Condensed phase chemistry with the Effective Fragment Potential method

Lyudmila V. Slipchenko,

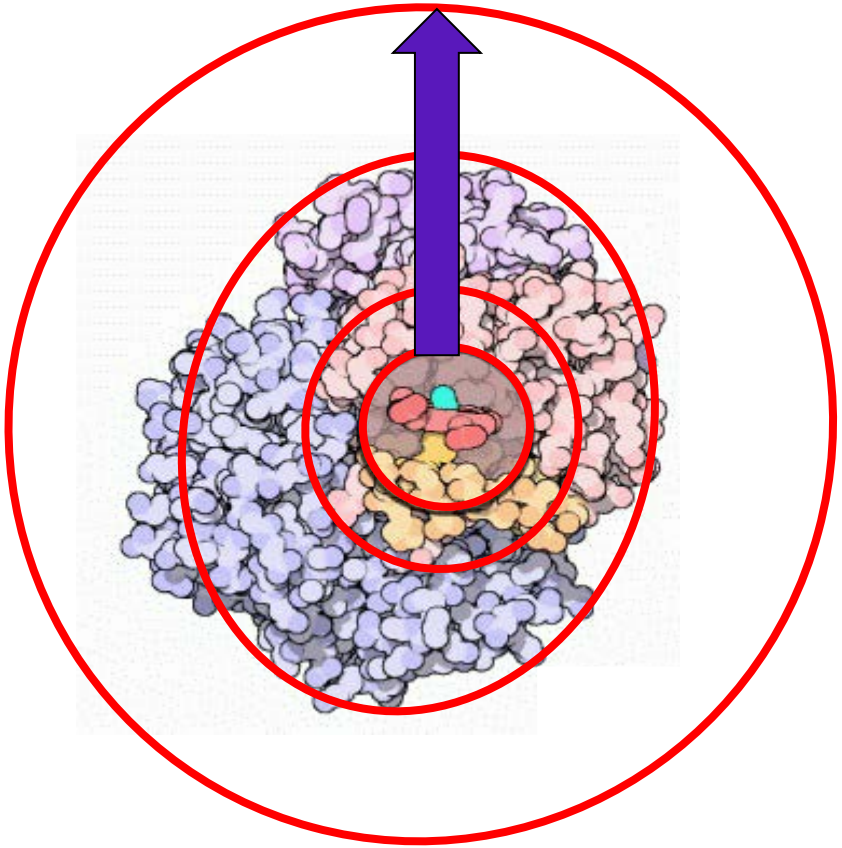
Department of Chemistry, Purdue University

Smart models for big problems

Computational cost and complexity

- Implicit solvent
- Explicit solvent: QM/MM
- Fragmentation techniques
- Semiempirical and DFT
- Linear scaling
- ….

Size of the considered system



Which way do we choose?

V. Vasnetzov: “A Knight at the Crossroads”

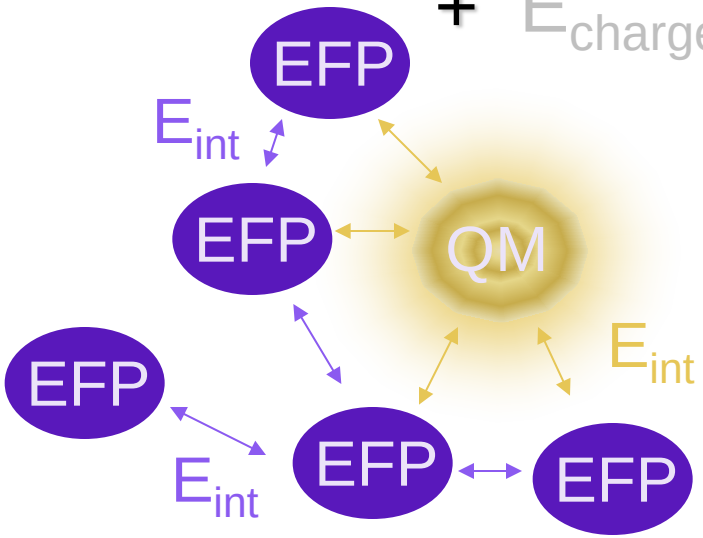
Effective Fragment Potential method

Perturbation theory applied to non-interacting fragments

$$E_{interaction} = E_{coulomb} + E_{polarization} + E_{dispersion} + E_{exchange\text{-}repulsion} + E_{charge\text{-}transfer}$$

long-range perturbation theory

short-range perturbation theory



distributed approach used for all terms

Day et al, *J. Chem. Phys.* **1996**, *105*, 1968-1986;
Gordon et al, . *Phys. Chem. A* **2001**, *105*, 293-307;
Gordon et al, *Ann. Rep. Comp. Chem.*, **2007**, *3*, 177-193;
Ghosh et al, *J. Phys. Chem. A* **2010**, *114*, 12739-12754

EFP set-up

1. Preparation of EFP fragment parameters

✓ general fragment: MAKEFP run (GAMESS)

a set of ab initio calculations on each unique fragment

- Coulomb: set of point multipoles (DMA)
- Polarization: static polarizability tensors at LMO (coupled HF)
- Dispersion: dynamic polarizability tensors at LMO (TDHF)
- Exchange-repulsion: wave function & Fock matrix (HF)

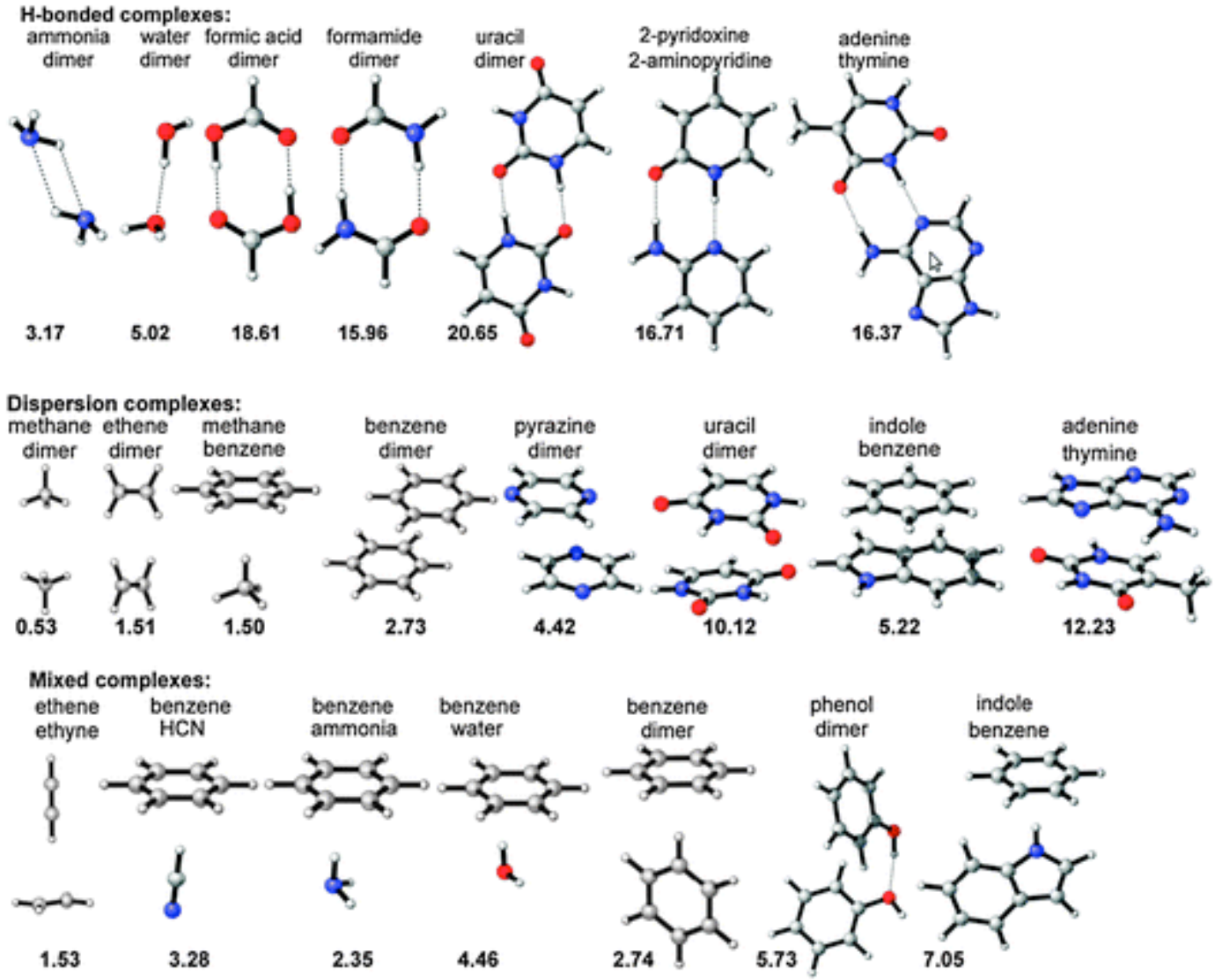
✓ precomputed EFP fragment from library

solvents, ions, DNA bases, amino-acid residues

2. EFP calculation (energy, optimization, MD, MC, …)

- EFP-EFP interactions by (semi)-classical formulas
- QM-EFP interactions as 1-electron terms in QM Hamiltonian

S22 dataset of intermolecular interactions



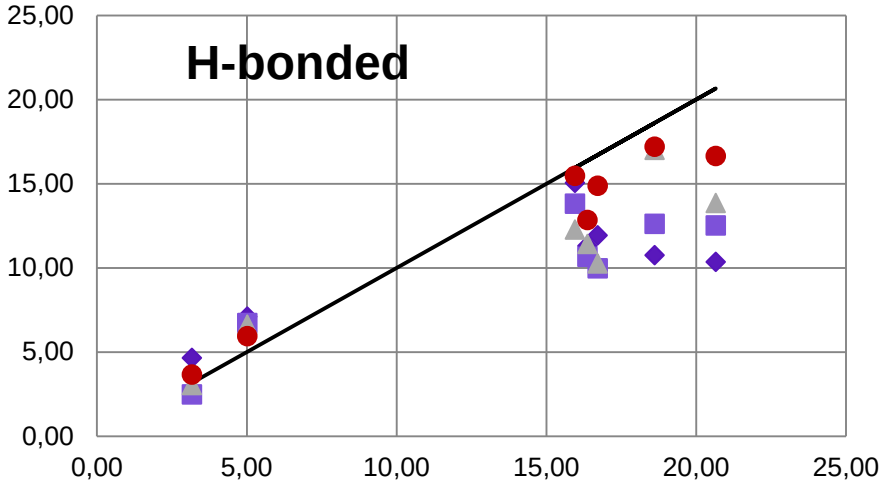
S22: performance of popular methods

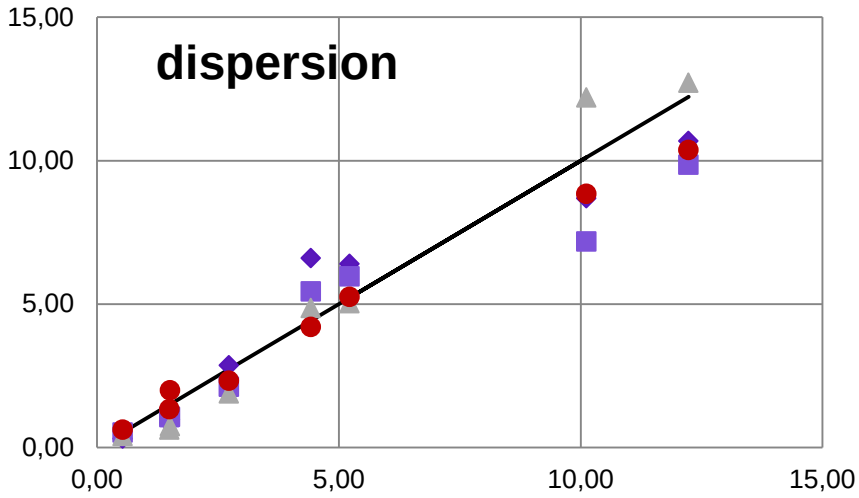
MAD, kcal/mol

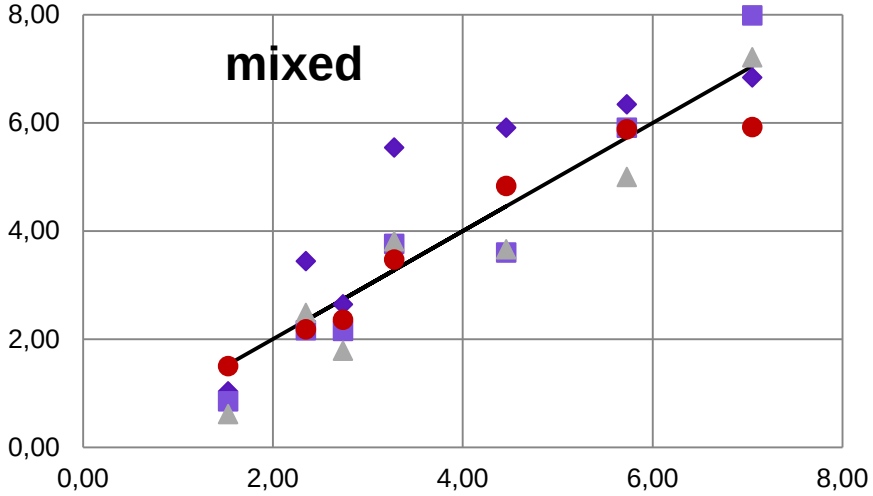
	HB	disp	mixed	overall
HF	3.29	7.24	3.15	4.56
B3LYP	1.77	6.22	2.64	3.54
PBE	1.13	4.53	1.66	2.44
M06	0.89	0.99	0.67	0.85
M06-2X	0.73	0.36	0.32	0.47
ωB97X-D	0.27	0.30	0.42	0.33
MP2	0.24	1.69	0.61	0.88
SCS-MP2	1.54	0.55	0.37	0.80
SCS-CCSD	0.40	0.23	0.08	0.24
Amber	4.64	0.98	0.89	2.12
OPLSAA	4.45	1.07	0.56	1.98
MMFF94	3.61	0.73	0.60	1.61
EFP	1.82	0.57	0.35	0.89
10% error	1.38	0.48	0.39	0.74

J. Chem Theory Comp., *8* (8), 2835–2843 (2012)

S22: performance of force fields





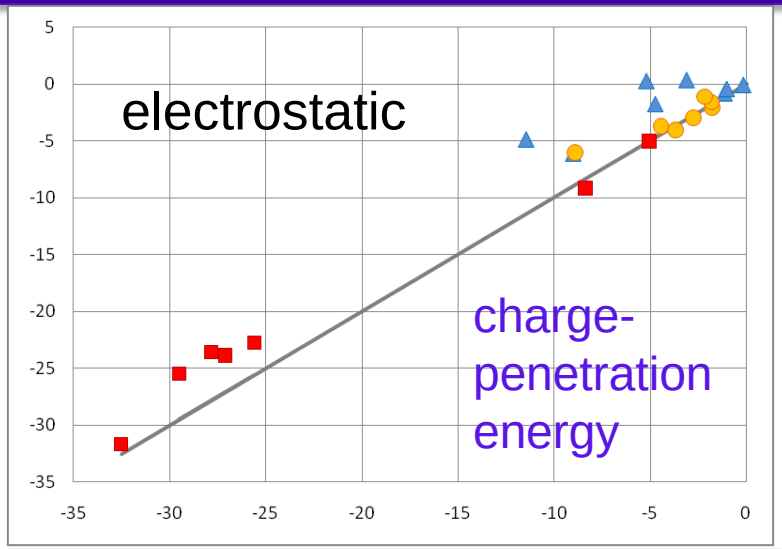


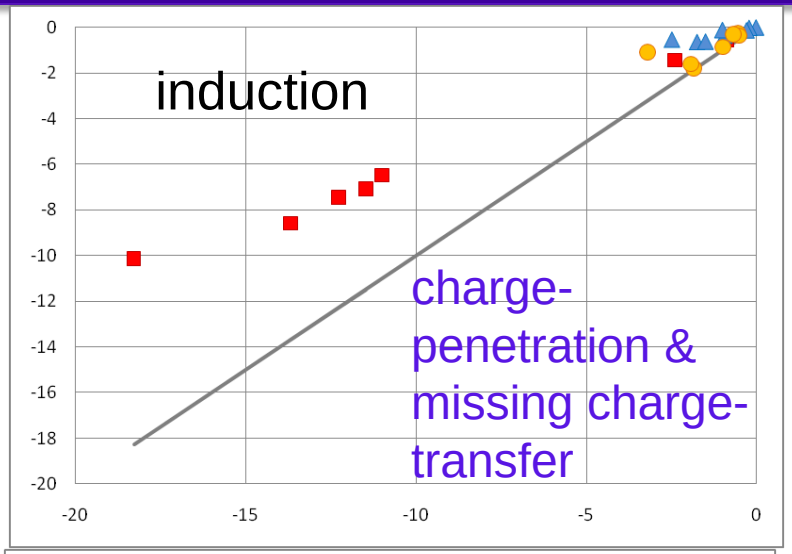
Amber
OPLSAA
MMFF94
EFP

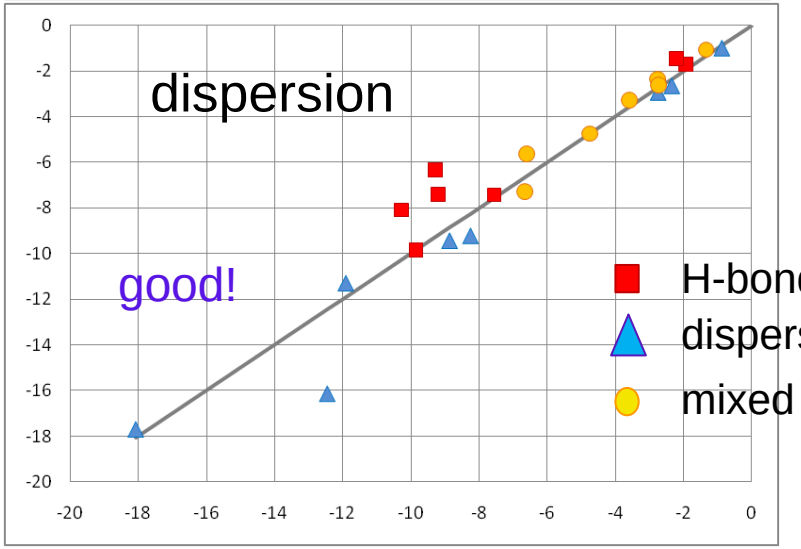
energies in kcal/mol

Paton et al, *J. Chem. Inf. Model. 2009, 49, 944–955*

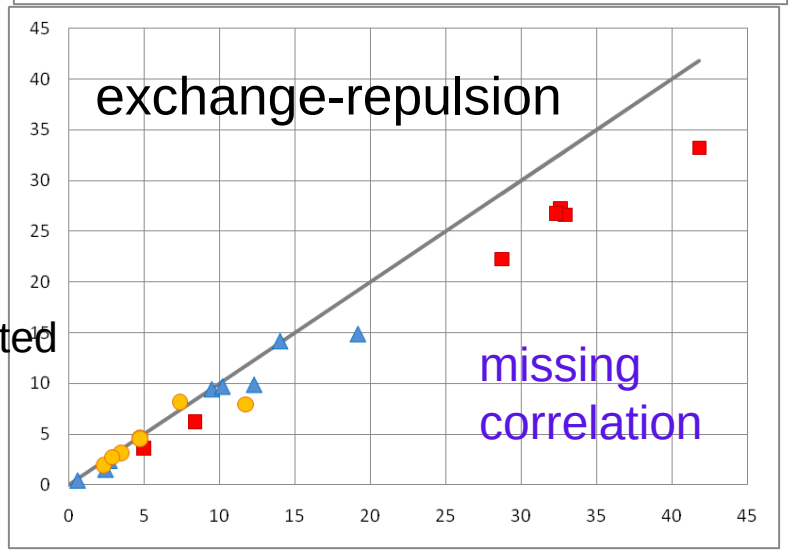
EFP vs SAPT







H-bonded
dispersion-dominated
mixed

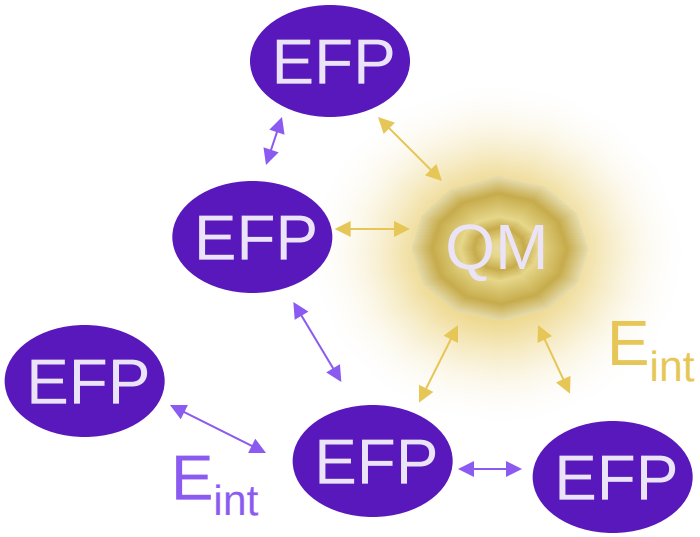


J. Chem Theory Comp., *8* (8), 2835–2843 (2012)

EFP in a nutshell

- rigid-geometry fragment-based polarizable force field
- all EFP force field parameters are obtained from a separate *ab initio* calculation: no fitted parameters
- provides physical insight into intermolecular interaction
- accuracy on S22 benchmark: MAD=0.9 kcal/mol (11-12% relative error)
- to further improve accuracy:
  - better treatment of short-range charge penetration effects (electrostatics & polarization)
  - correlation for exchange-repulsion, polarization and dispersion
  - computationally more affordable charge-transfer term

QM / EFP



solute

solvent

$$\hat{H} = \hat{H}_{QM} + \hat{H}_{EFP} + \hat{H}_{QM/EFP}$$

coupling term

$$\hat{H}_{QM/EFP} = \hat{H}^{el} + \hat{H}^{pol} + \hat{H}^{disp} + \hat{H}^{exch-rep}$$

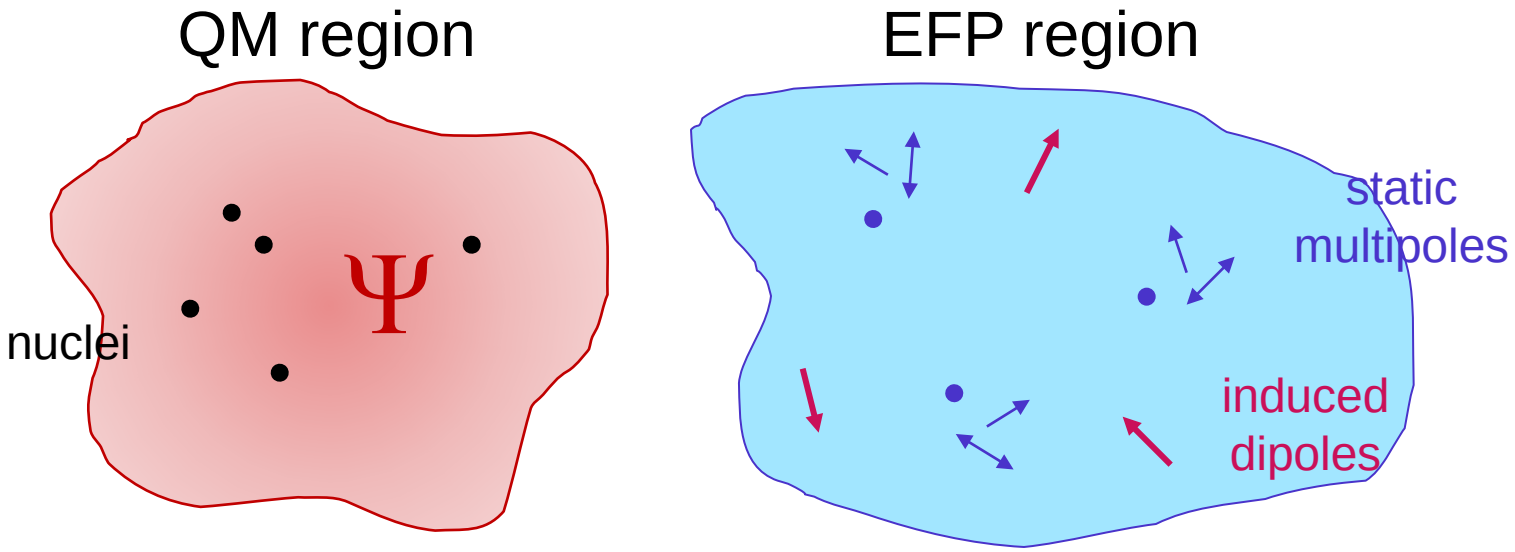
one-electron terms
in quantum Hamiltonian

under development:

Annu. Rev. Phys. Chem., *64,* 553-78 (2013);

J. Chem. Phys. *136*, 244107 (2012)

Self-consistent polarization



Induced dipole

$$\mu_\gamma = \alpha_{\gamma\alpha} F_\alpha^{total}$$

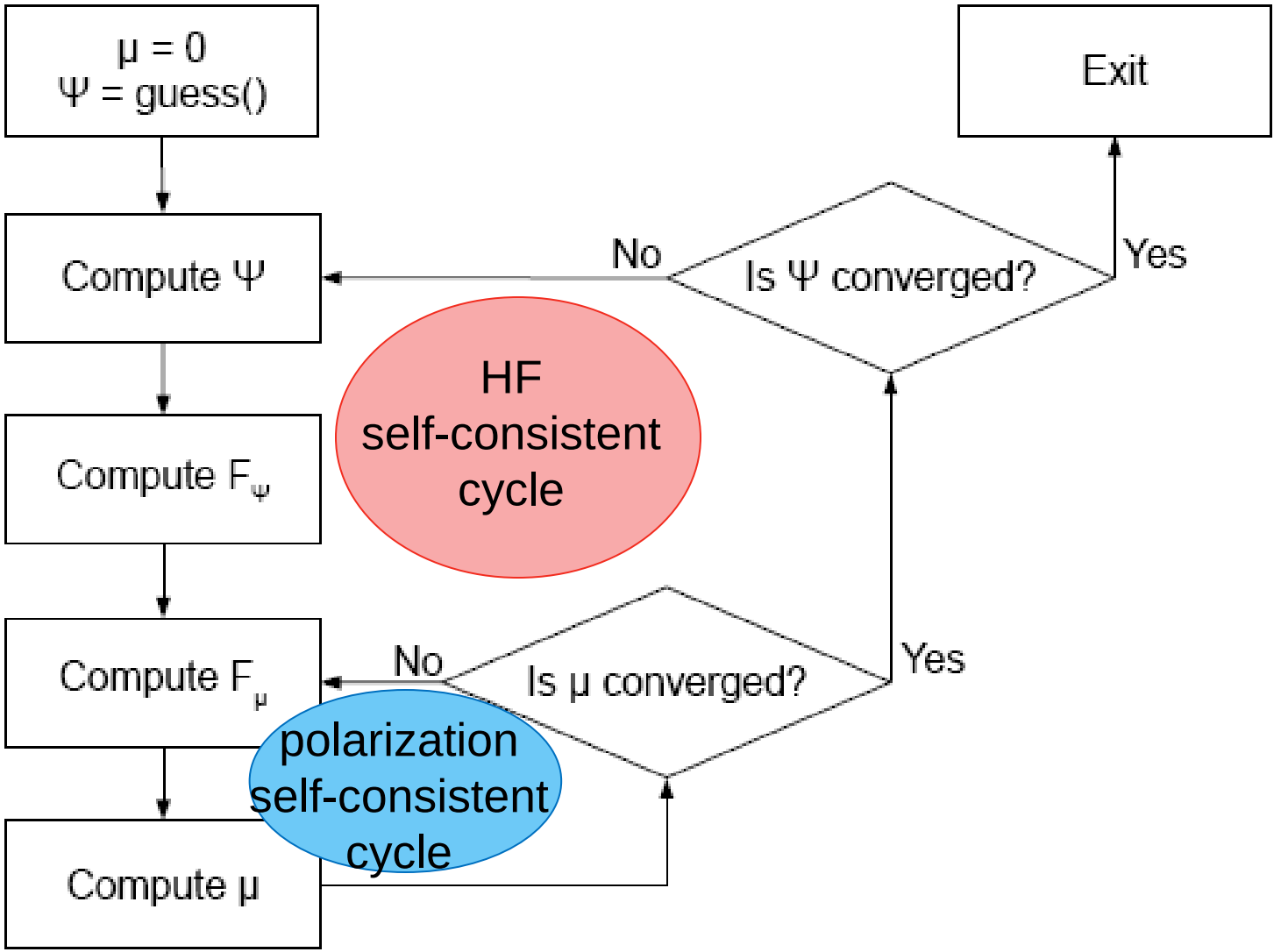
total field

polarizability tensors

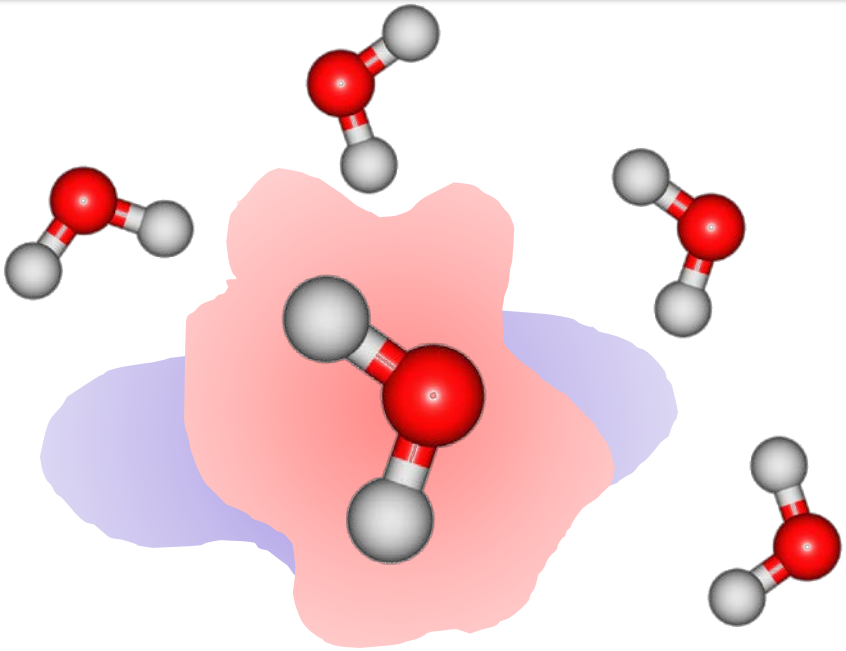
$$F^{total} = \Sigma (F^{mult} + F^{ind}) + F^{ai} + F^{ai\text{-}nuc}$$

$$E^{pol} = -\tfrac{1}{2} \Sigma \mu (F^{mult} + F^{ai\text{-}nuc}) + \tfrac{1}{2} \Sigma \mu F^{ai}$$

Polarization within HF cycle



QM/EFP for the electronic excited states



Generally, each excited state has different electron density & charge distribution ➡ different response from environment

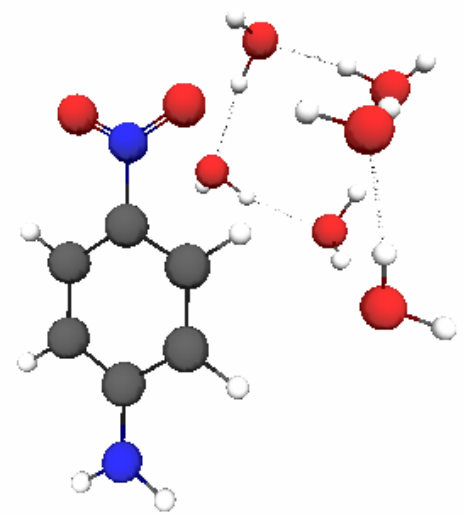
Polarization correction to the excitation energy due to polarizable environment (using one-electron excited state density):

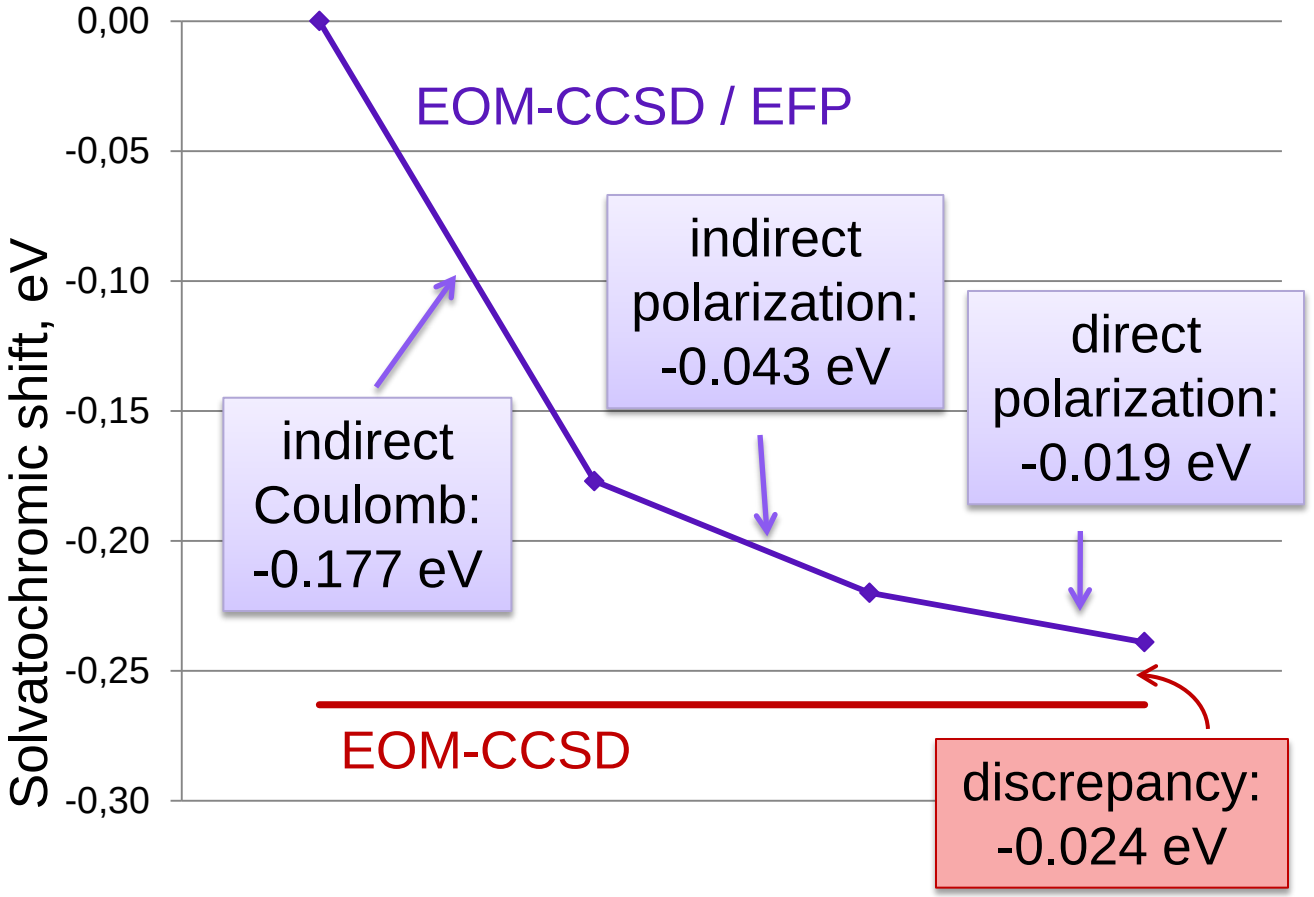
$$\Delta E^{pol} = E^{pol,ai}(\mu^{ex}) - E^{pol,gr}(\mu^{gr}) - \Sigma(\mu^{ex} - \mu^{gr})F^{ai,ex}$$

leading correction to the interaction between μ^{ex} and Ψ^{ex}

Thompson & Schenter, JPC 99, 6374 (1995)

Composition of solvatochromic shift

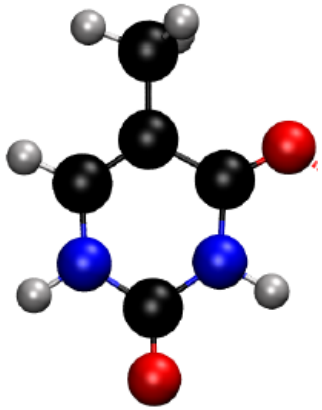


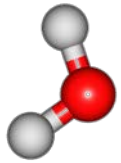


Indirect terms: orbital relaxation of the solute in the electrostatic field of the solvent
Direct polarization: repolarization of the environment as a response to a change of the electronic wave function in the excited state

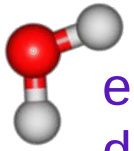
Vertical ionization energy of hydrated thymine

Dr. Debashree Ghosh (USC)

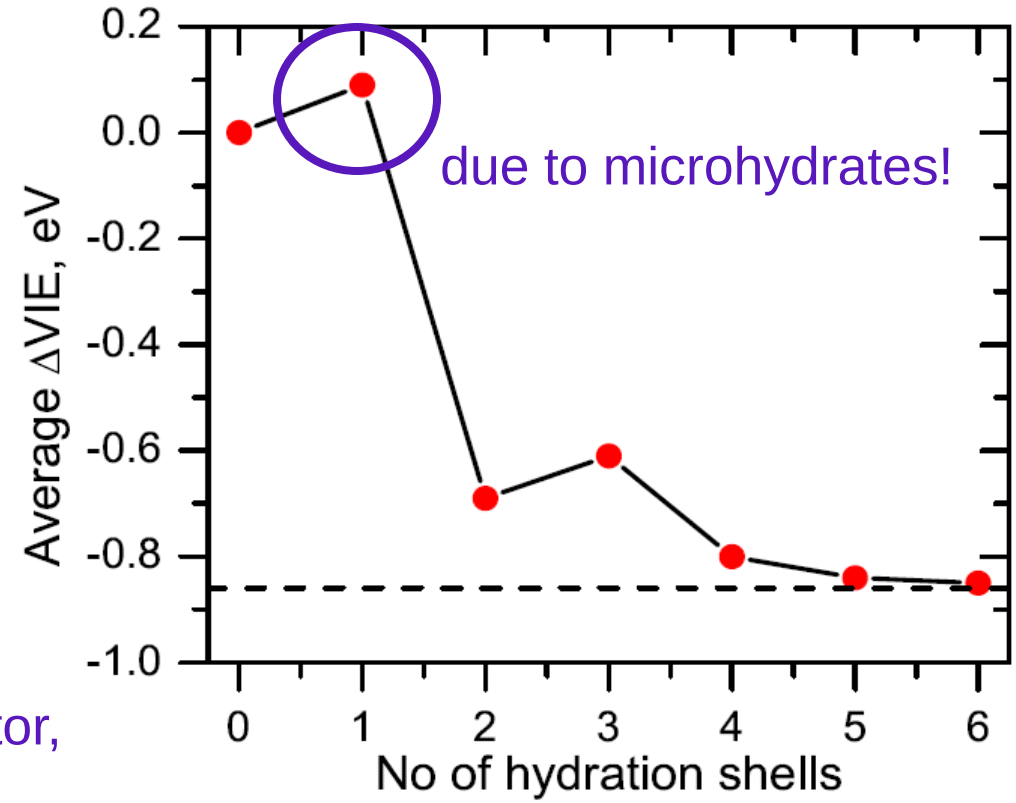




electron acceptor, increases VIE



electron donor, decreases VIE

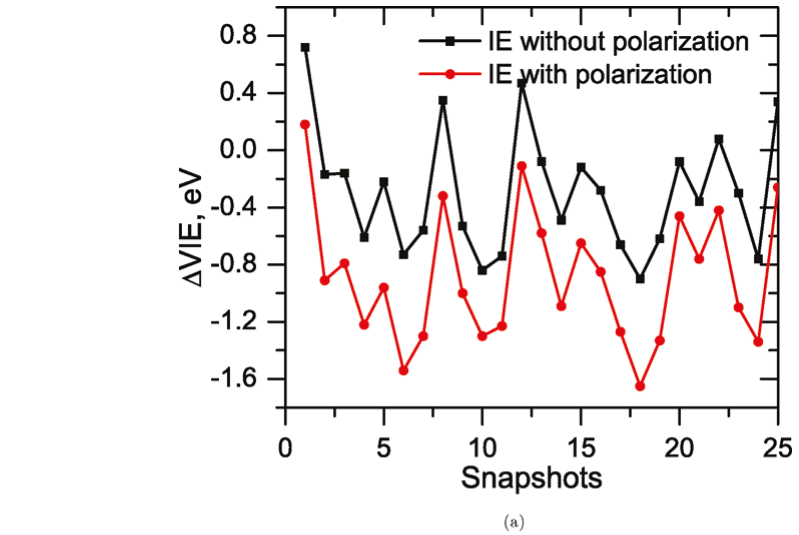


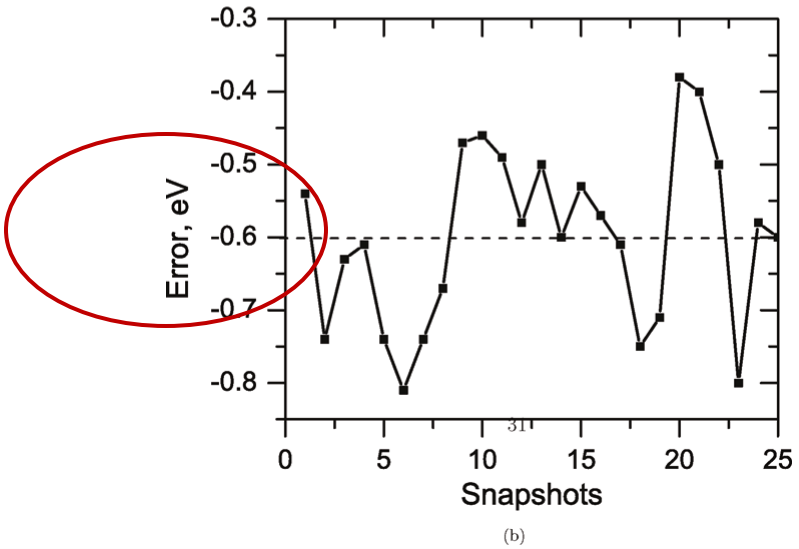
EOM-IP-CCSD/EFP

Ghosh, Isayev, Slipchenko, Krylov, JPCA **115**, 6028 (2011)

Vertical ionization energy of hydrated thymine

Polarization of environment is extremely important!





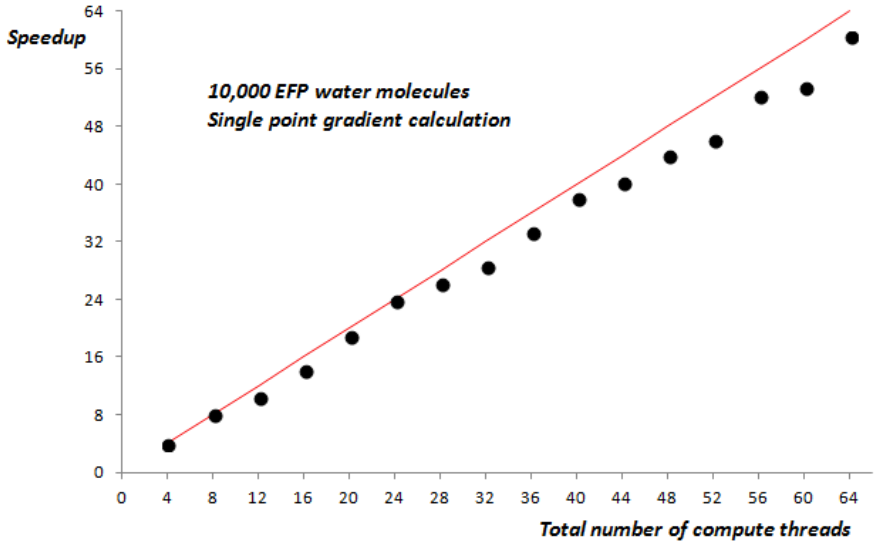
LIBEFP: stand-alone EFP implementation

- written in standard C99
- uses native EFP data format generated by GAMESS
- 2-clause BSD license
- uses BLAS wherever possible for better performance
- available as a shared or static library
- parallelization across multiple nodes using hybrid MPI/OpenMP

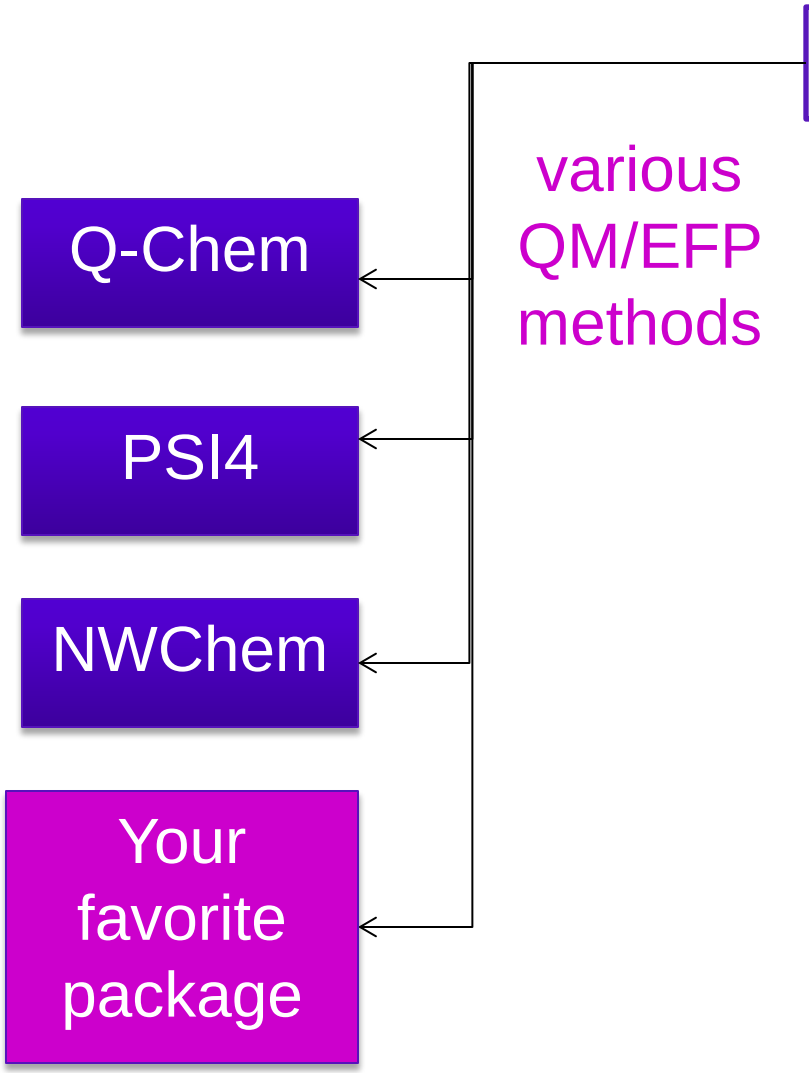
Kaliman and Slipchenko, JCC 34, 2284 (2013)

Dr. Ilya Kaliman

http://www.libefp.org/

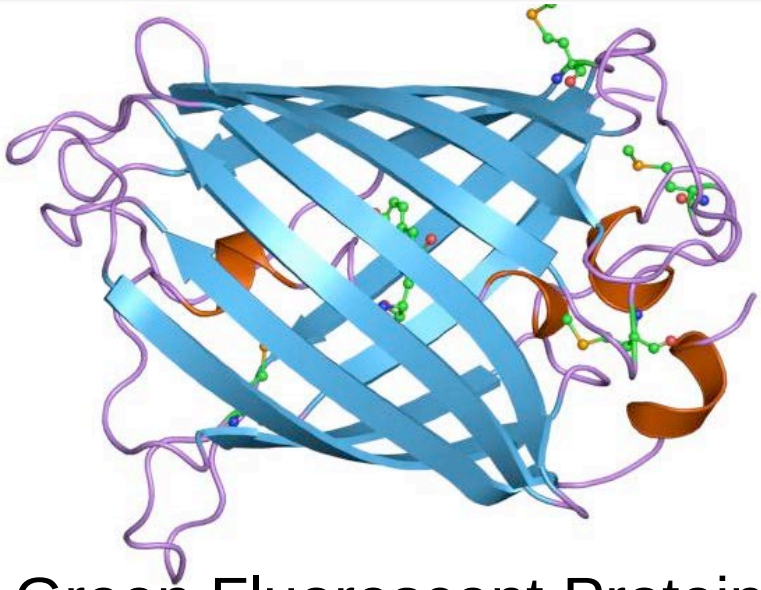


LIBEFP

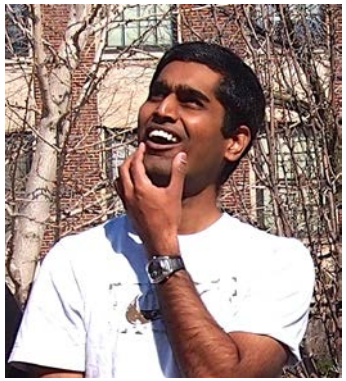


- distributed with *LIBEFP* code
- single point energy and analytical gradient calculation
- geometry optimization using efficient LBFGS optimizer
- molecular dynamics in NVE, NVT, and NPT ensembles
- seminumerical Hessian and normal mode analysis
- simulation of periodic systems

Macromolecules and polymers



Green Fluorescent Protein



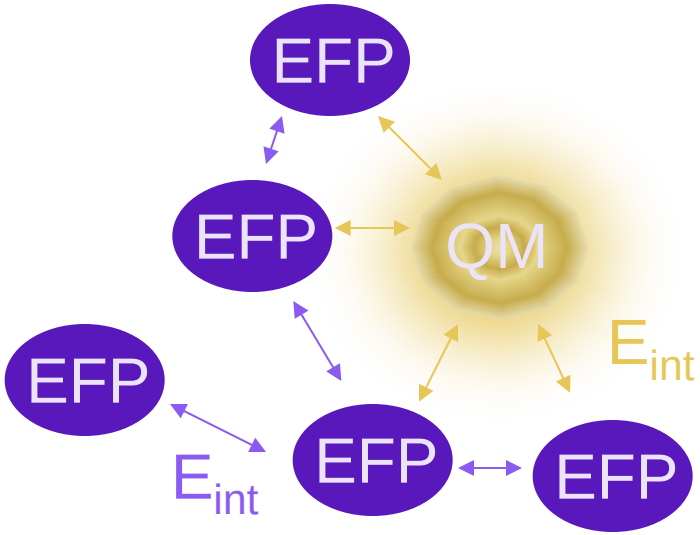
Pradeep Gurunathan

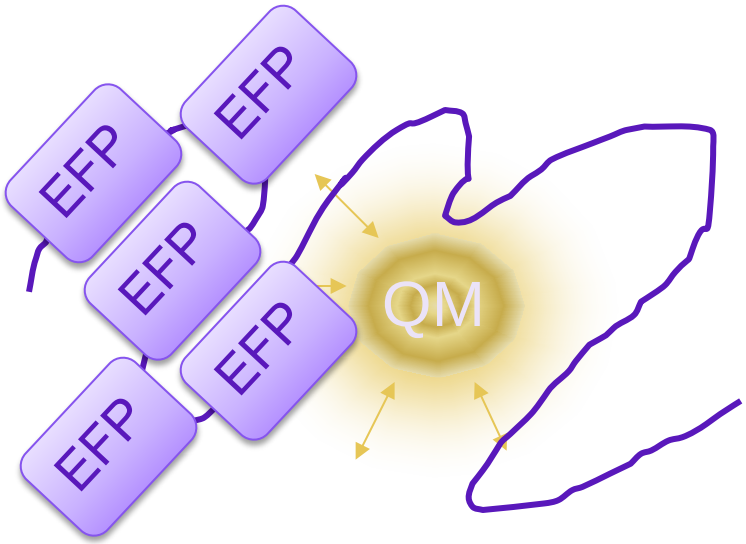
- Is polarization important in biology and materials?
- Is accurate electrostatics needed there?
- Will we obtain a qualitatively different answer substituting simple classical force fields with a more detailed representation of macromolecules?

Challenge:

extend QM/EFP to macromolecules and polymers

BioEFP: EFP for polymers





Original EFP

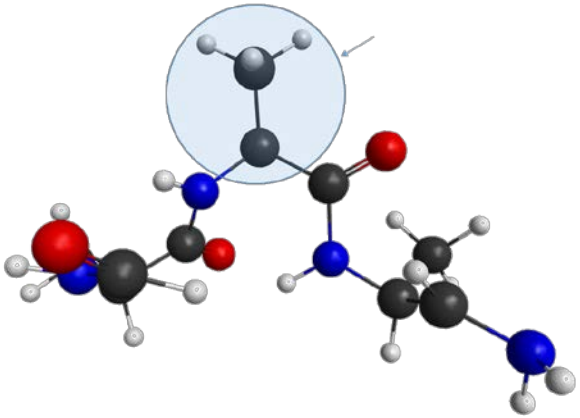
- rigid-geometry fragment-based polarizable force field
- EFP parameters are obtained from *ab initio* calculations on a gas phase fragment
- describes intermolecular interactions

BioEFP

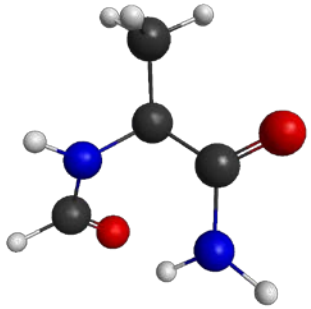
- split macromolecule into fragments
- prepare parameters for each fragment
- develop mechanism to describe covalent interactions between neighboring fragments
- watch out for polarization madness

Preparing parameters for bio-fragments

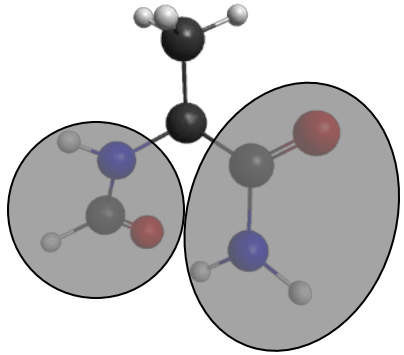
Target fragment



- groups to the left and right are added
- fragmented bonds are saturated with hydrogens

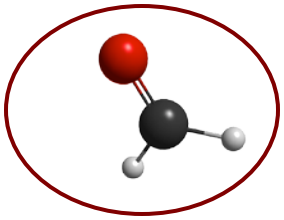


- parameters for the ‘extended’ fragment are generated

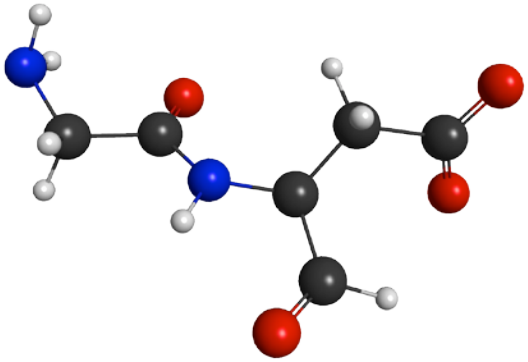


- only parameters of the target fragment are left,
- all extra points are deleted

Polarization in QM/BioEFP



CH_2O: QM



LYS-ASP
EFP: 1 fragment
BioEFP: 3 fragments

Shifts, eV

CH_2O, gas phase	3.9735
CH_2O + LYS-ASP	
full QM	0.0417
QM/EFP	0.0410
QM/BioEFP	0.0432

BioEFP reproduces original EFP results

BioEFP summary

BioEFP provides a parameter-free description of environment effects on photochemical events in biology and materials

Automatic preparation of the system:

PDB file ->

geometries of fragments ->

calculation of fragment parameters (jobs submitted to GAMESS) ->

removing extra points ->

generating input file for QM/BioEFP

Computational cost:

- cost of QM calculation on a chromophore
- generating EFP parameters (e.g., for GFP protein: ~2 days at 40 cores)

Geometry can be relaxed:

MD of frozen-geometry fragments covalently linked by classical potentials is implemented

Conclusions

- EFP is first-principles based polarizable force field
- EFP is similar in accuracy to MP2; superior to classical force fields
- *LIBEFP* stand-alone EFP implementation ready for interfacing with *ab initio* software
- QM/EFP methods:
  - polarizable embedding for the electronic excited states
  - robust tool for systems with complicated electronic structure in non-homogeneous environments
- BioEFP: extension of EFP to polymers
  - work in progress

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Ksenia Bravaya
Adele Laurent

Group:
Ben Nebgen
Pradeep Gurunathan
Carlos Borca
Yen Bui
SungMin Hong

Former group members:
Dr. Mandy Green
Dr. Ilya Kaliman
Dr. Dmytro Kosenkov
Mike Hands
Dr. Frank Emmert
Dr. Levi Haupert
Stephanie Thompson
Joanna Flick