Physical Principles in Biology

Biology 3550

Spring 2025

Lecture 31

The Hydrophobic Effect and Amphiphilic Molecules

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The Hydrophobic Effect

- The basic observation: Water and oil don't mix!
- A 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?

Clicker Question #1

Why don’t oil and water mix?

A) Water and oil molecules repel one another.

B) Oil molecules stick together very tightly.

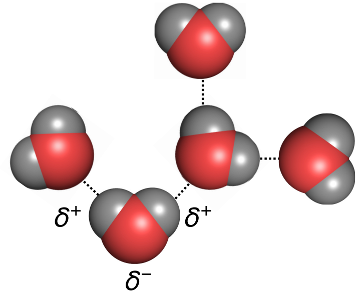
C) Water molecules stick together very tightly.

D) All of the above.

E) None of the above.

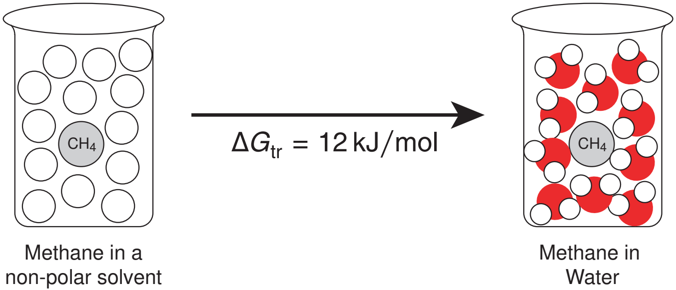
All answers count for now!

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



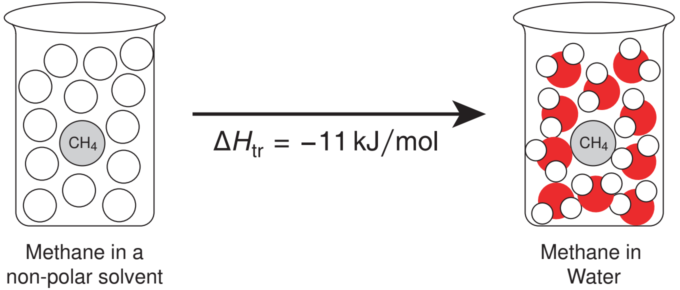
- Non-polar molecules do <u>not</u> form hydrogen bonds with water!
- Do water hydrogen bonds break to allow non-polar molecule in?
  That would be unfavorable, and would explain low solubility.
- Much of what we know (or think we know) about this comes from thermodynamic measurements.

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.

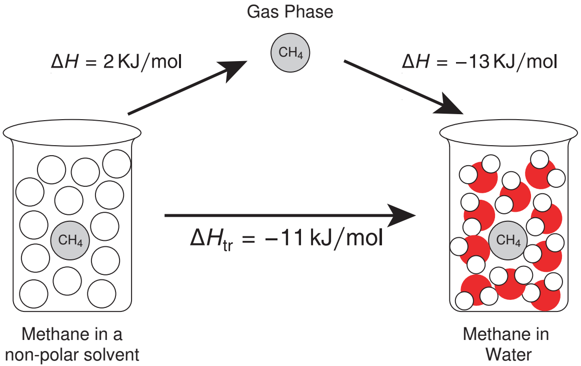
Thermodynamics of Transfer of a Non-polar Molecule to Water



- A negative ΔH_{tr} is not what we expect for breaking hydrogen bonds!
- Suggests that favorable interactions are being <u>formed</u> 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?

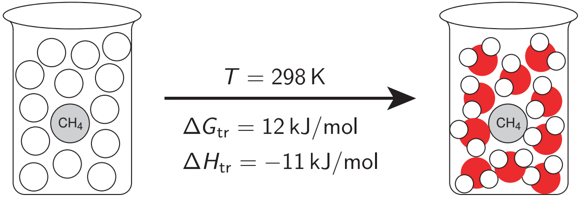
Thermodynamics of Transfer of a Non-polar Molecule to Water

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 <u>formed</u> when non-polar molecule is introduced into water!

Clicker Question #2



Methane in a non-polar solvent

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

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

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

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

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

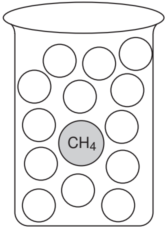
$$\Delta G_{\text{tr}} = \Delta H_{\text{tr}} - T\Delta S_{\text{tr}}$$

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

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

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

Thermodynamics of Transfer of a Non-polar Molecule to Water



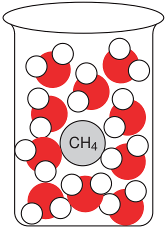
Methane in a
non-polar solvent

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

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

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

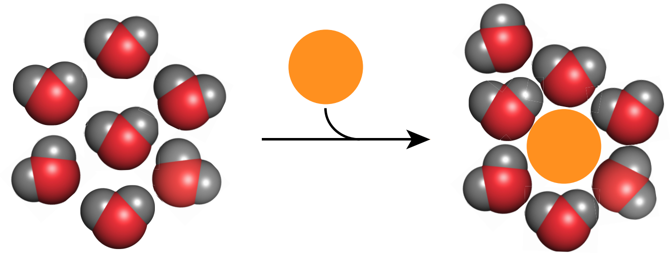
$\Delta S_{\mathrm{tr}} = -77\,\mathrm{J/(mol \cdot K)}$



Methane in
Water

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

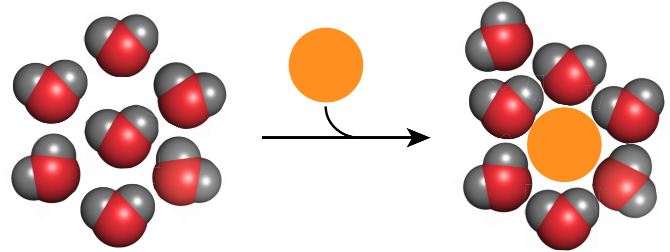
Transfer of a Non-polar Molecule to Water

- The change in heat capacity for a process:

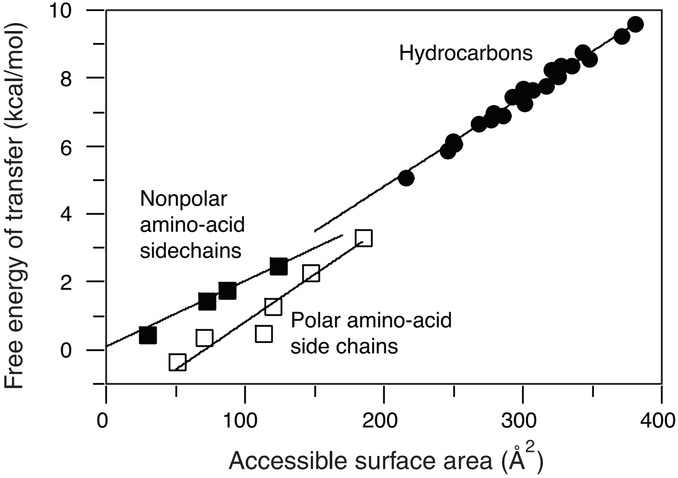
  $$\Delta C_{\mathrm{p}} = C_{\mathrm{p},2} - C_{\mathrm{p},1}$$

  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.

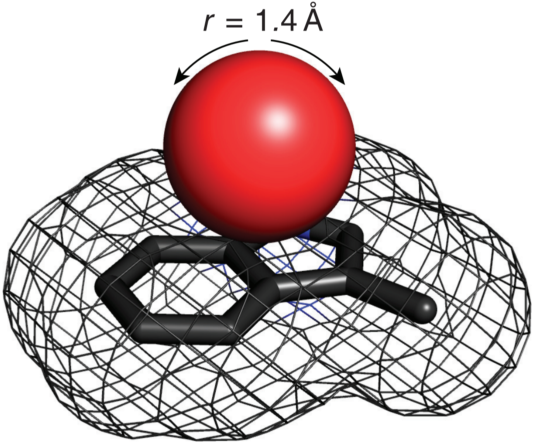


Transfer Free Energy versus Molecular Size



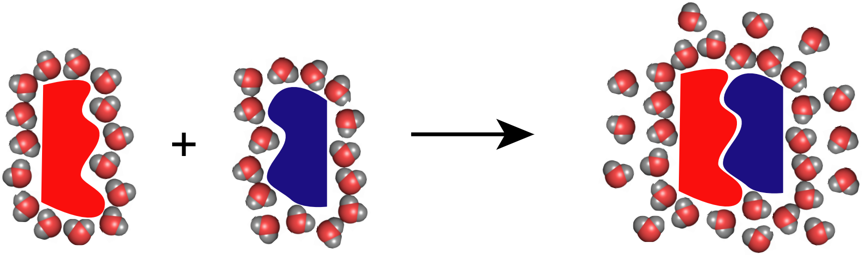
Adapted from: F. M. Richards. Areas, volumes, packing and protein structure. *Annu. Rev. Biophys. Bioeng.*, 6:151–176, 1977. http://dx.doi.org/10.1146/annurev.bb.06.060177.001055

Accessible Surface Area



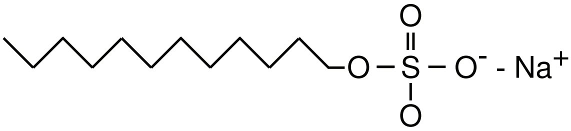
- Surface of the molecule that can contact a water molecule, represented by a sphere with radius of 1.4 Å.
- Ball is rolled over the surface of the molecule and accessible surface is defined by path of the ball.
- ASA is strongly correlated with free energies of transfer from non-polar solvents to water.

Bimolecular Association can be Entropically Favorable!



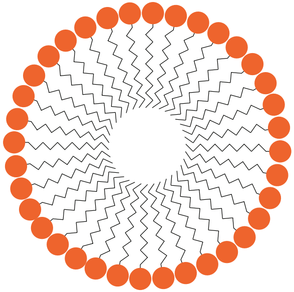
- Associating molecules lose entropy.
- Water molecules near hydrophobic surfaces become less ordered.
- Ions bound to charged groups can have similar effect.

An Amphiphilic Molecule: Sodium Dodecyl Sulfate



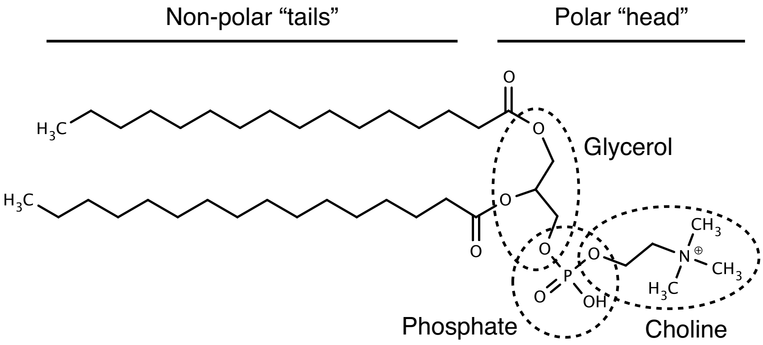
- Two parts:
  - Tail: 12-carbon hydrocarbon - highly insoluble in water
  - Head: Sulfate group - highly soluble in water
- Typical structure of ionic detergents
- Common ingredient of shampoos and other common cleaning products

Self Assembly of Detergents: Micelles



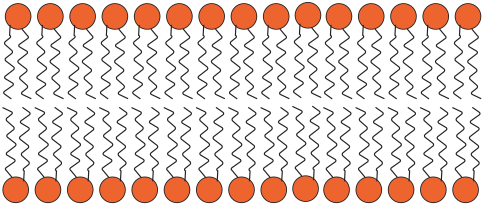
- Roughly spherical structures.
- Hydrocarbon tails are sequestered away from water.
- Polar head groups interact with water.
- Structural specificity:
  For a given detergent, micelles will have limited range of sizes that optimizes packing of molecules.
- Soaps and detergents act by dissolving non-polar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

A Phospholipid: Phosphatidylcholine



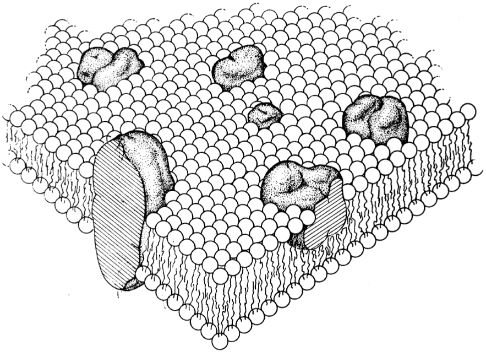
- Two hydrocarbon tails linked together through glycerol.
- Polar head includes glycerol, phosphate group, and choline.
- Lots of variety in both hydrocarbon tails and polar groups.

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?

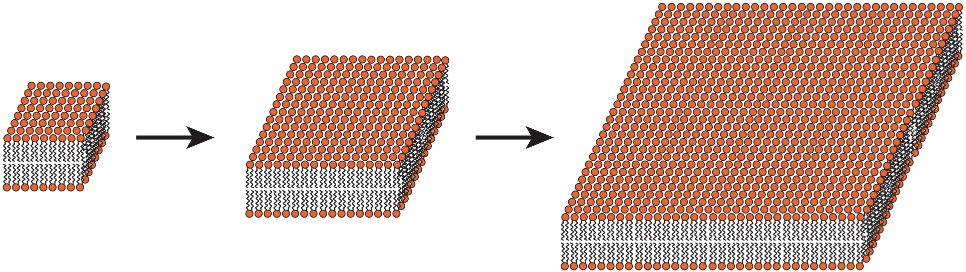
General Structure of Biological Membranes: The Fluid Mosaic Model



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

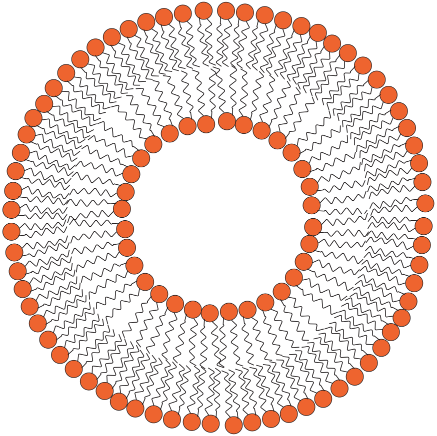
Singer, S. J.& Nicolson, G. (1972). The fluid mosaic model of the structure of cell membranes. *Science*, 175, 720–731.
http://dx.doi.org/10.1126/science.175.4023.720

Growth of Bilayer Sheets



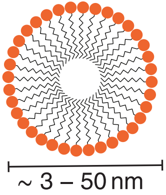
- As sheet grows, surface area of non-polar lipids exposed at edges grows.
- Hydrophobic effect counteracts resistance of the sheet to curve.

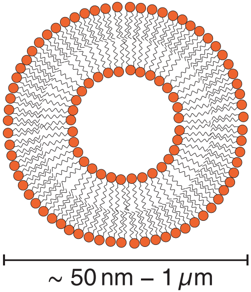
Bilayer Sheets Form Vesicles



- 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).