

Hydrophobic Hydration

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The hydrophobic effect

The term 'hydrophobic' is derived from *hydro-* (water) and *phobos* (fear). However, it is not so much that hydrophobic molecules 'fear' (that is, 'does not enjoy the company of') water as water 'fears' the hydrophobic molecules. Hydrophobic molecules in water generally tend to aggregate, so minimizing their surface contact, and associated surface energy, with water; hence 'oils and water do not mix'. Smaller hydrophobic materials do, however, dissolve to a small extent in water as water molecules can arrange around them without breaking hydrogen bonds or losing much energy and the hydrophobic molecule can interact with these water molecules with multiple van der Waals interactions, due to the small size of water molecules and flexibility in their spatial arrangement. The following thermodynamic effects are found on hydrophobic hydration [1376]:

- An increase in the chemical potential of the solute, indicative of its low solubility.
- A strong temperature dependence in the enthalpy of the system from exothermic at low temperatures (where the hydrophobic solute can fit into the pre-existing low density water network and gain multiple van der Waals interactions, that may be correlated and show synergism [1376]) to endothermic at high temperatures (where the cavity formation required for the hydrophobic solute absorbs energy).
- A large negative entropy of mixing compared with the formation of a hypothetical ideal solution.
- A decrease in the partial molar volume (it is lower by 5–20 cm³ mol⁻¹ in a dilute aqueous solution than in a nonpolar organic solvent), as the molecule fits into cavities in the water network.
- An increase in heat capacity (see below)

The "hydrophobic effect" of hydrophobic solutes in water (such as non-polar gases) is primarily a consequence of changes in the clustering in the surrounding water rather than water-solute interactions [1674]. Hydrophobic hydration (for reviews see [241]) produces a reduction in density and an increase in the heat capacity [821]. The expanded network causes the density decrease whereas the ordered bonds must be bent on increasing the temperature, so affecting the heat capacity. Thus, hydrophobic hydration behaves in an opposite manner to polar hydration, which increases the density and decreases heat capacity due to their associated disorganized hydrogen bonds being already bent or broken. Hydrophobic hydration is accompanied by a negative enthalpy change, due in part to the multiple van der Waals interactions between water and the hydrophobic material, a negative entropy change due to the increased order in the surrounding water and positive heat capacity change (C_p) due to the negative enthalpy change (*i.e.* the stronger hydrogen bonds at the surface). For example, adding CH₂ groups to aliphatic alcohols increases the heat produced on solution ($\Delta H/\text{CH}_2 = -5.4 \text{ kJ mol}^{-1}$) but causes a greater decrease in the entropy ($-T\Delta S/\text{CH}_2 = +7.1 \text{ kJ mol}^{-1}$) [1217]. The increased van der Waals attractions over the liquid gas interface causes $\gamma_{\text{ls}} < \gamma_{\text{lg}}$. There is also likely to be an overall reduction in volume due to more efficient solute packing density, only partially compensated by the localized solvent density decrease

[903]. These thermodynamic factors compensate to some extent but the entropy term is greatest so the free energy is generally positive, accounting for the low solubility of hydrophobic molecules in water.

A water layer with a thickness of up to 35 nm exists at hydrophobic surfaces. This layer is characterized by a more ordered network of hydrogen bonds than liquid water [1714], with stronger hydrogen bonding evident at lower temperatures but lost at higher temperatures [1944].¹ There are at least five (equivalent) ways of describing what happens to the structure of water at hydrophobic surfaces (see also vicinal water)

1. Water at a hydrophobic surface loses a hydrogen bond, therefore has increased enthalpy. Water molecules compensate for this by doing pressure-volume work, that is, the network expands to form low-density water with lower entropy (for example, see [318])
2. Water covers the surface with clathrate-like pentagons in partial dodecahedra, so avoiding the loss of most of the hydrogen bonds. This necessitates an expanded low-density local structure. Note that the formation of clathrate structures maximizes the van der Waals contacts between the hydrophobic solute and the water but without reducing the hydrogen bonding. The rotational restriction of the hydrogen bonds at the hydrophobic surface may be partially responsible for their increased strength. Such clathrate structures do not exist as rigid 'crystal-like' clusters but are minimum enthalpy structures and are easily and constantly disrupted by kinetic effects (for example, raised temperature). It has been found that at any^a instant some of these water molecules are much more rotationally fixed (immobilized) than the others, with the proportion 'fixed' dependent on the structure covered [1330].⁹ Also, some of these water molecules remain present for extended periods within the hydration shell [1894].
3. Water's chemical potential is raised due to the dangling bonds. Water decreases this potential by expanding the water network. This expansion has been verified at the hydrophobic air-water interface at about 6% using extended X-ray absorption fine structure (EXAFS) [415], about 6-12% over 2-5 nm by neutron reflectivity [487] and about 7-10% over 1-1.5 nm by X-ray reflectivity [486].
4. The high interfacial energy is compensated by forming low-density water.
5. The elasticity of water's hydrogen bonded network surrounds or squeezes out hydrophobic molecules dependent on their size and how well they can be accommodated within its network [507].

Where low-density water (LDW) overlays hydrophobic surfaces, there will be a tendency for surface minimization by surfaces interacting and excluding water, causing the formation of junction zones in many hydrocolloids. It is the incompatibility between the LDW and the hydrophobic surface that drives the structure formation. The formation of low-density water next to hydrophobic surfaces, and concomitant junction zone formation, is encouraged if this low-density water is also associated with high-density water created near to additional solute polar groups (for example, in polysaccharides). Alternatively, local strong hydrogen bonding may be able to create low-density water without assistance. It is likely that local weak water-water hydrogen bonding (and hence greater availability of water molecules) will discourage such junction zone formation because of its greater hydration capacity.

The hydrophobic effect decreases with increased pressure (or density) as it is dependent on the presence of tetrahedrally-placed water molecules (as in LDW), which reduce in number under the distorting influence of pressure [626]. In cold water, the hydrophobic effect increases with increasing temperature (that is, hydrophobic molecules become more sticky) due to the reduced

ease of clathrate formation increasing the energetic cost of the hydrophobe-water surface and reducing the hydrophobe-surface hydration. [Back to Top ▲]

Extensive hydrophobic interfaces

The behavior of liquid water at hydrophobic solid surfaces, and vapor interfaces is influenced by the necessary presence of dangling non-hydrogen bonded surface O-H groups when the clathrate structures can no longer form (that is, particles > 0.6- 0.7 nm diameter^e at ambient temperatures), which are necessarily compensated by stronger hydrogen bonding towards the bulk [213]. The liquid water lying against extended hydrophobic surfaces (with effective diameter greater than 1 - 2 nm at 0 °C reducing to below 0.5 nm at 100 °C [911]) has low density [1290],^a so encouraging non-polar gas accumulation,^f particularly if the surface is uneven. The drive to maximize hydrogen bonding by forming empty dome-shaped half clathrate structures is compensated by the tendency to fill the empty space and increase entropy. Overall, this is expected to cause dynamic sub-nanometer waves at the surface. Dissolved N₂ and O₂ gases reduce the hydrophobic surface density more than dissolved CO₂ gas and much more than Ar [890]; indicating perhaps that Ar is very soluble at these interfaces forming clathrate structuring but the other gasses form a thin gaseous phase. The character of this reduced density surface, in the presence of accumulated gas, is not clear with some evidence that it has fluctuating density (between that of vapor and liquid), without the sharp density transition that may have been expected of discrete nanobubbles (nanocavities) [890] and other evidence for the presence of the nanobubbles [506, 519]. Under reduced or negative pressure, such surface gas may expand into visible bubbles (cavities) [891]. Molecularly-flat hydrophobic surfaces show the low density layer but without large nanobubbles (nanocavities) [1175]. It seems likely that hydroxide ions may prefer the aqueous environment next to hydrophobic surfaces [1347] in much the same way as occurs at gas-water interfaces and easing the formation of nanobubbles. Thus the surface charge and zeta potential at extensive hydrophobe-water interfaces are negative.

Long range attractive effects occur between hydrophobic surfaces (also between hydrophilic and charged surfaces), which if not due to bridging nanoscopic gas cavities [629, 711] or the osmotic effect due to local nanobubble depletion [1433], may be due to organization^d within the water network (for a recent review see [235], for experiments showing the role of dissolved air see [459] and for the potential role of gas nanobubbles (strictly speaking these are nanocavities), containing up to 100,000 or so gas molecules [519] and up to tens to hundreds of nanometers in dimensions, see [506, 1172] and the gas-water interface page). This can be measured for distances up to 1000 Å, with 50% decay distances reported of about 7 Å or higher, in deaerated water, and 12-13 nm when dissolved gas is present [235]. Water between such close hydrophobic surfaces possesses such physical changes associated with increased hydrogen bond organization as increased thermal conductivity, depressed freezing point, reduced vapor pressure [406] and decreased dielectric [700]. Although these long range effects may be lost on removal of dissolved gas,^b a shorter range effect (< 25 nm [722]) and a stronger very short range effect (< 1 nm [722c]) remain between hydrophobic surfaces in deaerated water. This is much greater than expected from just van der Waals interactions and does not appear due to electrostatic effects as it is unaffected by the ionic strength of the solution. It may be due to the organization of the water at the interface such as the formation of cylindrical water clusters bridging the surfaces [1316]; such clusters being probably made up from concatenated ESclusters (for example see cartoon elsewhere). Additionally the tendency to reduce the liquid-solid interface through drying transitions (see below) will also cause strong attraction. Such drying transitions hold 'oily' particles together and are thought responsible for the poor dispersion of such particles but their good dispersion in de-gassed solutions [711].



Surface hydrophobicity is enhanced with increased nanoscale roughness with contact angles tending towards 180° (>150° represents 'superhydrophobicity' [1038]) and surface nanobubbles may become trapped with relatively large radii of curvature (that is, >100 nm). Relatively large changes in the volume and surface coverage of nanobubbles with temperature [842] may also confuse the experimental results.

The effects of dissolved gases are often ignored. However, they are usually present (even in distilled and de-ionized water), and may have important and varying effects. Some gases are essentially structuring (for example, O₂, N₂, Ar) fitting into dodecahedral clathrate cavities [831], whereas others are water destructuring (for example, CO₂, which imposes its own structure on water). Structuring gases, even with their low solubility, may accumulate at hydrophobic surfaces (including the formation of tiny gas bubbles [459] extending to a thin, ~nm, gas gap [825]) where they are more soluble (the water here possessing effectively very low dielectric constant [700]) and so increase their structuring effects. Such dissolved gas has a major effect on emulsion stabilization and flocculation (degassing stabilizing the emulsions) and confusing any Hofmeister effects [671]. They may also be responsible for other apparent artifacts such as free radical production in electromagnetic fields.

The incompatibility between low-density water (near hydrophobic surfaces) and most common salts is key to the functioning of reverse-osmosis water purification (desalination) cellulose ester membranes. [[Back to Top ▲](#)]

Solubility effects

In a manner similar to that causing the solubility minimum for non-polar gases, hydrophobic saccharides may become less soluble as the temperature increases [187]. However, the solubility behavior of such compounds in water is complicated by entropic factors due to their size and/or charge plus specific structural effects.^c The cavity radius around hydrophobic polycyclic aromatics remains constant between 23 °C and 90 °C, indicating clathrate formation with strengthening of the surrounding hydrogen bonds [510] (see also [794b]). Certainly if an optimal clathrate structuring is formed there will be only a third as many hydrogen bonds between water molecules in the first and second shells as within the shells, as shown by the connectivity map. Outside this first shell, hydrogen bonding may be weaker [794], due perhaps to the pressure-volume work and the necessary reduced entropy. This means that water molecules within the hydration shell possess both stronger (within shell) and more broken (to outside shell) hydrogen bonds. As the specific heat (C_p) is proportional to $\langle(\delta H)^2\rangle_{TPN}$ (that is, enthalpy fluctuations squared), this still results in increased heat capacity change (*i.e.* $+\Delta C_p$). Where the hydrophobic molecule is at high concentrations and fewer water molecules are available, the dynamics within the first (clathrate) hydration sphere becomes highly suppressed with only the rotational motions, attributed to the hydrophobic group(s) allowed [1424]. The solubility of volatile organic (*i.e.* hydrophobic) compounds undergo a change on supercooling the solution as, then, their solubility decreases with decreasing temperature [1590]. This is likely due to them being expelled from the more numerous smaller clathrate cages of ES formed. [[Back to Top ▲](#)]

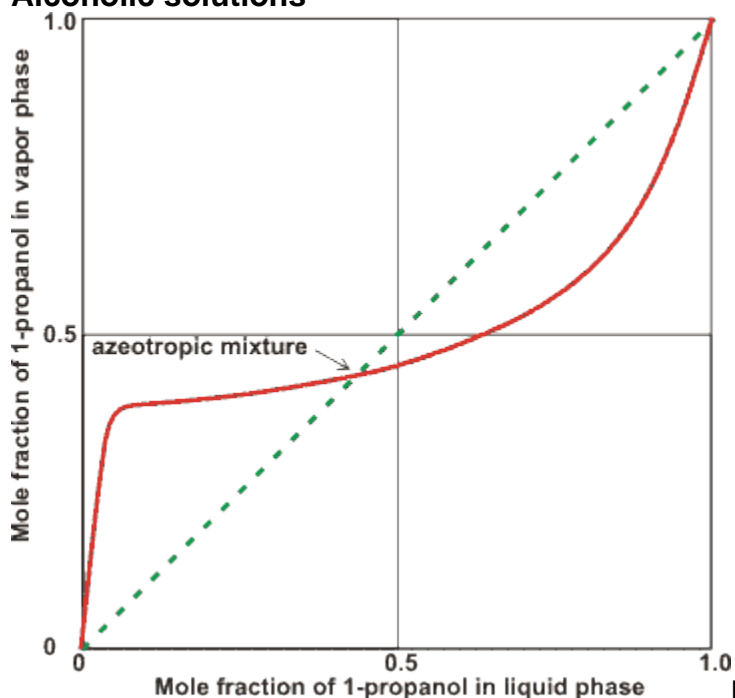
Salting-out and salting-in

Salt solutions have been used both to stabilize and destabilize hydrophobic surfaces causing molecules with sufficient non-polar character to become more (salting-in) or less (salting-out) soluble (see also the Hofmeister series). Recent molecular dynamics simulations have confirmed the importance of the surface charge density of the ions on the process [1243a]. They report salting-out as being entropically-driven by ions with high charge density (the effect increasing with charge

density [1243b]), and less polarizability, that form strong hydration complexes away from the hydrophobic surfaces, whereas salting-in, is caused by ions with lower charge density, and greater polarizability, that exhibit preferential binding at the hydrophobic surfaces and stabilized by entropic or enthalpic effects. At lower concentrations, ions with lower charge density can also increase hydrophobic aggregation of hydrophobic particles, stabilizing "micelle-like" structures but, with increasing salt concentration the micellar particles disperse rather than aggregate further [1243b], due to a greater ionic charge being better spread over their more extensive surface area.

The mechanism of 'salting-out' (phase separation of amphiphilic molecules from aqueous solution) has been further studied using NaCl and *t*-butanol [550a]. At low concentrations *t*-butanol is hydrated by a clathrate-like cage of about 20 water molecules [1239]. In relatively concentrated solution, the *t*-butanol molecules tend to form loose dimers through hydrophobic interactions of their methyl groups with no noticeable interaction between their alcohol groups (spectroscopically confirmed [952]). Introduction of NaCl causes the further interaction of the butanol residues indirectly through their alcohol groups, due to their mutual interaction with the anions (Cl⁻), and increasing both the tendency for further amphiphile clustering and tendency for phase separation. The conclusions of this work [550a], indicating the importance of the anion rather than the cation in such salting-out phenomena, has been (inconclusively) challenged [550c]. [\[Back to Top ▲\]](#)

Alcoholic solutions



Low molecular weight alcohols freely mix with water and are widely used as solvents and, in the case of ethanol, in alcoholic drinks. The solutions, however, are microheterogeneous with the alcohols tending to form linear hydrogen-bonded chains with each other (with increasing effect with alcohol hydrophobicity) whereas the water molecules forms tetrahedral clusters [776], mostly excluding the alcohol molecules (although at higher temperatures, mixed clusters predominate [1569]). Such solutions may contain several distinct liquid phases dependent on solutes, temperature and pressure [1297]. In line with their hydrophobic nature, the alcohols preferentially occupy surface sites, up to maximum values equivalent to about a monolayer, and lower the surface tension [777]. At higher concentrations (molar alcohol:water > 0.1), clear micro-aggregation occurs [777]. Binary mixtures of low molecular weight alcohols (e.g. ethanol, 1-propanol and 1-butanol but not methanol) with water show

azeotropy^h caused by the change of the evaporation properties of the solution with composition. This is shown for 1-propanol opposite [1746]. At low 1-propanol composition, water hydrogen-bonded clustering excludes the alcohol so that the alcohol evaporates more readily whereas at high alcohol content, clustering of the alcohol molecules due to inter-alkyl van der Waals' plus hydrogen-bonding interaction excludes the water molecules so that the water evaporates preferentially [1746]. [[Back to Top ▲](#)]

Footnotes

^a In contrast, interfaces involving moderately (but not extremely) hydrophobic liquids (for example, CCl₄) have residual (for example, van der Waals interactions) and fluid interactions between the interfacial molecules, so reducing the water-water hydrogen bonding within interfacial water [214]. This effect can also be found at lipid bilayers, where there is sufficient water penetration to allow its passage across [1425]. [[Back](#)]

^b Degassing is usually achieved by freeze-thaw cycles under reduced pressure. An efficient method of degassing is helium washing [1825]. [[Back](#)]

^c There is still some debate over the situation concerning methane [1276]. There is evidence that the hydrophobic molecule methane can be accommodated within the normal structure of water without significant local ordering around the methane molecules [853], and it should be noted that methane is a very small molecule being similar in size to a water molecule and only poorly fits into more capacious empty water clathrate cages endowing it with little stability from collapsing puckering. Neutron diffraction, indicates that the water may be forming a clathrate shell of about 19 water molecules around methane [1356]. Also, partial clathrate cages are found using molecular dynamics and increase in size with lowered temperature [1460]. [[Back](#)]

^d The very-long range interaction may be due to either the very strong forces involved in cavitation (that is, a drying transition) of the intervening water introduced during measurement [1073] or the weaker osmotic effects [1433]. [[Back](#)]

^e The report that hydrophobic molecules as small as neopentane, C(CH₃)₄ with diameter 0.54 nm, behave like an extensive hydrophobic surface [1232a,c] is disputed [1232b] and seems flawed. [[Back](#)]

^f Some studies show an effect of dissolved gasses and others do not. Differences may be due to the structure and history of the surface and the concentration of the dissolved gas. [[Back](#)]

^g These rotationally retarded water molecules may be thought of as the inwardly 'puckered' water in the clathrate model (see similar but greater ion effects), where their closer approach to the hydrophobic molecule prevents any bifurcating water aiding rotation. [[Back](#)]

^h An azeotropic mixture is one that has the same composition in the vapor and liquid phases and therefore cannot be separated by distillation. [[Back](#)]

ⁱ This Raman experimental finding is contrary to that previously loudly-proclaimed but subtly, in reality, inconclusive theoretical and neutron diffraction data. [[Back](#)]