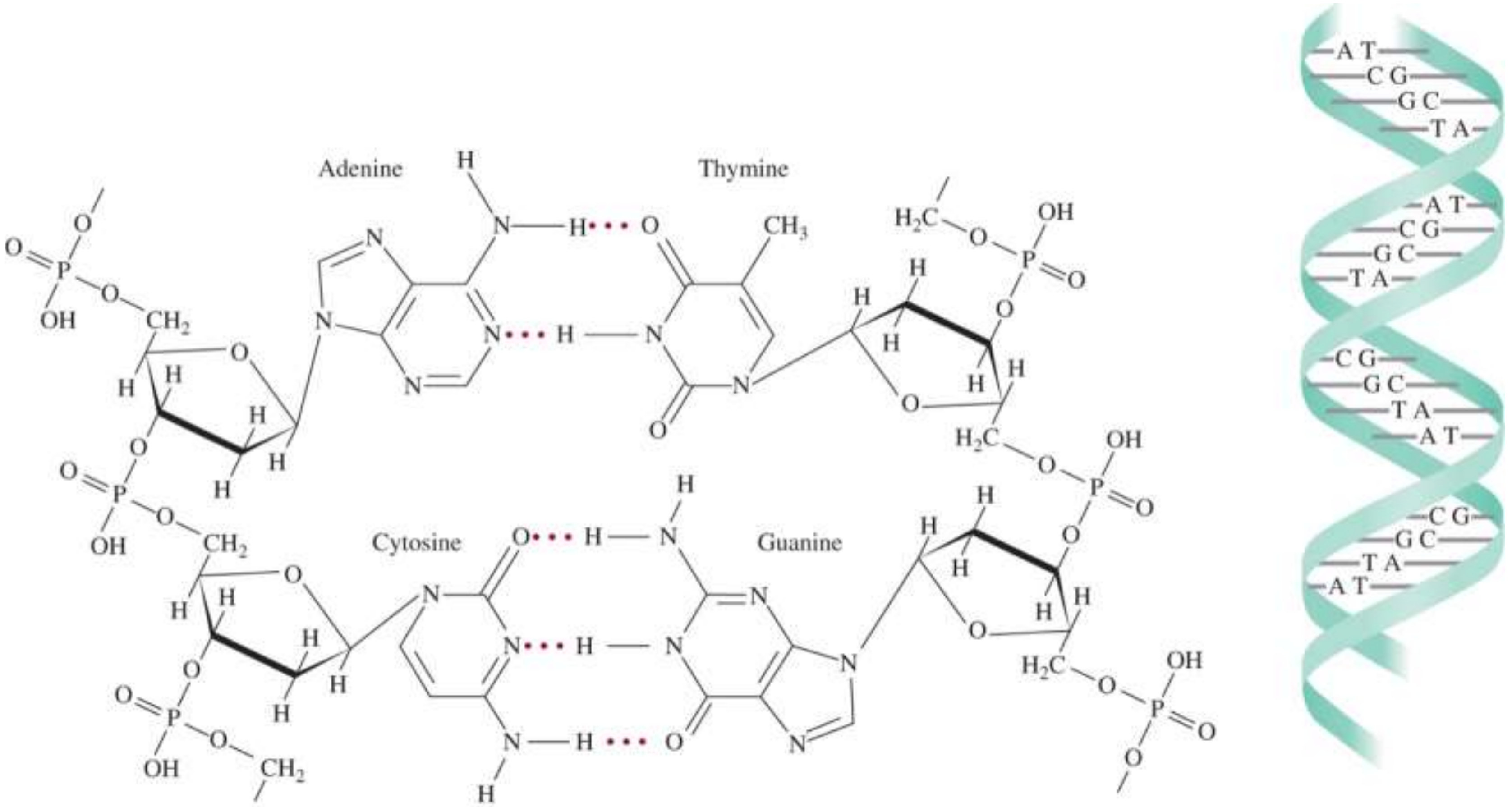
glutamic acid



valine

Structure of DNA

- The double helix structure of DNA is only stable due to the extensive hydrogen bonding holding each strand together.



(a) (b)

Drug design

- Drugs are now designed to target specific sites or receptors.
- Very often the structure of the drugs are designed to compliment the site.
  - –Often this means creating strong intermolecular interactions between drug and target.