Solvation

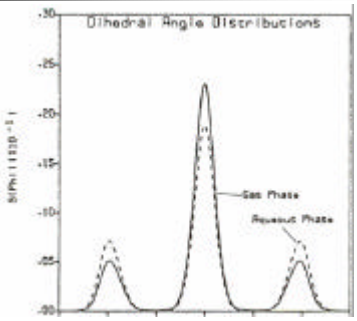
CHEM8711/7711

Solvent Influence

- Solvent influence levels
  - Direct interaction (or reaction) with solute
  - Solvent provides environment (anisotropic, for example) that influences solute behavior (mean field effect)
  - Solvent acts as bulk medium affecting solute properties

Bulk Solvent Effect Example

Butane Conformation Distribution

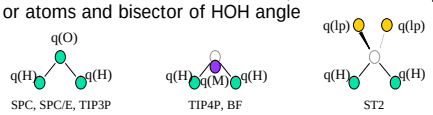


Solvation Treatment

- Explicit
  - System includes actual solvent molecules
  - Required for any direct solvent-solute interaction
  - Problems
    - System becomes quite large if long-range effects are to be handled well
    - Sampling of solvent configurations required
    - Simulation times increase
- Implicit
  - System does not include actual solvent molecules

Explicit Water Models

- Simple Pairwise Potentials
  - Interaction sites defined on atoms, atoms and lone pairs, or atoms and bisector of HOH angle



  - VDW interactions may be simplified to one per pair of water molecules
  - Individual molecule dipole moments (~2.25D) approximate liquid water (2.6D) rather than gas phase (1.85D)
- Polarizable

Implicit Solvent Models

- Dielectric Screening
- Continuum Representations
  - Attempt to represent three contributions to solvation free energy:

$$\Delta G_{sol} = \Delta G_{elec} + \Delta G_{vdw} + \Delta G_{cav}$$

  - Widely used methods addressing ΔG_{elec}:
    - Born model (we will discuss generalized Born model, which also addresses ΔG_{vdw} and ΔG_{cav})
    - Poisson-Boltzmann

Dielectric Screening

- Polar solvents screen (reduce) electrostatic interactions
- Electrostatic function: $V = \frac{q_1 q_2}{Dr}$
- Common solvent dielectric constants:
  - gas phase: 1
  - water: 78.3
  - alkanes: 3
  - aqueous/membrane interface: 10

Limitation

- The influence of solvent includes an electrostatic and an entropic contribution
  - The electrostatic component is due to solvent polarization (and screening of charge interactions due to intervening solvent molecules)
  - Entropic contributions are due to formation of solvent cavities around solutes
  - The solvent dielectric only reflects the screening of charge interactions

Class Exercise

- Compute the conformational populations for either butane or 1,4-butanedione (coordinate with another student to make sure both are covered) with the solvent dielectric set to 1
- Recompute the conformational populations with the solvent dielectric set to 80

if you have a database of conformations, you can reset the dielectric using Window->Potential Control and then get energies for reminimized structures:

db_ComputeEnergy ['database.mdb','source field','destination field',1]

Exercise Analysis

- Consider the following questions:
  - Are the lowest energy conformations the same with different solvent dielectrics?
  - If not, how do they differ (structurally)?

Generalized Born Method

- Solvation free energies can be expressed as a sum of a solvent cavity term, a solvent-solute van derWaals term and an electrostatic polarization term

  $G_{sol} = G_{cav} + G_{VDW} + G_{pol}$
- The cavity and van derWaals terms are related to the solvent-accessible surface area

  $G_{cav} + G_{VDW} = ?\sigma_k SA_k$

  σ_k: parameter for atom type k; SA_k: solvent accessible surface area for atoms of type k
- Electrostatic term form:

$$\Delta G_{elec} = -\frac{1}{2}\left(1-\frac{1}{e}\right)\sum_{i=1}^{N}\sum_{j=1}^{N}\frac{q_i q_j}{f\left(r_{ij}, q_{ij}\right)}$$

r_{ij}: Interparticle distance; q_{ij}: Born radii

Implicit Solvation of Butane

	ε=1	ε =80
Anti	23.4317 (99.98421%)	25.6143 (99.98420%)
Gauche$^+$	24.3669 (0.00789%)	26.5494 (0.00790%)
Gauche$^-$	24.3669 (0.00789%)	26.5494 (0.00790%)

Changes in conformational distribution due to solvation of hydrophobic molecules are largely NOT electrostatic in nature

GB/SA Results for Butane

	No Solvent	GB/SA water
Anti	-5.076 (99.92605%)	-3.04947 (99.88116%)
Gauche$^+$	-4.29374 (0.03697%)	-2.31422 (0.05942%)
Gauche$^-$	-4.29374 (0.03697%)	-2.31422 (0.05942%)

Inclusion of the cavity and van derWaals effects of solvation improves the calculated influence of solvent

Poisson Equation

Charge density

$$\underbrace{\nabla^2 f(r)}_{\text{Variation in potential }(\phi)} = -\frac{4\pi r'(r)}{\underbrace{e}_{\text{Medium constant dielectric}}}$$

$$\nabla \bullet \underbrace{e(r)}_{\text{Dielectric field varies with position}} \nabla f(r) = -4\pi r(r)$$

Boltzmann Distribution of Ions

Number density of ions at r

Bulk number density

Energy change of ion transfer from infinity to r

$$n(r) = \mathrm{N} \exp\left(\frac{-u(r)}{k_B T}\right)$$

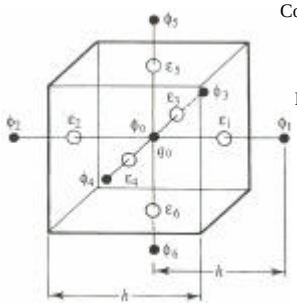
Linearized Poisson-Boltzmann Equation

$$\nabla \bullet e(r) \nabla f(r) - k' f(r) = -4\pi r(r)$$

$$k' = \frac{8\pi N_A e^2 I}{1000 k_B T}$$

- Must be solved numerically

Finite Difference Method



Constant charge density in cube:

$$r_0 = \frac{q_0}{h^3}$$

Potential at grid point 0:

$$f_0 = \frac{\sum e_i f_i + 4\pi \frac{q_0}{h}}{\sum e_i + k_0'^2}$$

potential influenced by surrounding grid points – iterate until consistent solution achieved

Reading

- Chapter 4, section 14
- Chapter 11, sections 9-12