L7 - Classical Mechanics 3

Molecular mechanics: dynamics

Born-Oppenheimer Molecular Dynamics (BOMD)

Second Newton's law:

$$M_\alpha \frac{d^2\mathbf{R}_\alpha}{dt^2} = -\nabla_\alpha E_K\left(\mathbf{R}\right)$$

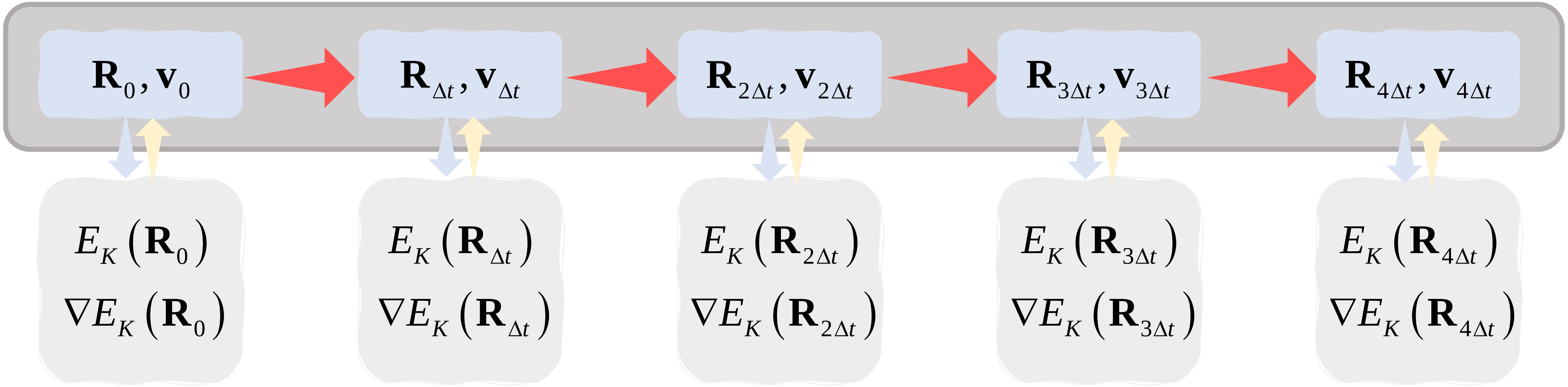
Solve it numerically, for instance, with Velocity Verlet:

$$\mathbf{R}_\alpha(t+\Delta t) = \mathbf{R}_\alpha(t) + \mathbf{v}_\alpha(t)\Delta t + \tfrac{1}{2}\mathbf{a}_\alpha(t)\Delta t^2$$

$$\mathbf{v}_\alpha(t+\Delta t) = \mathbf{v}_\alpha\left(t\right) + \tfrac{1}{2}\left(\mathbf{a}_\alpha\left(t\right) + \mathbf{a}_\alpha(t+\Delta t)\right)\Delta t$$

BOMD

Classical EOM



$\mathbf{R}_0, \mathbf{v}_0$ → $\mathbf{R}_{\Delta t}, \mathbf{v}_{\Delta t}$ → $\mathbf{R}_{2\Delta t}, \mathbf{v}_{2\Delta t}$ → $\mathbf{R}_{3\Delta t}, \mathbf{v}_{3\Delta t}$ → $\mathbf{R}_{4\Delta t}, \mathbf{v}_{4\Delta t}$

$E_K(\mathbf{R}_0)$

$\nabla E_K(\mathbf{R}_0)$

$E_K(\mathbf{R}_{\Delta t})$

$\nabla E_K(\mathbf{R}_{\Delta t})$

$E_K(\mathbf{R}_{2\Delta t})$

$\nabla E_K(\mathbf{R}_{2\Delta t})$

$E_K(\mathbf{R}_{3\Delta t})$

$\nabla E_K(\mathbf{R}_{3\Delta t})$

$E_K(\mathbf{R}_{4\Delta t})$

$\nabla E_K(\mathbf{R}_{4\Delta t})$

The nuclei move on the potential energy surface $E_K(\mathbf{R})$ of electronic state *K*

$$\left(T_{elec}(\mathbf{r})+V(\mathbf{r},\mathbf{R})\right)\varphi_K(\mathbf{r};\mathbf{R})=E_K(\mathbf{R})\varphi_K(\mathbf{r};\mathbf{R})$$

How do we get this surface?

- Precompute
  - ✓ Fitting
  - ✓ Modeling

- Compute as needed

PES type		**Pros**	**Cons**
Precomputed	Fitted	• May consider nonlocal effects (tunneling, …)	• Curse of dimensionality • Difficult procedure • Expensive preparation
	Modeled	• May consider nonlocal effects (tunneling, …)	• Lack of functional flexibility • Expensive preparation
Computed as needed		• Offer QM flexibility (easy to change methods)	• Miss nonlocal effects • Expensive dynamics

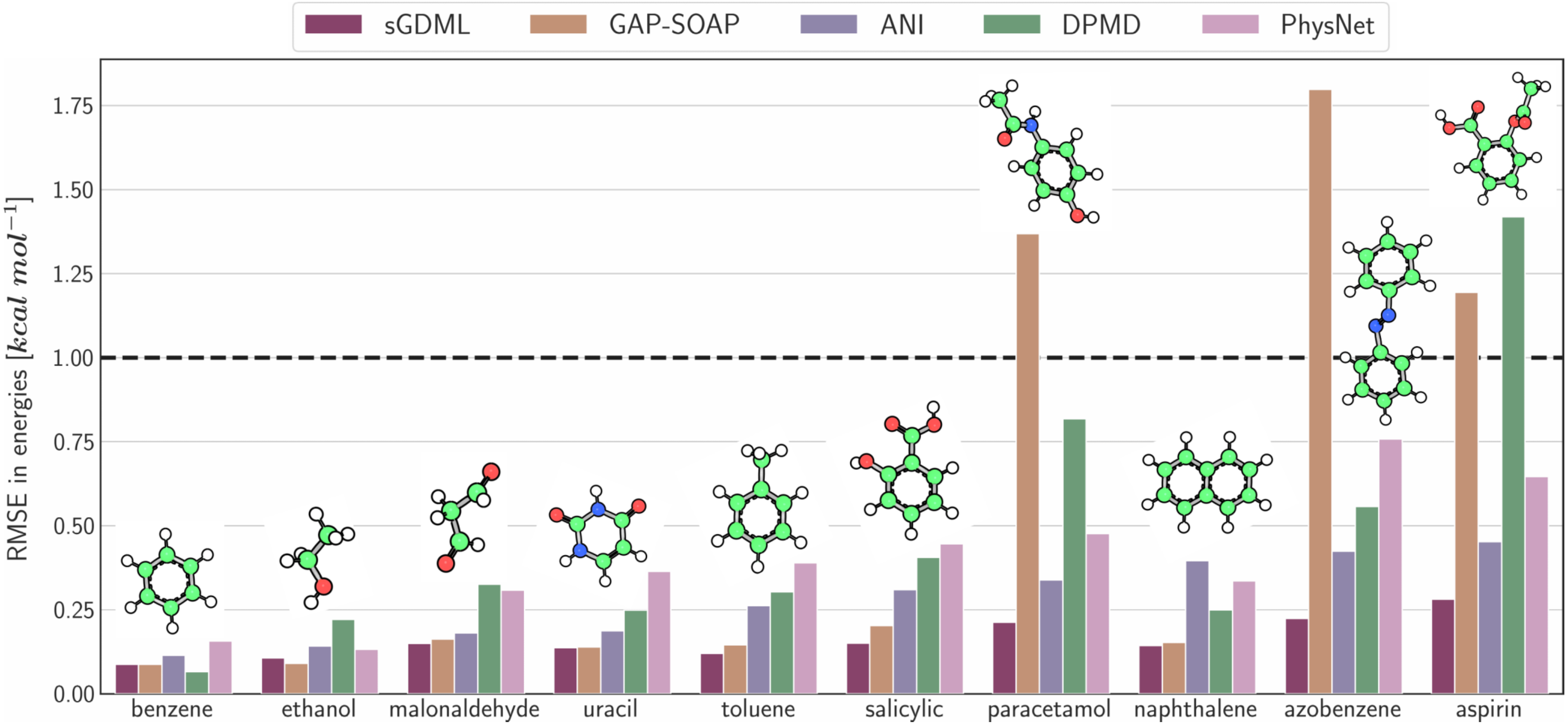
Fitted precomputed PES

A collection of fitted potential energy surfaces is available at comp.chem.umn.edu/potlib/form.cgi

Non-fitted datasets:
- MD17 & MD22: www.sgdml.org/#datasets
- QM-22: github.com/jmbowma/QM-22
- WS22: zenodo.org/record/6985377

Machine learning is reviving the field

1. Build a dataset of energies and energy gradients (100 k points)
2. Train a machine (kernel, NN) to predict energies and gradients for unseen geometries



- MD17 Database
- Energy + Force
- N_{train} = 1k; N_{model} = 20; N_{test} = 20k

Pinheiro Jr *et al*. *Chem Sci* **2021**, *12*, 14396

Model PES

Model Hamiltonians assume that the PES has some specific shape.

Thus, the amount of computed data is smaller than in fitted surfaces.

They are needed to parameterize the model.

Examples of model Hamiltonians:

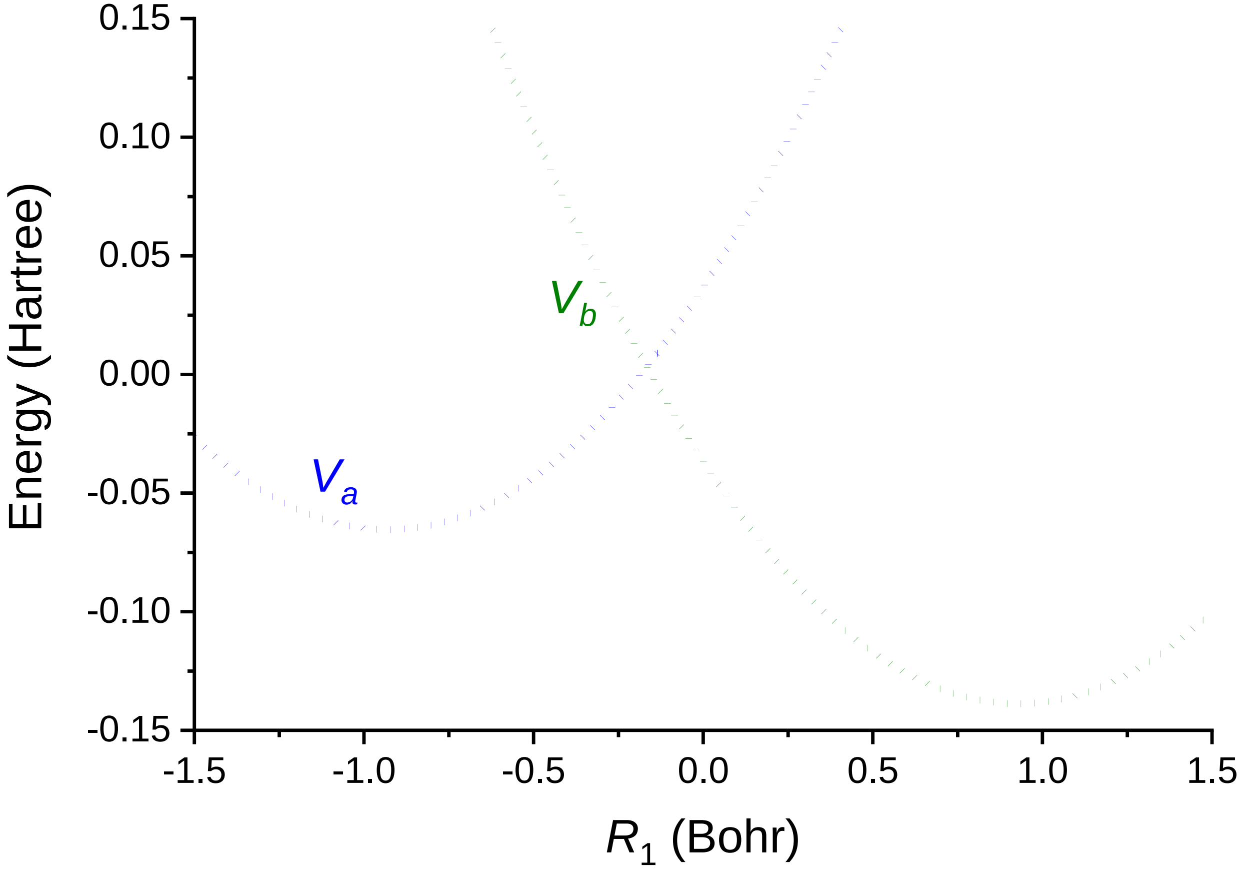
- Spin-Boson Hamiltonian
- Linear Vibronic Coupling
- Molecular mechanics force fields

Example: Spin-Boson model

$$V_a(\mathbf{R}) = \varepsilon_0 + \frac{1}{2}\sum_{j=1}^{N} M_j \omega_j^2 R_j^2 + \sum_{j=1}^{N} g_j R_j$$

$$V_b(\mathbf{R}) = -\varepsilon_0 + \frac{1}{2}\sum_{j=1}^{N} M_j \omega_j^2 R_j^2 - \sum_{j=1}^{N} g_j R_j$$

$$V_{ab} = -v_0$$



Leggett et al. *Rev Mod Phys* **1987,** *59*, 1

Full dimensional H-models [($3N_a$-6)D]

H Model	# states	# parameters	Pros	Cons
SBH	2	$2(3N_a\text{-}5)$	Analyt. adiabatic rep.	Low flexibility

SBH: Leggett et al. *Rev Mod Phys* **1987,** *59*, 1
Example of dynamics with SBH: Landry; Subotnik. *J Chem Phys* **2011**, *135*, 191101

Full dimensional H-models [$(3N_a\text{-}6)$D]

H Model	# states	# parameters	Pros	Cons
SBH	2	$2(3N_a-5)$	Analyt. adiabatic rep.	Low flexibility
LVC	N_s	$(3N_a-6)N_s(N_s+1)/2$	Number of states	Parameterization
. . .				

SBH: Leggett et al. *Rev Mod Phys* **1987,** *59*, 1
Example of dynamics with SBH: Landry; Subotnik. *J Chem Phys* **2011**, *135*, 191101
LVC: Koppel; Domcke; Cederbaum. *Adv Chem Phys* **1984,** *57*, 59
Example of LVC parameterization: Aleotti *et al. J Chem Phys* **2021**, *154*, 104106

PES models like Spin-Boson and LVC should be parameterized for each molecule. They are not transferrable.

Their formulation using normal modes makes finding correspondence with real molecules difficult.

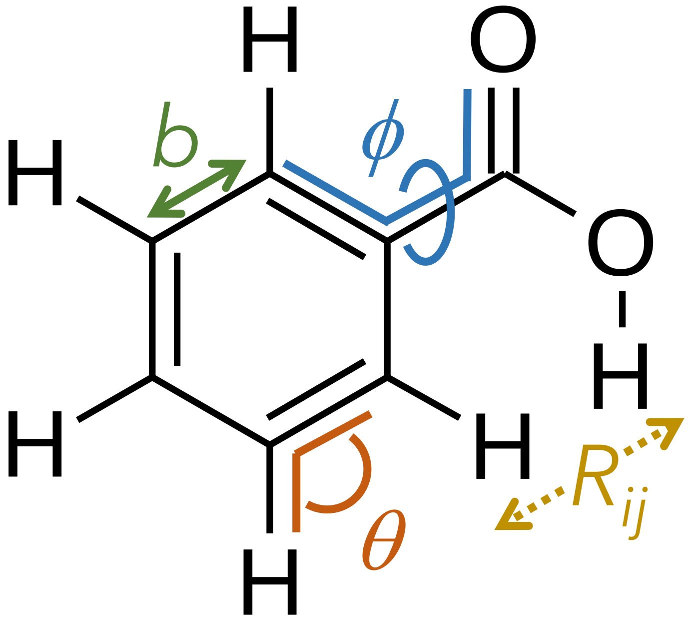
Combining these models with hybrid QM/Model approaches is not straightforward.

All these problems are avoided with **Force Field** models.

Force fields

Force-field potential energy surface:

$$E = \sum_{bonds} V_b(b) + \sum_{angles} V_a(\theta) + \sum_{dihedrals} V_d(\phi) + \sum_{i<j}\left[V_e(R_{ij}) + V_{vdW}(R_{ij})\right]$$



b - distance between two bonded atoms

θ - angle between three bonded atoms

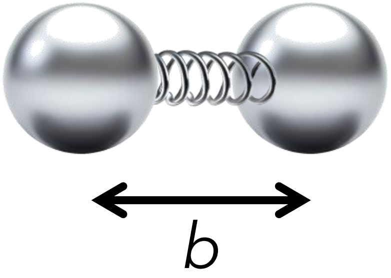
ϕ - dihedral between four bonded atoms

R_{ij} – distance between two atoms in different molecules or separated by four or more bonds

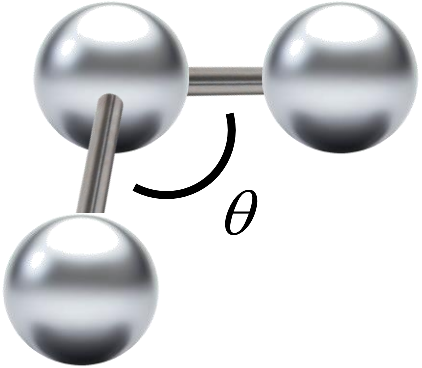
Groenhof, In *Biomolecular simulations: Methods and protocols*, **2013**

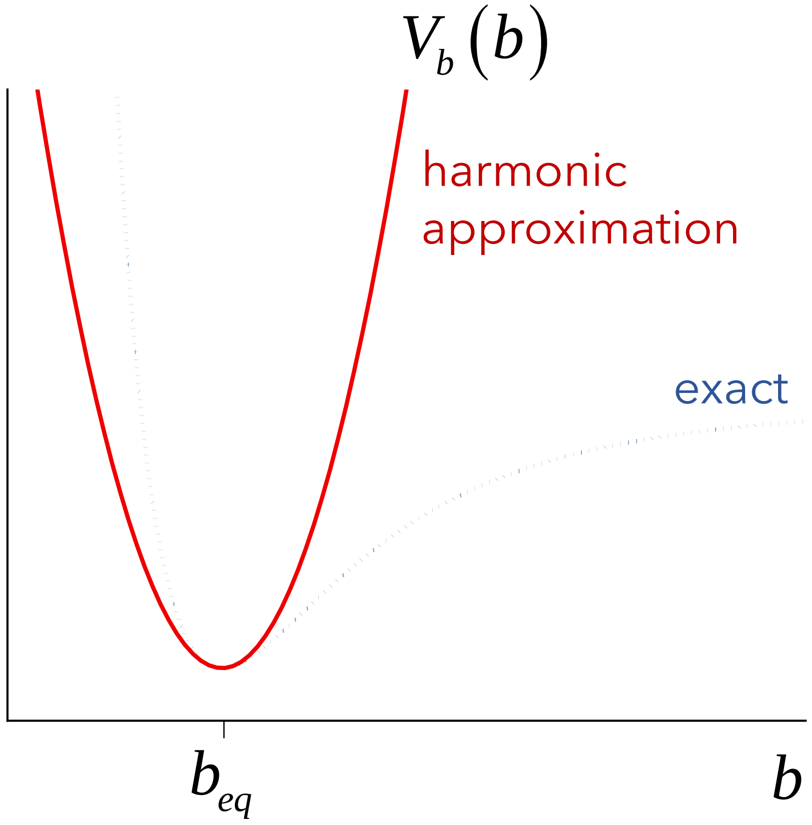
Bonds and angles are harmonic

$$V_b(b) = K_b\left(b - b_{eq}\right)^2$$



$$V_a(\theta) = K_\theta\left(\theta - \theta_{eq}\right)^2$$

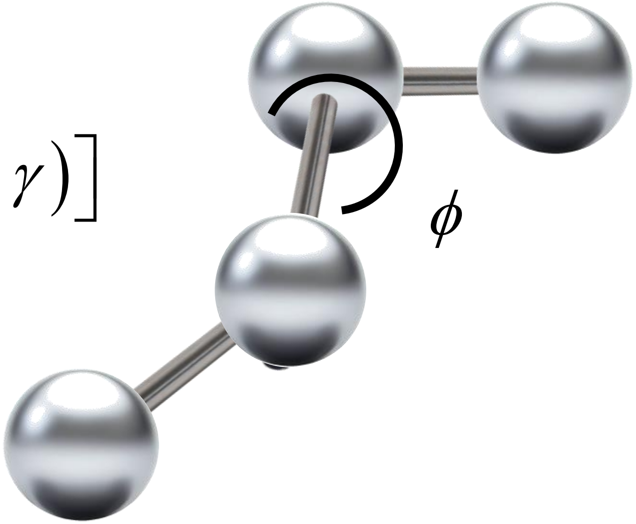


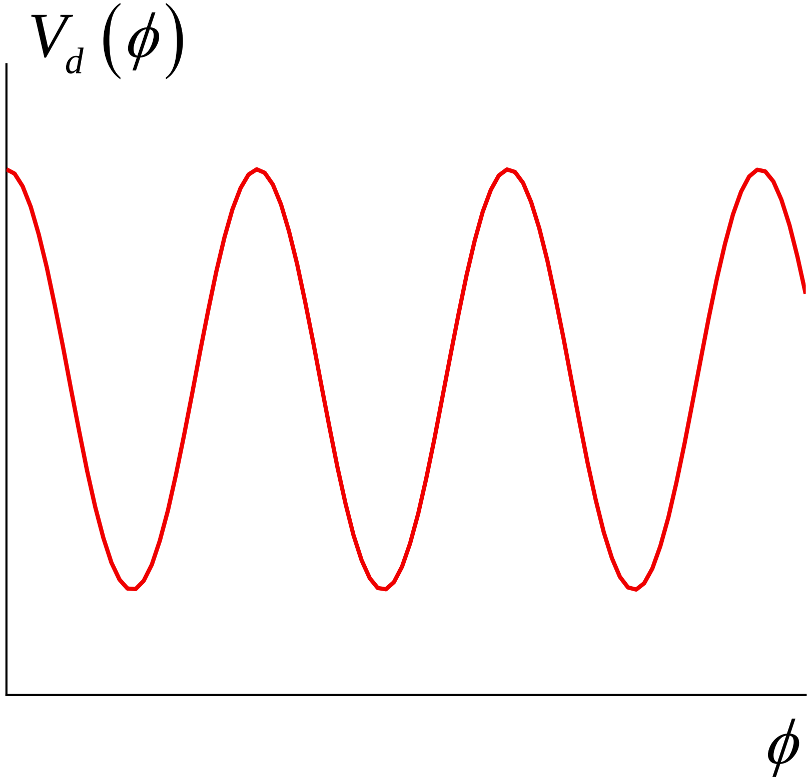


Restrict to low temperatures.
No dissociation or bond formation.

Dihedrals follow a periodic potential

$$V_d = \frac{V_n}{2}\left[1 + \cos\left(n\phi - \gamma\right)\right]$$

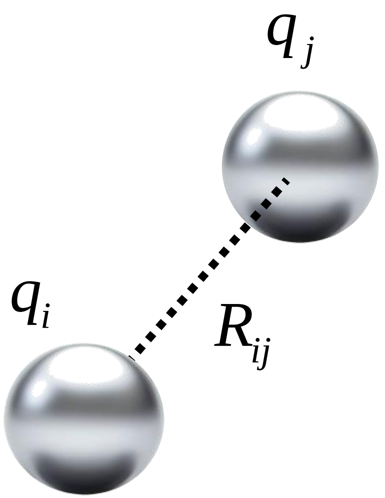


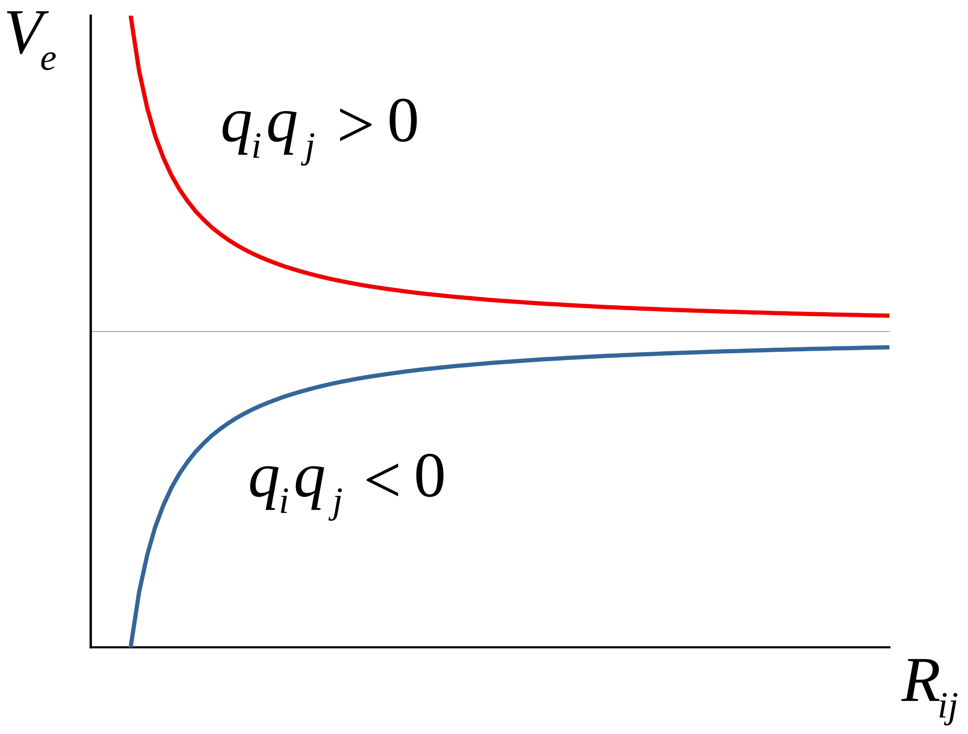


Non-bonded interactions have two components

1. Electrostatic (Coulomb)

$$V_e = \frac{q_i q_j}{\varepsilon R_{ij}}$$

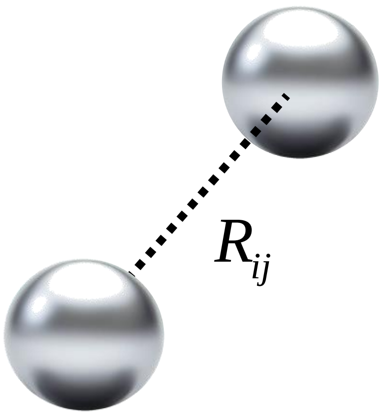


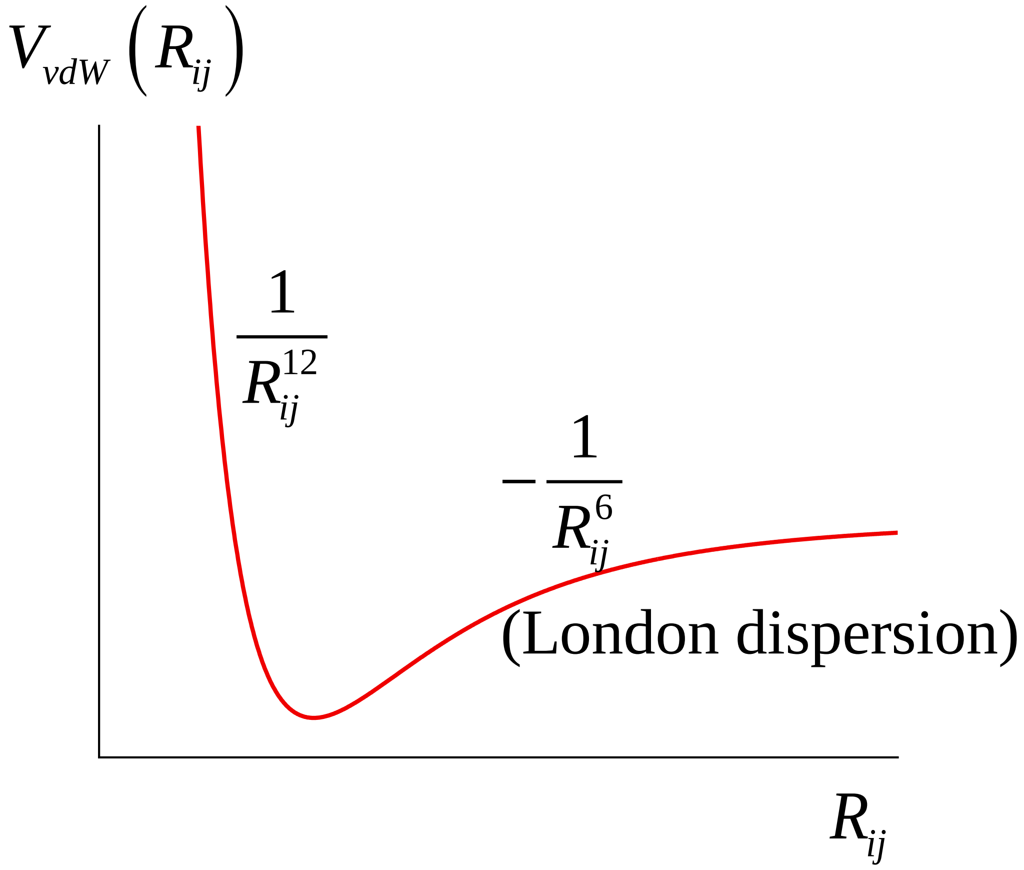


Non-bonded interactions have two components

2. Van der Waals
[Lennard-Jones potential]

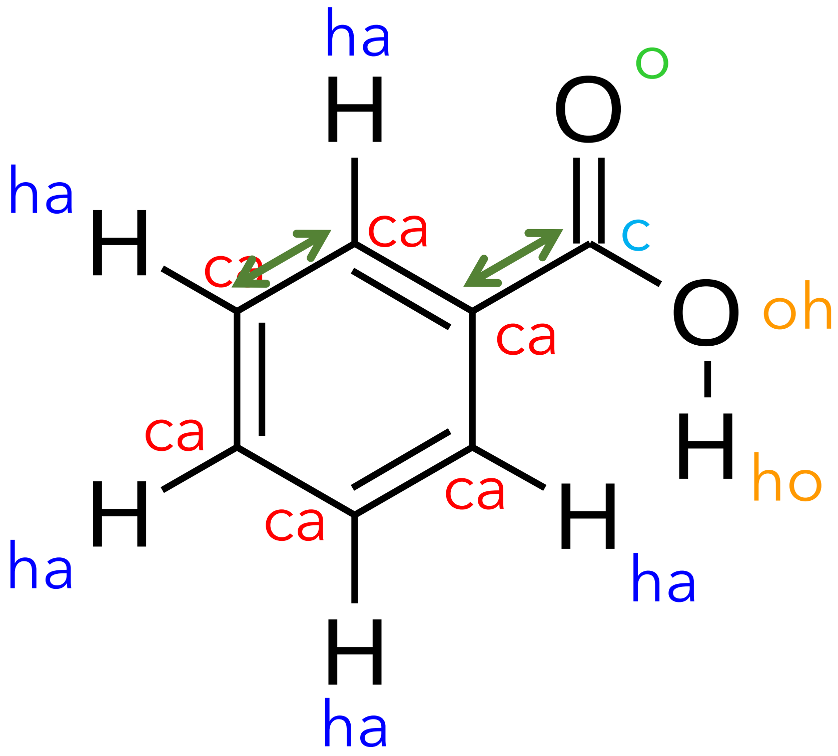
$$V_{vdW} = \frac{A_{ij}}{R_{ij}^{12}} - \frac{B_{ij}}{R_{ij}^{6}}$$





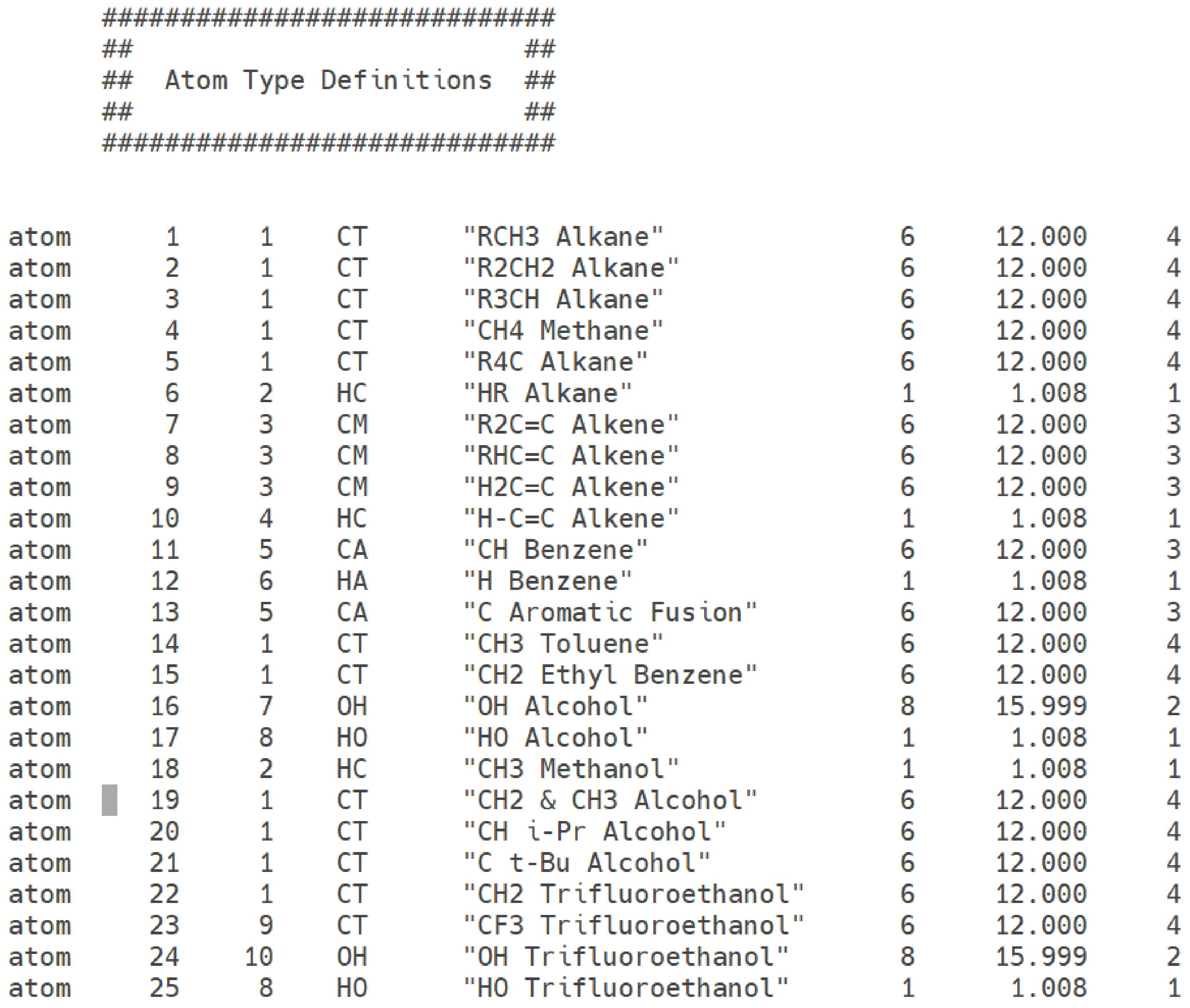
Force-field potential energy surface:

$$E = \sum_{bonds} K_b \left(b - b_{eq}\right)^2 + \sum_{angles} K_\theta \left(\theta - \theta_{eq}\right)^2 + \sum_{dihedrals} \frac{V_n}{2}\left[1 + \cos\left(n\phi - \gamma\right)\right] + \sum_{i<j}\left[\frac{A_{ij}}{R_{ij}^{12}} - \frac{B_{ij}}{R_{ij}^{6}} + \frac{q_i q_j}{\varepsilon R_{ij}}\right]$$



$$\sum_{bonds} K_b^{(ca-ca)} \left(b - b_{eq}^{(ca-ca)}\right)^2 \neq \sum_{bonds} K_b^{(ca-c)} \left(b - b_{eq}^{(ca-c)}\right)^2$$

AMBER force field: Duan *et al. J Comput Chem* **2003**, *24*, 1999



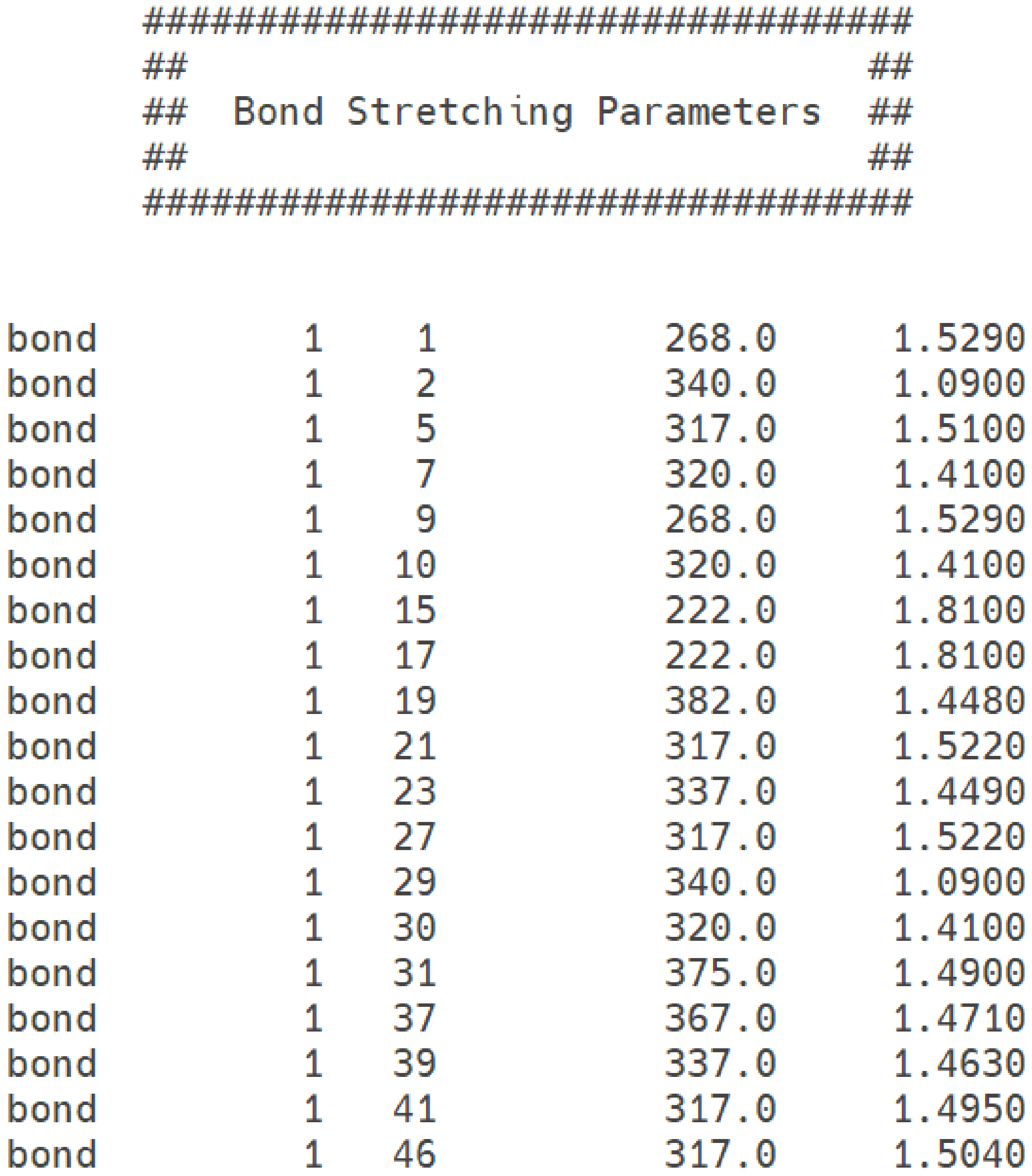
```
      ##############################
      ##                          ##
      ##  Atom Type Definitions   ##
      ##                          ##
      ##############################


atom      1    1    CT     "RCH3 Alkane"                 6    12.000    4
atom      2    1    CT     "R2CH2 Alkane"                6    12.000    4
atom      3    1    CT     "R3CH Alkane"                 6    12.000    4
atom      4    1    CT     "CH4 Methane"                 6    12.000    4
atom      5    1    CT     "R4C Alkane"                  6    12.000    4
atom      6    2    HC     "HR Alkane"                   1     1.008    1
atom      7    3    CM     "R2C=C Alkene"                6    12.000    3
atom      8    3    CM     "RHC=C Alkene"                6    12.000    3
atom      9    3    CM     "H2C=C Alkene"                6    12.000    3
atom     10    4    HC     "H-C=C Alkene"                1     1.008    1
atom     11    5    CA     "CH Benzene"                  6    12.000    3
atom     12    6    HA     "H Benzene"                   1     1.008    1
atom     13    5    CA     "C Aromatic Fusion"           6    12.000    3
atom     14    1    CT     "CH3 Toluene"                 6    12.000    4
atom     15    1    CT     "CH2 Ethyl Benzene"           6    12.000    4
atom     16    7    OH     "OH Alcohol"                  8    15.999    2
atom     17    8    HO     "HO Alcohol"                  1     1.008    1
atom     18    2    HC     "CH3 Methanol"                1     1.008    1
atom     19    1    CT     "CH2 & CH3 Alcohol"           6    12.000    4
atom     20    1    CT     "CH i-Pr Alcohol"             6    12.000    4
atom     21    1    CT     "C t-Bu Alcohol"              6    12.000    4
atom     22    1    CT     "CH2 Trifluoroethanol"        6    12.000    4
atom     23    9    CT     "CF3 Trifluoroethanol"        6    12.000    4
atom     24   10    OH     "OH Trifluoroethanol"         8    15.999    2
atom     25    8    HO     "HO Trifluoroethanol"         1     1.008    1
```

Force-field potential energy surface:

$$E = \sum_{bonds} K_b \left(b - b_{eq}\right)^2 + \sum_{angles} K_\theta \left(\theta - \theta_{eq}\right)^2 + \sum_{dihedrals} \frac{V_n}{2}\left[1 + \cos\left(n\phi - \gamma\right)\right] + \sum_{i<j}\left[\frac{A_{ij}}{R_{ij}^{12}} - \frac{B_{ij}}{R_{ij}^{6}} + \frac{q_i q_j}{\varepsilon R_{ij}}\right]$$

Types	K_b	b_{eq}	K_θ	θ_{eq}	V_n	n	γ	A_{ij}	B_{ij}	q_i	q_j
ca-ca	#	#	-	-	-	-	-	#	#	#	#
ca-c	#	#	-	-	-	-	-	#	#	#	#
…											
ca-ca-ca	-	-	#	#	-	-	-	-	-	-	-
ca-ca-c	-	-	#	#	-	-	-	-	-	-	-
…											
ca-ca-ca-ca	-	-	-	-	#	#	#	-	-	-	-
ca-ca-ca-c	-	-	-	-	#	#	#	-	-	-	-
…											



```
      ##################################
      ##                              ##
      ##  Bond Stretching Parameters  ##
      ##                              ##
      ##################################


bond         1    1          268.0     1.5290
bond         1    2          340.0     1.0900
bond         1    5          317.0     1.5100
bond         1    7          320.0     1.4100
bond         1    9          268.0     1.5290
bond         1   10          320.0     1.4100
bond         1   15          222.0     1.8100
bond         1   17          222.0     1.8100
bond         1   19          382.0     1.4480
bond         1   21          317.0     1.5220
bond         1   23          337.0     1.4490
bond         1   27          317.0     1.5220
bond         1   29          340.0     1.0900
bond         1   30          320.0     1.4100
bond         1   31          375.0     1.4900
bond         1   37          367.0     1.4710
bond         1   39          337.0     1.4630
bond         1   41          317.0     1.4950
bond         1   46          317.0     1.5040
```

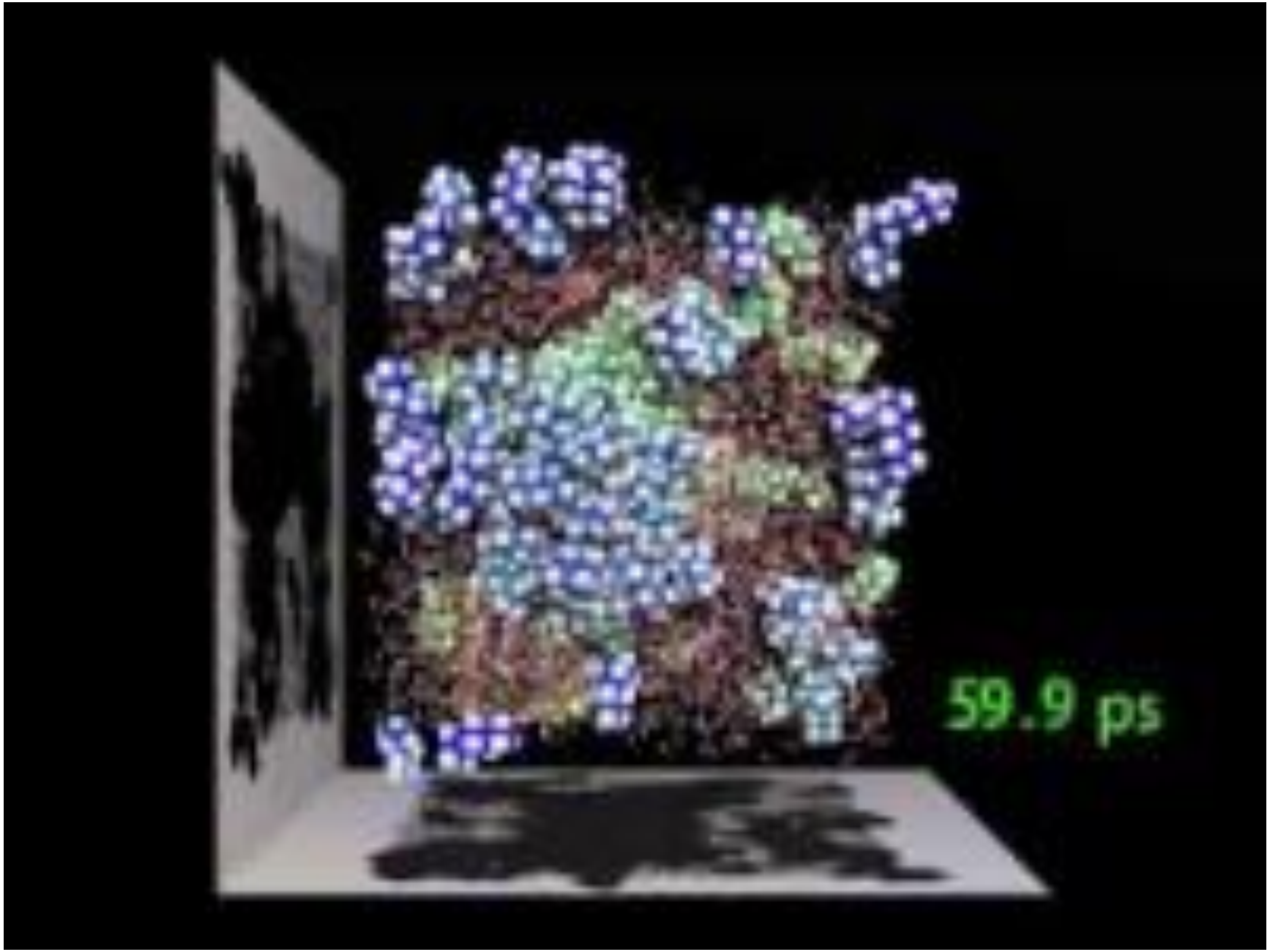
Force fields

- AMBER
- CFF
- CHARMM
- COSMOS-NMR
- CVFF
- ECEPP
- GROMOS
- IFF
- MMFF
- MM2
- OPLS
- QCFF
- UFF
- …

en.wikipedia.org/wiki/Force_field_(chemistry)
en.wikipedia.org/wiki/Molecular_mechanics

MD Software

- AMBER
- CHARMM
- COSMOS
- CP2K
- GROMACS
- GROMOS
- LAMMPS
- SPARTAN
- TINKER
- …

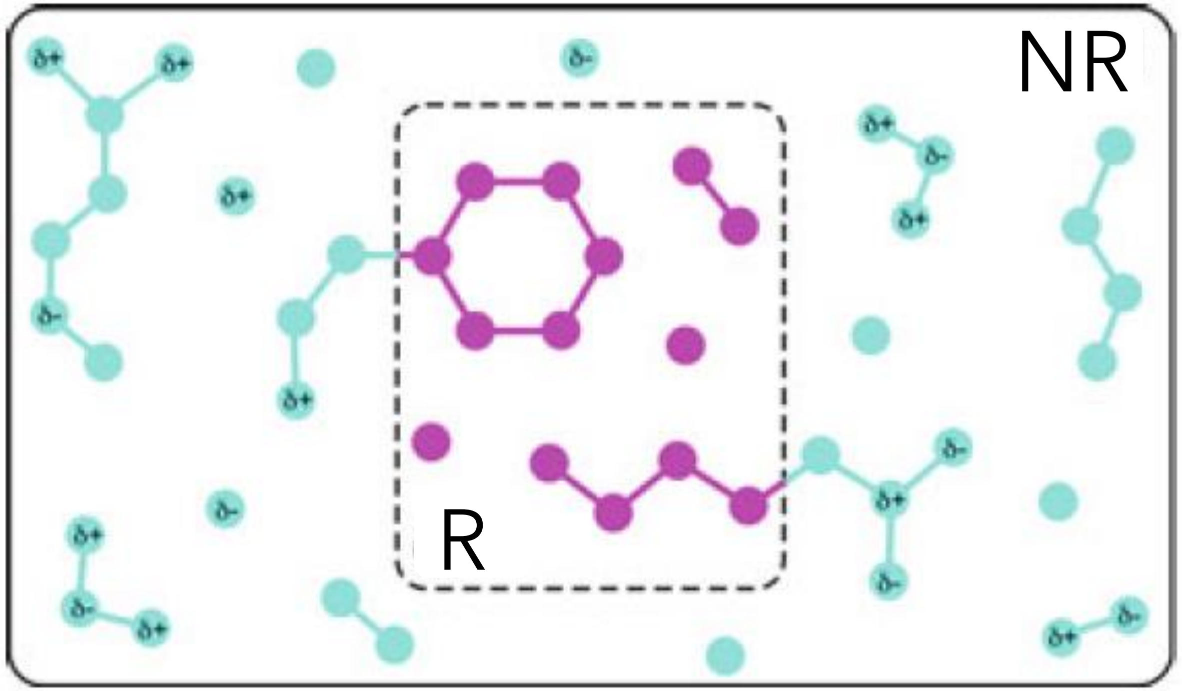


youtu.be/xcMSHy3CqXA

QM/MM PES

Hybrid methods combining QM and MM allows to treat reactive events like bond formation and dissociation.

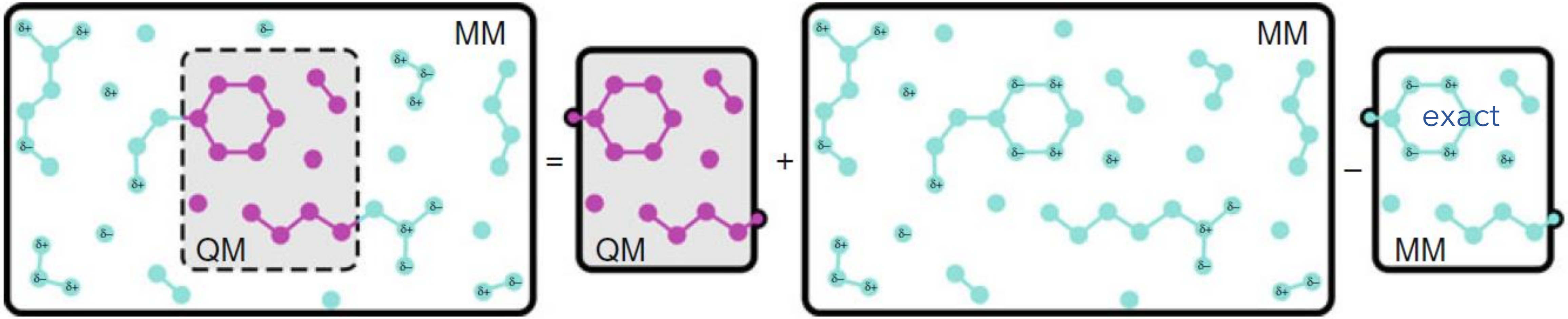
The system is split into reactive (R) and nonreactive (NR) regions.



Groenhof, In *Biomolecular simulations: Methods and protocols,* **2013**

Subtractive QM/MM (ONIOM)

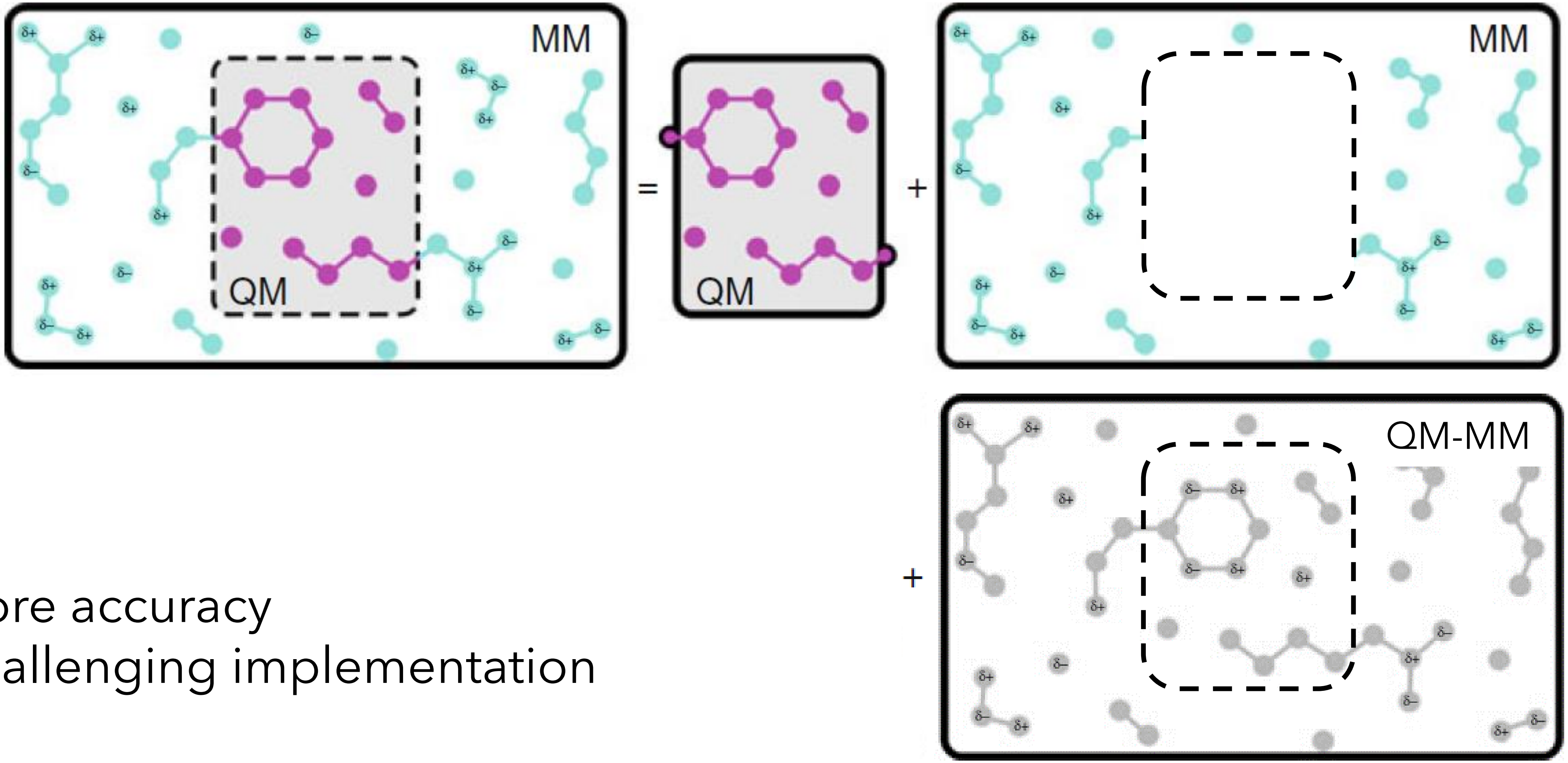
$$E_{QM/MM} = V_{MM}\left(R+NR\right) + V_{QM}\left(R\right) - V_{MM}\left(R\right)$$



☺ No communication between QM and MM routines
☹ Require FF for R region
☹ No polarization of R due to NR

Additive QM/MM

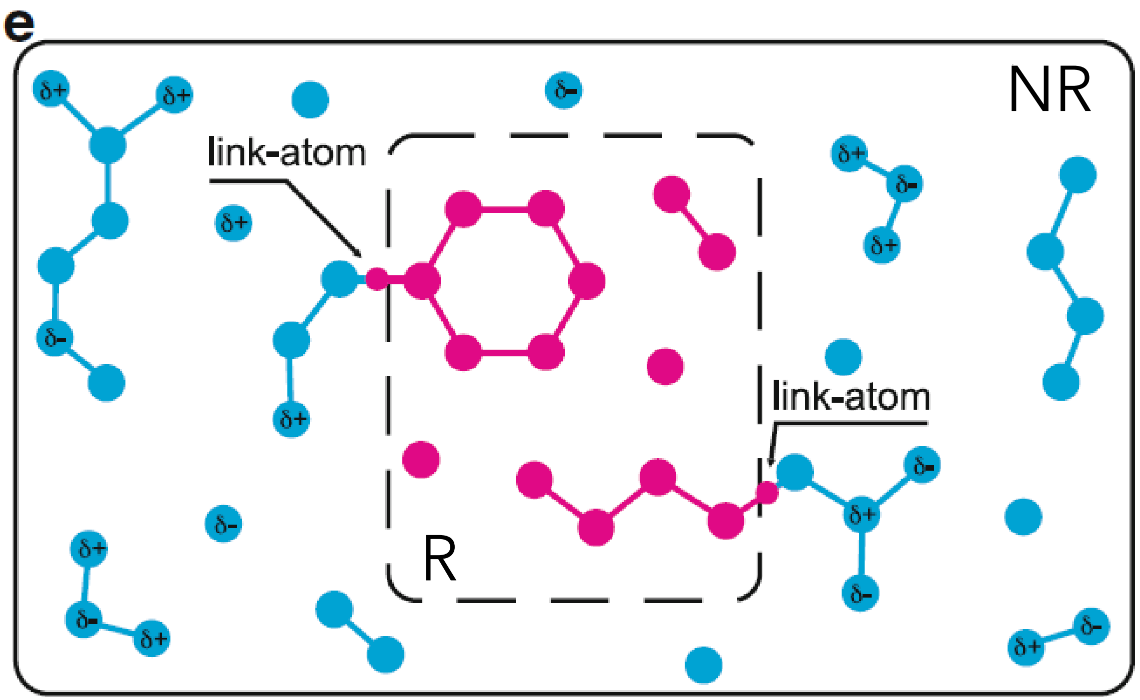
$$E_{QM/MM} = V_{QM}\left(R\right) + V_{MM}\left(NR\right) + V_{QM-MM}\left(R + NR\right)$$



☺ More accuracy
☹ Challenging implementation

$$E_{QM/MM} = V_{QM}\left(R\right) + V_{MM}\left(NR\right) + V_{QM-MM}\left(R + NR\right)$$

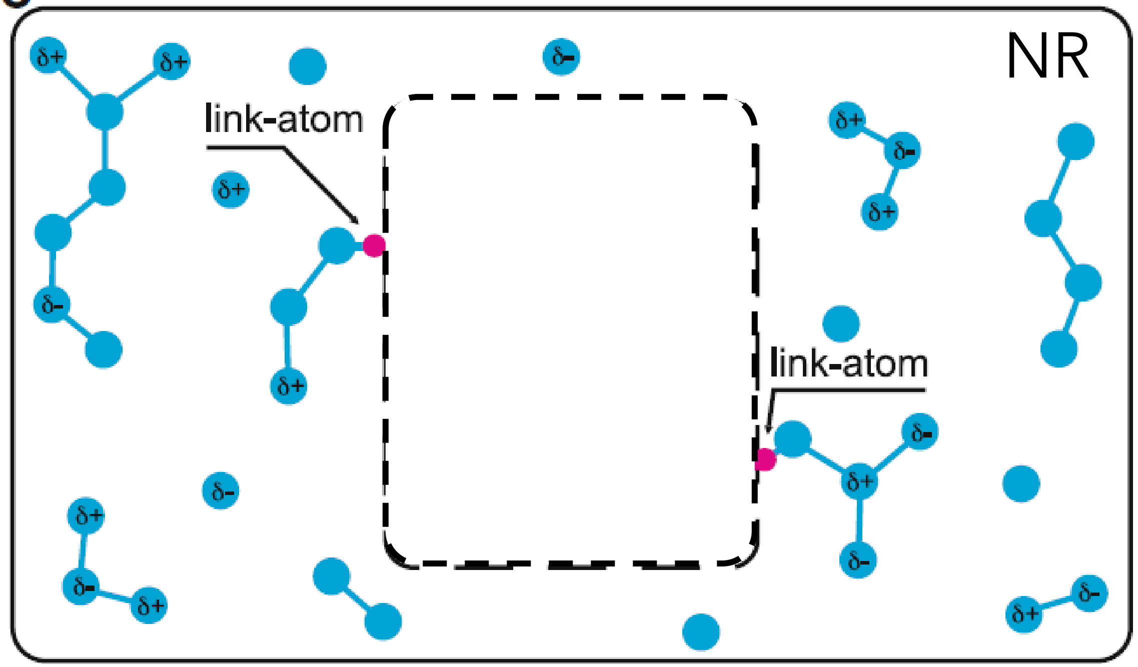
$V_{QM}(R)$ gets virtual
link atoms



$$E_{QM/MM} = V_{QM}(R) + V_{MM}(NR) + V_{QM-MM}(R+NR)$$

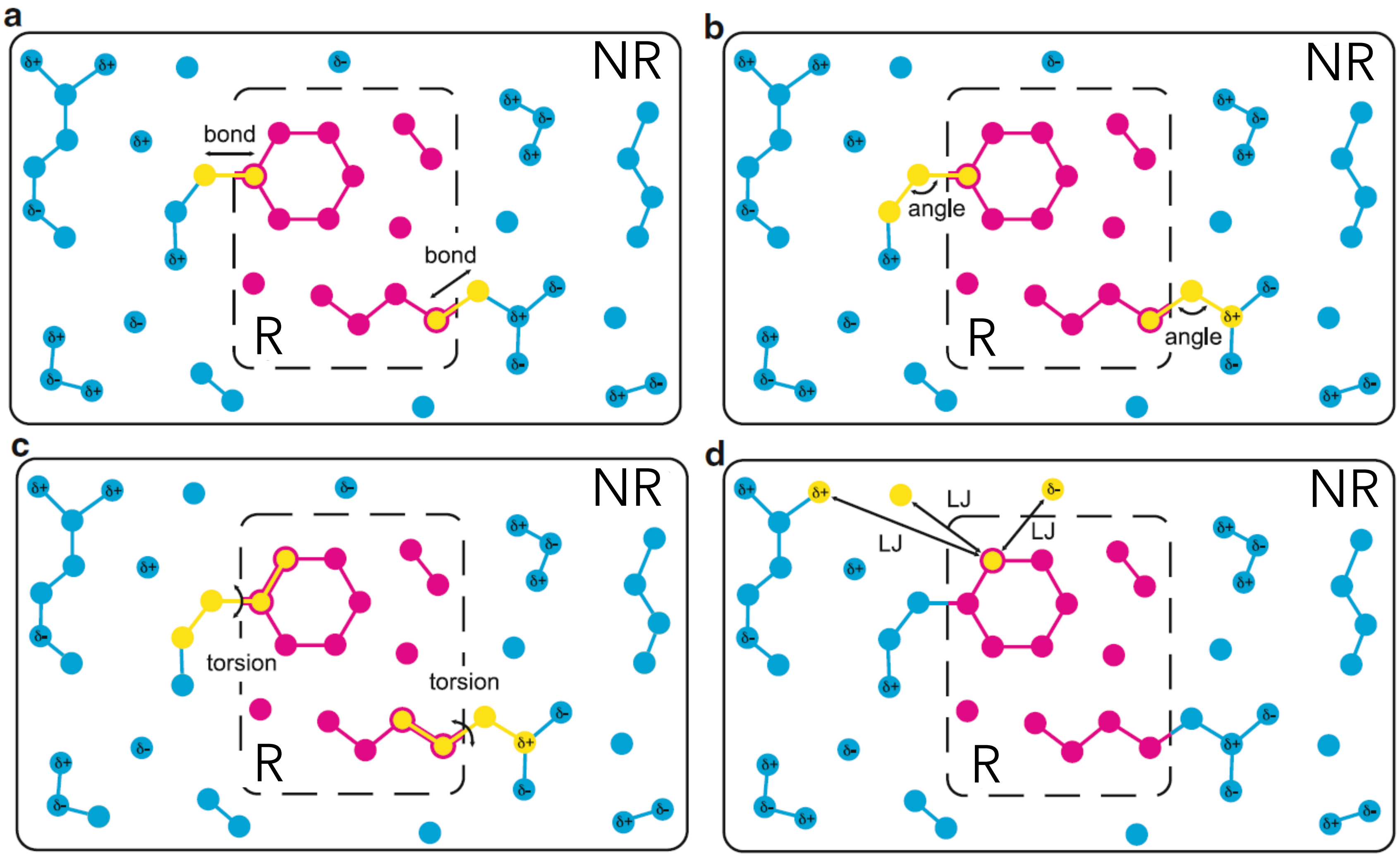
MM doesn’t need parameters for *R*

e



$$E_{QM/MM} = V_{QM}\left(R\right) + V_{MM}\left(NR\right) + V_{QM-MM}\left(R + NR\right)$$

$V_{QM\text{-}MM}(R+NR)$ is handled by FF



$$E_{QM/MM} = V_{QM}\left(R\right) + V_{MM}\left(NR\right) + V_{QM-MM}\left(R+NR\right)$$

Electrostatic interactions in $V_{QM\text{-}MM}(R+NR)$:

1. Mechanical embedding

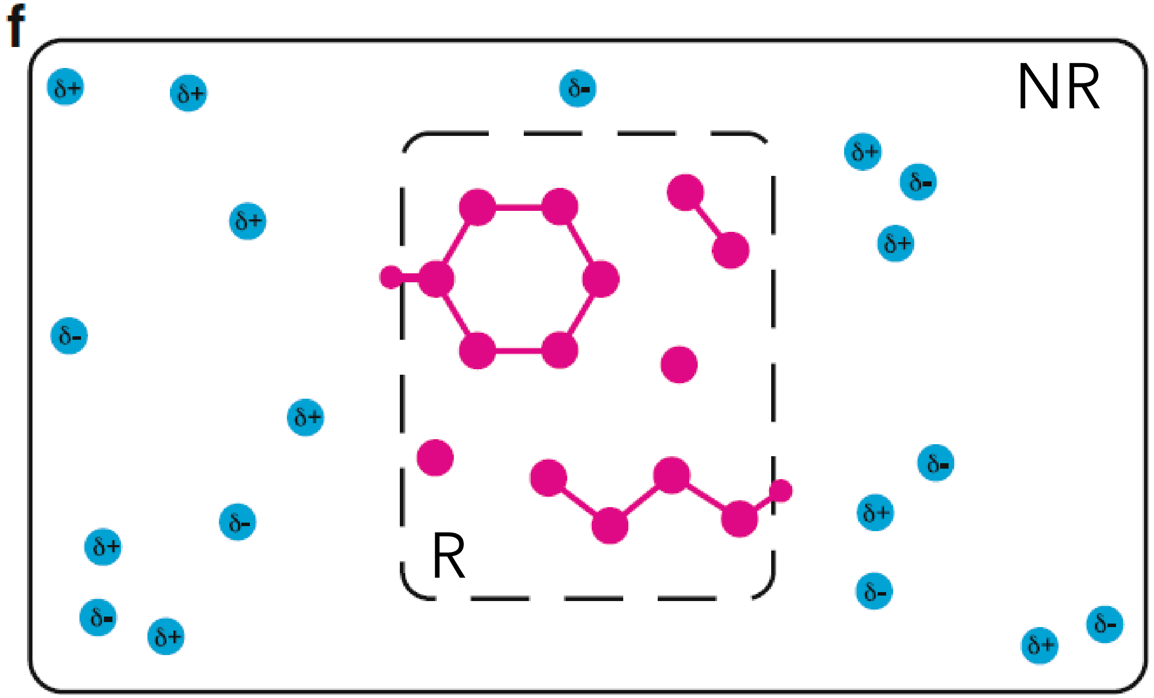
$$H_{QM} = H_{QM}\left(R\right)$$

$$V_e\left(R-NR\right) = \sum_{\substack{i\in R\\ j\in NR}} \frac{q_i q_j}{\varepsilon R_{ij}}$$

2. Electrostatic embedding

$$H_{QM} = H_{QM}\left(R\right) + \sum_{i\in NR} q_i$$

$$V_e\left(R-NR\right) = 0$$



Electrostatic embedding is mandatory for problems involving charge transfer and excited states.

Baker. *Wires* **2015**, *5*, 241

Some advanced aspects in QM/MM

- Certain cases may require polarization of NR too.
  This is done with **polarizable force fields**.
  Baker. *WIREs: Comp Mol Sci* **2015**, *5*, 241

- R and NR regions may change during dynamics.
  It is addressed with **adaptive QM/MM**.
  Duster *et al*. *WIREs: Comp Mol Sci* **2017**, *7*, e1310

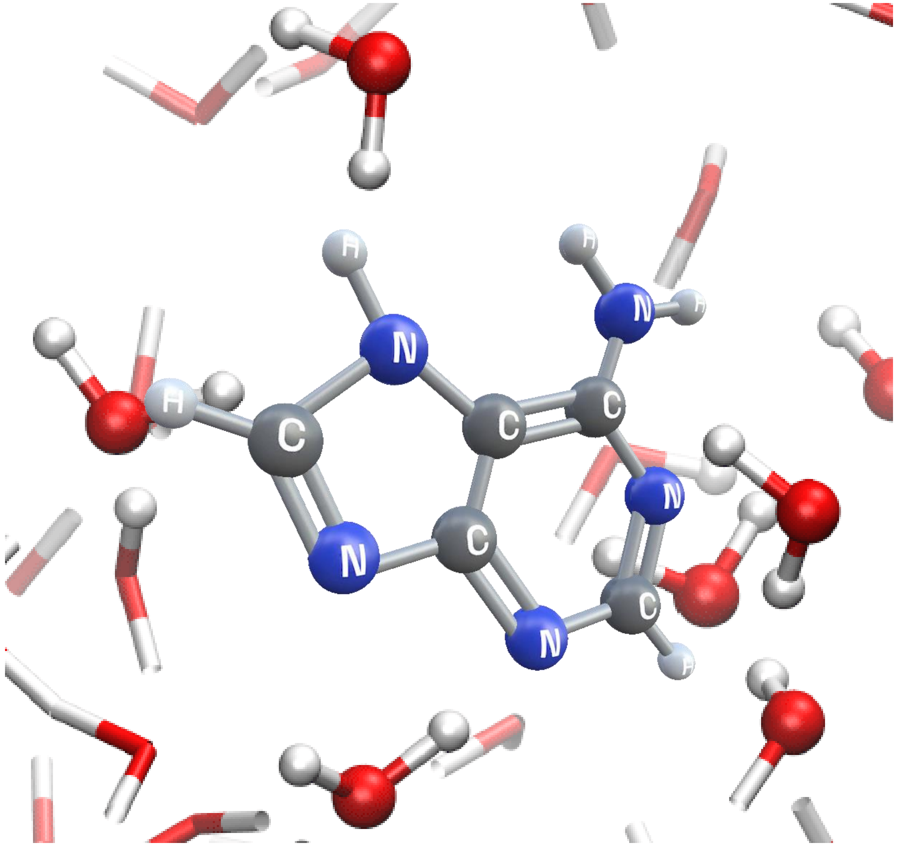
- QM/MM input is prone to errors (too many steps).
  Input automatization is fundamental.
  Pedraza-González *et al. J Chem Theory Comput* **2019**, *15*, 3134

Software allowing QM/MM

- QMMM (Truhlar’s group)
- ChemShell (Molcas,Turbomole, …)
- COBRAMM
- CP2K
- Gaussian
- Gamess
- Q-Chem
- NWChem
- ORCA
- MOPAC
- …

Continuum models

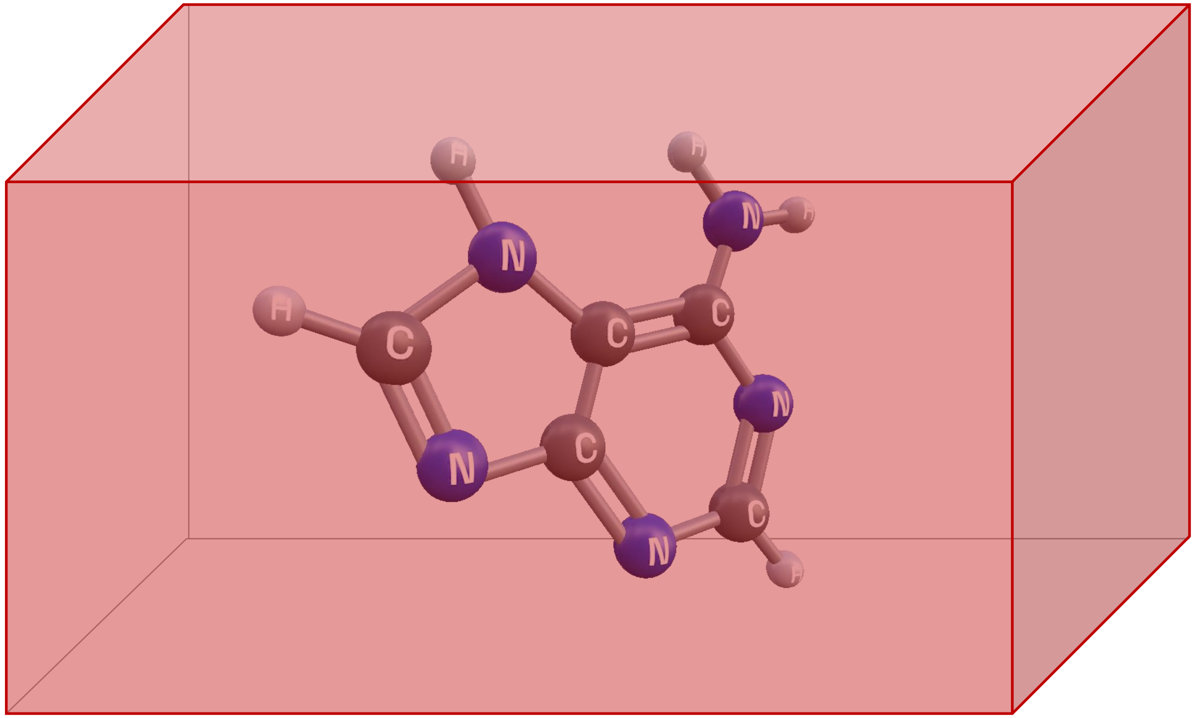
Consider a solvated molecule.



Replace the solvent with a continuum medium.

The molecular charges polarize the medium.

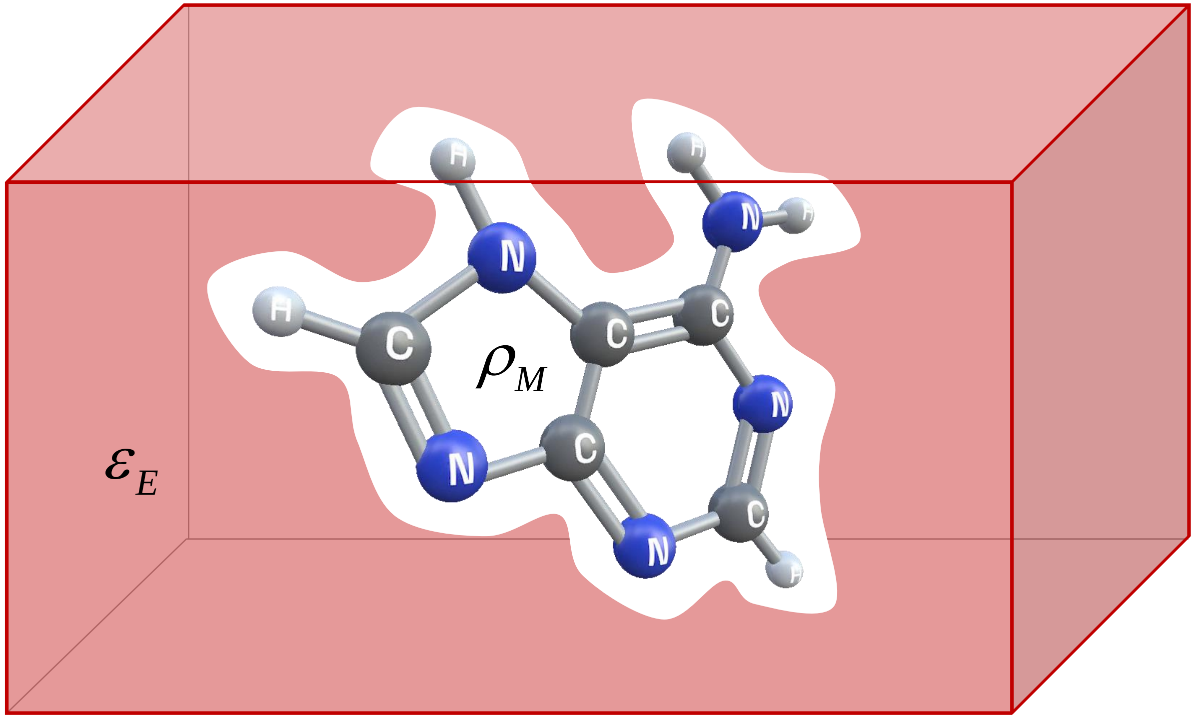
The polarized medium affects the molecular charges.



Continuum (or implicit) solvation models describe the molecular electronic energy changes due to the influence of a polarized continuum medium.

Electrostatic potential *V* of the polarized medium (V_E) plus the molecule (V_M) is given by the Poisson equation

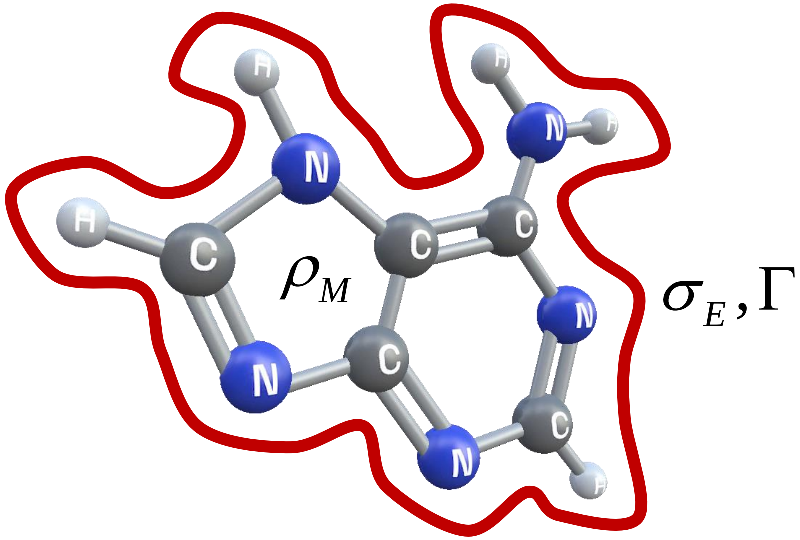
$$\nabla^2 V = -\frac{4\pi\rho}{\varepsilon_E}$$



Mennucci. *WIREs: Comp Mol Sci* **2012**, *2*, 386.

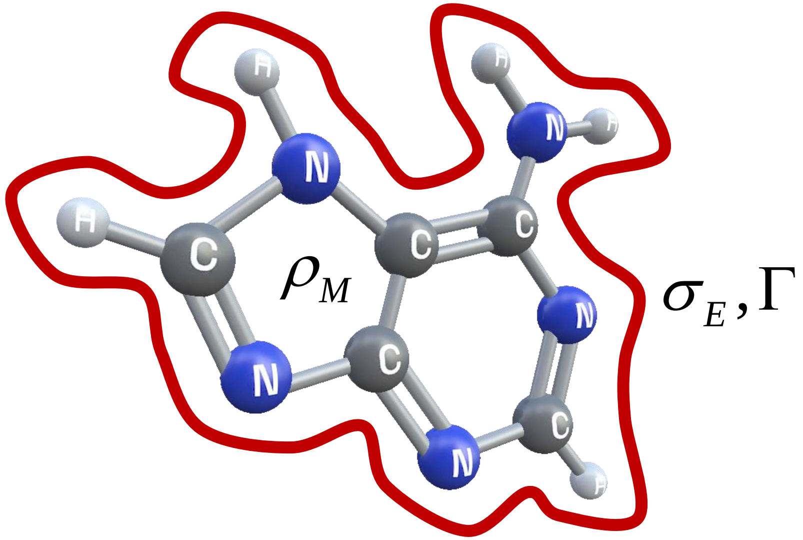
This problem is equivalent to finding the potential of a fictitious charge distribution σ_E on the surface of the cavity between the molecule and the medium.

$$V_\sigma(\mathbf{r}) = \int_\Gamma \frac{\sigma_E(\mathbf{s})}{|\mathbf{r}-\mathbf{s}|} d^2\mathbf{s}$$



Once σ_E is found, the contribution of the solvent to the molecular energy can be computed.

$$G_E = \frac{1}{2}\int_{\Gamma} \sigma_E(\mathbf{s}) \left[\int_{vol} \frac{\rho_M(\mathbf{r})}{|\mathbf{r}-\mathbf{s}|} d^3\mathbf{r} \right] d^2\mathbf{s}$$

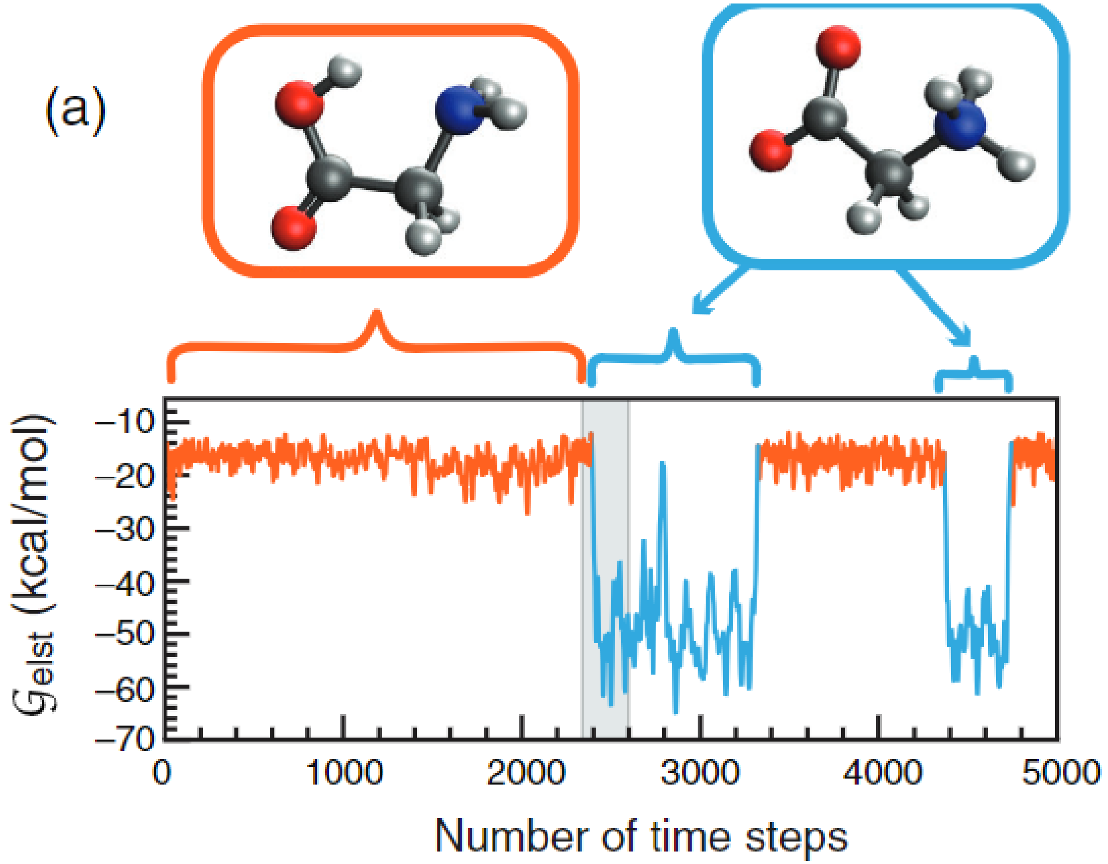


Most implicit models may not describe:

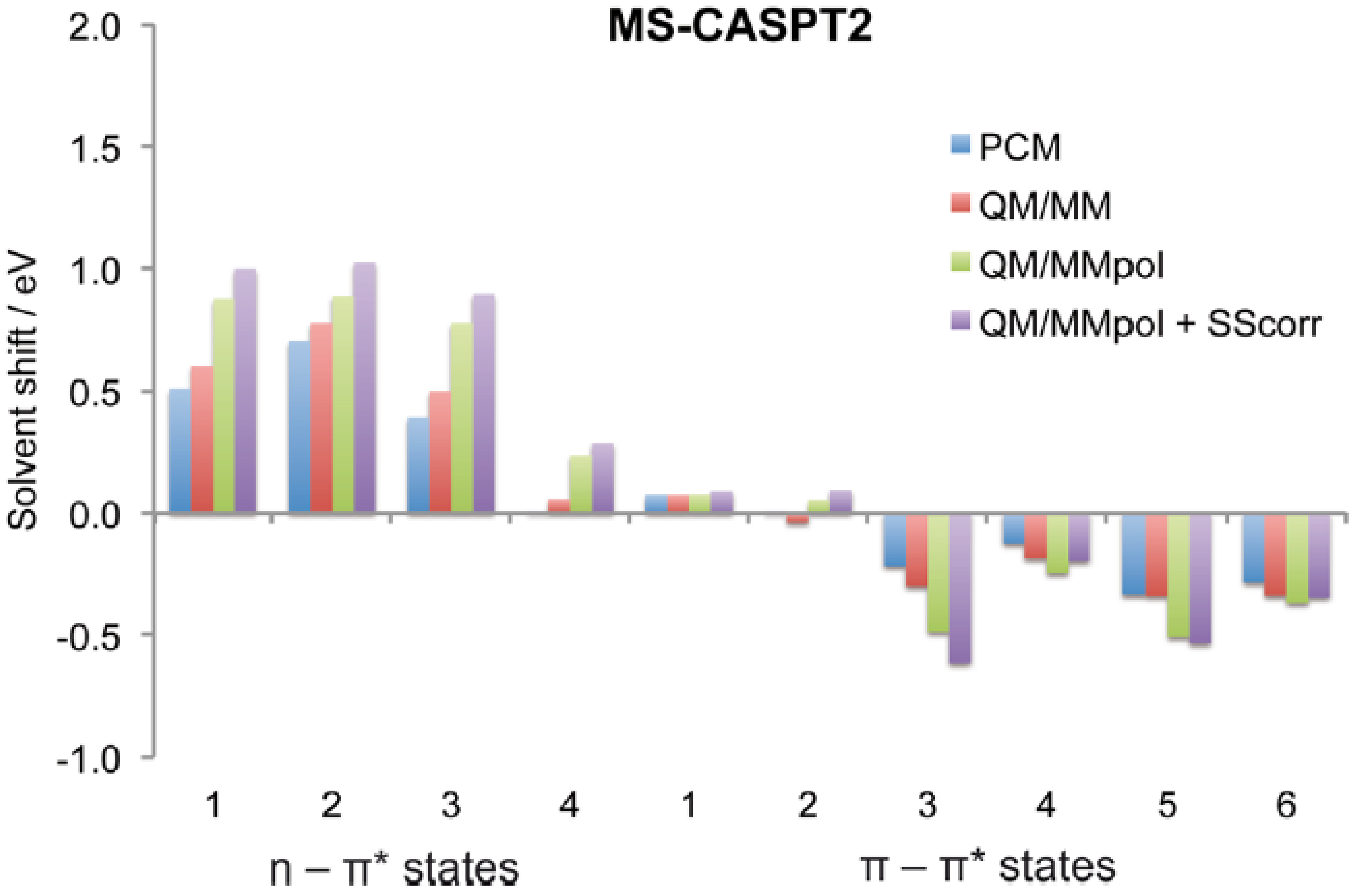
- Charge transfer
- Hydrogen bonds
- Anisotropic and inhomogeneity effects
- Electronic density equilibration after a state change.

They may also have PES discontinuities, which are critical for dynamics.

Charge transfer and discontinuities are well treated with SwiG-PCM.



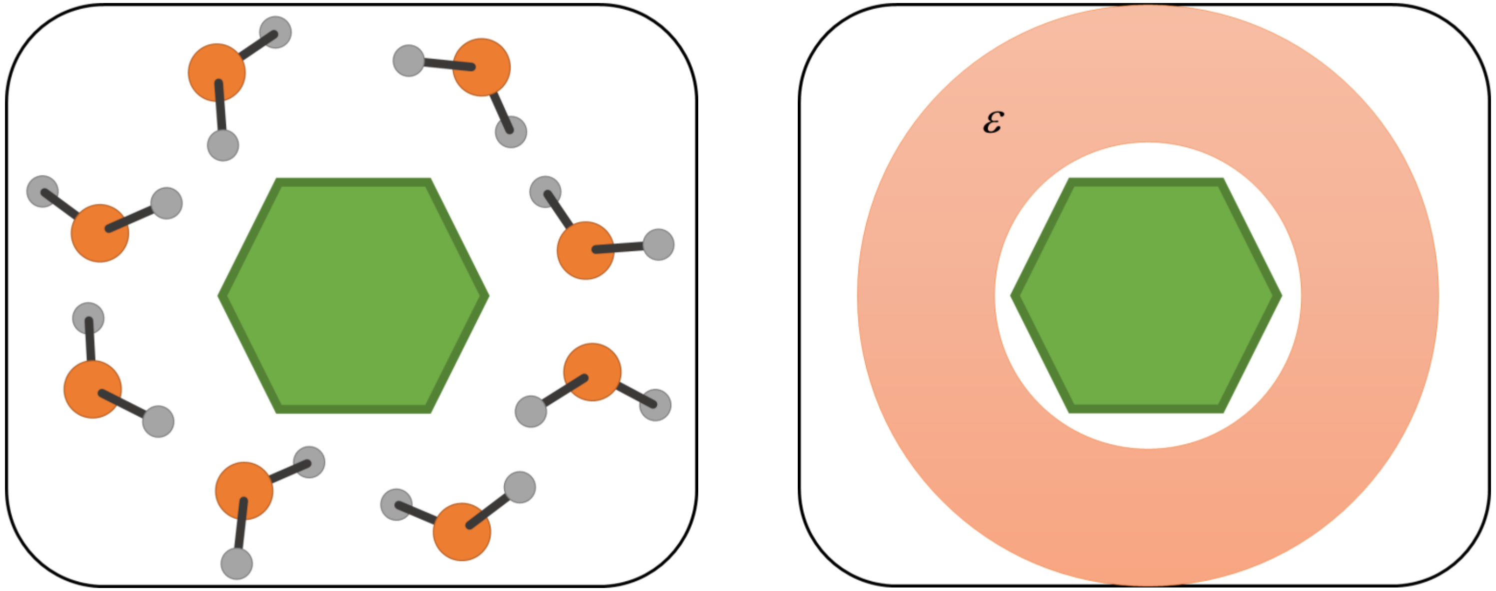
Herbert. *WIREs: Comp Mol Sci* **2021**, *11*, e1519



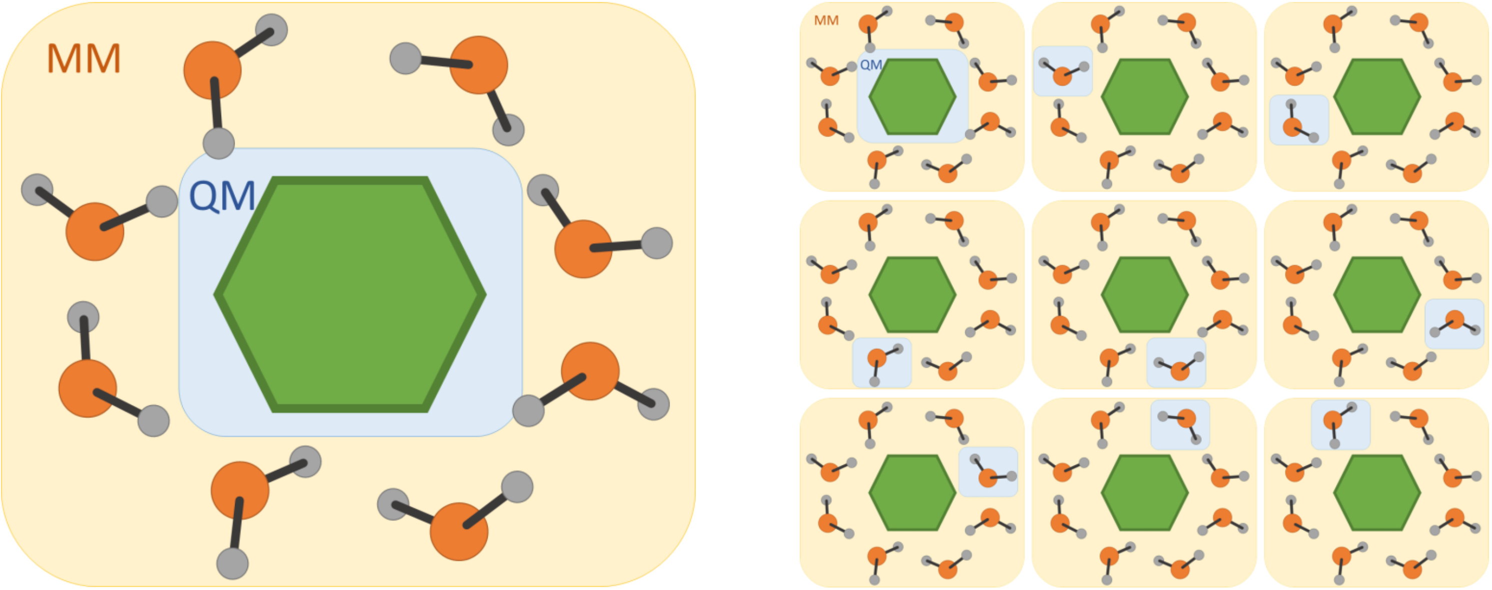
Li *et al. J Chem Theory Comput* **2015**, *11*, 1674

More comparisons: Klamt *et al. J Chem Theory Comput* **2015**, *11*, 4220

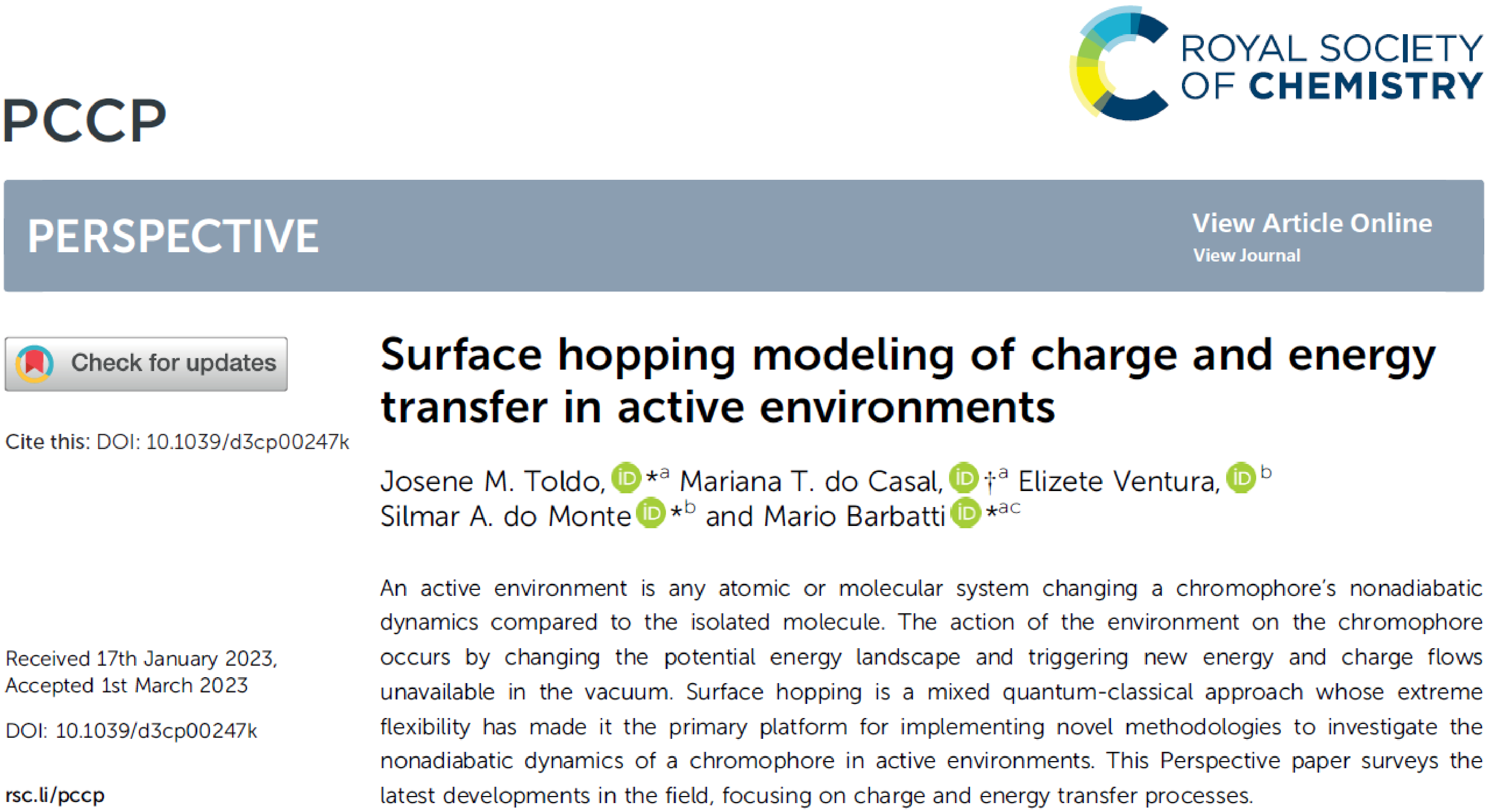
Photophysics in active environments


(a) Complete QM

(b) Implicit environment


(c) QM/MM

(d) Fragment QM/MM



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Surface hopping modeling of charge and energy transfer in active environments

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Silmar A. do Monte *[b] and Mario Barbatti *[ac]

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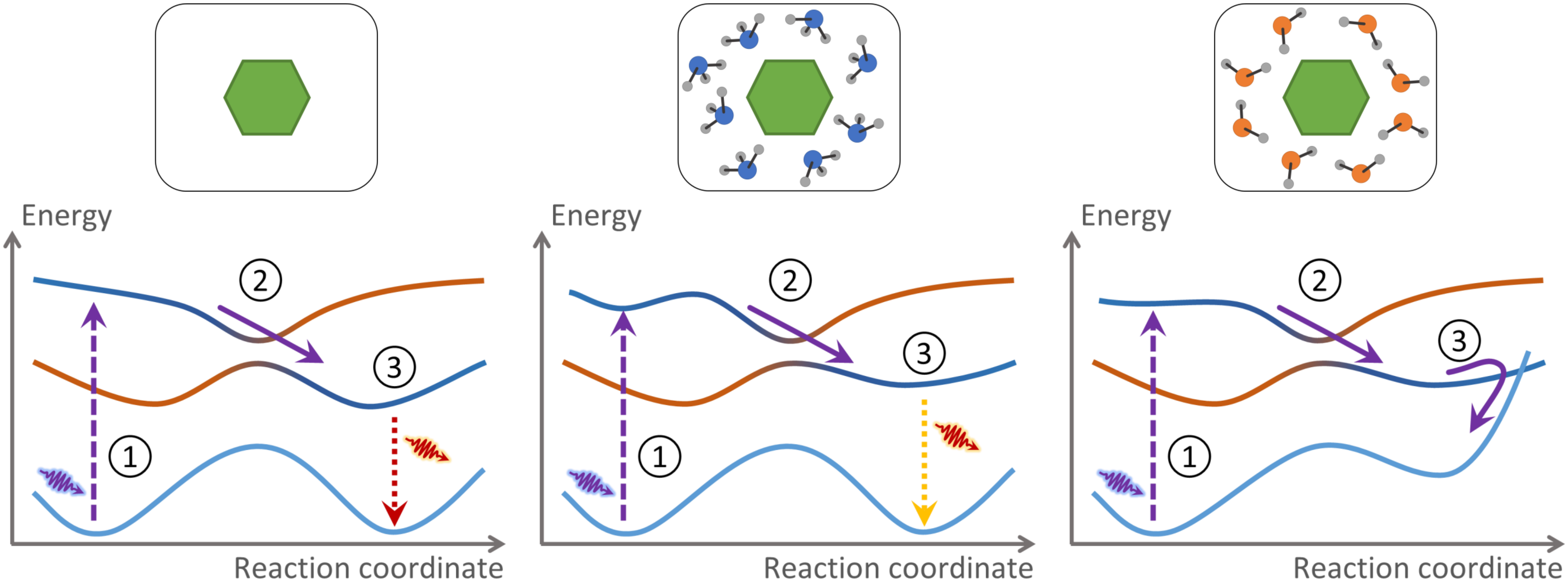
An active environment is any atomic or molecular system changing a chromophore's nonadiabatic dynamics compared to the isolated molecule. The action of the environment on the chromophore occurs by changing the potential energy landscape and triggering new energy and charge flows unavailable in the vacuum. Surface hopping is a mixed quantum-classical approach whose extreme flexibility has made it the primary platform for implementing novel methodologies to investigate the nonadiabatic dynamics of a chromophore in active environments. This Perspective paper surveys the latest developments in the field, focusing on charge and energy transfer processes.

Toldo *et al.* *PCCP* **2023**, *25*, 8293

What’s an active environment?

An active environment change the photophysics of the chromophore



(a) Isolated chromophore

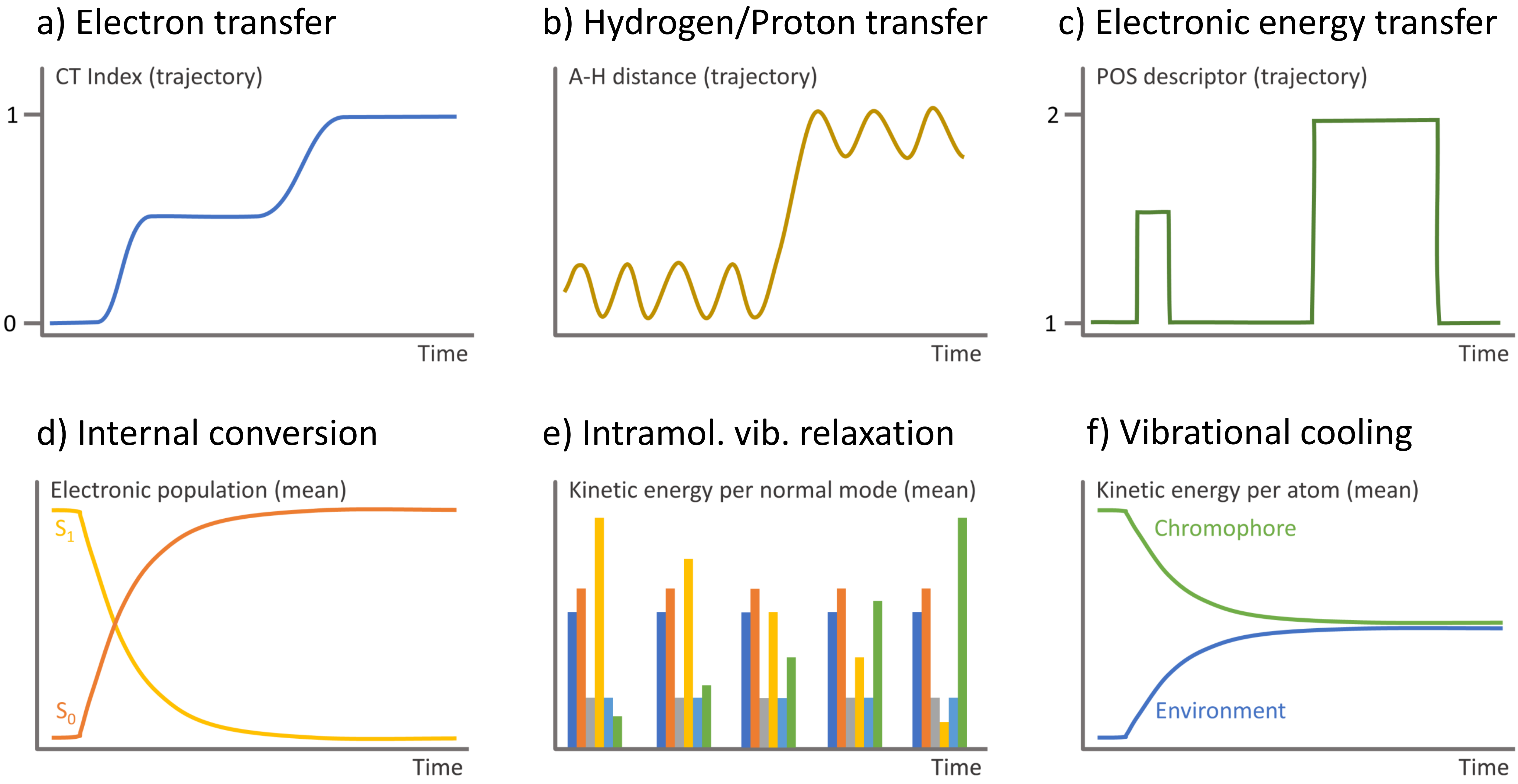
(b) Passive environment

(c) Active environment

Processes in active environments

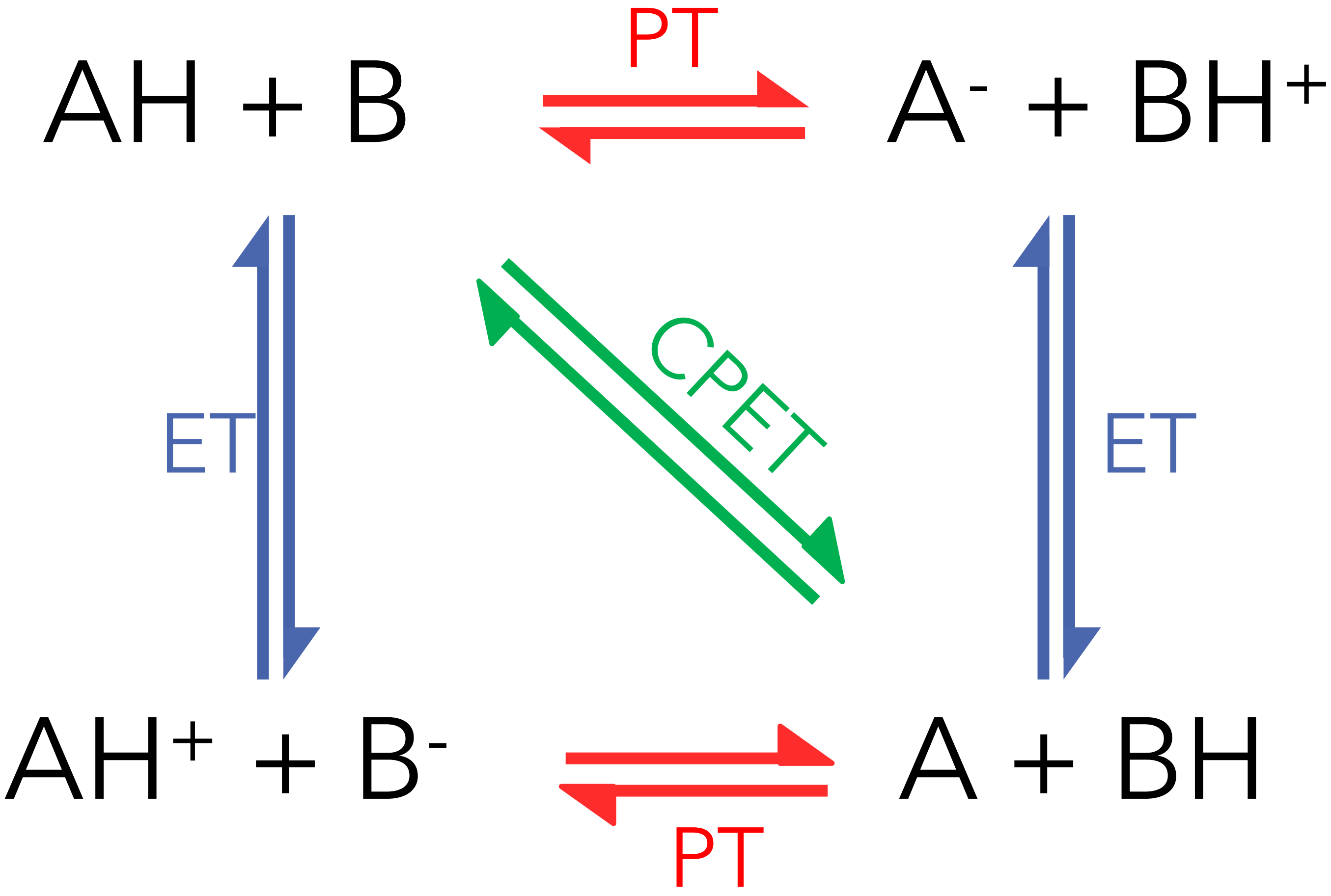
- Charge transfer
  - Electron transfer
  - Proton transfer

- Energy transfer
  - Electronic energy
  - Vibrational energy


a) Electron transfer
CT Index (trajectory)
1
0
Time
b) Hydrogen/Proton transfer
A-H distance (trajectory)
Time
c) Electronic energy transfer
POS descriptor (trajectory)
2
1
Time
d) Internal conversion
Electronic population (mean)
S_1
S_0
Time
e) Intramol. vib. relaxation
Kinetic energy per normal mode (mean)
Time
f) Vibrational cooling
Kinetic energy per atom (mean)
Chromophore
Environment
Time

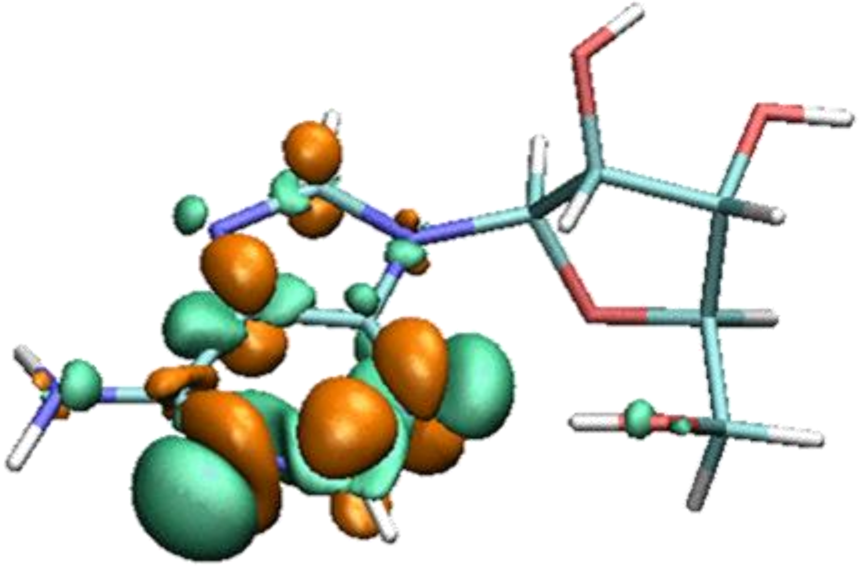
Charge transfer

Electron and proton transfer processes



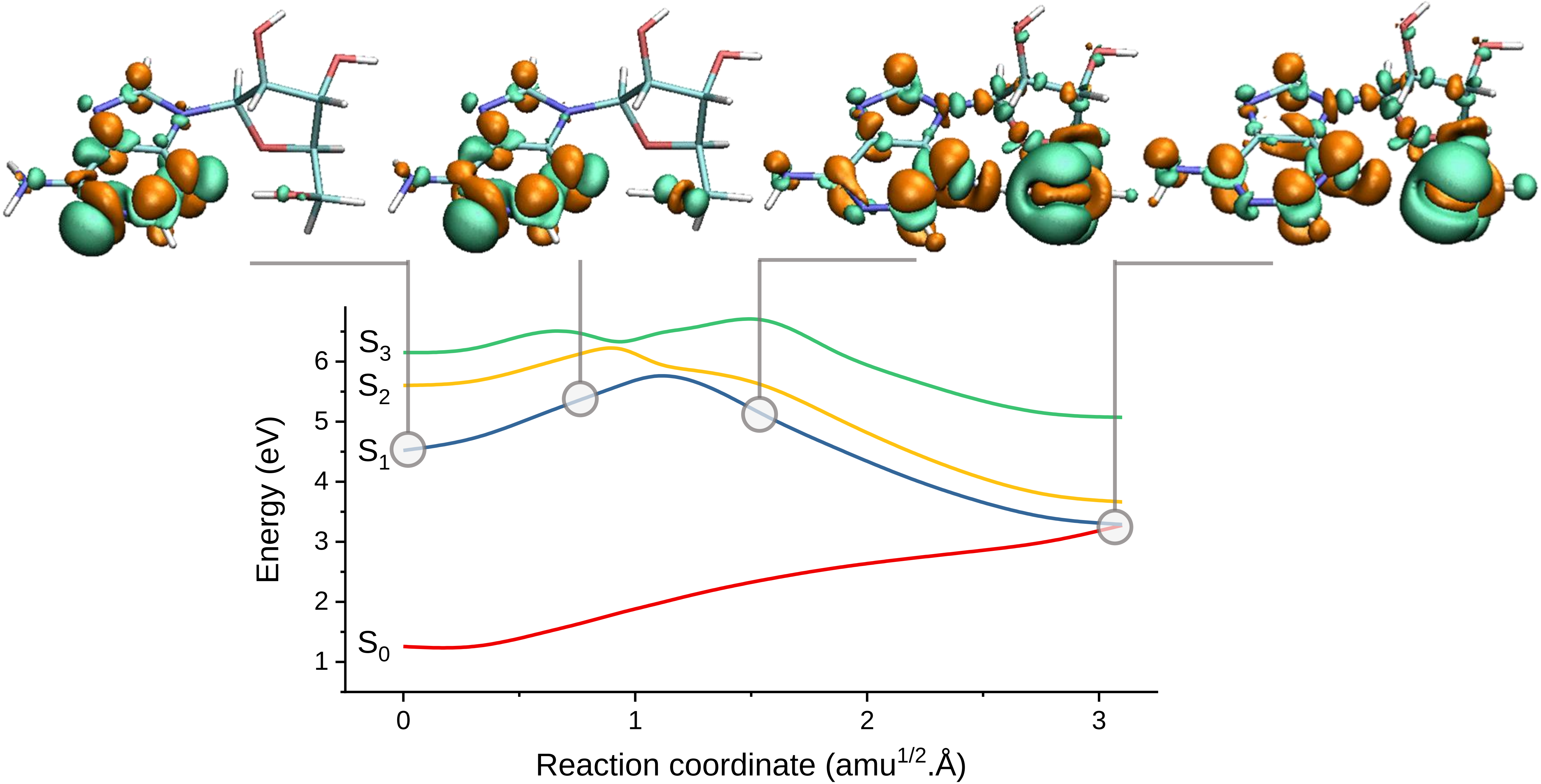
$$\begin{tikzcd}
AH + B \arrow[r, shift left, "PT"] \arrow[d, shift left] \arrow[dr, shift left, "CPET"] & A^- + BH^+ \arrow[l, shift left] \arrow[d, shift left] \\
AH^+ + B^- \arrow[u, shift left, "ET"] \arrow[r, shift left] & A + BH \arrow[l, shift left, "PT"] \arrow[u, shift left, "ET"'] \arrow[ul, shift left]
\end{tikzcd}$$

H-transfer pathway in adenosine



Electron goes from GREEN to ORANGE

Mansour *et al. J Phys Chem Lett* **2022**, *13*, 6194


S3
S2
S1
S0
Energy (eV)
1
2
3
4
5
6
0
1
2
3
Reaction coordinate (amu$^{1/2}$.Å)

Be careful with BOMD involving proton transfer.

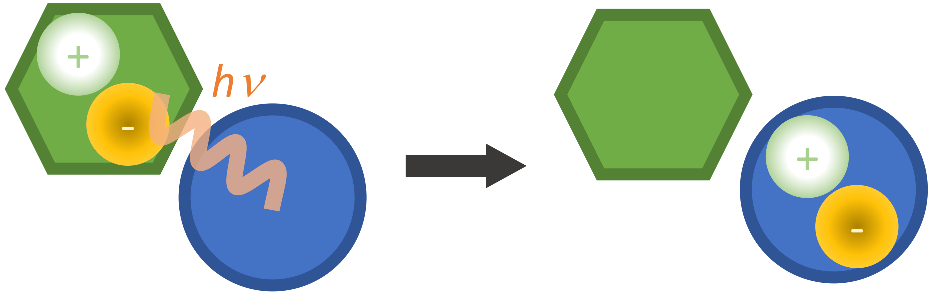
The large proton delocalization may require a quantum treatment.

Hammes-Schiffer. *Philos Trans R Soc A* **2022**, *380*, 20200377

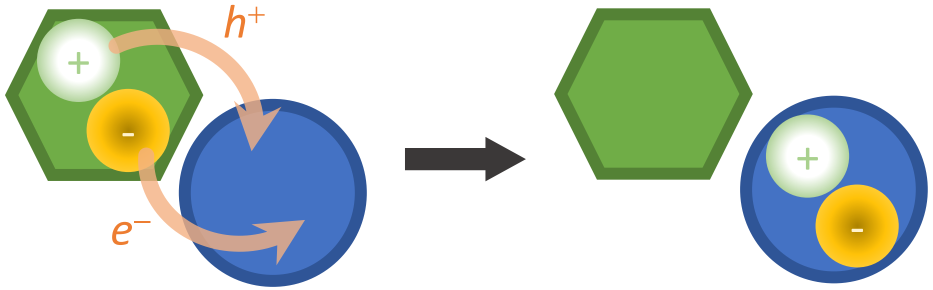
Energy transfer

Electronic energy transfer

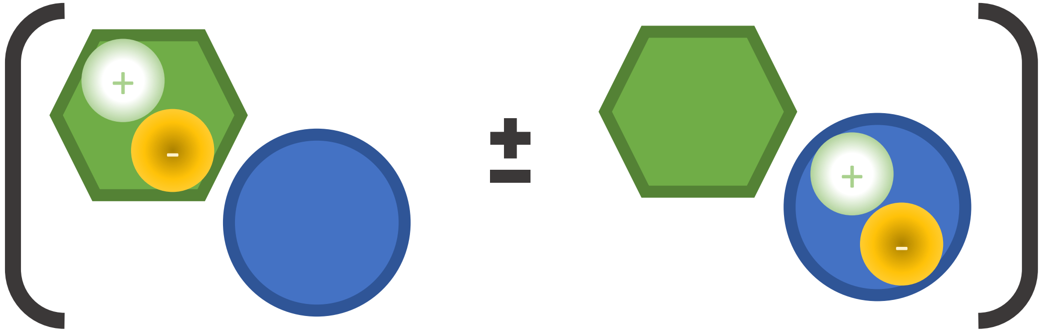
a) Förster resonance energy transfer (FRET)



b) Dexter energy transfer

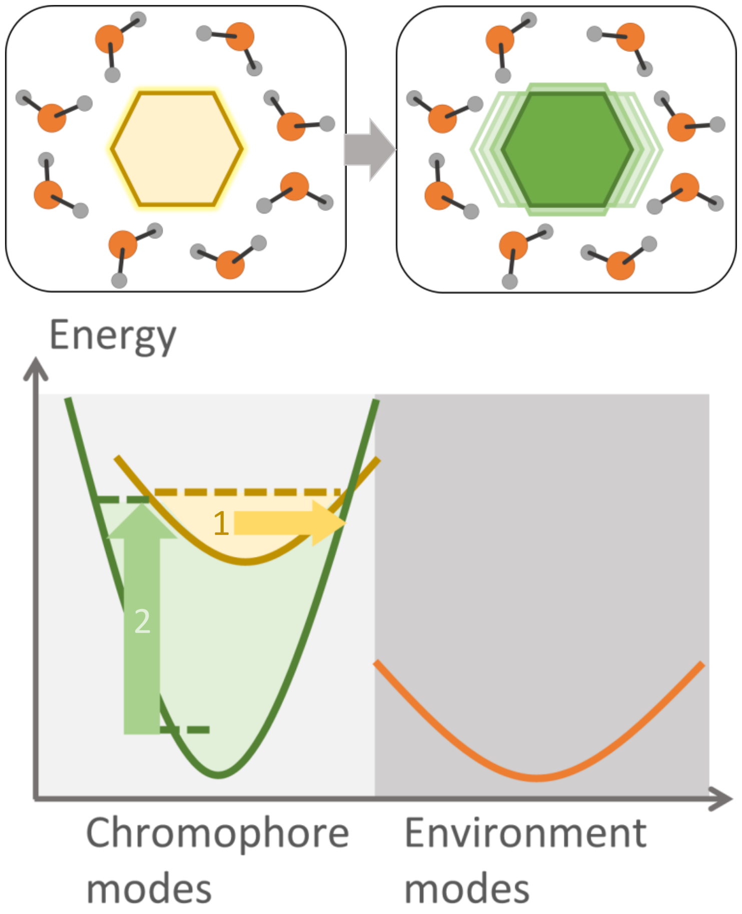


c) Coherent transport

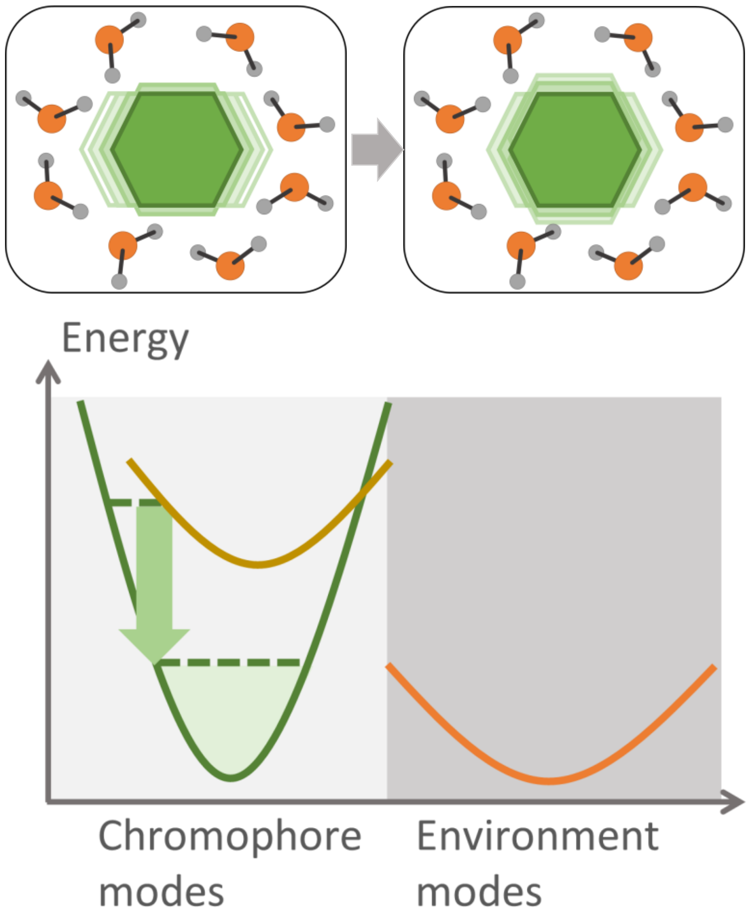


Vibrational energy transfer

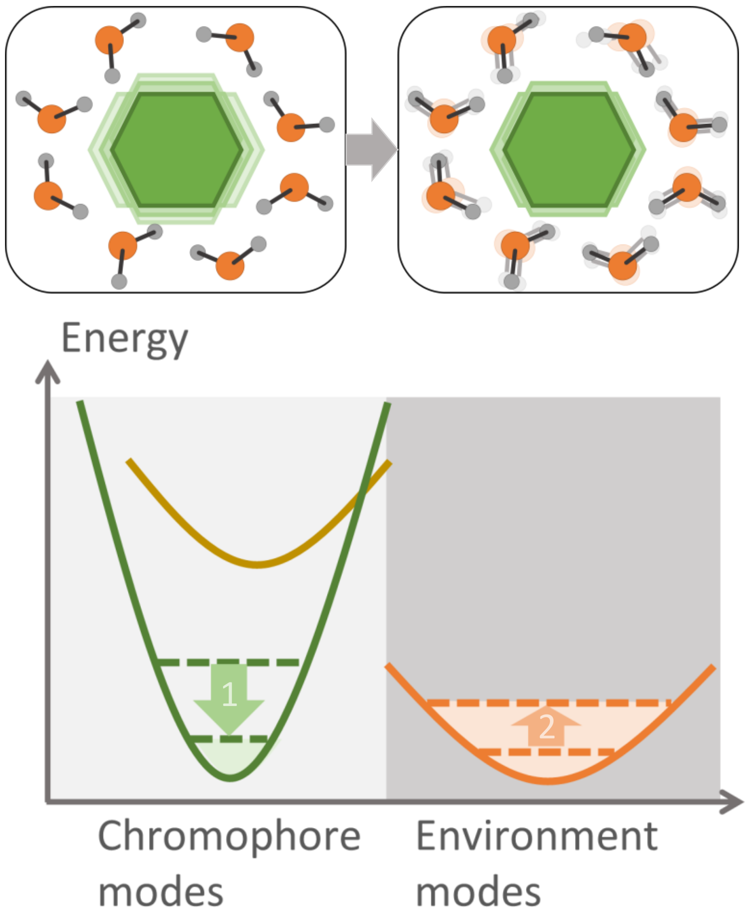
a) Internal conversion



b) Intramol. vib. redistribution

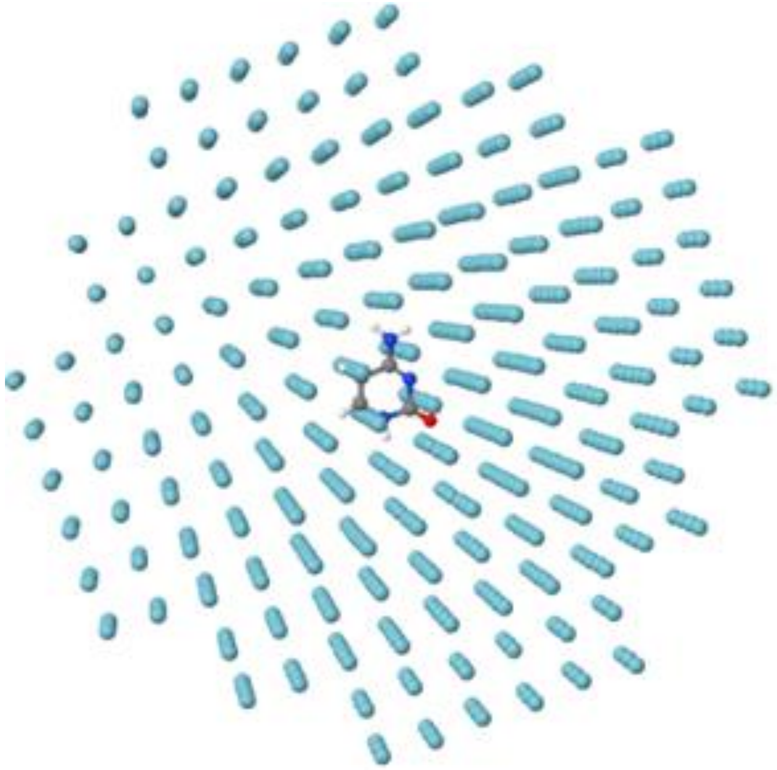


c) Vibrational cooling



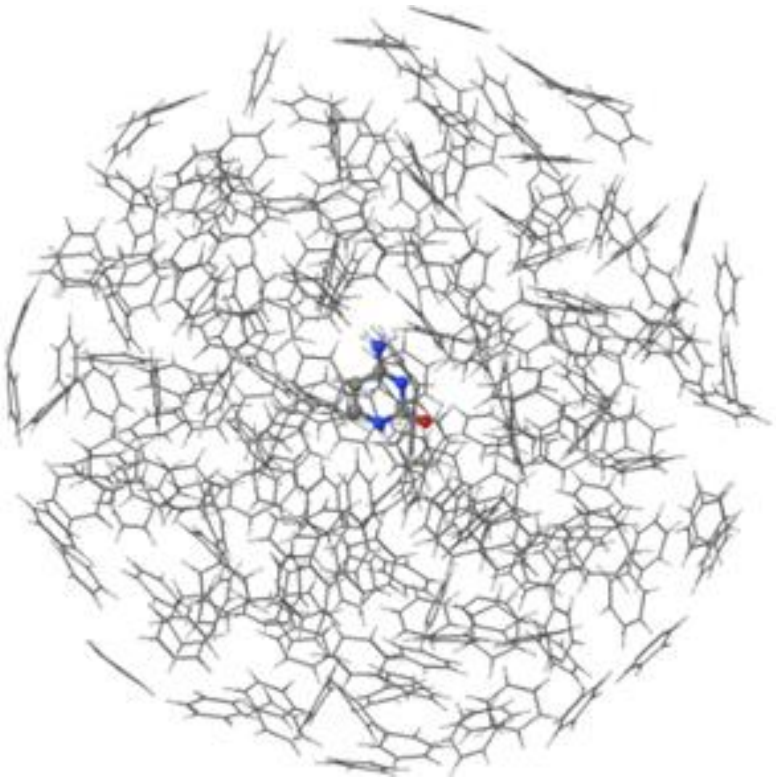
Cytosine in

Argon



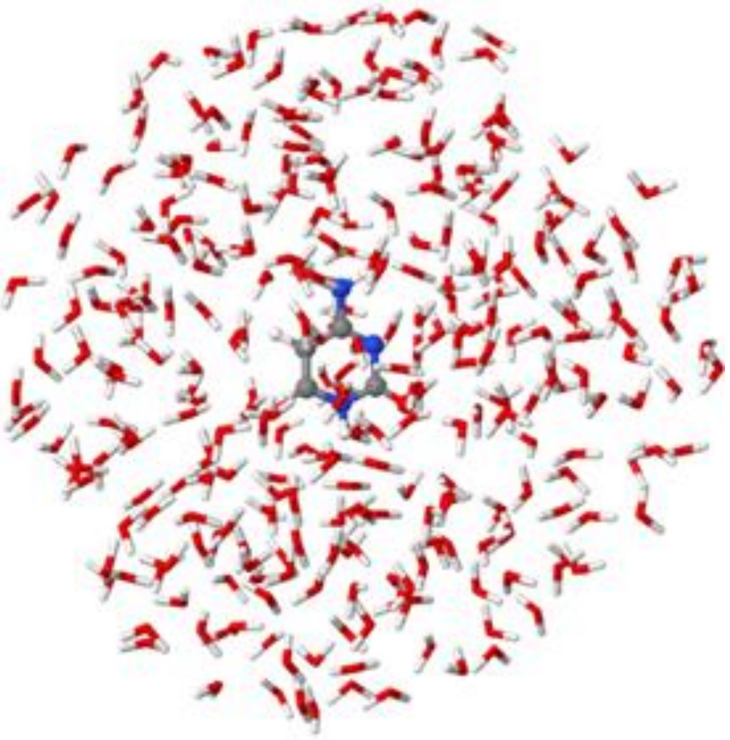
25 ps

Benzene



4 ps

Water



1 ps

Ventura *et al.* *PCCP* **2022**, *24*, 9403

To know more:

QM/MM

- Groenhof, *In Biomolecular simulations,* **2013**

Active environments

- Toldo *et al. PCCP* **2023**, *25*, 8293