

Very large system

molecular systems

fragm. methods

density

(compute density
of the whole system)

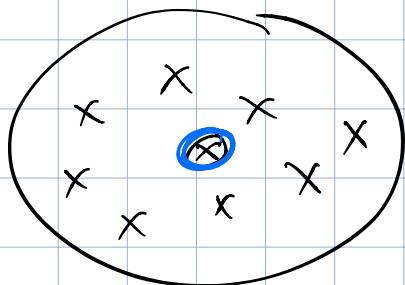
then compute energy

FMO, DC

→
energy is
computed
directly from
fragments

SFM, MFCC

FMO fragment molecular orbital



monomer density
is computed in
electrostatic field
of other fragments

$$\tilde{F}^x C^x = S^x C^x \Sigma^x$$

$$\tilde{F}^x = \tilde{h}^x + G^x$$

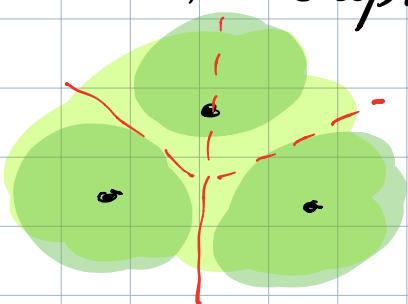
$$\tilde{h}_{\mu\nu}^x = h_{\mu\nu}^x + \sum_{A \in K} \left\langle \mu \left| \frac{-Z_A}{r - r_A} \right| \nu \right\rangle +$$

$$+ \sum_{\lambda, \delta \in k} D_{\lambda \delta}^k \langle \mu | \delta \rangle$$

k-other fragment

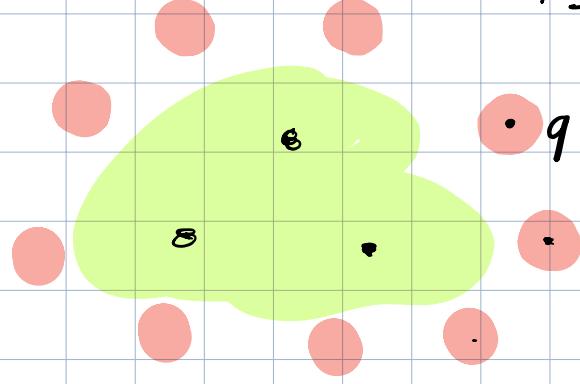
Can be approximated $\sum_{A \in k} \left\langle \mu \left| \frac{P_A}{r - r_A} \right| \delta \right\rangle$

P_A - partial charges
how to compute partial charges?



can be determined
by summing density
near atoms,
density is separated
by density gradient
surfaces

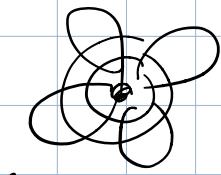
AIM (atom-in-molecule)



q_i , compute potential
on this charge due
to molecule
error ($\sum_i^{\text{grid}} (V_{QM}^{(i)} -$
 $V_{\text{charges}}^{(i)})^2 = \min$

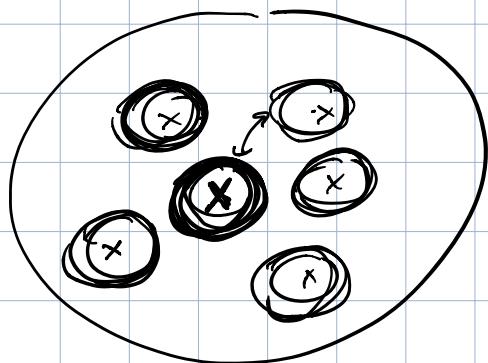
ESP (el. potential) charges
RESP

Mülliken & Löwdin charges



charge is computed
based on contributions
from atomic orbitals

FMO: Mülliken charges
or ESP charges



Nelectrons
no fragments
cost $\sim N^3$

FMO: n fragments

Step 1:
self-consistent
loop over
densities of
all fragments

$$\text{cost} \sim hf \left(\frac{N}{n}\right)^3 =$$

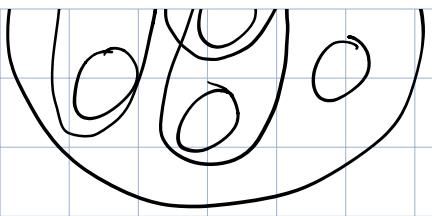
$$= f \frac{N^3}{n^2}$$

f - prefactor

Step 2:



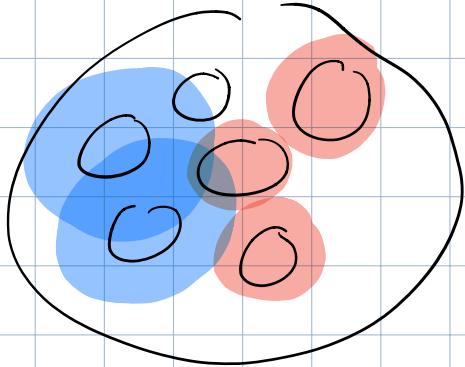
dimer calculations
in presence of
bath



$$E^{\text{FM02}} = \sum_i^{n_{\text{frag}}} E_i + \\ + \sum_{i>j}^{n_{\text{frag}}} (E_{ij} - E_i - E_j)$$

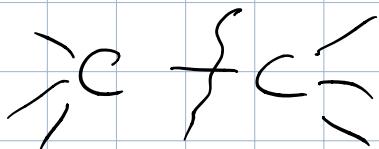
Problems:

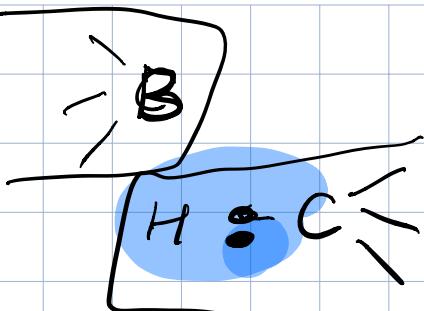
- 1) hard to describe systems with delocalized electrons
~ graphenes, metallic crystals,
...
- 2) basis set convergence



charge-transfer
between fragments
becomes large

- 3) splitting of covalent systems into fragments is not easy
(done but questionable)

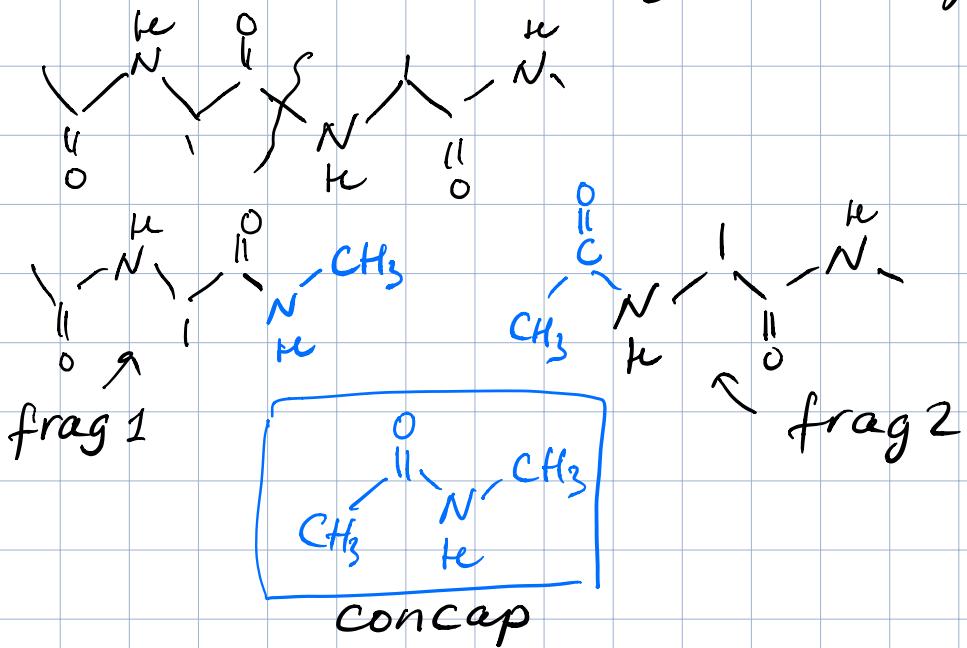




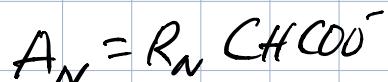
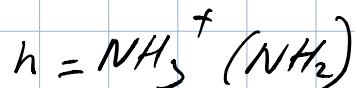
blue orbital is kept frozen

MFCC

nuclecular fragmentation
with conjugated caps



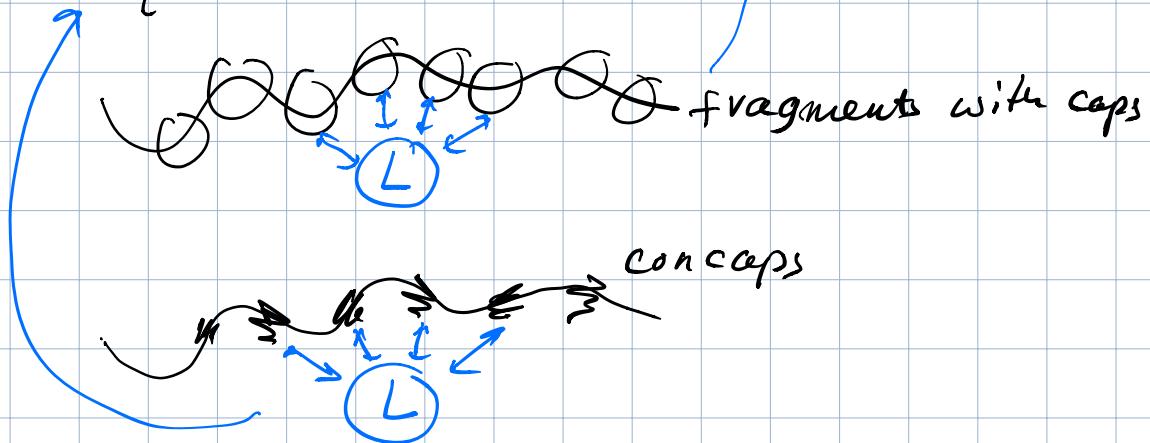
$$P = n A_1 A_2 A_3 \dots A_N$$



Goal: compute protein-ligand interactions

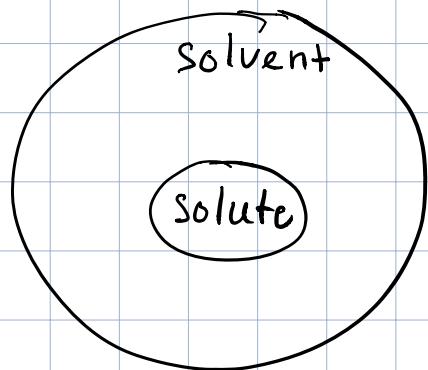
$$E(P-L) = \sum_i^N E(L - Cap^{i-1+} A_i Cap^i) -$$

$$-\sum_i^{n-1} E(L - \text{Cap}^i * \text{Cap}^i)$$



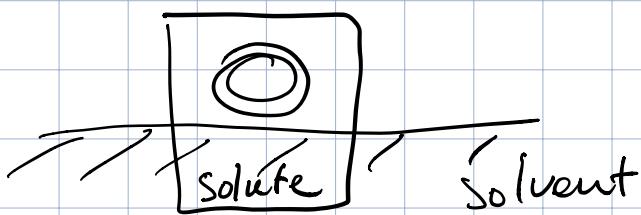
density $\sim \rho = \sum_i \rho_{Ai} - \sum_i \rho_{ci}$

ONIOM

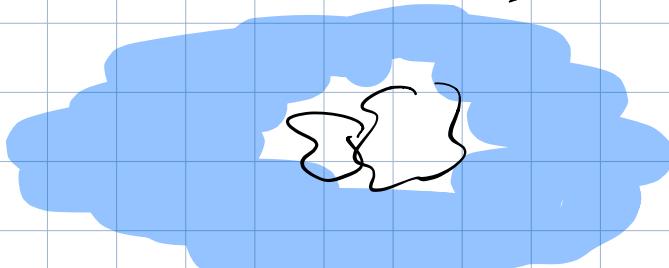


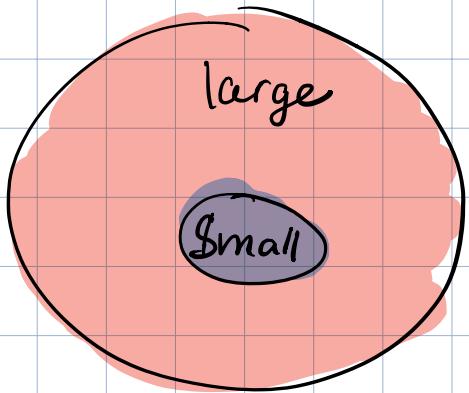
Morokuma

reactions on surface



reactions in solvent





$$E = E_{\text{large}}^{\text{MM}} - E_{\text{small}}^{\text{QM}} + E_{\text{small}}$$

$\text{large} = \text{full system}$
 $(\text{large} - \text{small}) = \text{solvent}$

QM/MM models

MM - molecular mechanics

- how to describe interactions between QM and MM parts
- boundaries between QM and MM regions

MM \equiv FF force field

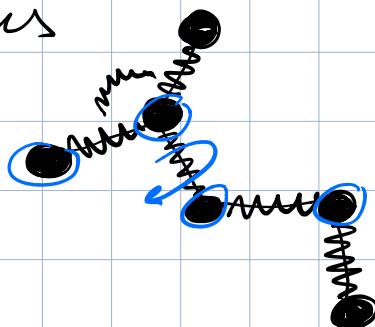
FF : Bonded terms

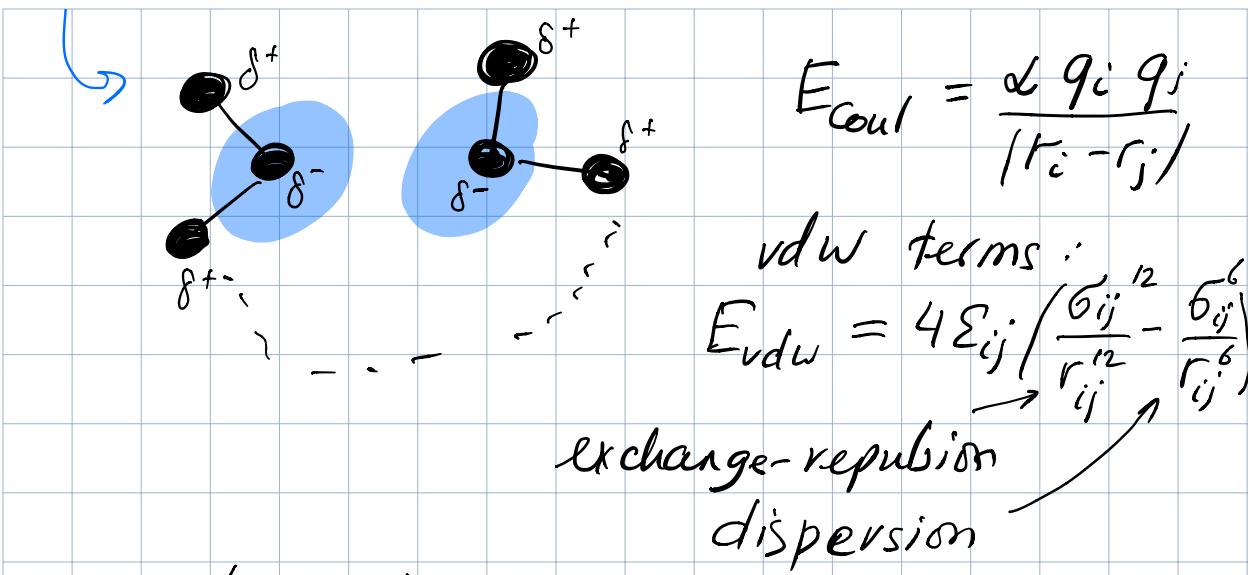
non-bonded terms

$$E_{\text{bond}} = \frac{1}{2} k_b (r - r_0)^2$$

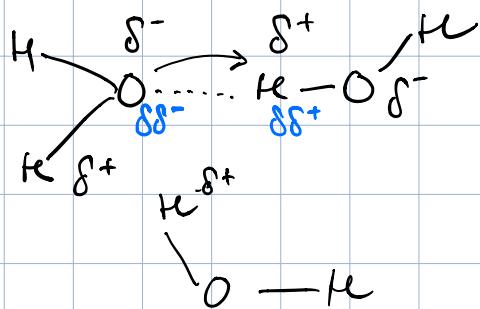
$$E_{\text{angle}} = \frac{1}{2} k_a (\theta - \theta_0)^2$$

$$E_{\text{dihedral}} \sim \dots$$





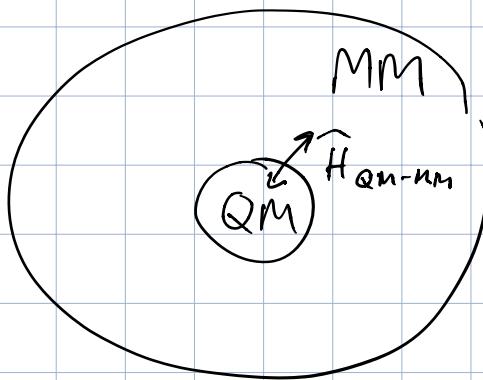
polarization



1) flowing charge with constraints

2) induce dipoles

$$\mu_{ind} = \int F_{polariz. field} \, d\mu$$



$$\hat{H} = \hat{H}_{QM} + \hat{H}_{MM} +$$

$$+ \underbrace{\hat{H}_{QM-MM}}_{\text{coupling term}}$$

1) mechanical embedding (ME)

QM-MM interactions = electrostatic

$+ v_{\text{vdw}}$
described at MM level

need q_i & v_{vdw} parameters for
QM region

problem when QM region changes
no QM-MM response

2) electrostatic embedding

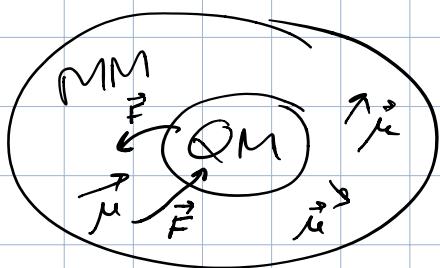
$$\langle 4 | \hat{H}_{\text{QM-MM}} | 4 \rangle = \Delta E_{\text{vdw}} +$$
$$+ \sum_{k \in \text{nuclei}}^{\text{QM}} \sum_{m=1}^{\text{MM}} \frac{Z_k q_m}{r_{km}} + \langle 4 | \sum_{i=1}^{\text{electrons}} \sum_{m=1}^{\text{MM}} \frac{q_m}{r_{im}} | 4 \rangle$$

Charges

QM is aware of MM,
but MM does not know what
happens to QM

3) polarizable embedding

polarizable FF



feedback between
electrostatic fields
in QM and MM