Chemistry 4612: Introduction to Macromolecular, Supramolecular and Nanoscale Chemistry

- B.S. degrees from UMSL are certified by the American Chemical Society as meeting their educational standards

- Coverage of the topics of this course have recently been added as a requirement for B.S. degrees by the ACS

- The requirement is that coverage (of all three topics combined) be equivalent to 1 semester credit hour

- Why the new requirement? Supramolecular chemistry and nanoscale chemistry have grown exponentially in research activity and significance over the past two decades and have become key areas of modern chemistry, macromolecular chemistry is a much older field but has become highly important in many everyday applications and continues to experience much innovation in research

- These subjects draw upon some prior knowledge of chemistry, such as having some understanding of organic structure and physical properties of organic molecules, some common organic reactions, coordination chemistry, acid-base chemistry, oxidation and reduction reactions, basic knowledge of proteins and DNA, and some basic thermodynamics. Other concepts will be introduced through the course.

- Unfortunately, there is no book that provides a concise introduction to these three topics and is at the right level. There are many texts available for each of these 3 topics separately and some are quite long and too detailed

Supramolecular Chemistry

Jean-Marie Lehn (b. 1939), received Nobel Prize in 1987 for his work on molecules known as 'cryptands' that are cage-like molecules. He introduced many of the concepts of supramolecular chemistry and defined the field as 'chemistry beyond the molecule' involving two (or more) molecules held together in an organized assembly (structure) by intermolecular forces. These assemblies are also called 'self-organized' as they arise spontaneously upon combination of the chemical species and there are no covalent bonds forming.

Consider molecules A and B

A -------- B   held together by non-covalent forces could be called a 'supramolecule'
                                      A and B could be ions, or A could be a molecule and B an ion

A ------- B
 ¦   ¦   If multiple molecules are held together by non-covalent forces then we can call this a
 ¦   ¦   'supramolecular assembly', a common example of a non-covalent force would be a
 ¦   ¦   hydrogen-bond of some type.
 ¦   ¦
B ------- A
                    Supramolecular forces are also responsible for having many large molecules such as
                    macromolecules have a preferred structure, for example the proper folding of proteins

                    There are both natural supramolecular systems (e.g. proteins, DNA, polysaccharides,
                    minerals) and also synthetic supramolecular systems prepared by chemists (many kinds)

Nanoscale Chemistry

Nanotechnology involves the creation and application of devices or materials through the control of matter in the size range generally given as 1 – 1000 nanometers (1 nm = 10^{-9} m).

The study of the properties of matter and living systems in this size range is referred to as nanoscience, and the study of the properties of living systems in this size range can be referred to as nanobioscience. In this regard, much of biochemistry and many aspects of biology (life science) can be considered as a part of this topic, provided that the properties of individual cells, viruses, organelles, etc. are the focus.

Nanomedicine involves the development of materials or devices in the size range of 1 nm – 1000 nm designed to interact with living systems for disease diagnosis or treatment

Nanoscale chemistry includes using chemical approaches to prepare nanoscale materials or to synthetically modify them, there are many examples of nanoscale materials such as nanoparticles made of many different types of materials (can be a single element, e.g. gold; or more complex such as of compound like CdS; or of a covalent material such as TiO_2 or SiO_2), and of materials such as nanotubes of carbon, and other nanoscale shapes

In the nanoscale size range, the properties of a material can change such as its melting point, electronic, optical properties and others

Macromolecular Chemistry

Study of larger molecules made of linkages between defined units known as 'monomers'.

Macromolecules are also called polymers and various names for types of polymers (copolymers, dendrimers, etc..)

Simplest case: all the same monomer and linear covalent attachments
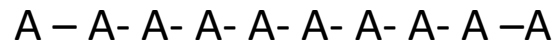
      A – A- A- A- A- A- A- A- A –A   physical properties will depend on chain length

However, an important question is that when even a simple polymer is synthesized, there can be chains of differing length and the properties of the chains can depend on their solvent environment, such as being coiled up or stretched out

If there are two monomers, we have a copolymer

      A-B-A-B-A-B-A-B-A-B   alternating copolymer
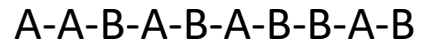
      A-A-B-A-B-A-B-B-A-B   random copolymer, the composition can be varied
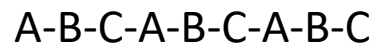
      A-B-C-A-B-C-A-B-C   triblock copolymer

Polymers are what we know at least in common experience as the many kinds of plastics, and there are many many ways to create polymers of varied structures. There are also many natural polymers such as polysaccharides, and biopolymers (DNA, proteins, for example)

Module 1: Supramolecular Forces

Survey of the forces that hold together supramolecules and supramolecular assemblies, these forces will be important to understand so we can understand how molecules interact with each other often in organized or directional ways

The strengths of **covalent bonds** range from about 150 kJ mol^{-1} for a weak bond such as I – I (two iodines) to strongest C≡O with strength of 1080 kJ mol^{-1}. This is the energy required to break a mole of such bonds. For supramolecular forces we need to consider many other kind of interactions such as:

Ion-ion interaction

Ion-dipole interaction

Dipole-dipole interaction

Dipole – (induced dipole) interaction

Induced dipole – induced dipole interaction (London dispersion)

Hydrogen bond

Cation – (π) interaction

π-π interaction

Hydrophobic effects (this is an effect based on entropy changes and not an actual 'force')

Steric interference

The strength of the same intermolecular interactions will generally be stronger in the gas phase than in solvent because the interactions of the molecules with the solvents are also contributing

The term 'van der Waals' forces includes dipole-dipole, induced dipole – dipole, and induced dipole – induced dipole interactions

Relative strength of interactions is generally:

Ion-Ion > hydrogen-bonding > dipole – dipole > (induced dipole – dipole and induced dipole – induced dipole)

Charged species such as cations or anions interact by 'ionic' interactions (also called charge-charge interactions or ion-ion interactions), the attraction of unlike charges for each other and the repulsion of like charges

NaCl (s) → Na⁺ (g) + Cl⁻ (g) $\Delta H = 785$ kJ mol⁻¹ 298 K, 1 atm

However,

NaCl (s) + ∞H₂O(l) → Na⁺ (aq) + Cl⁻ (aq) $\Delta H = 4$ kJ mol⁻¹ 298 K, 1 atm
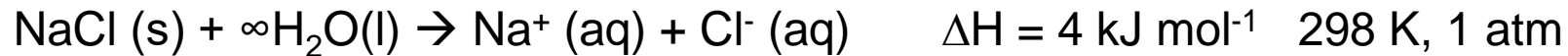
The strong interactions between the ions and the water molecules stabilize the dissolved ions by diminishing the attractions between sodium and chloride ions

The distribution of electrons favors the oxygen atom since it is more electronegative than hydrogen.

The δ- and δ+ are partial charges.

A dipole is two opposite charges separated by a fixed distance.

If a single + and a single – charge are separated by a distance r, then the dipole moment is equal to e r

e is the charge of an electron   1.60 x 10^{-19} C

Dipole moments are expressed in units of Debye, **1 D = 3.336 x 10^{-30} C m**

$\delta-$

$\delta-$
O

H   H

$\delta+$ $\delta+$

$\mu = 1.8$ D
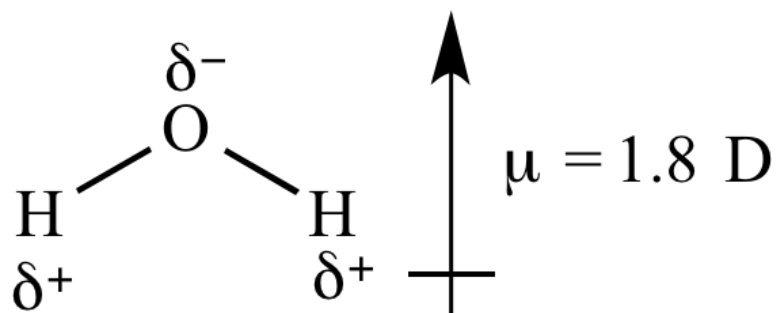
negative end of dipole

positive end of dipole

$\delta+$ = +0.417 e $\delta-$ = -0.834 e

The dipole moment of water is found by experiment to be *equivalent to* A unit positive and a unit negative charge separated by 0.38 Å

1 Å = 10^{-10} m   0.38 x 10^{-10} m x 1.60 x 10^{-19} C = 6.08 x 10^{-30} C m = **1.82 D**

Ion – Dipole Interaction

ion-dipole interactions are responsible for the orientation of water molecules around cations and anions.

KEY

Sodium ion (Na^+)

Chloride ion (Cl^-)

Oxygen atom

Hydrogen atom

δ^+: Partially positive

δ^-: Partially negative
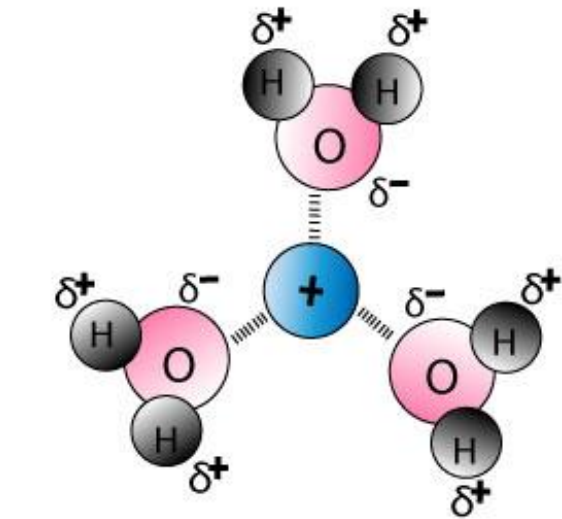
sodium ion surrounded by water molecules with the partially negative oxygen atom pointing towards it
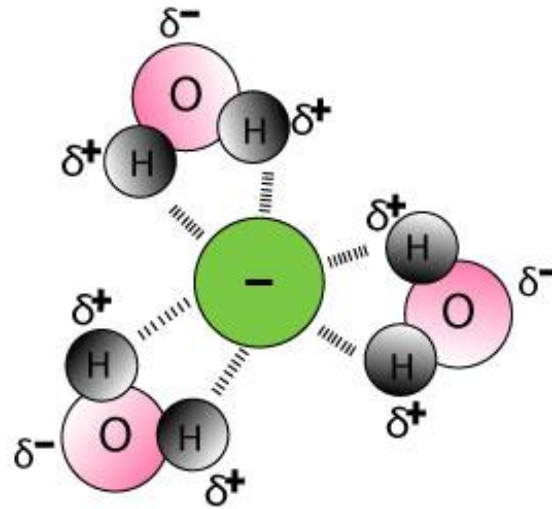
chloride ion surrounded by water molecules with the partially positive hydrogen atom pointing towards it

https://masterconceptsinchemistry.com/index.php/2017/10/24/how-does-sodium-chloride-nacl-dissolve-in-water/

The presence of a charge nearby a neutral molecule with no net dipole moment will distort the electron distribution and 'create' (induce) a dipole in that molecule How much of a dipole is created is a function of the *polarizability* of the molecule, a property that determines how easily the electron clouds in a molecule are distorted by a nearby charge. Heavier atoms with more electrons tend to be more polarizable, and so are pi electrons such as those in benzene.

The interaction of the induced dipole moment with the charge is called an **ion – induced dipole interaction**.
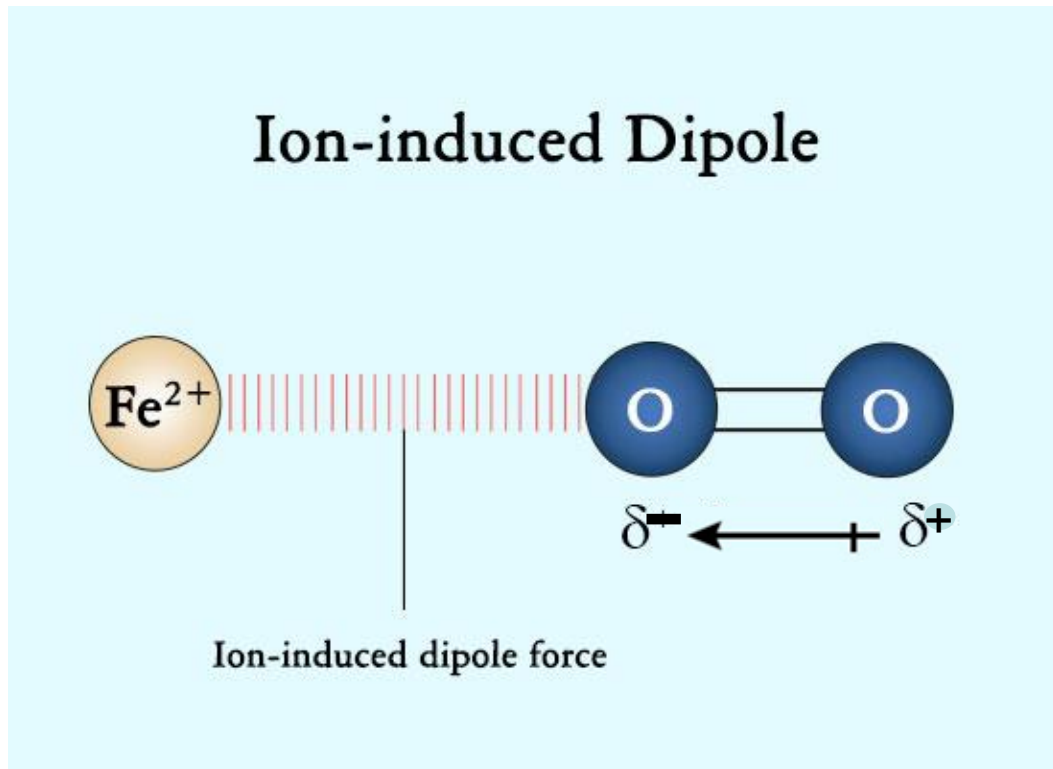
The ion being near the neutral molecule induces a dipole moment in the molecule by distorting the electron cloud

Ion-induced Dipole

Ion-induced dipole force
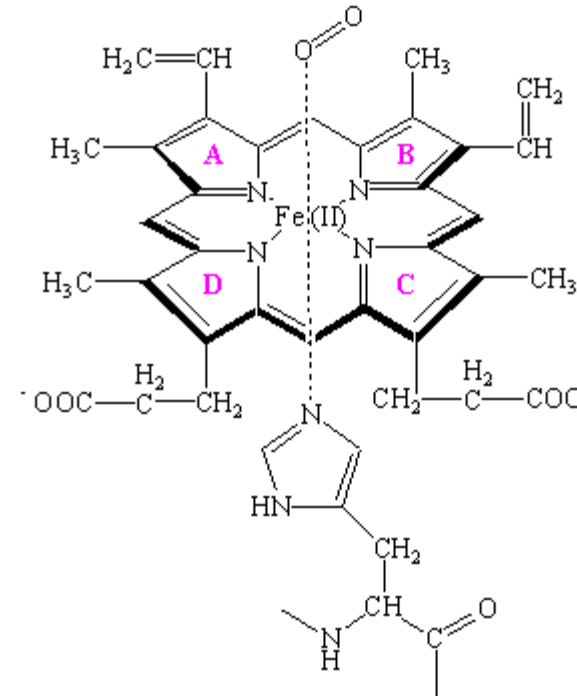
This interaction occurs between iron and oxygen in hemoglobin

Two neutral molecules with no overall dipole moment that are near each other will induce transient (oscillating versus time) dipole moments in each other and will be attracted to each other by **induced dipole-induced dipole interaction** that are known as **London dispersion forces** *(not named after the city, but after Erwin London).*
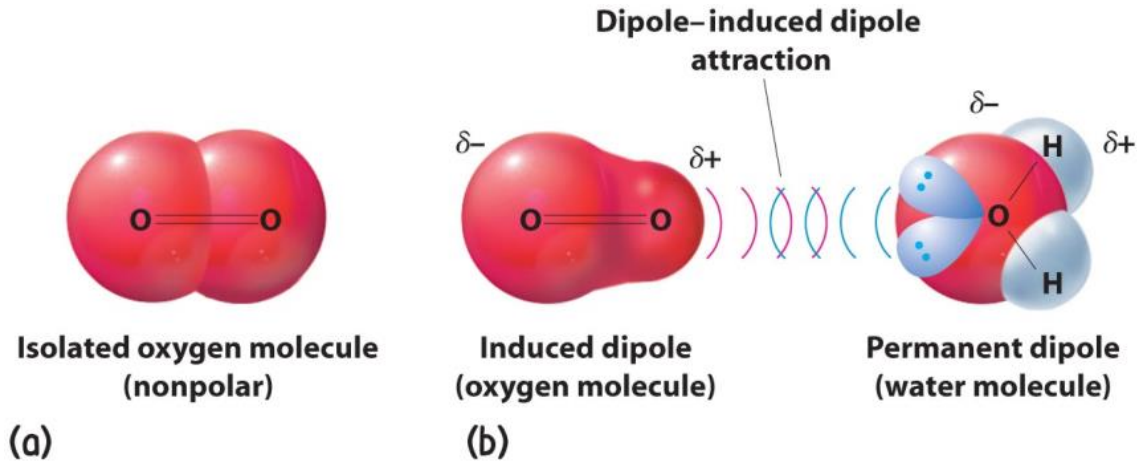
London dispersion forces are always present as a contribution to the interaction between molecules or atoms. For atoms such as in solid argon, they are the only forces present. The strength of the London forces increases with polarizability, e.g. Ar is more polarizable than Ne because it has more electrons.
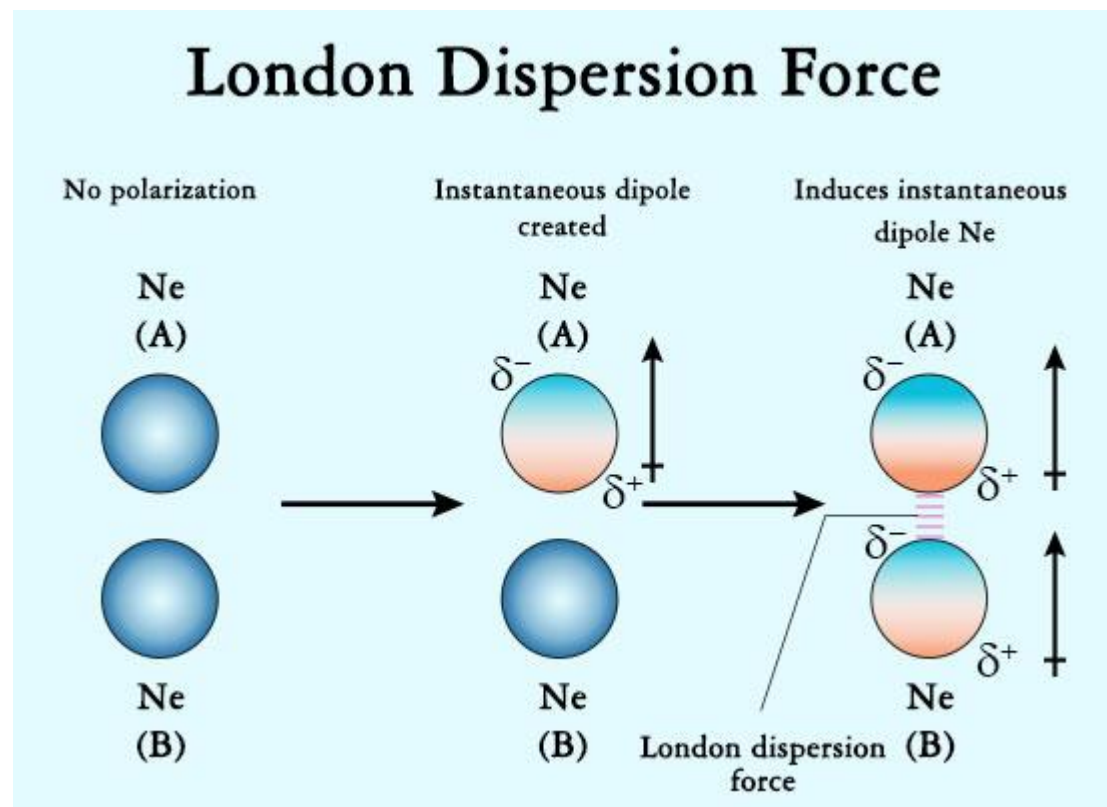
Dipole – dipole forces : dipoles interact more favorably when they are pointing in opposite directions

$\delta+$ $\delta-$
I—Cl

$\delta-$ $\delta+$
Cl—I

or

$\delta+$ $\delta-$ $\delta+$ $\delta-$
I—Cl ---------- I—Cl

dipole – induced dipole

Dipole–induced dipole
attraction

Isolated oxygen molecule
(nonpolar)

Induced dipole
(oxygen molecule)

Permanent dipole
(water molecule)

(a)

(b)
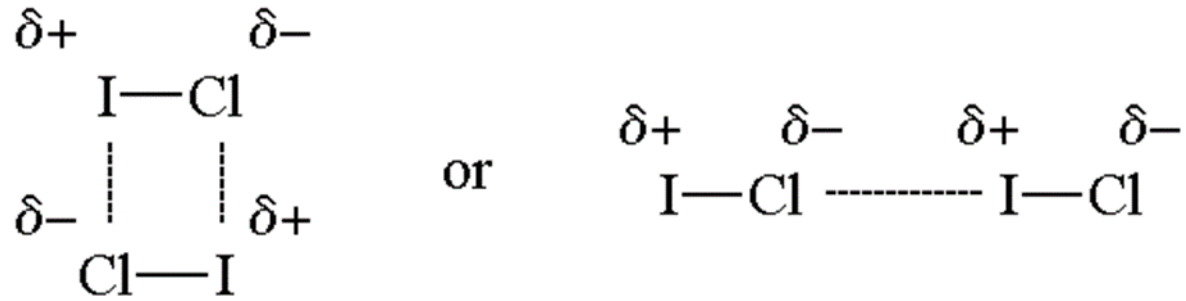
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https://socratic.org/questions/5a64204ab72cff7b83554c78

Steric repulsions – molecules or parts of molecules don't like to brought too close together because electron clouds overlap

<u>Hydrogen Bond</u> – A hydrogen atom covalently attached to (for example) a N, C, or O can form a weak partial bond to another atom that has a lone pair of electrons.

<u>Hydrogen-bond donor</u> = atom to which the H is bonded
<u>Hydrogen-bond acceptor</u> = atom with lone pair accepting a partial bond to H
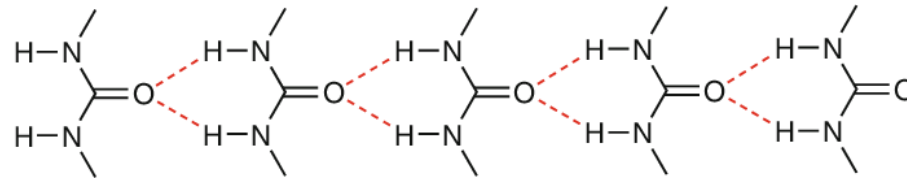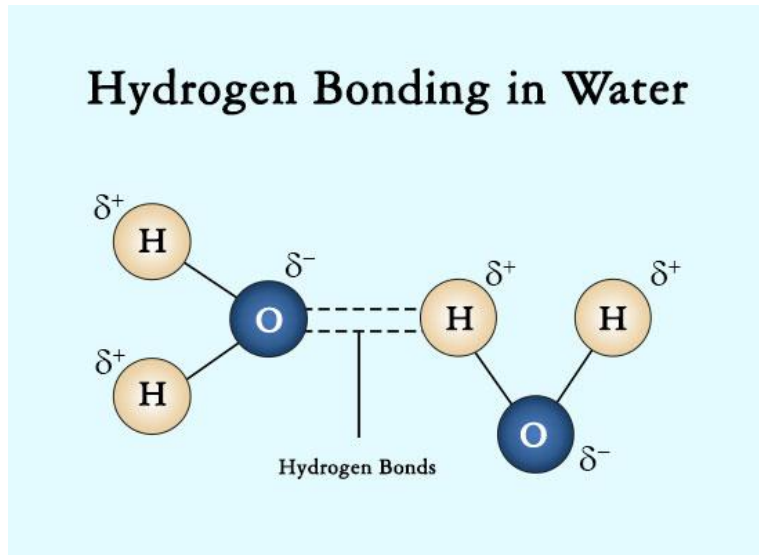
Urea-Urea hydrogen bonding

Strength of a hydrogen-bond in gas phase is about 15-20 kJ mol^{-1} versus about 400 kJ mol^{-1} for typical covalent bonds. (compared in gas phase)

In water, the strength is lower due to interactions with water, there is a competition between hydrogen-bonding to water and to another species.

Urea-Urea hydrogen-bond strength in water is 5 kJ mol^{-1}, good peptide model

Polynucleotides

Example of hydrogen-bonds in biochemistry

Adenine-Thymine

2 H-bonds

In RNA, uracil
subsitutes for thymine

cytosine-guanine

3 H-bonds

Consequence:

C - G stronger
than A - T
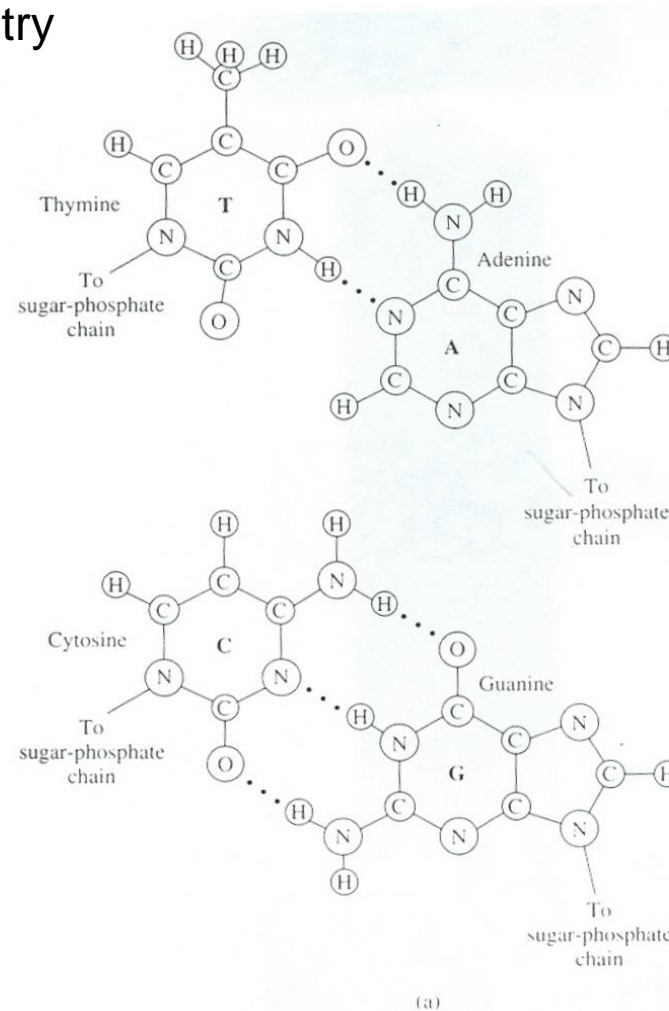
note the negative charges on the
phosphates, these repel each other

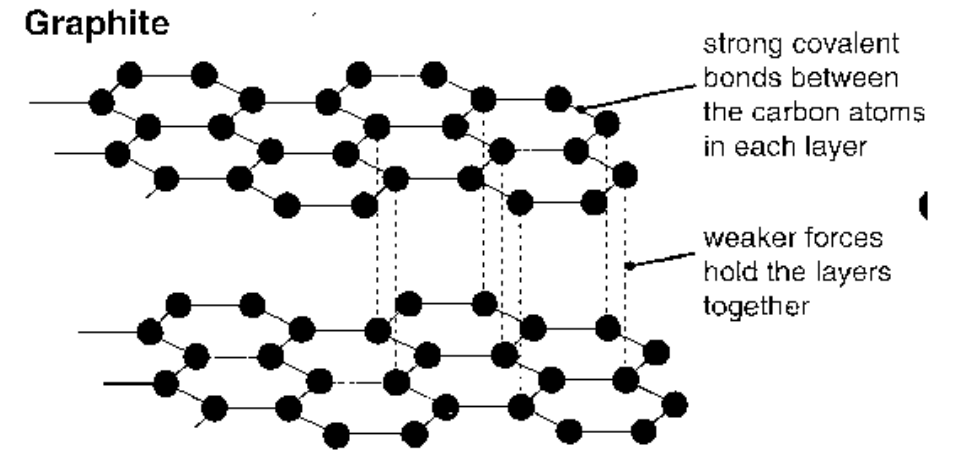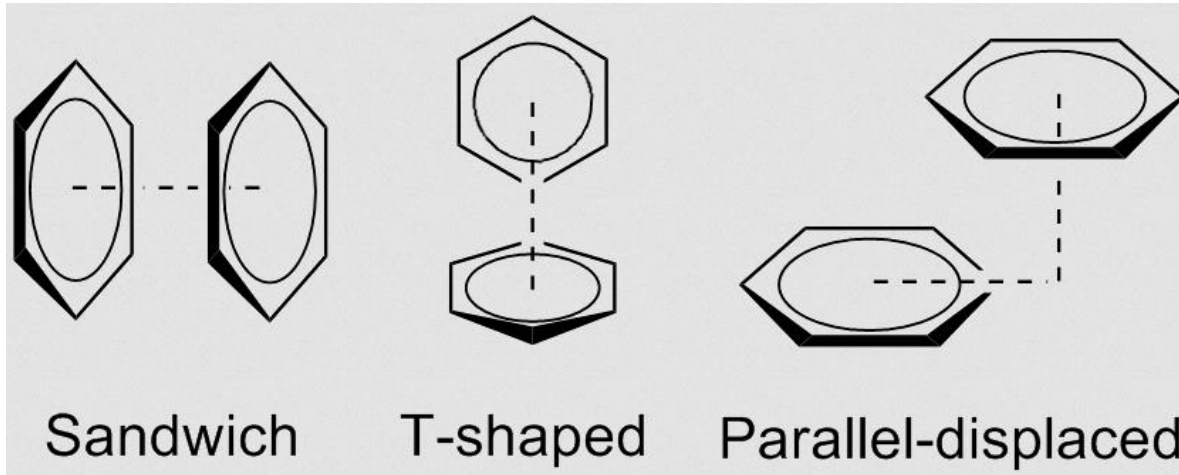positive counterions in the solution (Na$^+$)
may screen Coulomb repulsions.
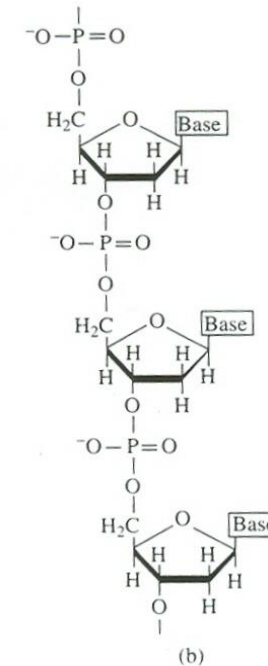
Phosphodiester bonds

▲ FIGURE 3.6

(a) The Watson–Crick base pairs found in DNA. Adenine is complementary to thymine (A·T), and guanine is complementary to cytosine (G·C). In RNA, uracil substitutes for thymine (A·U). (b) The sugar–phosphate chain in RNA differs only in that the sugar is ribose instead of deoxy-ribose. In the structures shown in (a), a covalent bond, whether it is a single or a double bond, is represented by a solid line; a hydrogen bond is represented by a dotted line.

From Tinoco, Physical Chemistry: Principles and Applications in Biological Sciences, 5th edition

$\pi - \pi$ interactions

Sandwich   T-shaped   Parallel-displaced

Graphite

strong covalent bonds between the carbon atoms in each layer

weaker forces hold the layers together

$\pi - \pi$ interactions are also known as stacking

the 'sandwich' or face-to-face orientation is responsible for the structure of graphite, and also for the stacking of nucleobases in the double helix of DNA

The 'T-shaped' or edge to face orientation is considered a weak hydrogen-bond – the hydrogens around the ring have a partial positive charge and are attracted to the electron rich π – cloud. The parallel-displaced orientation is based on similar interactions

The strength of the interactions will vary with substituents around the ring, for example

Cation – π interactions

A noncovalent interaction between a cation and an electron rich π-system such as in an olefin, or in an aromatic molecule such as benzene

Acetylcholine

Tryptophan
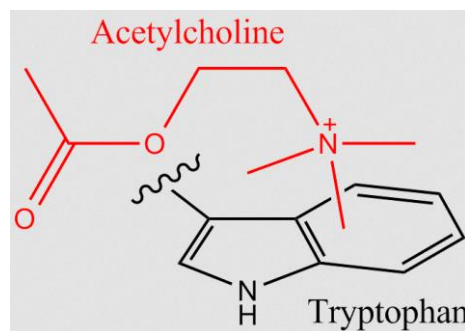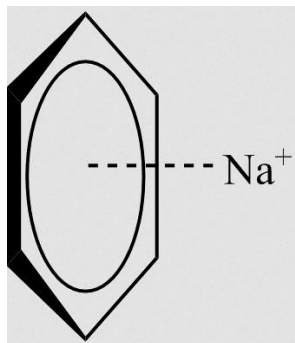
see Cation–pi_interaction,pdf

M^+	Li^+	Na^+	K^+	NH_4^+	Rb^+	NMe_4^+
-ΔG [kcal/mol]	38	27	19	19	16	9
r_{ion} [Å]	0.76	1.02	1.38	1.43	1.52	2.45

The strength of the interaction is stronger for smaller size cations.
These values are for the interaction in the gas phase.
In water, the interaction is still present but is weaker.
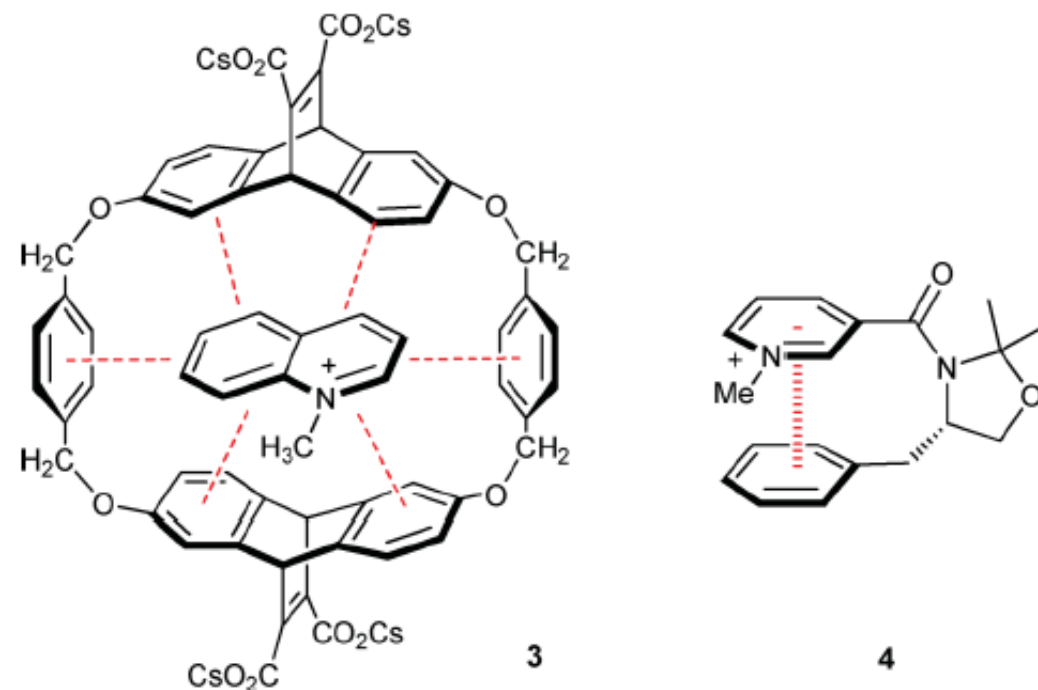
Fig. 3 Supramolecular guest-host ensemble **3**, utilising pyridinium–π interactions and a Yamada pyridinium–π construct **4**.

https://pubs.rsc.org/en/content/articlepdf/2011/ob/c1ob05228d

Lennard – Jones potential (6-12 potential) is used mathematically to describe van der Waal's forces between molecules
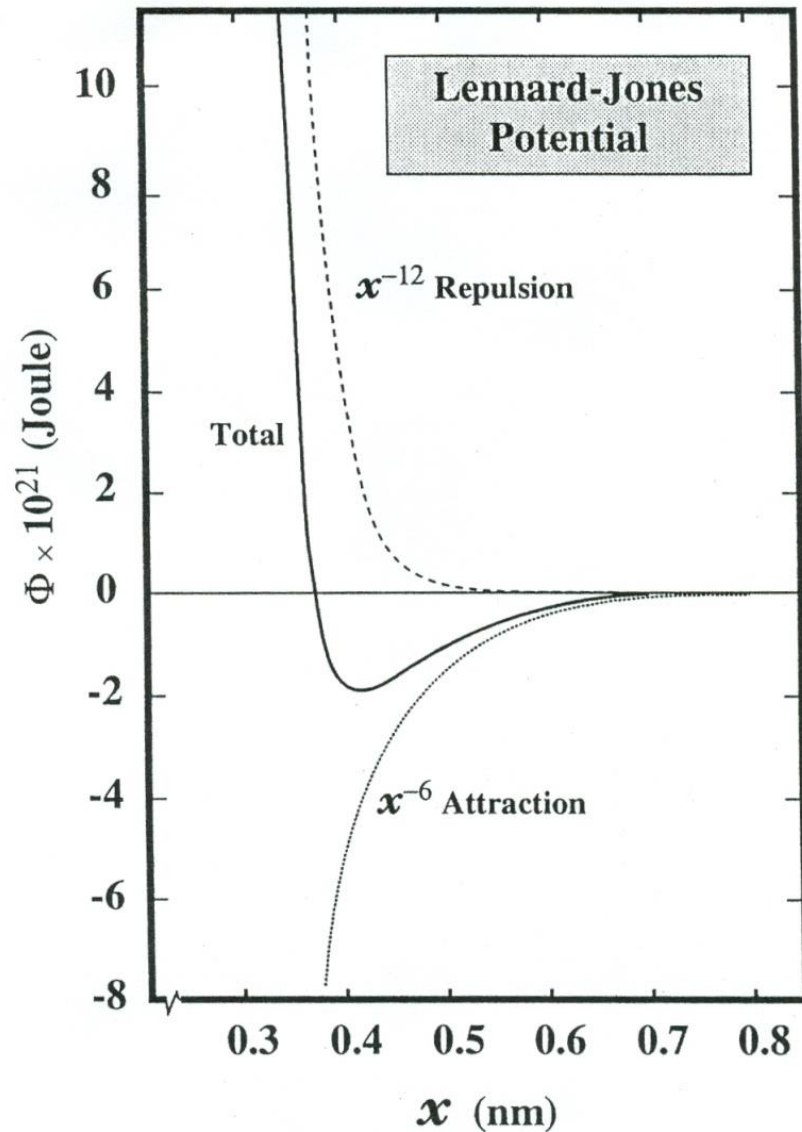
FIG. 10.2 Potential energy versus distance of separation for two methane molecules.

$$\Phi(r) = \xi \cdot r^{-12} - \beta \cdot r^{-6}$$

$$\frac{\partial \Phi(r)}{\partial r} = 0$$

$$r_{min} = \left(\frac{2 \cdot \xi}{\beta}\right)^{1/6}$$

$$\Phi_{min} = -\frac{\beta}{2} \cdot r_{min}^{-6} = -\xi \cdot r_{min}^{-12}$$

$$\beta = -2 \cdot \Phi_{min} \cdot r_m^6$$

$$\xi = -\Phi_{min} \cdot r_m^{12}$$

$$\Phi(r) = \Phi_{min}\left[\left(\frac{r}{r_{min}}\right)^{-12} - 2\left(\frac{r}{r_{min}}\right)^{-6}\right]$$

The parameters ξ and β depend on the electronic structure of the molecule, can be determined experimentally or calculated (estimated) using theoretical approaches

The L-J potential does not model other interactions well

Hydrophobic Effect

If a hydrocarbon (such as propane) is introduced into water, a disturbance is introduced. The water molecules around the propane molecule are re-oriented so that they can hydrogen-bond to each other and end up more ordered and sort of 'frozen'.
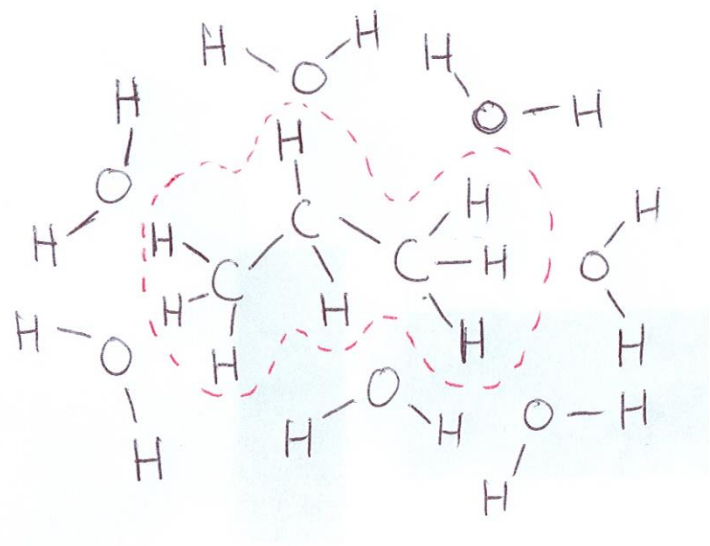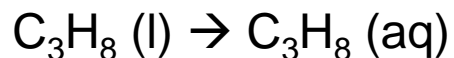
Even though ΔG is positive, some propane dissolves in water.

$$\Delta H^o_{298} \approx -8 \text{ kJ mol}^{-1}$$

$$\Delta S^o_{298} \approx -80 \text{ J K}^{-1} \text{ mol}^{-1}$$

$$\Delta G^o_{298} \approx +16 \text{ kJ mol}^{-1}$$

The water molecules are released if the propane molecule is transferred from water to another solvent.

C_3H_8 (l) → C_3H_8 (aq)

R(aq) + R (aq) → [R(aq) R (aq)] (clustered)   where R is a hydrophobic alkyl chain

Releases some water back to its undisrupted bulk state and is favorable, $\Delta S > 0$ and ΔH is small, and then ΔG is < 0

Clustering is not because of the attractions between these molecules, it is because the entropy change of the water molecules is favorable enough to make $\Delta G < 0$ and the assembly of the alkyl chains spontaneous.

The <u>hydrophobic effect</u> is what drives the assembly of hydrophobic molecules (or parts of molecules) to organize away from water molecules

Lipids which make up cell membranes are amphiphilic molecules:

phospholipid

Polar head-group   Hydrocarbon chains
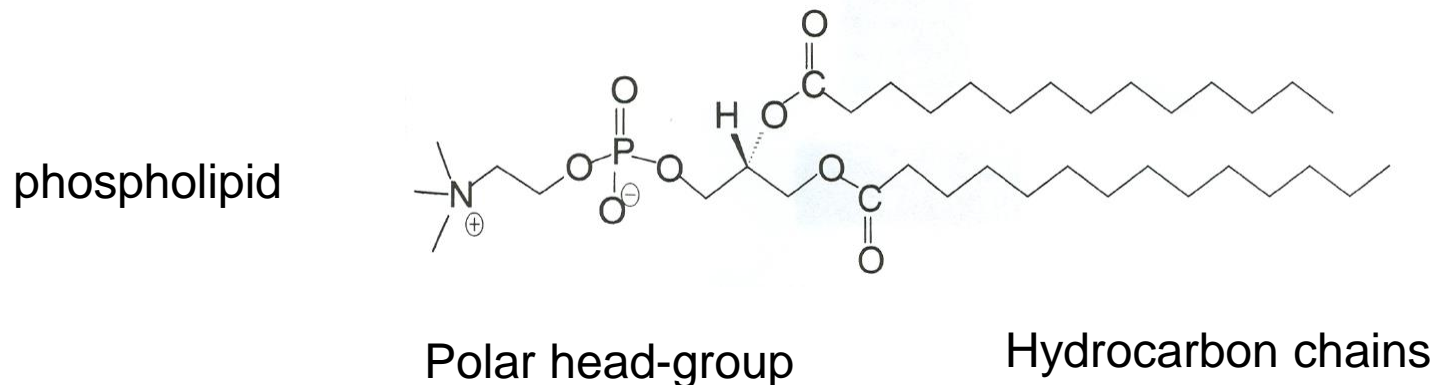
In water, even alone, these molecules form bilayers like those of cell membranes (liposomes)

Liposomes – these are structures formed by phospholipids in water as a result of the hydrophobic effect

Will form by sonicating a lipid dispersion in aqueous solution

Choice of preparation method can result in different sizes.

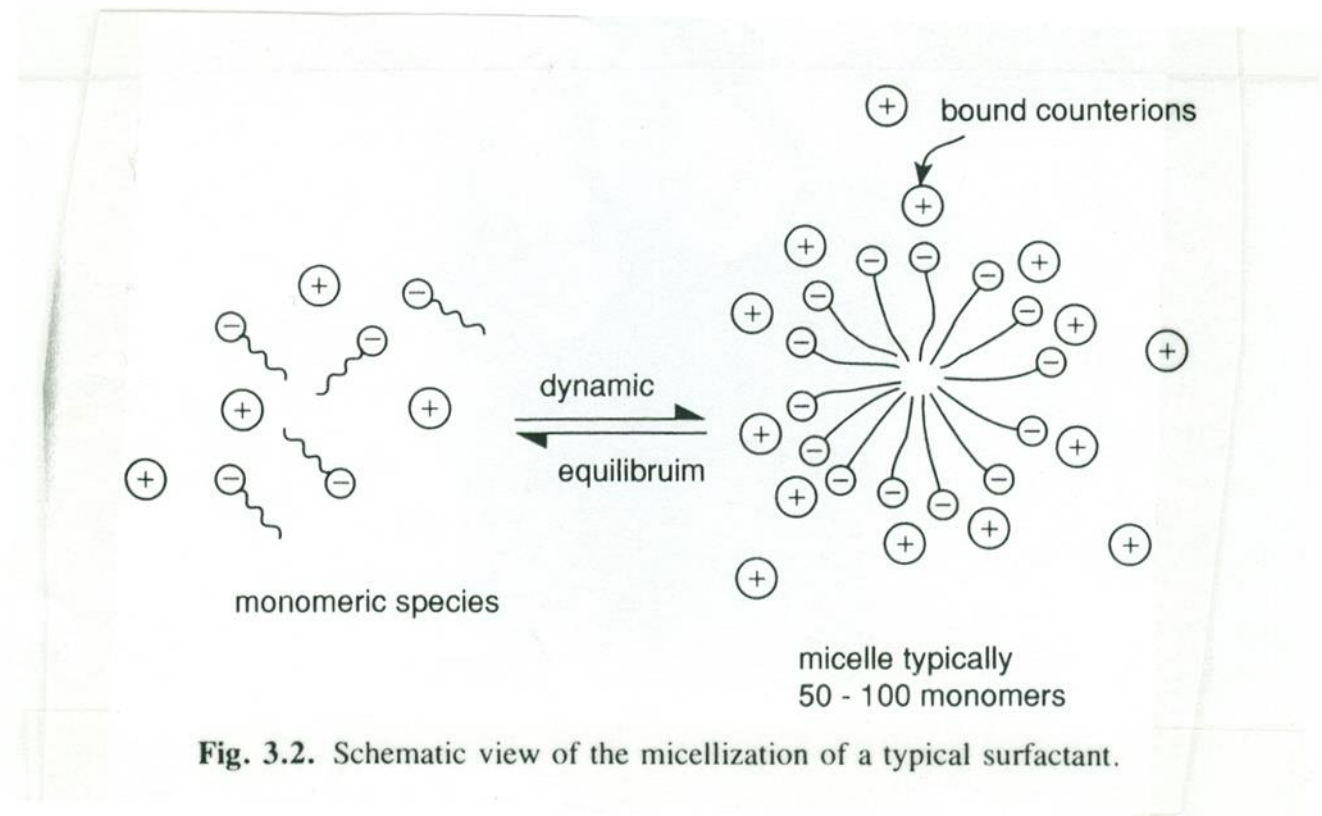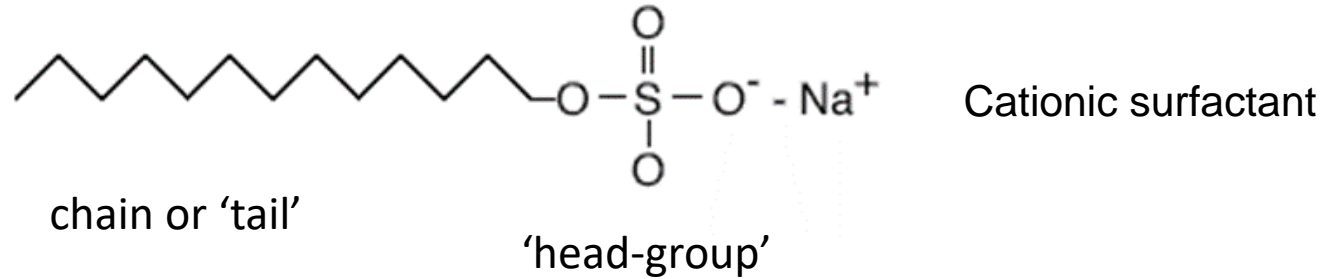Extrusion through solid membranes of defined pore size can yield liposomes of a fairly uniform size.

100 nm diameter (small unilamellar) up to 50 um (visible under microscope) giant liposomes
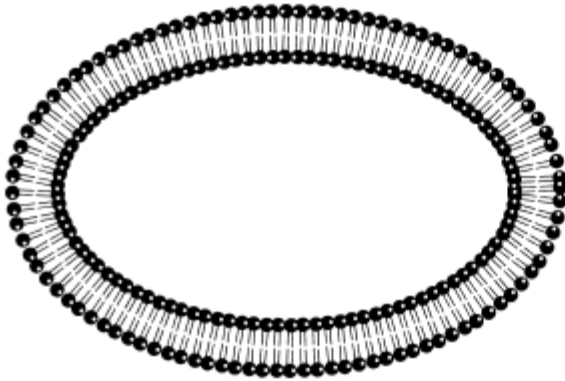
Can vary lipid composition, applications include drug delivery

Membrane proteins can be reconstituted (added into) into liposomes.

Another example of the hydrophobic effect is micelle formation

chain or 'tail'

'head-group'

Cationic surfactant

bound counterions

dynamic

equilibruim

monomeric species

micelle typically
50 - 100 monomers

Fig. 3.2. Schematic view of the micellization of a typical surfactant.

Micelles form above a certain concentration known as the critical micelle concentration

Detergency – micellar dispersions in water carry away greasy molecules by their being solubilized into the hydrophobic micellar cores

From Micelles, Monolayers and Biomembranes, by Jones and Chapman, 1995

Examples

An example of an ion-ion interaction of great significance is a salt bridge that occurs in proteins between cationic and anionic amino acids (in biochemistry it is called a salt bridge). It is an _electrostatic interaction_. As we will see later, salt bridges are important for holding proteins in their proper structure
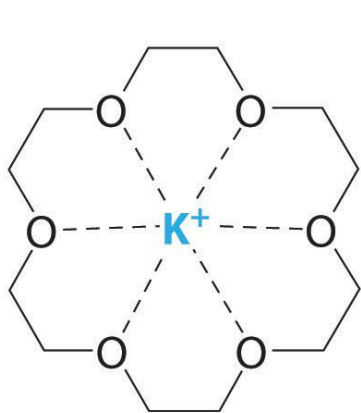

Arginine – aspartic acid

https://www.nature.com/articles/s41598-018-31935-z.pdf
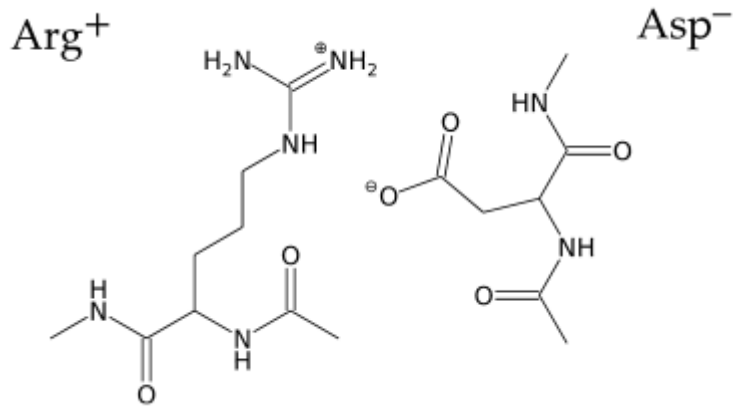
Salt bridges can occur between aspartic acid and glutamic acid (deprotonated) and lysine, arginine, or histidine

Interactions Governing Polypeptide Tertiary Structure

Illustration by G. Bergtrom
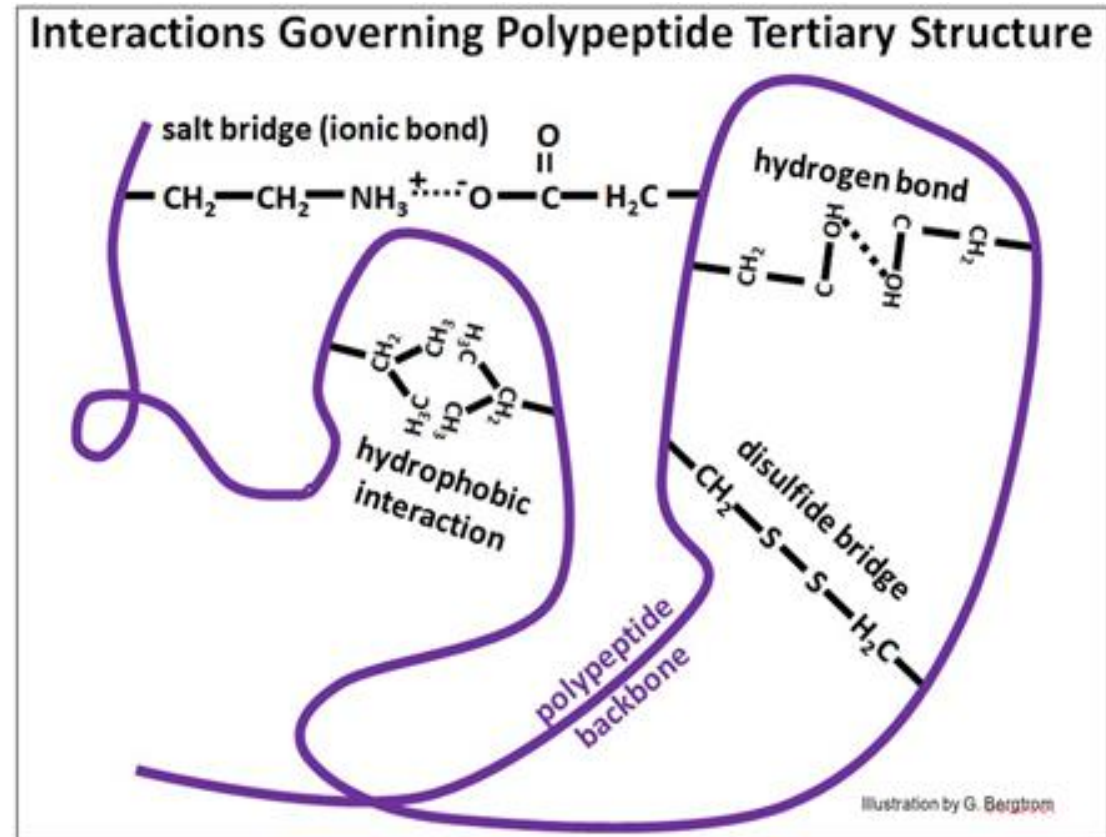
https://bio.libretexts.org/Bookshelves/Cell_and_Molecular_Biology/Book%3A_Basic_Cell_and_Molecular_Biology_(Bergtrom)/3%3A_Details_of_Protein_Structure/3.2%3A_Levels_(Orders)_of_Protein_Structure
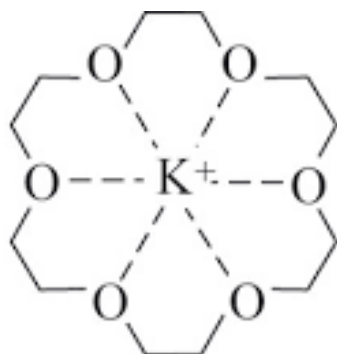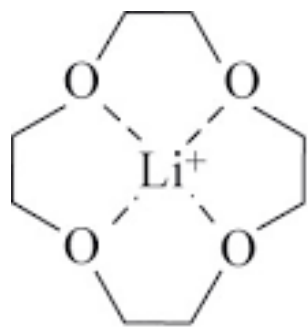
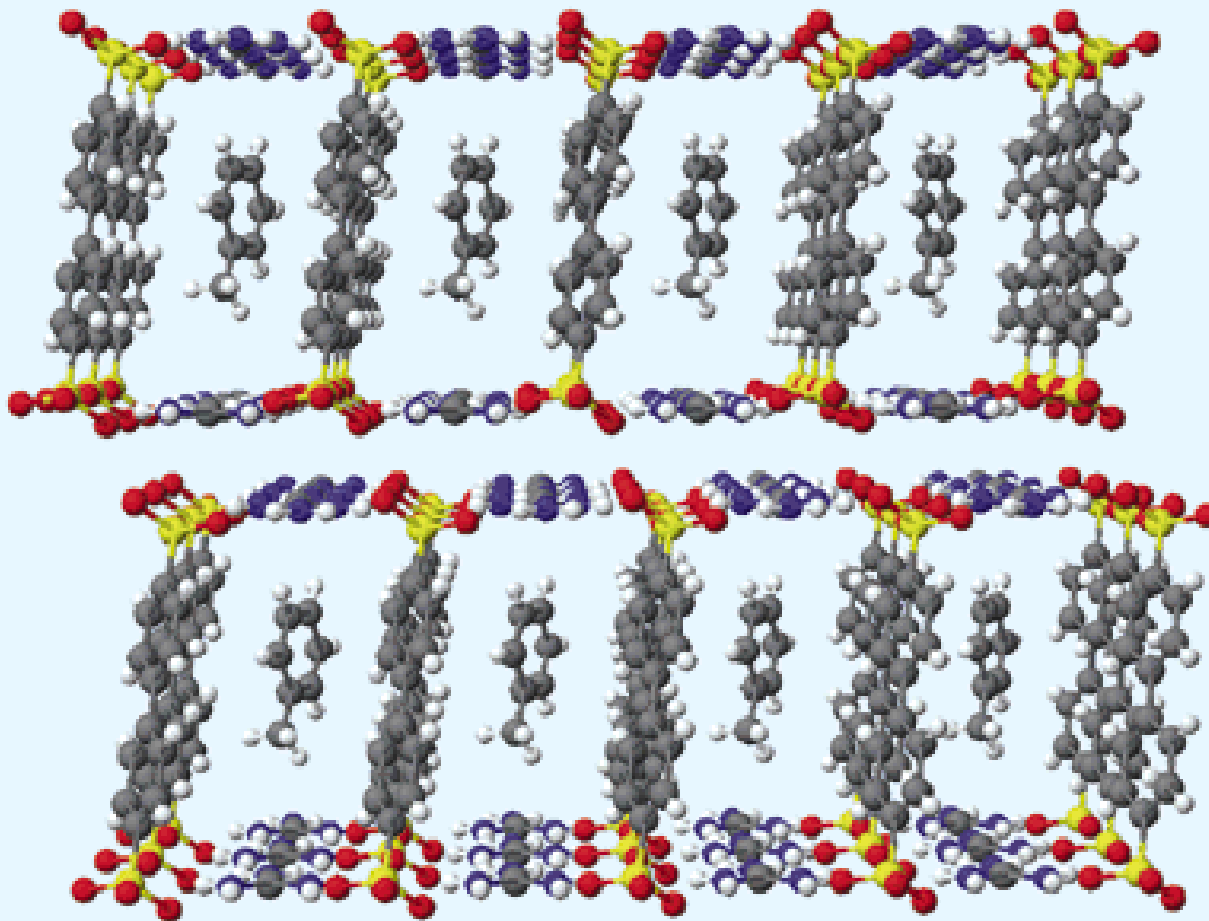# Ion-dipole interactions in crown ethers and cryptands

(a) Crown ether

(b) Cryptand

Crown ethers – different sizes are best for complexes different size cations

Hydrogen-bonds

Hydrogen-bonding can be used to design uniquely ordered solids

The example has a hydrogen-bonded framework with molecules trapped (hosted) inside the structure

This is an example of 'crystal engineering'

Hydrogen bonds are also crucial in biomolecules – for determining the shape of proteins, of the DNA helix, and other structures

https://science.sciencemag.org/content/276/5312/543