Physical Principles in Biology
Biology 3550
Spring 2024

Lecture 31

The Hydrophobic Effect and Amphiphilic Molecules

Monday, 1 April 2024

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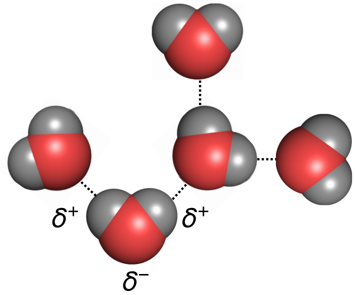
The Hydrophobic Effect

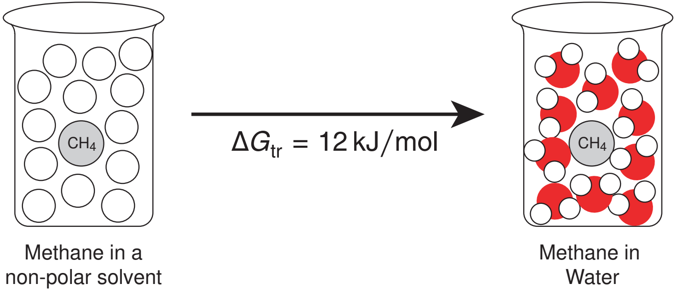
- The basic observation: Water and oil don't mix!
- confusing and still controversial subject, partly because of terminology.
- Non-polar molecules are poorly soluble in water.
- Are non-polar molecules afraid of water?
- What happens when a non-polar molecule does dissolve in water?

What Happens to Water Hydrogen Bonds When a Non-polar Molecule is Introduced?



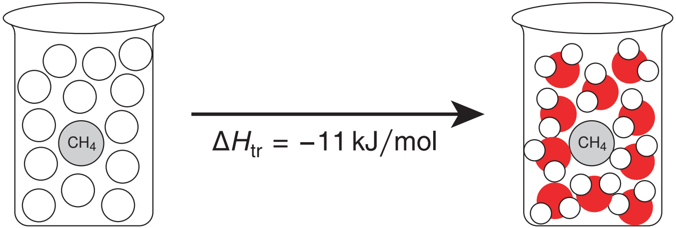
- Non-polar molecules do <u>not</u> form hydrogen bonds with water!
- Do water hydrogen bonds break to allow non-polar molecule in? That would be unfavorable, and would explain low solubility.
- Much of what we know (or think we know) about this comes from thermodynamic measurements.

Thermodynamics of Transfer of a Non-polar Molecule to Water



- ΔG_{tr} is measured by comparing solubilities of the same molecule in non-polar solvent and water.
- The positive ΔG_{tr} confirms that transfer to water is unfavorable.

Thermodynamics of Transfer of a Non-polar Molecule to Water



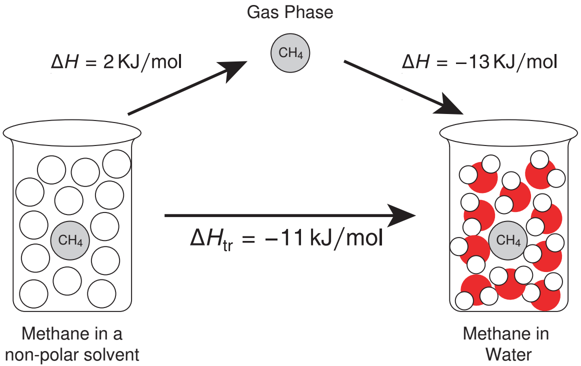
Methane in a non-polar solvent

Methane in Water

- A negative ΔH_{tr} is not what we expect for breaking hydrogen bonds!
- Suggests that favorable interactions are being formed when the non-polar molecule is transfered to water!
- Does this happen when molecule is removed from non-polar solvent or when it is added to water?

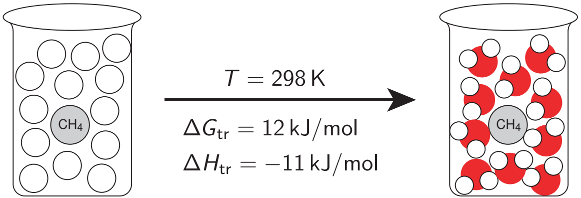
Thermodynamics of Transfer of a Non-polar Molecule to Water

A path through the gas phase from the non-polar solvent to water



- Removing molecule from non-polar solvent breaks some favorable interactions.
- Favorable interactions are being formed when non-polar molecule is introduced into water!

Clicker Question #1



Methane in a non-polar solvent

$T = 298\,\mathrm{K}$

$\Delta G_{tr} = 12\,\mathrm{kJ/mol}$

$\Delta H_{tr} = -11\,\mathrm{kJ/mol}$

Methane in Water

What is the entropy change?

A) $\approx 80\,\mathrm{kJ/(mol \cdot K)}$

B) $\approx 80\,\mathrm{J/(mol \cdot K)}$

C) 0

D) $\approx -80\,\mathrm{J/(mol \cdot K)}$

E) $\approx -80\,\mathrm{kJ/(mol \cdot K)}$

The Entropy Change for Transfer of a Non-polar Molecule to Water

$$\Delta G_{\text{tr}} = 12\,\text{kJ/mol}$$

$$\Delta H_{\text{tr}} = -11\,\text{kJ/mol}$$

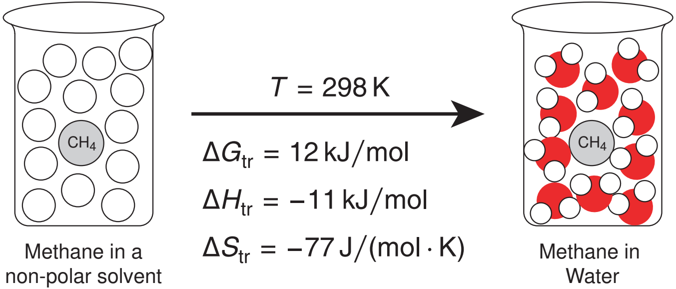
$$\Delta G_{\text{tr}} = \Delta H_{\text{tr}} - T\Delta S_{\text{tr}}$$

$$\Delta S_{\text{tr}} = \frac{\Delta G_{\text{tr}} - \Delta H_{\text{tr}}}{-T} = \frac{\Delta H_{\text{tr}} - \Delta G_{\text{tr}}}{T}$$

$$\Delta S_{\text{tr}} = \frac{-1.1 \times 10^4\ \text{J/mol} - 1.2 \times 10^4\ \text{J/mol}}{298\,\text{K}} = -77\,\text{J/(mol} \cdot \text{K)}$$

- This is the general approach for determining entropy changes experimentally.

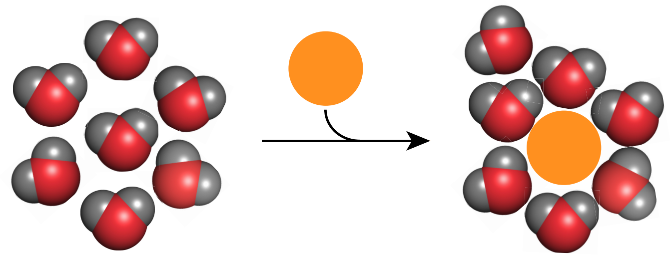
Thermodynamics of Transfer of a Non-polar Molecule to Water



- $\Delta G_{tr} = \Delta H_{tr} - T\Delta S_{tr}$
- ΔG_{tr} is positive because ΔS_{tr} is negative!

  (an "entropically driven" process).
- Something becomes more ordered when non-polar molecule is introduced into water.

The "Iceberg Model"



- Introduction of a non-polar molecule causes water molecules to become more ordered.
- Either new hydrogen bonds form or existing ones become stronger, leading to negative ΔH.
- Why do water molecules do this, instead of just allowing hydrogen bonds to break?
- I don't know! (And, I don't think that anyone else really does either.)

Specific Heat Capacities of Some Liquids

Liquid	C_p (J/(K · g))
Methanol	2.14
Ethanol	2.44
Octane	2.22
Water	4.18

- Large heat capacity of water is attributed to hydrogen bonds.
- Heat is absorbed by breaking or weakening of hydrogen bonds.

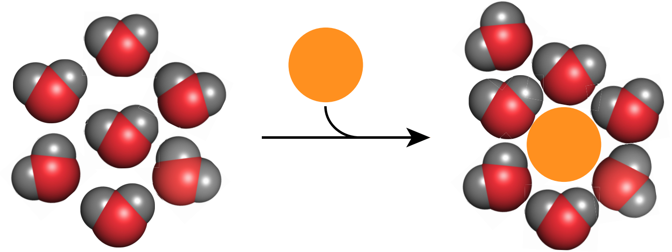
Data from https://en.wikipedia.org/wiki/Table_of_specific_heat_capacities

Transfer of a Non-polar Molecule to Water

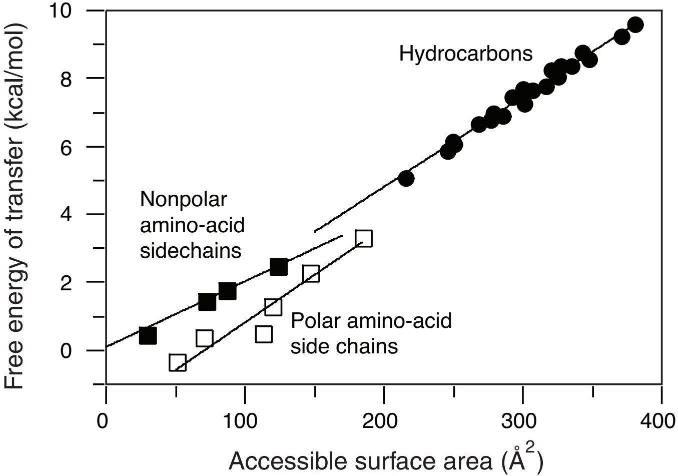
- The change in heat capacity for a process:

  $$\Delta C_p = C_{p,2} - C_{p,1}$$

  The heat capacity changes for phase transitions are very large, as intermolecular interactions are cooperatively broken or formed.
- ΔC_p for transfer of a non-polar molecule is positive.
- Consistent with the formation of more or stronger hydrogen bonds.

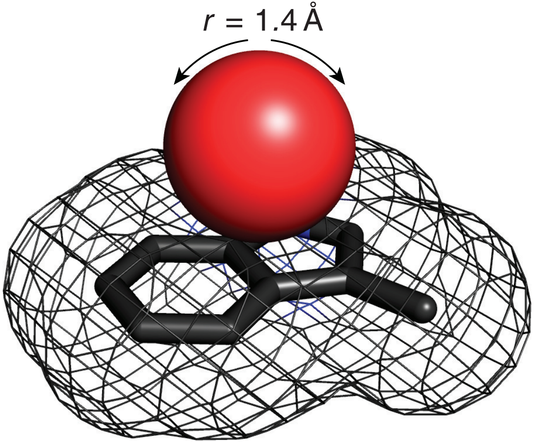


Transfer Free Energy versus Molecular Size



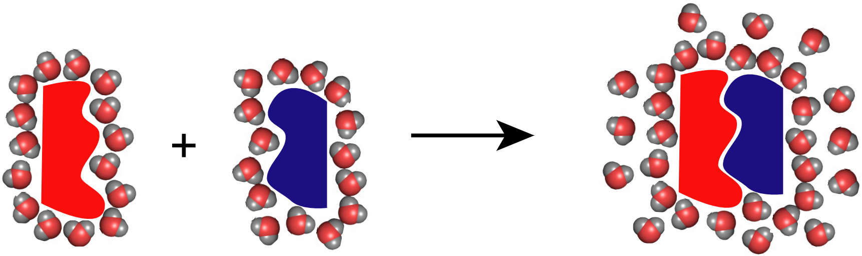
Adapted from: F. M. Richards. Areas, volumes, packing and protein structure. *Annu. Rev. Biophys. Bioeng.*, 6:151–176, 1977. http://dx.doi.org/10.1146/annurev.bb.06.060177.001055

Accessible Surface Area



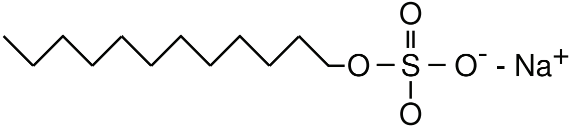
- Surface of the molecule that can contact a water molecule, represented by a sphere with radius of 1.4 Å.
- Ball is rolled over the surface of the molecule and accessible surface is defined by path of the ball.
- ASA is strongly correlated with free energies of transfer from non-polar solvents to water.

Bimolecular Association can be Entropically Favorable!



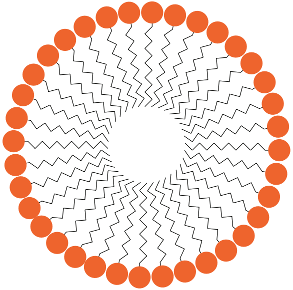
- Associating molecules lose entropy.
- Water molecules near hydrophobic surfaces become less ordered.
- Ions bound to charged groups can have similar effect.

An Amphiphilic Molecule: Sodium Dodecyl Sulfate



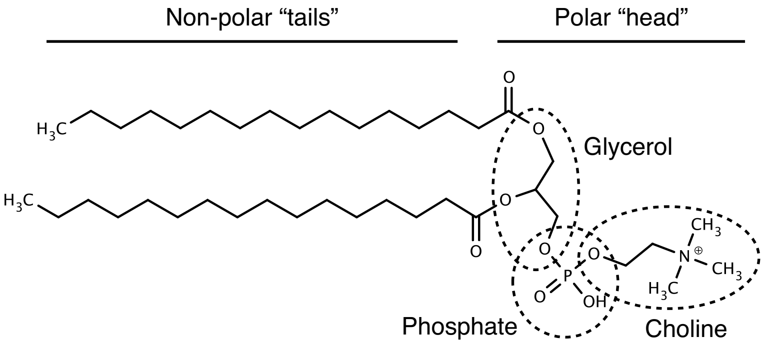
- Two parts:
  - Tail: 12-carbon hydrocarbon - highly insoluble in water
  - Head: Sulfate group - highly soluble in water
- Typical structure of ionic detergents
- Common ingredient of shampoos and other common cleaning products

Self Assembly of Detergents: Micelles



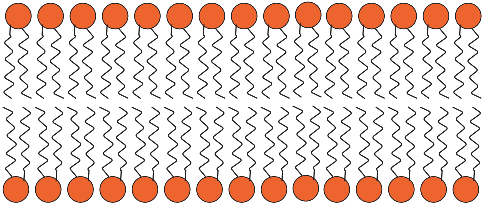
- Roughly spherical structures.
- Hydrocarbon tails are sequestered away from water.
- Polar head groups interact with water.
- Structural specificity:
  For a given detergent, micelles will have limited range of sizes that optimizes packing of molecules.
- Soaps and detergents act by dissolving non-polar molecules in core of micelles.

A Phospholipid: Phosphatidylcholine



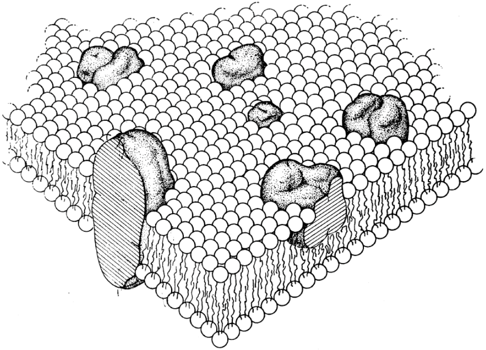
- Two hydrocarbon tails linked together through glycerol.
- Polar head includes glycerol, phosphate group, and choline.
- Lots of variety in both hydrocarbon tails and polar groups.

Phospholipids and Bilayers



- Large two dimensional sheets.
- Non-polar tails sequestered away from water.
- Polar head groups exposed to water on each side.
- Why don't phospholipids form micelles, like detergents do?

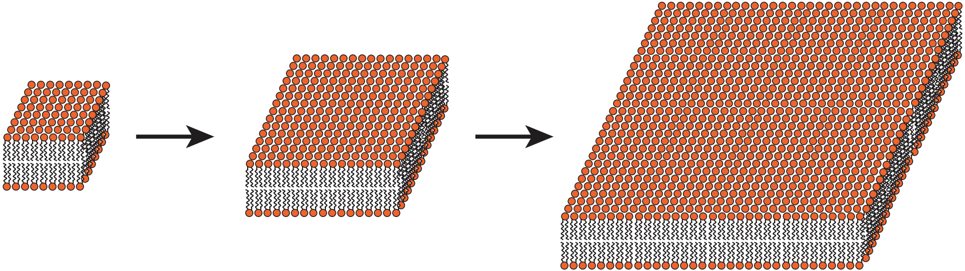
General Structure of Biological Membranes:
The Fluid Mosaic Model



- Proteins embedded in bilayer control passage of other molecules.
- Many other functions of membrane proteins!

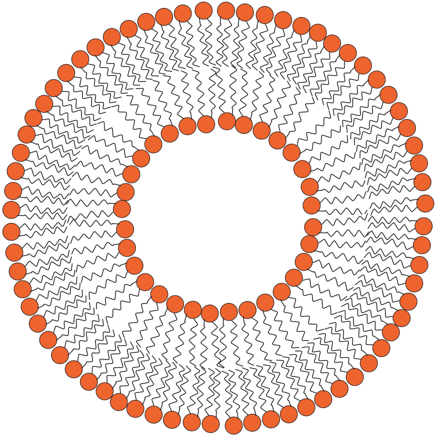
Singer, S. J.& Nicolson, G. (1972). The fluid mosaic model of the structure of cell membranes. *Science*, 175, 720–731.
http://dx.doi.org/10.1126/science.175.4023.720

Growth of Bilayer Sheets



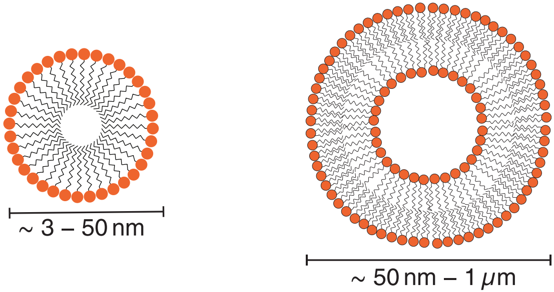
- As sheet grows, surface area of non-polar lipids exposed at edges grows.
- Hydrophobic effect counteracts resistance of the sheet to curve.

Bilayer Sheets Form Vesicles



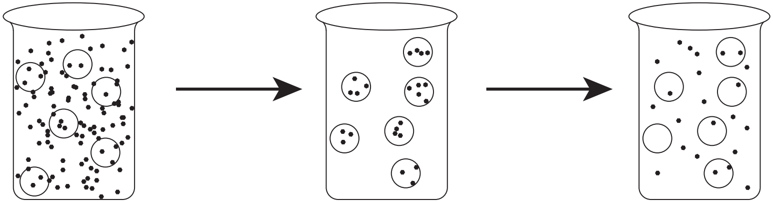
- Bilayers close on themselves to eliminate edges.
- 50 nm–1 μM in diameter.
- Function in vivo to store and transport specific molecules (*e.g.*, neurotransmitters)
- Formed experimentally by vigorously mixing bilayers in water.

Micelles Versus Vesicles



- Micelles are formed by detergents and soaps; vesicles are formed by phospholipids.
- Micelles are made up of a single shell of detergent or soap molecules; vesicles are made up of lipid bilayers.
- Micelles are generally much smaller than vesicles.
- Different shapes and sizes of the micelles and vesicles reflect the different shapes of detergents and soaps (∼conical) and phospholipids (∼cylindrical).

Using Vesicles to Measure Permeability of Bilayers



- Form vesicles in presence of molecules of interest.
- Separate vesicles from external molecules.
- Allow molecules to diffuse across bilayers for a period of time.
- Separate vesicles from external molecules and measure concentrations.
- What determines rate of escape?
  Fick's first law!