Modeling in Solution

1

Important Observations

Various electrostatic effects for a solvated molecule are often less important than for an isolated gaseous molecule when the molecule is dissolved in a solvent having a high dielectric constant.

Charge separations in a solvated molecule are often stabilized in a polar solvent.

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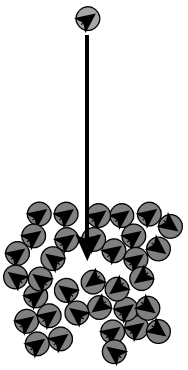
Energy Concepts



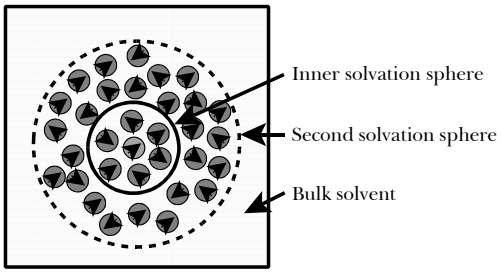
The molecular energy is

E(solvated) = E(gaseous) + E(dissolution)

with a corresponding change in the Hamiltonian

$\mathcal{H}$(solvated) = $\mathcal{H}$(gaseous) + $\mathcal{H}$(dissolution)

3



$\mathcal{H}$(dissolution) typically contains hundreds of interaction terms for solute-inner solvation sphere, inner solvation sphere-second solvation sphere, ..., bulk solvent.

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"Expense" and Accuracy I

Rigorous or Molecular

- "Brute Force" Method
  - Model solute molecule
  - Model solute molecule + 1 solvent molecule
  - Model solute molecule + 2 solvent molecules
  - Model solute molecule + 3 solvent molecules
  - Continue until no change in results
  - Drawbacks
    - Need adequate description of solvent-solute and solvent-solvent interactions
    - Several hundred calculations

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- Dynamics or Monte Carlo Method
  - Model solute molecule
  - Insert all solvent molecules
  - Run molecular "dynamics simulator"
  - Average results
- Effective Fragment Potential (EFP) Method
  - Model solute molecule
  - Represent each solvent molecule by single analytical fragment potential
  - Using solvent clusters can simplify calculations

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“Expense” and Accuracy II

Less Rigorous

- QM-MM Mixture Method
  - Model solute molecule
  - Model solvent using molecular mechanics
- Langevin Dipole Method
  - Model solute molecule
  - Place three-dimensional array of rotatable point dipoles around solute (slide 3)
  - Minimize energy
  - Iterate

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- QM-Continuum Method
  - Model solute and inner solvation sphere
  - Model remainder of solvent as continuum
- Continuum Solvent Methods
  - Assume solvent does not react directly with solute by formation of covalent bonds
  - Place solute in “cavity” of solvent
  - More in a couple of minutes (slide 10)

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“Expense” and Accuracy III

Empirical / QSPR

- Virial equations using empirical parameters
- Group additivity methods

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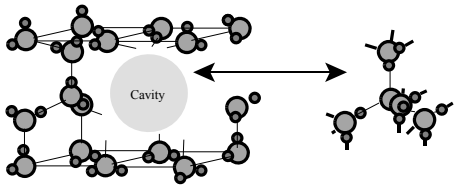
Details on Self-Consistent Reaction Field (SCRF) Methods

Continuum Methods

- Concepts
  - Solvent is a continuum of uniform dielectric constant
  - Solute molecule is placed in a cavity
  - Cavity creation is destabilization of energy



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- Energy stabilization between solute and solvent
  - Solute within cavity induces a polarization in solvent
  - Solvent polarization induces an electric field in cavity (reaction field)
  - Reaction field interacts with solute dipole
  - Note: if there is no dipole moment of solvent, then solution results are identical to those of isolated gaseous molecule

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- SCRF Methods differ by
  - Description of solute (MM, semi-empirical, QM)
  - Description of charge density
  - Size and shape of cavity
  - Description of solvent
  - Description of polarization effects

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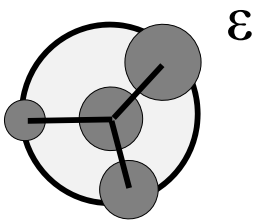
Onsager Model

- Spherical or ellipsoidal cavity
  - Radius from gas phase structure
  - Empirical radius from density and molar mass
  - Choice of radius is important for accuracy
- Charge distribution of solute expressed in terms of a dipole or multipole expansion
  - Multipole needed for nonpolar solute
- Electrostatic interactions calculated analytically
- Good first approximation for other methods



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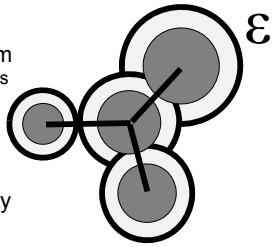
Tomasi Polarizable Continuum Model (PCM)

- Cavity based on union of spheres centered on each atom
  - Radius of sphere ~1.2 van der Waals radius
- Electrostatic interactions calculated numerically
  - Iterated
- Better approximations for cavity are the Connally surfaces



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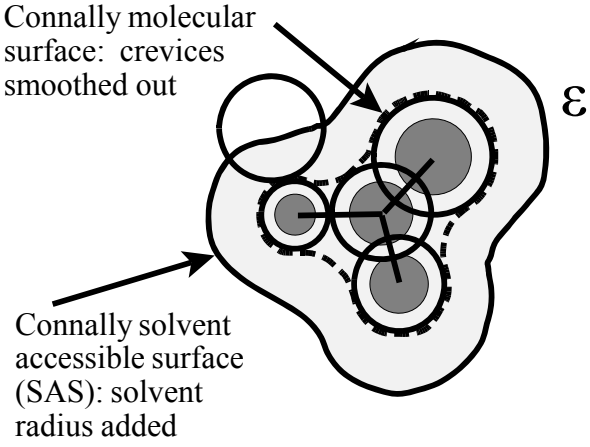

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Isodensity Polarized Continuum Model (IPCM)

- Cavity based on isosurface of electron density
  - SCF calculations on the cavity until converges
- Electrostatic interactions calculated numerically
- Self-Consistent Isodensity Polarized Continuum Model (SCI-PCM)
  - Cavity calculation embedded in SCF differently

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Conductor-like Screening Model (COSMO)

- Cavity based on solvent accessible surface
- Electrostatic interactions are more approximate
  - Solvent is considered a conductor except close to cavity
  - Interactions based on a conducting polygonal surface and calculated numerically
  - SCF calculations until convergence

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Solvation Model "*x*" (SM*x*)

- Solvent molecular interactions based on orbital overlap
  - SM1 - SM3 apply to aqueous solutions
  - SM4 applies to alkanes
  - SM5 applies to general solvents

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Accuracy of Continuum Models

Usually

PCM > Onsager > COSMO

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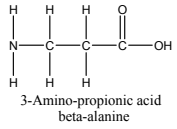
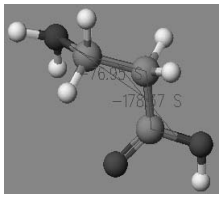
Effect of High Dielectric Constant on Structure



3-Amino-propionic acid
beta-alanine



PM3 conformational analysis (2 labels)

E_{min}(g) = -100.388 kcal mol^{-1}

E_{min}(aq) = -115.895 kcal mol^{-1}

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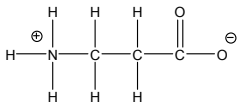

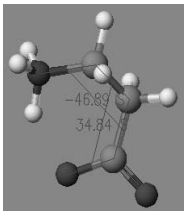

PM3 conformational analysis (2 labels)

E_{min}(g) = -67.502 kcal mol^{-1}

E_{min}(aq) = -131.957 kcal mol^{-1}

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In gas phase
E(molecule) - *E*(zwitterion) =
(-100.388) -(-67.502) = -32.886 kcal mol^{-1}
Molecular form is preferred structure.

In aqueous phase
E(molecule) - *E*(zwitterion) =
(-115.895) -(-131.957) = 16.062 kcal mol^{-1}
Zwitterion is preferred structure.

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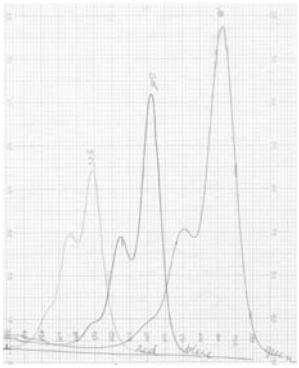
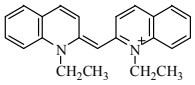
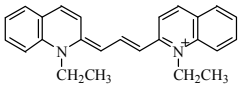
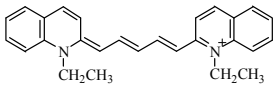
Effect of Dissolution on UV-vis Spectra









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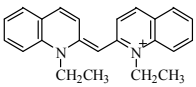
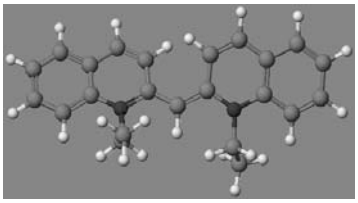


ZINDO PM3

gas λ = 473 nm
in CH_3OH λ = 475 nm
(did not adjust cavity)
exp CH_3OH λ = 523 nm



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