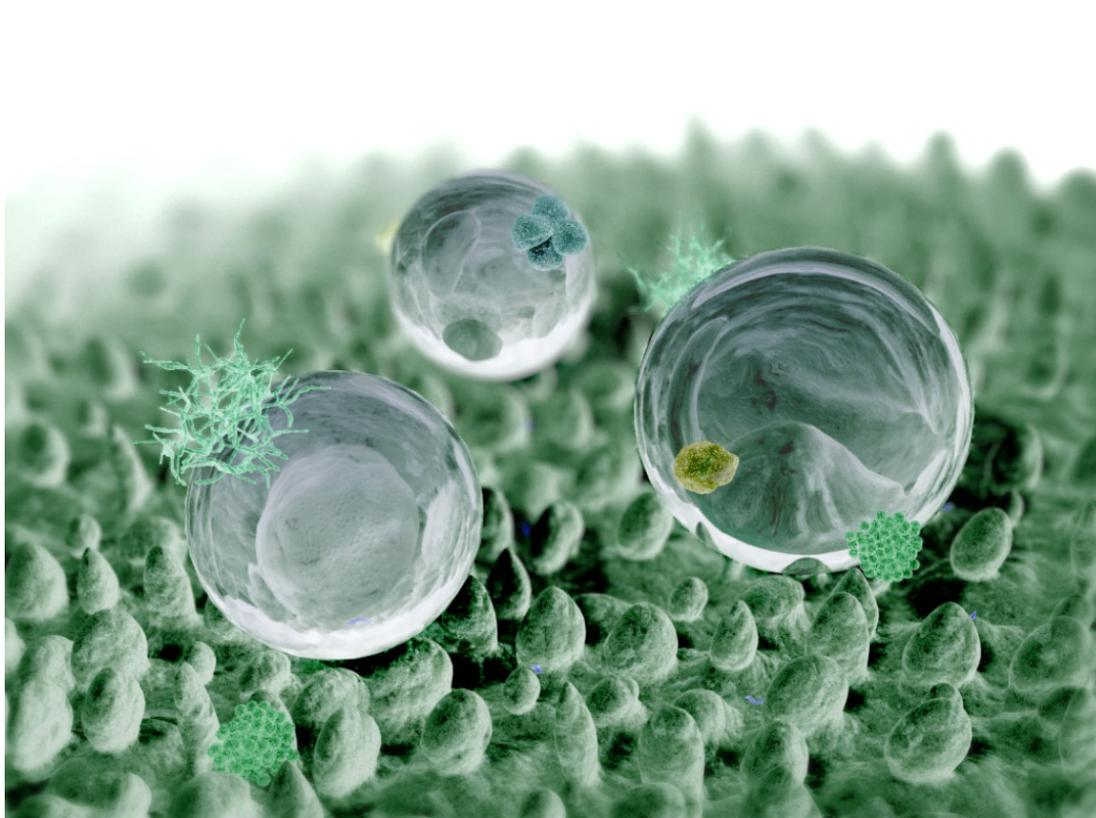
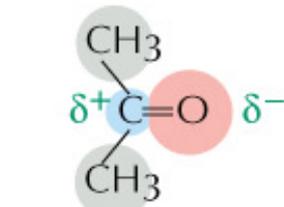


Hydrophobic effect

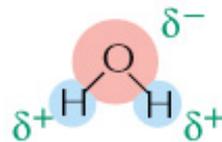
This is not an intermolecular force, but rather the effect due to the peculiar solvent – water.



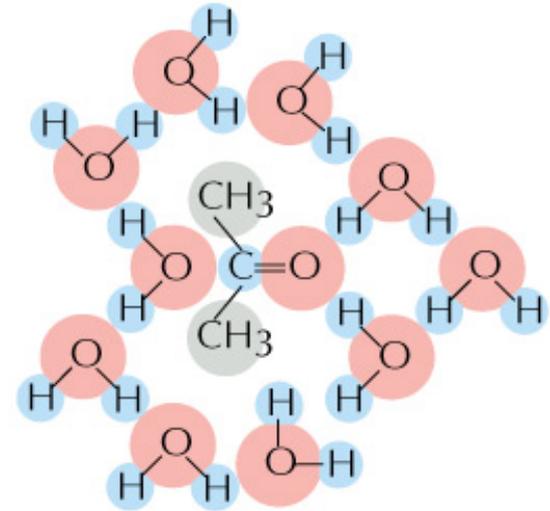
Polar molecule dissolved in water



acetone

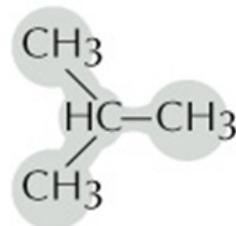


water

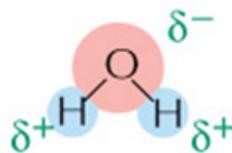


acetone in water

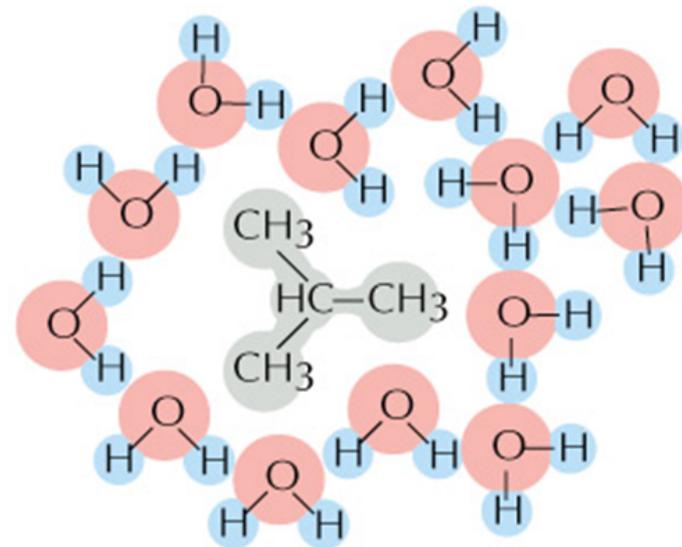
Non-polar molecule dissolved in water



2-methyl propane



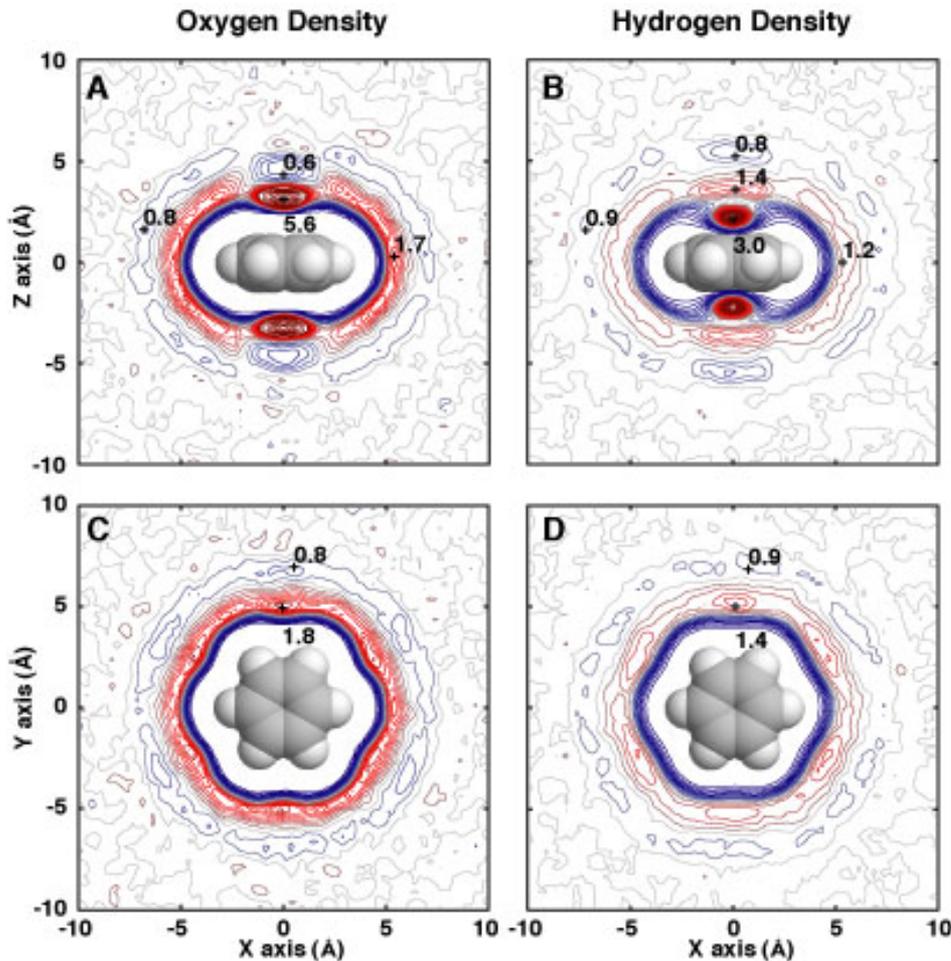
water



2-methyl propane in water

Water is ordered by the presence of solutes

Water structure is different around the solute molecules:

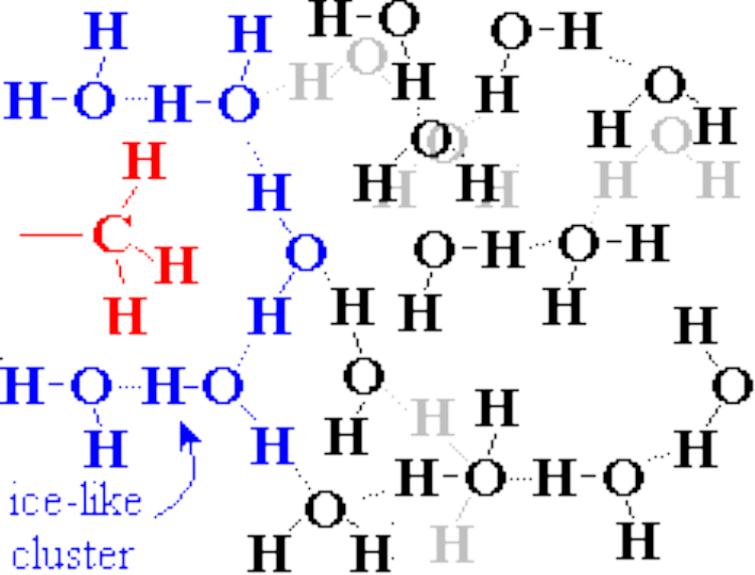


Water Density Surrounding Benzene

The water **oxygen** density maps reflect the average position of the water molecules surrounding the solutes.

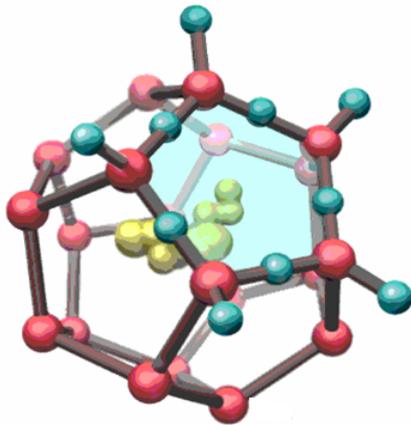
The **hydrogen** density maps contain orientation information.

The water molecules located in the peak regions above and below the benzene ring are in a hydrogen-bonding orientation, with the global **H** density peak located between the benzene center and the **O** density peak.



At the interface between water and a non H-bonding group, there are fewer opportunities for H-bond exchange. This leads to longer H-bond lifetime, and creation of ice-like ordered water clusters at the interface, and consequent loss of entropy.

For n-butane in water at 25 °C.



Water molecules form cage-like structure to encase hydrophobic molecule.

$$\Delta G = \Delta H - T\Delta S = + 24.5 \text{ kJ/mol}$$

$$\Delta H = - 4.3 \text{ kJ/mol}$$

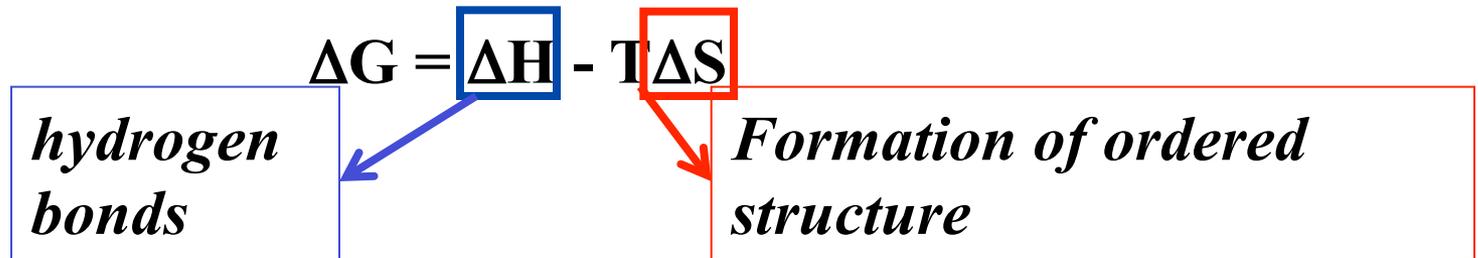
$$-T\Delta S = +28.7 \text{ kJ/mol}$$

It is *enthalpically favorable* but it is very *entropically unfavorable*.

Solubility in water

Water is a polar solvent: dissolves charged or polar compounds by replacing solute-solute H-bonds with solute-water H-bonds.

Water structure is different around the solute molecules:



$$\Delta G < 0$$

Soluble compound

$$\Delta G > 0$$

Hydrophobic/ insoluble compound

*Compounds that dissolve easily in water are **hydrophilic**.*

Non-polar** molecules such as lipids and side chains of some amino acids are **hydrophobic

***Amphipathic** molecules have **polar** or charged regions, as well as **non-polar** regions.*

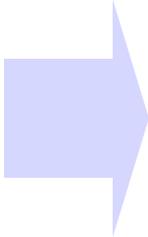
There is no “hydrophobic force”!!!

Often a small ΔH , but a large, favorable ΔS component.

Lipid suspension

❖ Water concentration – 55 M

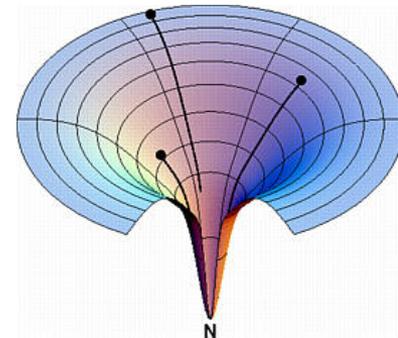
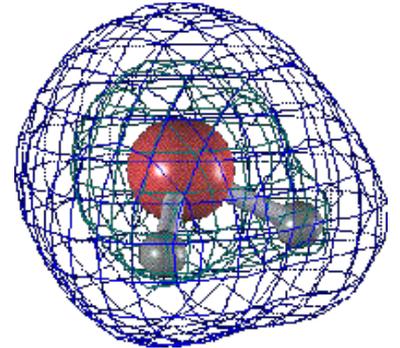
❖ Lipid concentration < 1 μM


$$\frac{\text{water molecules}}{\text{lipid molecules}} \approx 5.5 \times 10^7$$

❑ The water molecules easily change orientations, or move to new neighboring locations.

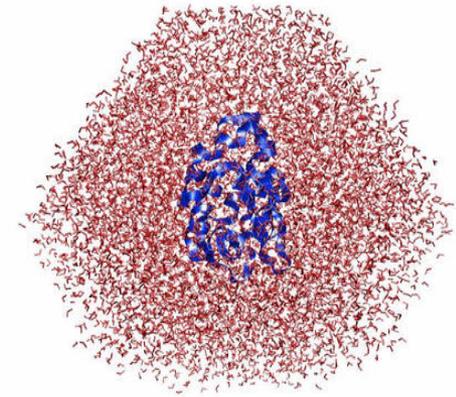
❑ System explores different conformations through diffusion and random thermal motion.

❑ System will stay with the lowest energy conformation it encounters.



Hydration of macromolecules

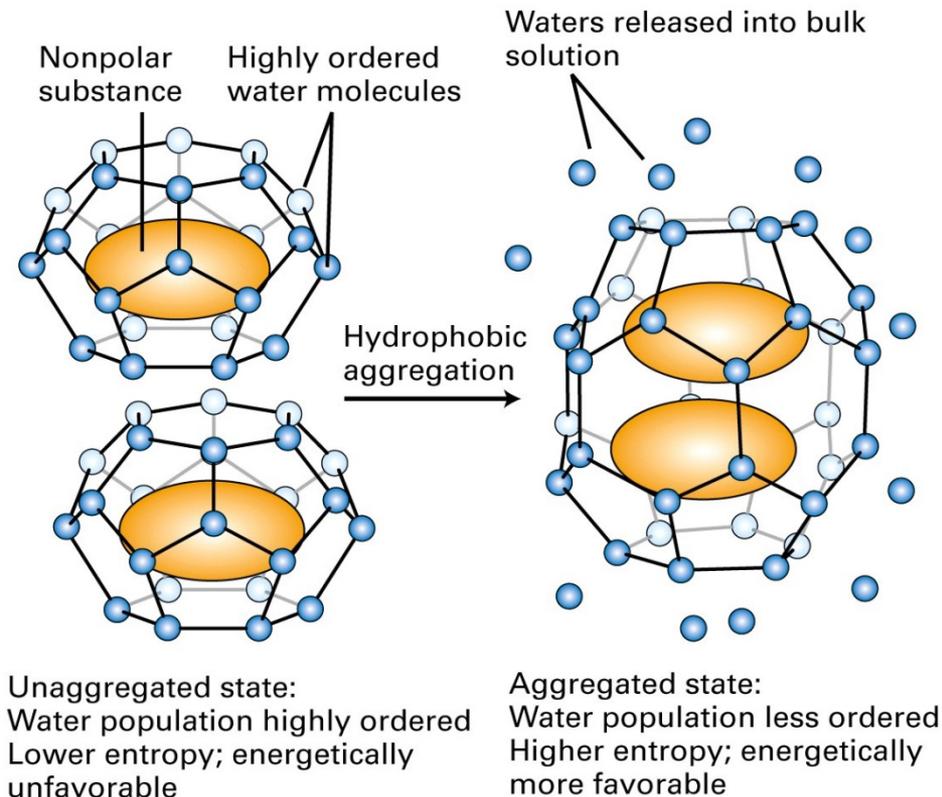
When a macromolecule moves, it displaces many small solvent molecules.



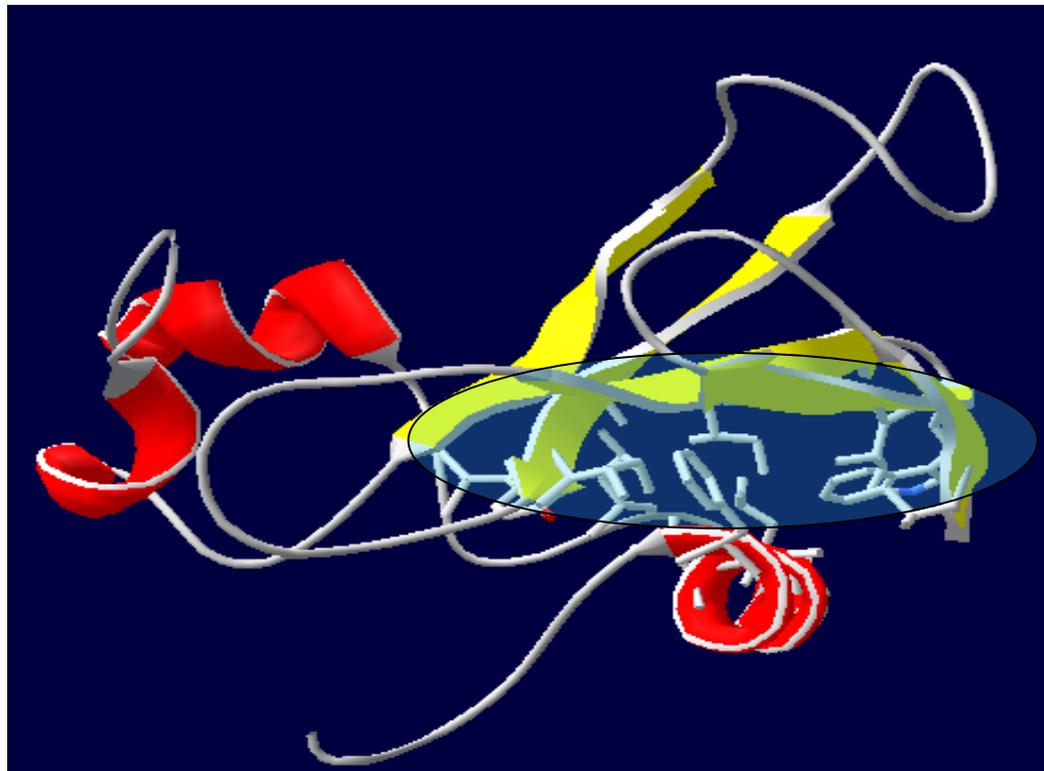
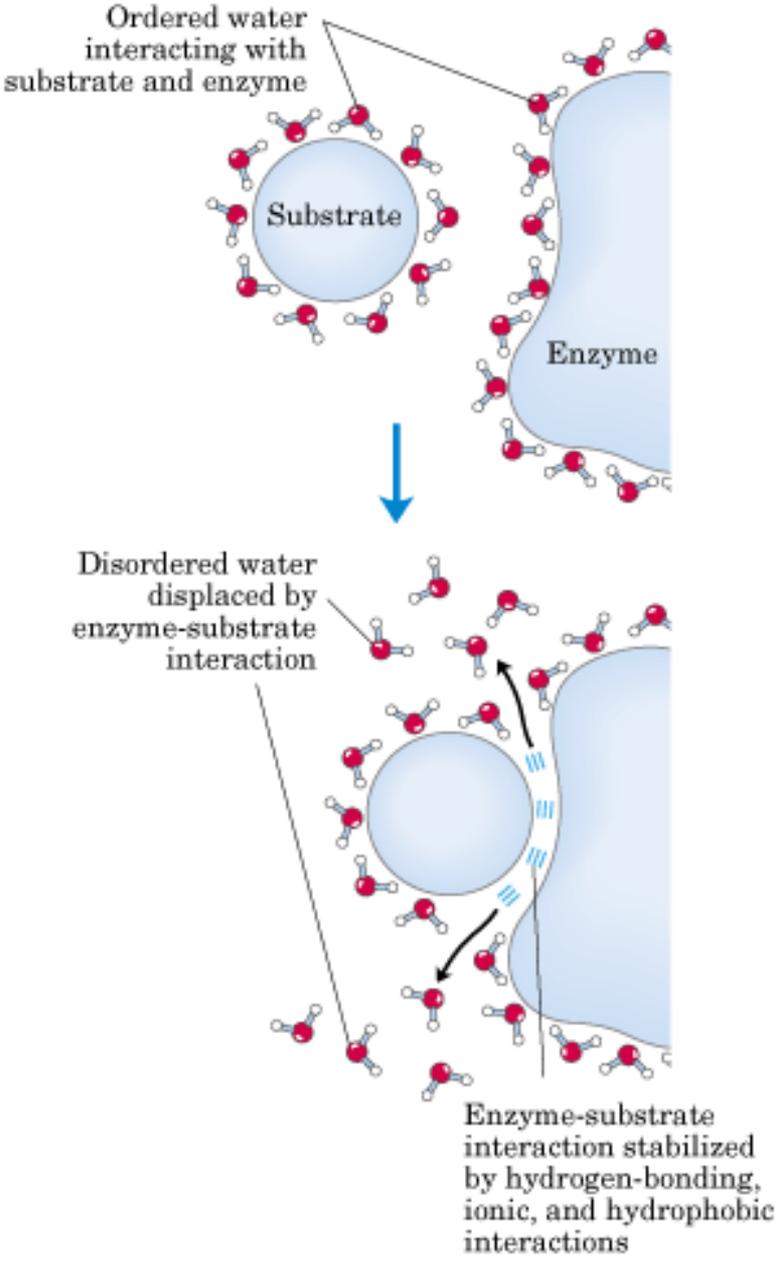
Lysozyme in water

+ *Introduction of a hydrocarbon molecule creates a unfavourable cavities in water.*

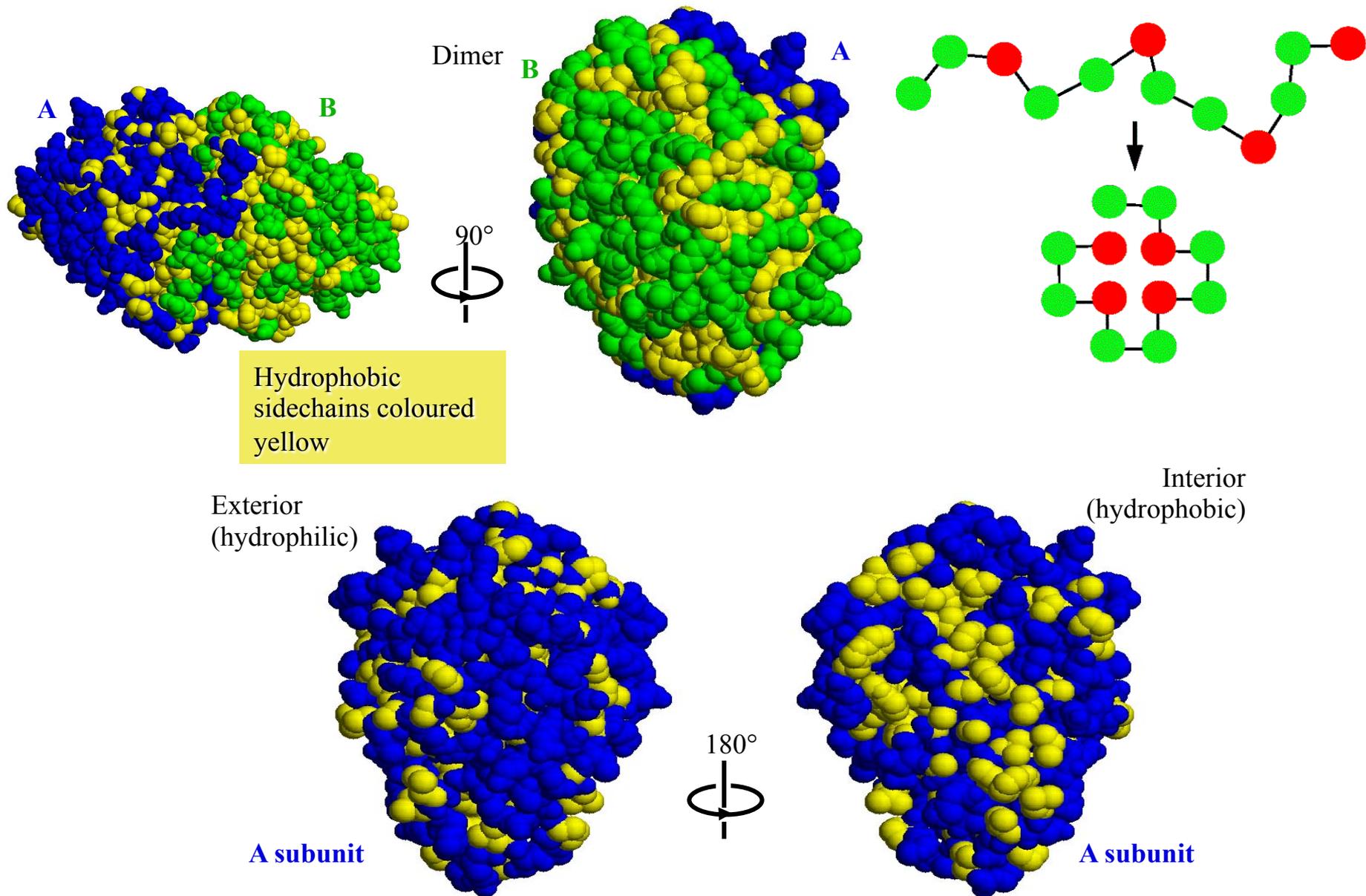
+ *By clumping together in water hydrophobic molecules can reduce the total surface area of the cavity ($\Delta S > 0$).*



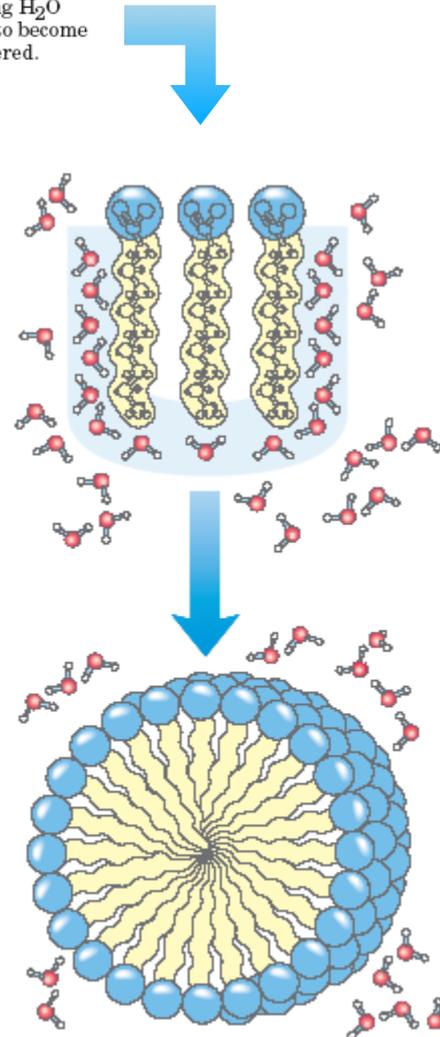
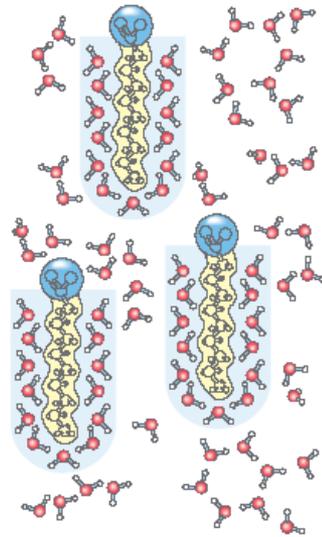
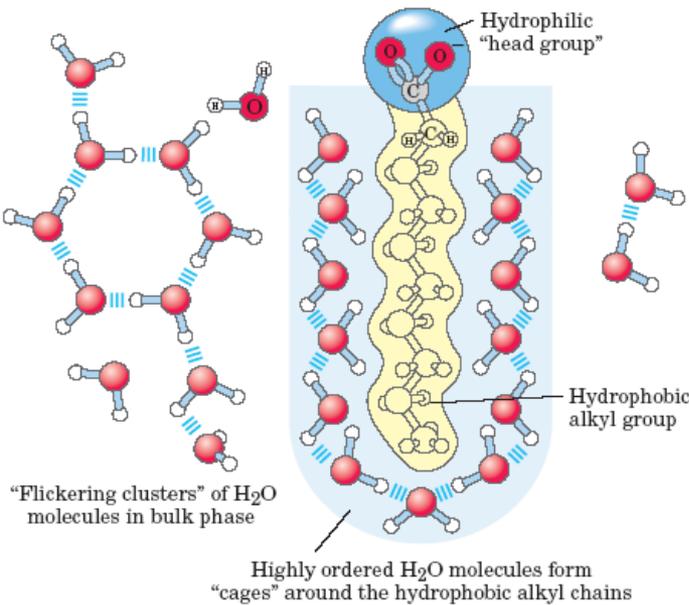
Hydrophobic effect in interactions of macromolecules



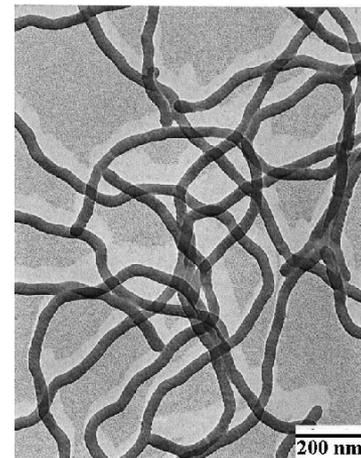
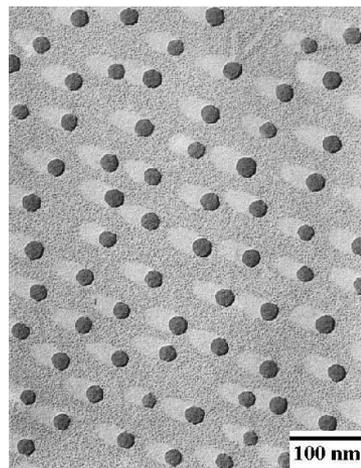
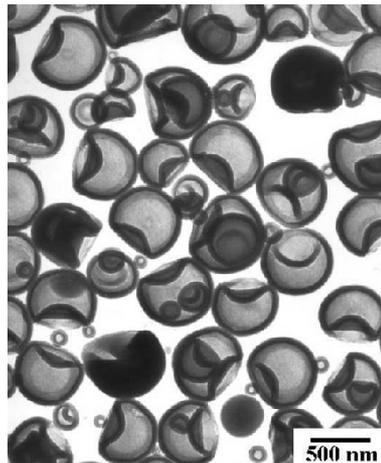
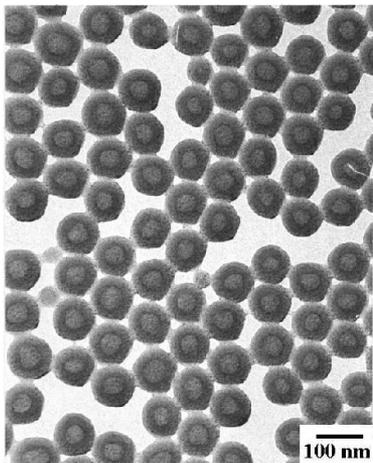
Alcohol dehydrogenase (homodimer)



Hydrocarbons in water



Hydrocarbons and nonpolar molecules are insoluble because water-water interactions are stronger than water-hydrocarbon interactions. So water molecules force nonpolar molecules together and surround them.



At equilibrium, the free energy or chemical potential of x is the same in both phases:

$$\mu_{x,org} = \mu_{x,org}^{\circ} + RT \ln[x]_{org} = \mu_{x,aq}^{\circ} + RT \ln[x]_{aq} = \mu_{x,aq}$$

$$\Delta G_{tr}^{\circ} = \mu_{x,aq}^{\circ} - \mu_{x,org}^{\circ} = -RT \left(\frac{\ln[x]_{aq}}{\ln[x]_{org}} \right) = -RT \ln K_p$$

$$\Delta G_{tr}^{\circ} = \Delta H_{tr}^{\circ} - T\Delta S_{tr}^{\circ}$$

Free energy, enthalpy and entropy of transfer for small alkanes

Alkane	ΔG_{tr}° (298K) kJ/mol	ΔH_{tr}° kJ/mol	ΔS_{tr}° J/mol.K	$-T \Delta S_{tr}^{\circ}$ (298K) kJ/mol
CH ₄	+10.9	-11.7	-76	+22.6
C ₂ H ₆	+15.9	-9.2	-84	+25.1
C ₃ H ₈	+20.5	-7.1	-93	+27.6
C ₄ H ₁₀	+23.8	-6.3	-100	+30.1

The biological system is a spatial organization of two phases: hydrophilic and hydrophobic separated by the interface.

The partition coefficient of a substance X is a measure of the tendency of a compound to be in water, compared to a vapor state, and it is defined as:

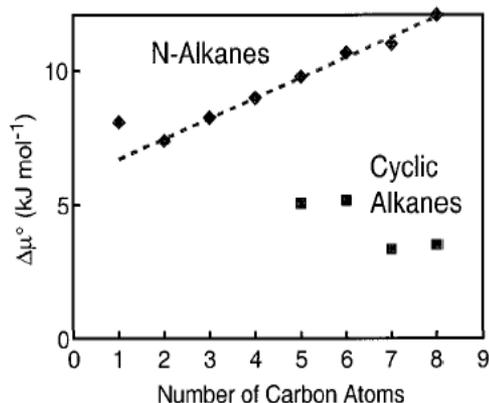
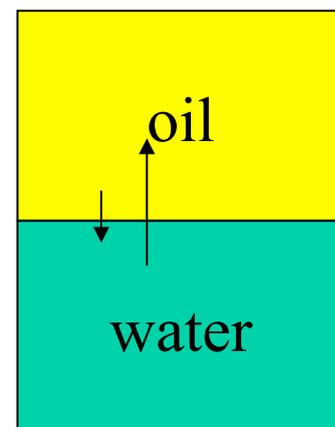


Figure 4. Alkane transfer free energies. For the normal alkanes (diamonds), except methane, there is a linear correlation between number of carbon atoms and free energy. This relationship fails to describe the cyclic alkanes (squares). From A. Ben-Naim, *Solvation Thermodynamics*; Plenum Press: New York, 1987.

$$K_D = \frac{[H]_{water}}{[X]_{vapor}}$$



partition coefficient
(equilibrium constant)

$$[C]_{water}/[C]_{oil}$$

[X] refers to the concentration of X in the corresponding environment.

The molecular packing parameter, P.

This dimensionless parameter is given by the following equation:

$$P = \frac{v}{a_0 l_C}$$

v - the volume occupied by the hydrophobic portion of the surfactant,

l_C - the critical chain length of the hydrophobic portion,

a_0 - the representative surface area occupied by the surfactant.

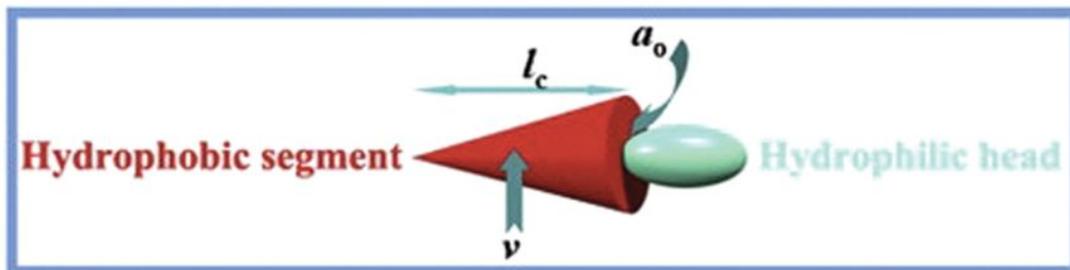
The value of P can be used to predict the supermolecular self-assembled structures of a surfactant solution.

This molecular perspective of the geometric packing is related to parameters of the macroscopic aggregate structural geometry by

$$P = \frac{v}{a_0 l_C} = 1 + Hl_C + \frac{Kl_C^2}{3}$$

where H is the mean curvature and K is the Gaussian curvature.

Graphic representation of individual surfactant geometry and the corresponding aggregate structure.



Packing shape

Cone

Truncated cone

Truncated cone

Cylinder

Wedge



$$P = \frac{v}{a_0 l_c}$$

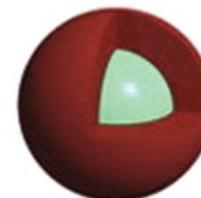
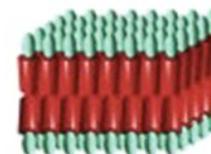
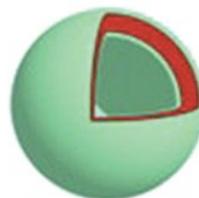
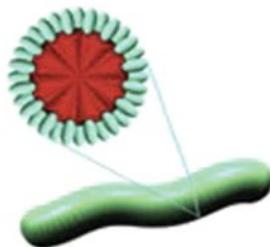
<1/3

1/3-1/2

1/2-1

~1

>1



Assembled structure

Spherical micelle

Cylindrical micelle

Vesicle or flexible bilayer

Planar bilayer

Inverted structure

Mosley G L et al. Journal of Laboratory Automation
2012;2211068212457161

Packing Parameter as a Geometric Constraint – the Micelle case.

R is the radius of micelle,

N is the number of surfactant molecules in one micelle (i.e., the aggregation number).

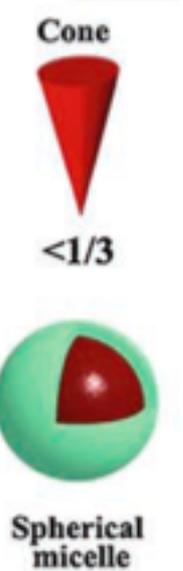
$$4\pi R^2 = a_0 N$$

For spherical micelles in an aqueous solution, we have the following equation for the surface area and spherical volume in terms of R and N:

$$\frac{4}{3}\pi R^3 = \nu N$$

$$N = \frac{4\pi R^3}{3\nu}$$

$$N = \frac{4\pi R^2}{a_0}$$



This results in individual surfactant molecules occupying space in the shape of shallow cones:

$$\frac{\nu}{a_0 R} = \frac{1}{3}$$

$$\frac{\nu}{a_0 R} < \frac{1}{3}$$

Cylindrical micelles

L is the length of the cylinder, we have the following equation for the cylindrical volume and surface area,

$$\pi R^2 L = vN \quad 2\pi RL = a_0 N$$

$$\frac{v}{a_0 l_c} < \frac{1}{2}$$

Because $R < l_c$, we have the following:

Because surfactant systems transition from spherical to cylindrical micelles as the packing parameter value increases, we can plug in the spherical micelle

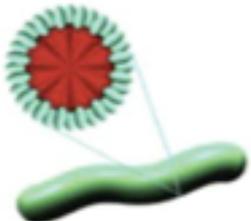
$$\frac{1}{3} < \frac{v}{a_0 l_c} < \frac{1}{2}$$

Truncated cone to arrive at for cylindrical micelles.



1/3-1/2

The number of surfactant molecules in the end caps is typically much smaller than the number of surfactant molecules present in the rest of the cylinder; therefore, end effects can be neglected.



Cylindrical micelle

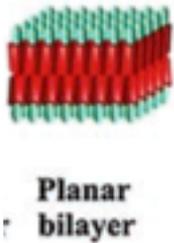
The shape occupied by the individual surfactant molecules in a cylindrical micelle is described as a

The packing parameter of a vesicle follows a different approach.

A flat bilayer is considered. Because there is no curvature for this self-assembled supermolecular structure, the surface area occupied per molecule on the top and bottom are equal, giving a cylindrical or rectangular prism shape with a

$$\frac{v}{a_0 l_c} \approx 1$$

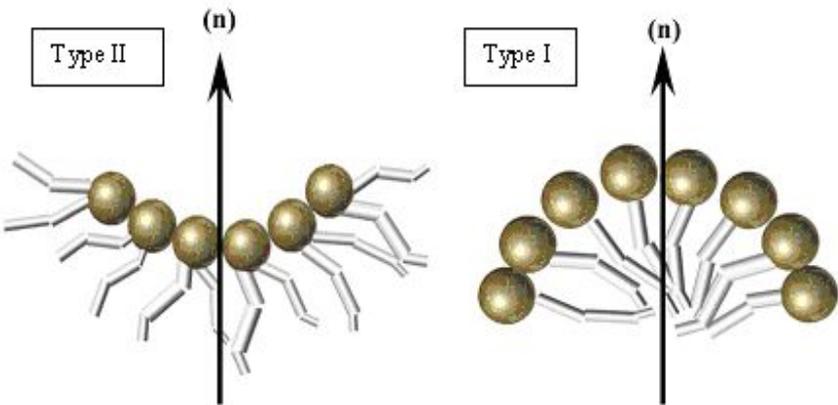
$$v \approx a_0 l_c$$



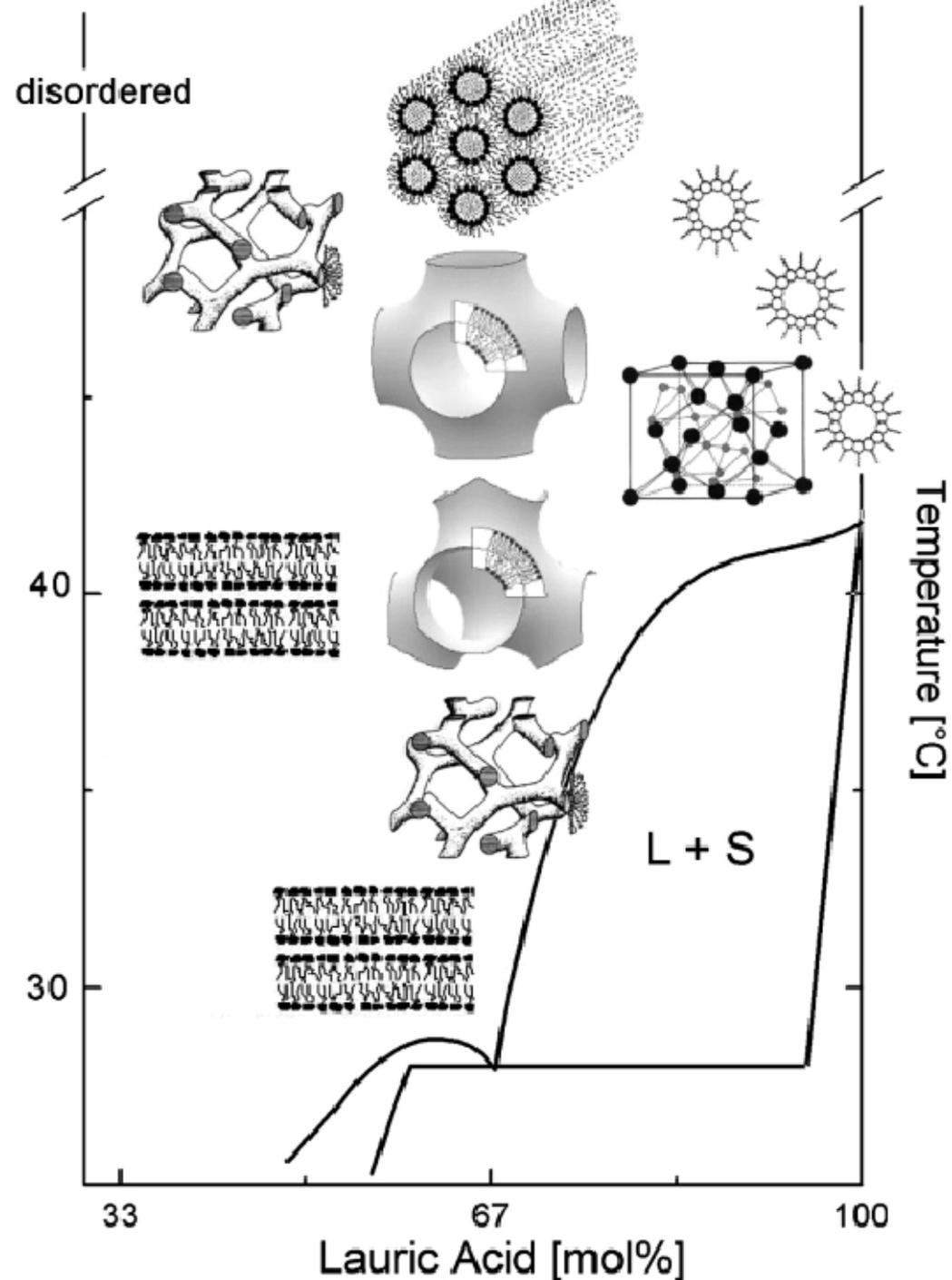
Because the vesicle morphology is an intermediate between a flat bilayer and a cylindrical micelle, the packing parameter values for a vesicle are given by:

$$\frac{1}{2} < \frac{v}{a_0 l_c} < 1$$

Lyotropic Phases



DLPC/LA pseudo-binary phase diagram.



Reconstitution

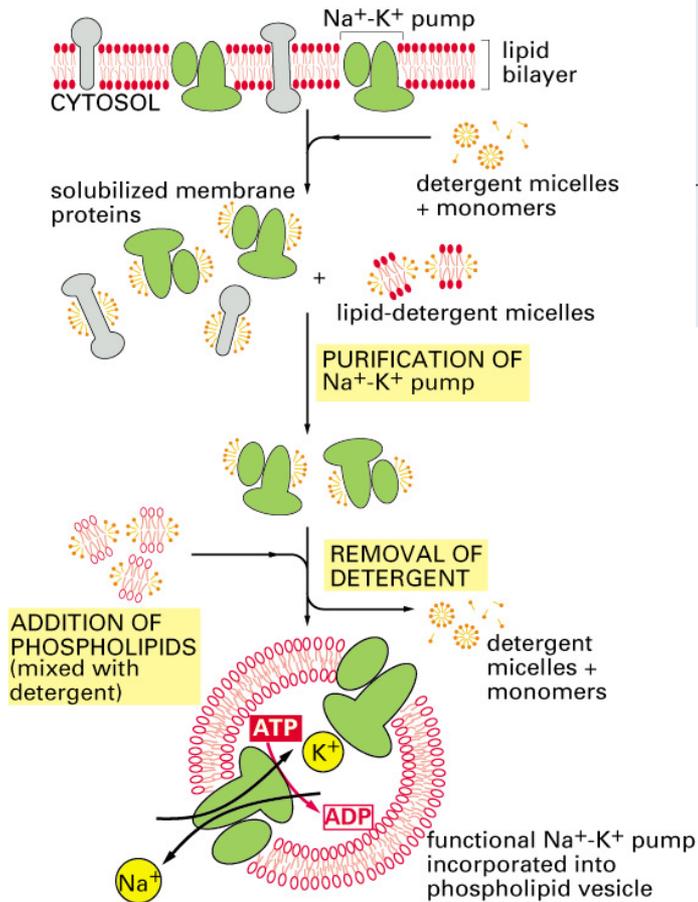
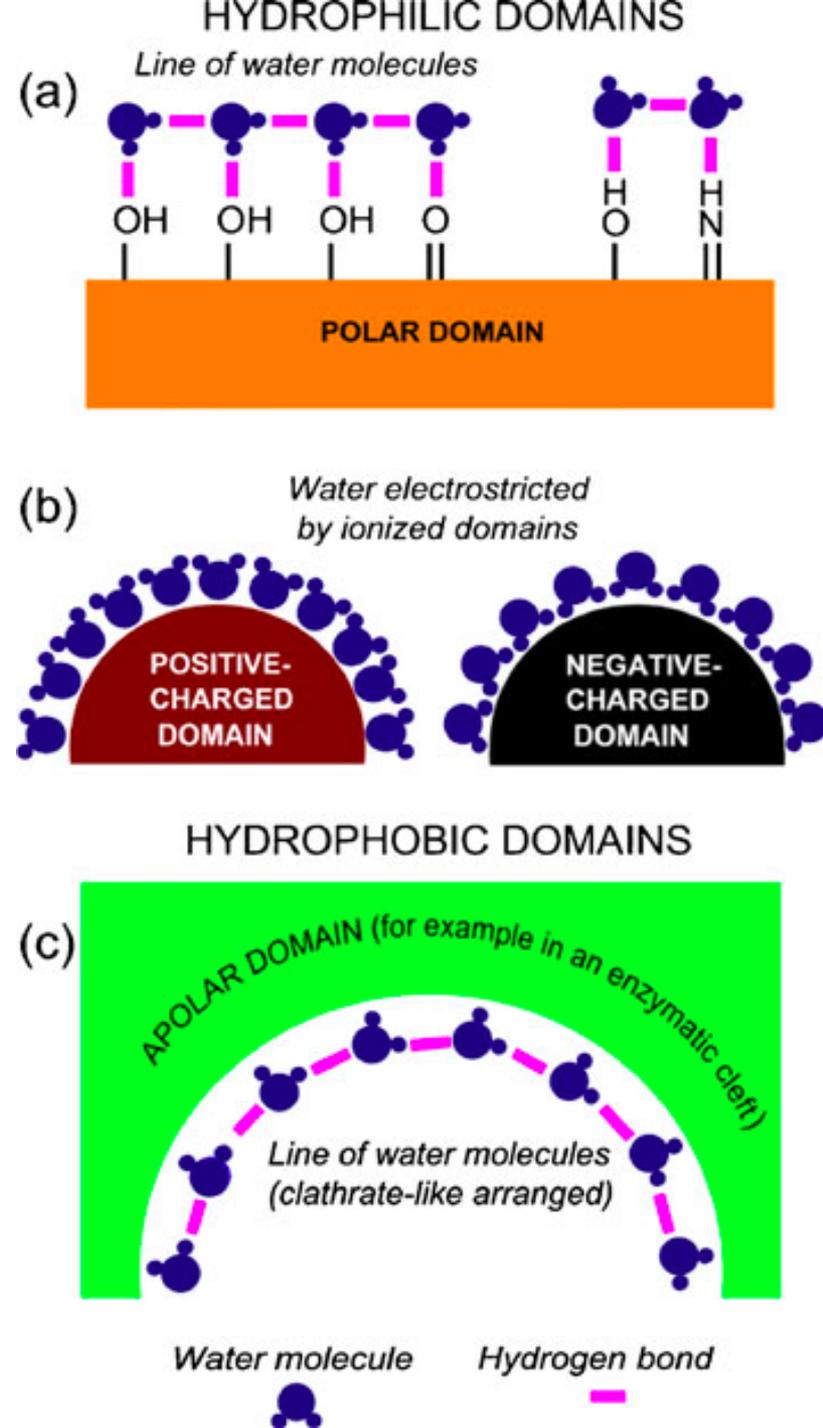


Figure 10-26. Molecular Biology of the Cell, 4th Edition.

Structure	M _r	CMC	Micelle M _r
Triton X-100 $\text{CH}_3 - \underset{\text{CH}_3}{\overset{\text{CH}_3}{\text{C}}} - \text{CH}_2 - \underset{\text{CH}_3}{\overset{\text{CH}_3}{\text{C}}} - \text{C}_6\text{H}_4 - (\text{OCH}_2\text{CH}_2)_{10} - \text{OH}$	625	0.24 mM	90–95,000
Octyl glucoside $\begin{array}{c} \text{CH}_2\text{OH} \\ \\ \text{H} \quad \text{O} \\ \quad \backslash \quad / \quad \text{O} - (\text{CH}_2)_7 - \text{CH}_3 \\ \quad \quad \\ \text{H} \quad \text{OH} \quad \text{H} \\ \quad \\ \text{H} \quad \text{OH} \end{array}$	292	25 mM	
C₁₂E₈ (Dodecyl octaoxyethylene ether) $\text{C}_{12}\text{H}_{25} - (\text{OCH}_2\text{CH}_2)_8 - \text{OH}$	538	0.071 mM	
$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_2 \\ \\ \text{O} \\ \\ \text{O} = \text{S} = \text{O} \\ \\ \text{O}^- \quad \text{Na}^+ \end{array}$			

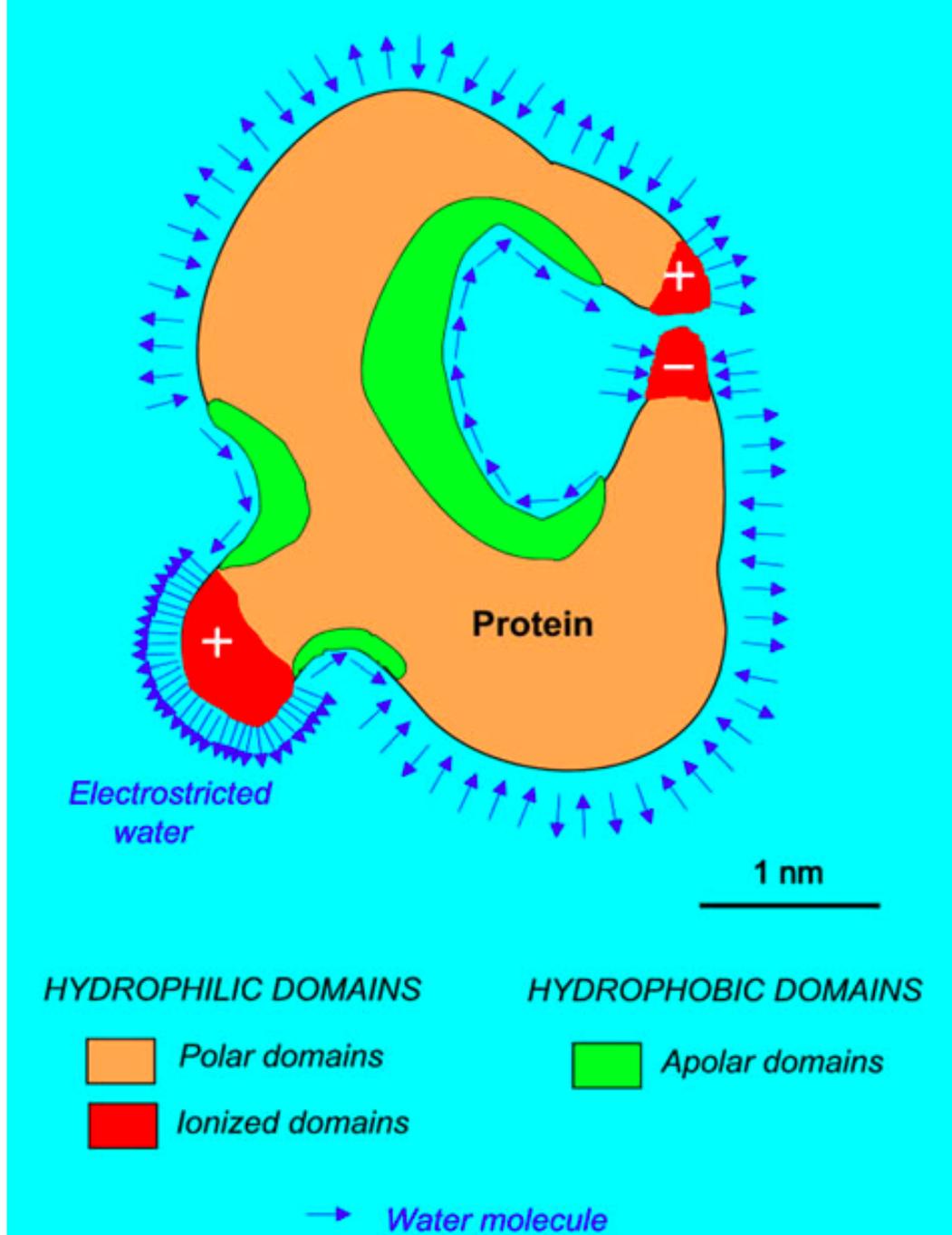
sodium dodecyl sulfate (SDS)

- *Principal types of organization of water at the contact of hydrophilic domains (a and b) and hydrophobic domains (c).*
- *Lines of H-bonded water molecules are good conductors of protons.*
- *They can form along sequences of polar amino acids in polypeptide chains (a), or in clathrate-like structures covering hydrophobic domains (c). They do not form at the contact of highly charged surfaces.*



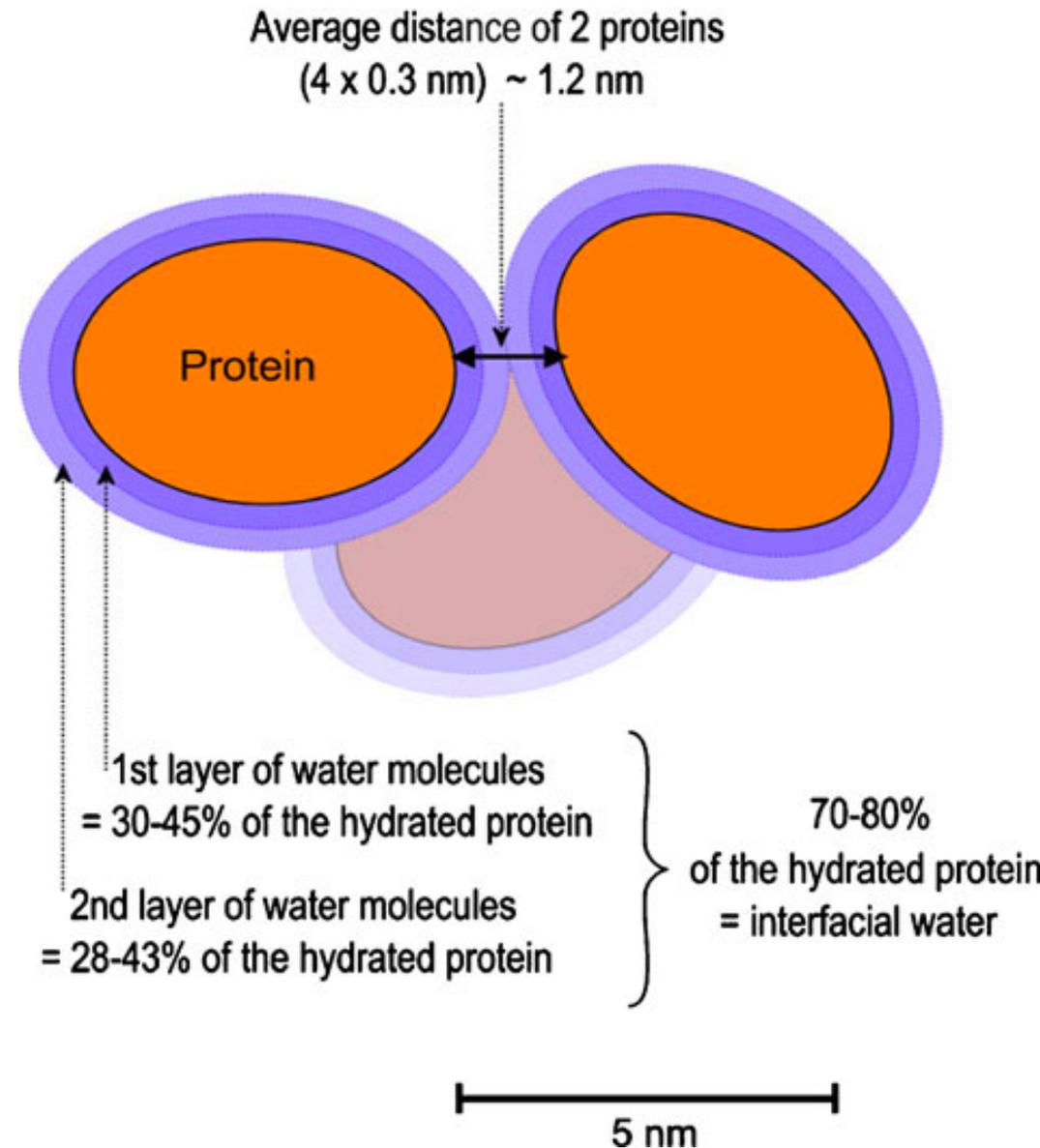
Schematic representation of the first layer of interfacial water at the surface of a protein. Its highly heterogeneous structure reflects the heterogeneity of the macromolecule surface.

- Interfacial water presents a large range of densities.
- Changes in protein configuration must involve changes in volume, therefore mechanical effects

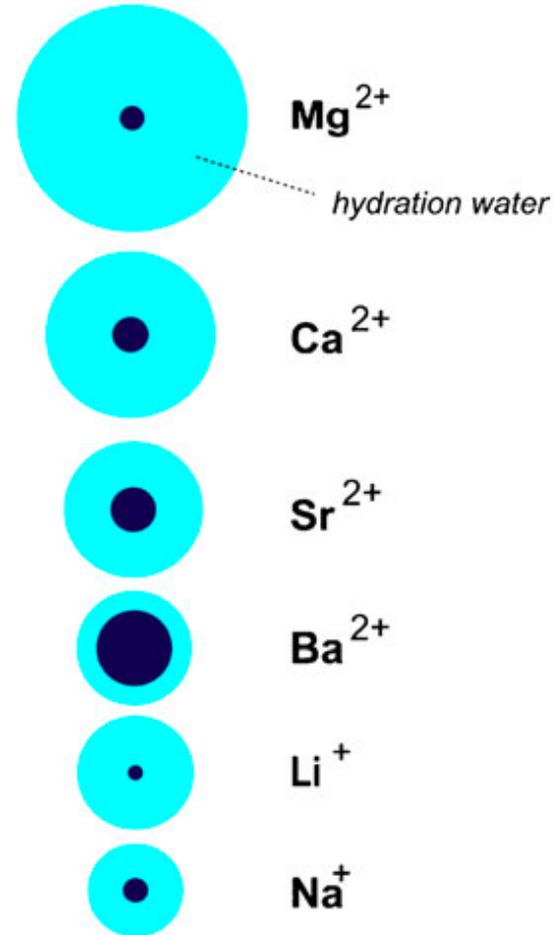


The whole cell water (70–80% of the total mass), statistically, is distributed into only two to three hydration layers around macromolecules.

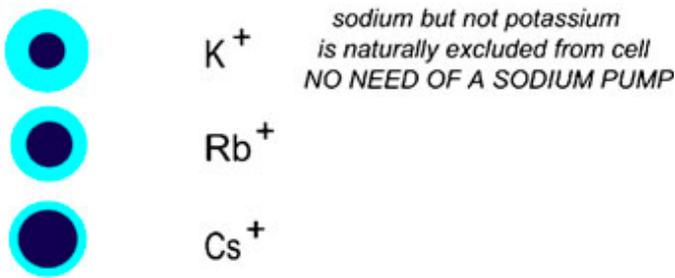
The size of a water molecule being 0.3 nm, the film of interfacial water between cell macromolecules is probably not very different from 1.2 nm.



KOSMOTROPIC (= structure making) IONS
strongly excluded from INTERFACIAL WATER

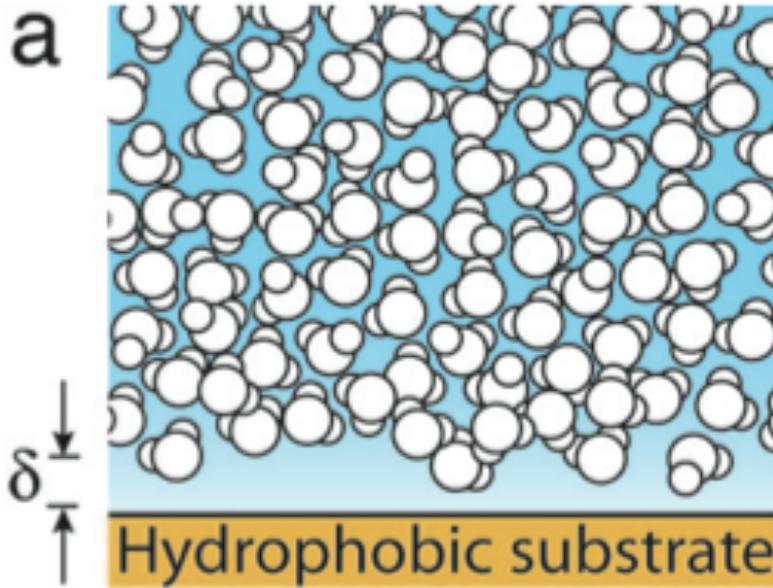


CHAOTROPIC (= structure breaking) IONS
little or not excluded from INTERFACIAL WATER

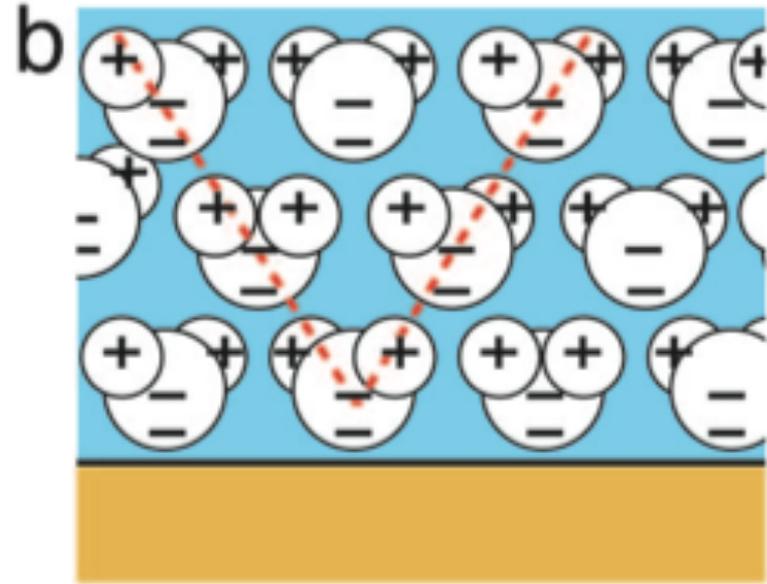


The cation Hofmeister series

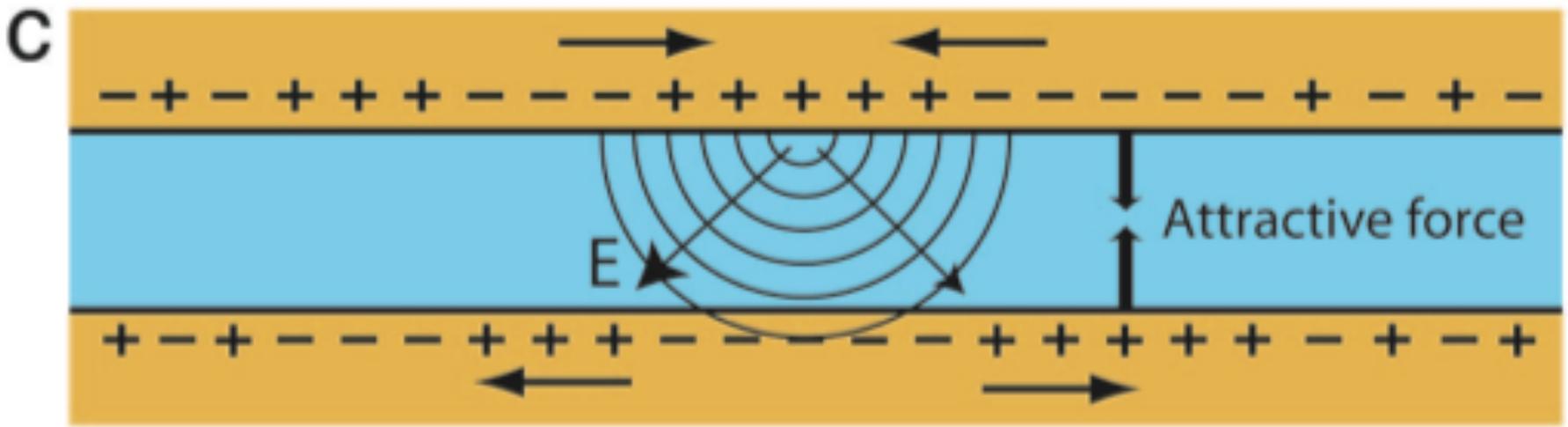
Possible mechanisms for long-range attraction between hydrophobic surfaces.



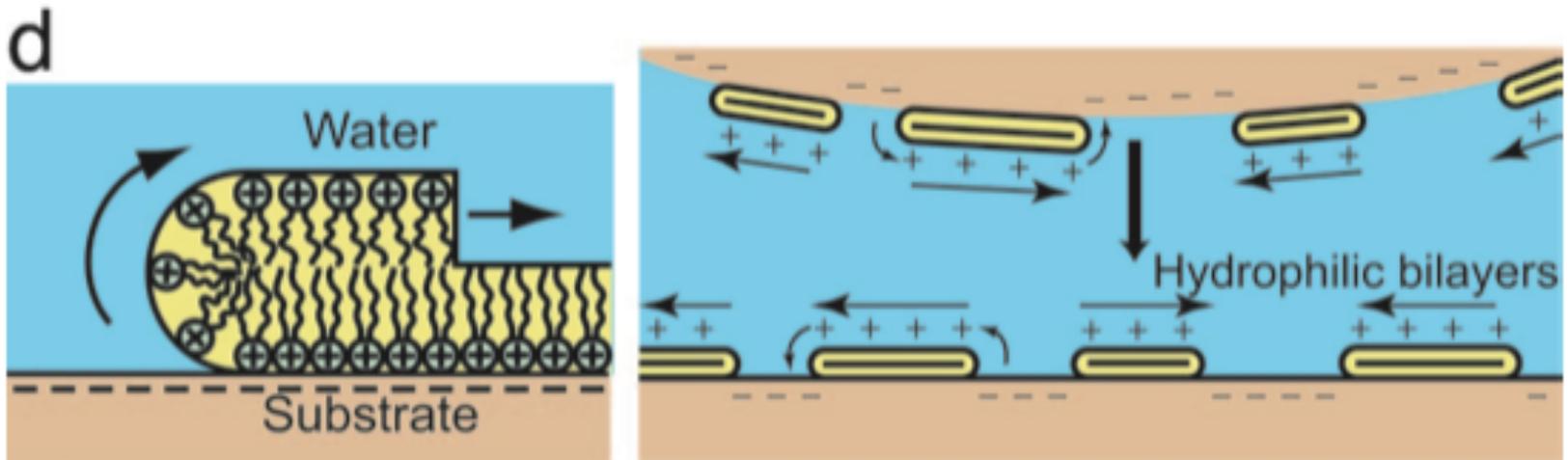
Although a depletion layer exists next to a hydrophobic surface, the range of thickness of this layer is typically only one to two water molecules, suggesting that only a short-range force should be operating.

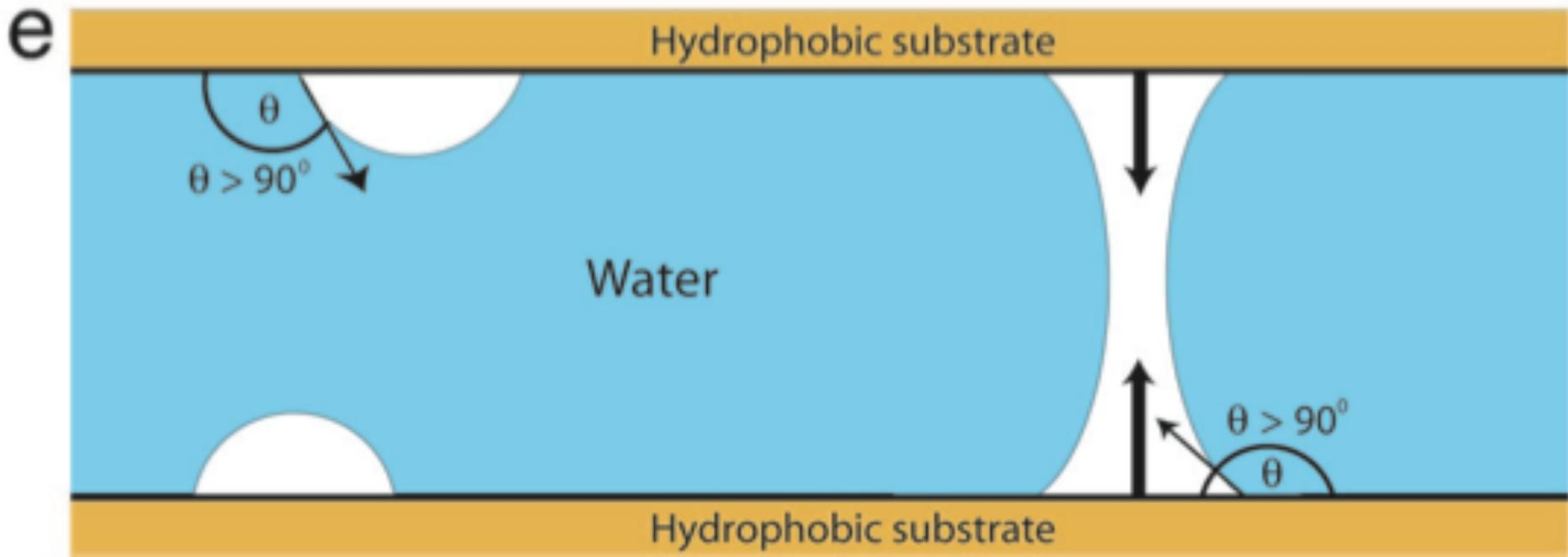


The presence of a hydrophobic solute (or ion) also affects the local orientation of the surrounding water molecules, an effect that can propagate many molecular layers into the bulk.



Local charge fluctuations at one surface can influence the charge density of the opposing surface, causing a long-range attractive electrostatic interaction, such as that seen with patchy bilayers.





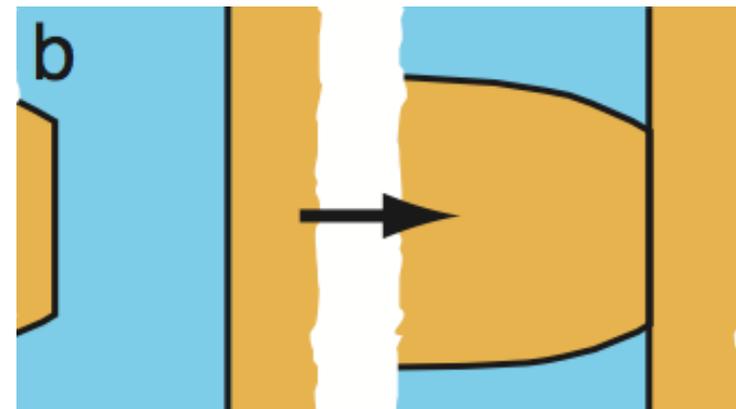
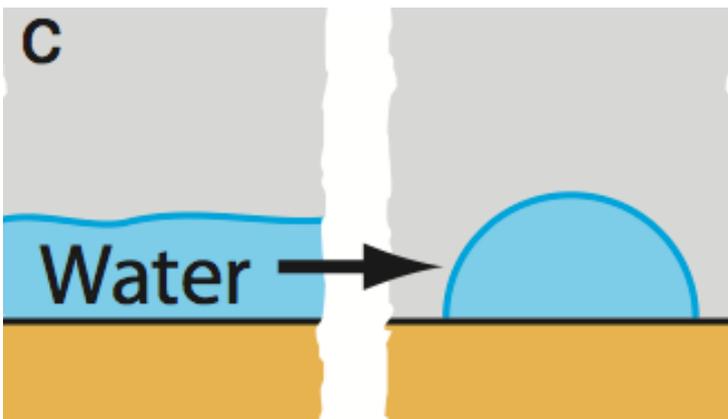
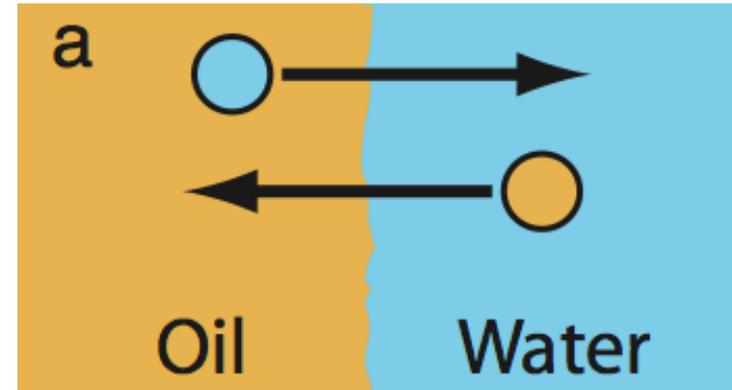
When present on hydrophobic surfaces, nanobubbles can coalesce, leading to an attractive Laplace pressure at large range.

Manifestations of the hydrophobic effect.

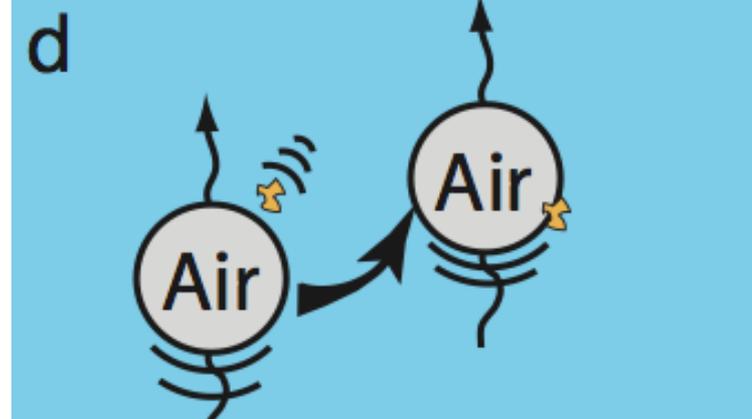
The low solubility of hydrophobic solutes (e.g., oil) in water and vice versa.

The strong adhesion between solid hydrophobic surfaces.

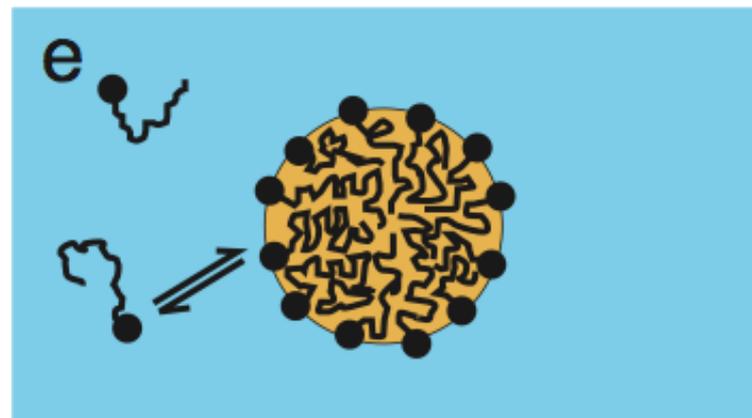
The dewetting phenomena leading to a large contact angle.



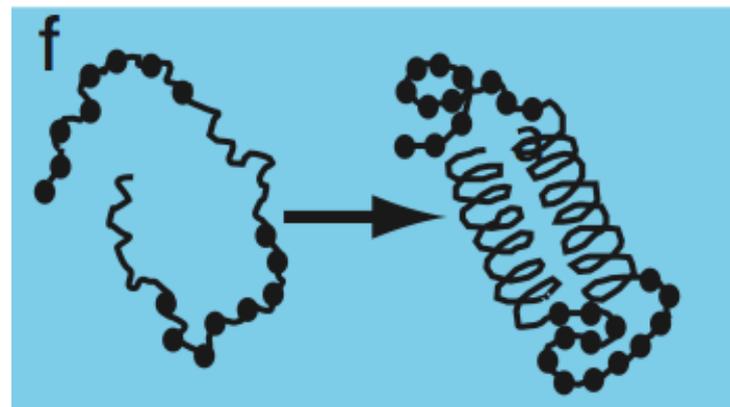
Hydrophobic contaminants or pollution adsorbing at the air–water interface



Micelle formation,



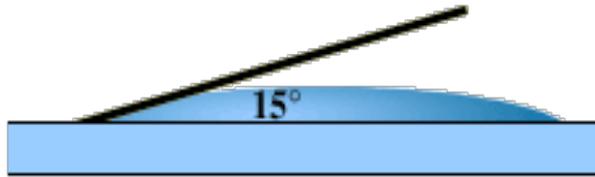
Protein folding



Wetting & Beading

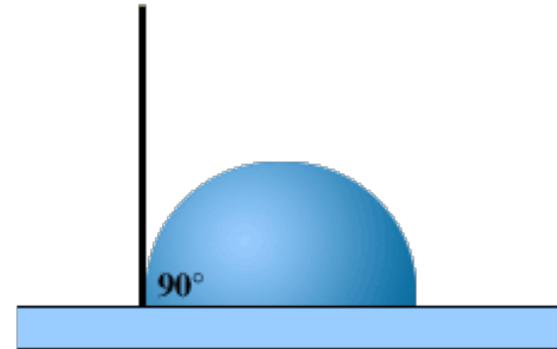
Good wetting

Contact angle $< 90^\circ$



Poor wetting (beading)

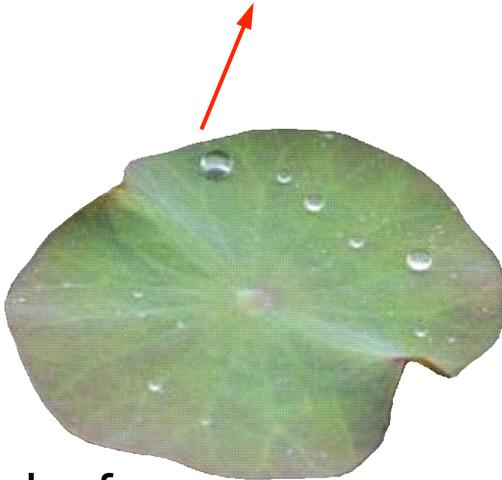
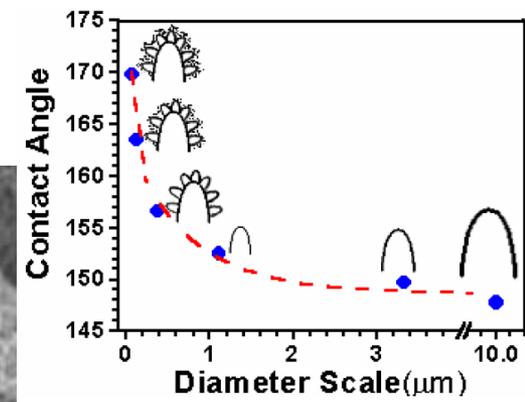
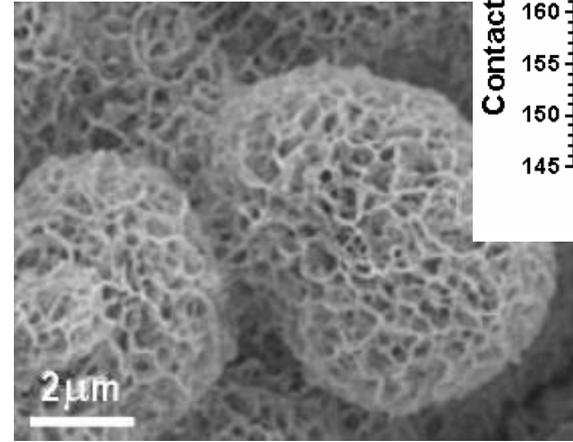
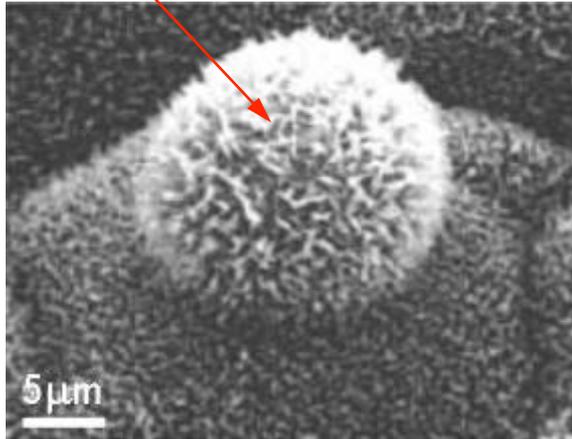
Contact angle $> 90^\circ$



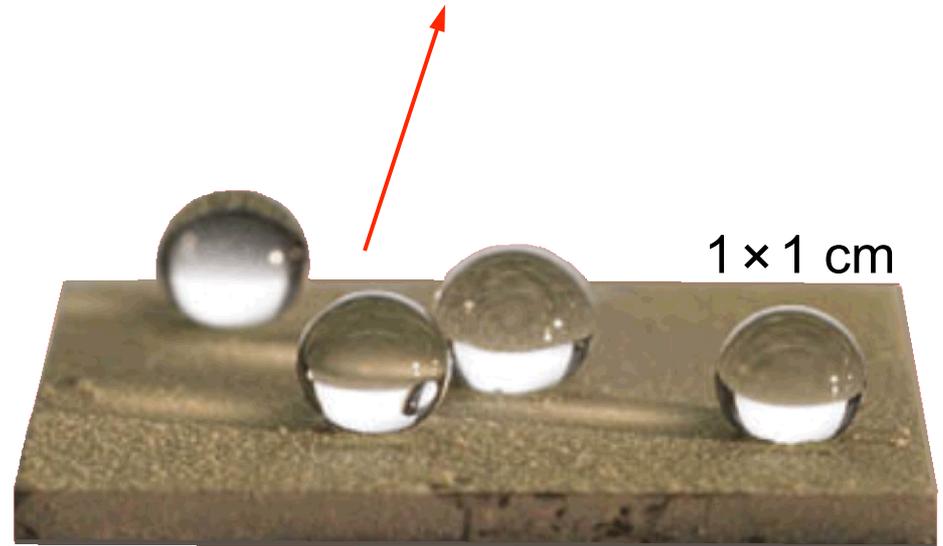
Contact angles below 90° indicate good wetting, while contact angles above 90° indicate poor wetting (beading).



Secondary structure



Lotus leaf



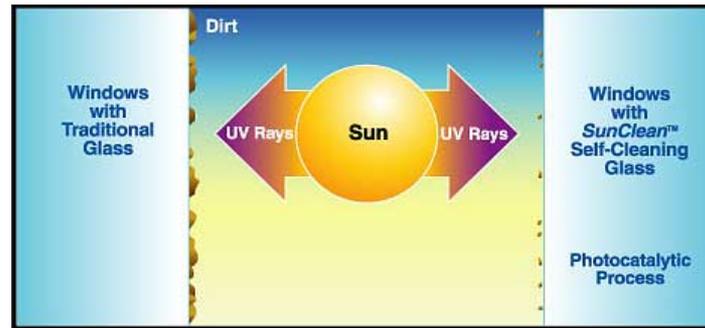
engineering imitation

The Lotus-Effect extended

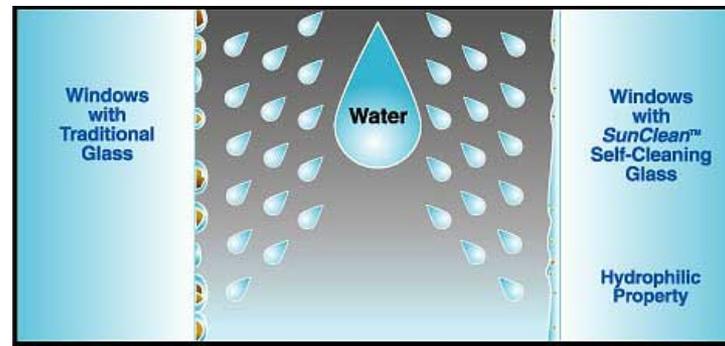
Self cleaning glass has a nanolayer of titanium dioxide coating on the surface.

This acts in two ways:

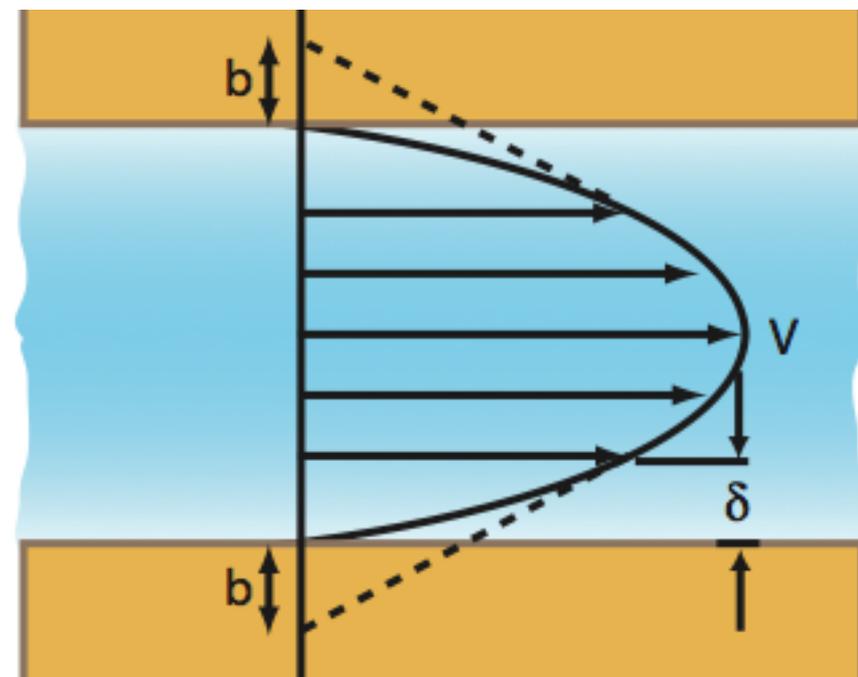
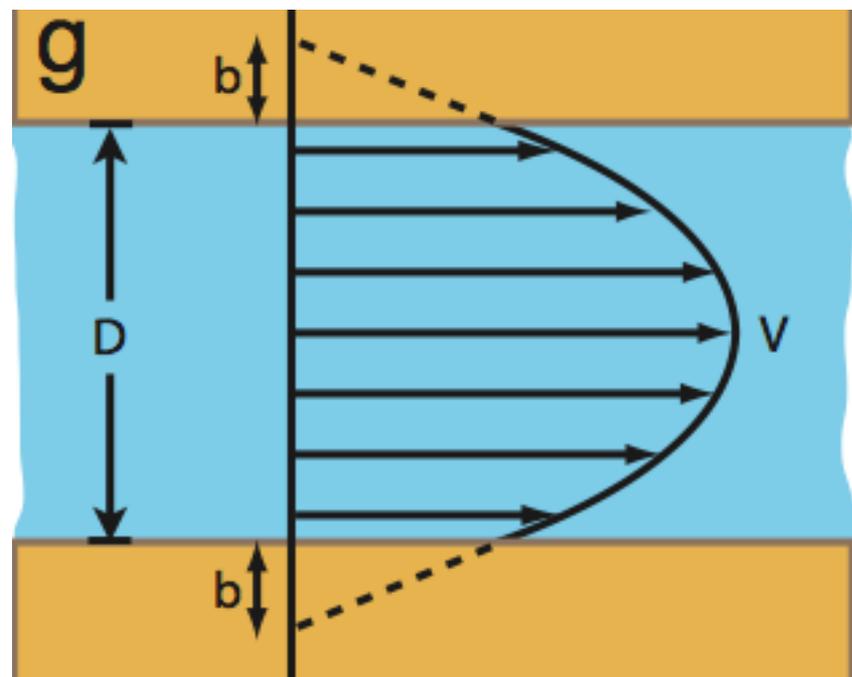
- it is photocatalytic: UV rays, abundant on even the cloudiest of days, cause the glass to react chemically with dirt and organic deposits, breaking them down and loosening them from the surface of the glass.



- it is hydrophilic: it attracts water, which slides down and off the surface of the glass without forming into separate droplets. This ensures that loose particles of dust and dirt are easily washed off during normal rainy weather.



Flow through hydrophobic surfaces leading to an observed slip length at the solid–liquid interface. The slip length, b , is approximately related to the thickness of the depletion layer, (through b).



Fog catching



made by nature (Namib desert)



The Darkling-Beetle-Effect



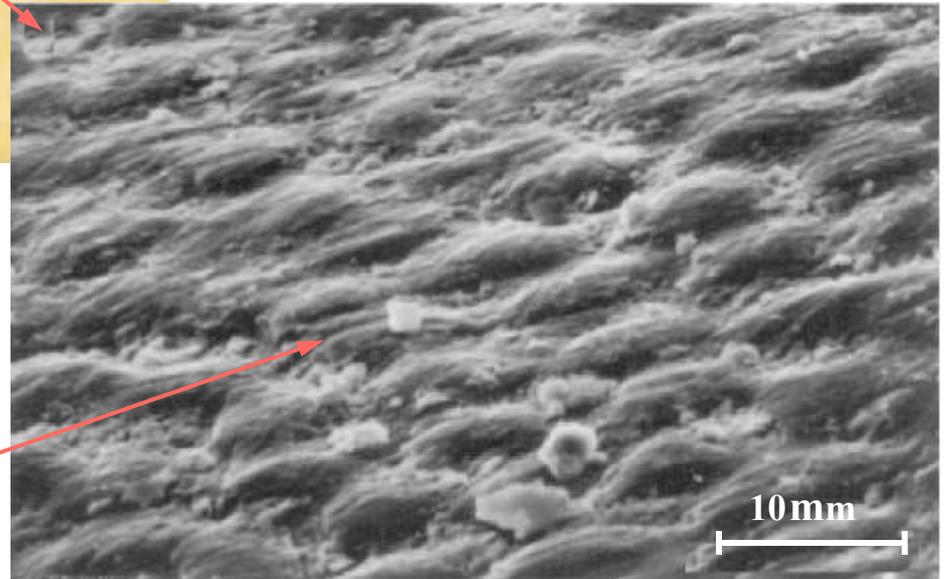
made by humans



Darkling beetle of the Namib desert
(*Stenocara* sp.)

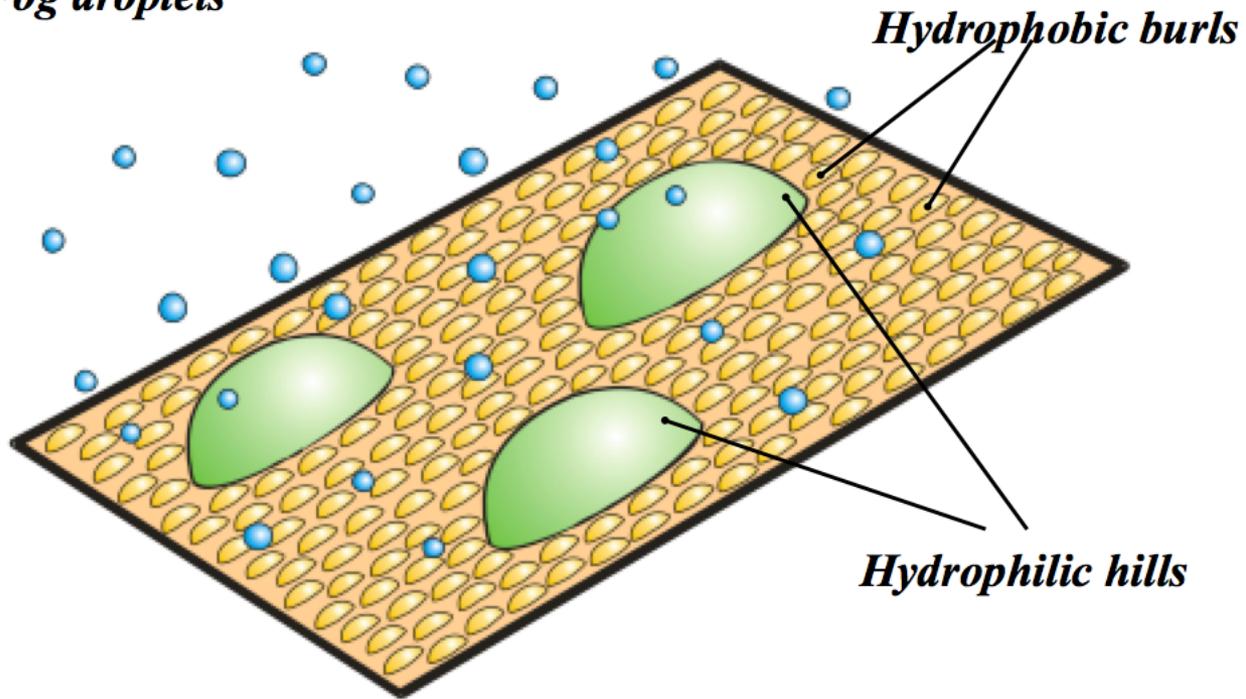
Hydrophilic peaks

Hydrophobic burred lowland
similar to the Lotus-Effect[®]



Andrew R. Parker and Chris R. Lawrence

Fog droplets



Hydrophobic burls

Hydrophilic hills

