Protein Folding, Nonbonding Forces, and Free Energy

ΔG Gibbs Free Energy

$e^{-\Delta G/kT}$ Boltzman Probability Distribution

Entropy

- Entropy – a measure of disorder

$$\Delta S_{total} = \Delta S_{system} + \Delta S_{surroundings}$$

$$\Delta S_{total} = \Delta S_{system} - \Delta H_{system} / T$$

H = enthalpy
T = temperature (Kelvins)

Entropy

- Entropy – a measure of disorder

$$\Delta S_{total} = \Delta S_{system} + \Delta S_{surroundings}$$

$$\Delta S_{total} = \Delta S_{system} - \Delta H_{system} / T$$

H = enthalpy
T = temperature (Kelvins)

$$-T\Delta S_{total} = \Delta H_{system} - T\Delta S_{system}$$

Free Energy

$$-T\Delta S_{total} = \Delta H_{system} - T\Delta S_{system} \quad = \Delta G$$

- 2nd Law of Thermodynamics – the total entropy of a system and its surroundings always increases for a spontaneous process.

Since we have already seen that:

$$\Delta S_{total} = \Delta S_{system} - \Delta H_{system} / T$$

Total entropy will only increase if:

$$\Delta S_{system} > \Delta H_{system} / T \qquad (T\Delta S_{system} > \Delta H_{system})$$

Therefore, $\Delta G < 0$ for a spontaneous process

Free Energy and Protein Folding

$$\Delta G = \Delta H_{system} - T\Delta S_{system} \quad < 0$$

Water and the hydrophobic 'effect'

Bonding Energies

Disulfides, bound ions, etc.

Nonbonding Energies

Electrostatic

Hydrogen Bonds

Van der Waals

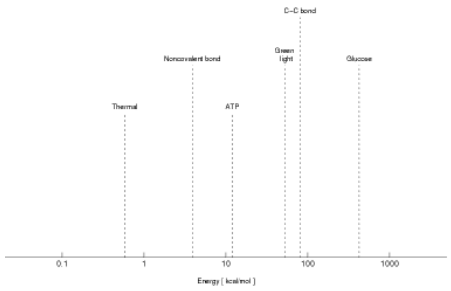
Non-Bonding Interactions

Amino acids of a protein are joined by covalent bonding interactions. The polypeptide is folded in three dimension by non-bonding interactions. These interactions, which can easily be disrupted by extreme pH, temperature, pressure, and denaturants, are:

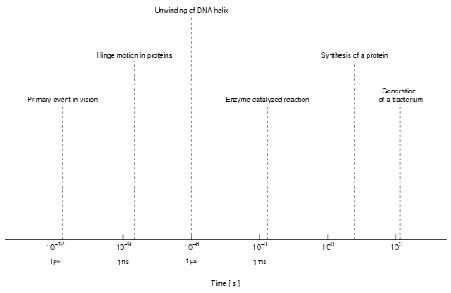
- Electrostatic Interactions (5 kcal/mol)
- Hydrogen-bond Interactions (3-7 kcal/mol)
- Van Der Waals Interactions (1 kcal/mol)
- Hydrophobic Interactions (< 10 kcal/mol)

The total inter-atomic force acting between two atoms is the sum of all the forces they exert on each other.

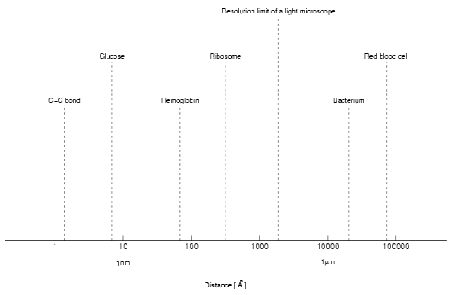
Space, Time, Energy



Space, Time, Energy



Space, Time, Energy

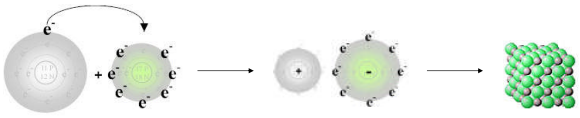


Electrostatic Interactions

Charged groups attract or repel each other. The force F of such an electrostatic interaction is given by Coulomb's law:

$$F = \frac{q_1 q_2}{Dr^2}$$

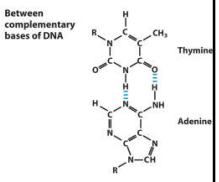
q_1 and q_2 are the charges
r is the distance
D is the dielectric constant



Coulomb's law is also used to determine interactions between uncharged, but polar atoms.

Hydrogen bonds

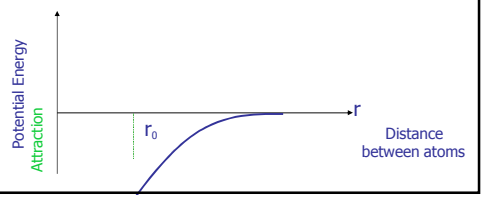
In a hydrogen bond, a hydrogen atom is shared between two other atoms. The atom to which the hydrogen is more tightly linked is called the hydrogen donor, the other atom is called the hydrogen acceptor.



Van der Waals Interactions

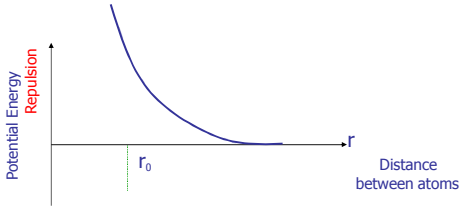
The distribution of electronic charges around an atom changes with time, and a transient asymmetry in the charges around one atom induces a similar asymmetry in the electron distribution around its neighboring atoms.

This is essentially an electrostatic interaction and results in a small distant-dependent (R^{-6}) attractive force.



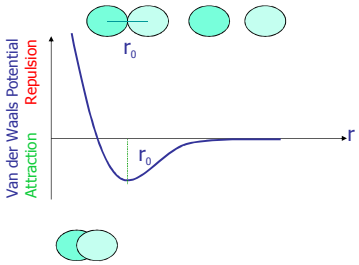
Van der Waals Interactions

As atoms get too close, their electron clouds will clash, resulting in a distant-dependent (R^{-12}) repulsive potential energy.

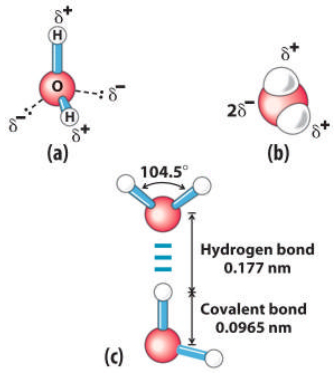


Lennard-Jones Potential

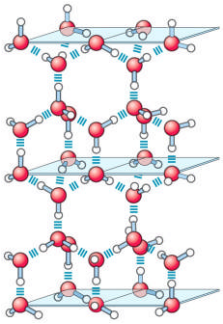
The attractive and repulsive terms can be summed together to describe a distance-dependent interatomic potential energy.



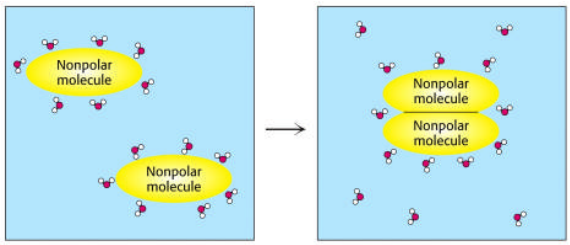
Water



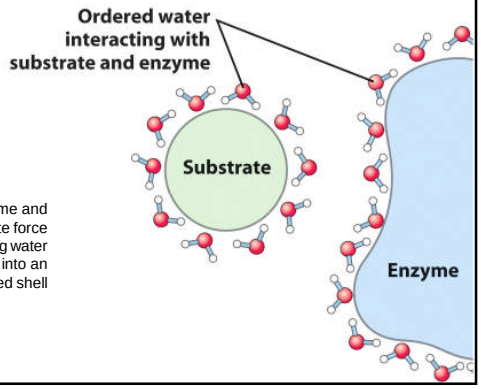
Ice



The Hydrophobic Effects



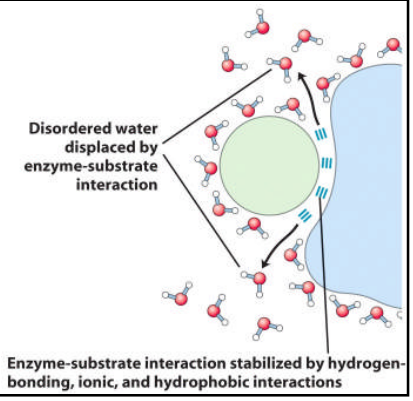
Enzyme-Substrate Binding



Both enzyme and substrate force neighbouring water molecules into an ordered shell

Enzyme-Substrate Binding

The release of ordered water favors the formation of the enzyme-substrate complex!



Hydrophobic Interactions in Proteins

- Hydrophobic interactions minimize interactions of non-polar residues with solvent.
- Non-polar regions of proteins are usually buried in the molecules interior.
- However, non-polar residues can also be found on the surface of a protein. They may participate in protein-protein interactions.
- This type of interaction is entropy driven.