WATER SOLUTIONS AND HYDRATION:
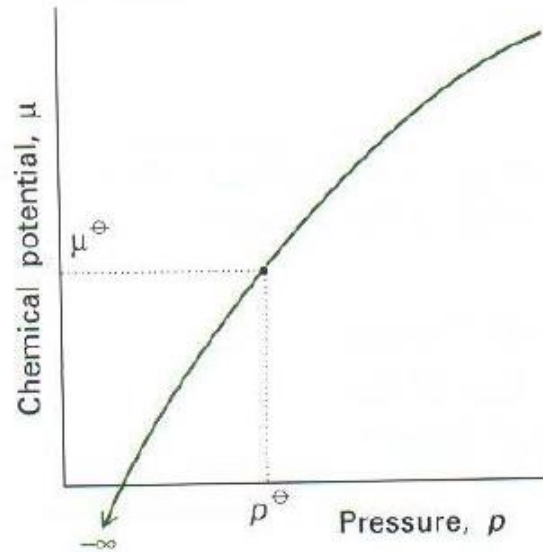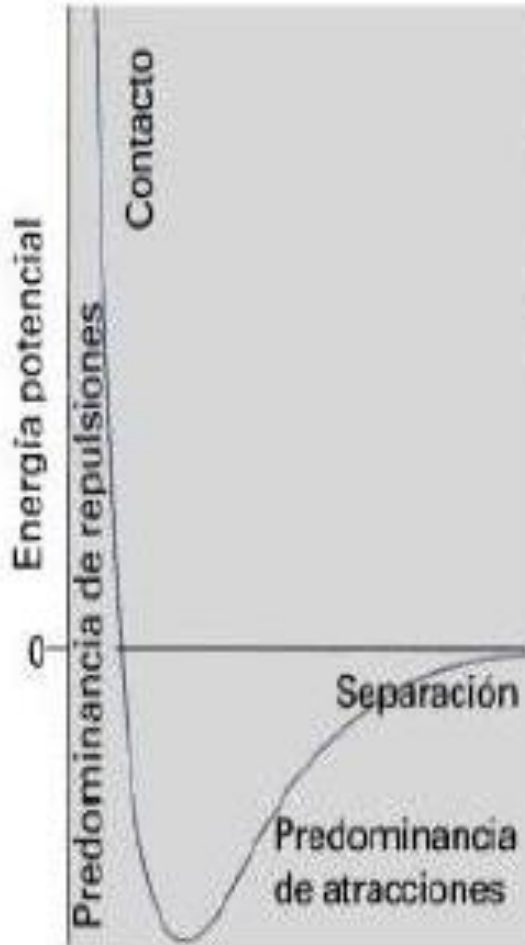
(J. Raúl Grigera, Temas de Biofisicoquimica, Ed. Eudeba)
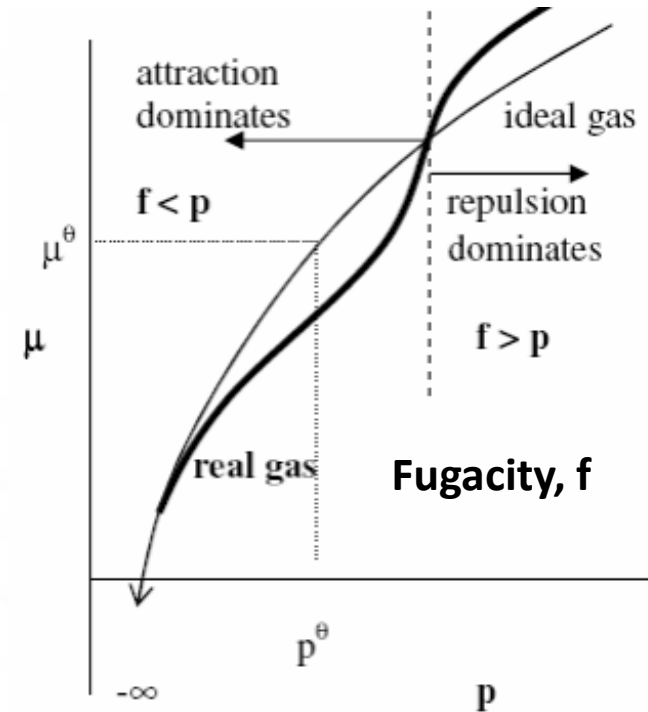
Ideal and real gases:

Energía potencial

Contacto

Predominancia de repulsiones

0

Separación

Predominancia de atracciones

Chemical potential, μ

$\mu^{\ominus}$

$-\infty$

$p^{\ominus}$ Pressure, p

5.5 The chemical potential, μ, of a perfect gas is proportional to ln p, and the standard state is reached at $p^{\ominus}$. Note that, as $p \rightarrow 0$, μ becomes negatively infinite.

$$\mu = \mu^{\ominus} + RT \ln (p/p^{\ominus})$$

From Atkin's book

attraction dominates

$f < p$

ideal gas

repulsion dominates

$\mu^{\ominus}$

μ

$f > p$

real gas   **Fugacity, f**

$p^{\ominus}$

$-\infty$ p

5.6 The chemical potential of a real gas. As $p \rightarrow 0$, coincides with the value for a perfect gas (shown by the pale line). When attractive forces are dominant (at intermediate pressures), the chemical potential is less than that of a perfect gas and the molecules have a lower 'escaping tendency'. At high pressures, when repulsive forces are dominant, the chemical potential of a real gas is greater than that of a perfect gas. Then the 'escaping tendency' is increased.

Mixture of ideal gases: T = const: $\Delta H_{mix} = 0$

n_a n_b $n_a + n_b$
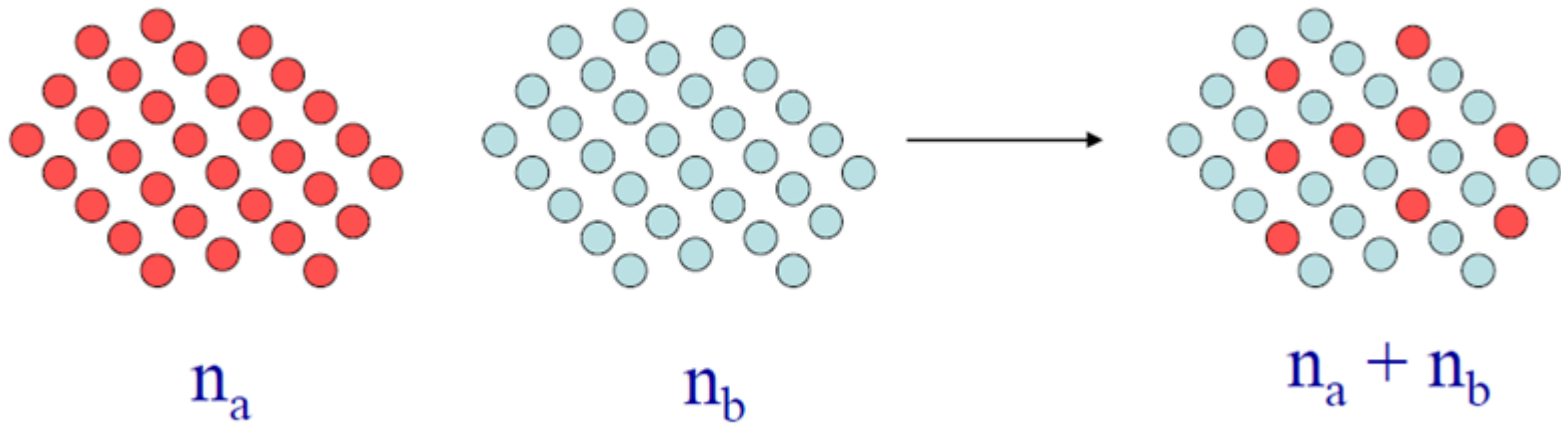
Non ideal mixture: $\Delta E_{mix} \neq 0$, $\Delta H_{mix} \neq 0$

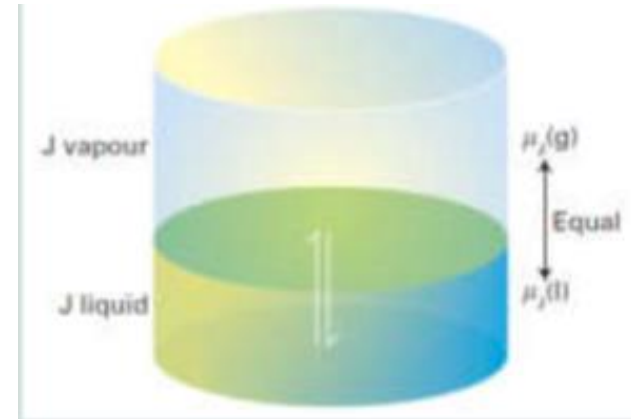n_a n_b $n_a + n_b$
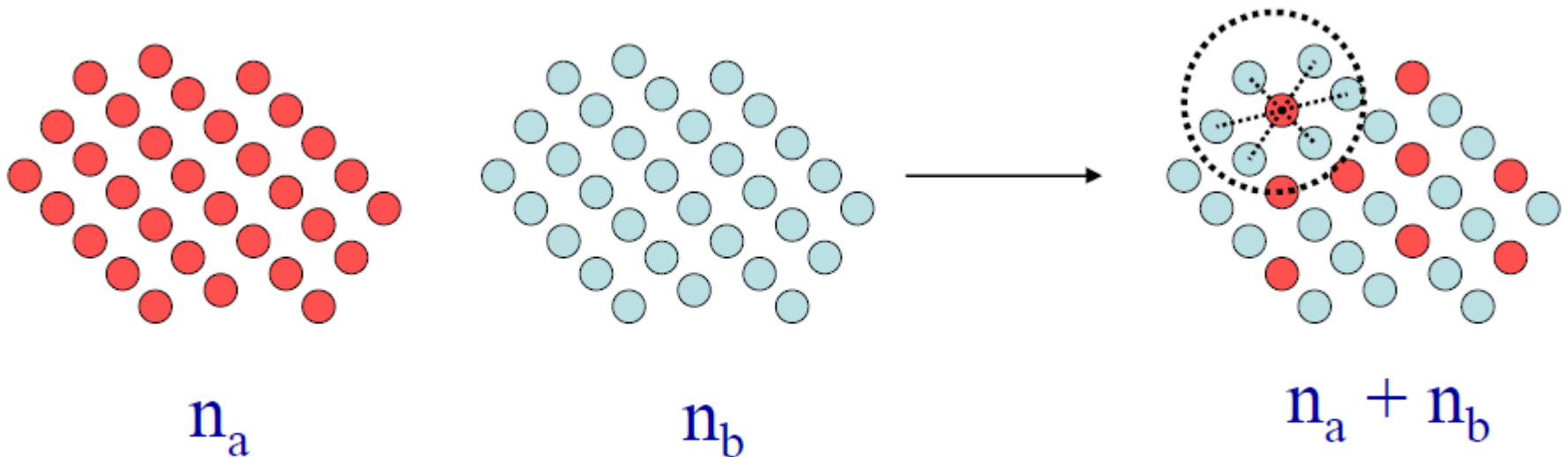
LIQUID MIXTURES: SOLUTIONS

CHEMICAL POTENTIAL OF SOLUTIONS
Ideal solution:

$$\mu_i = \mu_i^* + R\,T\,\ln x_i$$

where R is the gas constant, T the absolute temperature, x_i the molar fraction of component i and μ_i^* the chemical potential of the reference state.

Real solutions, activity (a_i): Activity ("effective concentration") is the product of the molar fraction multiplied by the activity coefficient (Υ_i), which depends on pressure, temperature and concentration.

$$\mu_i = \mu_i^* + R\,T\,\ln a_i = \mu_i^* + R\,T\,\ln x_i\,\Upsilon_i$$

At *infinit dilution* both Υ_i of solute and solvent are equal to unity and the solutions behaves ideally. $\eta = \eta^+ + \eta^-$. Electrolyte estequiometric coefficients, cation and anion.

$$\mu = (\eta^+ \mu^+ + \eta^- \mu^-) \qquad \mu^\pm = \eta^+ \mu^+ + \eta^- \mu^- / \eta \qquad a^\pm = [a_+^{\eta^+} a_-^{\eta^-}]^{1/\eta} \qquad \gamma^\pm = [\gamma_+^{\eta^+} \gamma_-^{\eta^-}]^{1/\eta}$$

Experimental measurements consider the solution as a whole, providing information on the **average value of a_i and Υ_i** (mean ionic values), and not for each particular ion. **But several biological problems require specificity.**

Activity of individual ions

Considering that **activity is a kind of effective concentration** the expressions of μ can be extended to electrolytes, thus considering the existence of an **individual activity of ions.**
There are several experimental techniques that depend on μ and allow the calculation of Υ_i, such as osmotic pressure, vapor pressure, and electromotive force of galvanic cells.
It is possible to measure the individual activity of ions using electrodes that are selectively sensitive to a particular ion. However, there are difficulties with reference and calibration.

$$E = E_j + (RT/z_A F)\ln(a_A)$$

Ej??? Juncture potential
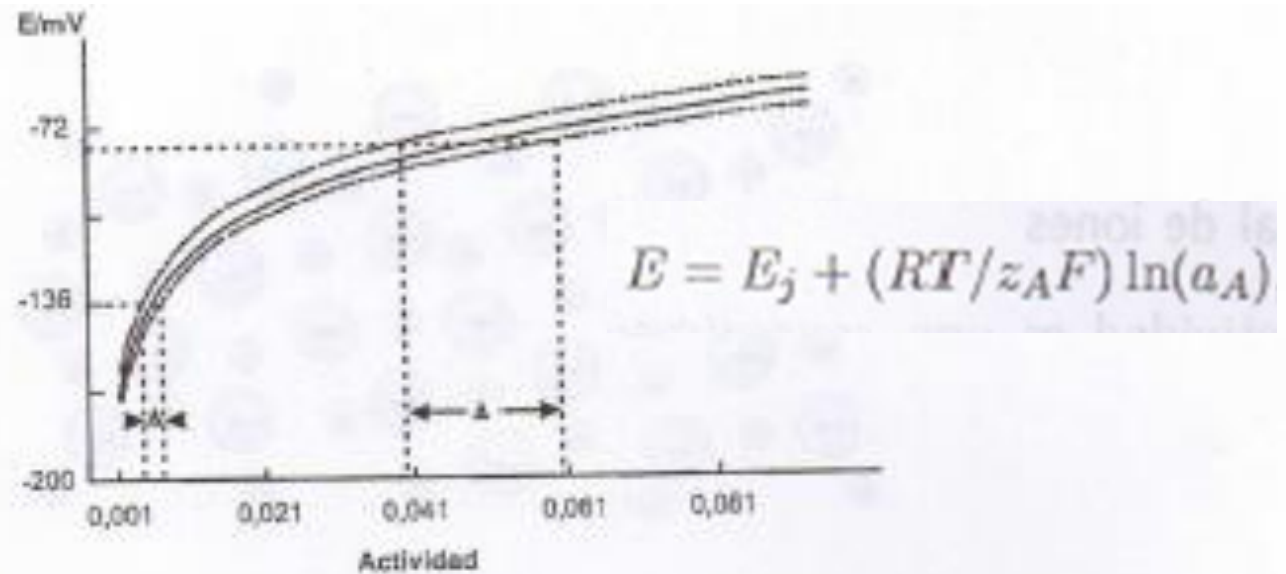
$$E = E_j + (RT/z_A F) \ln(a_A)$$
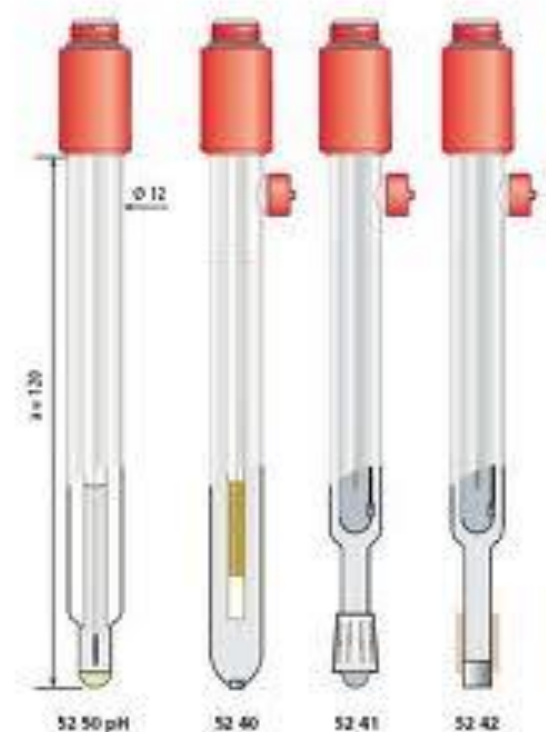
Figura II.1: Fuerza electromotriz generada en una pila con un electrodo selectivo en función de la actividad iónica. La línea llena corresponde al valor con $E_j = 0$ y las líneas de puntos al resultado con $E_j \pm 5 mV$. Se han señalado dos valores de E y su correspondiene error (Δ) debido a los errores en el potencial de juntura. El error aumenta abruptamente con E.

Considering that there are great difficulties in accurately measuring activity experimentaly, **could a theory give an acceptable value of activity?**

# Theory of ionic activity. Theory of Debye-Hückel

When a strong electrolyte dissolves in water, each ion is surrounded by water molecules. The properties of the ions depend on ion-ion and ion-solvent interactions.

The **Debye-Hückel** (DH) model accounts for these interactions by treating the **solvent as a continuum and the ions as point charges**. Each ion is surrounded by an ionic cloud (counter-ions) that exactly cancels its charge. The potential between two ions is:

$U_{ij}(r) = e\, z_i\, z_j\, /\, 4\pi\epsilon_0\epsilon\, r_{ij}$, where e is the electron charge, z the cahrge of the ion, r the distance between ions and ϵ the electrical permitivity of the solvent.

Postulates:

1. Strong electrolytes completely dissociate into ions.

2. Observed deviations from the ideal behavior of solutions are attributed to electrical interactions between ions.

3. The ion attracts charges of opposite sign and repels charges of the same sign, so that its electric field is partly shielded, so the basic postulate of the theory is the concept that each ion is surrounded by an ionic atmosphere of oppositely charged ions.
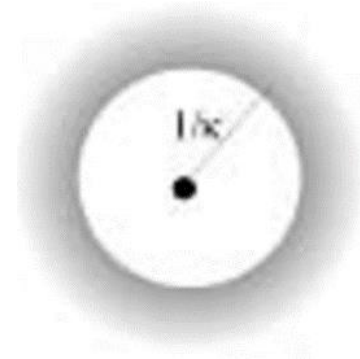
In a medium of dielectric constant ε_r, the potential $\psi(r)$ due to an ion of charge ze at a distance r is (suposing there are not other free ions in the environment):

$$\psi(r) = \frac{ze}{4\pi\varepsilon_0\varepsilon_r r}$$

The presence of other free ions alters such potential $\psi(r)$. Debye-Hückel's theory allows to calculate the electrical work of introducing an electrical charge into the radius of influence of the central ion i. Solving Poisson's equation with the approximation that the concentration of counter-ions is proportional to the interaction energy with the central ion.
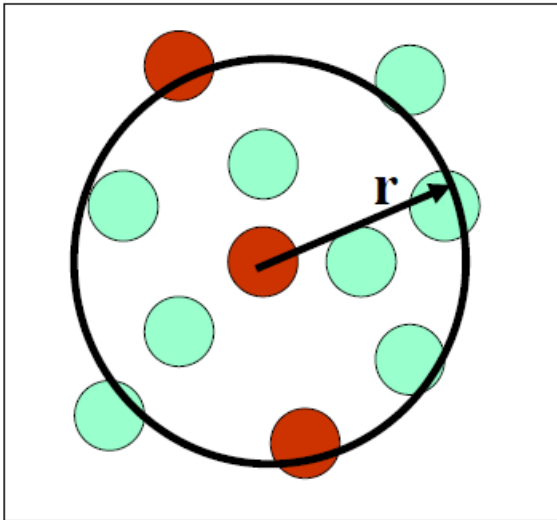
$$\psi(r) = \frac{ze}{4\pi\varepsilon_0\varepsilon_r r}\exp(-\kappa r)$$

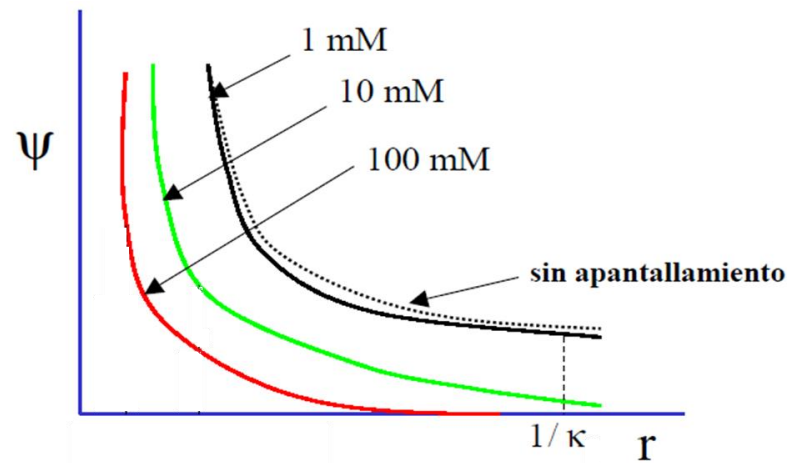K is the inverse Debye length, it has units of length^{-1}

So, the ionic distribution is a function of a single parameter, the inverse Debye length (k)

1) Ionic strength (I) / Charge concentration

2) Thermal energy

3) Density and dielectric constant of the solvent

* Efecto sobre el potencial ψ de una nube iónica formada por una sola especie iónica con $z=1$, para diversos valores de la concentración de dicha especie

$$\kappa = \left(8\pi N_A e^2/1000\epsilon T\right)^{1/2} I^{1/2},$$

where ε is the electric permitivity, *T the absolute temperature*, N_A Avogadro's number and *I the ionic force: $I = \frac{1}{2} \Sigma\, c_i z_i^2$ where c is concentration (mol /l)*

$$\mu_{REAL} - \mu_{IDEAL} = N_A W = \frac{N_A z e_0}{2}\Psi = -\frac{N_A (z_i e_0)^2}{2\varepsilon\kappa^{-1}} = RT ln\gamma_i$$

$$\log \gamma_{\pm} = -[1.824\times10^6/(\varepsilon T)^{3/2}]\,|z_+ z_-|\,\sqrt{I}$$

$$\log \gamma_{\pm} = -0.509|z_+ z_-|\sqrt{I}$$

Limit of application: Only valid for extremely diluted solutions (*c < 0, 001 mol/l*) The most serious error of the DH theory is that it does not take into account ionic size. **With this approximation all ions of equal charge have exactly the same properties**.

Mean Spherical Approximation (MSA)

Extention of D-H theory where the ionic size is taken into account by considering the **ions as rigid charged spheres.**

A parameter called **2Γ** takes the place of k, also representing a reciprocal length that depends not only on the ionic charges and the concentration but also on the diameter of the ions (σ).

$$\Gamma^2 = (\pi e^2 1000 / 4\pi \epsilon_0 \epsilon RT) \left\{ \Sigma\, c_i\, (z_i / (1 + \sigma_i \Gamma)) \right\}^2$$

Using MSA, the individual ion activities for salt solutions or salt mixtures can be easily calculated. The electrostatic contribution of the individual ion activity in a solution is calculated by:

$$\Delta \ln \Upsilon_{\pm} = - e^2 1000 / 4\pi \epsilon_0 \epsilon RT \left(\Gamma\, \Sigma\, c_i\, z_i^2 / (1 + \Gamma \sigma_i) \right)$$
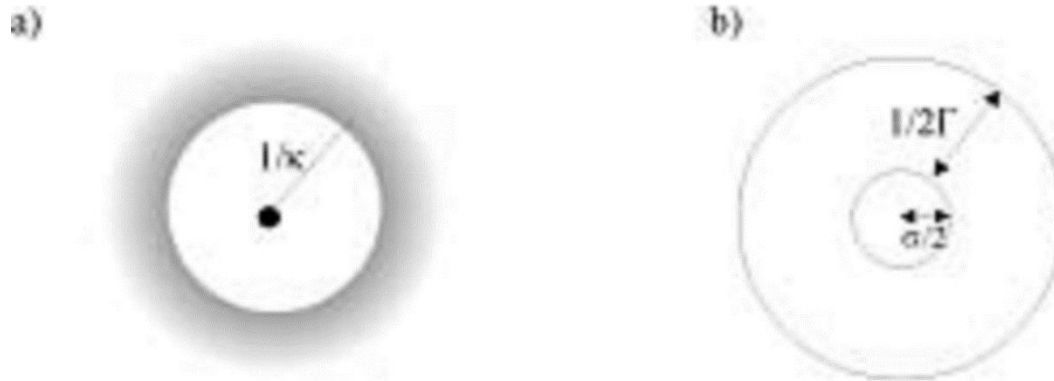

Figura 2.3: Dos representaciones de la distribución de contra-iones en una solución electrolítica: (a) un ion central y su nube de contra-iones y (b) un condensador esférico equivalente.

The ionic diameter introduced in the theory must consider both the excluded volume generated by the ion and the hydration water, which interacts with the ion generating a hydration sphere. The diameter of this theory is actually an *effective diameter,* σ_i : $\qquad \sigma_i = \sigma_i^0 (1 + \alpha_i\, c_i)$, where σ_i^0 y α_i are adjustment parameters. We can see that σ_i is a function of the concentration. *Predictions closer to experiments!*

IONIC HYDRATION

Formation of the solution: interaction of the solute with the solvent molecules.
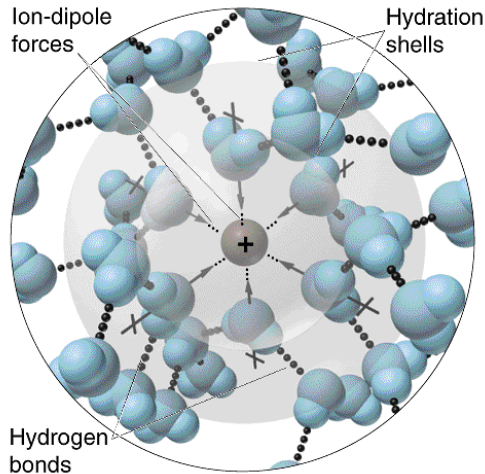
Dissolved ion:

Solvent ion interface (spheres or hydration layers)

Changes in the order of solvent molecules around the ion.

Discontinuity in the hydrogen bond network.

This ion-water orientational force competes with water-water interactions (hydrogen bonds) and with the destructive effect of thermal noise.
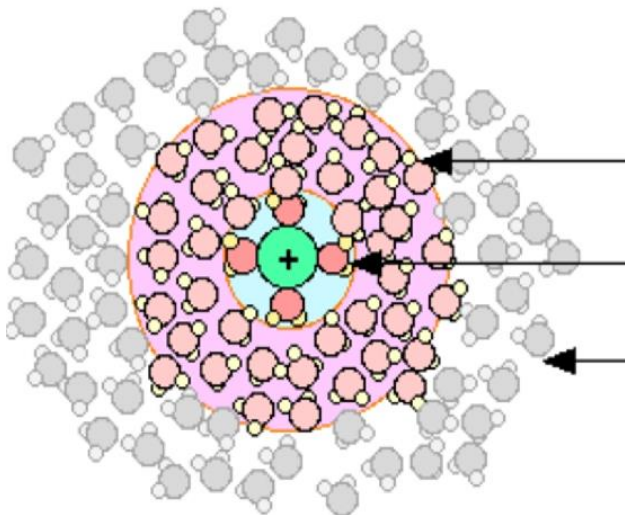

Secondary hydration: At large distances (lower electric field), water is less oriented, but the effect is still enough to perturbate water structure (more **disordered** than pure water).

Primary hydration: Close to the ion, large electric field, water molecules are strongly oriented and **ordered.**

Normal water: At large distances. Bulk water. Unperturbed.

ION-ION INTERACTIONS IN WATER

Each ion in solution interacts with neighboring water molecules, i.e., its *hydration sphere*. The orientation of the water molecules in this sphere is determined by the charge and size of the ion, forming the **primary hydration sphere**. Other water molecules located at a greater distance are incorporated but their orientation will not be well defined. Thus, **the interaction between oppositely charged ions is mediated by the surrounding water.** Whether or not the ions interact will depend on the rigidity of the first sphere and the energy cost between establishing a water-mediated contact or loosing the second sphere.
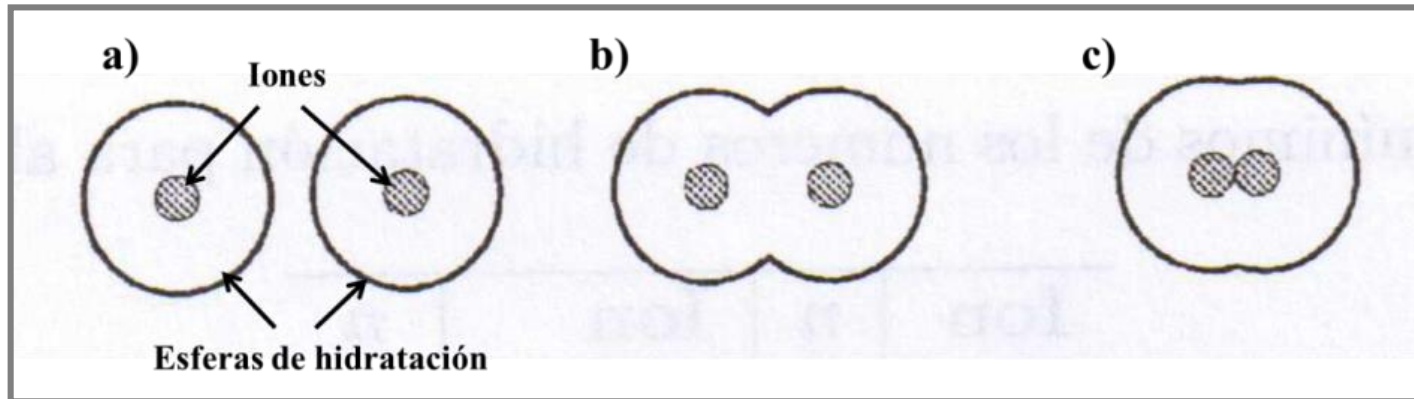
Three cases of ion-ion interaction: a) The hydration spheres do not interact, b) The proximity of the ions causes part of the spheres to overlap, the ions remaining separated by some water molecules, c) The ions are in contact. For cases b) and c) the **entropy change is positive** since water molecules move from a restricted mobility condition at the hydration sphere to the bulk where mobility is enhanced.

Hydration numbers (n)

An approximate way of establishing the degree of hydration is to establish **how many water molecules are present in the first hydration sphere**. Hydration numbers can be obtained as a measure of the average number of water molecules surrounding the ion. The stability of the sphere is short-lived and its value will depend on the property used to determine it as well as the experimental time. It can be estimated from an effective radius by means of hydrodynamics.

In general, a high concentration of salts decreases the value of n, this is because the availability of water for each ion decreases and in turn a charge screening effect is produced which decreases the attraction of water.

Ion	n	Ion	n
Li^+	6	Mg^{++}	14
Na^+	4	Ba^{++}	14
K^+	4	La^{+++}	22

Minimum hydration numbers for certain ions

Charge density
Z value

Hydration dynamics

$R = t_i / t_a$ The parameter R describes an average value of the hydration time. t_a is the average time during which a water molecule remains next to another water molecule in the bulk liquid and t_i is the average time during which a water molecule remains next to the ion. They are called *residence times*.

If $t_i > t_a$ and thus R > 1, we have *positive hydration.*
If $t_i < t_a$ and thus R < 1, we have *negative hydration.*

Residence times can be obtained by different experimental techniques such as dielectric relaxation, nuclear magnetic resonance, fast pulse laser and viscosity.
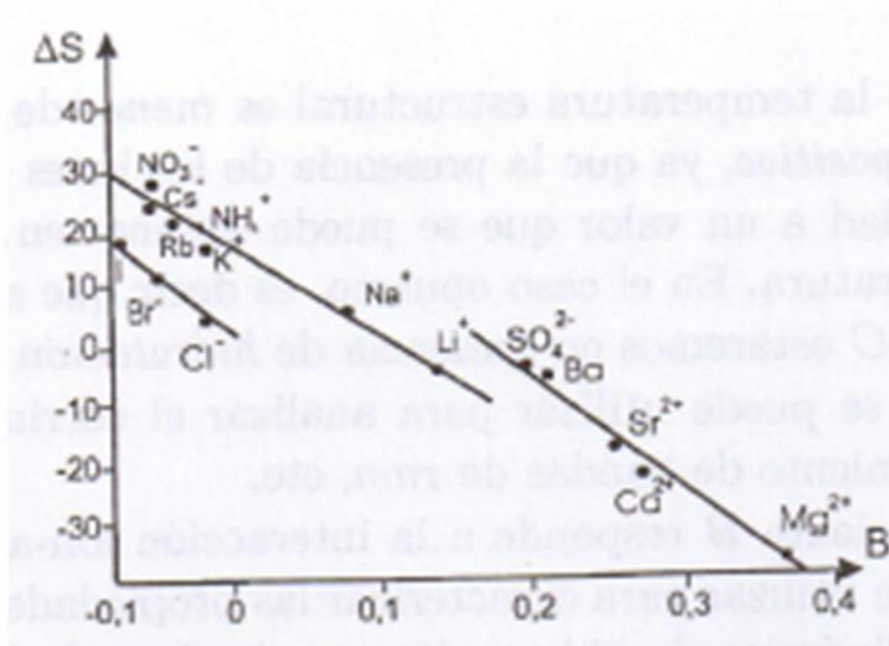
Hydration and viscosity

The relative viscosity (η_r) of a solution (solution viscosity/pure solvent viscosity) provides valuable information on hydration dynamics. The relative viscosity of a solution can be expressed as:

$\eta_r = 1 + Ac^{1/2} + Bc + ...$

This equation is called the *Jones-Dole equation*, where c is the concentration of the solution and **the coefficient B is related to the solute-solvent interaction**.

Cuadro II.5: Valores del coeficiente B de la ecuación de Jones-Dole para algunos iones.

Li^+	Na^+	K^+	Rb^+	Cs^+	Ba^+
0,149	0,086	-0,007	-0,03	0.005	0,22

Mg^{++}	Cl^-	Br^-	I^-	NO_3^-	SO_4^{--}
0,585	-0,007	-0,042	-0,068	-0,046	-0,209

B > 0, positive hydration: water molecules more restricted by the ions (less mobile water; negative ΔS).
Rigid hydration sphere increases friction, thus viscosity.

B < 0, negative hydration (less restricted or more mobile water; positive ΔS). Less friction

Figura II.6: Entropía unitaria de iones en función del coeficiente B. Se observa un comportamiento lineal para diferentes familias de iones.

Hydration and "structural temperature"

Another parameter that provides information on the hydration dynamics is the **structural temperature**. It is defined as the temperature at which *pure water* has the value for a given property as the solution at 25ºC, considering properties such as viscosity.

Structural temperature < 25ºC → positive hydration since the presence of the *ions has increased the viscosity* to a value that can only be obtained for pure water by reducing temperature to a value lower than 25ºC.
Large residence times of the water molecules around the ions → rigid hydration layer → increased friction → increased viscosity.

Structural temperature > 25ºC → negative hydration. *The ions have reduced viscosity* to a value that is obtained for bulk water at a higher temperature.

Hydration structure

The ordering of water as a whole will depend on the order-disorder balance between the different spheres of hydration. This balance is reflected in the parameters that define positive and negative hydration, but there are also structural phenomena. X-ray diffraction and computer simulation provide information on the possible hydration structure.

The crystallographic radii r_c (X-ray diffraction) are not compatible with the transport properties in aqueous solution. It is necessary to speak of *hydrodynamic radii r_h* which consider the sphere of hydration. The r_h can be obtained by equivalent conductivity.

Ion	masa atómica	$r_c/\text{Å}$	$r_h/\text{Å}$
Li$^+$	6,941	0,6	3,83
Na$^+$	22,989	0,95	3,65
K$^+$	39,098	1,33	3,48
Mg^{++}	24,305	0,65	4,39
Ba^{++}	136,327	1,35	4,00

Size, "bound" water, strength

r_h and r_c do not follow the same size trend. The hydrated radius is actually an equivalent radius referred to a sphere such that it has the same transport properties as the ion studied.

Although we talk about structure "promoting" and "destroying" ions, this is not rigorous.

An experimental way to quantify the hydration shell around an ion is through the **hydration radius or Stockes radius** (r_H), which is determined by studying the limiting speed v that this ion reaches in the aqueous medium when subjected to an electric field E. Approximating the ion to a sphere of radius r_H, charge q, and if η is the **viscosity** of water:

$$qE = 6\pi\eta r_H v \Rightarrow r_H = \frac{qE}{6\pi\eta v}$$

Similarly, the effective radius of the ion (r) is related to the **diffusion coefficient** by Einstein's equation and, thus, can be experimentally determined:

$$D = \frac{RT}{N}\frac{1}{6\pi\eta r}$$

Hydration structure (results from computer simulations)

Density of water around different ions. It can be seen that the relative sizes of the hydration sphere differ in each case. Considering that the electrostatic interaction depends on the inverse of the distance to the charge center, it is expected that a small ion like Li^+ will have a more rigidly bound sphere around the ion.
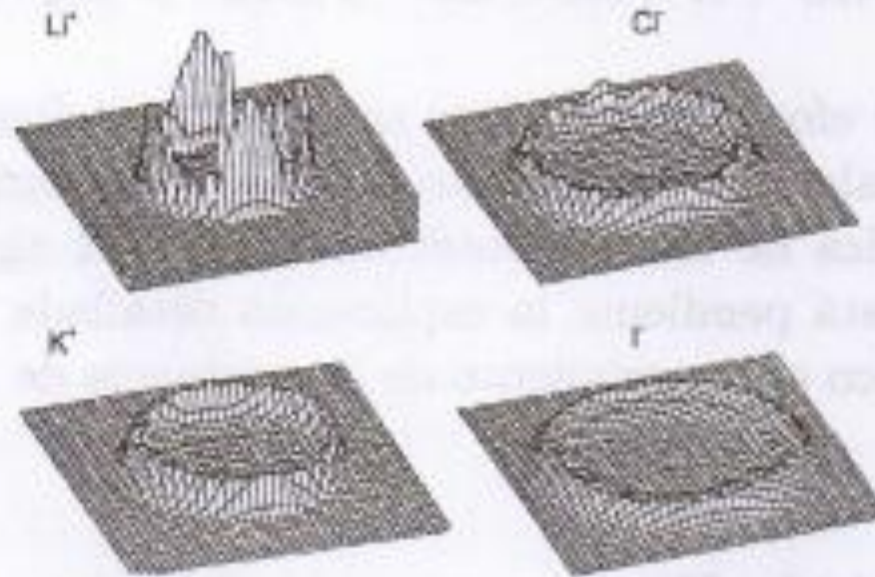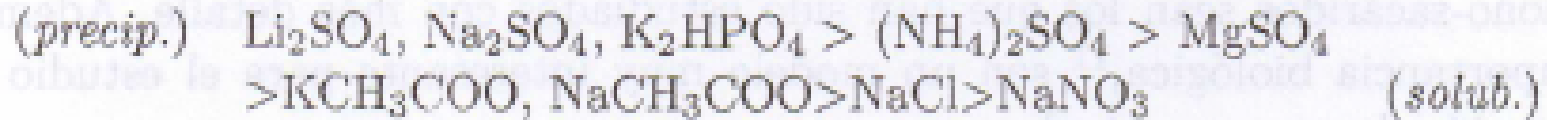

Figura II.7: Distribución de agua alrededor de Li^+, K^+, Cl^- y I^- de acuerdo con simulaciones de dinámica molecular [de K. Heinzinger, in *Water: Biomolecule Interactions*, editado por M. U. Palma and M. B. Palma-Vittorelli, Soc. Italiana di Fisica, Bologna, (1993)].
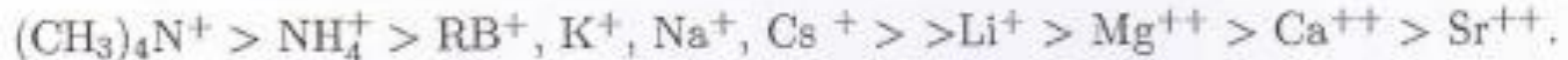
The liotropic series

In 1888, Hofsmeister found that certain salts increased the solubility of globular proteins while others produced precipitation.

$$(precip.) \quad Li_2SO_4, Na_2SO_4, K_2HPO_4 > (NH_4)_2SO_4 > MgSO_4$$
$$> KCH_3COO, NaCH_3COO > NaCl > NaNO_3 \qquad (solub.)$$

para aniones

$$SO_4^= > CH_3COO^- > Br^- > NO_3^- > ClO_4^- > I^- > CNS^-,$$

para cationes

$$(CH_3)_4N^+ > NH_4^+ > RB^+, K^+, Na^+, Cs^+ > > Li^+ > Mg^{++} > Ca^{++} > Sr^{++}.$$

The effect is not easy to explain, but it is known that it depends on charge, ionic radius, the specific interaction of different ions with water and the ionic polarizability. The existence of this so-called *liotropic series* has relevant practical consequences.

A **cosmotrope** would generate "order" in water, with cosmotrope-water interactions prevailing and therefore minimizing protein hydration and preventing its denaturation or stabilizing it since water could attack backbone hydrogen bonds which are responsible for the protein structure

In the absence of ions, water interacts with the solute.

A **chaotrope** (promotes chaos or disorder) would interact poorly with water and encourage water to interact with the protein, favoring its hydration and therefore its destabilization or denaturation.
However, the interaction with the side chains, mainly the charged ones, is also important.
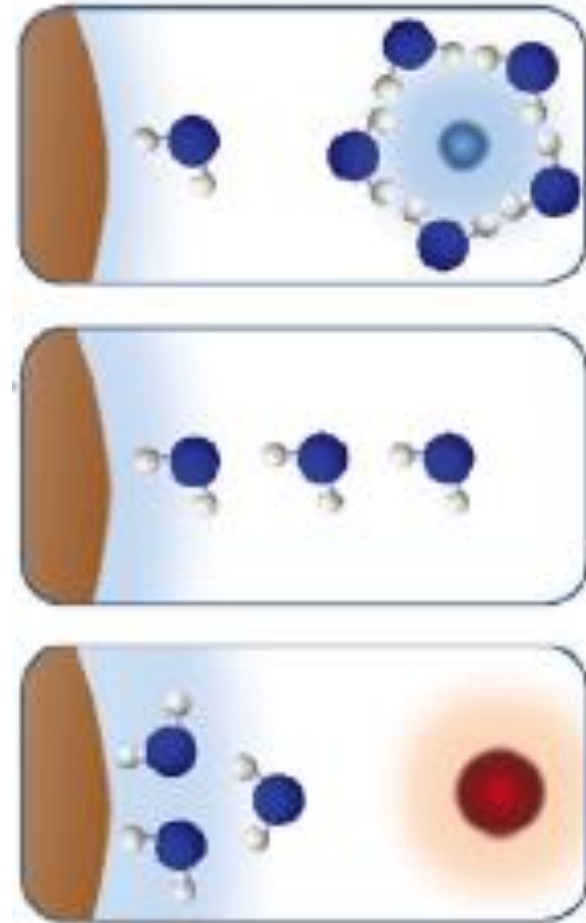
HYDROPHILIC SUBSTANCES

They have no net charge but still have an affinity for water. Most of these substances have **sites that form hydrogen bonds**. In these cases, the energies involved are lower compared to ions. Water-site interactions through hydrogen bonds are energetically of the same order of magnitude as water-water interactions.

**Criteria to be taken into account in these cases:**
We should speak of "hydration sites" instead of hydration sphere.
The distribution of these sites on the surface does not have to be uniform.
The solute-solvent interaction determines the conformation and **depends on the arrangement of the hydrogen bonds** rather than on the hydration number.
The hydration number depends not only on the hydrogen bond-forming sites but also on their **spatial orientation.**
- The solubility of sorbitol at 25°C is 2.5 times greater than that of mannitol and has much greater diffusion.
- α-anomer of glucose is 45% soluble in org. solvent and 37% in water. 3OH equatorials that would form better HB than the axial ones. The β-anomer has 4 equatorials. Also, more compatible with water network.

Sorbitol   Mannitol

Glucose
$C_6H_{12}O_6$

α-D-glucose β-D-glucose
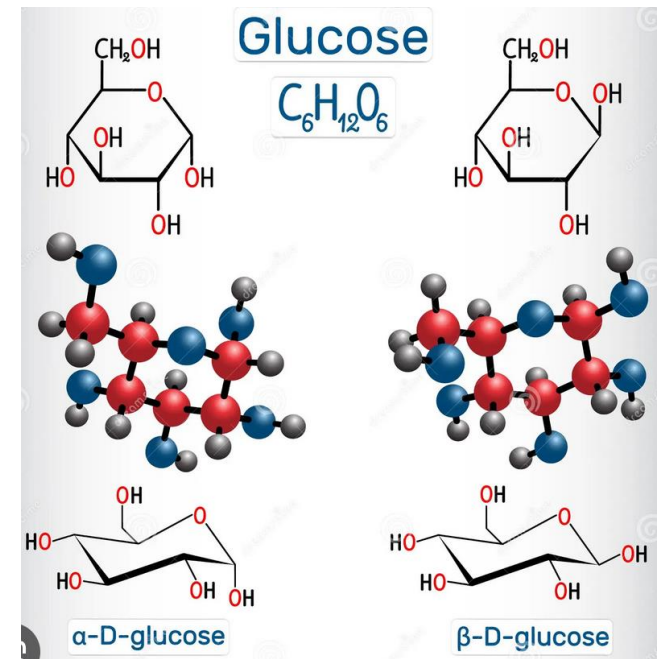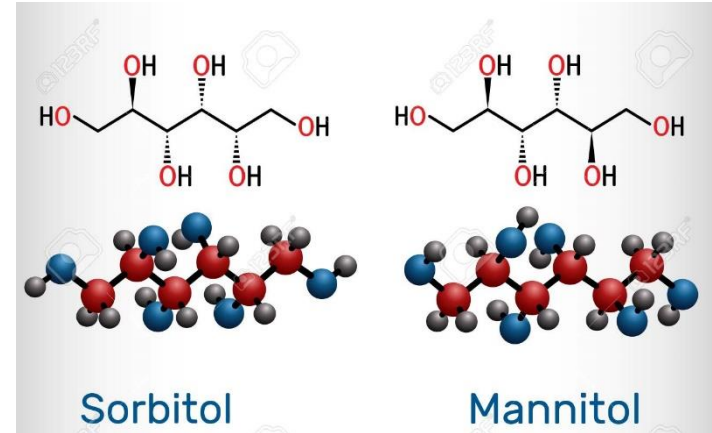
HYDROPHOBIC SUBSTANCES: SMALL HYDROPHOBES - CLATHRATES

Hydrophobicity. However, water does not lose hydrogen bond coordination. They can encapsulate small molecules such as noble gases, methane, etc.
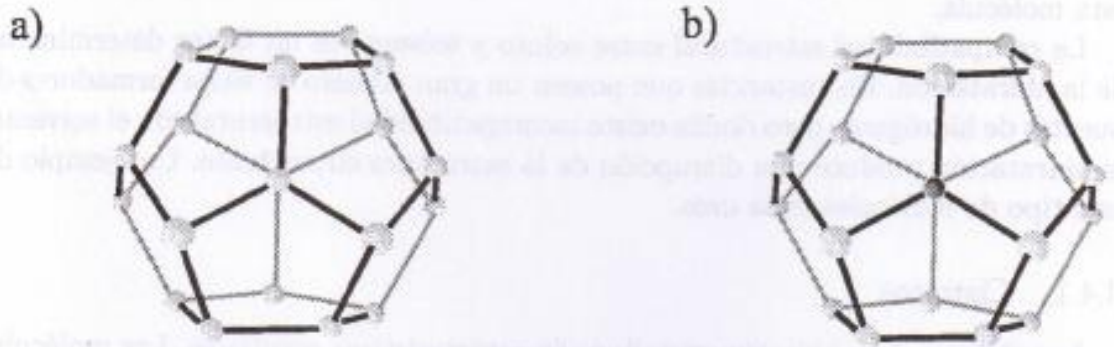

Figura II.9: Estructura de clatratos, (a) Tipo I y (b) Tipo II (redibujado de D. W. Davidson, in *Water: A Comprehensive Treatise*, Vol. 2, editado por F. Franks, Plenum Press, New York, 1973).
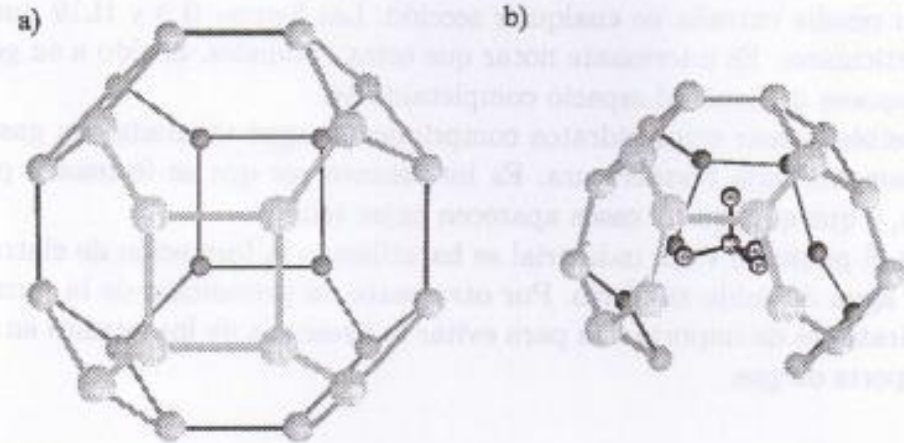

Figura II.10: a) Caja (octaedro truncado ideal) encontrada en $HPF_6 \cdot 6H_2O$, y (b) Forma distorsionada de $(CH_3)_4NOH \cdot 5H_2O$ (redibujado de Davidson, *op. cit.*).

Nonpolar solutes attract each other in water, as if pulled by certain "force". Hydrophobic effect. Water looses hydrogen bonds → reduce interface by removing water towards bulk (entropic effect). Barrier: cost of dehydration.
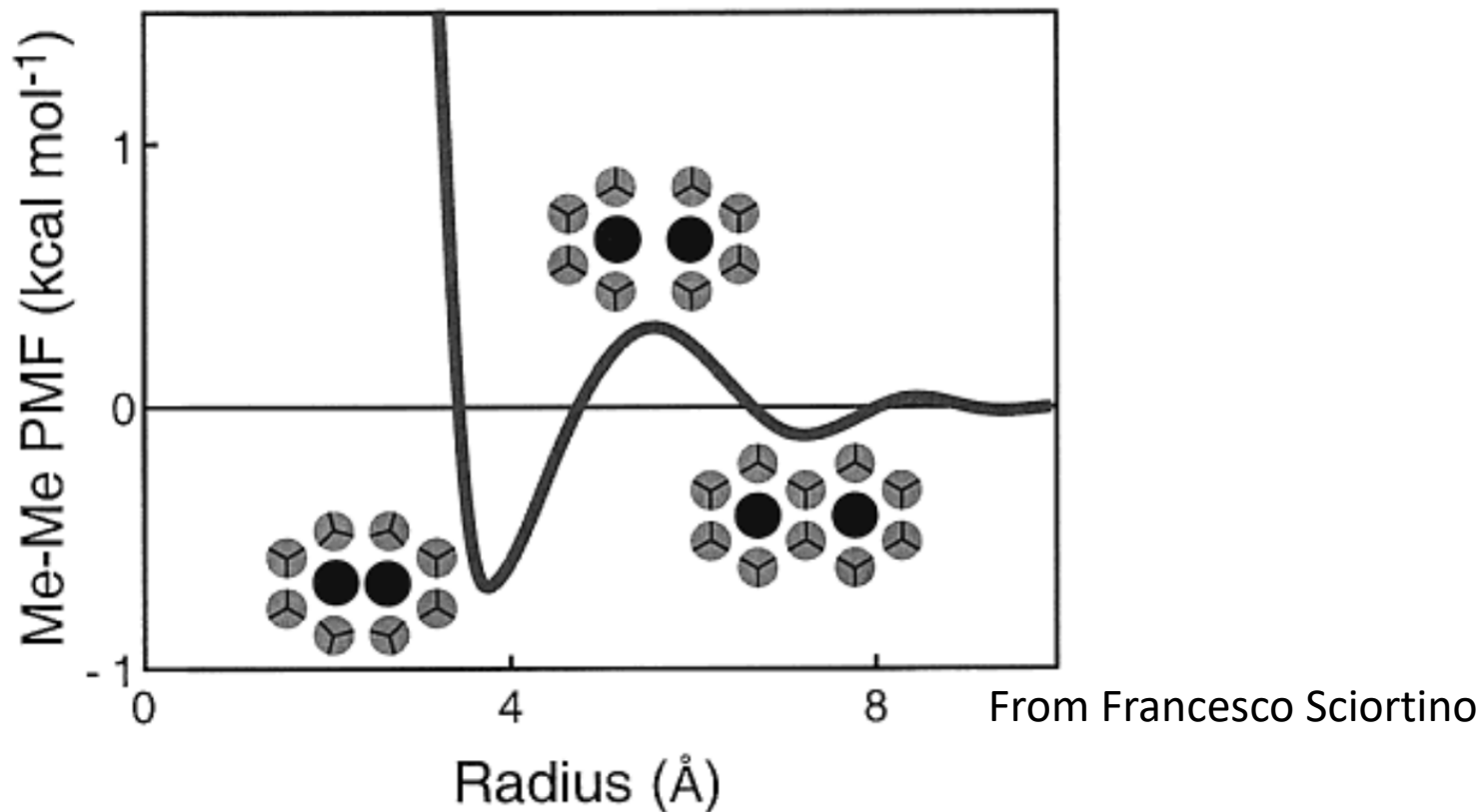

From Francesco Sciortino

Figure 15. Methane−methane potential of mean force. Idealized potential of mean force between two methanes as a function of distance in angstroms. Left: methanes (in black) at contact, middle: at the barrier distance (which has an unfavorable free energy), and right: in a solvent-separated configuration. Adapted from D. E. Smith, and A. D. J. Haymet, J. Chem. Phys. **1993**, *98*, 6445.

Extensive hydrophobic surfaces: Flat, structureless, non-attractive (or repulsive) smooth surfaces. Hydrogen bond loss. Depletion of density at the surface (predicted theoretically, David Chandler and others)
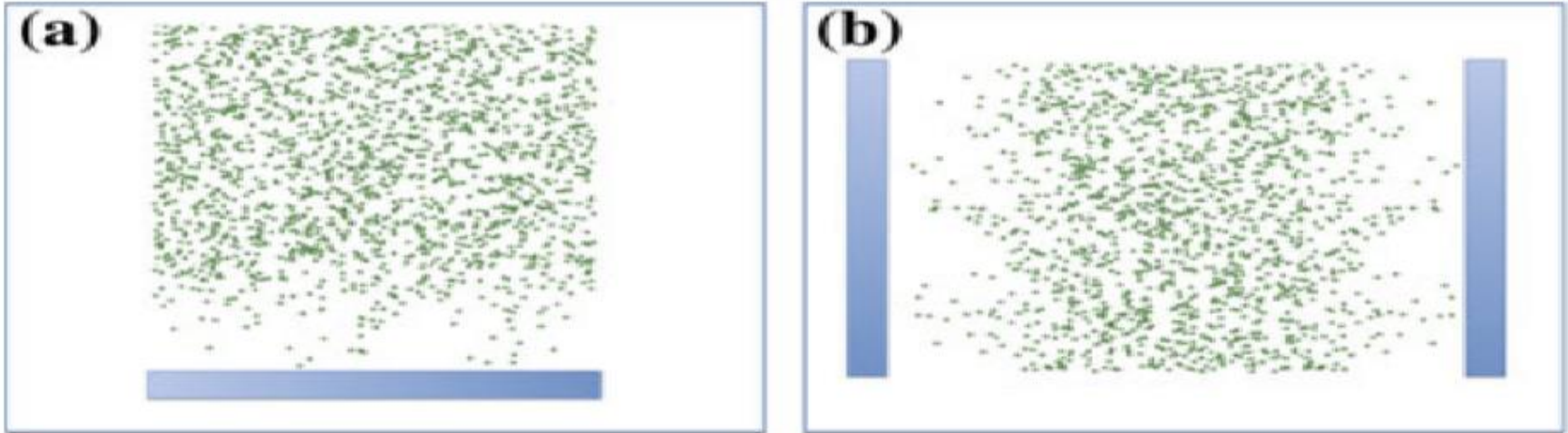
The hydrophobic effect between water molecules (*green*) and a non-polar (*blue*) material. **a** A non-polar surface (for example, a plastic sheet) is introduced in water; as a result, the water molecules tend to maximise their entropy by retreating from the plastic surface. **b** Two non-polar surfaces in water have the effect of creating two such regions of reduced density: as soon as the two surfaces are approached, water molecules tend to escape from the region between the two.

The two plates collapse to each other. Hydrophobic attraction (hydrophobic collapse is relevant in protein folding).

Next step: Study the nature of the hydrophobic interaction. We will see that entropy is the driving force.

Not completely structureless or slightly attractive (very low van der Waals forces). The behavior at a single plate is hydrophobic but no depletion length. Water density profile indeed shows layering. Anyway, two plates also attract each other (hydrophobic interaction)
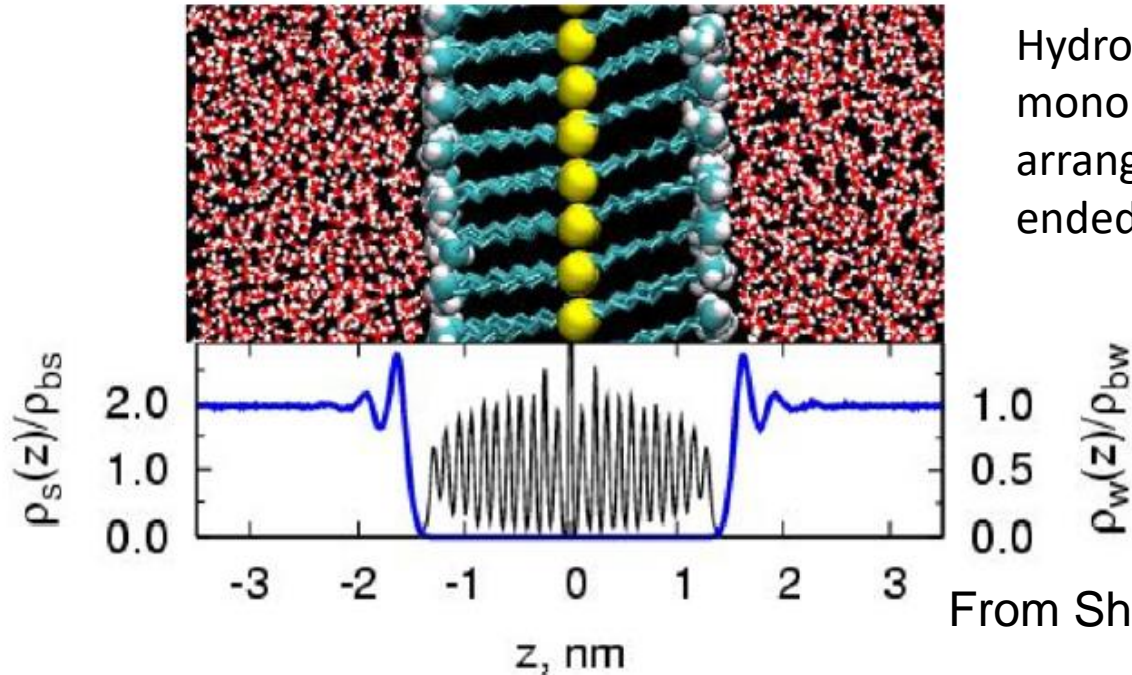
Hydrophobic self-assembled monolayer (SAM): arrangement of alkylic chains, ended in methyls (CH_3).

From Shekhar Garde's group

Fig. 1. The SAM water system. (*Upper*) A snapshot of the $-CH_3$ SAM system. The sulfur atoms (yellow) and surfactant head groups (cyan and white) are shown in spacefill representation. The alkane tail (cyan) and water (red and white) are shown with sticks. (*Lower*) Average density of SAM and water phases normal to the surface divided by their respective bulk densities ($\rho_{bs} = 935$ kg/m^3 and $\rho_{bw} = 985$ kg/m^3). The SAM bulk density was calculated by averaging over the region excluding the sulfur and head group atoms.