
Solvation Methods

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Outline

Motivation (*including some examples of chemical reactions*)

Fundamentals (*Maxwell equation, Poisson(-Boltzmann) equation, Born, Onsager Kirkwood*)

Continuum Solvation Models (*CSM, SCRF, PCM*)

COSMO-RS theory



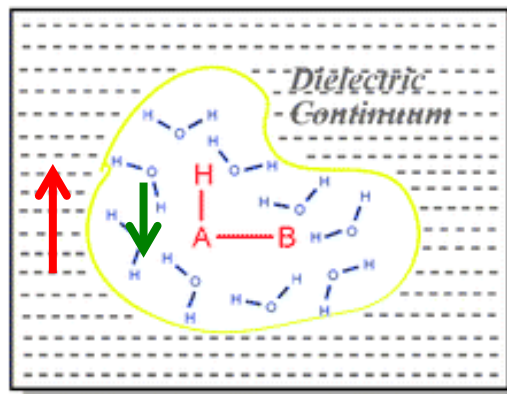
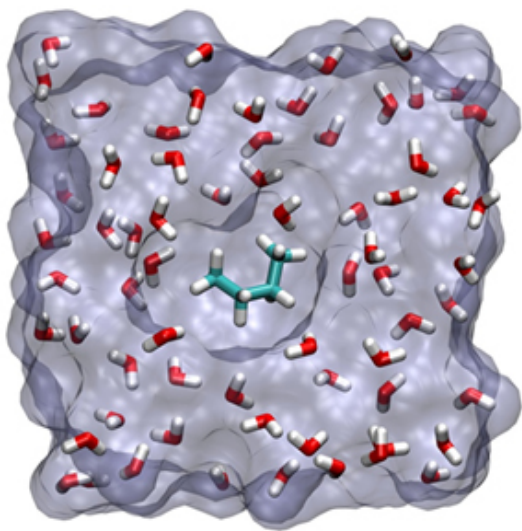
At first sight, modelling of condensed phase might seem trivial

- Explicit solvation(!)

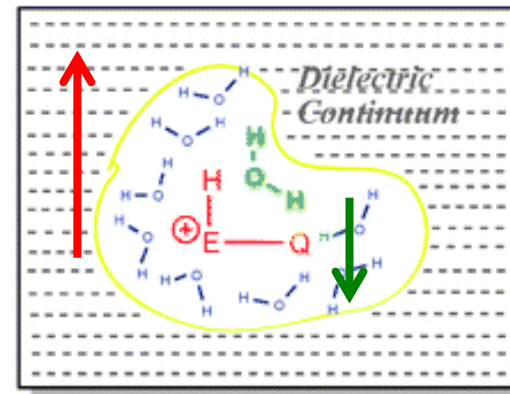
Problems: large number of solvent molecules, conformationally intractable

⇒ Remove the huge number of solvent molecules and replace by

continuous medium



(i) neutral solute



(ii) charged solute



Solvation Energy

$$\Delta G_S^0(\mathbf{A}) = \lim_{[A]_{sol} \rightarrow 0} \left\{ -RT \ln \frac{[A]_{sol}}{[A]_{gas}} \Big|_{eq} \right\}$$

!!! Standard state concentrations (definition)

Equilibrium electrostatic interactions ≤ 0 (= 0 for noble gases)

→ Reaction field

Balance between increasing solute and solvent polarity and the energy cost paid for it on the side of solvent and solute

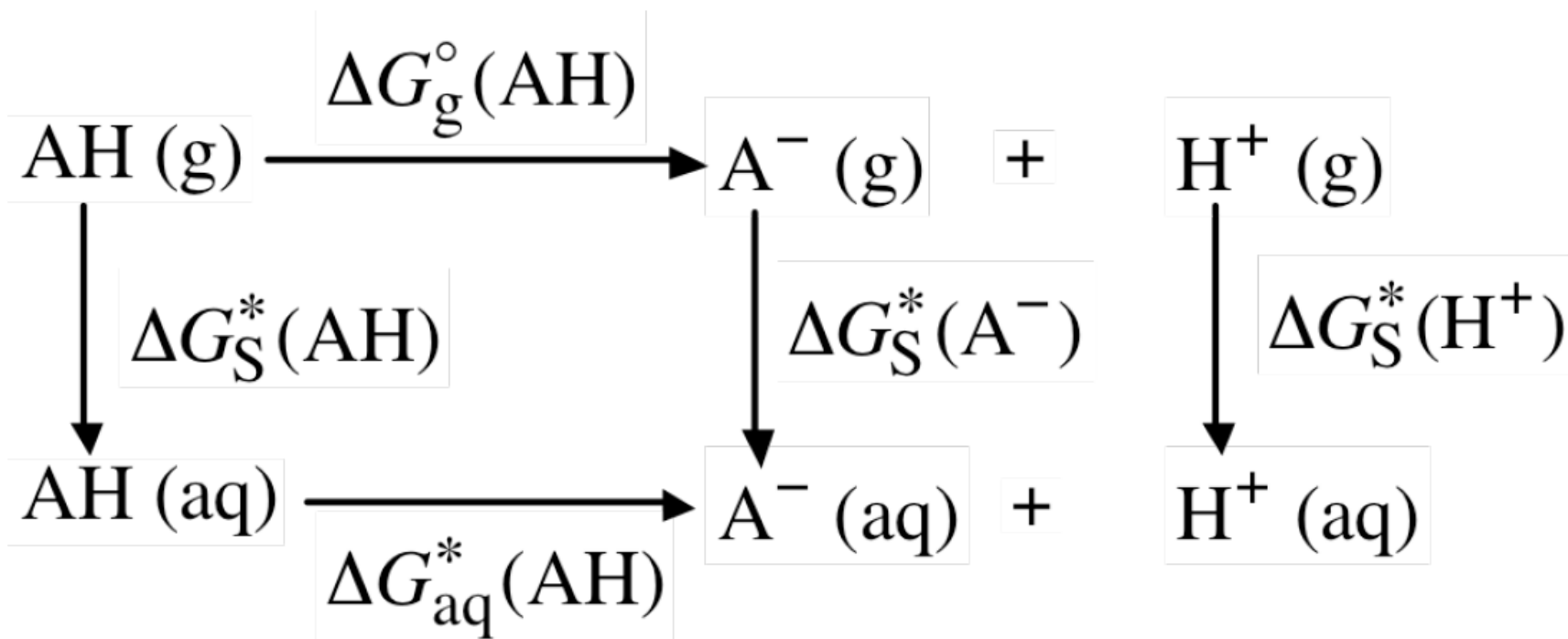
Linear response theory: $\Delta E_{cost} = \frac{1}{2} E_P$

Solvation changes the solute electronic structure and properties

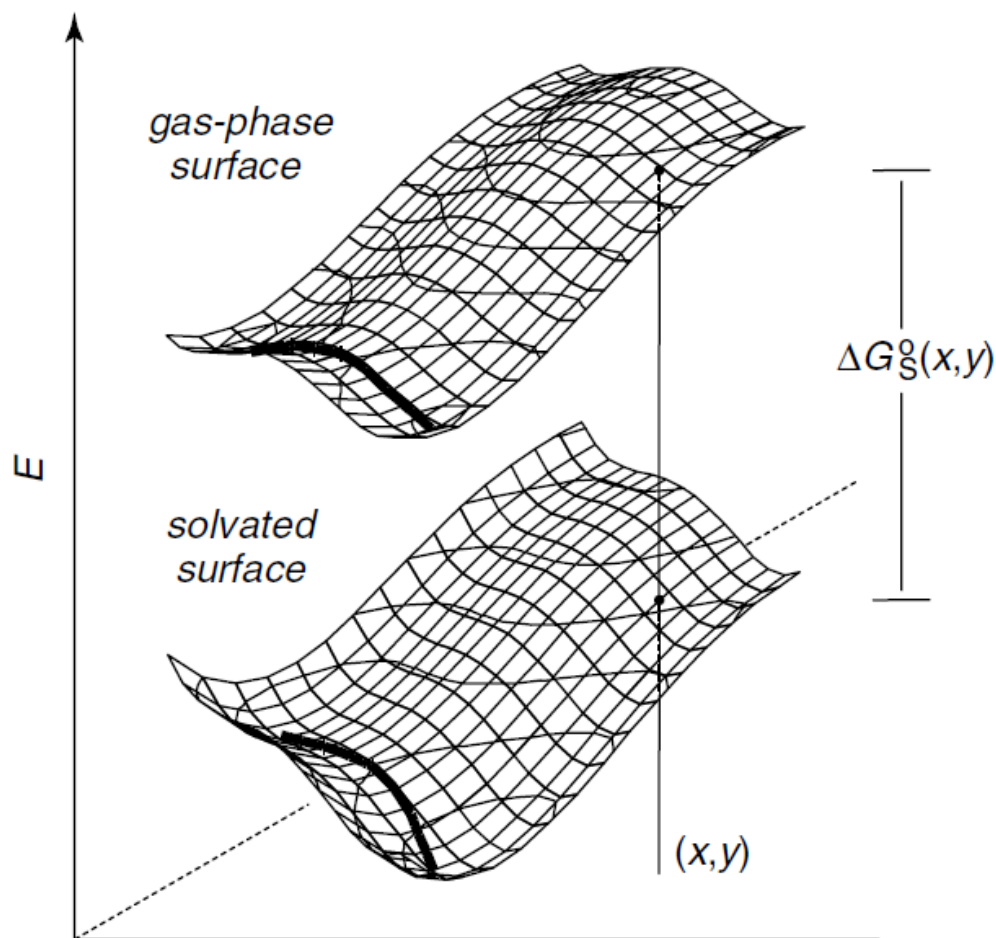
Cavitation, Dispersion Energies, ... (loss of orientational freedom – hydrophobic effect)



Thermodynamic Cycle (Lecture 1 and Lecture 7)

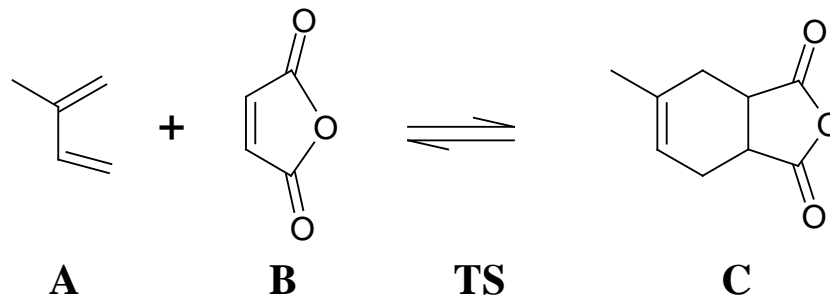


Solvation Effects (Examples)



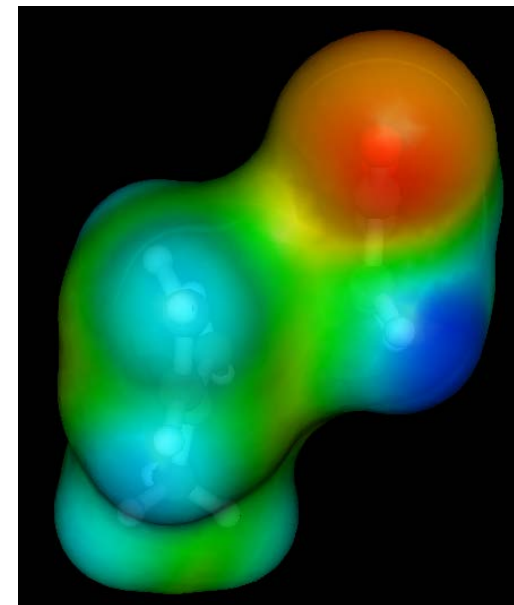
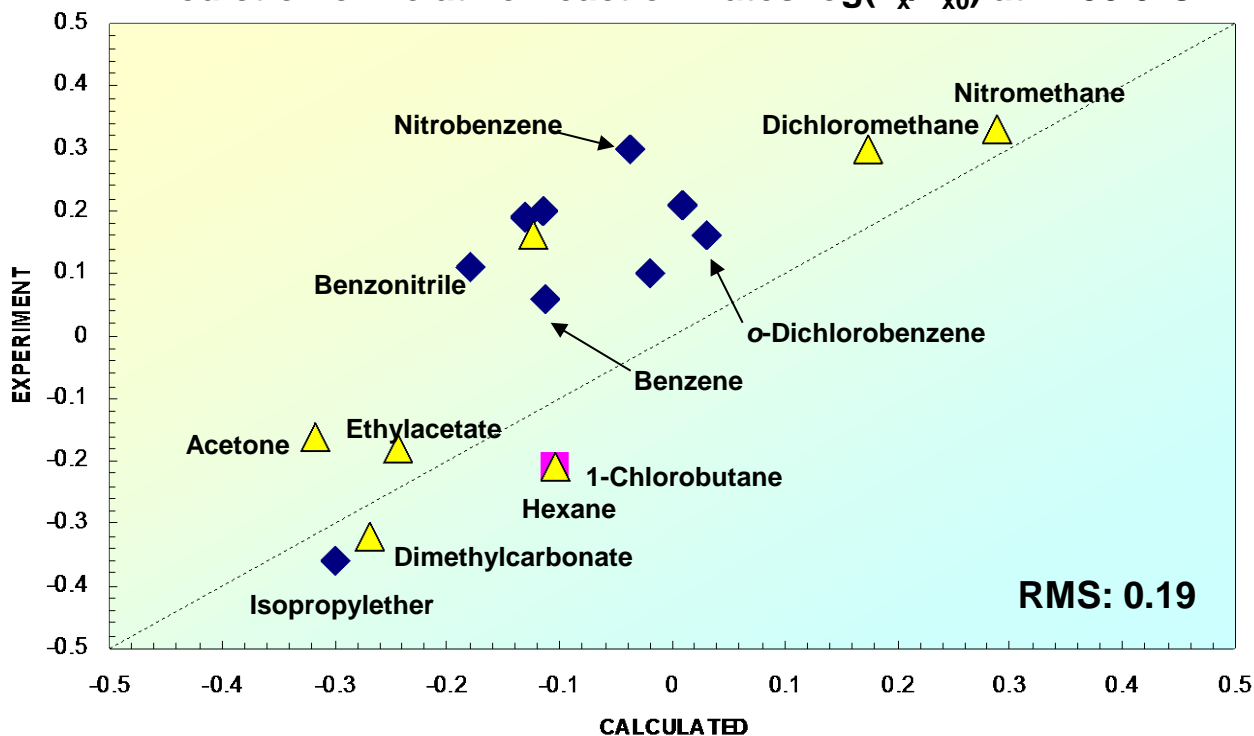
from Cramer, C. J.: *Essentials of Computational Chemistry*

Diels-Alder Reaction



$$k_x = k_{x0} \left(\frac{\gamma_A \gamma_B}{\gamma_{TS}} \right)$$

Prediction of Relative Reaction Rates $\log(k_x/k_{x0})$ at $T=30.0^\circ\text{C}$



Non-polar Transition State

Experimental Data:

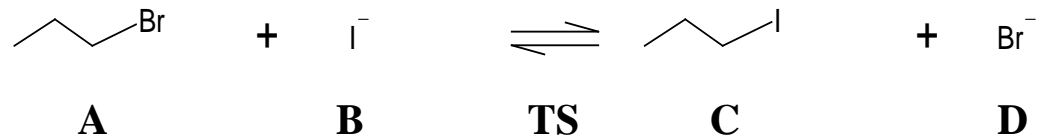
Dewar and Pyron., *J. Am. Chem. Soc.* 92, 3098 (1970).

Grieger et al., *Trans Faraday. Soc.* 66, 2579 (1970).

Snyder and Eckert, *AIChE J.* 19, 1126 (1973).



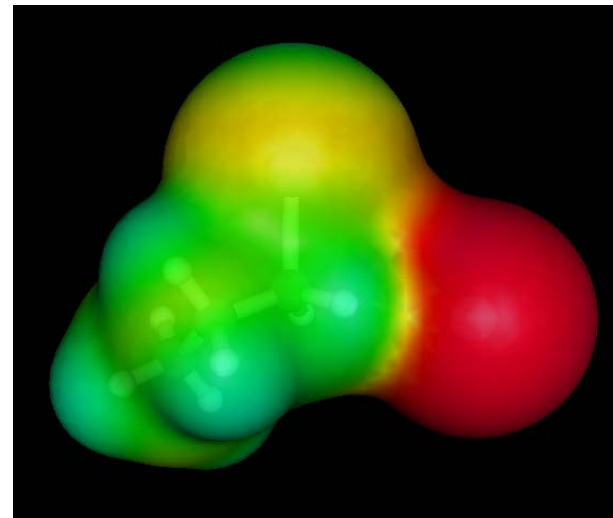
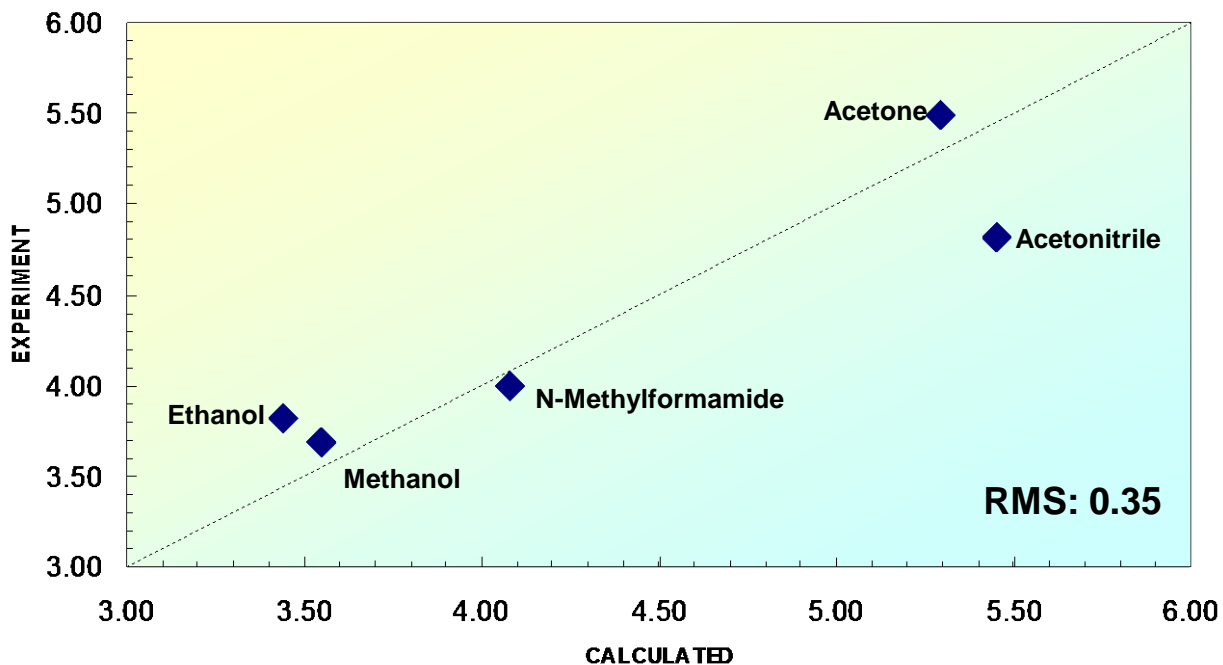
SN₂ Reaction



$$k_x = k_{x0} \left(\frac{\gamma_A \gamma_B}{\gamma_{TS}} \right)$$

$$\log(k_{x0}) = -5.8$$

Prediction of Relative Reaction Rates $\log(k_x)$ at T=50.0°C



Ionic Transition State

Experimental Data:
Eckert, Hsieh and McCabe, *AIChE J.* 20, 20 (1974).



Fundamentals

Electrostatic interactions with Continuum

Work required to create charge distribution

$$G = -\frac{1}{2} \int_{\text{solute}} \rho(\mathbf{r})\varphi(\mathbf{r})d\mathbf{r}$$

G_p (polarization free energy) ... *difference between the charging of the system in gas-phase and in the continuum*

All that is needed $\varphi(\mathbf{r})$ in continuum and in the gas-phase



The Poisson Equation

$$\nabla^2 \phi(\mathbf{r}) = -\frac{4\pi\rho(\mathbf{r})}{\varepsilon}$$

In non-homogenous medium

$$\nabla\varepsilon(\mathbf{r}) \cdot \nabla\phi(\mathbf{r}) = -4\pi\rho(\mathbf{r})$$

Poisson-Boltzmann equation (*non-zero ionic strength*)

$$\nabla\varepsilon(\mathbf{r}) \cdot \nabla\phi(\mathbf{r}) - \varepsilon(\mathbf{r})\lambda(\mathbf{r})\kappa^2 \frac{k_{\text{B}}T}{q} \sinh\left[\frac{q\phi(\mathbf{r})}{k_{\text{B}}T}\right] = -4\pi\rho(\mathbf{r})$$

With Debye-Hückel parameter $\kappa^2 = \frac{8\pi q^2 I}{\varepsilon k_{\text{B}}T}$



The Born Equation

$$G_P = -\frac{1}{2} \left(1 - \frac{1}{\epsilon}\right) \frac{q^2}{a}$$

The Kirkwood-Onsager Equation

$$G_P = -\frac{1}{2} \left[\frac{2(\epsilon - 1)}{(2\epsilon + 1)} \right] \frac{\mu^2}{a^3} \quad G_P = -\frac{1}{2} \sum_{l=0}^L \sum_{m=-l}^l \sum_{l'=0}^L \sum_{m'=-l'}^{l'} M_l^m f_{ll'}^{mm'} M_{l'}^{m'}$$

In the QM context: non-linear SchrEq, stationary dipole moment, Self-Consistent Reaction Field (SCRF) Calculations

$$\left\{ H - \frac{1}{2} \left[\frac{2(\epsilon - 1)}{(2\epsilon + 1)} \right] \frac{\langle \Psi | \mu | \Psi \rangle}{a^3} \mu \right\} \Psi = E \Psi$$



‘PB Solver’: non-ideal (arbitrary cavities)

Numerical solution to

$$G = -\frac{1}{2} \int_{\text{solute}} \rho(\mathbf{r})\varphi(\mathbf{r})d\mathbf{r} \quad (11.3)$$

1. Divide space according to a three-dimensional grid.
2. Define the molecular cavity and assign gridpoints the appropriate dielectric constant – in classical calculations, the interior is often assigned a dielectric constant between two and four to mimic solute polarizability.
3. ‘Discretize’ the solute charge distribution onto interior grid points using some algorithm – e.g., divide every atomic partial charge equally over the nearest grid point and its 14 nearest neighbors.
4. Determine the electrostatic potential at each grid point by numerical solution of the PB equation; this process is typically iterative.
5. Once the potential is available, evaluate Eq. (11.3) as a pointwise sum over points carrying non-zero charge.



Generalized Born model

$$G_P = -\frac{1}{2} \left(1 - \frac{1}{\varepsilon}\right) \sum_{k,k'}^{\text{atoms}} q_k q_{k'} \gamma_{kk'} \quad (11.20)$$

where

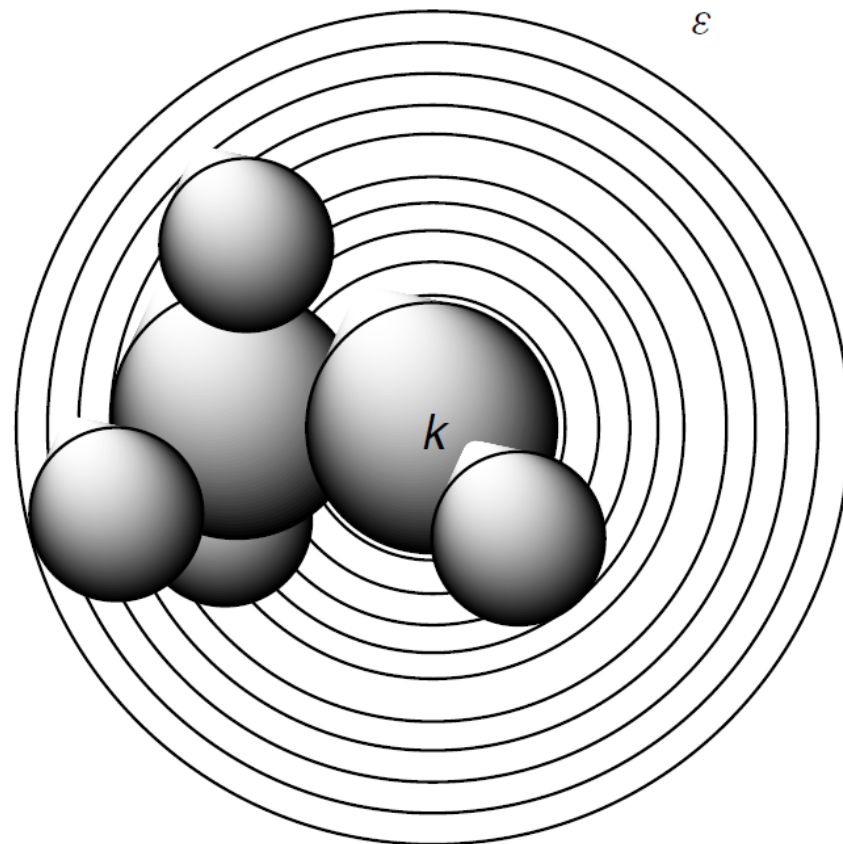
$$\gamma_{kk'} = \left(r_{kk'}^2 + \alpha_k \alpha_{k'} e^{-r_{kk'}^2 / d_{kk'} \alpha_k \alpha_{k'}} \right)^{-1/2}$$

1. Assign atomic radii to all atoms for purposes of defining the cavity.
2. Compute effective Born radii α for all atoms using the procedure outlined above.
3. Using those effective Born radii, compute all values of $\gamma_{kk'}$.
4. Compute or arbitrarily assign the atomic partial charges.
5. Evaluate Eq. (11.20).



$$G_{P,kk} = -\frac{1}{2} \left(1 - \frac{1}{\varepsilon}\right) q_k^2 \int_{\rho_k}^{\infty} \frac{A(r, \{\rho_{k'}\})}{4\pi r^4} dr$$

$$= -\frac{1}{2} \left(1 - \frac{1}{\varepsilon}\right) \frac{q_k^2}{\alpha_k}$$



Continuum Solvation Models (Polarized Continuum Models)

$$\left(H - \frac{1}{2} V \right) \Psi = E \Psi$$

when Ψ is a Slater determinant then

$$(F_i - V) \psi_i = e_i \psi_i$$

Seminal paper S. Miertus, E. Scrocco, J. Tomasi, "Electrostatic Interaction of a Solute with a Continuum. A Direct Utilization of Ab Initio Molecular Potentials for the Prevision of Solvent Effects." *Chem. Phys.* 1981, 55, 117.

Rather than solving the PB equation on a three-dimensional grid, the differential equation can be recast into a boundary element problem by representing the potential using a charge density spread over the molecular surface

Tomasi, J.; Mennucci, B.; Cammi, R.: **Quantum Mechanical Continuum Solvation Models.** *Chem. Rev.* **2005**, 105, 2999-3093.



Continuum Models for Non-electrostatic Interactions

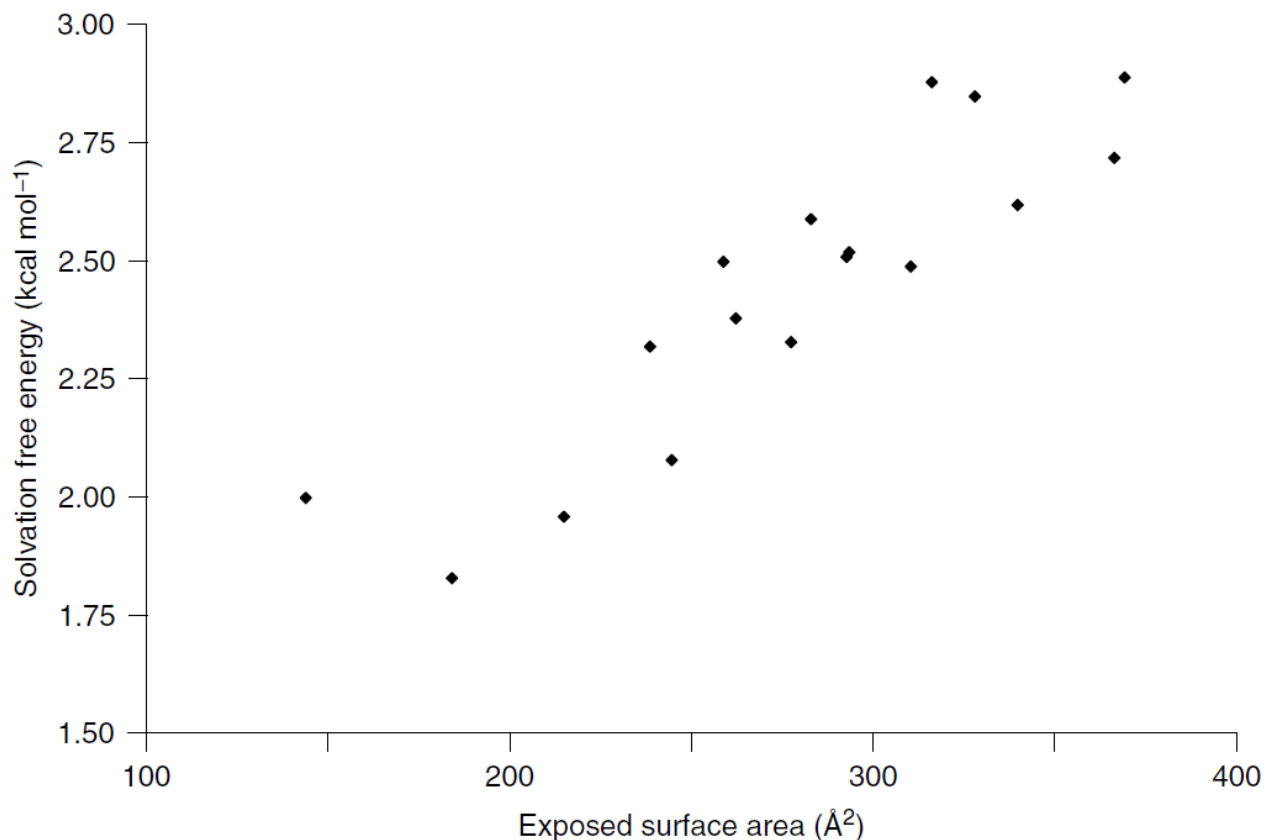


Figure 11.8 Approximately linear relationship between solvation free energy and solvent-accessible surface area for linear and branched alkanes. A best fit line passing through zero has a slope of $8.6 \text{ cal mol}^{-1} \text{ \AA}^{-2}$, which may be taken as the σ value for alkane surface area in Eq. (11.22) (Giesen, Cramer, and Truhlar 1994)

$$G_{CDS} = \sum_k A_k \sigma_k$$

A_k ... exposed surface area

σ_k ... characteristic 'surface tension'

SASA

GB/SA, PB/SA methods

Core of PCM methods'



Equilibrium vs. Non-Equilibrium Solvation

Fast and slow component of the solvation

Photoexcitations, fluorescence, etc...

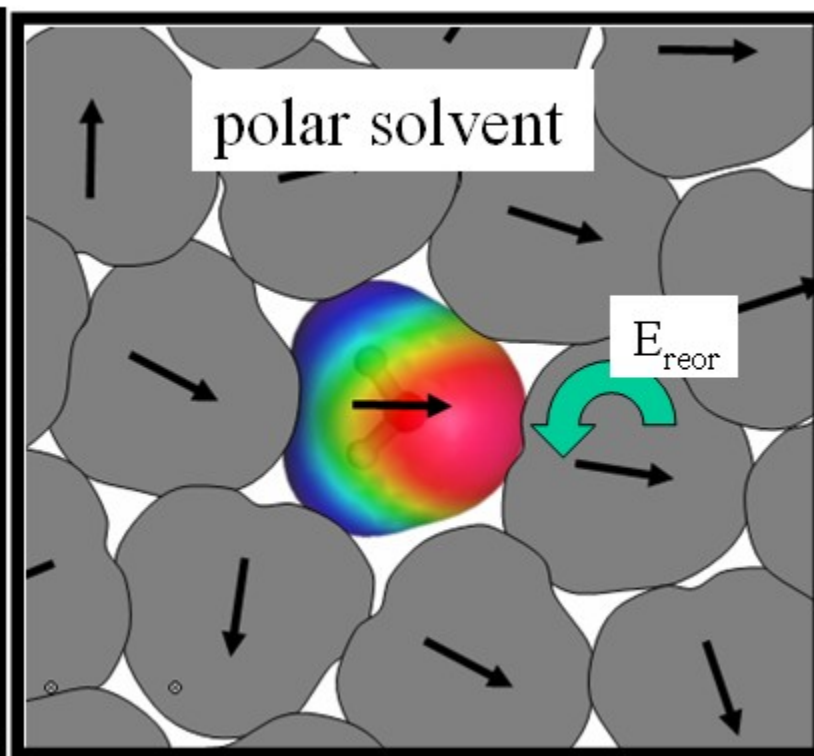
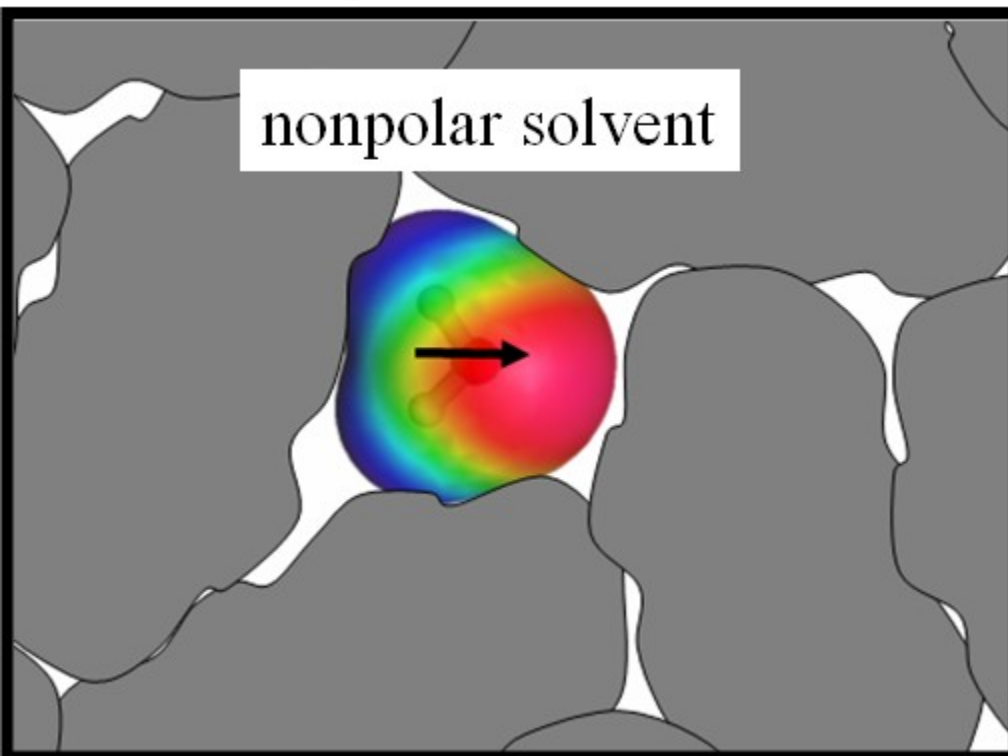


Conductor-like screening model (COSMO)

... for realistic solvation (COSMO-RS)



Why are Continuum Solvation Models wrong for polar molecules in polar solvents



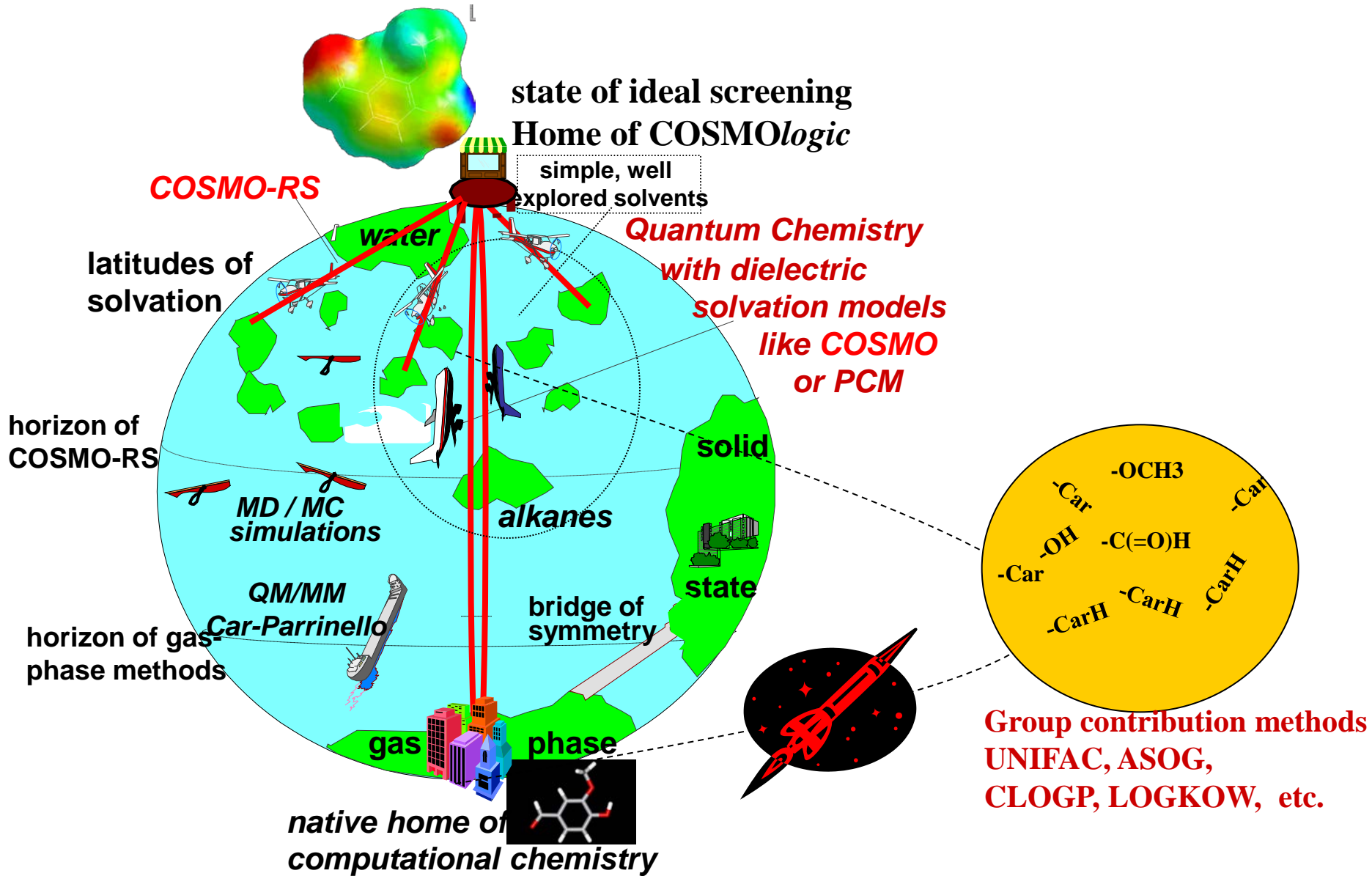
- only electronic polarizability
- homogeneously distributed
- linear response up to very high fields

→ dielectric continuum theory should

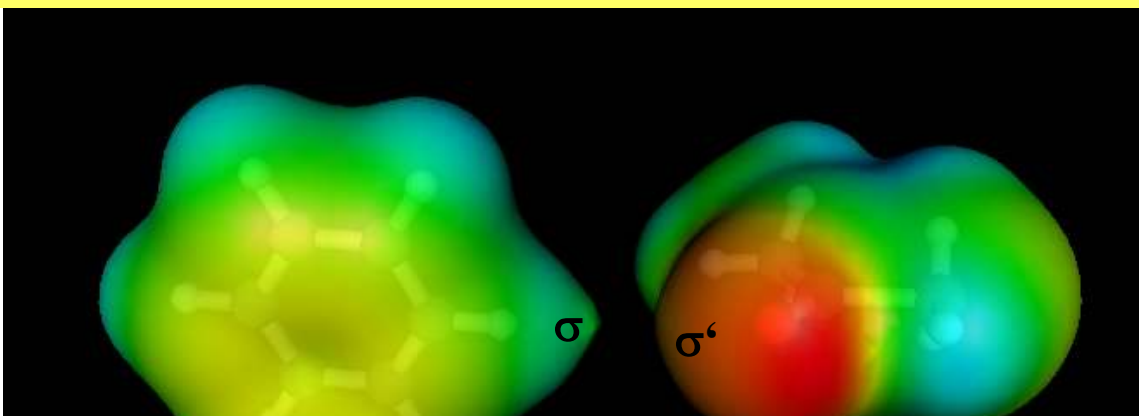
be reasonably applicable

- discrete permanent dipoles
 - mainly reorientational polarizability
 - linear response requires $E_{reor} \ll kT$
 - typically $E_{reor} \sim 8$ kcal/mol !!!
- no linear response, no homogeneity

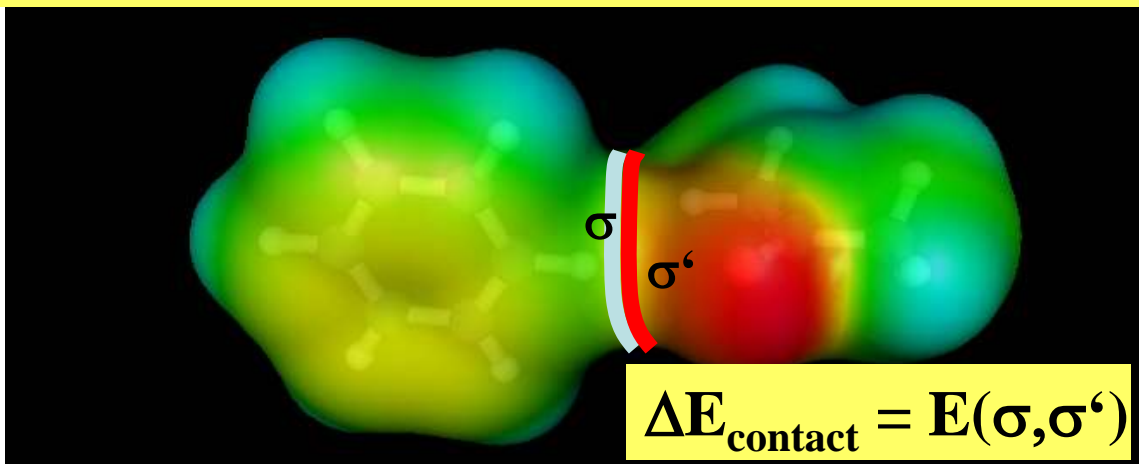
How to come to the latitudes of solvation?



COSMO-RS: Starting point: molecules in conductor



Basic idea of COSMO-RS: Quantify interaction energies as local interactions of COSMO polarization charge densities σ and σ'

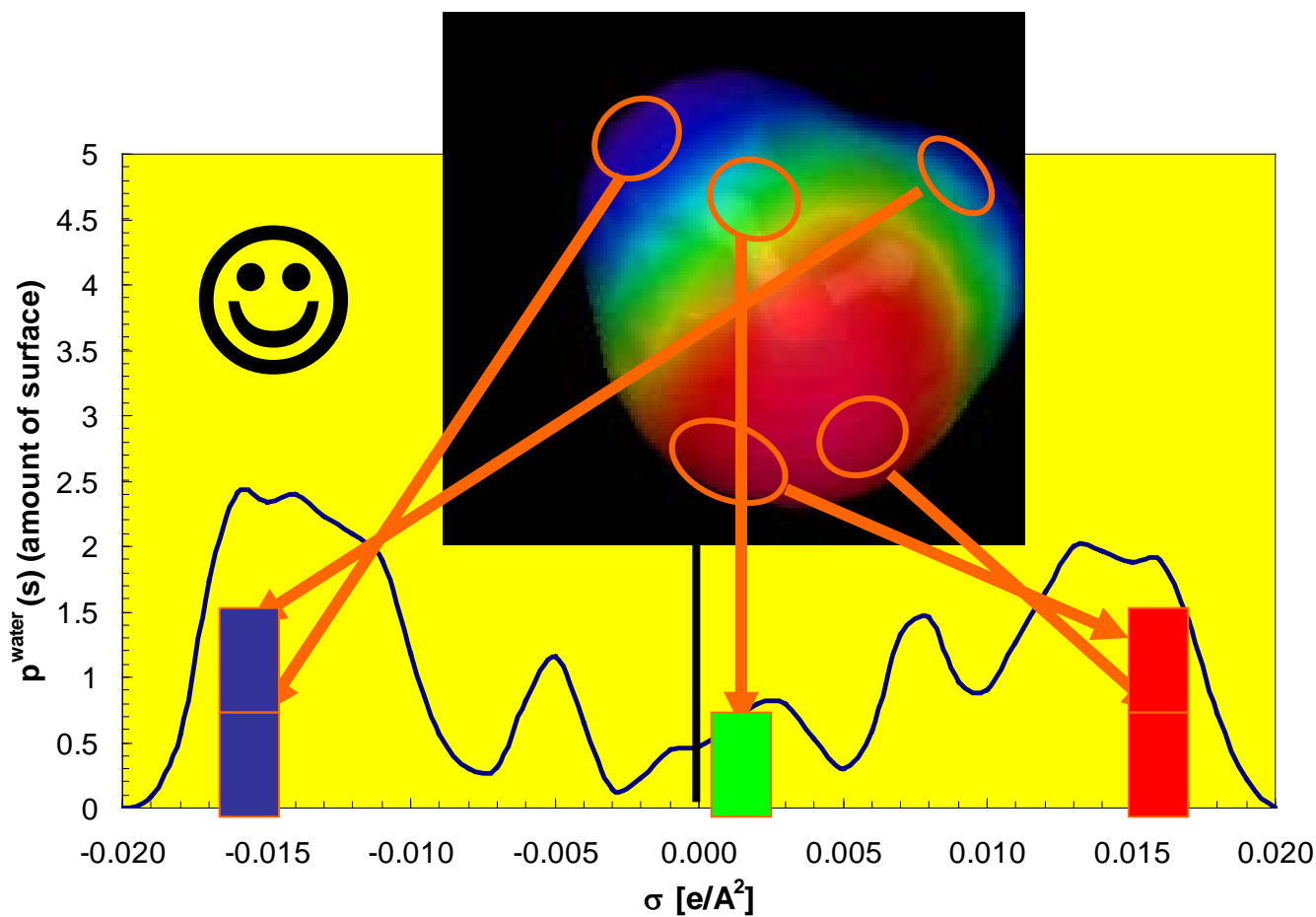


$$E_{\text{misfit}}(\sigma, \sigma') = a_{\text{eff}} \frac{\alpha'}{2} (\sigma + \sigma')^2$$

$$E_{\text{hb}}(\sigma, \sigma') = a_{\text{eff}} c_{\text{hb}}(T) \min\{0, \sigma\sigma' + \sigma_{\text{hb}}^2\}$$

COSMO-RS

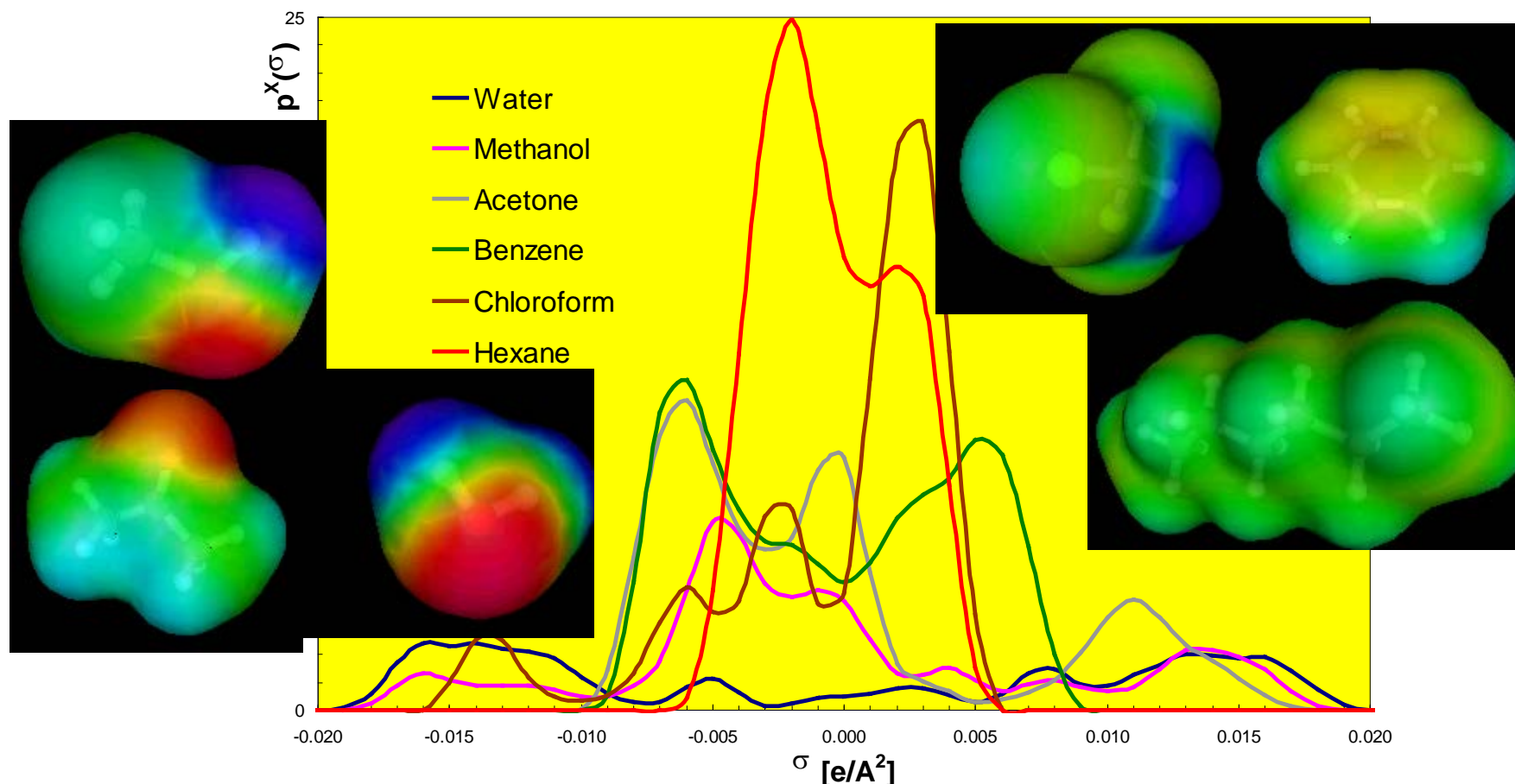
For an efficient statistical thermodynamics reduce the ensemble of molecules to an ensemble of pair-wise interacting surface segments !



**Screening charge distribution on molecular surface
reduces to " σ -profile"**

For an efficient statistical thermodynamics reduce the ensemble of molecules to an ensemble of pair-wise interacting surface segments !

(same approximation as is UNIFAC)

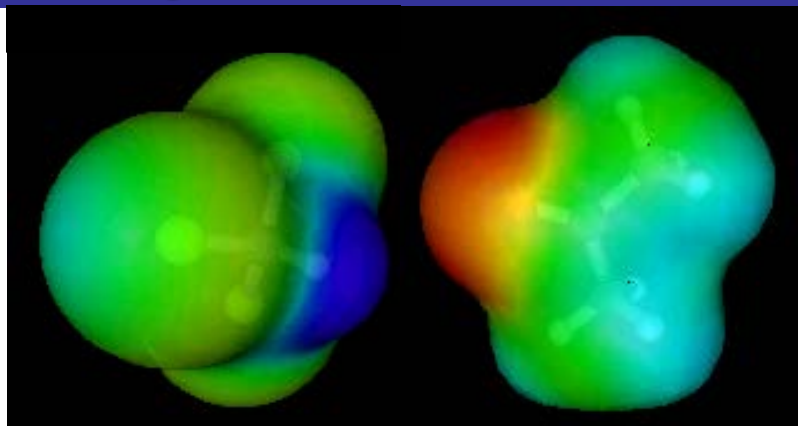


**Screening charge distribution on molecular surface
reduces to " σ -profile"**

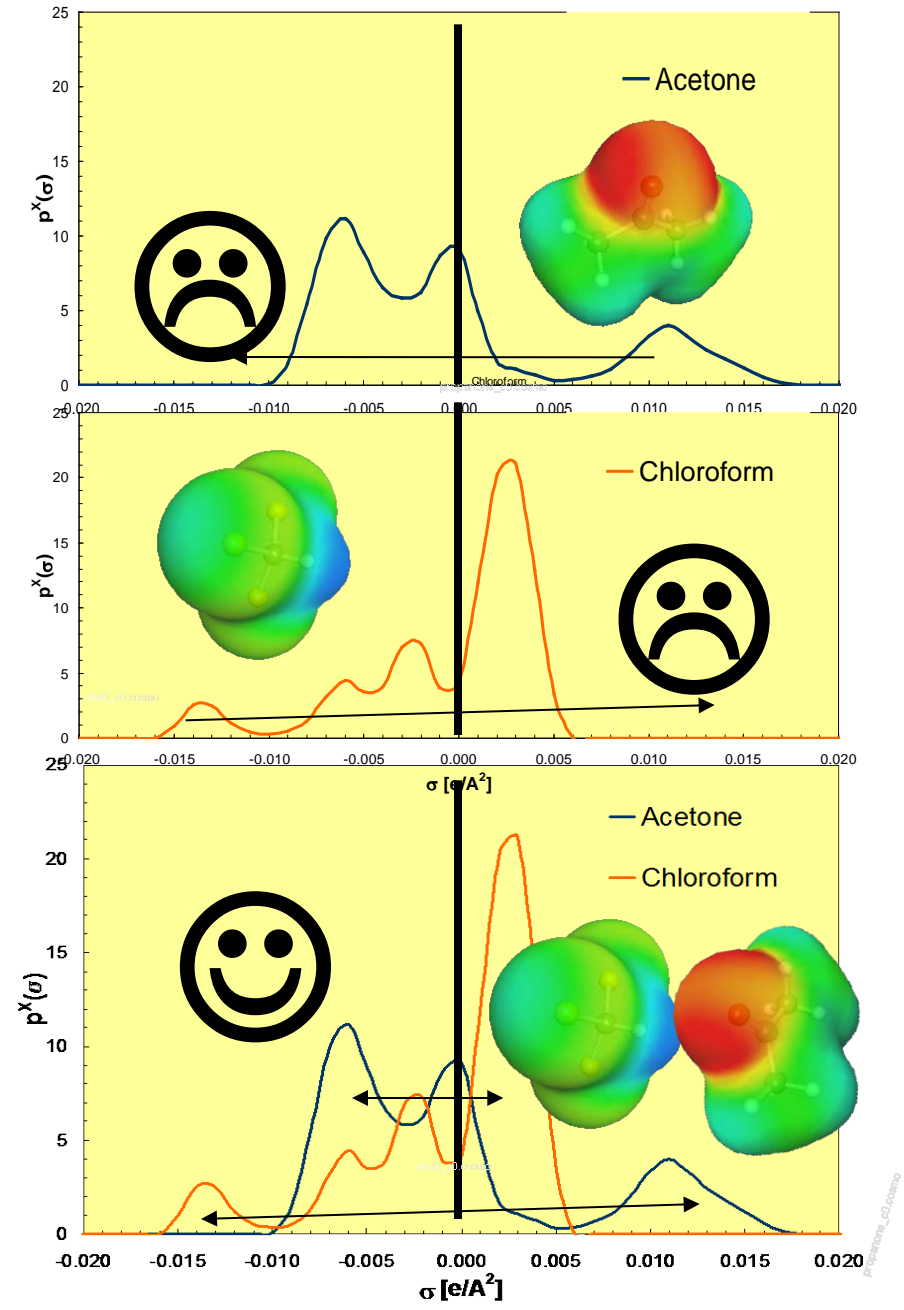
Qualitative thermodynamics based on σ -profiles

profiles

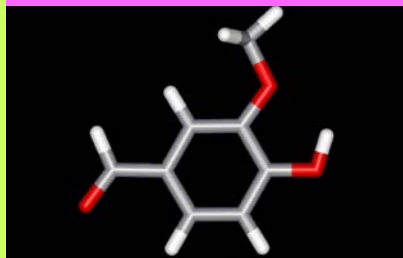
Why does it get warm when you mix acetone and?



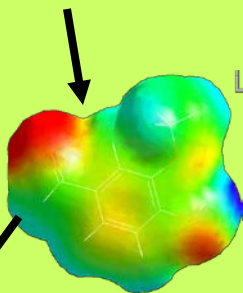
Because their σ -profiles are almost complementary!



Chemical Structure



Quantum Chemical
Calculation with COSMO
(full optimization)



ideally screened molecule
energy + screening charge
distribution on surface

Database of
COSMO-files
(incl. all common
solvents)

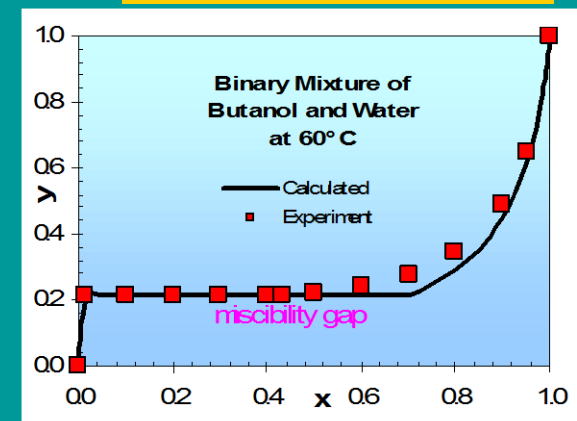
other compounds

DFT/COSMO

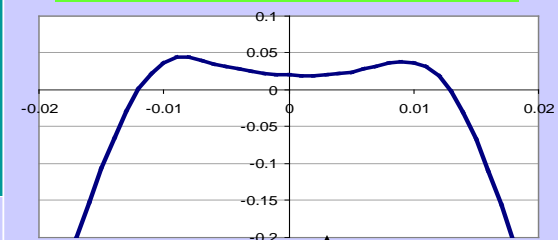
Flow Chart of COSMO-RS

Equilibrium data:
activity coefficients
vapor pressure,
solubility,
partition coefficients

Phase Diagrams



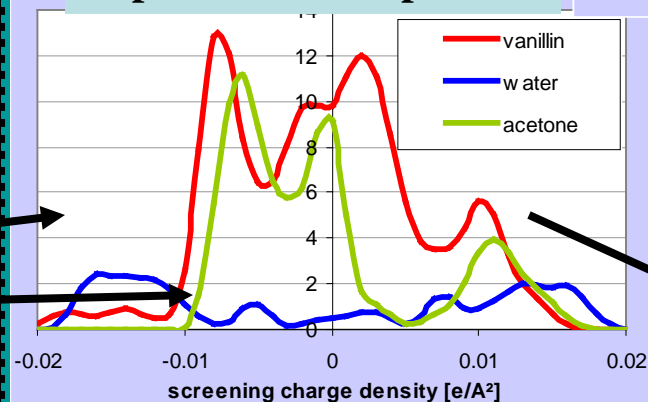
σ -potential of mixture



Fast Statistical
Thermodynamics

σ -profile
of mixture

σ -profiles of compounds



COSMOtherm