QM/MM methods: theory and applications

1st topical seminar, Canon, fall 2004

QM/MM methods

Embedding ~ combined ~ hybrid scheme
- "bridging the gap between theory and experiment"

Most of the experimental characteristics are rather sensitive to the system geometry:

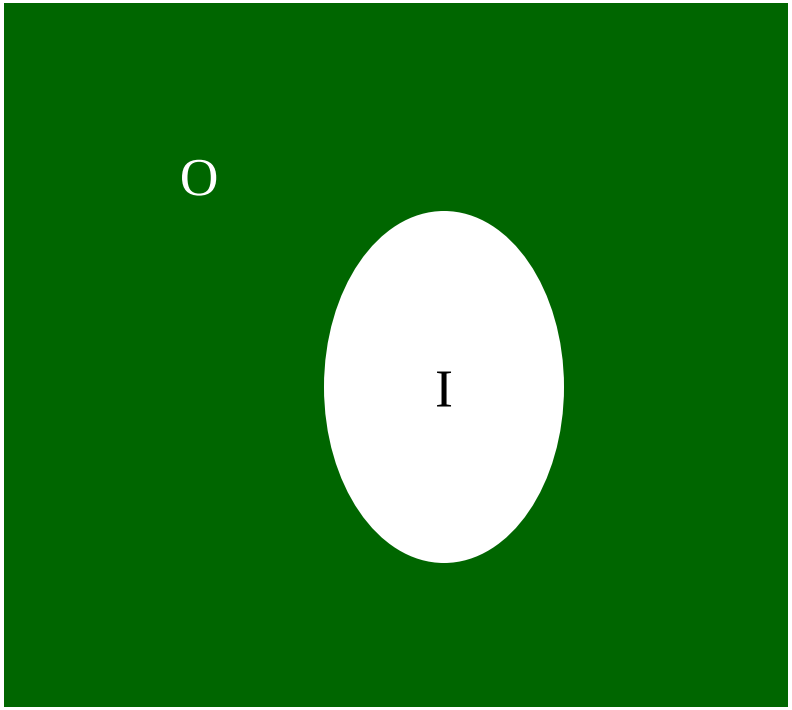
- IR, NMR, EPR, UV-vis,...

Embedding scheme:

+ effect of the long-range interaction
+ changes in the active site geometry due to the interaction with the surrounding atoms
+ proper geometry constraints

- charge transfer across the bondary

General Embedding Scheme



S

S … system

I … inner part

O … outer part

S = I + O

Definition of periodic boundary conditions

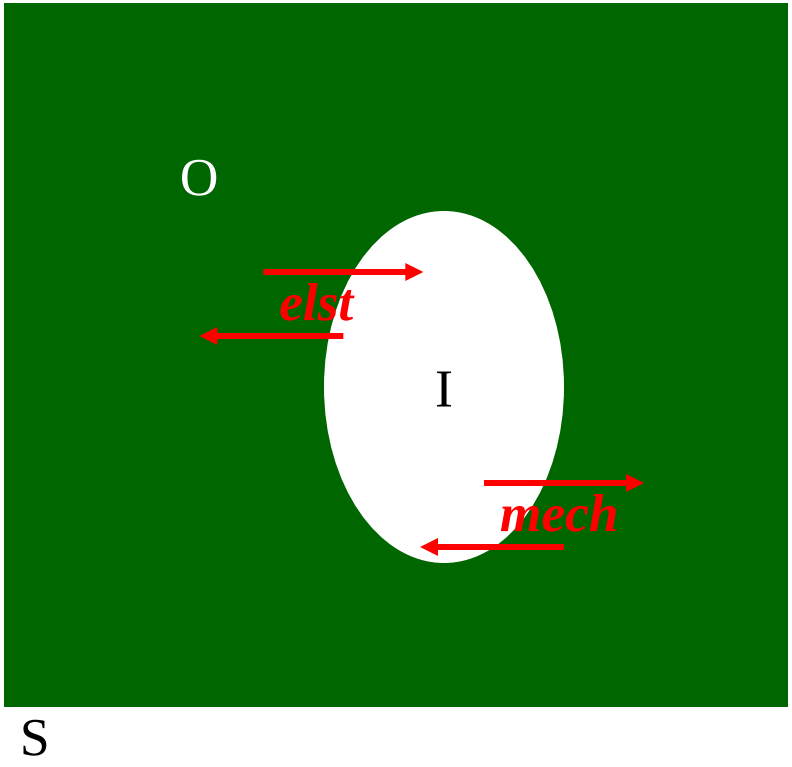
Two approaches:

1) additive scheme
   connection
2) subtraction scheme
   embedding

$$E^S = E^I_{high-level} + E^O_{low-level} + E^{I-O}_{coupling}$$

$$E^S = E^S_{low-level} + E^I_{high-level} - E^I_{low-level}$$

General Embedding Scheme



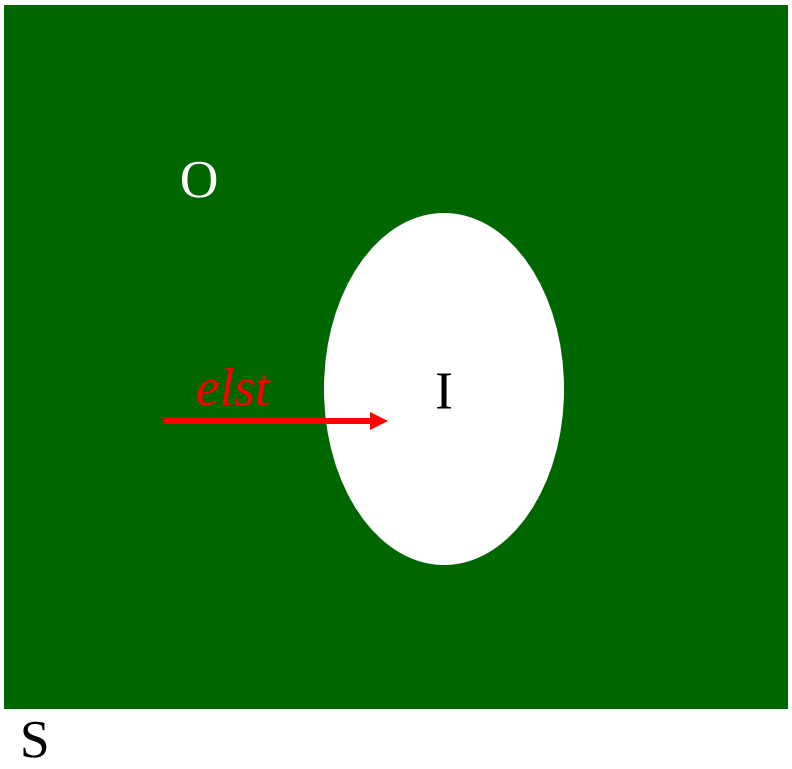
Interaction between I and O regions:

- electrostatic interaction
- mechanical interaction

- *Interaction in one or both directions*
- *Any combination possible*

Mechanical embedding	vs.	Electrostatic embedding

General Embedding Scheme



Interaction between I and O regions:

- electrostatic interaction
- mechanical interaction

- *Interaction in one or both directions*
- *Any combination possible*

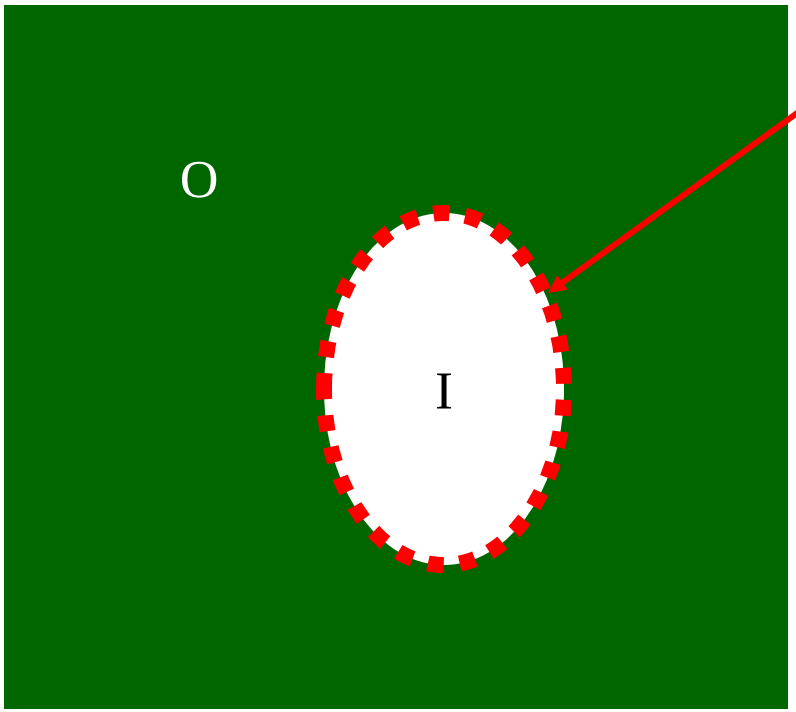
Electrostatic effect of outer part atoms on inner part:

$$\hat{H}^{I}_{O-elst} = \left\langle \Psi \left| -\sum_{i}^{N}\sum_{m}^{M} \frac{q_m}{r_{im}} \right| \Psi \right\rangle$$

i=1,…,N - inner part electrns

m=1,…,M - outer part atoms

General Embedding Scheme



PROBLEM:

I-O boundaries

Increasing difficulty

- No bonds across the boundary
- Purely ionic bonds
- Covalent bonds
- Polar bonds

System of interest	=>	boundaries
	=>	interactions across the boundary required

Large variety of embedding schemes and number of slightly different programs available

The simple case - BOUNDARIES THROUGH SPACE

A) unpolarized interactions

simple additive scheme

$$E^S = E^I_{high-level} + E^O_{low-level} + E^{I-O}_{coupling}$$

Solute-solvent interaction:

Jorgensen (J. Phys. Chem. B 102 (1998) 1787): AM1/OPLS

Solute: AM1

Solvent: OPLS

$$E^{I-O}_{coupling} = \sum_i^{solute} \sum_j^{solvent} \left[\frac{\alpha q_i q_j}{r_{ij}} + 4\varepsilon_{ij} \left(\frac{\sigma_{ij}^{12}}{r_{ij}^{12}} - \frac{\sigma_{ij}^{6}}{r_{ij}^{6}} \right) \right]$$

Just simple electrostatic + Lennard-Jones interaction
Example of explicit solvent model

Does not work too well -

- does not account for polarization
- continuum solvation models woks better!

The simple case - <u>BOUNDARIES THROUGH SPACE</u>

B) polarized high-level/unpolarized low-level

simple additive scheme

$$E^{S} = E^{I}_{high-level} + E^{O}_{low-level} + E^{I-O}_{coupling}$$

Many implementations, *e. g.*, HF/TIP3

Solute: HF

Solvent: TIP3

$$E^{I-O}_{coupling} = \sum_{i}^{\substack{solute\\electons}} \sum_{J}^{\substack{solvent\\atoms}} \left[\frac{q_J}{r_{iJ}} \right] + \sum_{I}^{\substack{solute\\nuclei}} \sum_{J}^{\substack{solvent\\atoms}} \left[\frac{Z_I q_J}{r_{IJ}} + 4\varepsilon_{IJ} \left(\frac{\sigma_{IJ}^{12}}{r_{IJ}^{12}} - \frac{\sigma_{IJ}^{6}}{r_{IJ}^{6}} \right) \right]$$

$$= \left\langle \Psi \middle| - \sum_{i}^{N} \sum_{J}^{M} \frac{q_J}{r_{iJ}} \middle| \Psi \right\rangle$$

Coupling term is just sum over one-electron integrals => computationally easy

The simple case - BOUNDARIES THROUGH SPACE

C) fully polarized interactions

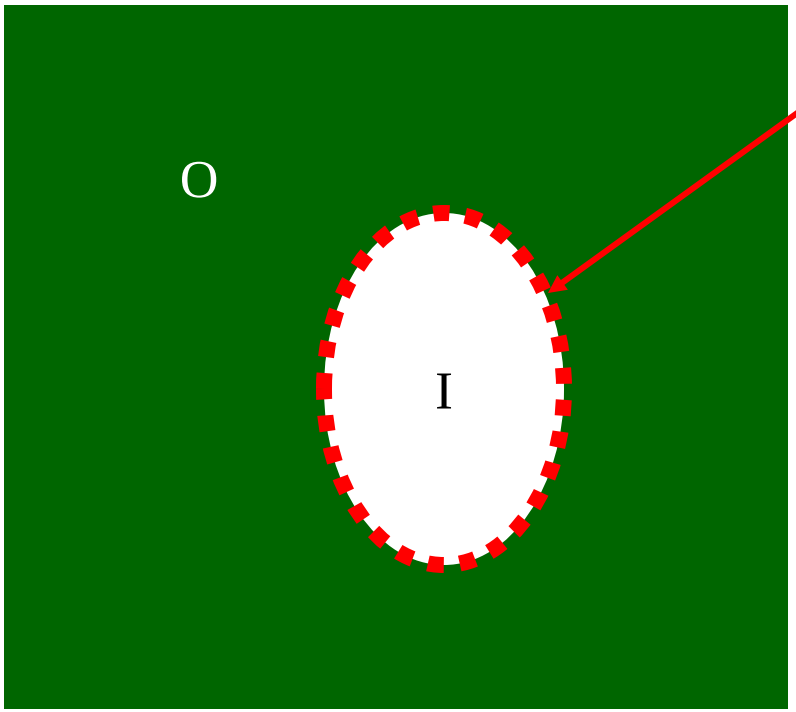
Low-level potential must allow for polarization

I-polarization & O-polarization => evaluation must proceed iteratively until self-consistency

=> order of magnitude more demanding

=> the profit is questionable in many cases

General Embedding Scheme



PROBLEM:

I-O boundaries

Increasing difficulty

- No bonds across the boundary
- Purely ionic bonds
- Covalent bonds
- Polar bonds

Ionic crystals - ELECTROSTATIC EMBEDDING

I … cluster (neutral) - QM or DFT

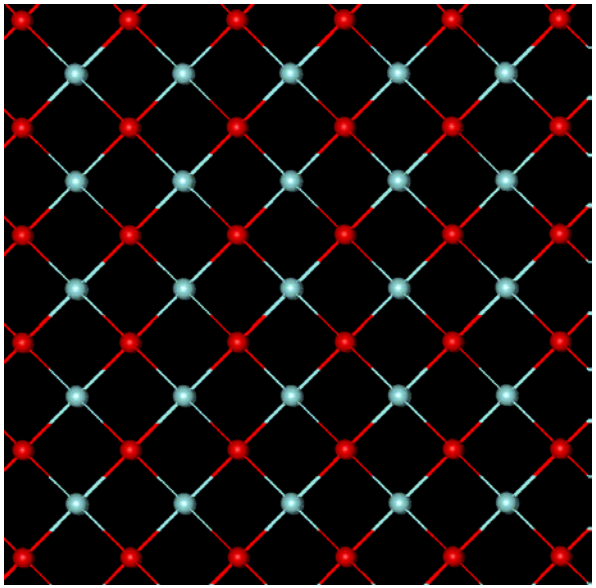
O… point chargec (PC) fixed at the crystal positions

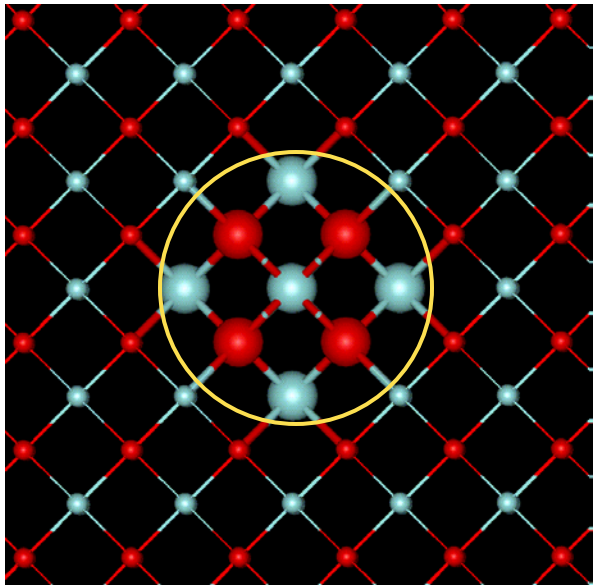
Additive scheme $E^S = E^I_{high-level} + E^O_{low-level} + E^{I-O}_{coupling}$

neglected

$$\hat{H}^I_{O-elst} = \langle \Psi | - \sum_i^N \sum_m^M \frac{q_m}{r_{im}} | \Psi \rangle$$

=> E^S is just simple QM description augmented by O-elst potential

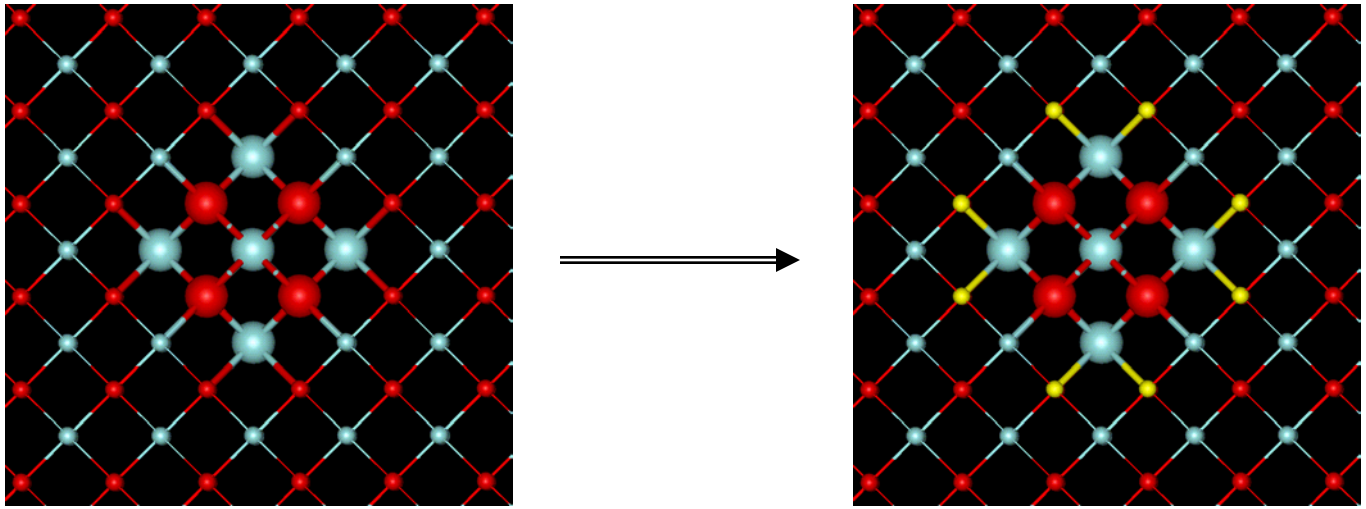




Ionic crystals - ELECTROSTATIC EMBEDDING

O atoms adjacent to I region have too strong effect on the Ψ^I

=> use of ECP on these atoms



Notation:

DFT/PC

DFT/ECP/PC

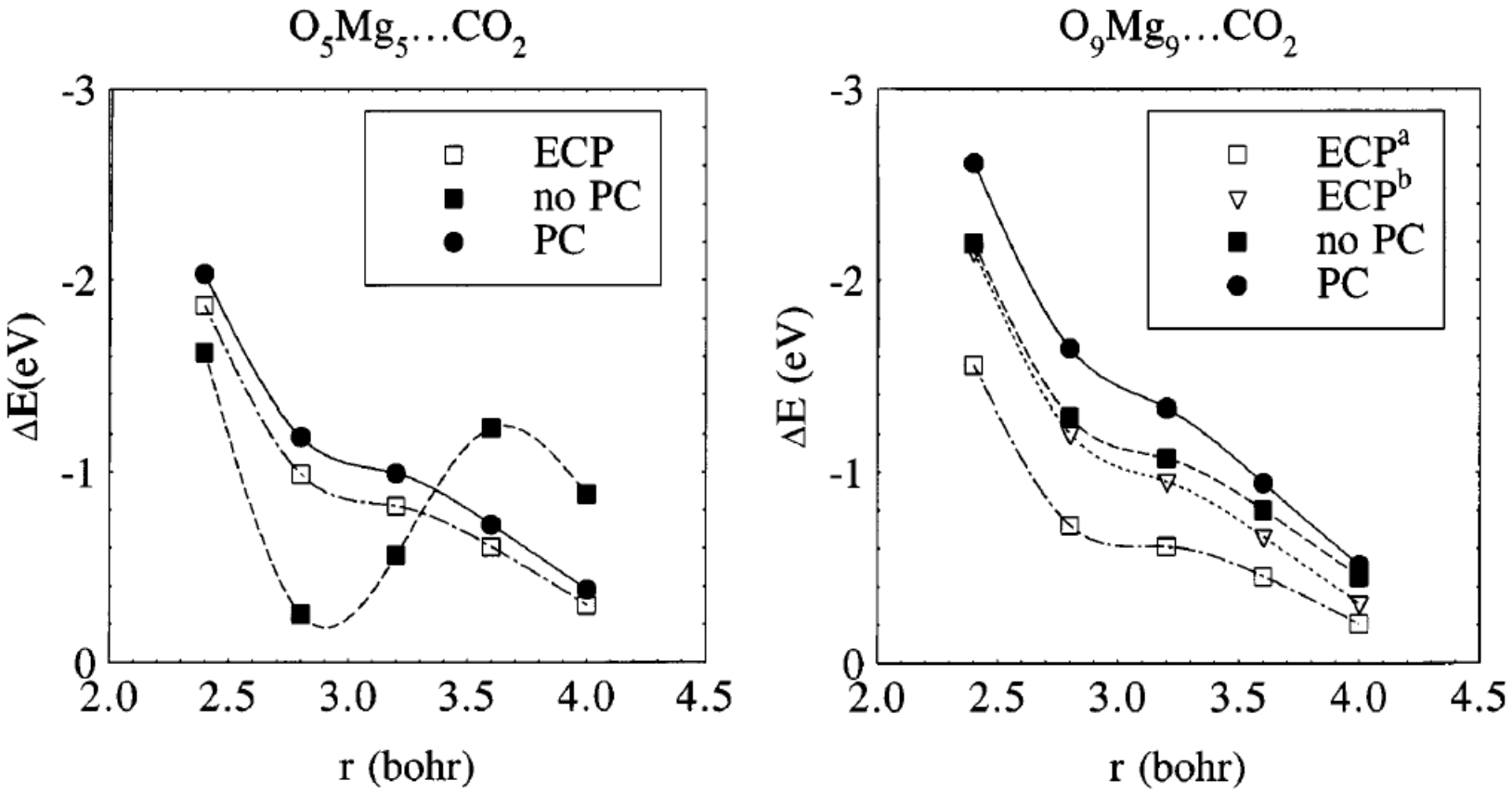
Describes effect of Madelung potential

Electronic (band) structure of solid not reproduced well with clusters

=> some properties not described too well

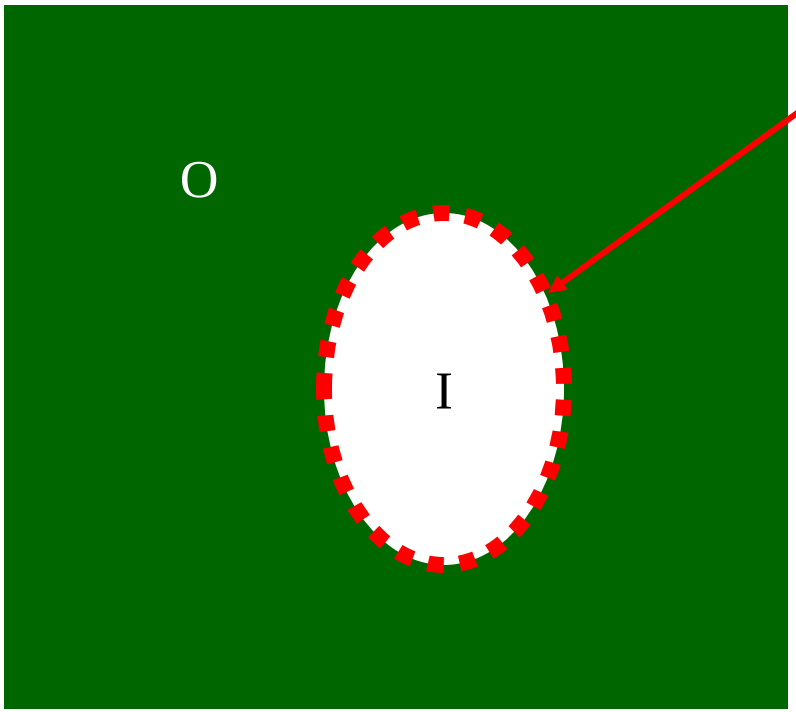
Ionic crystals - ELECTROSTATIC EMBEDDING

Example: CO_2 adsorption on MgO surface
(Illas, J. Comput. Chem. 18 (1996) 617)



Periodic DFT appears to be much more suitable !

General Embedding Scheme



S

PROBLEM:

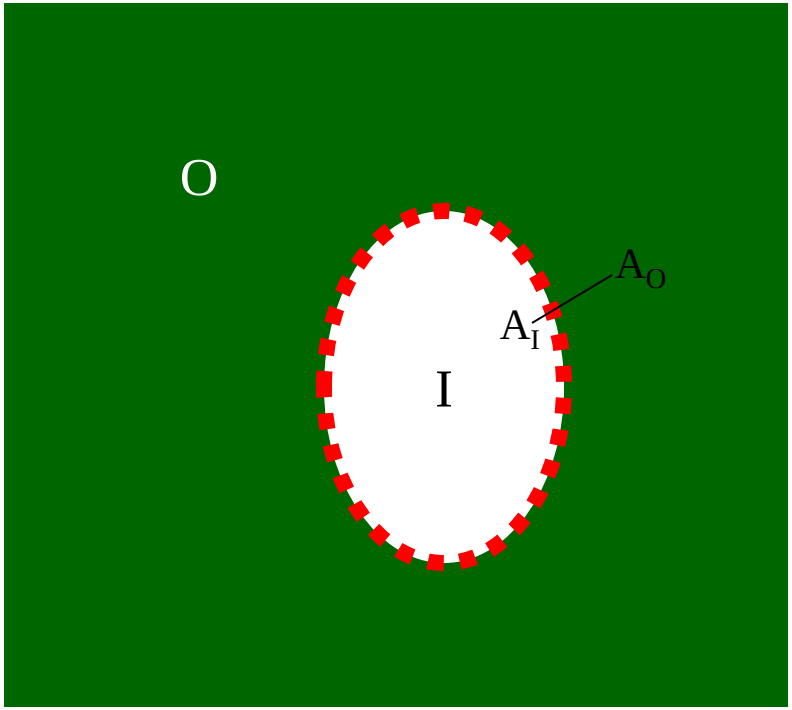
I-O boundaries

Increasing difficulty

- No bonds across the boundary
- Purely ionic bonds
- Covalent bonds
- Polar bonds

a) boundary cuts through bonsd => use of link atoms
(H, CH_3, F, pseuodatom)
b) boundary through atom => pseudoatoms on the I/O boundary

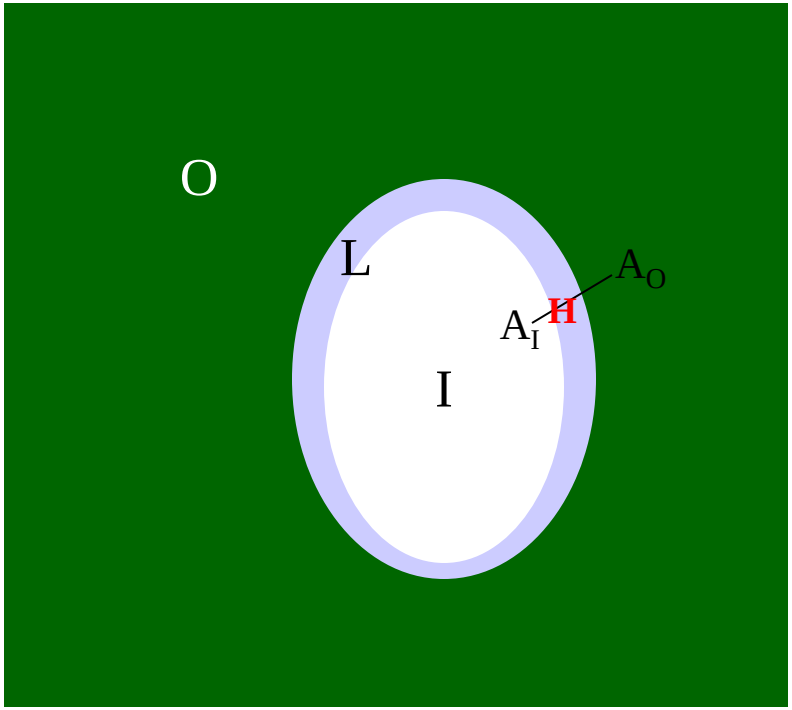
Mechanical Embedding - using H atom saturation



I-O boundary cuts through the bond:

- tolopogical effect
  treated via I-O coupling term
- electronic structure effect
  huge perturbation - saturation required

Mechanical Embedding - using H atom saturation



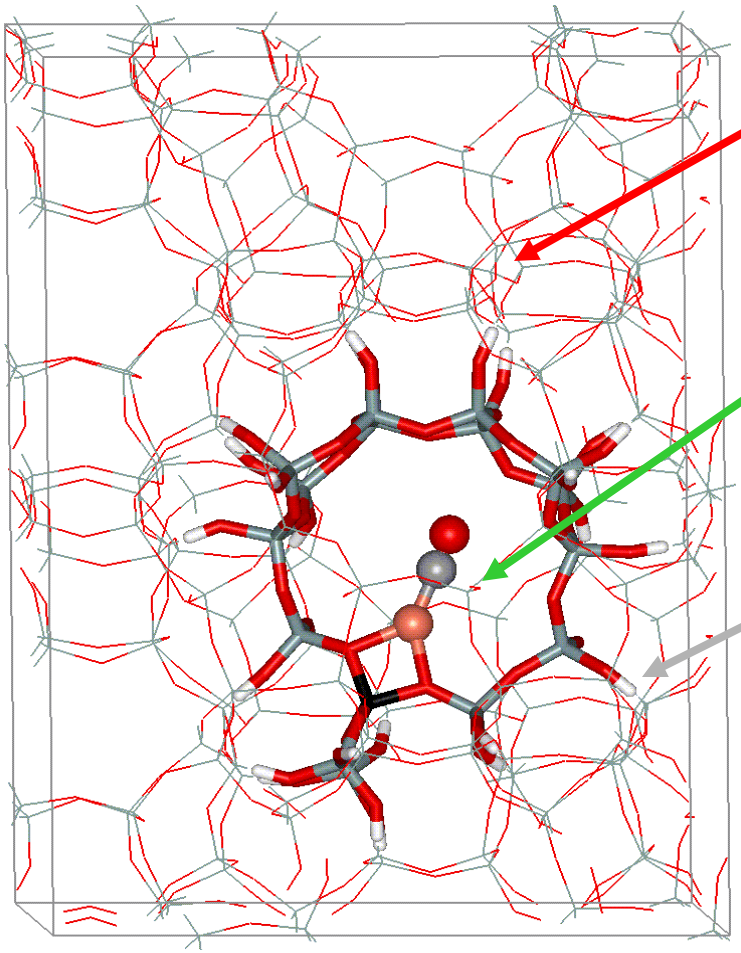
Link atoms introduced (hydrogen)

- link atoms not present in the real system
- makes perturbation on Ψ smaller
- should replace atoms with similar electronegativity (Si, C, …)
- link atoms placed along the A_I-A_O bond at fixed r(A_I-H) distance
- no interaction with atoms from O
- no direct effect on ∇E

Cluster: Cl = I + L

$$E^S = E^S_{low-level} + E^I_{high-level} - E^I_{low-level} \Rightarrow E^S = E^S_{low-level} + E^{Cl}_{high-level} - E^{Cl}_{low-level}$$

Mechanical Embedding - using H atom saturation



Outer part
- surrounding periodic zeolite framework (192 T atoms, 384 O atoms)
- shell model ion-pair potential

Inner part
- metal ion, adsorbed molecule and neighboring atoms

3-10 T atoms, **B3LYP** (DZP/TZP)
BSSE included

Link atoms
saturating the oxygen atoms on the inner part boundary

Outer vs. Inner part
core-shell model ion-pair potential

PBC - periodic boundary conditions

[a] Sierka, M., Sauer, J.: J. Chem. Phys. 112, (2000), 6983

Mechanical Embedding - using H atom saturation

Link atoms only approximately simulate the electronic effect of the outer part
No charge transfer across the boundary
Electrostatic interactions across the boundary at low-level!
Approximative expression for E^S

Sauer - Biosym implementation, 1994
Gale - Phys. Rev. B 54 (1996) 962
Morokuma - J. Chem. Phys. 105 (1996) 1959
Sauer - J. Comput. Chem. 18 (1997)463

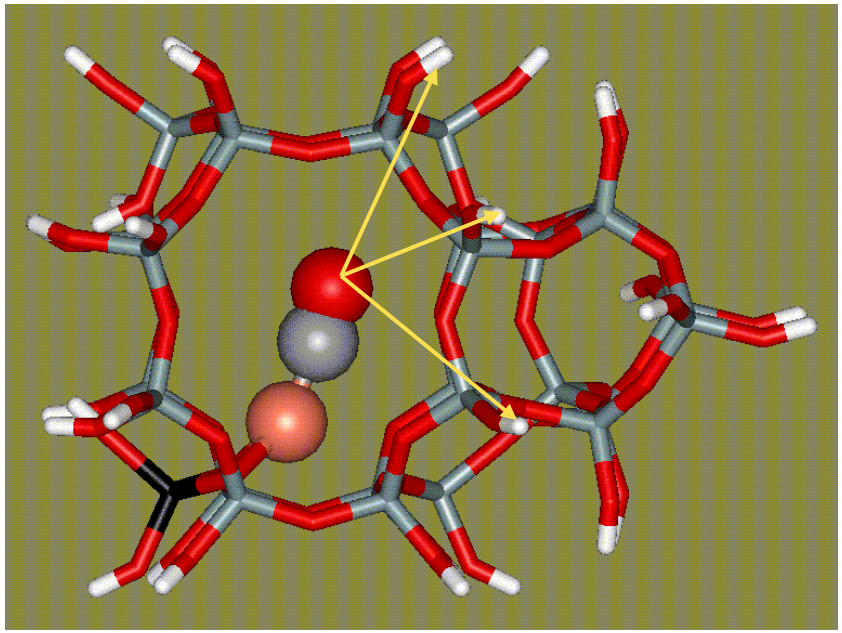
$$E^S = E^S_{low-level} + E^{Cl}_{high-level} - E^{Cl}_{low-level}$$

Approximation, error Δ: $\Delta = -E^L_{high-level} - E^{L-I}_{high-level} + E^L_{low-level} + E^{L-I}_{low-level}$

- In order to minimize Δ the use of *ab initio* derived potentials is mandatory !
- Interatomic potentials for inner part atoms must be also defined!
- Calculations for systems with 3-D strucutre must be done with great care!
- Inner part size convergence should be always tested!

Mechanical Embedding - using H atom saturation

Example:
$CO/Cu^{+}/Z$



All link atoms must be far from embedded $Cu^{+}CO$!
=> large inner part definition required

Gaussian 98/03 embedding scheme - ONIOM

Keiji Morokuma

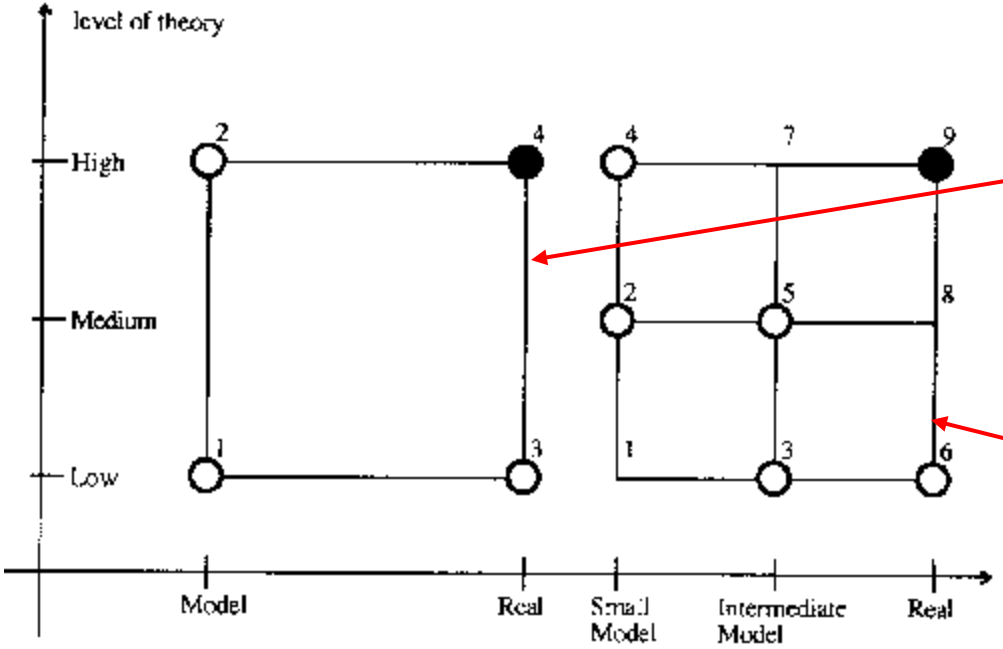
IMOMM - *J. Comput. Chem. 16 (1995) 1170*

IMOMO - *J. Chem. Phys. 105 (1996) 1959*

ONIOM - *J. Phys. Chem. 100 (1996) 19357*

"Our own n-layered integrated molecular orbitals and molecular mechanics"

Subtraction scheme (2- or 3-layer):



$$E_{ONIOM\,2} = E_3 - E_1 + E_2$$

$$E^S = E^S_{low-level} + E^I_{high-level} - E^I_{low-level}$$

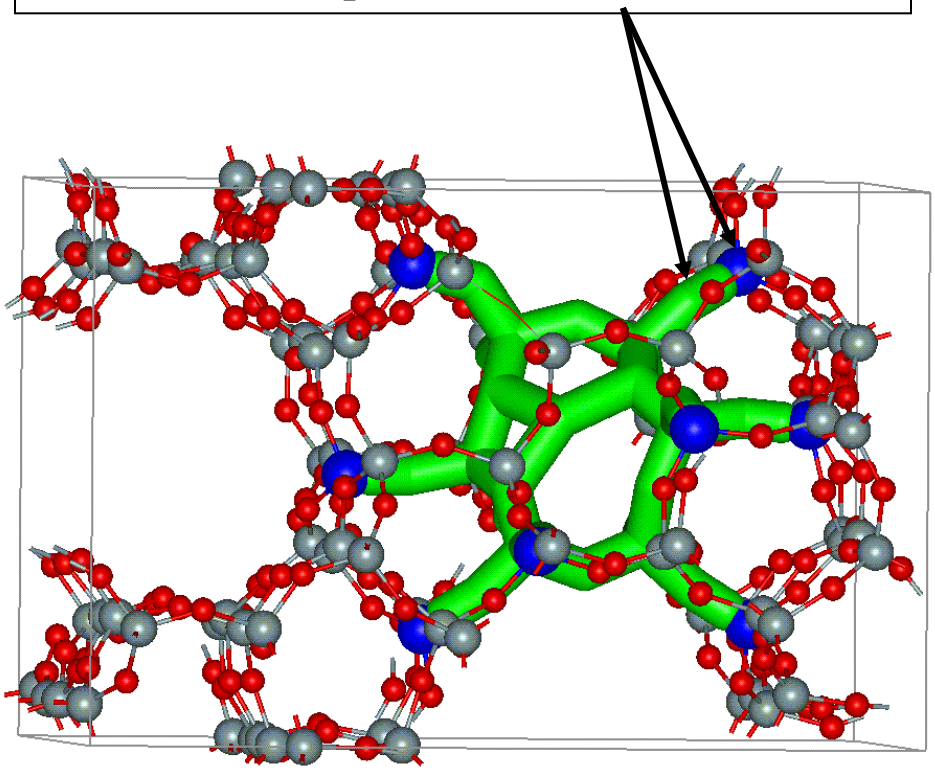
$$E_{ONIOM\,3} = E_6 - E_3 + E_5 - E_2 + E_4$$

Electrostatic Embedding - using H atom as link atoms

Includes electrostatic effects of outer part atoms on inner part at QM level:

$$\hat{H}^{I}_{O-elst} = \langle \Psi | - \sum_{i}^{N} \sum_{m}^{M} \frac{q_m}{r_{im}} | \Psi \rangle$$

Problem: link atoms too close to some atoms from O part



SCREEP "The Surface Charge Representation of the Electrostatic Embedding Potential Method"
Truong, J. Phys. Chem. B 102, 1998, 3018

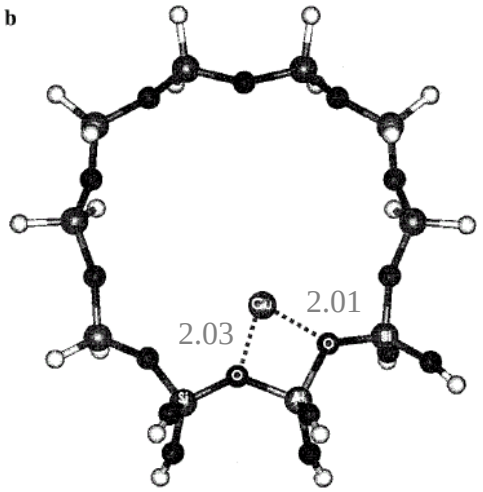
- Inner part of the cluster - VdW radii of the cluster atom
- Madelung potentail of the outer part is represented by the point charges at the surrounding surface.
- Some "close" ions explicitely (up to 4.0 A)

Additive scheme
Positions of O-part atoms cannot be varied in geometry optimization

Electrostatic Embedding - using H atom as link atoms

Cu^+

Cu^+ interaction with ZSM-5 zeolite
B3LYP/6-31G* level



Model	E^b(QM) [kcal/mol]	E^b(QM/MM) [kcal/mol]	Q(Cu)
3T	180	234	0.61
5T	184	196	0.58
7T	186	180	0.55
10T	187	164	0.55

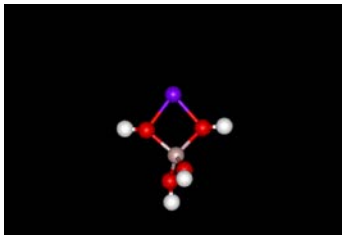
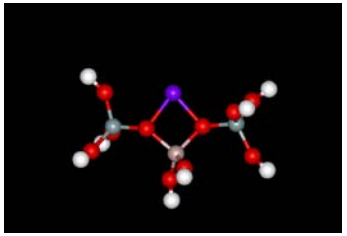
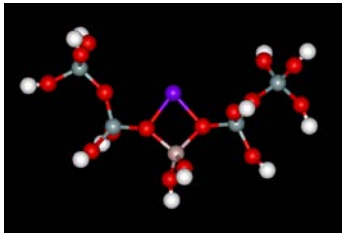
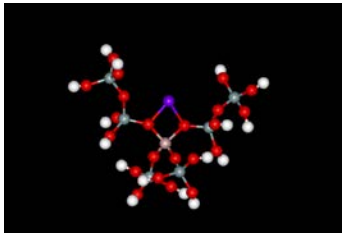
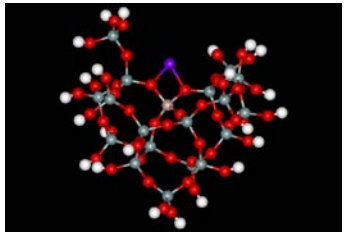
Convergence ?

Embedded 3T model - far from convergence
Can this be used for study of other properties ?

Treesukol et al.,
J. Phys. Chem. B 105 (2001) 2421

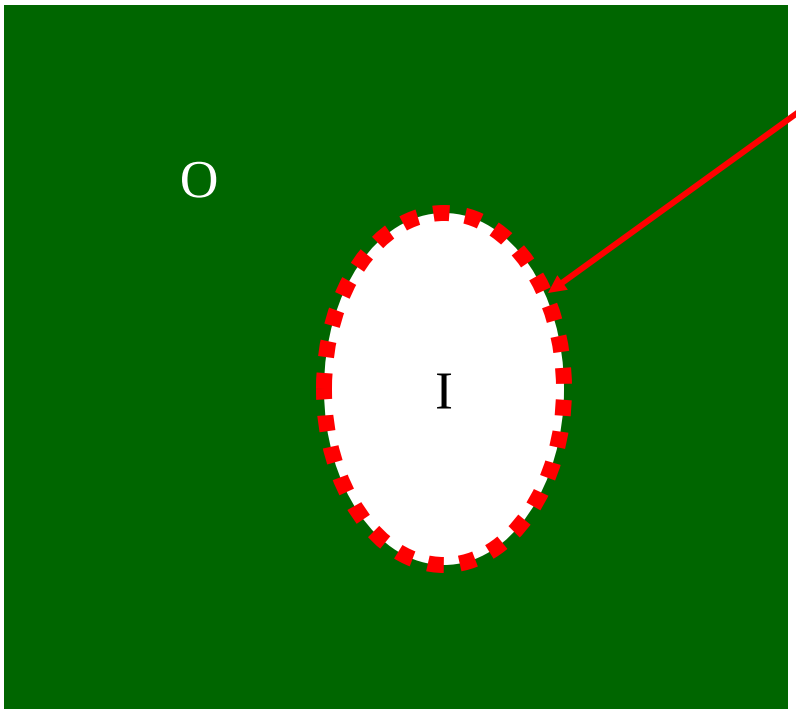
Mechanical Embedding - using H atom saturation

Results insensitive on the embedded cluster size:

1T	3T	5T	7T	19T
				
10 atoms	22 atoms	34 atoms	46 atoms	94 atoms
E^b(QM/MM) [kcal/mol]: 153	148	146	146	145
E^b(QM) [kcal/mol]: 181	174	174	164	165

Embedded 3T cluster model gives well converged results !!!

General Embedding Scheme



S

PROBLEM:

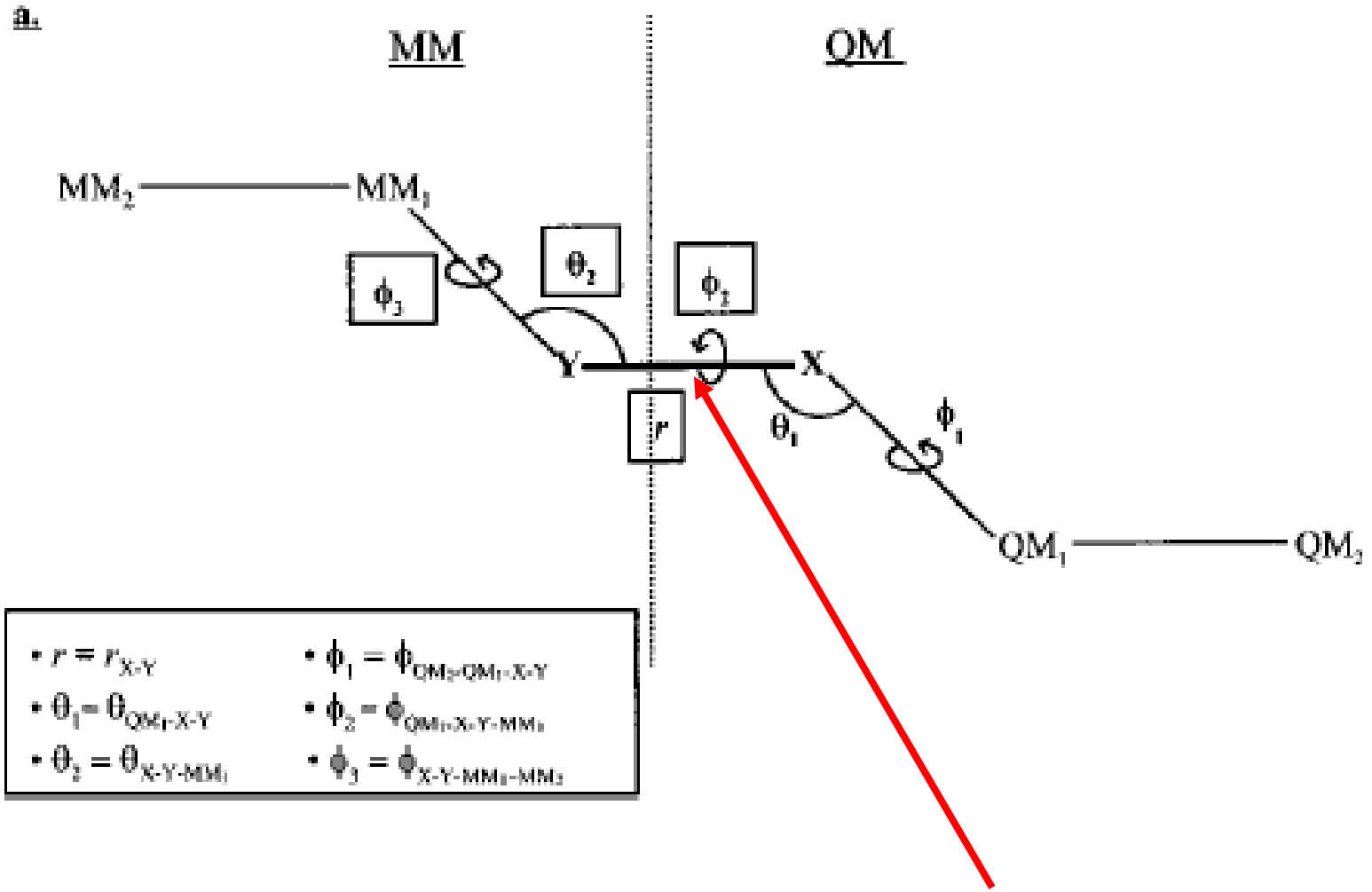
I-O boundaries

Increasing difficulty

- No bonds across the boundary
- Purely ionic bonds
- Covalent bonds
- Polar bonds

a) boundary cuts through bonsd => use of link atoms
(H, CH_3, F, pseuodatom)
b) boundary through atom => pseudoatoms on the I/O boundary

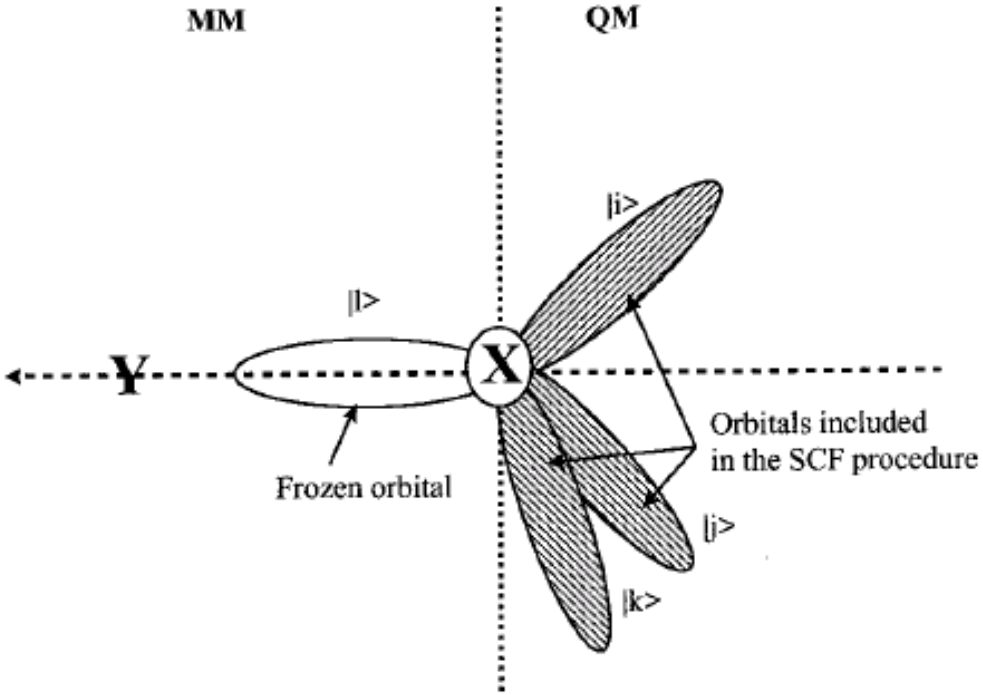
LSCF ("Local SCF") Method



Replacing X-Y bond by strictly localized bond orbital (SLBO)

- Assuming that X-Y bond is far from region of interest
- Electron density assumed to be constant for studied phenomenon
- SLBO obtained from calculations no model compound
- SLBO is kept frozen during the SCF - SLBO represents effective potential for other electrons during SCF

J. Comput. Chem. 15 (1994) 269



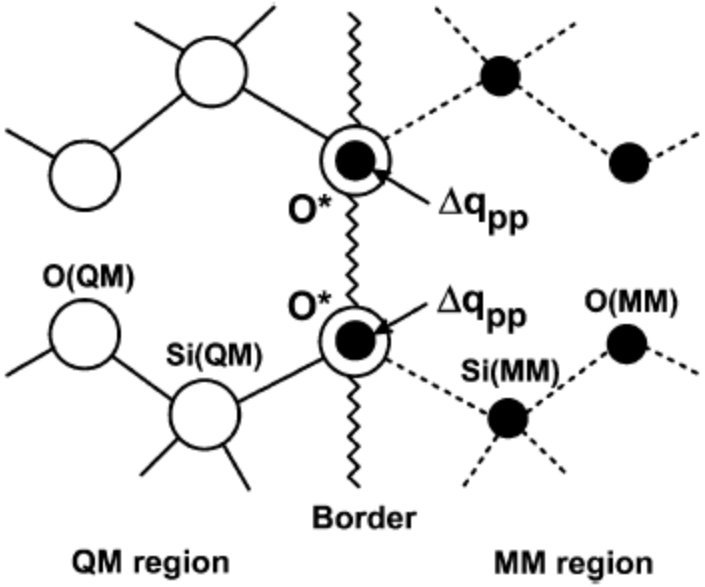
Suitable for semiempirical methods

Number of different “special” embedding schemes:

1. “Electron density partitioning scheme” - Weselowski (*J. Chem. Phys. 115 (2001) 4791)*

2. “Hybrid MP2/plane-waves DFT scheme” - Sauer (*Chem. Phys. Letters 387 (2004) 388)*

3. “Elastic polarizable environment cluster embedding approach” - Rosch (*J. Phys. Chem. B 107 (2003) 2228)*

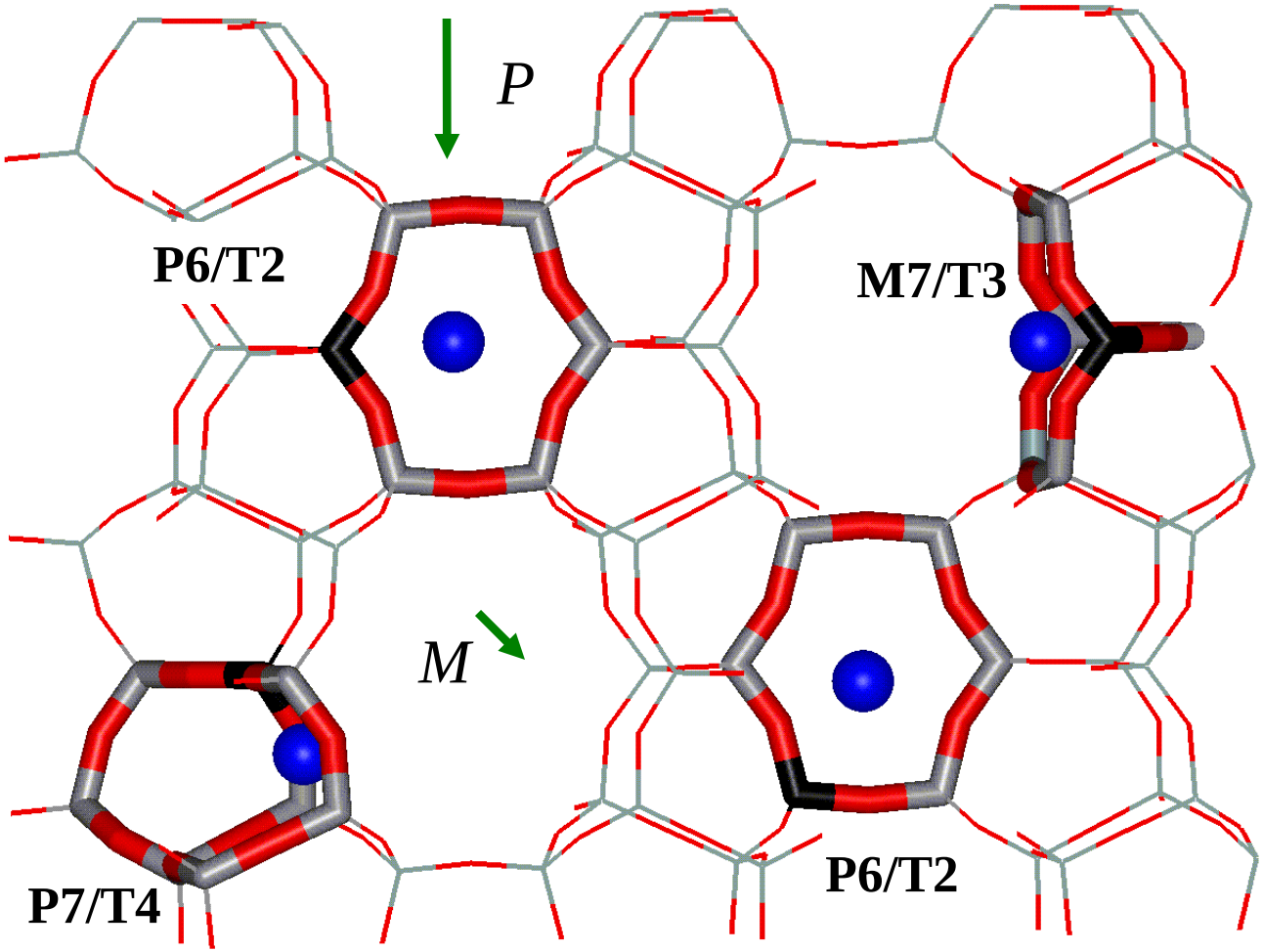


- Boundary through atom
- border atom chage splitted into I and O contribution
- special FF for boundary atoms must be fitted
- 7 electron boundary oxygen atom

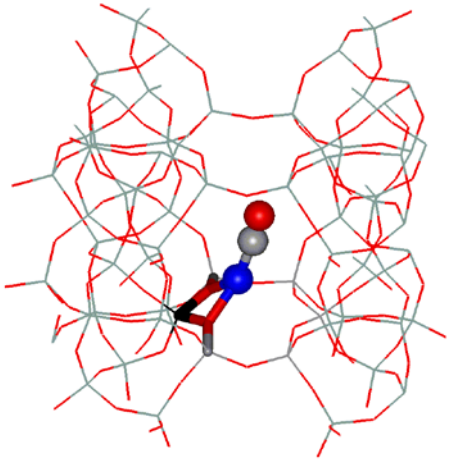
Example: Convergence of inner part size studied for CO/Cu^{+}/FER system

I … B3LYP/VTZP

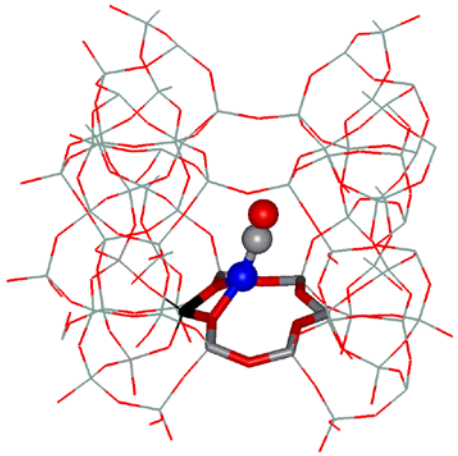
O… core-shell model polarizable potential



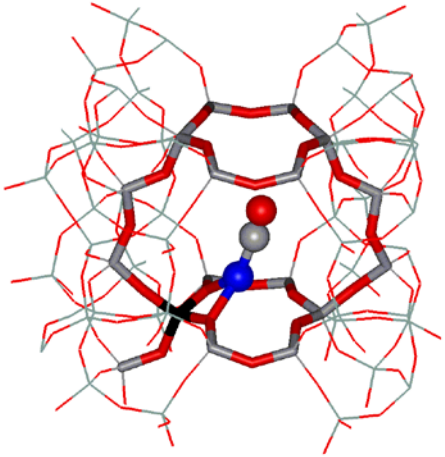
3-T

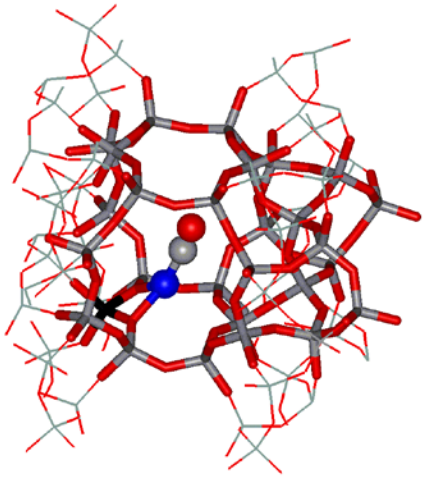


6-T



17-T





28-T

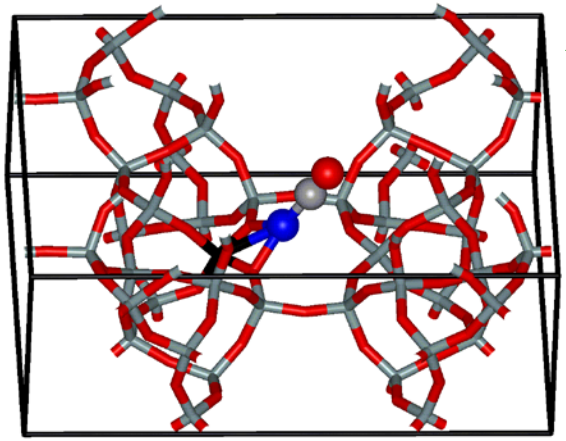


Table 2: Comparison of harmonic CO stretching frequencies and CO adsorption energies obtained at the QM-pot and periodic DFT levels.[a]

		r(CO)[b]	ν(CO)[c]	E_{ads}[d]
QM-pot[e]				
BLYP/PBE	1-T	1.14868	2137	-50.6
	3-T	1.14780	2142	-51.3
	6-T	1.14835	2138	-35.5
	6-T [no q(CO)][g]			-38.7
	8-Td	1.14779	2142	-35.7
	16T / 8 UC	1.14485	2158	
	17Td / 8 UC	1.14473	2159	-36.5
	28 T / 8 UC	1.14576	2153	-34.6
Periodic DFT[f]				
PBE	600 eV	1.14997	2154	-33.6
PBE	450 eV			-34.5
PBE	300 eV			-36.5
PW91	600 eV	1.14864	2154	

CONCLUSIONS:

- large variety of embedding schemes
- direct comparison of different embedding schemes for particular problem is lacking
- convergence of inner part size should always be tested

clara.uochb.cas.cz/public/petr/Topical_1-QM,MM.pdf