

5.1: Hydrophobic Solvation - Thermodynamics

Why do oil and water not mix? What is hydrophobicity? First, the term is a misnomer. Greasy molecules that do not mix with water typically do have favorable interaction energies, i.e., $\Delta H_{int} < 0$. Walter Kauzmann first used the term "hydrophobic bonding" in 1954. This naming has been controversial from the beginning, but it has stuck presumably, because in this case ΔG is what determines the affinity of one substance for another rather than just ΔH . Generally speaking, the entropy of mixing governs the observation that two weakly interacting liquids will spontaneously mix. However, liquid water's intermolecular interactions are strong enough that it would prefer to hydrogen bond with itself than solvate nonpolar molecules. It will try to avoid disrupting its hydrogen bond network if possible.

The hydrophobic effect refers to the free energy penalty that one pays to solvate a weakly interacting solute. Referring to the thermodynamic cycle above, ΔG_{sol} , the reversible work needed to solvate a hydrophobic molecule, is dominated by step 1, the process of forming a cavity in water. The free energy of solvating a hydrophobic solute is large and positive, resulting from two factors:

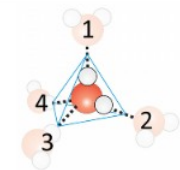
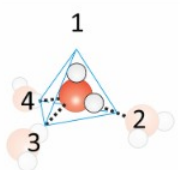
1. $\Delta G_{sol} < 0$. The entropy penalty of creating a cavity in water. We restrict the configurational space available to the water within the cavity. This effect and the entropy of mixing (that applies to any solvation problem) contribute to ΔS_1 .
2. $\Delta G_{sol} > 0$. The energy penalty of breaking up the hydrogen bond network (ΔH_1) is the dominant contributor to the enthalpy. This can be estimated from a count of the net number of H-bonds that needs to be broken to accommodate the solute: ΔH_{sol} increases by 1-3 kcal mol⁻¹ of hydrogen bonds. The interaction energy between a hydrocarbon and water (ΔH_2) is weakly favorable as a result of dispersion interactions, but this is a smaller effect. (At close contact, van der Waals forces lower the energy by ~ 0.1 -1.0 kcal mol⁻¹). Therefore $\Delta H_{sol} \approx \Delta H_1$.

The net result is that ΔG_{sol} is large and positive, which is expected since water and oil do not mix.

These ideas were originally deduced from classical thermodynamics, and put forth by Frank and Evans (1945) in the "iceberg model", which suggested that water would always seek to fulfill as many hydrogen bonds as it could—wrapping the network around the solute. This is another misnomer, because the hydrophobic effect is a boundary problem about reducing configurational space, not actual freezing of fluctuations. Hydrogen bonds continue to break and reform in the liquid, but there is considerable excluded configurational space for this to occur. Let's think of this as solute-induced *hydrogen-bond network reorganization*.

Water Configurational Entropy

Let's make an estimate of ΔG_{sol} . Qualitatively, we are talking about limiting the configurational space that water molecules can adopt within the constraints of a tetrahedral potential.

Approximation							
Bulk water: 4 HBs/tetrahedron							
Within a tetrahedral lattice the orientation of an H ₂ O has:							
6 configurations:	<table border="0"> <tr> <td>1,2</td> <td>1,3</td> <td>1,4</td> </tr> <tr> <td>2,3</td> <td>2,4</td> <td>3,4</td> </tr> </table>		1,2	1,3	1,4	2,3	2,4
1,2	1,3	1,4					
2,3	2,4	3,4					
$\Omega_{bulk} = 6$							
At a planar interface, you satisfy the most hydrogen bonds by making one dangling hydrogen bond pointing toward the surface							
3 configurations							
<table border="0"> <tr> <td>1,2</td> <td>1,3</td> <td>1,4</td> </tr> </table>			1,2	1,3	1,4		
1,2	1,3		1,4				
$\Omega_{surface} = 3$							

So an estimate for the entropy of hydrophobic solvation if these configurations are equally probable is $\Delta S_{sol} = k_B \ln(\Omega_{surf}/\Omega_{bulk}) = -k_B \ln 2$ per hydrogen bond of lost configurational space:

$$-T\Delta S_{sol} = k_B T \ln 2$$

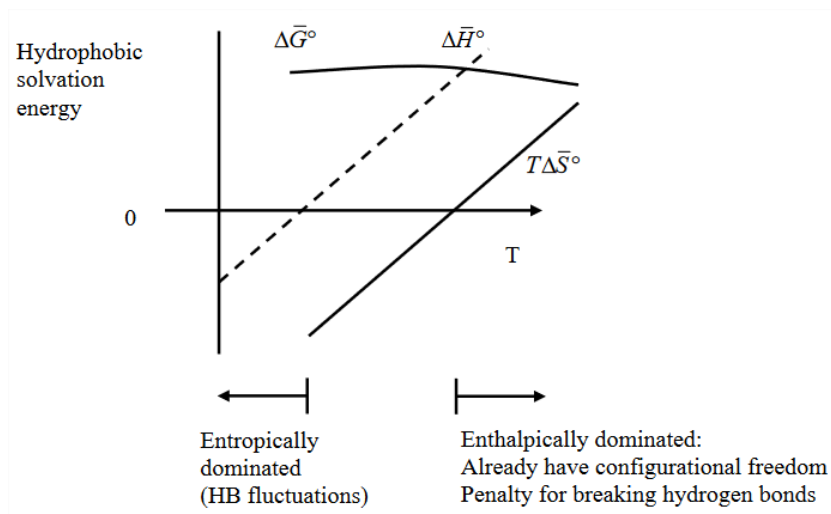
Evaluating at 300 K,

$$\begin{aligned}
 -T\Delta G_{sol} &= 1.7 \text{ kJ/mol water molecules @ 300 K} \\
 &= 0.4 \text{ kcal/mol water molecules}
 \end{aligned}$$

This value is less than the typical enthalpy for hydrogen bond formation, which is another way of saying that the hydrogen bonds like to stay mostly intact, but have large amplitude fluctuations.

Temperature Dependence of Hydrophobic Solvation

From ΔS_{sol} we expect ΔG_{sol} to rise with temperature as a result of the entropic term. This is a classic signature of the hydrophobic effect: The force driving condensation or phase-separation increases with temperature. Since the hydrogen-bond strength connectivity and fluctuations in water's hydrogen-bond network change with temperature, the weighting of enthalpic and entropic factors in hydrophobic solvation also varies with T . Consider a typical temperature dependence of ΔG_{sol} for small hydrophobic molecules:



The enthalpic and entropic contributions are two strongly temperature-dependent effects, which compete to result in a much more weakly temperature-dependent free energy. Note, this is quite different from the temperature dependence of chemical equilibria described by the van 't Hoff equation, which assumes that ΔH is independent of temperature. The temperature dependence of all of these variables can be described in terms of a large positive heat capacity.

$$\begin{aligned}\Delta C_{p, \text{sol}} &= \frac{\partial \Delta H_{\text{sol}}^0}{\partial T} = T \frac{\partial \Delta S_{\text{sol}}^0}{\partial T} \\ &= -T \frac{\partial^2 G_{\text{sol}}^0}{\partial T^2} \quad (\text{Curvature of } \Delta G^0)\end{aligned}$$

At low temperatures, with a stronger, more rigid hydrogen-bond network, the ΔS term dominates. But at high temperature, approaching boiling, the entropic penalty is far less.

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