Excited States and Nonadiabatic Dynamics
Cybertraining Workshop 2022

QM/MM Simulation for Excited States

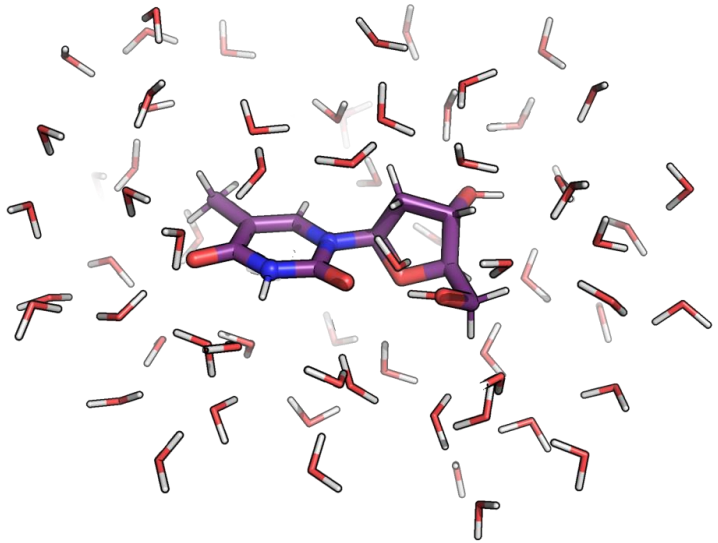
Davide Avagliano

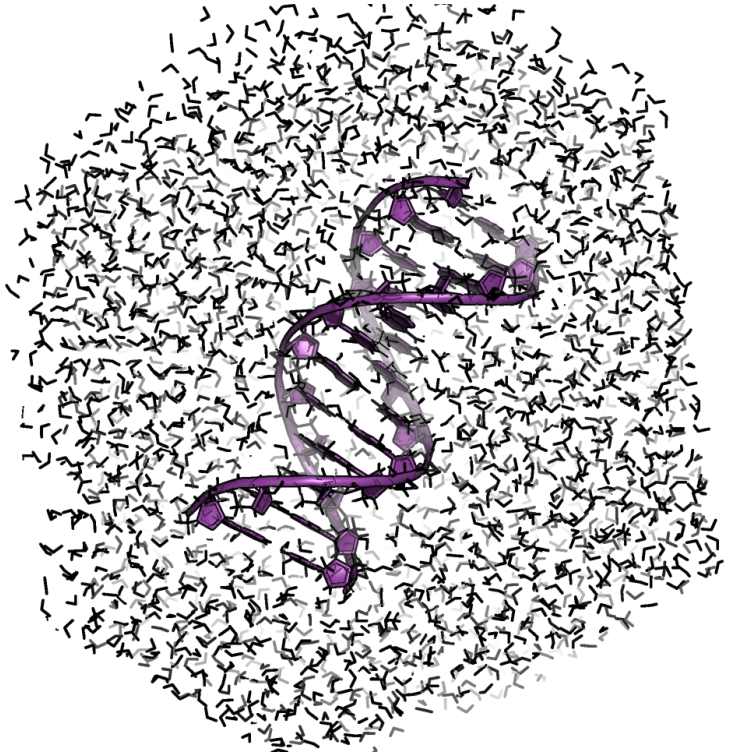
University of Bologna

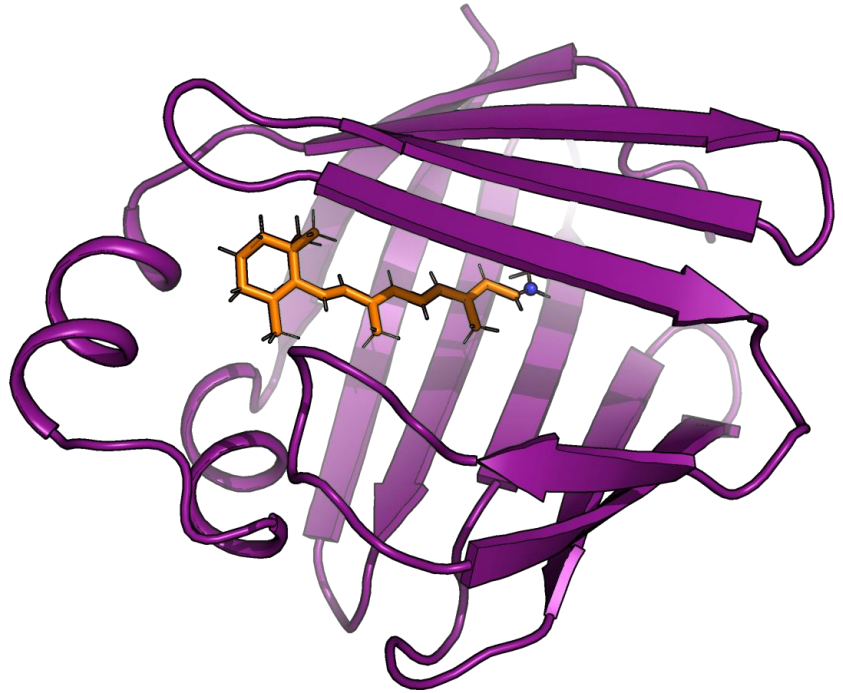
Buffalo, July 3-15 2022

Photo-induced processes

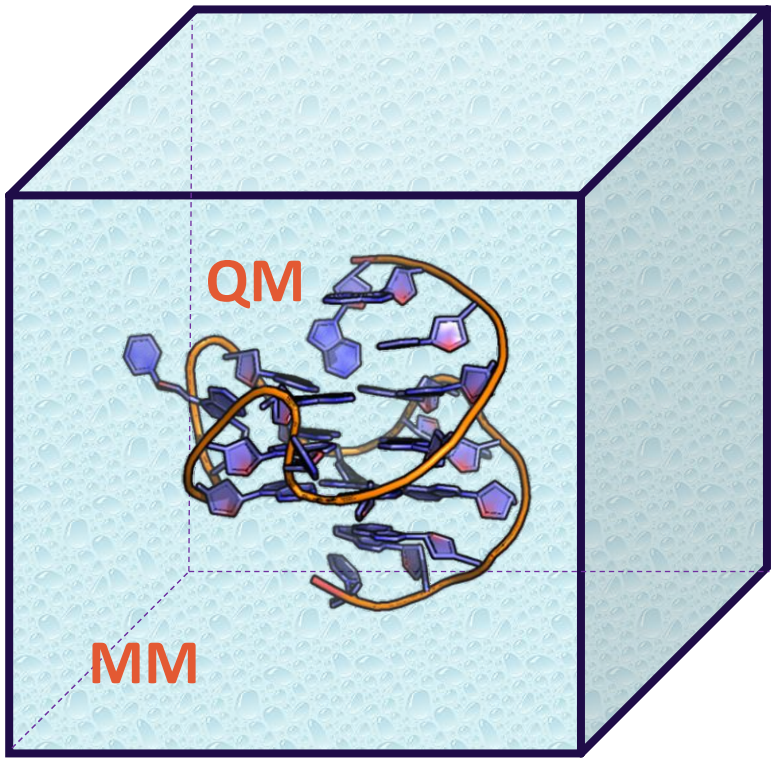
Photo-induced processes







QM/MM



$$i\hbar \frac{\partial}{\partial t} \psi(R,r,t) = \hat{H} \psi(R,r,t)$$

We know how to solve TDSE!

We know we cannot!

do we always need high accuracy?

for the full system?

we can introduce mindful approximations

QM/MM

J. Mol. Biol. (1976) **103**, 227–249

Theoretical Studies of Enzymic Reactions:

Dielectric, Electrostatic and Steric Stabilization of the Carbonium Ion in the Reaction of Lysozyme

A. Warshel and M. Levitt

Medical Research Council Laboratory of Molecular Biology
Hills Road, Cambridge CB2 2QH, England

and

Department of Chemical Physics
The Weizmann Institute of Science
Rehovot, Israel

(Received 12 September 1975, and in revised form 10 February 1976)

A general method for detailed study of enzymic reactions is presented. The method considers the complete enzyme–substrate complex together with the surrounding solvent and evaluates all the different quantum mechanical and classical energy factors that can affect the reaction pathway. These factors

$$i\hbar \frac{\partial}{\partial t} \psi(R,r,t) = \hat{H} \psi(R,r,t)$$

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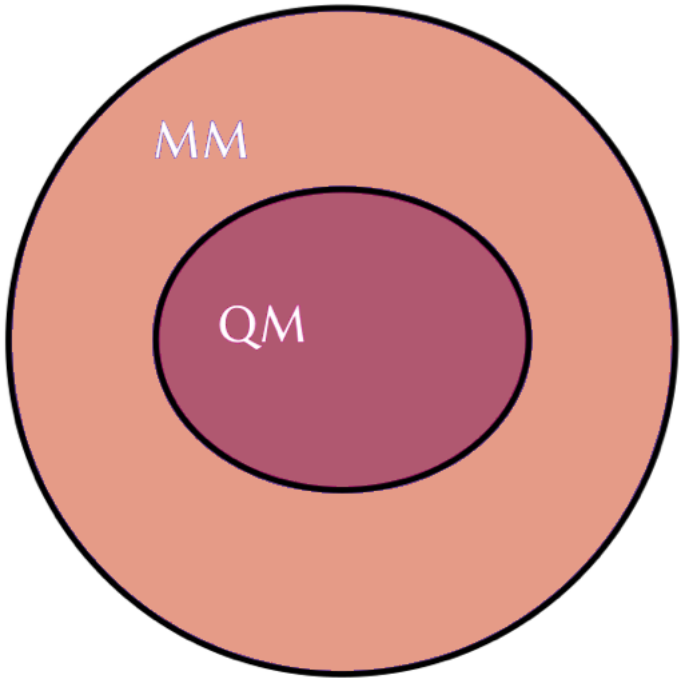
QM/MM energy

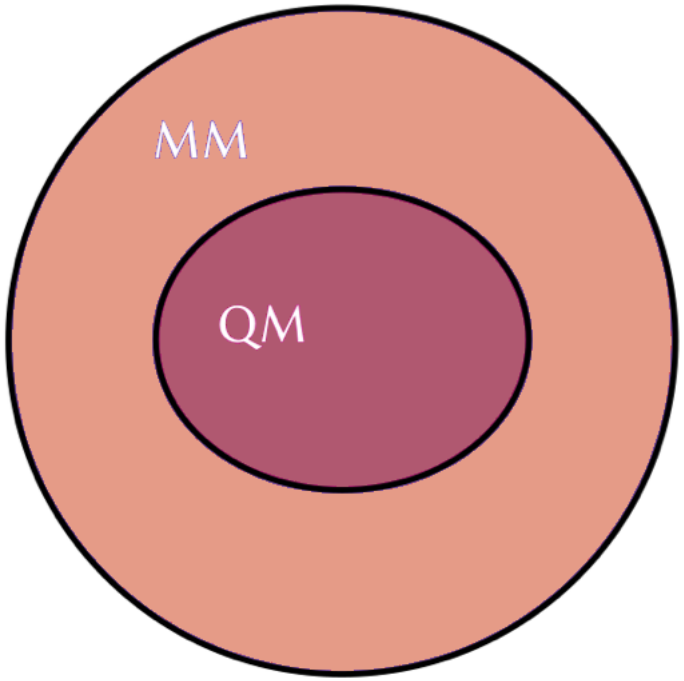
QM/MM energy



Divide the system in region treated at different levels of theory

e.g. quantum mechanically (QM) and classically (MM)

QM/MM energy



Divide the system in region treated at different levels of theory

e.g. quantum mechanically (QM) and classically (MM)

different schemes

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additive scheme

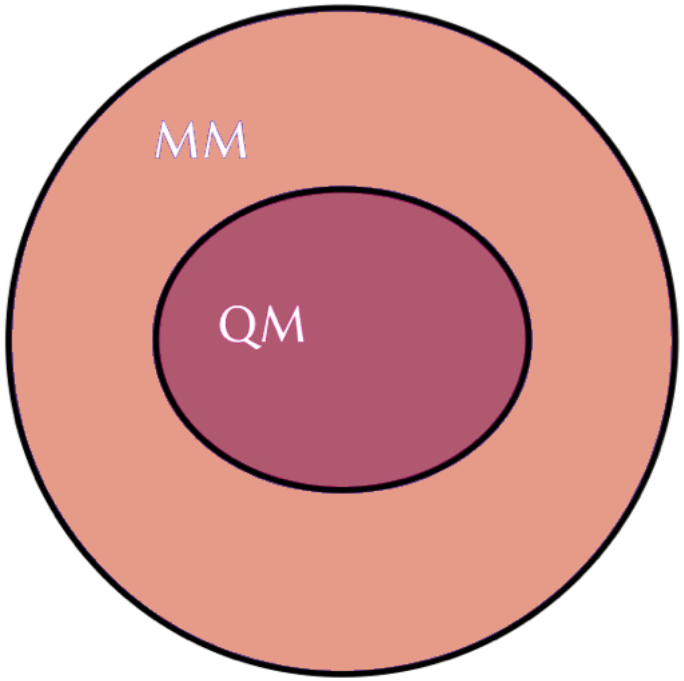
$$\hat{H}_{QM/MM} = \hat{H}_{QM} + \hat{H}_{MM} + \hat{H}_{emb}$$

---

subtractive scheme

$$\hat{H}_{QM/MM} = \hat{H}_{QM} + \hat{H}_{(QM+MM)} - \hat{H}_{QM[MM]} + \hat{H}_{emb}$$

QM-MM coupling



electrostatic and dispersive interactions to be included

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mechanical embedding

embedding interactions calculated at classical level

---

electrostatic embedding

MM point charges incorporated in the Hamiltonian

QM *e* density polarized by the charges

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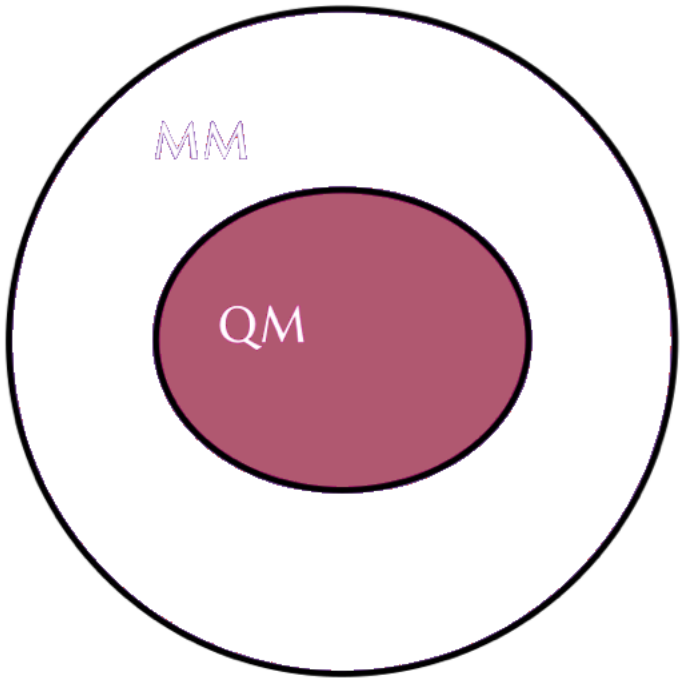
polarizable embedding

Each MM atom bears a charge and a polarizability

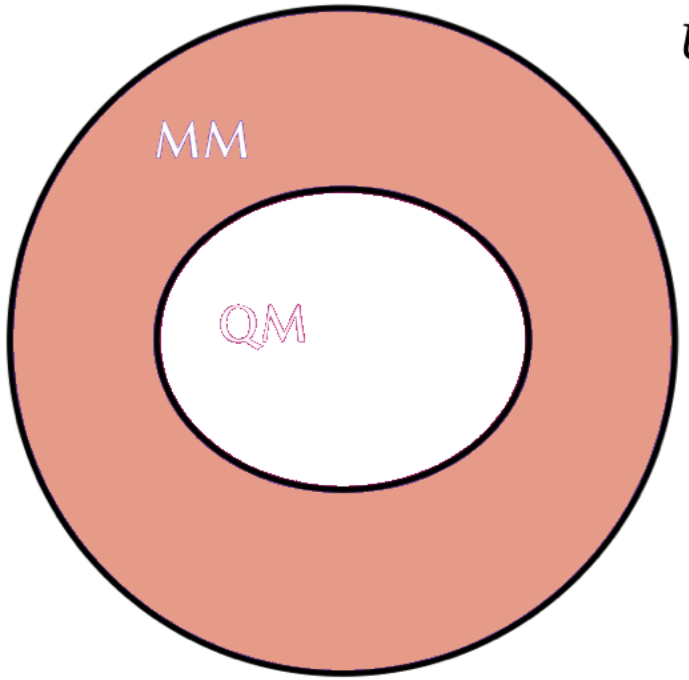
polarization induced by the electric field

QM energy



- Multi-configurational
  - CASSCF
  - RASPT2
  - CASPT2 (SS,MS,XMS)
- Single reference
  - CC
  - ADC
  - TD-DFT

MM energy



Force Field

$$U^{TOT} = U^{bonding} + U^{non-boding}$$

Bonding term

$$U_{stretching} = \sum_{bonds} k_b(r - r_{eq})^2$$

$$U_{bending} = \sum_{angles} k_\theta(\theta - \theta_{eq})^2$$

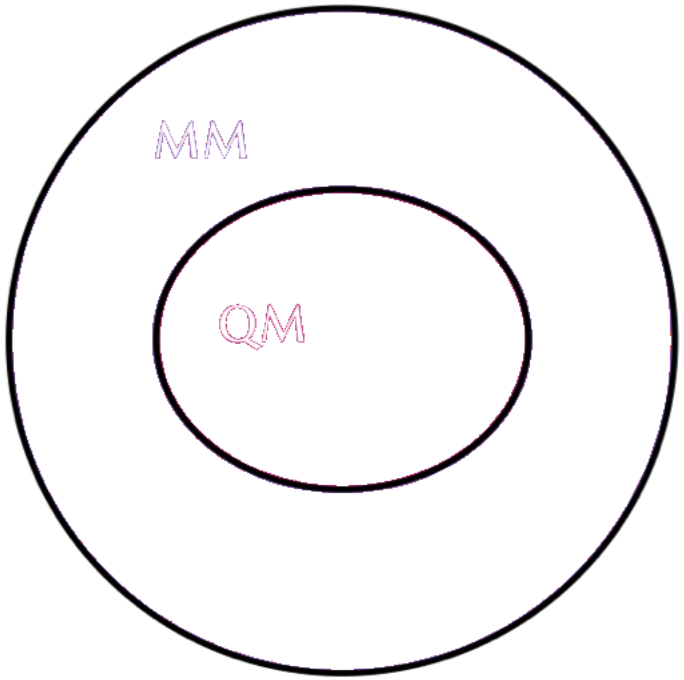
$$U_{dihedrals} = \sum_{dihedrals} \frac{k_d}{2}[\cos(n\tau)]$$

Non-bonding term

$$U_{LJ} = 4u\left[\left(\frac{\zeta}{R_{1,2}}\right)^{12} - \left(\frac{\zeta}{R_{1,2}}\right)^{6}\right]$$

$$U_{electrostatic} = \frac{q_1 q_2}{4\pi e_0 R_1 R_2}$$

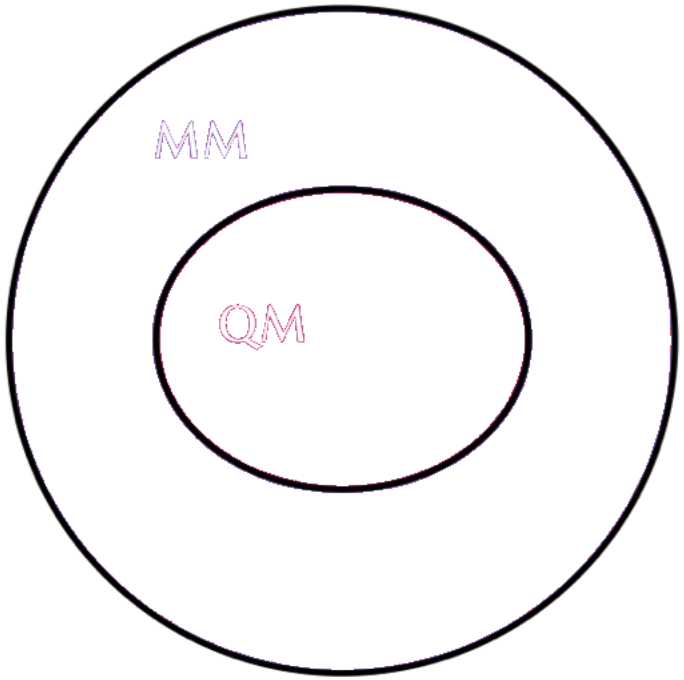
Boundary region



QM-MM boundary

System boundary

QM-MM boundary



QM-MM boundary

depends on the system

can involve covalent bonds

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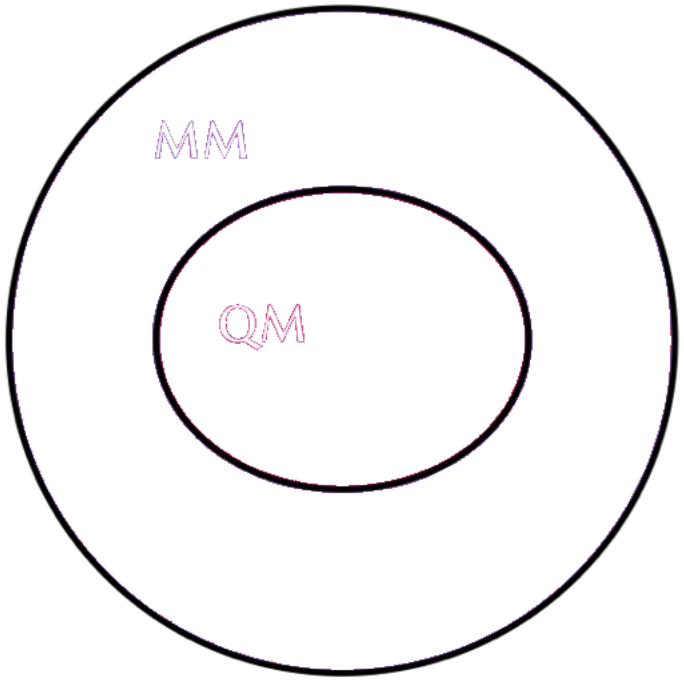
truncation of a covalent bond creates unrealistic and artificial system

enhanced over-polarization

QM-MM boundary



QM-MM boundary

covalent bonds

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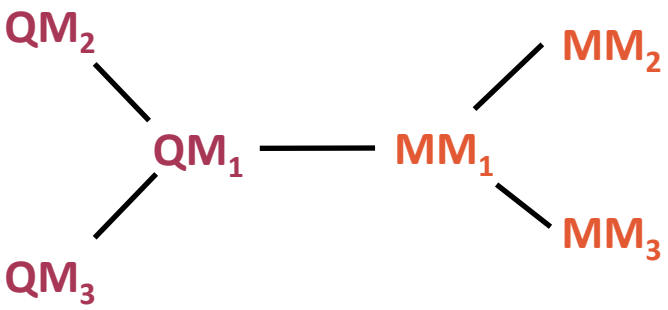
frozen orbital

boundary atom

link atom

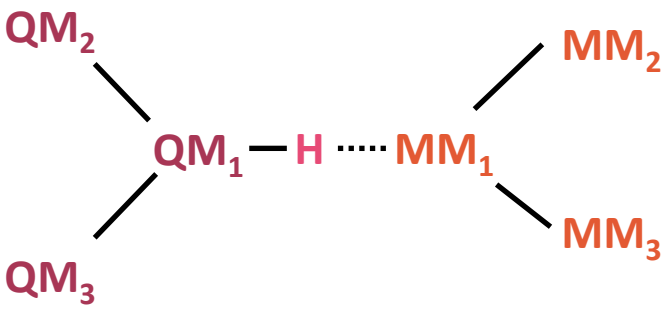
Link-atom

Link-atom



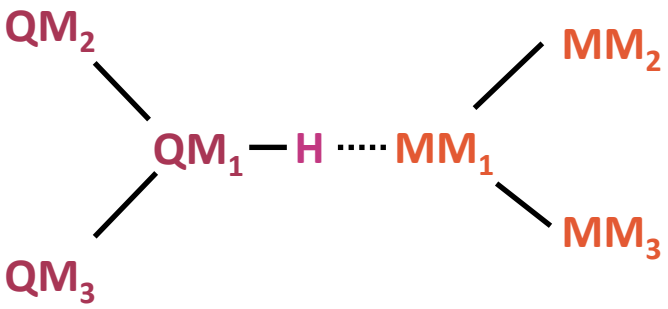
Link-atom

Link-atom

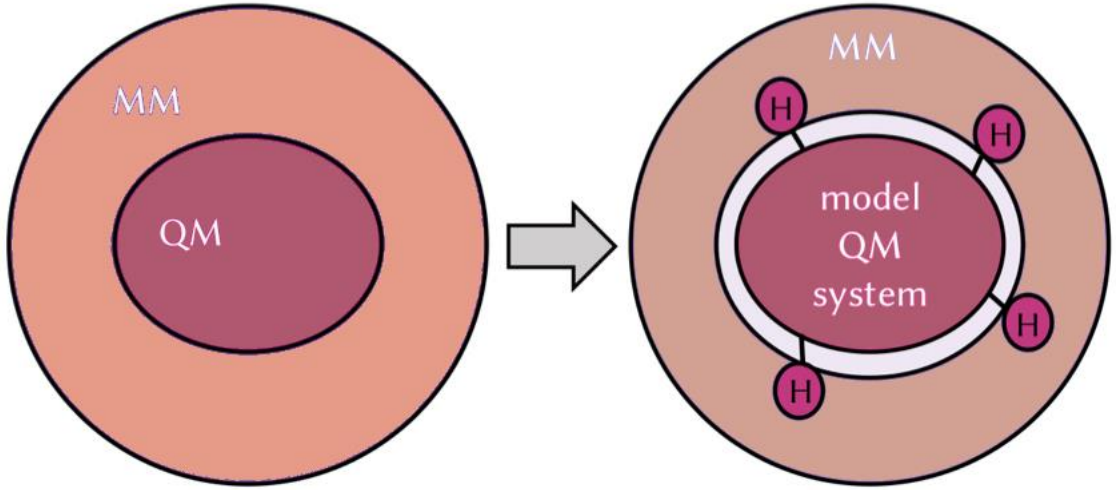


link-atom approach

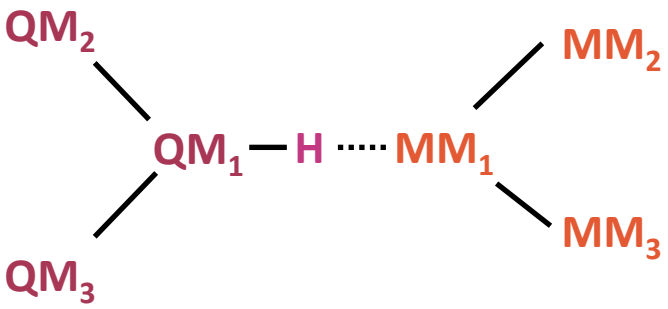
Link-atom

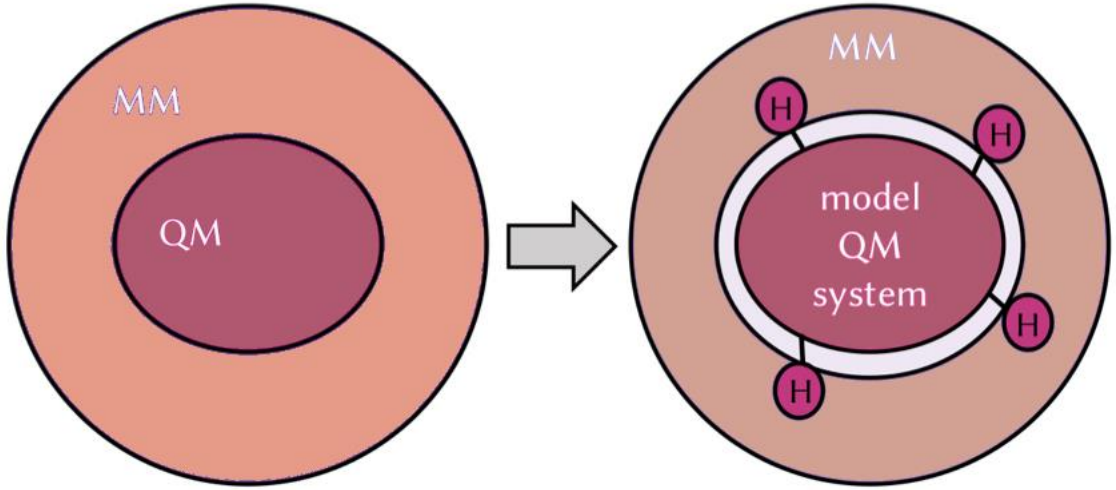


link-atom approach



Link-atom





link-atom approach

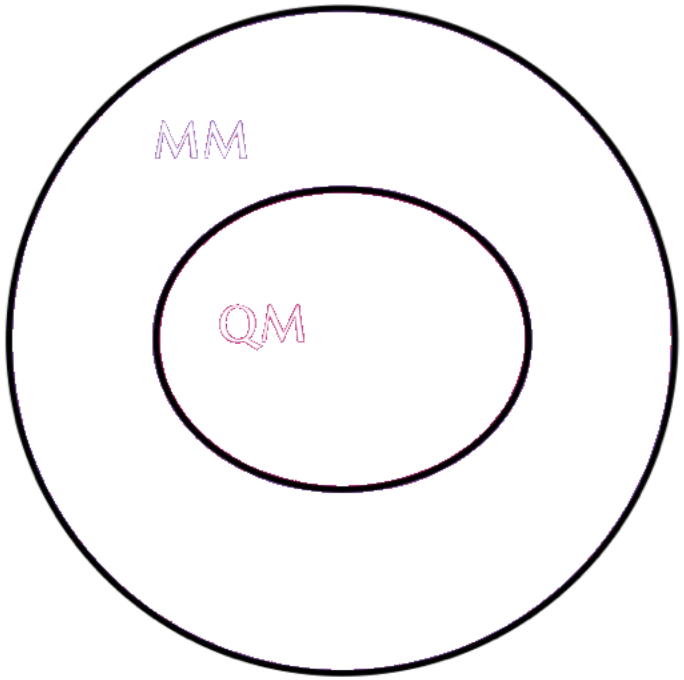
redistribution of the charge

MM blind to the H

distance QM_1-H constrained

gradient of H projected over QM_1 and MM_1

System boundary

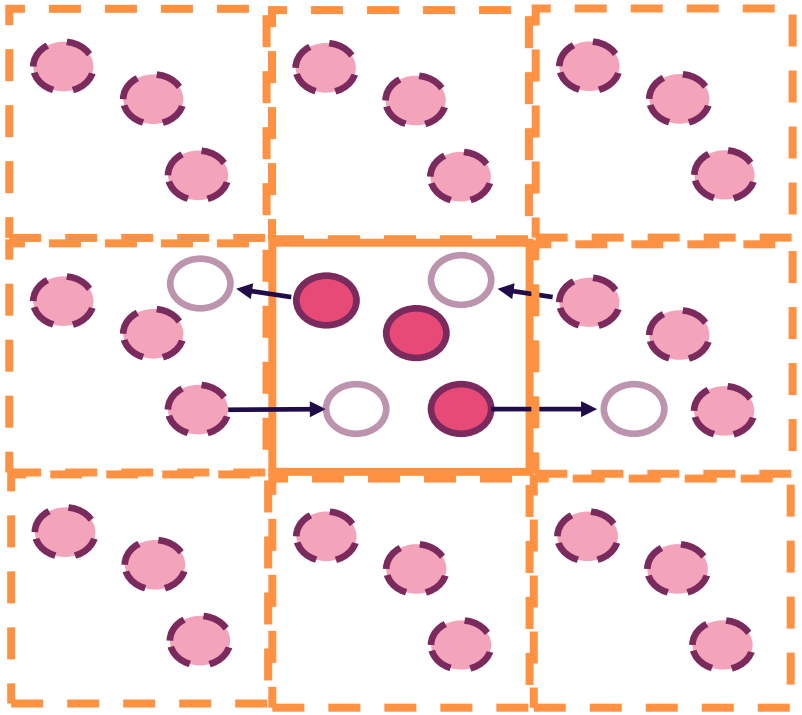


System boundary

System boundary

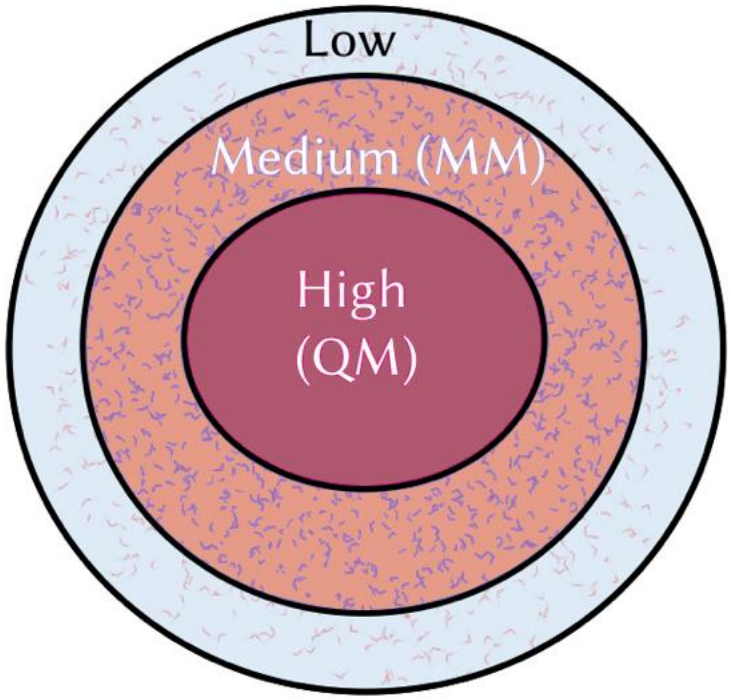
Periodic boundary condition

Ewald summation



finite-system approach - droplet

generalization to more layers (ONIOM-like)



Excited states and QM/MM

solvent and environment alter excited state:
energies, properties, decay..

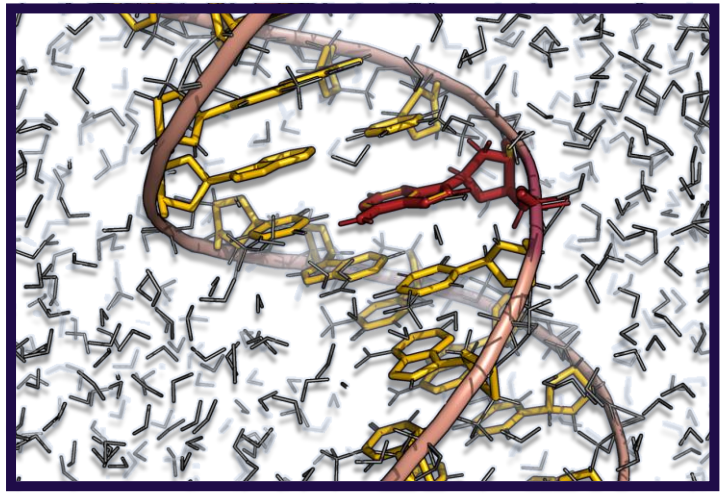
environment response slower than dynamics

solvent response is different for each electronic state

statistically meaningful representation

no FF parametrized ad hoc

small implementations required



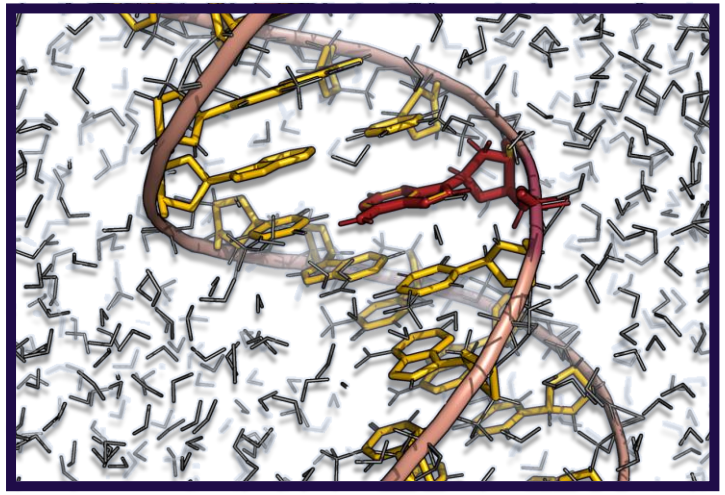
Methodology and test cases

Configurational and phase spaces sampling

spectroscopic proprieetis

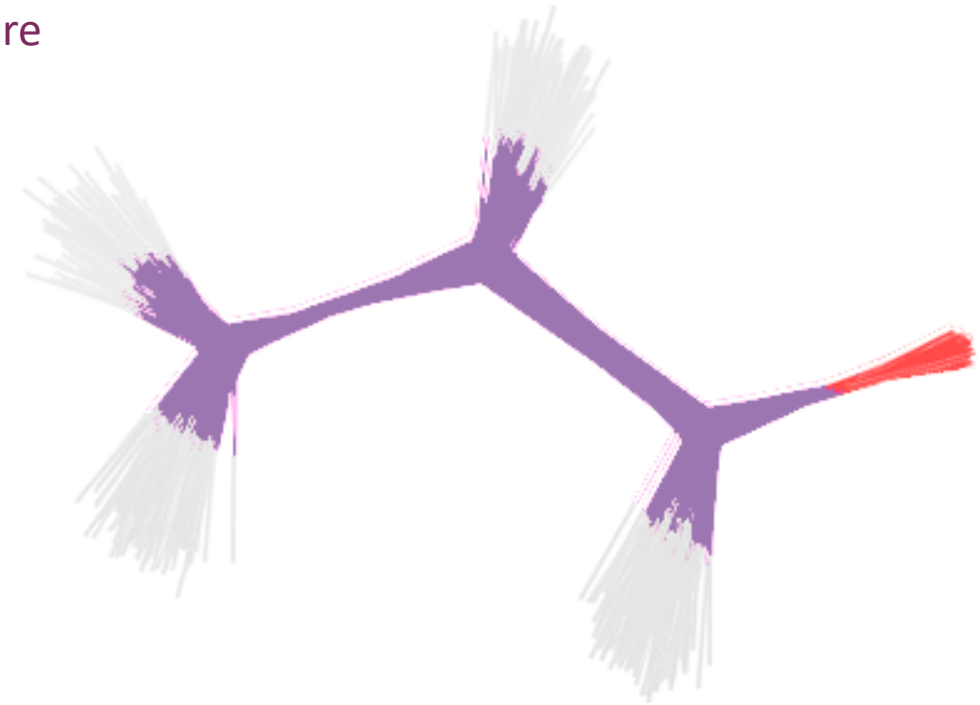
solvent response

static and dynamical approaches



Sampling

Solvated chromophore



Wigner distribution

probability to find molecule at position R
and with momentum p

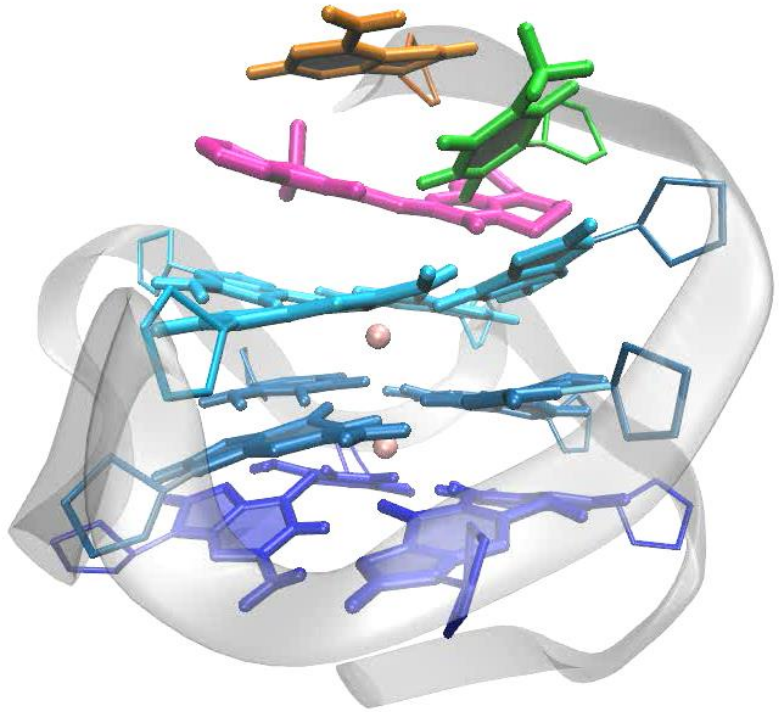
- Pick random (R,p) pair from Wigner distribution
- Distort R_{eq} in normal mode direction
- Repeat for each normal mode

Sampling

more complex environment

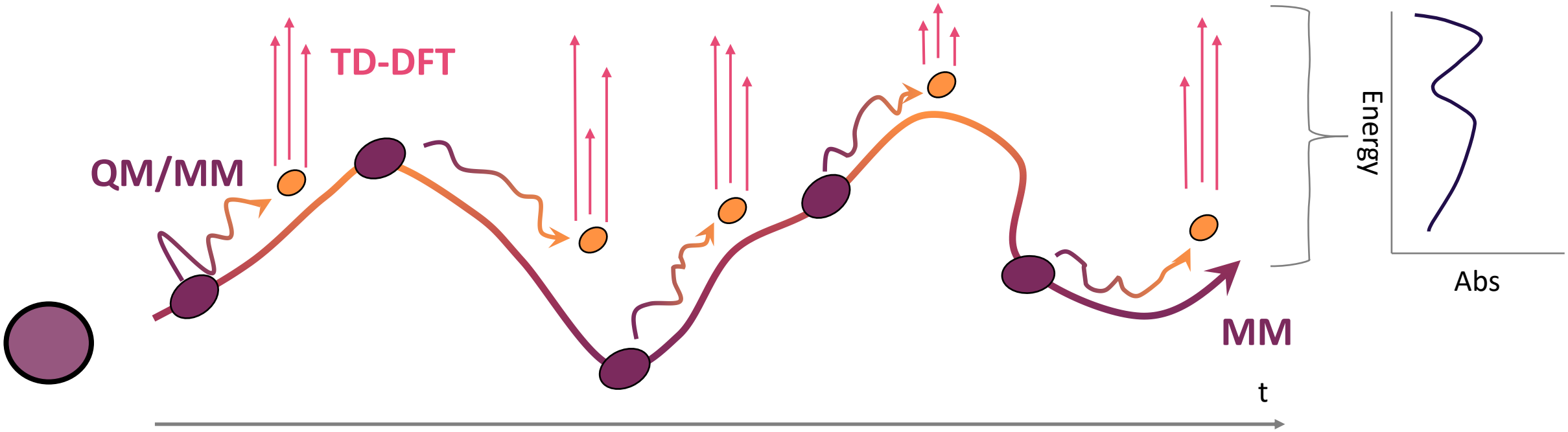
QM region:

- Guanine
- QMCH
- Thymine
- Adenine
- K^+



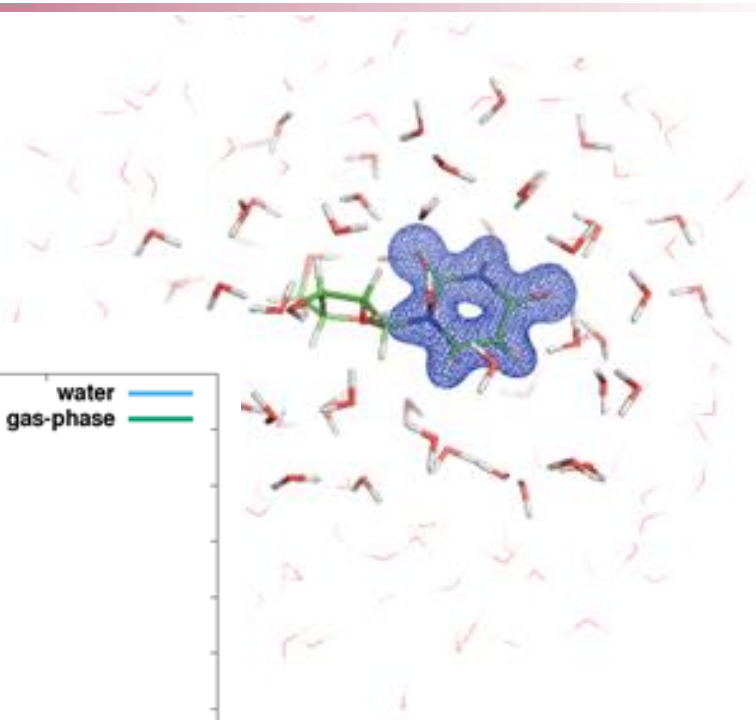
Sampling

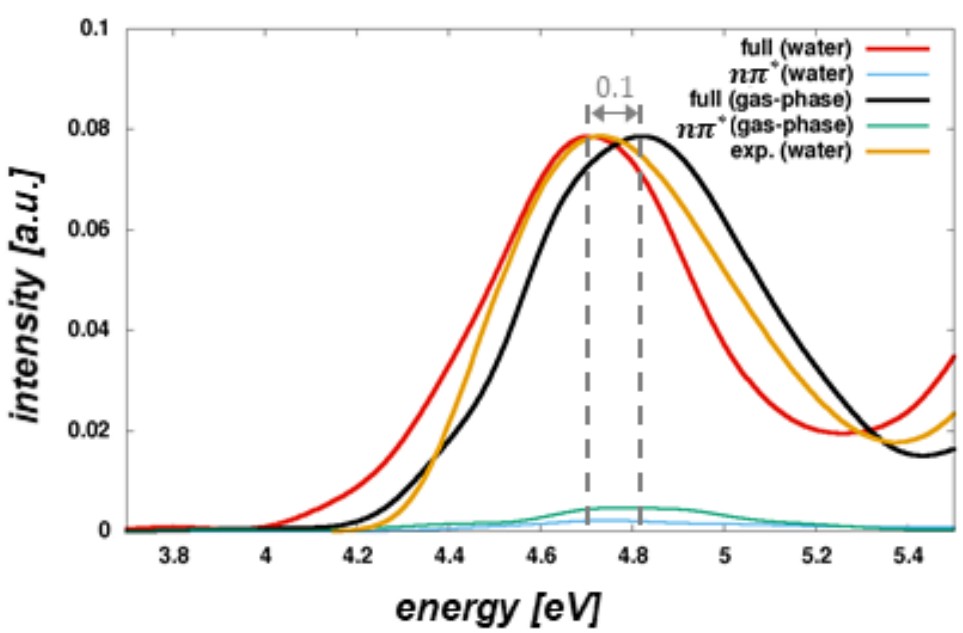
more complex environment

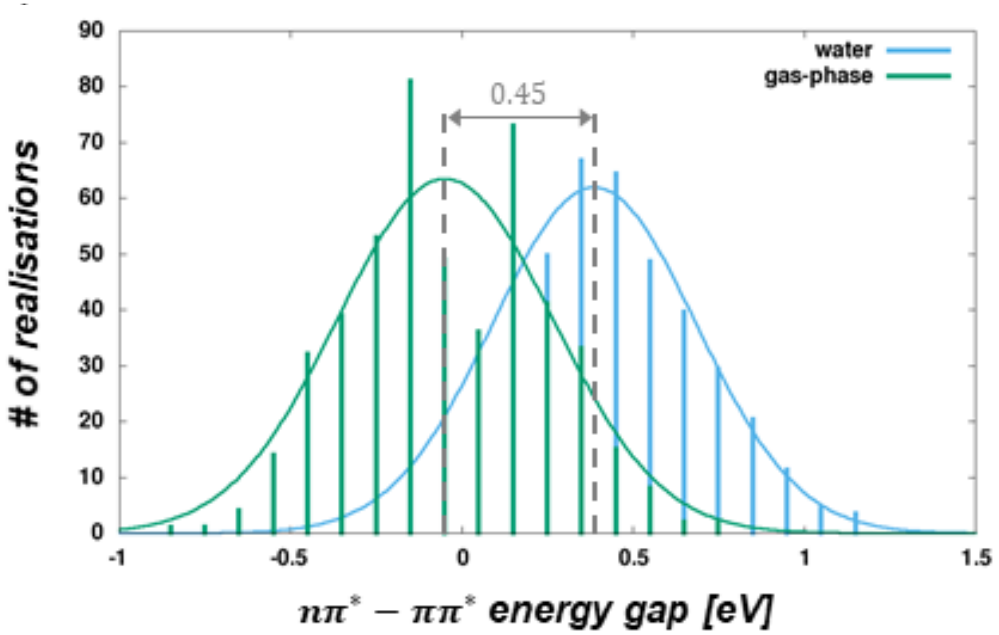


Spectroscopic properties

Solvated chromophore

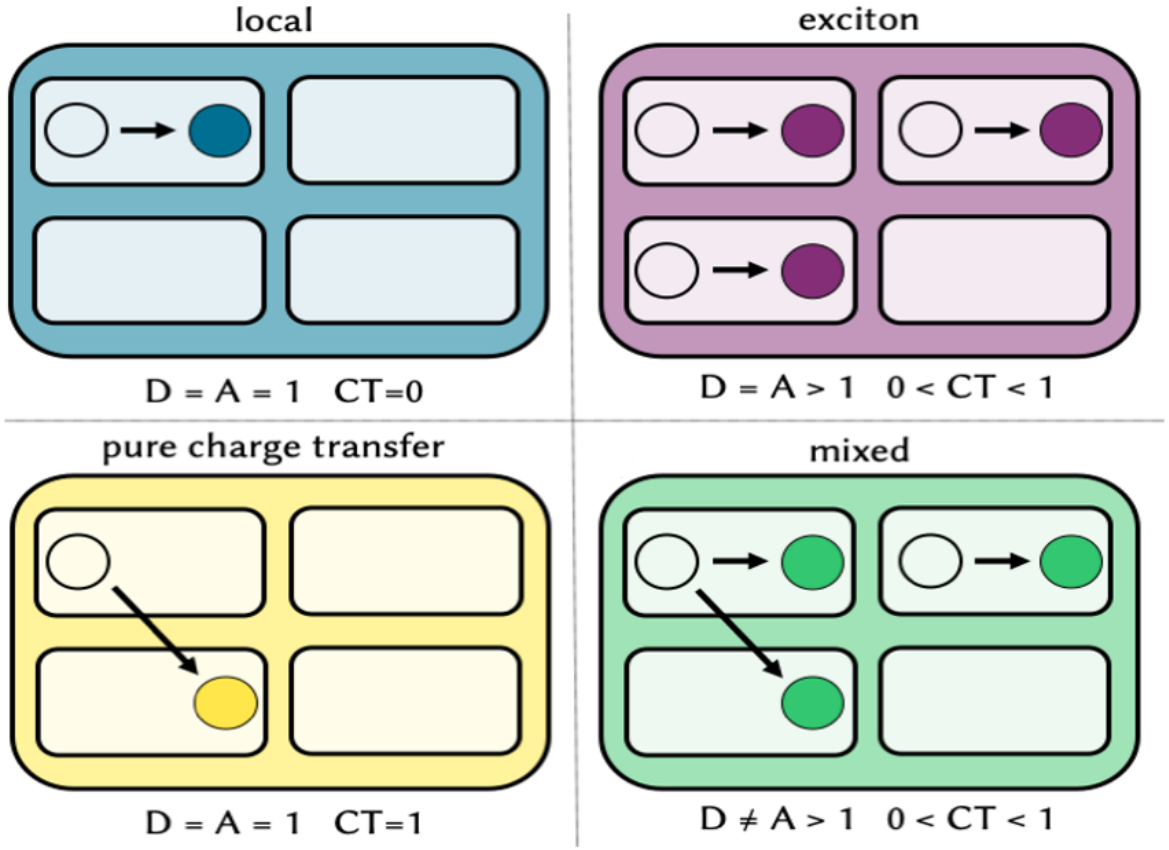




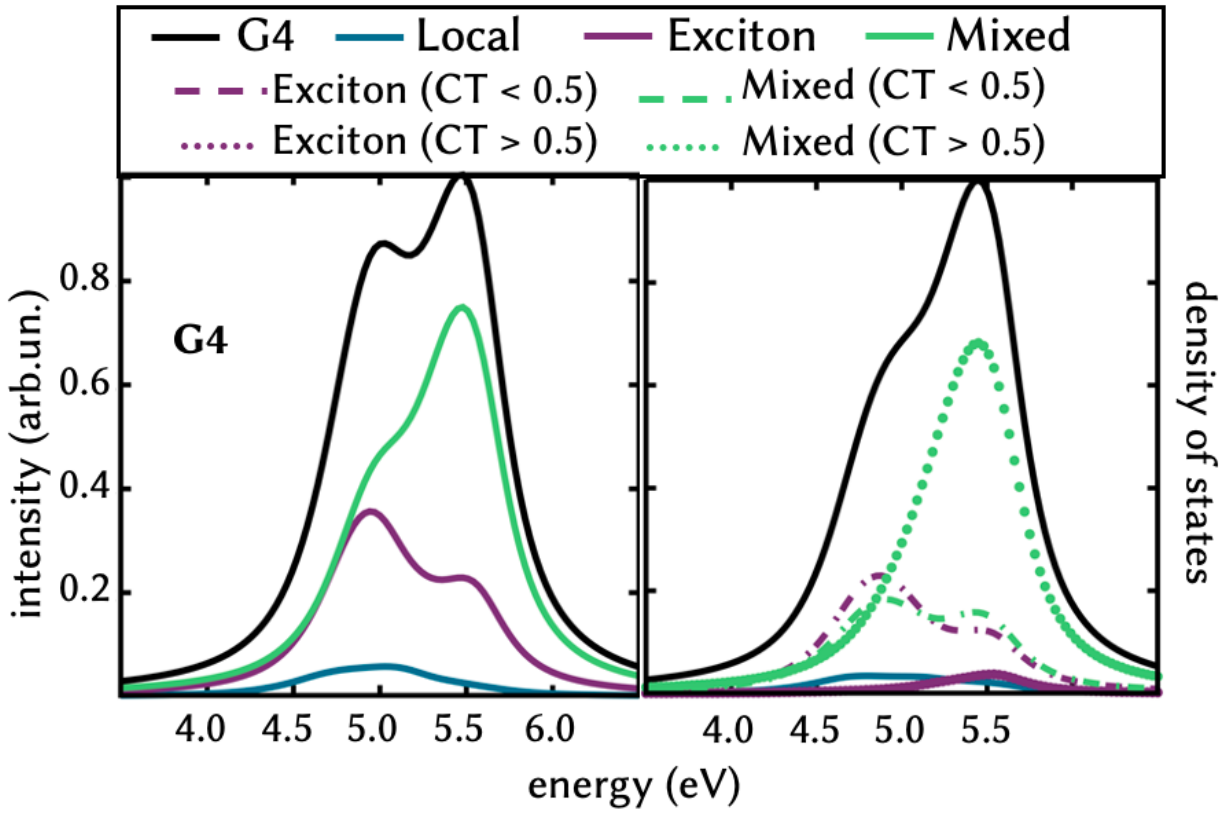


Nat. Comm. 12, 7285 (2021)

Spectroscopic properties

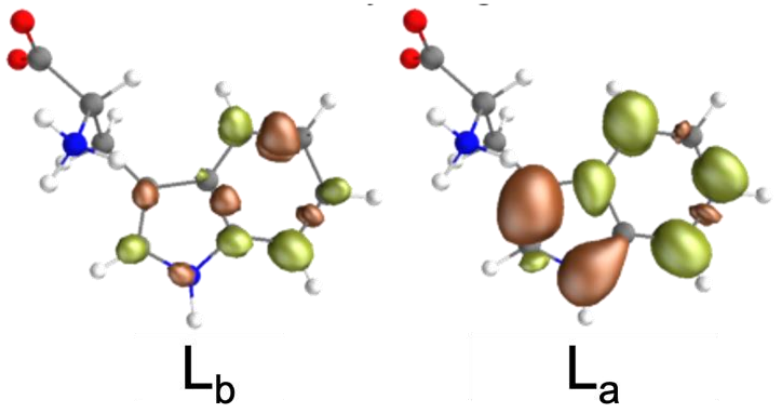


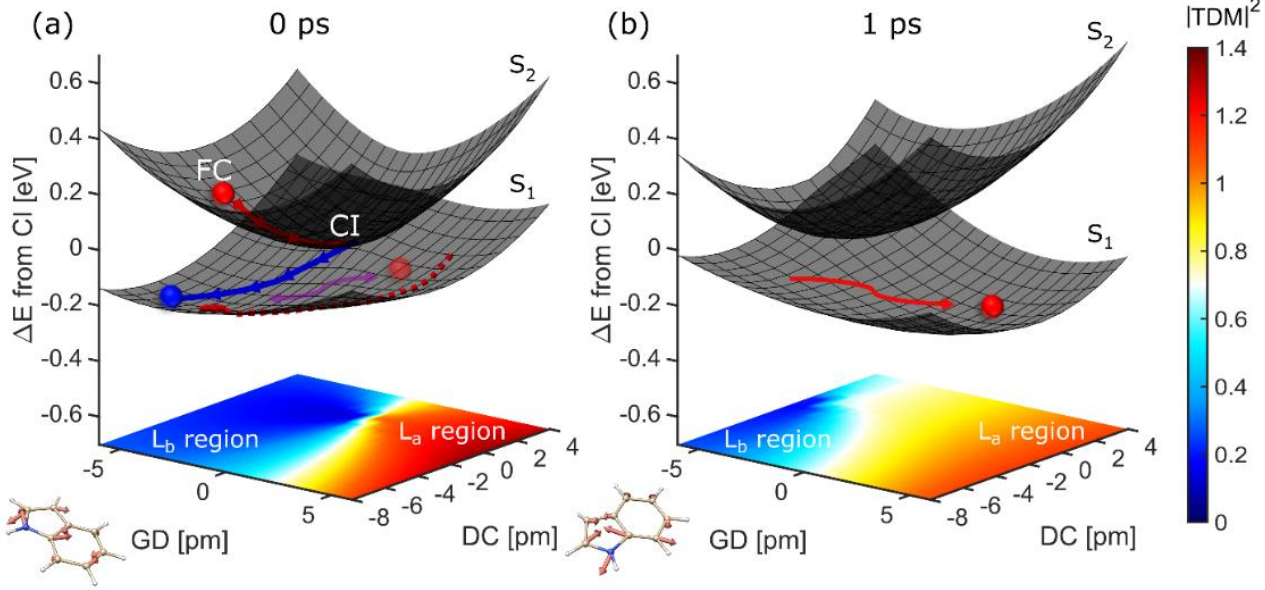
more complex environment

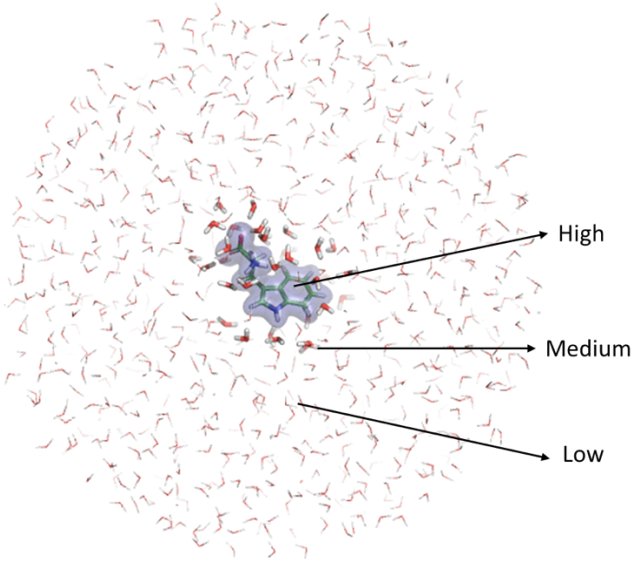


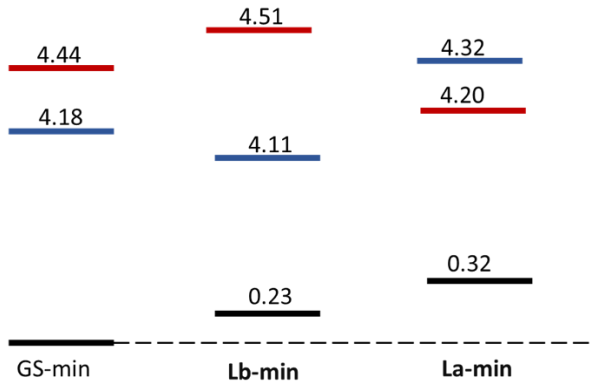
J.Phys.Chem.Lett.2020, 11, 10212−10218

Solvent response



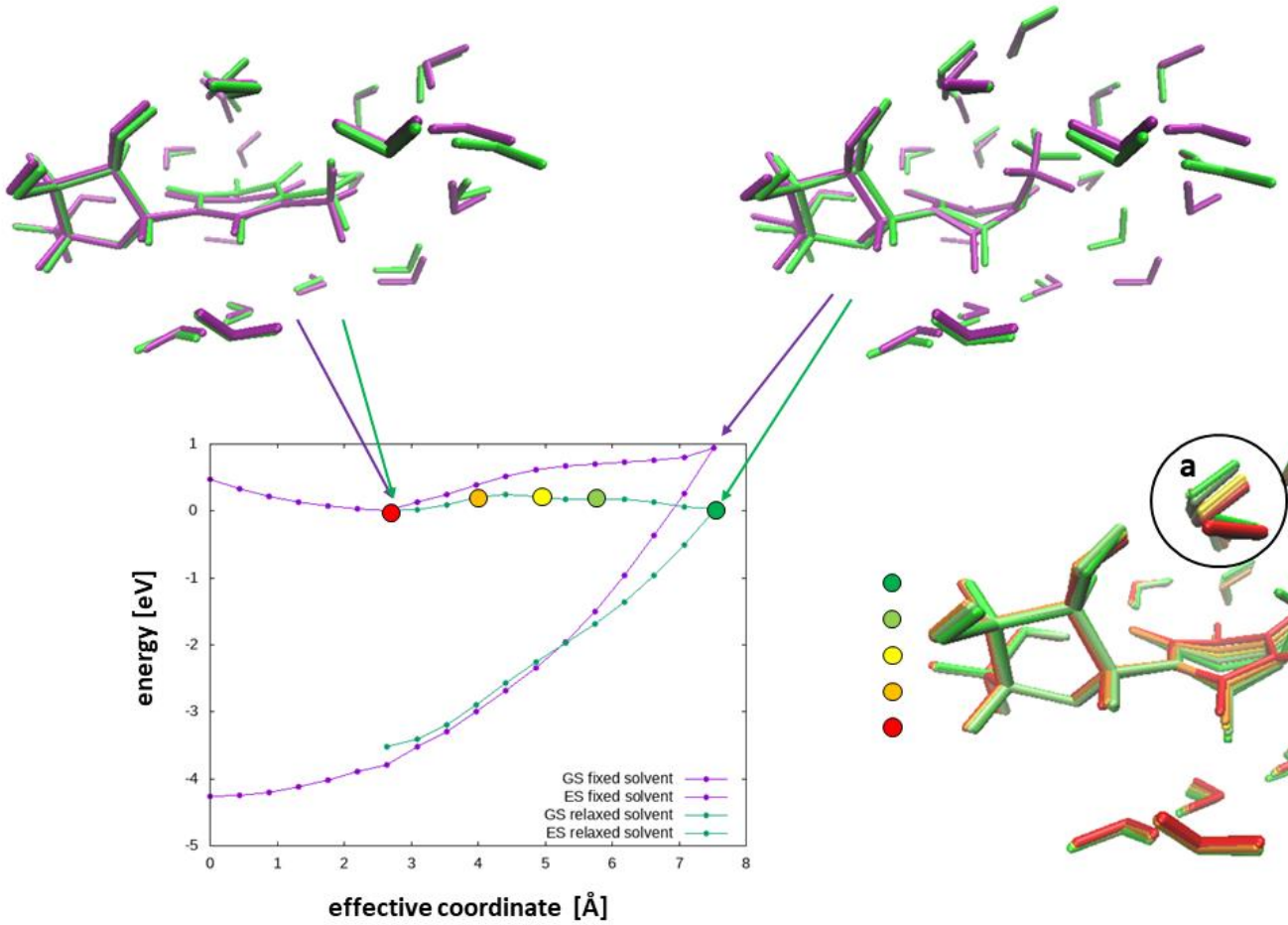






JACS, 2022 (just accepted)

Statical and dynamical approaches



Optimization techniques

separate algorithm

single gradient approach

Nat. Comm. 12, 7285 (2021)

Statical and dynamical approaches

Nonadiabatic dynamics

Wavefunction propagation on parametrized potentials

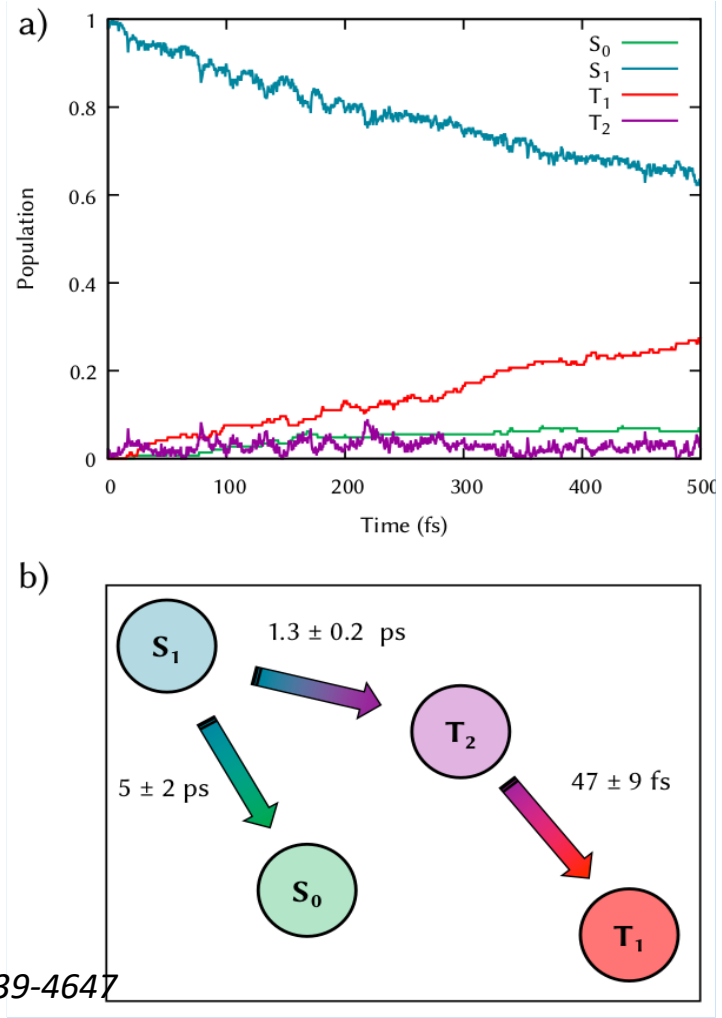
microsolvation

mean effect

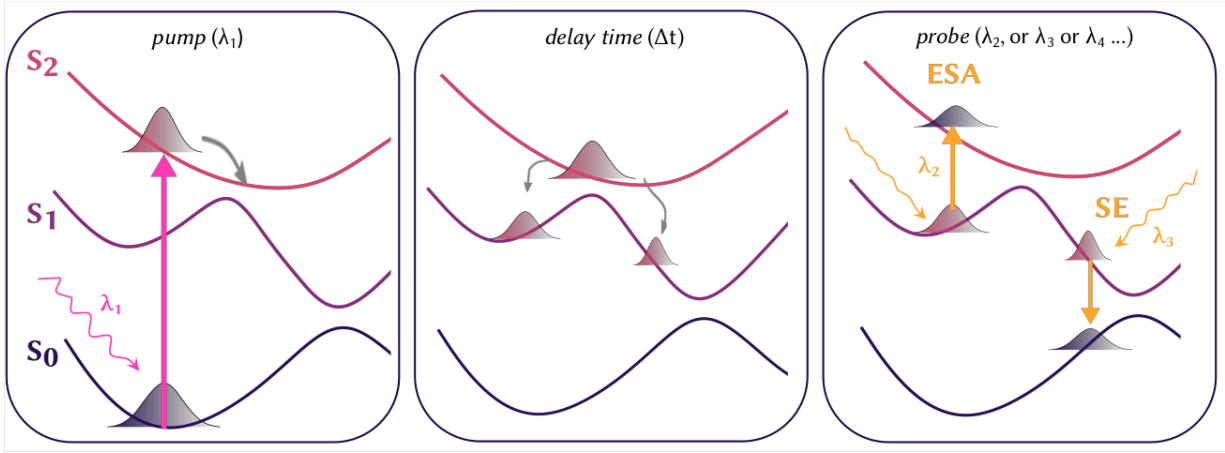
Trajectory-based methods

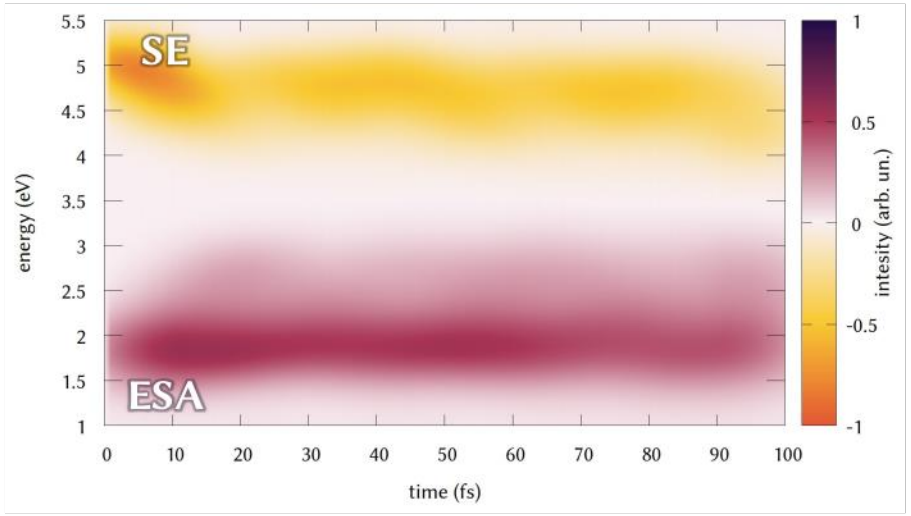
AIMS, FSSH

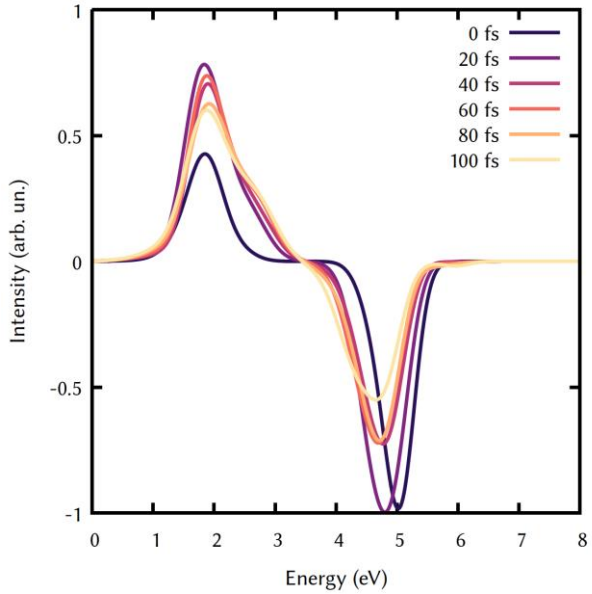
single initial condition solvation



J.Chem.Theory Comput., 2021,17,8,4639-4647







Dynamics and spectroscopy

J. Comp. Chem. (Just accepted)

COBRAMM

J. Mol. Model. 24, 271 (2018).

https://site.unibo.it/cobramm/en

COBRAMM

COBRAMM 2

subtractive QM/MM scheme

photochemical MEP and CI search

transient absorption

nonadiabatic couplings

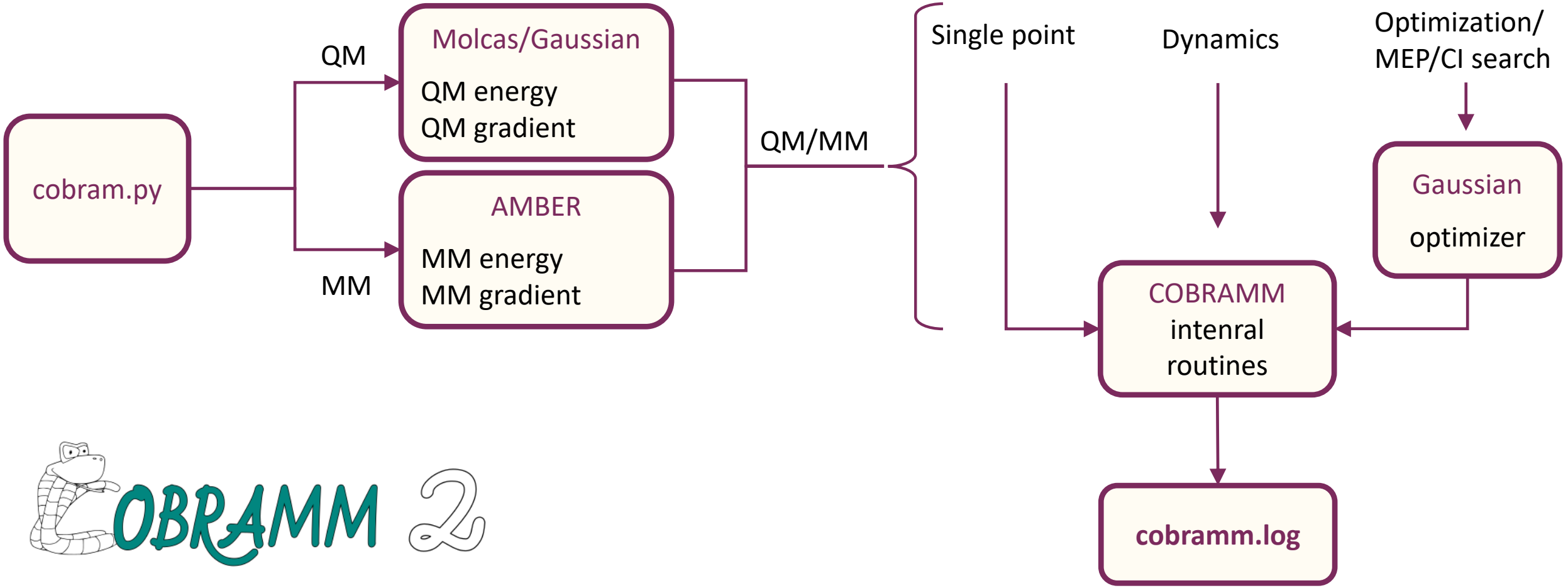
Fewest Switches Surface Hopping

many others...

J. Mol. Model. 24, 271 (2018).

https://site.unibo.it/cobramm/en

COBRAMM



COBRAMM 2

COBRAMM

cobram.command

```
!keyword
type=mdv
nproc=2
numproc=2
nsteps=200
qm-type=gauss
qmem=2000MB
tstep=0.5
surhop=persico
nacs=tdc
tdctype=2
hoptogs=0
backhop=1
velafterhop=1
?keyword

!sander
comment line
&cntrl
imin   = 1,
maxcyc = 0,
ntb    = 0,
igb    = 0,
ntr    = 0,
ibelly = 1,
cut    = 10
/
?sander

!gaussian
#p 6-31g* cam-b3lyp nosym tda=(nstates=5, root=2) density=current

gaussian input generated by COBRAMM

0 1
?gaussian
```

real_layers.xyz

```
C    0       22.495000     20.499000     21.682000  H
C    0       24.771000     19.638000     20.975000  H
C    0       22.359000     25.063000     23.693000  H
C    0       20.267000     23.572000     23.742000  H
N    0       25.607000     18.988000     20.559000  H
C    0       23.913000     20.589000     21.587000  H
C    0       24.515000     21.785000     22.085000  H
C    0       23.757000     22.839000     22.592000  H
C    0       22.382000     22.731000     22.713000  H
C    0       21.777000     21.526000     22.326000  H
H    0       21.604000     25.837000     23.509000  H
H    0       22.659000     25.219000     24.736000  H
H    0       23.166000     25.386000     23.023000  H
N    0       21.670000     23.791000     23.181000  H
H    0       19.553000     23.491000     22.912000  H
H    0       20.071000     24.501000     24.291000  H
H    0       20.177000     22.665000     24.353000  H
H    0       21.864000     19.731000     21.245000  H
H    0       25.591000     21.872000     21.962000  H
H    0       24.294000     23.728000     22.910000  H
H    0       20.700000     21.417000     22.411000  H
N    0       19.862000     32.097000     25.782000  M
C    0       18.920000     31.568000     25.296000  M
C    0       17.740000     30.925000     24.758000  M
H    0       18.151000     30.191000     24.065000  M
H    0       17.203000     30.366000     25.525000  M
H    0       17.079000     31.658000     24.294000  M
N    0       18.135000     19.671000     26.350000  M
C    0       19.124000     19.799000     26.750000  M
C    0       20.461000     19.959000     27.236000  M
H    0       20.450000     20.505000     28.179000  M
H    0       20.949000     18.987000     27.311000  M
H    0       20.954000     20.548000     26.462000  M
N    0       19.088000     27.801000     26.476000  M
C    0       19.853000     28.516000     26.984000  M
C    0       20.719000     29.400000     27.722000  M
```

real.top

model-H.top

AMBER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Welcome to Amber!
Amber is a suite of biomolecular simulation programs. It began in the late 1970's, and is maintained by an active development community; see our history page and our contributors page for more information.
The term "Amber" refers to two things. First, it is a set of molecular mechanical force fields for the simulation of biomolecules (these force fields are in the public domain, and are used in a variety of simulation programs). Second, it is a package of molecular simulation programs which includes source code and demos.

AMBER

PROGRAMS	FILES	PROTOCOL
tleap	pdb/mol2/ prep	minimisation
antechamber	frcmod	heating
parmchk		equilibration
sander	top	production
cpptraj	crd	

AMBER

pdb

```
ATOM      1  C    CHR     1       1.479   0.113   0.037  1.00  0.00           C
ATOM      2  C1   CHR     1       4.992   1.036  -0.107  1.00  0.00           C
ATOM      3  C2   CHR     1       0.724   1.247   0.398  1.00  0.00           C
ATOM      4  C3   CHR     1       5.656   2.200  -0.557  1.00  0.00           C
ATOM      5  C4   CHR     1      -0.666   1.201   0.399  1.00  0.00           C
ATOM      6  C5   CHR     1       7.037   2.290  -0.517  1.00  0.00           C
ATOM      7  C6   CHR     1      -1.317   0.015   0.030  1.00  0.00           C
ATOM      8  C7   CHR     1       7.821   1.220  -0.015  1.00  0.00           C
ATOM      9  C8   CHR     1      -0.580  -1.123  -0.338  1.00  0.00           C
ATOM     10  C9   CHR     1       7.152   0.052   0.429  1.00  0.00           C
ATOM     11  C10  CHR     1       0.808  -1.073  -0.333  1.00  0.00           C
ATOM     12  C11  CHR     1       5.770  -0.033   0.385  1.00  0.00           C
ATOM     13  N    CHR     1       2.914   0.053   0.105  1.00  0.00           N
ATOM     14  N1   CHR     1       3.566   1.057  -0.185  1.00  0.00           N
ATOM     15  H    CHR     1       1.227   2.184   0.687  1.00  0.00           H
ATOM     16  H1   CHR     1       5.075   3.052  -0.949  1.00  0.00           H
ATOM     17  H2   CHR     1      -1.251   2.092   0.686  1.00  0.00           H
ATOM     18  H3   CHR     1       7.525   3.210  -0.873  1.00  0.00           H
ATOM     19  N2   CHR     1      -2.802  -0.039   0.027  1.00  0.00           N
ATOM     20  O    CHR     1      -3.347  -1.060  -0.297  1.00  0.00           O
ATOM     21  O1   CHR     1      -3.421   0.940   0.348  1.00  0.00           O
ATOM     22  H4   CHR     1       9.629   2.041  -0.453  1.00  0.00           H
ATOM     23  H5   CHR     1       9.708   0.496   0.201  1.00  0.00           H
ATOM     24  N3   CHR     1       9.196   1.341   0.103  1.00  0.00           N
ATOM     25  H6   CHR     1      -1.101  -2.051  -0.630  1.00  0.00           H
ATOM     26  H7   CHR     1       7.730  -0.797   0.822  1.00  0.00           H
ATOM     27  H8   CHR     1       1.380  -1.970  -0.621  1.00  0.00           H
ATOM     28  H9   CHR     1       5.285  -0.956   0.744  1.00  0.00           H
```

mol2

```
@<TRIPOS>MOLECULE
geometry
   28    29     1     0     0
SMALL
bcc


@<TRIPOS>ATOM
      1 C           1.5390     0.0410    -0.0220 ca        1 CHR      0.154400
      2 C1          4.9390     1.2110     0.0230 ca        1 CHR      0.019400
      3 C2          0.7820     1.2250    -0.0180 ca        1 CHR     -0.124500
      4 C3          5.6570     2.4160     0.0140 ca        1 CHR     -0.039000
      5 C4         -0.6140     1.2100    -0.0110 ca        1 CHR     -0.069500
      6 C5          7.0580     2.4540     0.0450 ca        1 CHR     -0.217500
      7 C6         -1.2750    -0.0180    -0.0070 ca        1 CHR     -0.177200
      8 C7          7.7900     1.2730     0.1240 ca        1 CHR      0.193600
      9 C8         -0.5600    -1.2180    -0.0110 ca        1 CHR     -0.069500
     10 C9          7.1040     0.0600     0.0940 ca        1 CHR     -0.217500
     11 C10         0.8340    -1.1720    -0.0180 ca        1 CHR     -0.124500
     12 C11         5.7040     0.0360     0.0620 ca        1 CHR     -0.039000
     13 N           2.8910    -0.0240    -0.0250 ne        1 CHR     -0.232400
     14 N1          3.5850     1.2740    -0.0170 nf        1 CHR     -0.175400
     15 H           1.3120     2.1750    -0.0190 ha        1 CHR      0.160500
     16 H1          5.0920     3.3440    -0.0310 ha        1 CHR      0.149500
     17 H2         -1.1410     2.1560    -0.0070 ha        1 CHR      0.172000
     18 H3          7.5590     3.4130     0.0090 ha        1 CHR      0.138500
     19 N2         -2.7370    -0.0510     0.0020 no        1 CHR      0.313200
     20 O          -3.3030    -1.1590     0.0060 o         1 CHR     -0.209000
     21 O1         -3.3550     1.0280     0.0050 o         1 CHR     -0.209000
     22 H4          9.3760     1.4290    -1.0250 hn        1 CHR      0.409300
     23 H5          9.5800     0.4130     0.2700 hn        1 CHR      0.409300
     24 N3          9.2010     1.3060    -0.0300 nv        1 CHR     -0.836200
     25 H6         -1.0500    -2.1840    -0.0070 ha        1 CHR      0.172000
     26 H7          7.6270    -0.8880     0.0880 ha        1 CHR      0.138500
     27 H8          1.4120    -2.0940    -0.0200 ha        1 CHR      0.160500
     28 H9          5.1810    -0.9170     0.0520 ha        1 CHR      0.149500
@<TRIPOS>BOND
     1    22    24 1
     2    16     4 1
     3    24     8 1
     4    24    23 1
     1     1
```

frcmod

```
Remark line goes here
MASS
ca 12.010         0.360
ne 14.010         0.530
nf 14.010         0.530
ha 1.008          0.135
no 14.010         0.530
o  16.000         0.434
hn 1.008          0.161
nv 14.010         0.530              same as nh

BOND
ca-ca   461.10   1.398
ca-ne   389.30   1.408
ca-nf   389.30   1.408
ca-ha   345.80   1.086
ca-no   321.70   1.469
ca-nv   417.90   1.386        same as ca-nh, penalty score=  0.0
ne-nf   722.40   1.263
no-o    741.80   1.226
hn-nv   404.60   1.012        same as hn-nh, penalty score=  0.0

ANGLE
ca-ca-ca    66.600      120.020
ca-ca-ha    48.200      119.880
ca-ne-nf    70.400      115.170
ca-nf-ne    70.400      115.170
ca-ca-ne    67.800      120.610
ca-ca-nf    67.800      120.610
ca-ca-no    66.800      119.010
ca-ca-nv    68.300      120.950   same as ca-ca-nh, penalty score=  0.0
ca-no-o     68.700      117.760
ca-nv-hn    48.400      116.070   same as ca-nh-hn, penalty score=  0.0
o -no-o     76.700      125.080
hn-nv-hn    40.100      115.120   same as hn-nh-hn, penalty score=  0.0

DIHE
ca-ca-ca-ca    4    14.500       180.000          2.000
ca-ca-ca-ha    4    14.500       180.000          2.000
ca-ne-nf-ca    1     3.000       180.000         -2.000
ca-ne-nf-ca    1     2.800         0.000          1.000
ca-ca-ne-nf    2     0.000       180.000          3.000
```

AMBER

```
%VERSION  VERSION_STAMP = V0001.000  DATE = 06/23/22  17:27:35
%FLAG TITLE
%FORMAT(20a4)
geometry
%FLAG POINTERS
%FORMAT(10I8)
   12022       7   12004       19       19       25       41       35        0
   16123    3999       19       25       35       11       12        7       10
       0       0        0        0        0        0        0        2       28
       0
%FLAG ATOM_NAME
%FORMAT(20a4)
C   C1  C2  C3  C4  C5  C6  C7  C8  C9  C10 C11 N   N1  H   H1  H2  H3  N2  O
O1  H4  H5  N3  H6  H7  H8  H9  O   H1  H2  O   H1  H2  O   H1  H2  O   H1  H2
O   H1  H2  O   H1  H2  O   H1  H2  O   H1  H2  O   H1  H2  O   H1  H2  O   H1
H2  O   H1  H2  O   H1  H2  O   H1  H2  O   H1  H2  O   H1  H2  O   H1  H2  O
H1  H2  O   H1  H2  O   H1  H2  O   H1  H2  O   H1  H2  O   H1  H2  O   H1  H2
O   H1  H2  O   H1  H2  O   H1  H2  O   H1  H2  O   H1  H2  O   H1  H2  O   H1
H2  O   H1  H2  O   H1  H2  O   H1  H2  O   H1  H2  O   H1  H2  O   H1  H2  O
```

```
%FLAG CHARGE
%FORMAT(5E16.8)
  2.81352312E+00  3.53512620E-01 -2.26867635E+00 -7.10669700E-01 -1.26644985E+00
 -3.96335025E+00 -3.22899156E+00  3.52783728E+00 -1.26644985E+00 -3.96335025E+00
 -2.26867635E+00 -7.10669700E-01 -4.23486252E+00 -3.19619142E+00  2.92467915E+00
  2.72423385E+00  3.13423560E+00  2.52378855E+00  5.70722436E+00 -3.80846070E+00
```

```
%FLAG RESIDUE_LABEL
%FORMAT(20a4)
CHR WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT
WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT
WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT
WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT
WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT WAT
```

topology file

```
%FLAG BOND_FORCE_CONSTANT
%FORMAT(5E16.8)
  3.89300000E+02  4.61100000E+02  3.89300000E+02  3.45800000E+02  3.21700000E+02
  4.17900000E+02  7.22400000E+02  7.41800000E+02  4.04600000E+02  5.53000000E+02
  5.53000000E+02
%FLAG BOND_EQUIL_VALUE
%FORMAT(5E16.8)
  1.40800000E+00  1.39800000E+00  1.40800000E+00  1.08600000E+00  1.46900000E+00
  1.38600000E+00  1.26300000E+00  1.22600000E+00  1.01200000E+00  9.57200000E-01
  1.51360000E+00
%FLAG ANGLE_FORCE_CONSTANT
%FORMAT(5E16.8)
  7.04000000E+01  4.82000000E+01  6.66000000E+01  7.04000000E+01  6.78000000E+01
  6.78000000E+01  6.68000000E+01  6.83000000E+01  6.87000000E+01  4.84000000E+01
  7.67000000E+01  4.01000000E+01
%FLAG ANGLE_EQUIL_VALUE
%FORMAT(5E16.8)
  2.01009656E+00  2.09230160E+00  2.09474507E+00  2.01009656E+00  2.10504251E+00
  2.10504251E+00  2.07711723E+00  2.11097664E+00  2.05530061E+00  2.02580453E+00
  2.18305876E+00  2.00922390E+00
%FLAG DIHEDRAL_FORCE_CONSTANT
%FORMAT(5E16.8)
  2.80000000E+00  3.00000000E+00  3.62500000E+00  0.00000000E+00  6.00000000E-01
  1.05000000E+00  1.10000000E+00
%FLAG DIHEDRAL_PERIODICITY
%FORMAT(5E16.8)
  1.00000000E+00  2.00000000E+00  2.00000000E+00  3.00000000E+00  2.00000000E+00
  2.00000000E+00  2.00000000E+00
%FLAG DIHEDRAL_PHASE
%FORMAT(5E16.8)
  0.00000000E+00  3.14159400E+00  3.14159400E+00  3.14159400E+00  3.14159400E+00
```

Now we are ready for the Hands-on!!

Thank you for your attention!!