Entropy of Mixing:

One thermodynamic effect that favors high solubility of solutes in water (or any other solvent) is the increase in entropy when two pure compounds are mixed. The entropy of a system \( S \) can be calculated using the relationship derived by Boltzmann, which relates the number of conformations of a system \( W \) to the entropy of the system:

\[
S = R \ln W
\]

- Crystals have an entropy of zero because all of the atoms are fixed in position and there is only one way to arrange the atoms.
- Solutions of pure substances have low entropy because all of the molecules are identical. Since there can be a slight variation in the position of the molecules, as well as their orientation, the entropy is not zero. If we make the assumption that all molecules in solution are in the same orientation and their position is fixed to defined points in space, then the entropy of the liquid is also zero because all of the particles are interchangeable with each other.

**When two pure substances are mixed, there is an increase in entropy because we now have a mixture of two different molecules and there are many ways to arrange the molecules because the molecules are different. This is referred to as the entropy of mixing.**

In the following simple example, let’s look at the entropy of a bowl of fruit. If we have three oranges in the bowl, all of the oranges are identical and there is only one distinguishable way to organize the oranges, so the entropy of pure oranges is zero. If we interchange the position of two identical oranges, the system still looks the same.

Similarly, if we have three plums in a bowl the entropy of the plums is zero as well.

Now if we mix the oranges and plums, there are many different distinguishable ways to organize the oranges and plums. In this example, there are exactly 20 different ways to organize the six pieces of fruit, as shown below. Thus the entropy of the mixture is:

\[
S_{\text{mix}} = R \ln 20 = 24 \text{ J/mol-K.}
\]

This is also equal to the overall entropy changes, since the entropy of the reactants (unmixed fruit) was zero: 24 J/mol-K. This is also equal to the overall entropy changes, since the entropy of the reactants (unmixed fruit) was zero:

\[
\Delta S = S_{\text{Products}} - S_{\text{Reactants}} = (24 - 0) = 24 \text{ J/mol-K.}
\]

We can calculate the number of possible configuration of the mixed fruit using combinatorial theory:

The number of ways of arranging \( n \) things is \( n! \), which is 6x5x4x3x2x1 in this case.

However, the three oranges and three plums are identical, so this reduces the number of possible arrangements by \((3!)^2\), since there are 3x2x1 ways of arranging three objects. The total number of ways of arranging the three oranges and three plums is:

\[
6!/(3! 3!) = 20.
\]

Entropy and the Hydrophobic Effect:

Non-polar compound are not very water soluble. The low solubility is due to the entropy changes of the water. If we add a non-polar liquid (e.g. butane), the entropy of the dissolved butane is positive and favorable because it is no longer in pure butane. However, the water interacts with the dissolved butane by forming a cage of organized hydrogen bonded water around the butane, as illustrated on the right. This causes a large decrease in the entropy of the water, much more than the entropy of mixing, so the overall entropy change is negative, or unfavorable.
Lecture 2: Molecular Forces, Water & Hydrogen Bonds

Key Terms:
- Interactions:
  - Electrostatics
  - van der Waals
  - Entropy
- Polar bonds
- Electronegativity
- Polar solvents
- Water structure
- Hydrogen bond (donor & acceptor)
- Hydrophobic (nonpolar) compounds.
- Hydrophilic (polar) compounds.
- Interaction of salts with water.
- Amphipathic or amphiphilic compounds.

OLI Quiz Sequence:

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Navigation Tip:
Module 2 / 6. Primary Structure

Can type in page number (e.g. 56 = Schedule)

Functional Groups: Name the functional groups on these four amino acids (amino acids are the building blocks of proteins).

2A. Molecular Interactions

1) Electrostatics: The force between two charged particles is:

\[ F = \frac{1}{4\pi\varepsilon_0} \frac{q_1 q_2}{d^2} \]

\[ \varepsilon_0 = 8.854 \times 10^{-12} C^2/N\cdot m^2 \]

The force depends on the distance between the two charges and the dielectric constant (D) of the media. A high dielectric constant, such as that found in water (~80), is important because the forces between charges are attenuated, reducing charge interactions.

How strong are electrostatic interactions?
Na⁺ Cl⁻ = ~600 kJ/mol in vacuum
ii) van der Waals (induced dipole-induced dipole < induced dipole-dipole < dipole-dipole) - an electrostatic interaction that does not involve formal charges. Charges may be temporary (induced dipole) or permanent (dipole).

Boiling points of hydrocarbons:
- isobutane: 261 K
- butane: 272 K

Same number of cartons, why the difference in boiling points?

How strong are van der Waals forces?

2B. Polar bonds & Molecules
A bond is considered to be polar if there is a significant difference in the electronegativities of the participating atoms, giving an appreciable dipole moment. (The electronegativities increase across the periodic table).

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<tr>
<td>2</td>
<td>He</td>
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<tr>
<td>3</td>
<td>Li 1.0</td>
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</table>

The dipole moment, \( \mu \), is defined by the following equation:

\[
\mu = \sum q r_{\text{All atoms}}
\]

The size of the dipole moment can be approximated by the difference in the electronegativities of the two atoms: \( |\mu| = \Delta E \)

Polar molecule: A molecule is considered polar if it has a permanent dipole moment associated with it. Does \( \text{CO}_3 \) behave as a polar molecule? Why or why not?
2C. Structure of Water

i. Oxygen has the following electronic configuration: \[ 1s^22s^22p^4. \]
ii. The molecular orbitals in water are complex, however we can understand most of the properties of water by assuming that oxygen forms sp\(^3\) hybrid orbitals and H uses its 1s orb.
iii. The orbitals in oxygen are populated such that two orbitals are filled and two contain one electron each.
iv. The filled orbitals cannot form bonds and are often called lone pairs.
v. The half-filled orbitals participate in the formation of a sigma bond between oxygen and hydrogen.
vi. "Bent" water molecule generates a permanent dipole moment, making water a polar solvent with a high dielectric constant.

2D. Hydrogen Bonds

i) Formation of H-bonds is primarily an electrostatic attraction between:
- Electropositive hydrogen, attached to an electronegative atom is the hydrogen bond donor (i.e. NH)
- Electronegative hydrogen bond acceptor (e.g. the lone pairs of oxygen in the case of water, or C=O group of an amide).
- The energy released when H-bonds form depends on the distance and angle of the bond. The actual dependence will be explored in recitation and in the problem set. **You should know the ideal distance and angle.**

**Overall Energy:** 20 kJ/mole is released when an H-bond forms.

*How does this compare to the strength of a typical C-C bond?*
*Why might this difference be important in biochemistry?*

Biochemical Significance of Hydrogen Bonds in Water:

i). In ice, the hydrogen bonds cause the formation of cavities in the ice, lowering the density of the solid.
ii) In liquid water, the hydrogen bonds persist, and are transient, generating small short-lived (nsec) clusters of "ice" in liquid water.
iii) Hydrogen bonds are present over a wide temperature range 2-4 bonds/water at room temperature.
iv) The hydrogen bonds in water allow water to absorb heat without a large increase in temperature, giving water a high heat capacity.

2E. Solvation – It is all about reaching the lowest energy.

\( \Delta H^0 \): Enthalpy – A change in the electronic configuration of the system that either releases heat (\(\Delta H^0 <0\)) or absorbs heat (\(\Delta H^0 >0\)). **Release of heat is favorable.**

\( \Delta S^0 \): Entropy – A change in the number of configurations of the system (disorder). Either increasing the disorder (\(\Delta S^0 >0\)) or decreasing the disorder (\(\Delta S^0 <0\)). **Increase in entropy is favorable.**
2E. Solvation – It is all about reaching the lowest energy.

ΔH°: Enthalpy – A change in the electronic configuration of the system that either releases heat (ΔH° < 0) or absorbs heat (ΔH° > 0). Release of heat is favorable.

ΔS°: Entropy – A change in the number of configurations of the system (disorder). Either increasing the disorder (ΔS° > 0) or decreasing the disorder (ΔS° < 0). Increase in entropy is favorable.

ΔG° = ΔH° - TΔS°  ΔG° < 0 – favorable.

i) Solvation of ions (ΔH° < 0 & ΔH° > 0)
- Energy is required to break the ionic bonds in the crystal. ΔH° > 0. Heat was added to system, unfavorable.
- A large dipole moment on water means that the solvent molecules can interact favorably with charged solute molecules. This is energetically favorable. ΔH° < 0, releases heat.
- Overall ΔH° can be positive (unfavorable) or negative (favorable), depending on the balance of these two terms. It depends on the salt.

Question: Why does NH₄Cl readily dissolve in water, yet the solution becomes cold, indicating that the reaction consumes heat, and therefore should be unfavorable?

ii) Hydrophilic (water-loving, polar) compounds (e.g. methanol):
ΔH° < 0 – usually favorable
ΔS° > 0 – always favorable

iii) Hydrophobic (water-hating, nonpolar) compounds (e.g. methane).
ΔH° < 0 – favorable (stronger vdw with water than non-polar solvent)

ΔS° < 0

Hydrophobic effect.

http://chem.ps.uci.edu/~kcjanda/Group/Research_hydrates.html

iv) Amphipathic (or amphiphilic) compounds are both polar (usually charged) and have a substantial nonpolar section (e.g. fatty acids). These can form micelles if the nonpolar part is sufficiently large. Micelles are aggregates of amphipathic molecules that sequester the nonpolar part on the inside, much like the inside of an orange.