Liquids and Solutions

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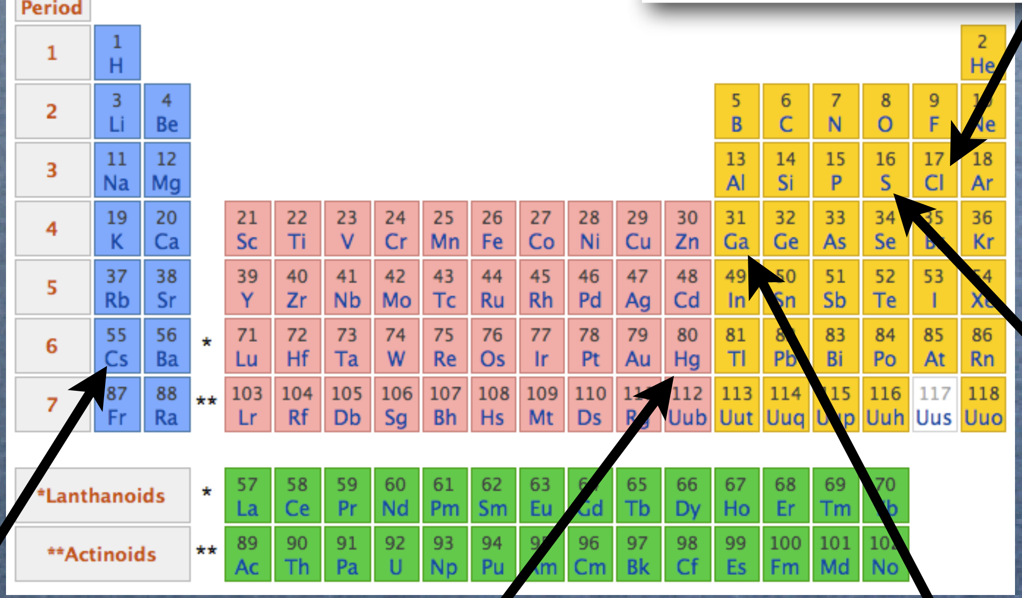
Rm 167 (Chemistry)

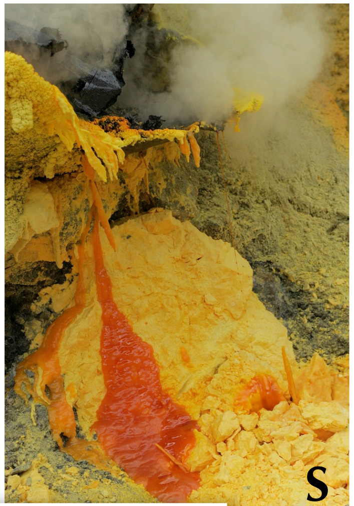
Outline

- Liquids!
- Between solids and gases
- Interactions within a liquid
- Classical models
- Mixed methods
- QM/MM methods
- Continuum methods

Liquids

- **Liquid form of any pure substance**
  - liquid Helium (He)
  - liquid Cesium (Cs)
  - liquid Mercury (Hg)
  - liquid Gallium (Ga)
  - liquid Sulphur (S)
  - liquid chlorine (Cl)

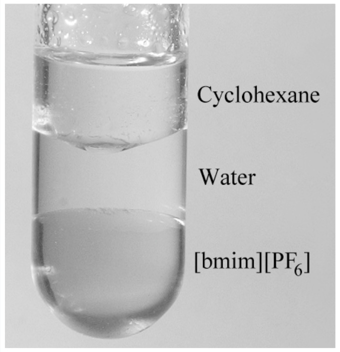


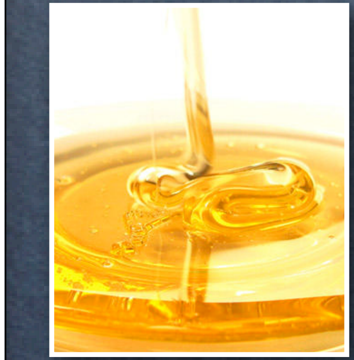


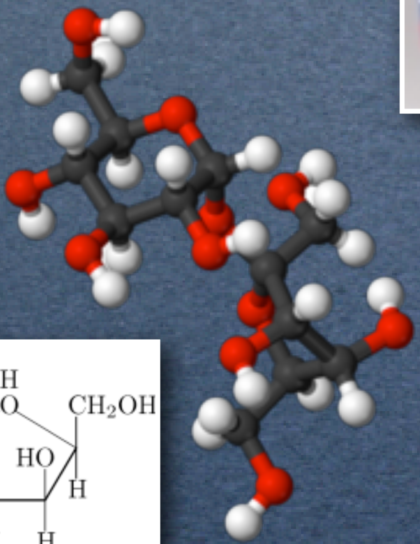
Liquids

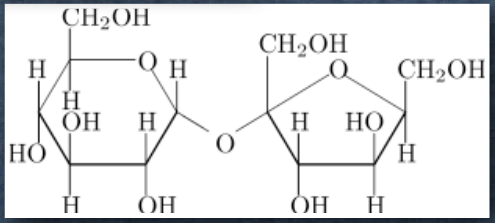
Pure molecular liquids

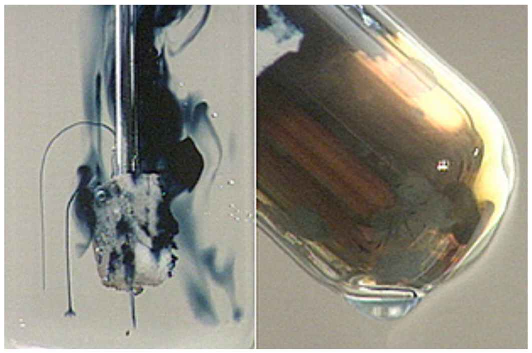
- water
- hydrocarbons
- polymers
- silicones
- sugars
- solvents (THF)
- ammonia







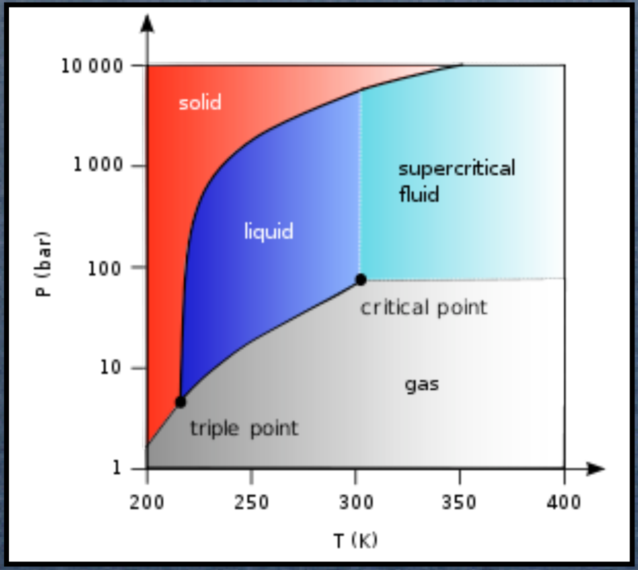




Borderline

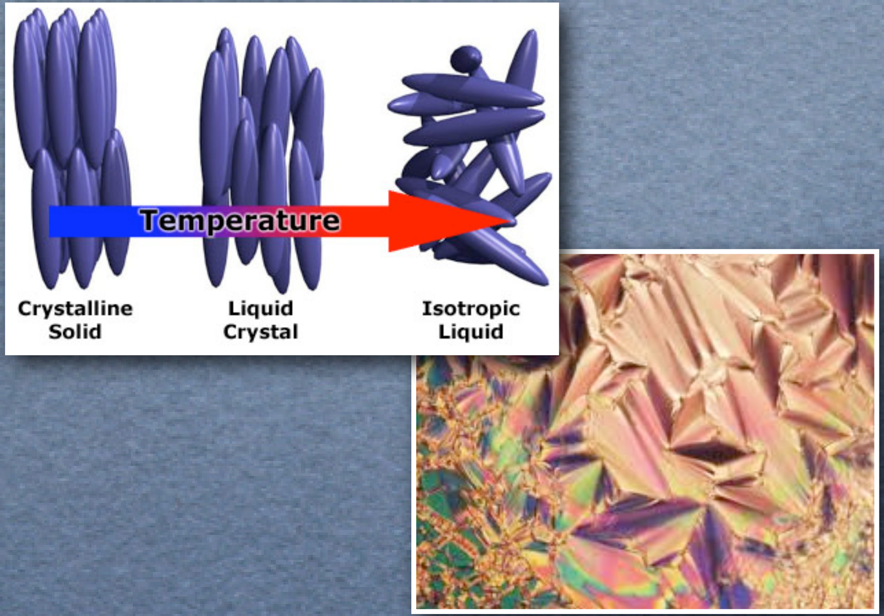
- **polymers**
  - transition from viscous oils, rubbers, malleable plastics, to waxes
  - cross-linked long flexible polymer chains, individual monomers have conformational freedom

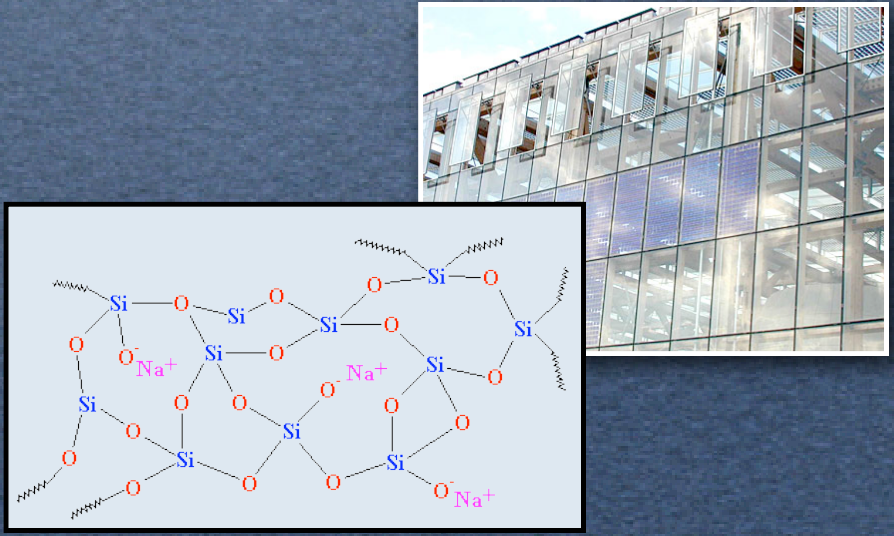
- **supercritical fluids**
  - density of gas and liquid are equal
  - no gas/liquid boundary



Borderline

- **liquid crystals**
  - long chain alkanes, polar groups
- **supercooled liquids**
  - avoid nucleation by rapid cooling
  - no time to move into thermodynamic minimum energy structures
- **glasses**
  - polar network amorphous “solids”
  - structurally similar to a solid but there is no regularity in the arrangements of the molecular constituents

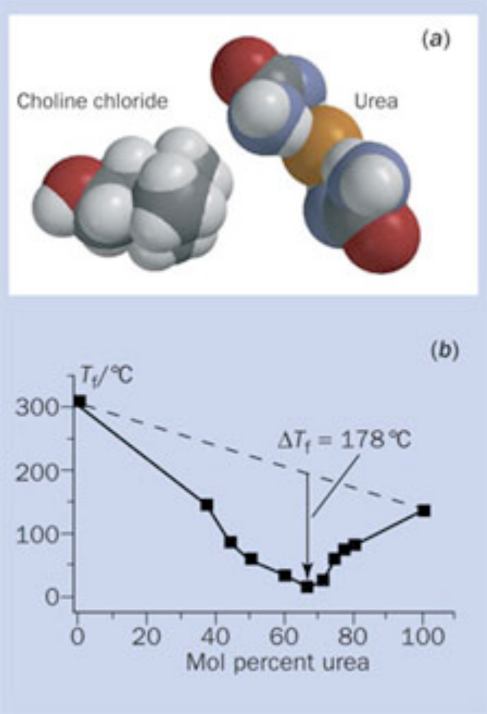




Complex Systems

- complex molten salts
- ionic liquids
  - different cations and anions
- mixtures of organic/polymers
- uniform mixture of two liquids
  - miscible liquids

mixture LiF and BeF_2



eutectic:
mixture of liquids that solidifies at a lower point than either of the pure liquids

Honey: mixture of sugars: fructose, glucose, sucrose

Solutes

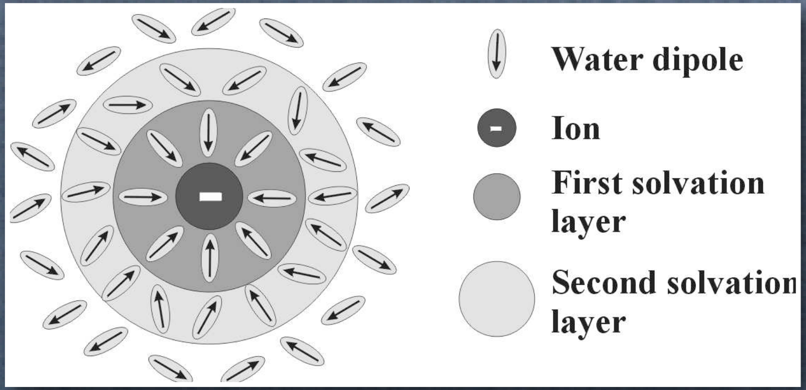
solute is a molecule or ion
dissolved in a liquid or solvent

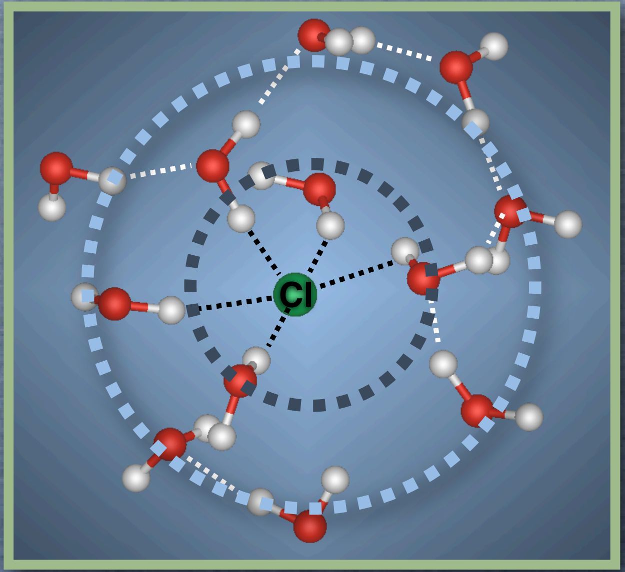
- **Dissolved substances**
  - dissolve gases (bubbles, CO_2)
  - suspend solids (slurries)
  - electrolytes (ionic solutes)
  - molecular solutes
- **Concentration**
  - dilute or concentrated
  - purity
- **Reality**
  - large number and type of species
  - biological
  - industrial effluents

http://www.dorlingkindersley-uk.co.uk/nf/ClipArt/Image

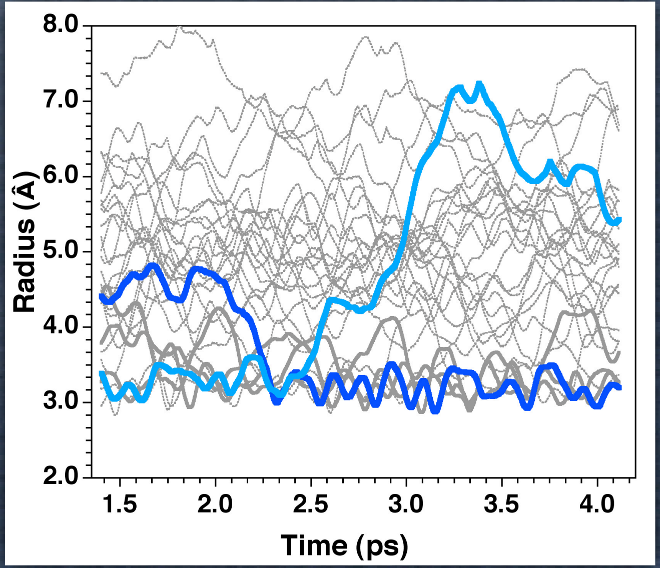
Solvation

- solute perturbs the solvent
- solvent “shells” around solute
  - first is highly perturbed
  - second less so
  - bulk environment





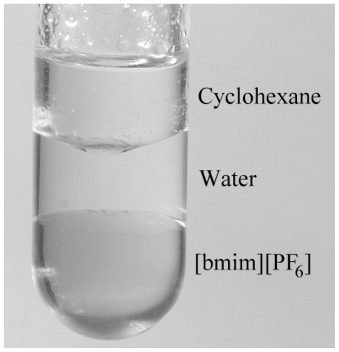
- not static
  - solvent molecules can enter and leave

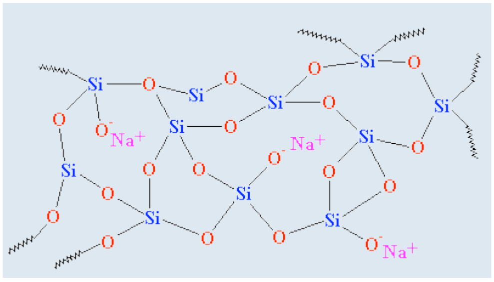


Cl-O distance for each water molecule

Summary

- elementally pure liquids
- molecular liquids
- borderline
- complex systems / mixtures
- solutes in solvents





be able to describe the different types of liquid

be able to give examples of systems that lie at the borders of liquid/solid and liquid/gas and identify their characteristic features

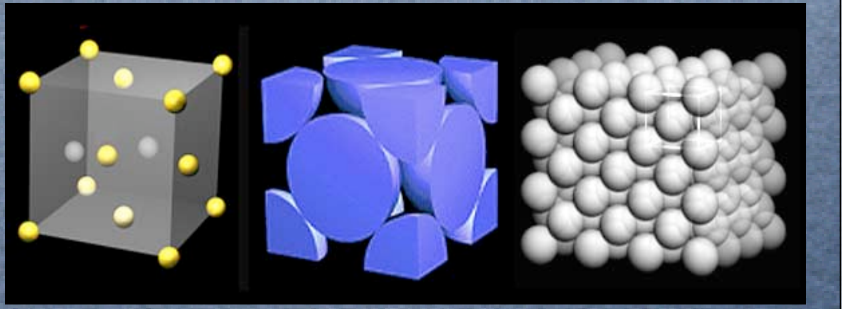
Non-aqueous Solvents by John R Chipperfield
(Oxford Chemistry Primer Series)

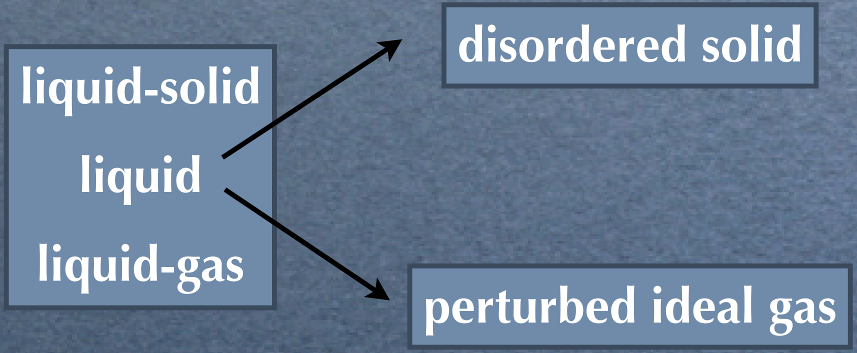
Liquid

lies between solid and a gas

Solid

- highly symmetrical
- small unit cell
- advantage of periodic boundary conditions





liquid-solid

liquid

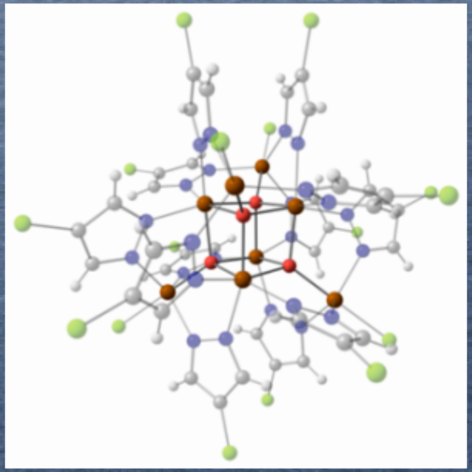
liquid-gas

disordered solid

perturbed ideal gas

Gas

- individual isolated molecules
- randomly distributed
- advantage of single molecule



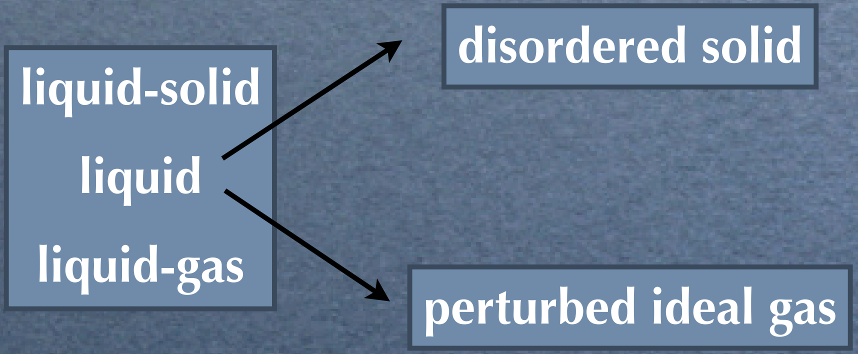
http://www.ndt-ed.org/EducationResources/CommunityCollege/Materials/Structure/metallic_structures.htm
http://research.chem.ox.ac.uk/john-mcgrady.aspx

Liquid

lies between solid and a gas

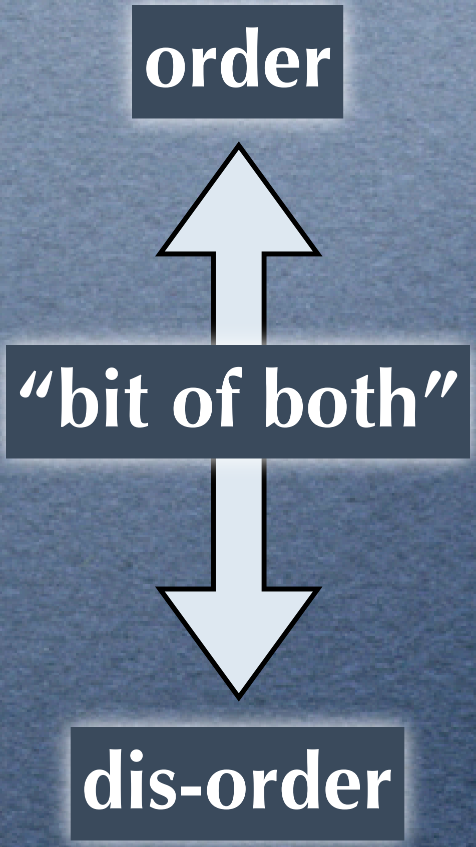
Solid

- highly symmetrical
- small unit cell
- advantage of periodic boundary conditions



Gas

- individual isolated molecules
- randomly distributed
- advantage of single molecule



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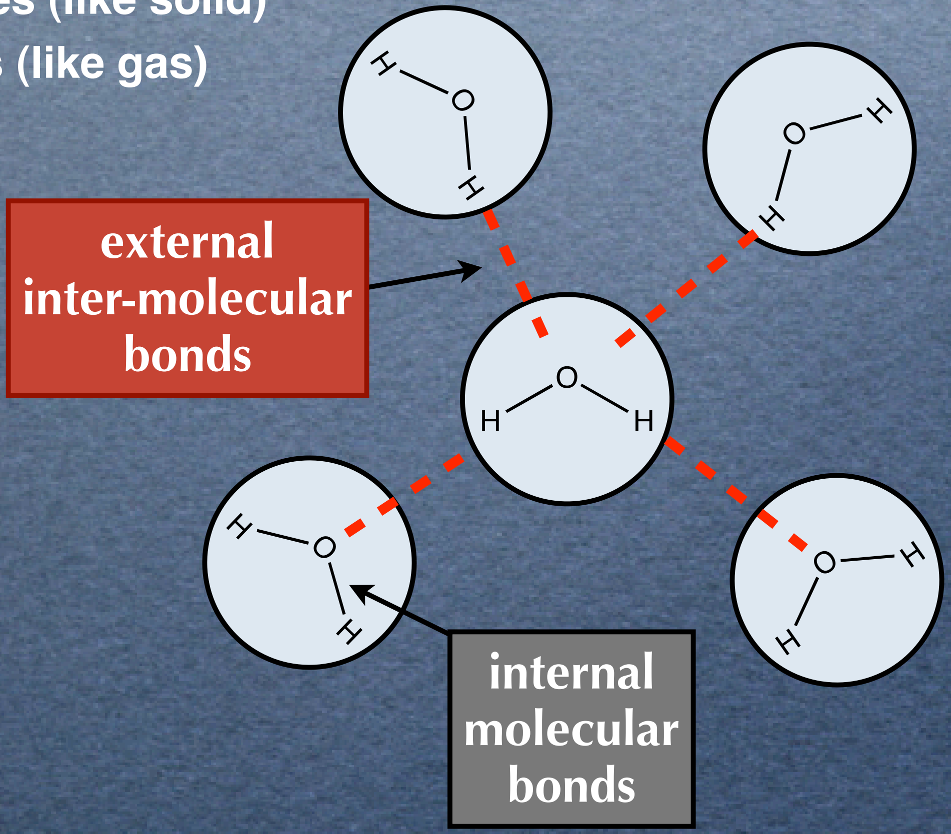
ΔG=ΔH-TΔS

Enthalpy

- association between molecules
- strong internal bonds in molecules (like solid)
- weak inter-molecular interactions (like gas)
- sliding scale of interactions



external inter-molecular bonds

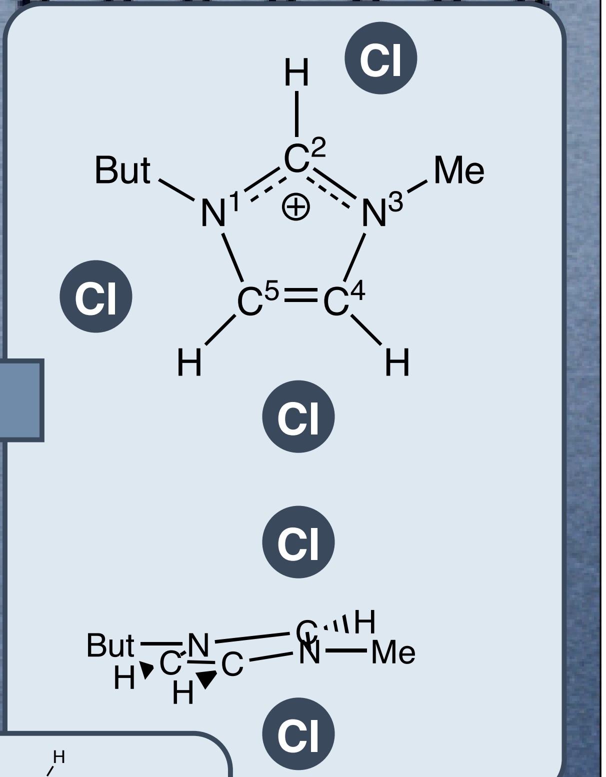
internal molecular bonds

ΔG=ΔH-TΔS

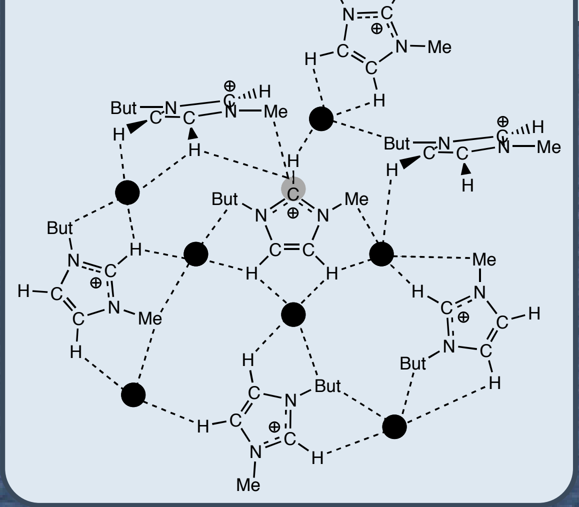
Entropy

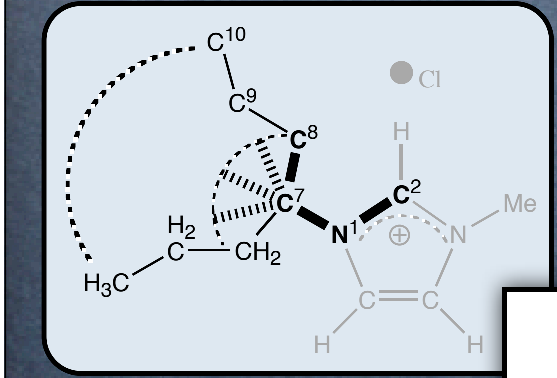
- **molecular/ionic short range order (like solid)**
- **long range disorder (like gas)**
- **disorder in**
  - ➠ conformation within molecules
  - ➠ arrangement whole molecules
  - ➠ connections between molecules
  - ➠ different molecular species (composition)

composition

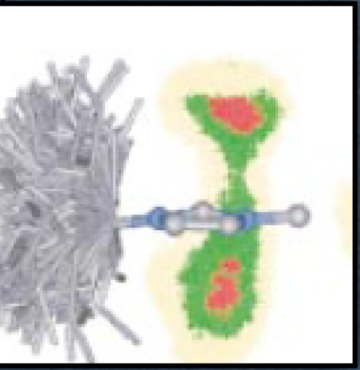


connections





multiple stable conformers



$\Delta G=\Delta H-T\Delta S$

- **Temperature**
  - can overcome different interactions at different temperatures
  - low energy interactions mobilised at low temperatures
  - strong interactions overcome at high temperatures
  - internal vibrations and rotations vs whole molecule translation and rotation

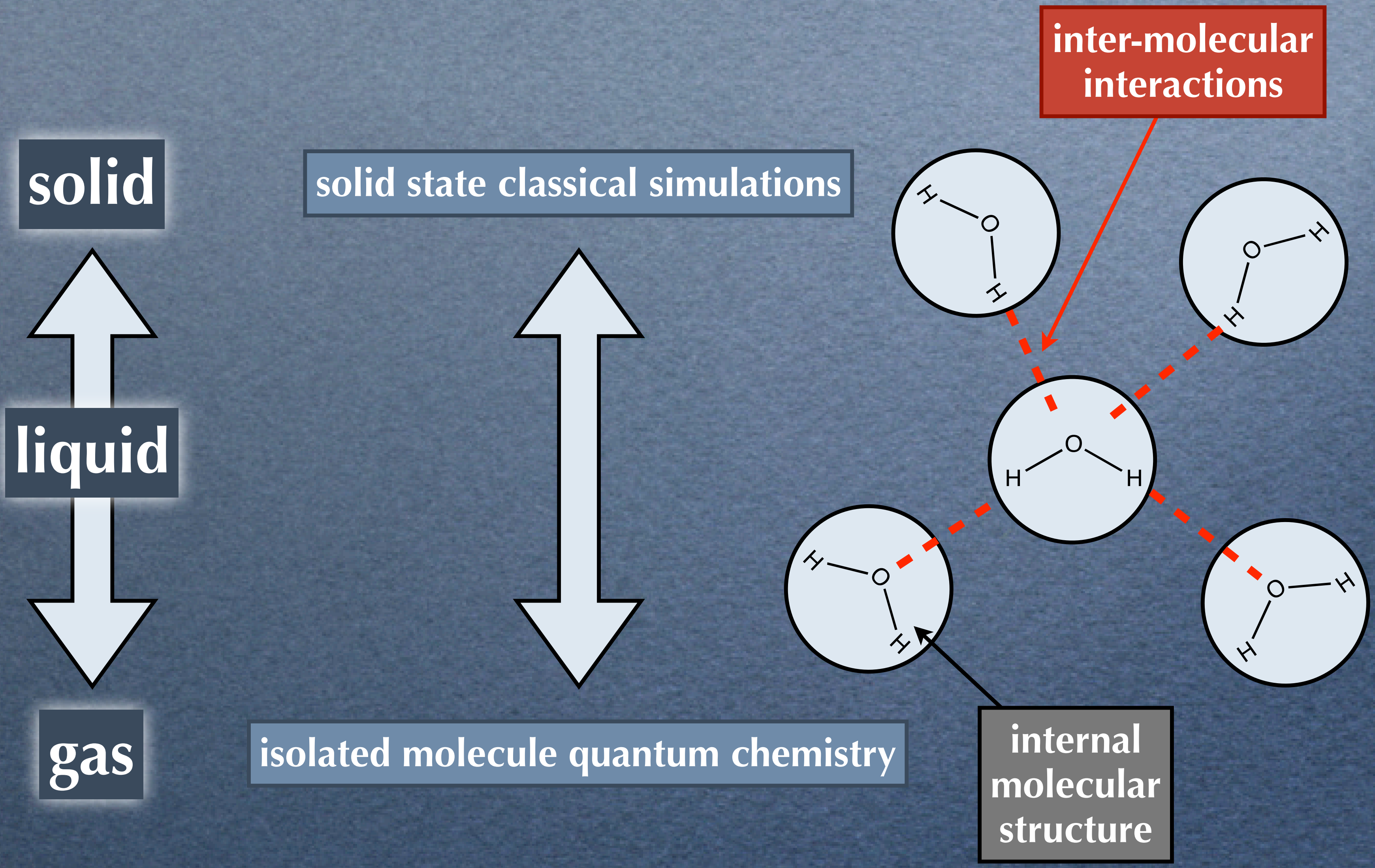
He -very weak interactions
remains liquid to just above 0K

NaCl -strong ionic interactions
melts ≈ 800ºC

W -strong covalent interactions
melts ≈ 3410ºC

glass transitions:
-alkyl rotations initiated
-molecular reorientations

Simulations/Modeling



solid

liquid

gas

solid state classical simulations

isolated molecule quantum chemistry

inter-molecular interactions

internal molecular structure

Properties

- **thermodynamic**
  - diffusion coefficients, conductivity
  - distribution functions
  - correlation functions
  - reorientation times
  - librational (collective) motions
  - thermal effects
  - freezing/melting/boiling/condensing

Classical

infinite (periodic boundary)
averages
movement/geometric
observable (potentially)

long range!
cost short range
dynamic
sampling

Properties

- **thermodynamic**
  - diffusion coefficients, conductivity
  - distribution functions
  - correlation functions
  - reorientation times
  - librational (collective) motions
  - thermal effects
  - freezing/melting/boiling/condensing
- **electronic**
  - molecular structure
  - zero-point-energy vibrations (molecular)
  - complex electron density
  - electrostatics
  - HOMO and LUMO (Fermi level)
  - structure energy relationships
  - electronic excitations
  - molecule-molecule interactions
  - spectra

Classical

infinite (periodic boundary)
averages
movement/geometric
observable (potentially)

long range!
cost short range
dynamic
sampling

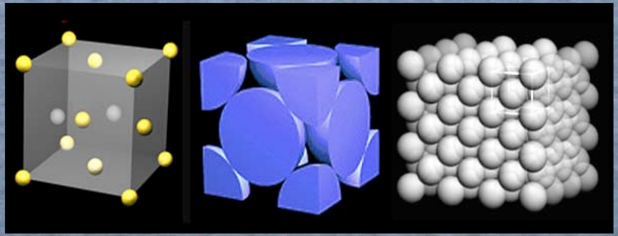
Quantum

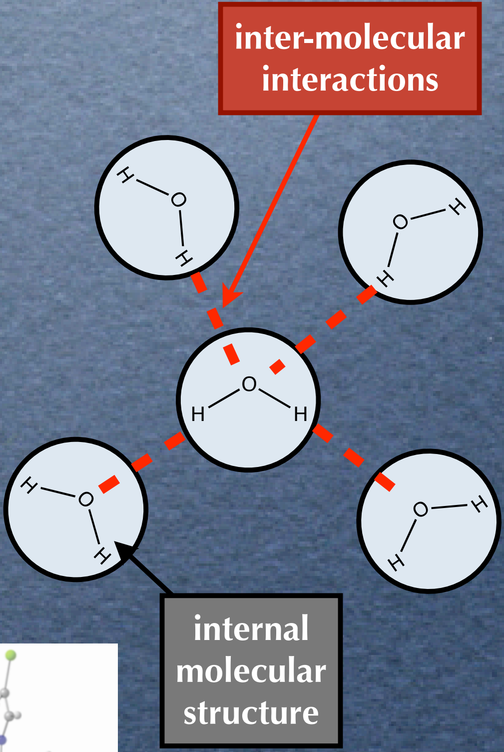
isolated molecule
specifics
energy / density
not-observable

short range!
cost long range
electronic
lowest energy

Summary

- between solids and liquids
- enthalpy / entropy / temperature
- the classical / quantum divide
- properties and quantities from computation





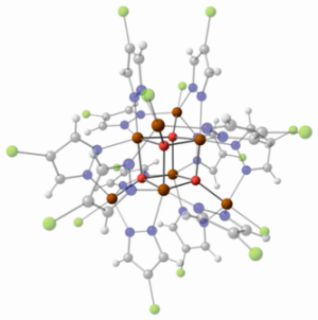
inter-molecular interactions

internal molecular structure

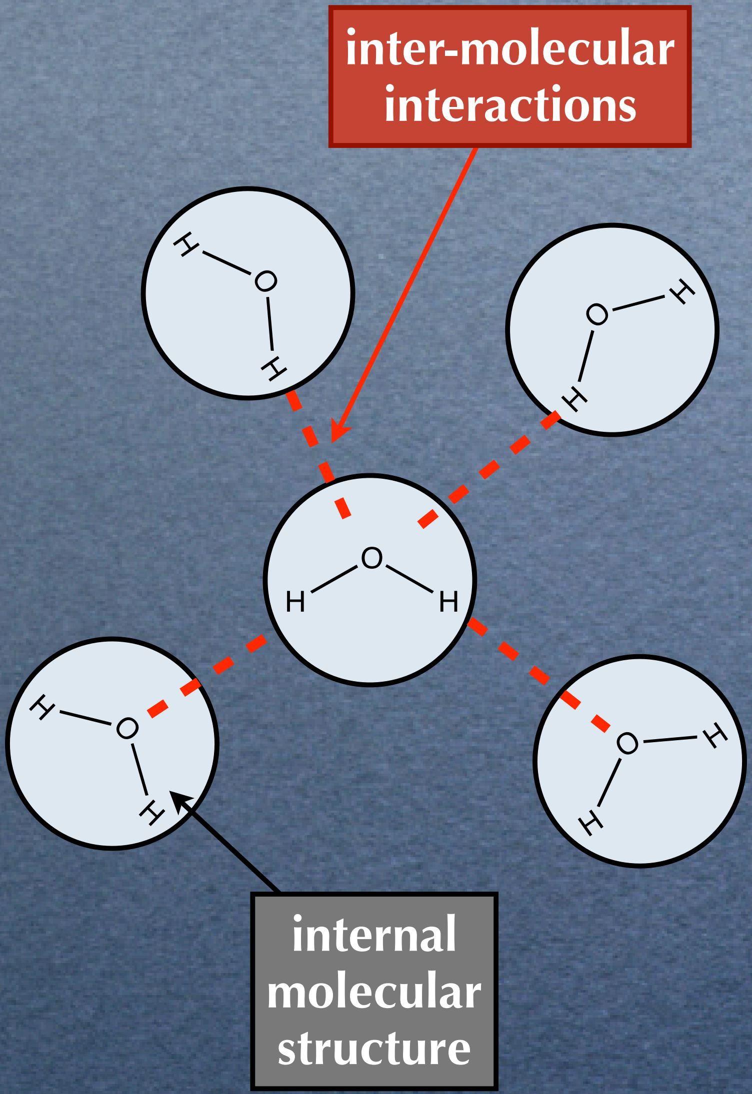
be able to describe the similarities and differences of a liquid to a solid and gas

be able to explain why enthalpy and entropy are important in describing liquids and be able to describe the effects of temperature

be able to identify properties that can be obtained from “classical” vs “quantum” level calculations



Interactions

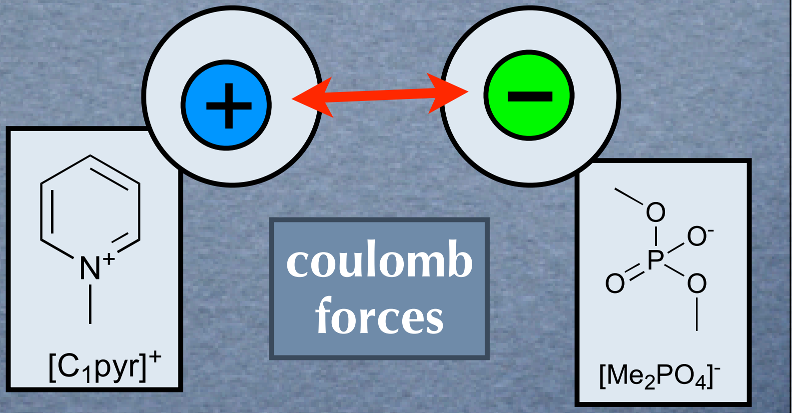


inter-molecular interactions

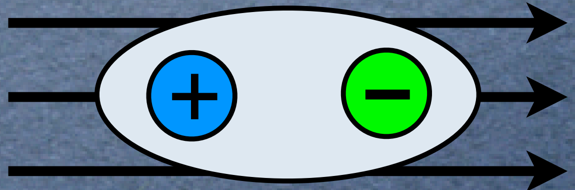
internal molecular structure

Interactions

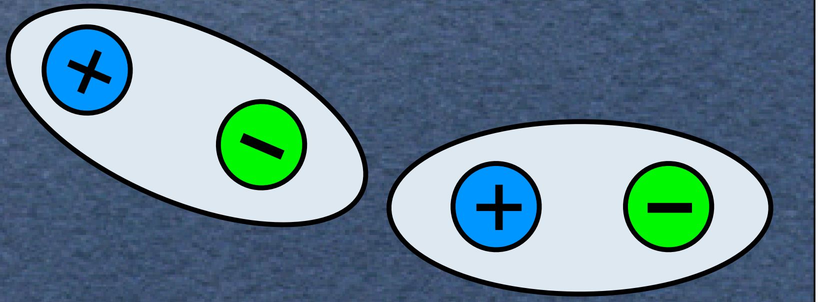
- **charge based coulomb interactions**
  - ◆ permanent charge-charge interactions
- **polarity / polarization**
  - ◆ induced interactions
- **Van der Waals forces**
  - ◆ chemist: correlation of electron clouds on different molecules or parts of the molecule
  - ◆ physics: indued dipole - dipole/induced dipole interactions



coulomb forces



response to an electric field

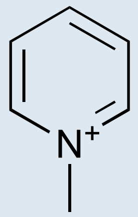


one molecule induces polarisation in another

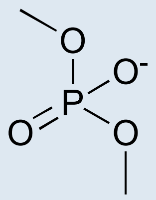
Interactions

- **covalent bonds**
  - internal structure
- **hydrogen bonding**
  - what is a Hydrogen bond?
- **donor-acceptor interactions**
  - what are donor-acceptor interactions?

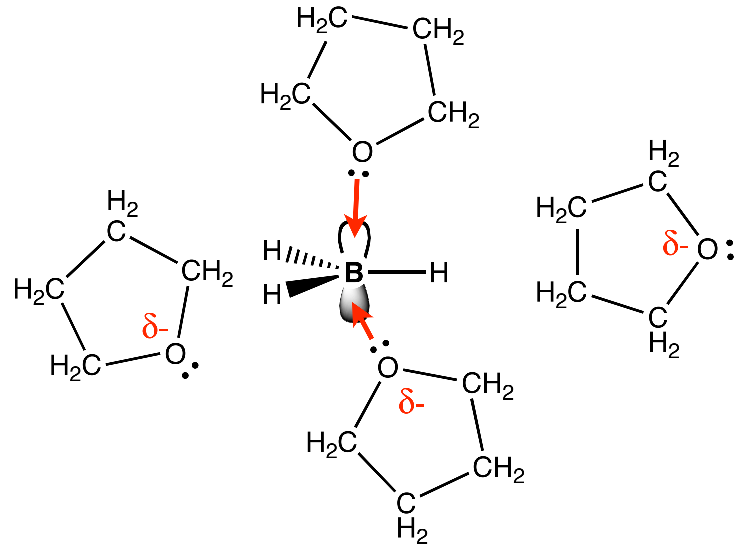
Prof Welton will talk more about these!

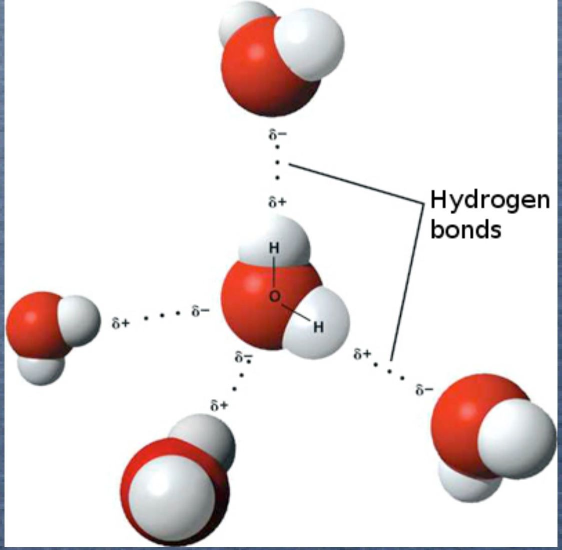


$[C_1pyr]^+$



$[Me_2PO_4]^-$

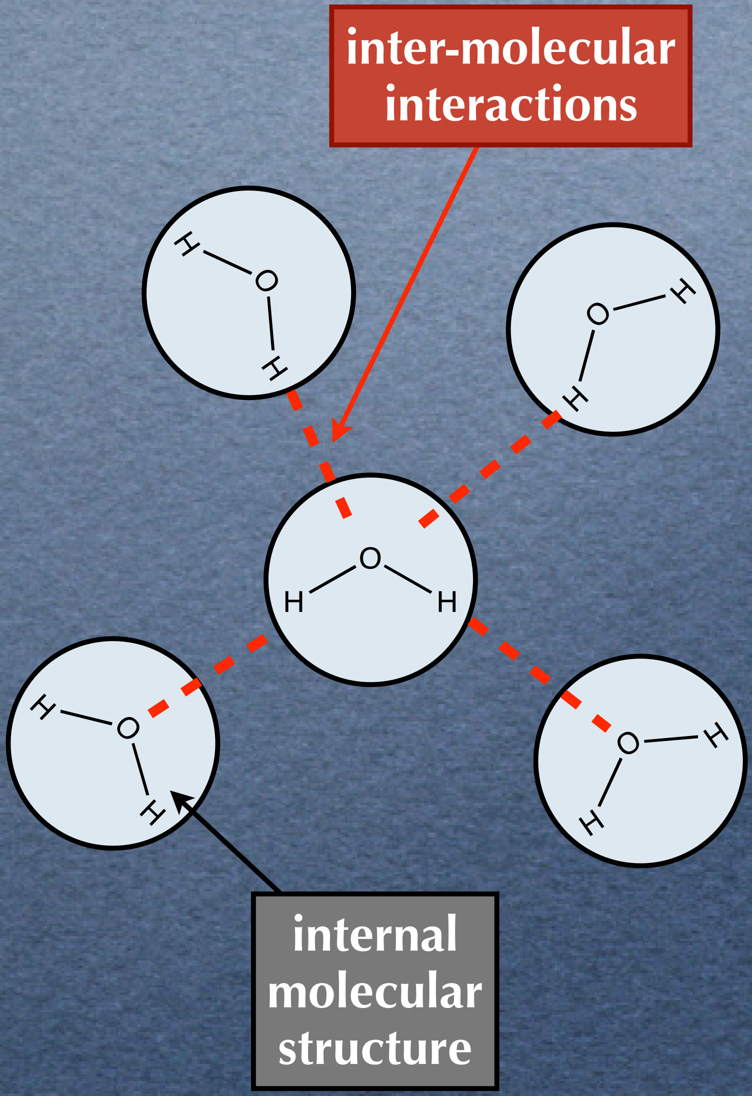




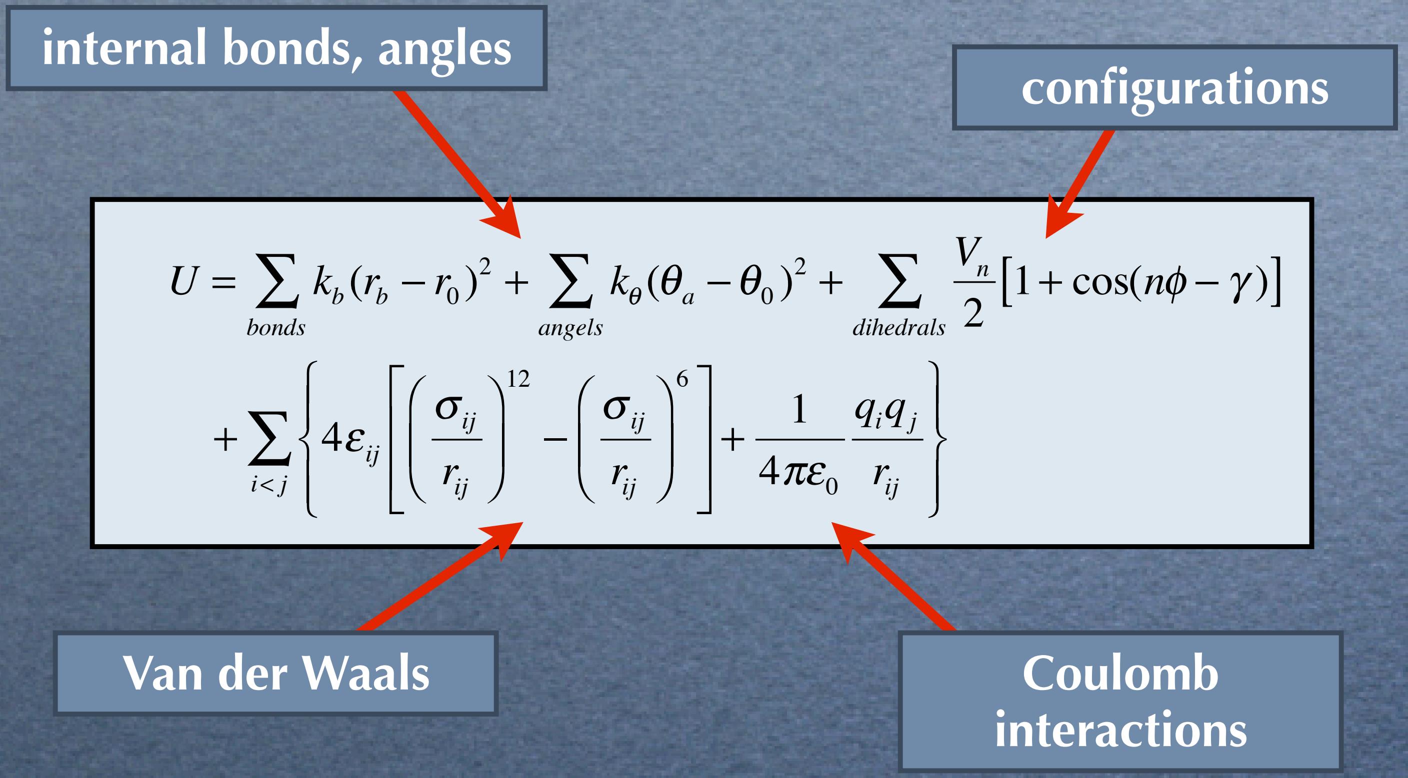
short range order
long range dis-order

Interactions

be able to describe the important interactions that must be included in order to model a liquid



Classical Methods



internal bonds, angles

configurations

$$U = \sum_{bonds} k_b (r_b - r_0)^2 + \sum_{angels} k_\theta (\theta_a - \theta_0)^2 + \sum_{dihedrals} \frac{V_n}{2}[1 + \cos(n\phi - \gamma)]$$
$$+ \sum_{i<j} \left\{ 4\varepsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^{6} \right] + \frac{1}{4\pi\varepsilon_0} \frac{q_i q_j}{r_{ij}} \right\}$$

Van der Waals

Coulomb interactions

where do these parameters come from?

Classical Methods

$$U = \sum_{bonds} k_b (r_b - r_0)^2 + \sum_{angels} k_\theta (\theta_a - \theta_0)^2 + \sum_{dihedrals} \frac{V_n}{2} [1 + \cos(n\phi - \gamma)]$$
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Empirical

adjust to experiment:

densities
heats of vapoursiation
free energies of hydration
heat capacity
compressibility

crystal cell parameters
viscosity
conductivity

Problems

- no experimental data for pure system!
- difficult to achieve accuracy required!
- cannot use Xray crystallography (solids) for liquids!
- Neutron diffraction obtained using MD or MC simulations => circular
- no parameters for design of new liquids

Classical Methods

$$U=\sum_{bonds}k_b(r_b-r_0)^2+\sum_{angels}k_\theta(\theta_a-\theta_0)^2+\sum_{dihedrals}\frac{V_n}{2}[1+\cos(n\phi-\gamma)]$$
$$+\sum_{i<j}\left\{4\varepsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12}-\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6}\right]+\frac{1}{4\pi\varepsilon_0}\frac{q_iq_j}{r_{ij}}\right\}$$

- **Simple geometric terms**
  - **bonds and angles and force constants**
    - experimental structures (crystal/ microwave /neutron), QM calculations
    - then adjusted to reproduce experimental normal modes
    - use small model compounds
  - **earlier and later models**
    - bonds and angles are fixed
    - united atom models (include H’s with heavy atom)
    - course grained models
    - run longer simulations, loose detail

setting up the AMBER potential

Title: A 2ND GENERATION FORCE-FIELD FOR THE SIMULATION OF PROTEINS, NUCLEIC-ACIDS, AND ORGANIC-MOLECULES
Author(s): CORNELL, WD; CIEPLAK, P; BAYLY, CI, et al.
Source: **JOURNAL OF THE AMERICAN CHEMICAL SOCIETY** Volume: **117**
Issue: **19** Pages: **5179-5197** Published: **MAY 17 1995**

Classical Methods

$$U = \sum_{bonds} k_b (r_b - r_0)^2 + \sum_{angels} k_\theta (\theta_a - \theta_0)^2 + \sum_{dihedrals} \frac{V_n}{2}\left[1 + \cos(n\phi - \gamma)\right] + \sum_{i<j}\left\{4\varepsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6}\right] + \frac{1}{4\pi\varepsilon_0}\frac{q_i q_j}{r_{ij}}\right\}$$

Torsions and Van der Waals

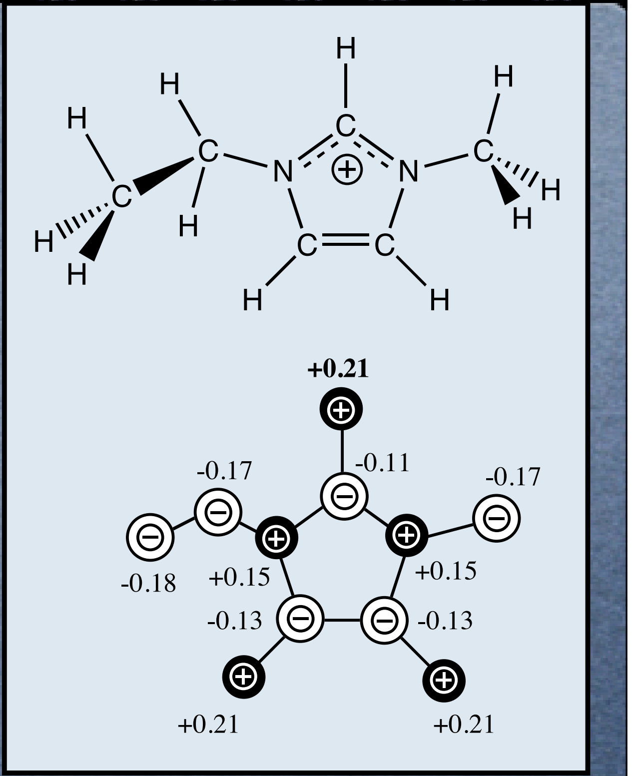
- **1-4 interactions are a balance between torsion and Van der Waals**
  - common to scale 1-4 interactions this varies with potential chosen
- **torsions**
  - use QM to produce a PES with multiple minima (simple molecule or small group molecules)
  - optimised for least number of terms that will fit
- **Wan der Waals**
  - use Monte-Carlo simulations and adjust
  - fit to simplest molecule with that dihedral and then assume transferability
  - eg for C-C use cyclopentane

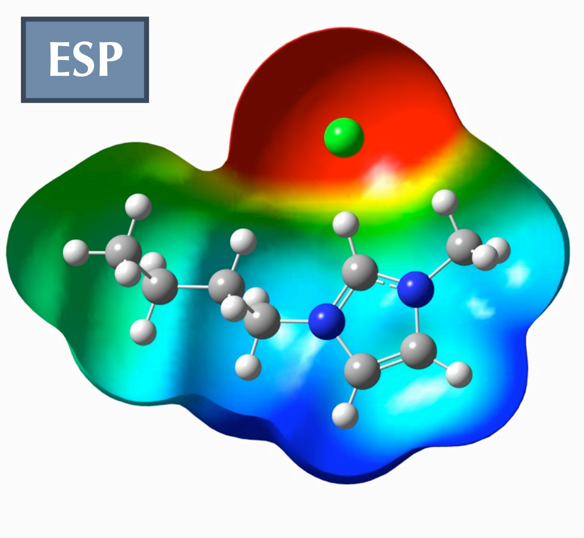
torsions and VdW

Title: OPTIMIZED INTERMOLECULAR POTENTIAL FUNCTIONS FOR LIQUID HYDROCARBONS
Author(s): JORGENSEN, WL; MADURA, JD; SWENSON, CJ
Source: **JOURNAL OF THE AMERICAN CHEMICAL SOCIETY** Volume: **106**
Issue: **22** Pages: **6638-6646** Published: **1984**

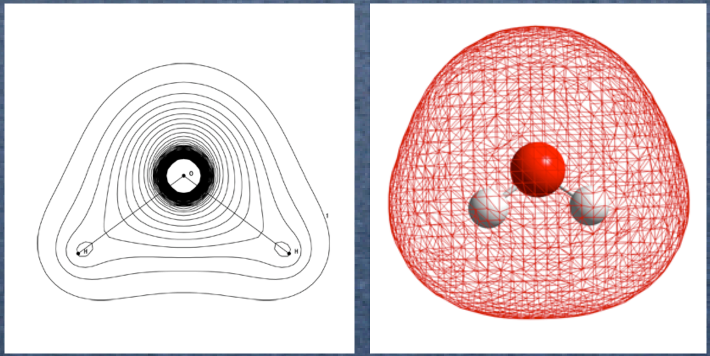
Charges

- ◆ **use point charges to recover the coulombic forces**
- ◆ **reality is an electron (and nuclear) charge density distributed over space**
- ◆ **methods for determining charges based on**
  - ➟ electrostatic potential
  - ➟ electronic density





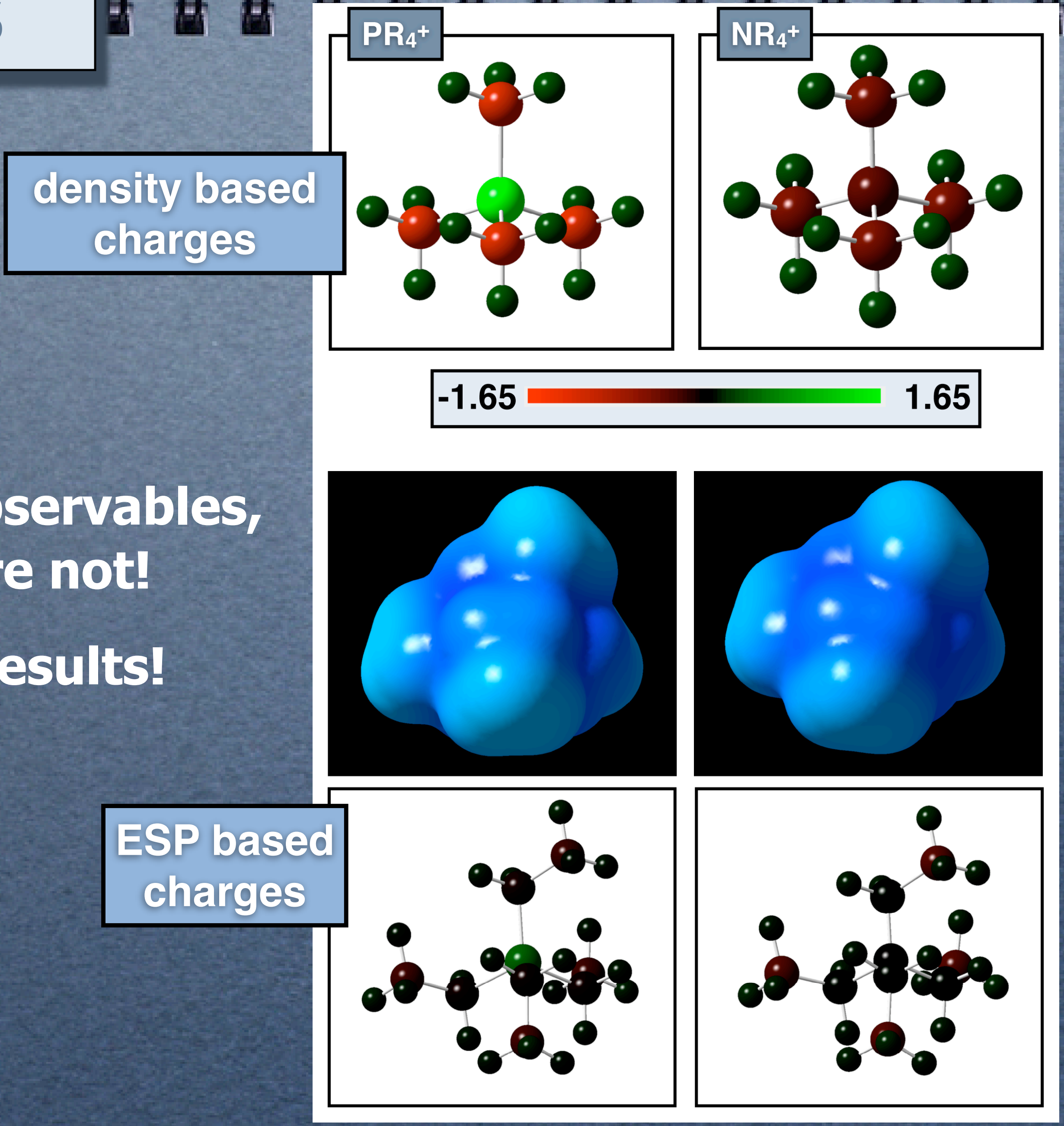
electron density



Charges

- **Method**
  - electrostatic potential
  - electronic density
- **both of these are observables, the point charges are not!**
- **give very different results!**

problem!



Charges

- ESP Fit
  - ESP determined at 1.2 times VdW radius
  - charges are varied to reproduce ESP at points on surface (least squares fit)
- Depends on
  - ESP used (HF/6-31G historical!)
  - number and distribution of points
- Impacts on
  - torsional profiles -> refitting!
  - eliminate 1-4 VdW interactions or scale them
- Restricted
  - atoms related by symmetry constrained to have same charge
  - H on same CH_3 have same charge
  - other restrictions are possible: for example require N atoms to be positive

More Problems:

Conformational freedom

- different conformers can produce very different charge distributions

how to recover these effects?

- MD recovers average properties so average over conformers
- requires fast motion of individual molecules (sometimes not realistic)

Underdetermination of charges

can we trust "local" structure?

- the outer charges are well defined
- interior charges can vary significantly
- not so important for hydrocarbons, much more important for other solvents: ionic or polar molecules

discusses charge issues

Title: Characterization of nano-domains in ionic liquids with molecular simulations
Author(s): Seduraman, A; Klahn, M; Wu, P
Source: **CALPHAD-COMPUTER COUPLING OF PHASE DIAGRAMS AND THERMOCHEMISTRY** Volume: **33** Issue: **3** Pages: **605-613** Published: **2009**

Ionic Liquids

- **Charge determination has been a significant problem for ionic liquids**
  - partial charges for simulations have varied widely

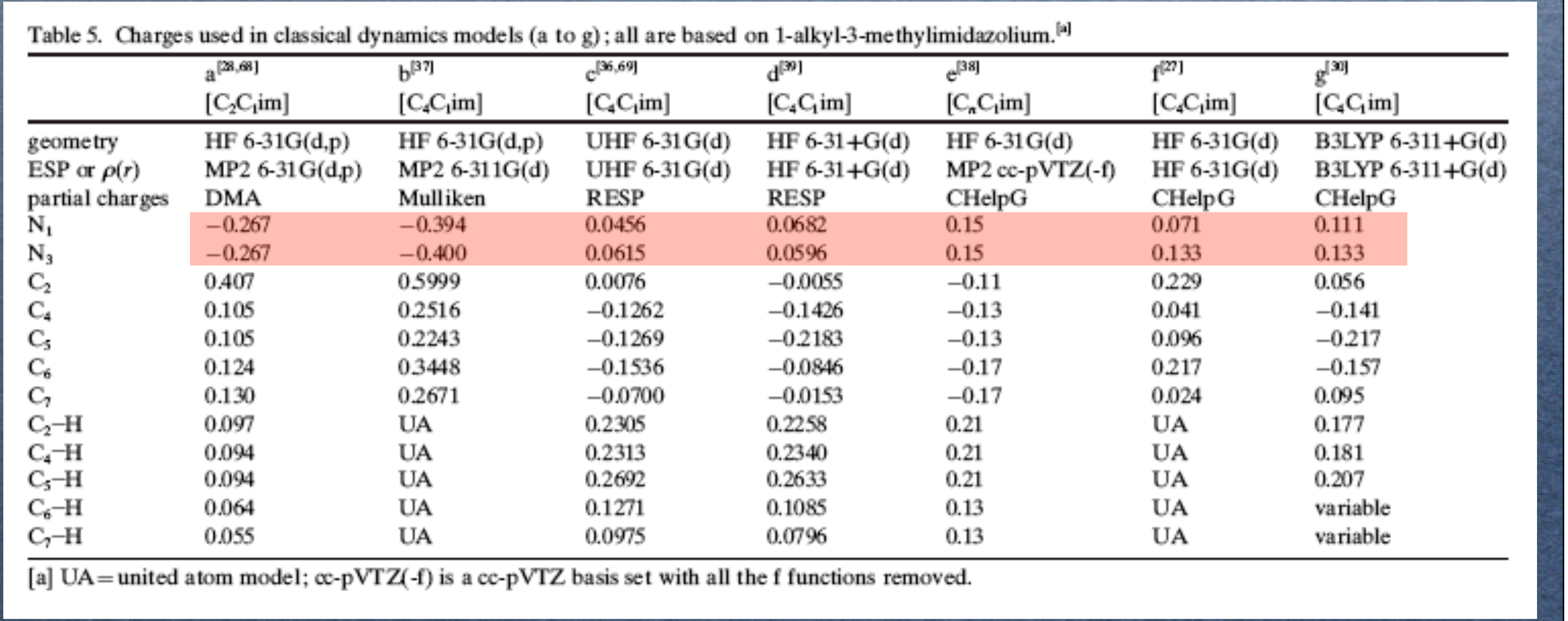


Table 5. Charges used in classical dynamics models (a to g); all are based on 1-alkyl-3-methylimidazolium.[a]

	a[28,68]	b[37]	c[36,69]	d[39]	e[38]	f[27]	g[30]
	[C_2C_1im]	[C_4C_1im]	[C_4C_1im]	[C_4C_1im]	[$C_nC_1$im]	[C_4C_1im]	[C_4C_1im]
geometry	HF 6-31G(d,p)	HF 6-31G(d,p)	UHF 6-31G(d)	HF 6-31+G(d)	HF 6-31G(d)	HF 6-31G(d)	B3LYP 6-311+G(d)
ESP or $\rho(r)$	MP2 6-31G(d,p)	MP2 6-311G(d)	UHF 6-31G(d)	HF 6-31+G(d)	MP2 cc-pVTZ(-f)	HF 6-31G(d)	B3LYP 6-311+G(d)
partial charges	DMA	Mulliken	RESP	RESP	CHelpG	CHelpG	CHelpG
N_1	−0.267	−0.394	0.0456	0.0682	0.15	0.071	0.111
N_3	−0.267	−0.400	0.0615	0.0596	0.15	0.133	0.133
C_2	0.407	0.5999	0.0076	−0.0055	−0.11	0.229	0.056
C_4	0.105	0.2516	−0.1262	−0.1426	−0.13	0.041	−0.141
C_5	0.105	0.2243	−0.1269	−0.2183	−0.13	0.096	−0.217
C_6	0.124	0.3448	−0.1536	−0.0846	−0.17	0.217	−0.157
C_7	0.130	0.2671	−0.0700	−0.0153	−0.17	0.024	0.095
C_2–H	0.097	UA	0.2305	0.2258	0.21	UA	0.177
C_4–H	0.094	UA	0.2313	0.2340	0.21	UA	0.181
C_5–H	0.094	UA	0.2692	0.2633	0.21	UA	0.207
C_6–H	0.064	UA	0.1271	0.1085	0.13	UA	variable
C_7–H	0.055	UA	0.0975	0.0796	0.13	UA	variable

[a] UA = united atom model; cc-pVTZ(-f) is a cc-pVTZ basis set with all the f functions removed.

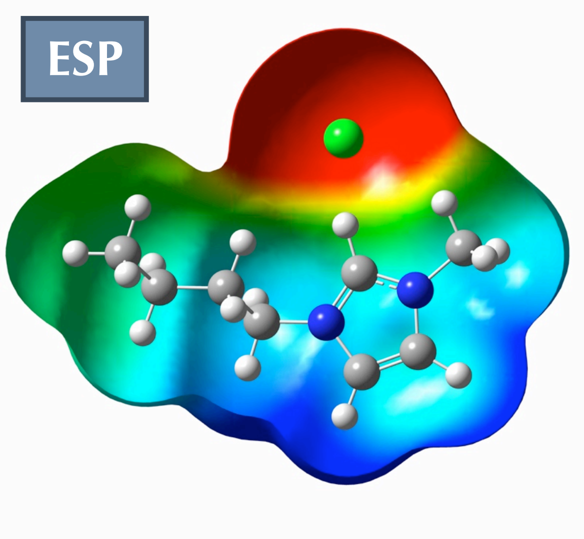
Summary

Classical potential terms

- How these are determined
- Importance of experimental information

Charges

- How charges are obtained: ESP vs density
- problems in determining the charges
- example from ionic liquids

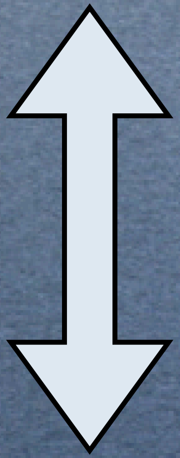


be able to discuss the terms of the classical potential and how they are obtained

be able to discuss the importance of experimental data, and relevant problems associated with gathering data

be able to discuss the generation of charges for use in classical potentials and problems encountered

Mixed Methods



Engineering Models

Classical MD

- ◆ Sequential
- ◆ QM/MM
- ◆ CPMD
- ◆ Onion
- ◆ Embedding
- ◆ Continuum

and others!

Quantum Mechanics

Highly active area of research and development

Mixed Methods

- **combine QM and MD**
  - **molecular mechanics (static)**
  - **molecular dynamics (include movement of nuclei or atomic centers)**
- **introduces**
  - **a periodic environment to QM**
    - polarisation of QM core due to the surrounding solvent
  - **a dynamic element to QM**
    - effects of a rearrangement of the solvent around QM region
  - **ability to describe electron movement or rearrangement to MM**
    - chemical reactions
    - electronic excitations
    - polarisation, charge transfer
- **partitioning of the problem**
  - **into QM core and MM surrounding**
  - **or high level QM computations build on an MD "structure"**
  - **or successive levels of simplification**
  - **expense vs accuracy**

How this is done is very important!

Mixed Methods

Sequential

- run MD of the liquid
- then extract a large cluster
- using MD atomic positions complete a single point QM

Oniom

- compute a large cluster at low level of theory
- and then simplified model at high level of theory
- obtain a more accurate energy than could be computed using low level method
- obtain it for a larger system than could be computed using high level method

$$E = E(low, complete) + [E(high, model) - E(low, model)]$$

Embedding

- have a QM core embedded in static point charges or a surrounding potential

CPMD

- treat orbitals as “classical particles” and run MD

QM/MM Methods

QM/MM

- have a QM core surrounded by a classical environment
- run a self consistent process
- run MD for X steps around QM core, then update QM core for MD environment

$$H = H_{QM} + H_{QM/MM} + H_{MM}$$

Hamiltonians

- H_{MM} standard MM force field
- H_{QM} standard molecular Hamiltionian
- $H_{QM/MM}$ varies with QM/MM method

$$H_{QM} = \left[-\frac{1}{2}\sum_{i} \nabla^2 - \sum_{i,a} \frac{Z_a}{R_{ia}} + \sum_{a<b} \frac{Z_a Z_b}{R_{ab}} + \sum_{i<j} \frac{1}{r_{ij}} \right]$$

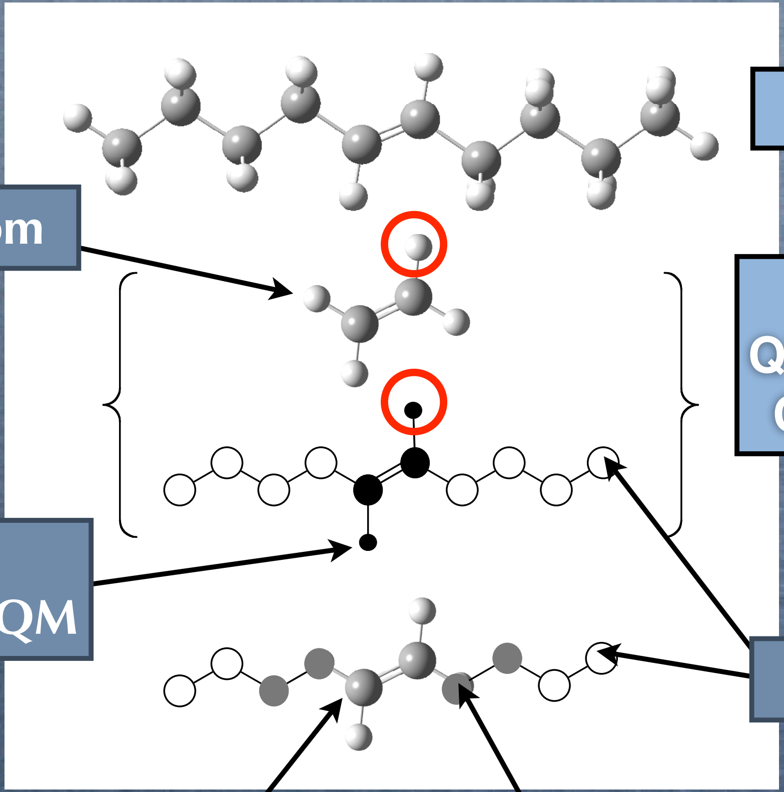
QM/MM Methods

QM/MM Hamiltonians

- **just add static external charge of MM to H**
  - problem! QM electrons attracted to MM positive charges
- **replace QM density with point charges and VdW**
  - how to model QM charges?
  - use frozen MM charges (so only geometric effects)
  - don't include full MM in QM part => QM is gas phase/small cell and does not interact with MM charges
  - no QM polarization due to environment
  - QM charges can be determined each cycle from QM ESP

$$H_{QM/MM} = \sum_{i}^{electrons} \sum_{k}^{MMatoms} \frac{Q_k}{R_{ik}} + \sum_{a}^{nuclei} \sum_{k}^{MMatoms} \frac{Z_a Q_k}{R_{ak}} + \sum_{a}^{nuclei} \sum_{k}^{MMatoms} \left\{ \frac{A_{ij}}{R_{ij}^{12}} - \frac{B_{ij}}{R_{ij}^{6}} \right\}$$

QM/MM Methods



capping atom

fully QM

minimal coupling:
QM core with capping atoms
QM atoms replaced by MM

MM
replaces QM

MM atoms

QM atoms

MM with PP

good coupling:
QM core sees MM atoms
PPs on close MM atoms

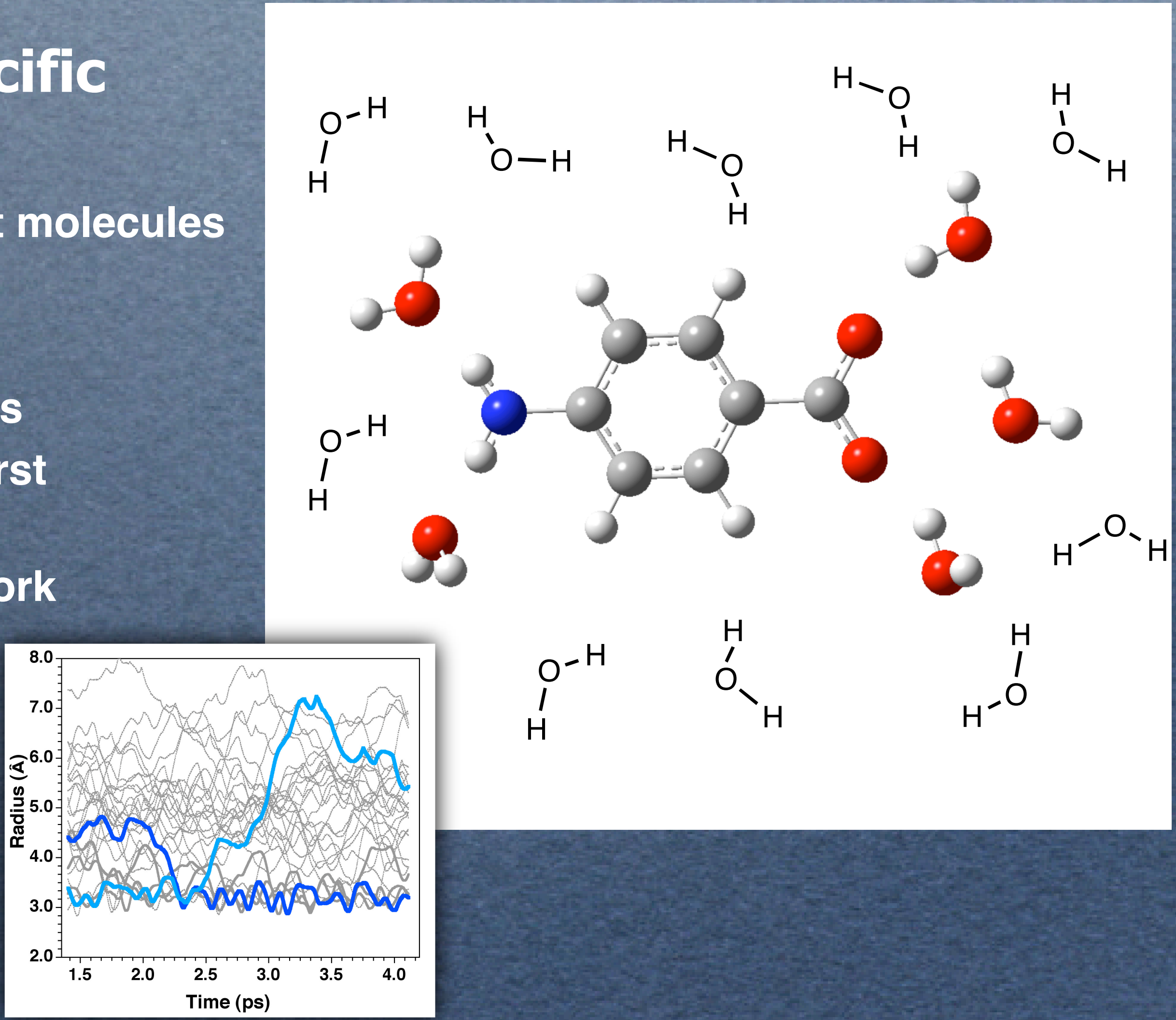
QM/MM Methods

QM/MM partitioning

- ◆ **how to partition QM/MM across a bond**
- ◆ **problem for interaction of atoms either side of the bond**
  - ➡ add an orbital to the MM atom to fill valency of QM atom
  - ➡ add caping atom terminating QM region
  - ➡ add caping “pseudo atoms” to both regions
  - ➡ add a pseudo-potential parametrised for the particular atom
- ◆ **problems with caping atoms**
  - ➡ effects are not subtracted from Hamiltonian
  - ➡ they are not at physical positions (real location of an atom)
  - ➡ may not satisfy larger electronic structure requirements, such as for delocalisation or aromatic regions
- ◆ **how to recover 1-2, 1-2-3, 1-2-3-4 interactions in MM?**
  - ➡ MM mechanics applied as soon as one atom is MM
  - ➡ complex
- ◆ **add pseudo-potential to close MM atoms**
  - ➡ avoids “over” attraction to MM atoms
  - ➡ don’t need to parameterize charges for QM subsystem
  - ➡ do need to parametrize pseudo-potential for MM atoms
  - ➡ only nearby MM atoms (cut-off about 8-12Å)

QM/MM Methods

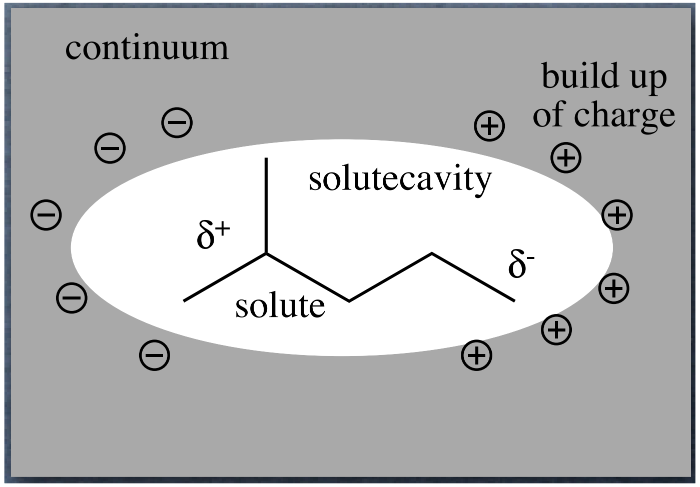
- **in a liquid need specific interactions**
  - keep some explicit solvent molecules
  - how many?
  - where to place cut-off?
  - what about dynamic effects
  - water coming in and out first solvation shell
  - but break H-bonding network



Continuum Methods

Set-up

- solvent described by a structureless polarizable medium
- polarization defined by the permittivity (ε)
- molecule inside a cavity
- inside cavity permittivity of a vacuum (ε_0)

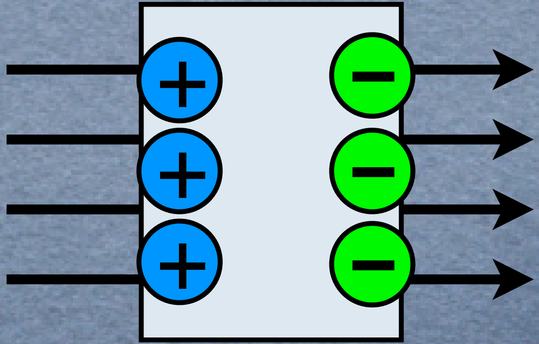


Assume

- pure solvent and dilute concentration of solute
- the permittivity is constant
- effect of solvent can be described by a local charge distribution “seen” by the solute on surface of the cavity walls

Permittivity

- **Response**
  - apply a field (E) to an object
  - charges inside the object polarize (move) and reduce the internal field (D)
  - ε is the permittivity, a response parameter

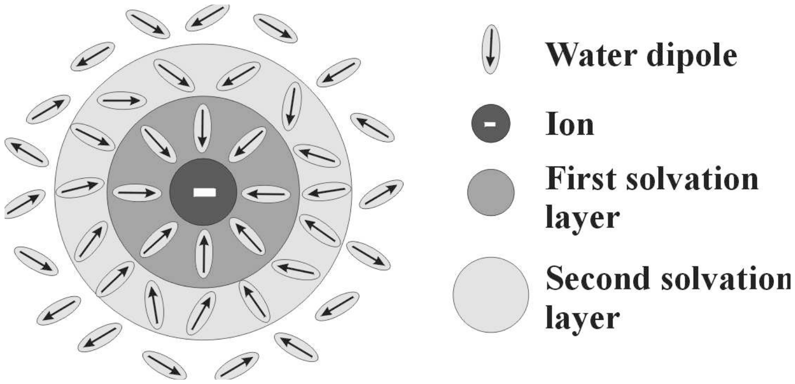


$$\tilde{D} = \varepsilon \tilde{E}$$

- **inside a liquid the permittivity reduces the ability of one charge to "perceive" another**
- **dielectric constants:**
  - vacumm 1
  - benzene 2.3
  - dichloromethane 9.1
  - n-butanol 18
  - methanol 33
  - water 80

$$V = \frac{1}{4\pi\varepsilon}\frac{q_1 q_2}{r_{12}}$$

solvent shields solute charges from each other



http://www.porous-35.com/electrochemistry-semiconductors-4.html

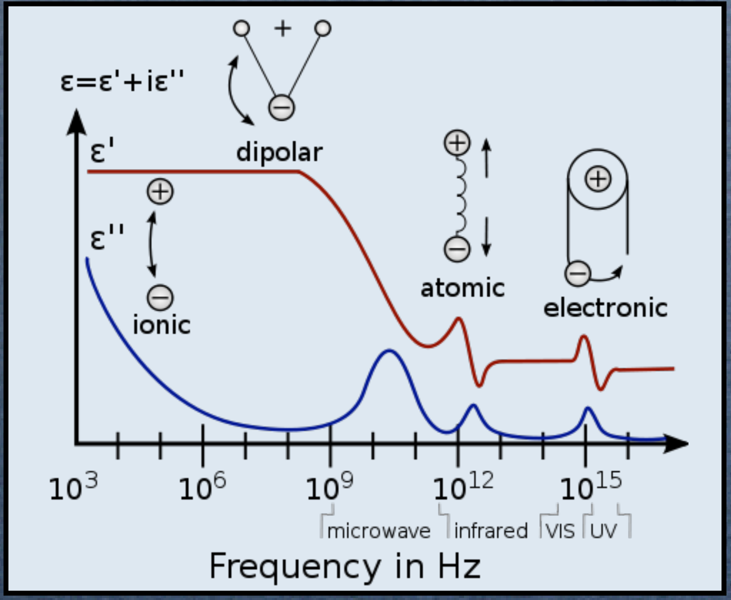
Permittivity

- **permittivity**
  - ε_0 permittivity of free space or vacuum
  - ε_r is the relative permittivity
  - ε_r also called dielectric constant

$$\boxed{\varepsilon = \varepsilon_0 \varepsilon_r}$$

continuum methods assume ε is constant!

- **permittivity is not a constant**
  - varies with position, field frequency, humidity, temperature
  - material does not respond instantly and there is a phase difference or lag



$$\boxed{\tilde{D} = \varepsilon \tilde{E}}$$

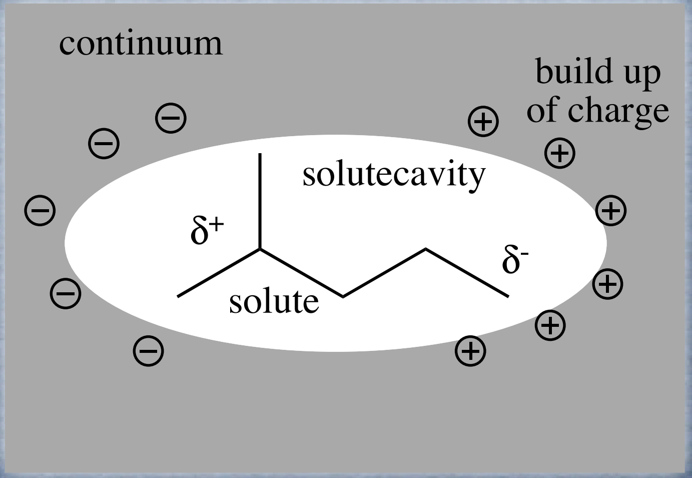
$$\boxed{D_0 e^{-iwt} = \varepsilon(w) E_0 e^{-iwt}}$$

$$\begin{aligned}
\varepsilon(w) &= \frac{D_0 e^{-iwt}}{E_0 e^{-iwt}} = \frac{D_0}{E_0} e^{-i\delta t} \\
&= \frac{D_0}{E_0}(\cos\delta - i\sin\delta) \\
&= \varepsilon'(w) + i\varepsilon''(w)
\end{aligned}$$

http://en.wikipedia.org/wiki/Permittivity

Continuum Methods

- **Self-consistent / Iterative solutions**
  - solvent effects are represented by a charge distribution on the cavity surface
  - these polarize the QM solute electronic structure
  - which then affects the charge distribution on the cavity surface



Continuum Methods

Notation

- H(c) Hamiltonian of quantum core (solute)
- H(s) Hamiltonian of solvent
- H(c,s) interaction Hamiltonian of solute and solvent

$$H = H(c) + H(s) + H(c,s)$$

Ignore bulk solvent!

$$\begin{aligned} H^{eff} &= H(c) + H(c,s) \\ &= H(c) + V^{\text{int}}(r) \end{aligned}$$

Look at local interaction around the solute

- effective Hamiltonian
- replace H(c,s) with a response function V
- response of QM core (c) to the electric field provided by the solvent
- electric field is determined by the charge distribution (Q) on the solute cavity surface

V(r) determined from Poisson equation:

$$\begin{aligned} -\nabla^2 V(r) &= 4\pi\rho_m(r) \quad \textit{inside} \\ -\varepsilon\nabla^2 V(r) &= 0 \quad \textit{outside} \end{aligned}$$

Continuum Methods

- **cross boundary conditions**
  - potentials inside and outside must be equal at the boundary
  - along vector perpendicular (n) to the cavity surface the differentials must be equal

$$[V] = V_{in} - V_{out} = 0$$

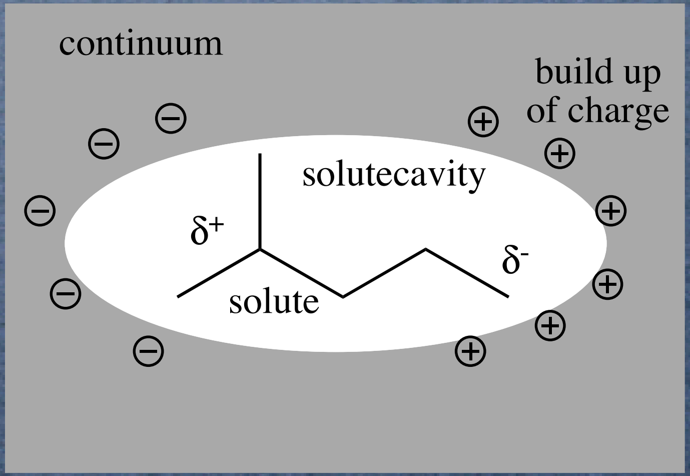
$$[\partial V] = \left(\frac{\partial V}{\partial n}\right)_{in} - \varepsilon\left(\frac{\partial V}{\partial n}\right)_{out} = 0$$

- **Continuum methods differ on how they treat these equations**

V(r) determined from Poisson equation:

$$-\nabla^2 V(r) = 4\pi\rho_m(r) \quad inside$$

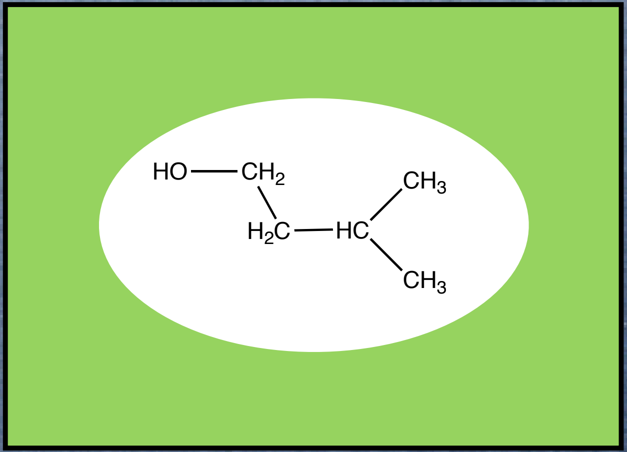
$$-\varepsilon\nabla^2 V(r) = 0 \quad outside$$



Solvent Cavity

How to define the cavity?

- **Requirements**
  - should have physical meaning!
  - contain largest part of charge of the molecule (density!)
  - areas where solvent molecules cannot enter should be described
- **simplest method**
  - spherical/oval cavities
  - BUT molecules are not spherical

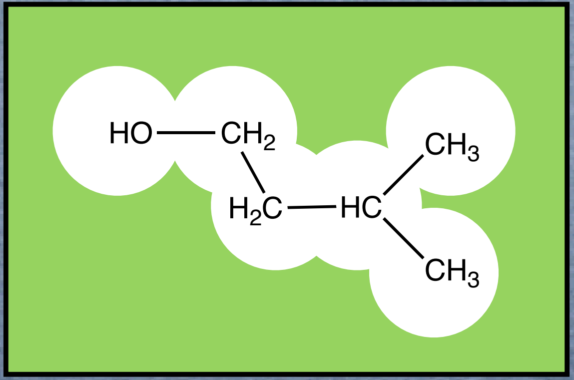


results are very sensitive to radius

Solvent Cavity

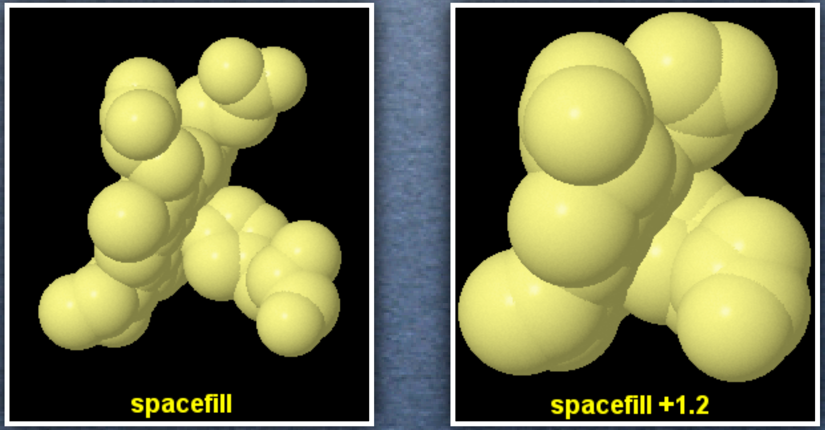
Atomic spheres

- use surface defined by an interlocking superposition of atomic spheres



Problems

- what radii do you use?
  - ➡ Bondi, Pauling, UFF, Van der Waals)
  - ➡ variation between methods
- are these accurate?
  - ➡ very old based on crystal structures
  - ➡ do not include charged or ionic species
  - ➡ do not account for changes in effective radii as a reaction proceeds
- actually expand Van der Waals radius ≈1.2-2.0 to account for solvent
  - ➡ depends on solute and not the solvent
  - ➡ small solvent molecules vs large solvent molecules

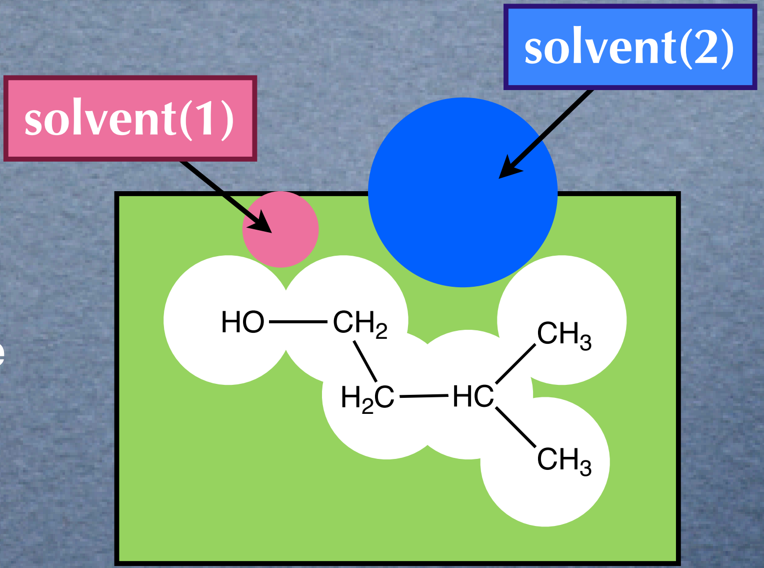


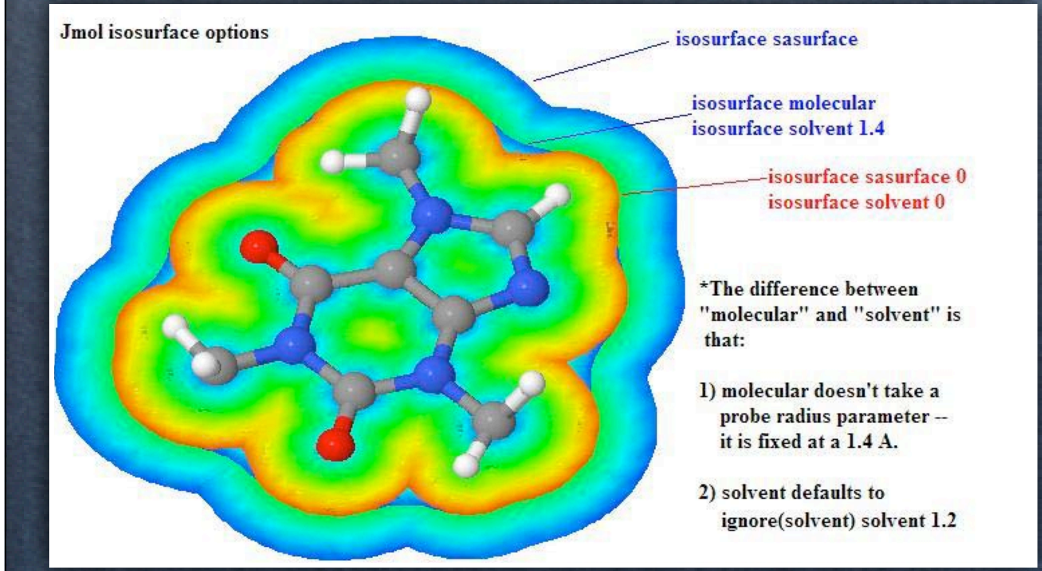
results are very shape sensitive

http://jmol.sourceforge.net/docs/surface/

Solvent Cavity

- **Solvent accessible surface**
  - ◆ roll a probe over the surface of the molecule
  - ◆ path mapped out by center of “solvent” sphere gives the solvent accessible surface SAS
  - ◆ eliminates pockets where solvent should not be able to enter
  - ◆ probe reflects solvent size

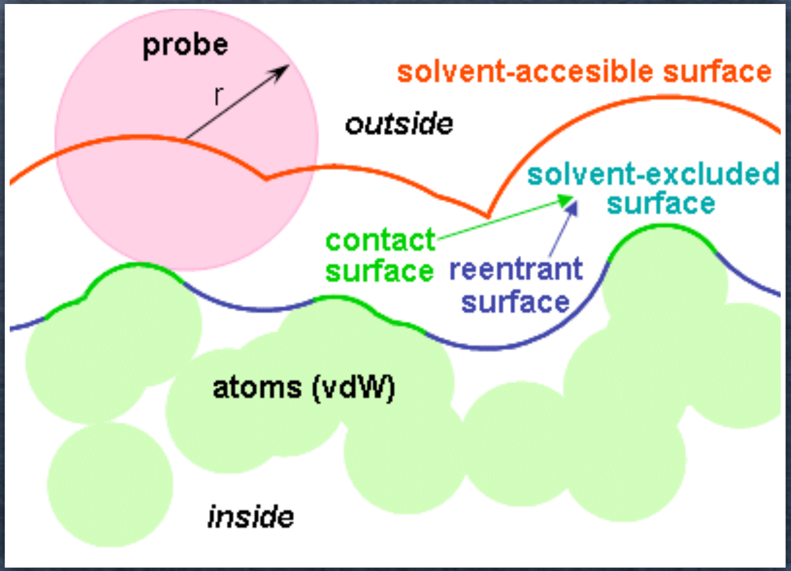




*The difference between "molecular" and "solvent" is that:

1) molecular doesn't take a probe radius parameter -- it is fixed at a 1.4 A.

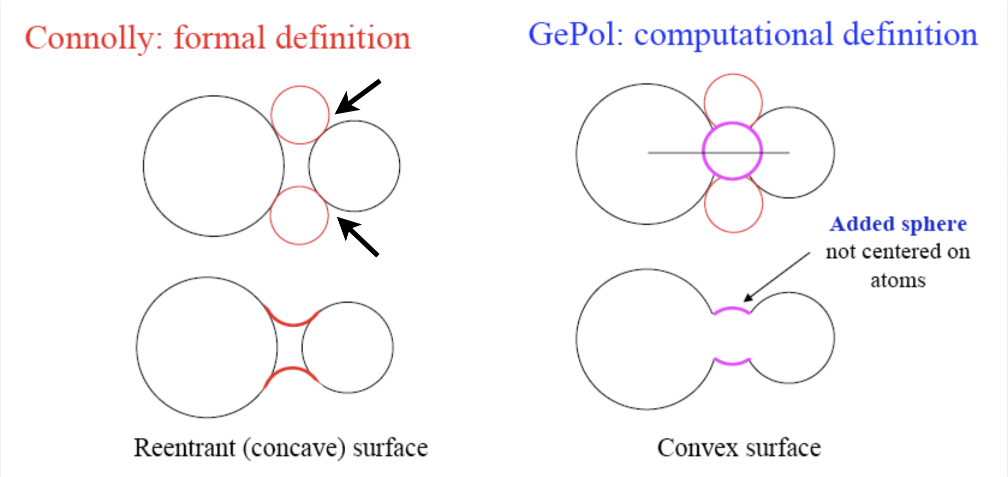
2) solvent defaults to ignore(solvent) solvent 1.2

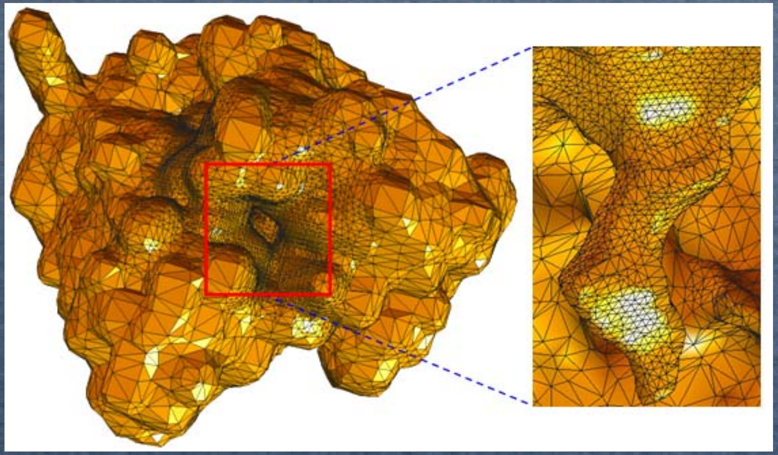


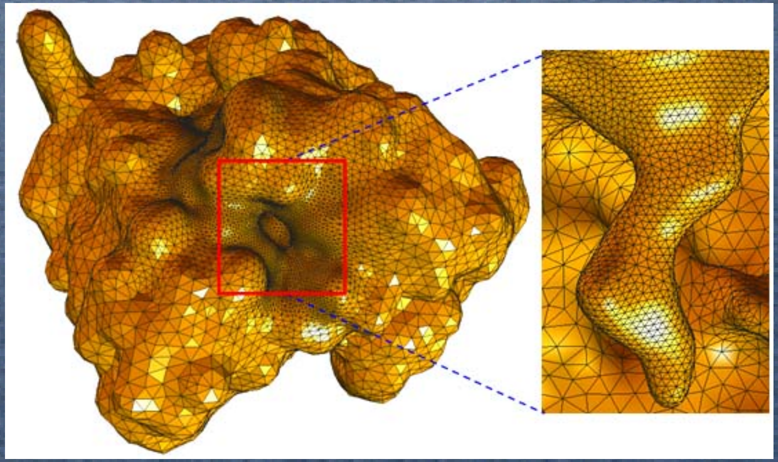
http://jmol.sourceforge.net/docs/surface/

Solvent Cavity

- **problems**
  - singularities and cusps
  - defining surface between atomic spheres
  - smoothing surfaces





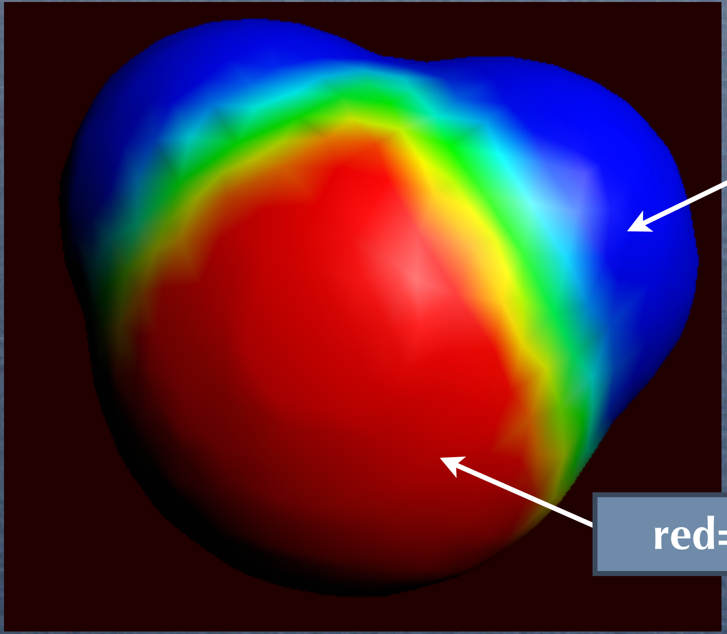


Continuum Methods

- **Surface charge methods**
  - assume a surface charge distribution spread over the cavity surface

integrated Poisson equation:

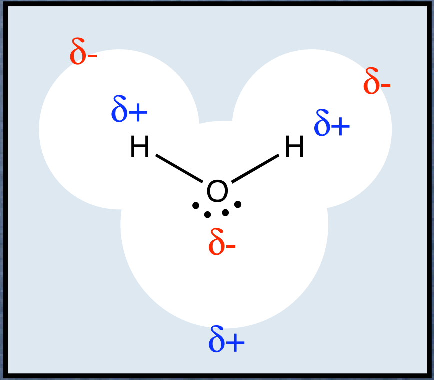
$$V_s(r) = \int_\Gamma \frac{\sigma(s)}{r-s}\, d^2 s$$



blue=negative

red=positive

surface charge distribution



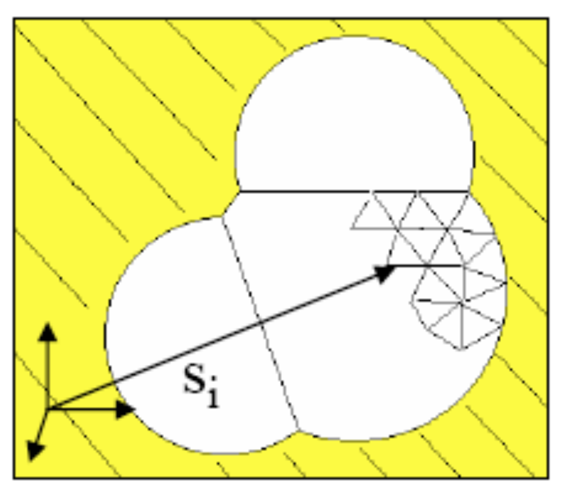
surface has opposite charge to molecule

http://en.wikipedia.org/wiki/COSMO_Solvation_Model

Continuum Methods

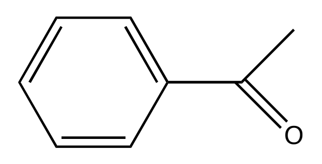
Tesserae

- replace continuous description with quantized one
- divide surface into small finite surface elements, called tesserae
- small enough that surface charge is constant
- define by a point charge
- local value of charge depends on surrounding charges, so solve iteratively

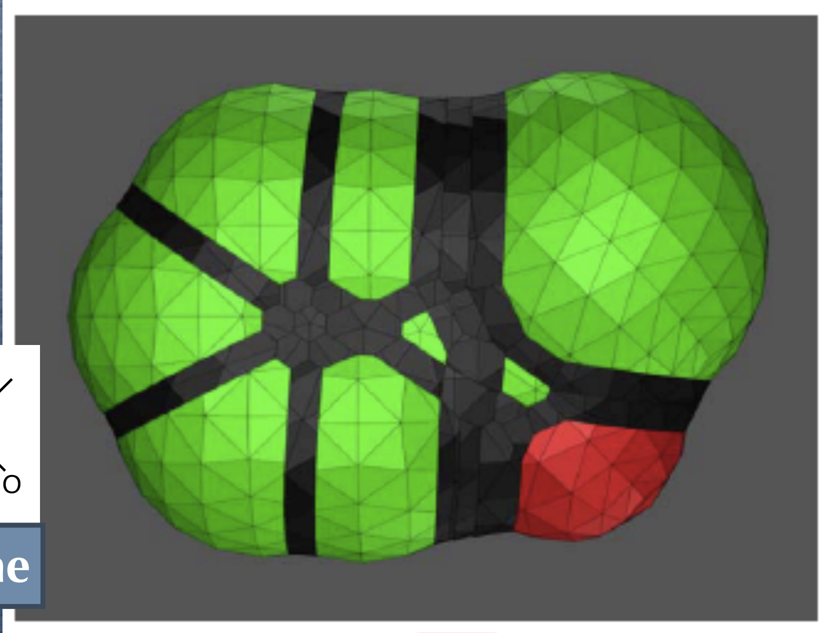


$$V_s(r) \approx \sum_k \frac{\sigma(s_k)A_k}{|r - s_k|} = \sum_k \frac{q_k}{|r - s_k|}$$

green spheres on carbon
red sphere on oxygen
H's summed into heavy atom
"added" spheres in black



acetophenone



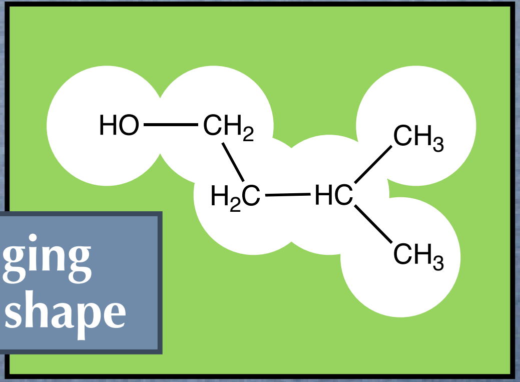
Continuum Methods

- basic
  - how many tesserae to use
  - how to divide up the surface
- different shapes of tesserae
  - small vs large tesserae
  - interactions between tesserae charges can become unbalanced
- discontinuities
  - smooth surfaces
  - introduces new tessera
- different numbers of tesserae
  - can appear and disappear as structure of solute changes
  - two solute cavities combine into one (chemical reaction)

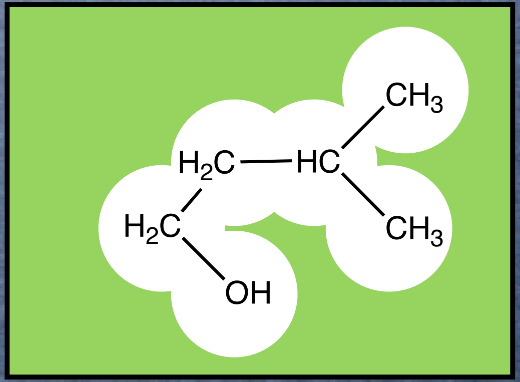
Problems for tesserae

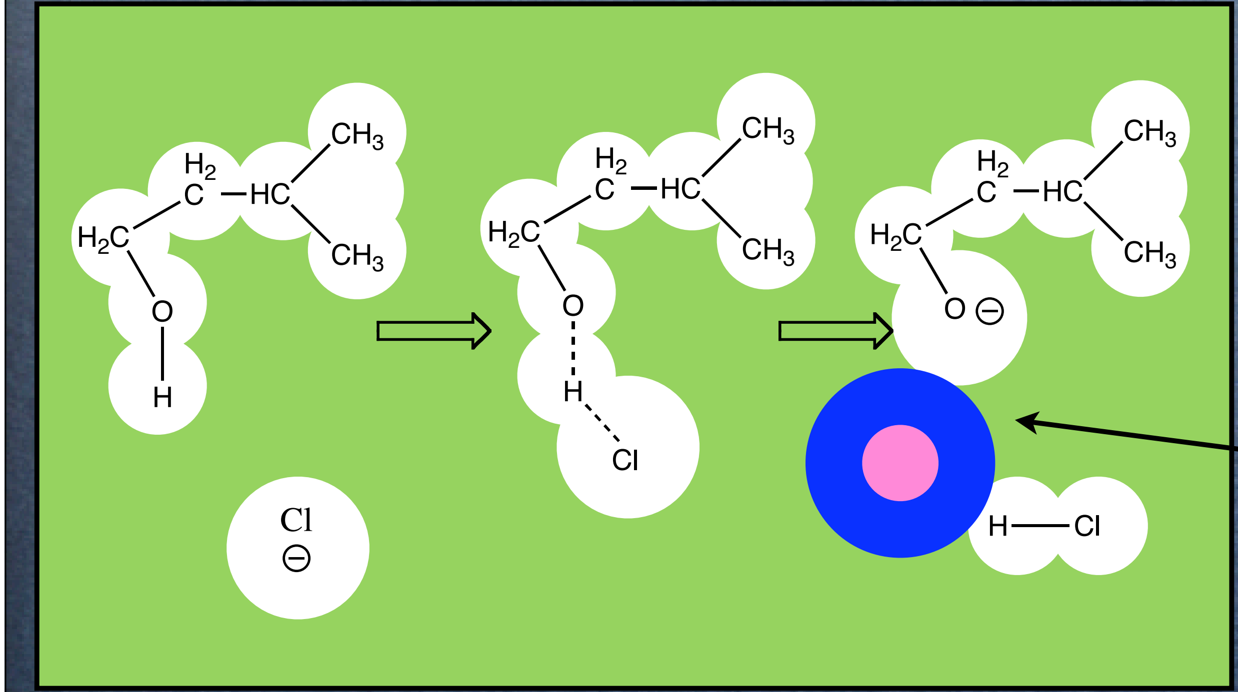
Solvent Cavity

- **changing molecule shape**
- **reactions**
  - atomic “radius” changes in reaction
  - shapes change dramatically
  - problems with solvent accessible areas



changing cavity shape

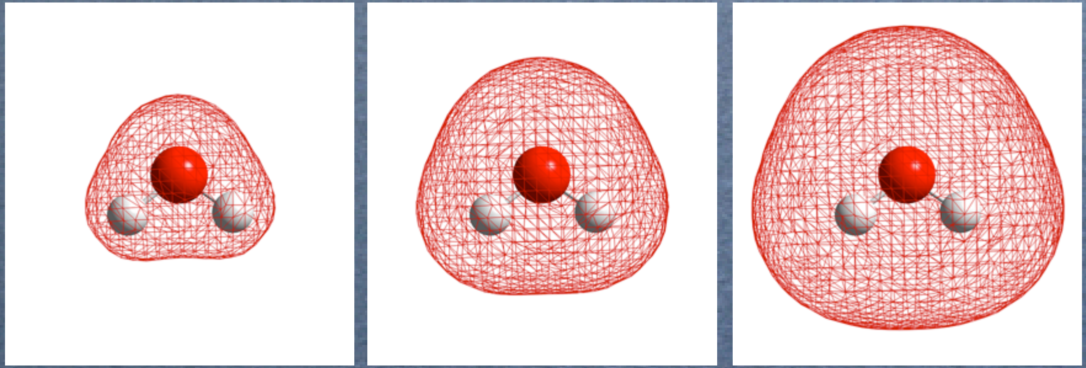


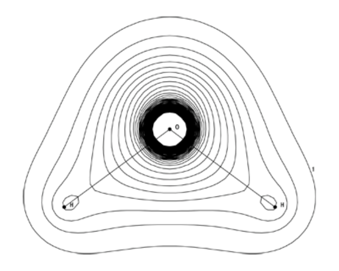


solvent accessible?

Solvent Cavity

- **Based on the electron density**
  - released G09 in 2010
  - can change with molecular shape
  - solved self consistently with electronic density
  - still problems with chemical reactions





density surfaces and contour map around a water molecule

Summary

Mixed Methods

- advantages of mixed methods
- outline of common methods

QM/MM methods

- basic physics
- boundary QM regions is an issue
- coupling QM to MM regions sensibly

Continiuum methods

- basic physics
- cavity construction
- surface charge distribution: tessarae
- problems with changing shape/structure

be able to discuss the advantages of mixed methods, with reference to features of the pure methods

be able to list and discuss briefly discuss a selection of mixed methods

be able to outline the physics behind the QM/MM method and discuss key issues relating to this method

be able to outline the physics behind the continuum methods and discuss key issues related to this method

Outline

- Liquids!
- Between solids and gases
- Interactions within a liquid
- Classical models
- Mixed methods
- QM/MM methods
- Continuum methods

THE END