Combined quantum/classical approaches for solvated systems: the role of mutual polarization

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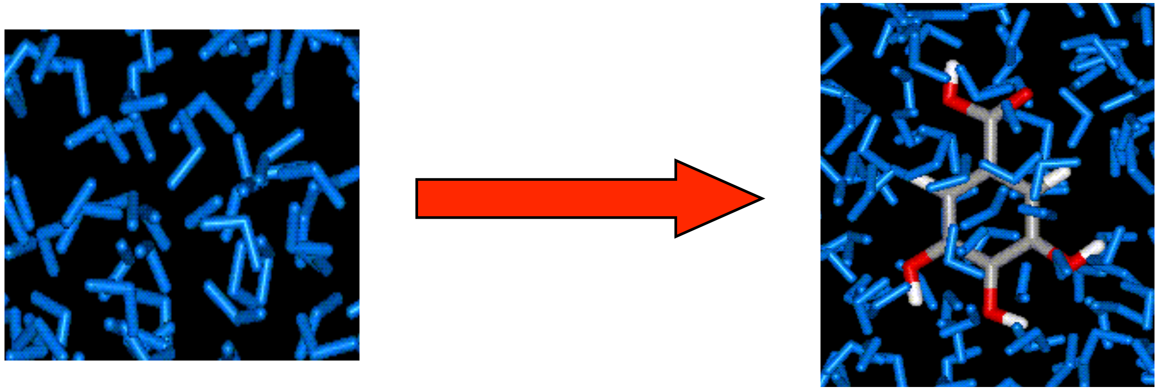
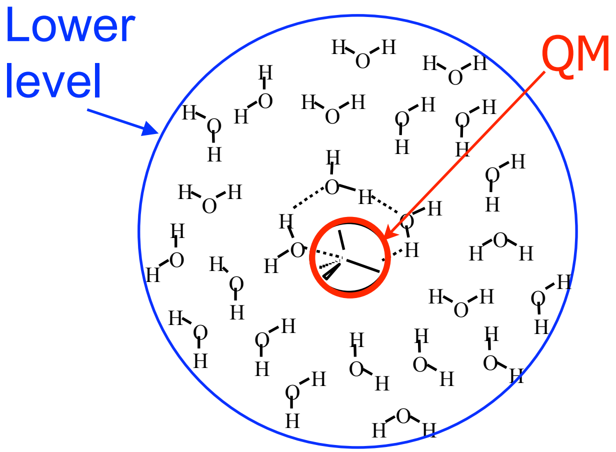
From condensed phases to “solvated” molecules: focused models



The system is hierarchically partitioned in two parts:
the part of interest (the solute) and the rest (the environment)

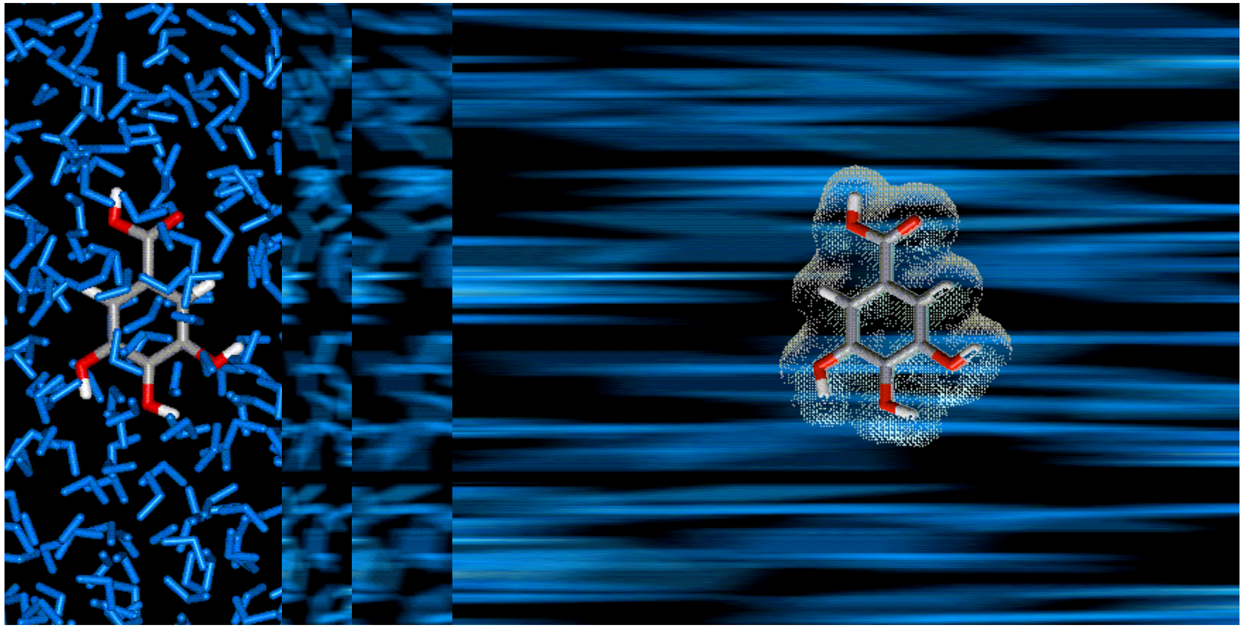


The solute is described at a quantum-mechanical level and the environment at classical level.

We need a proper integration of QM methods and environment models

Which model for the environment?

Discrete models

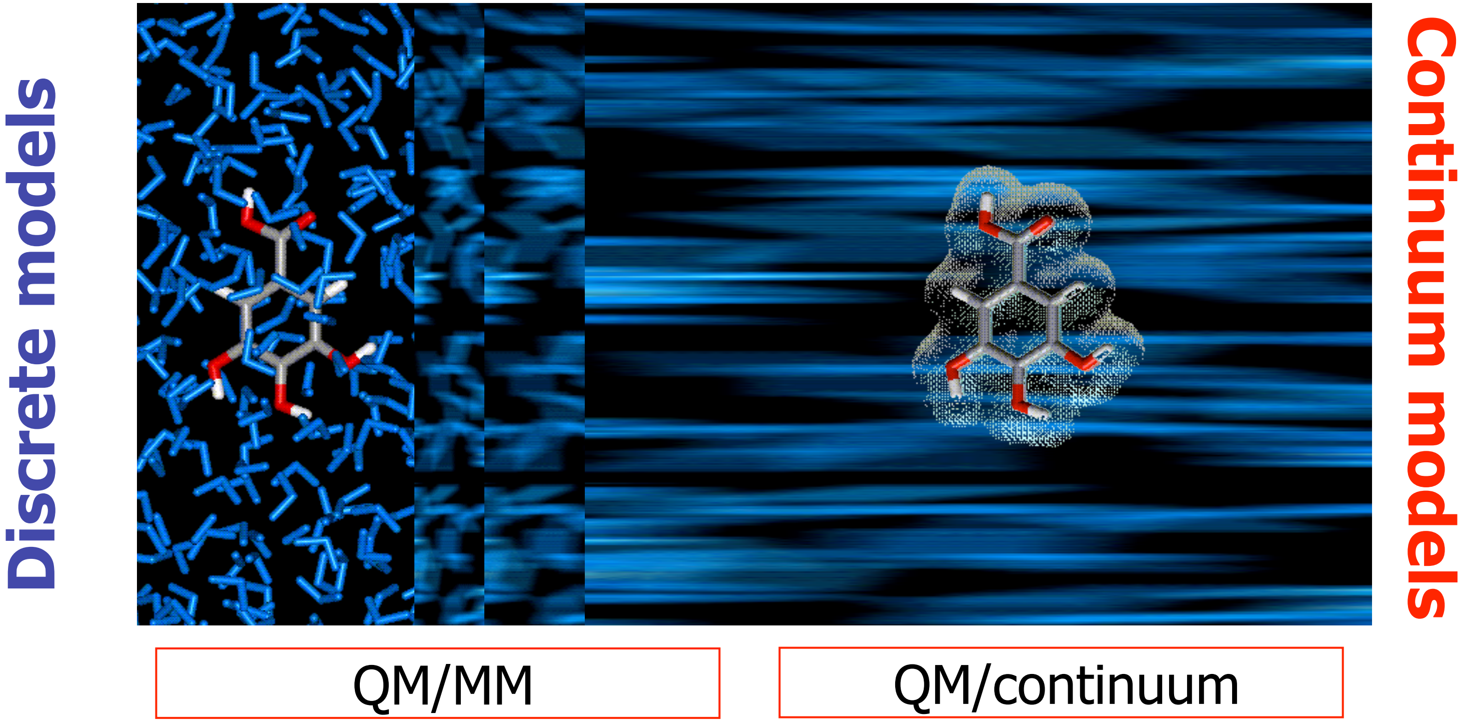


Continuum models

QM/MM

QM/continuum

Which model for the environment?



Effective Hamiltonian for the solute

$$H_{eff}|\Psi\rangle = (H_0 + H_{env})|\Psi\rangle = E|\Psi\rangle$$

$$H_{env} = \begin{cases} H_{QM/MM} + H_{MM} & \text{QM/MM} \\ H_{cont} & \text{QM/Continuum} \end{cases}$$

The Polarizable Continuum Model (PCM)

Solute + all solvent molecules

1. Continuum description

Solute (ρ) in a cavity within a continuum dielectric (ε)

$$\begin{cases} -\nabla^2 V = 4\pi\rho & \text{Inside the cavity} \\ -\varepsilon\nabla^2 V = 0 & \text{Outside the cavity} \end{cases}$$

2. PCM method

Solute in a cavity and an apparent charge on the cavity surface

$$V(\vec{r}) = V_\rho(\vec{r}) + V_\sigma(\vec{r}) \qquad V_\sigma(\vec{r}) = \int_\Gamma \frac{\sigma(\vec{s})}{\left|\vec{r}-\vec{s}\right|} d^2 s$$

The polarization of the solvent is described using only a charge distribution limited to a closed surface

J. Tomasi, B. Mennucci, R. Cammi, Chem. Rev., 105 (2005) 2999.

PCM: the apparent charges

The surface charge σ is solution of an integral equation (IEF-PCM):

A and g are two integral operators

$$A \cdot \sigma = -gV$$

E. Cancès, B. Mennucci, J. Tomasi, J. Chem. Phys., 107 (1997) 3032.

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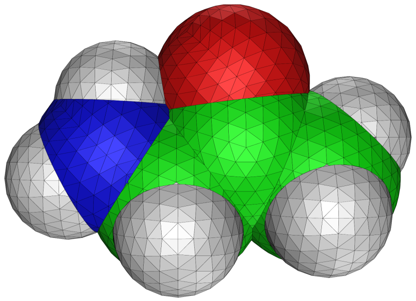
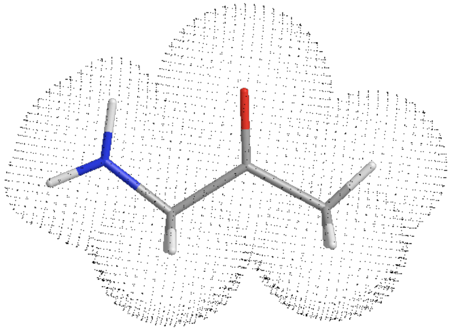
Use of a molecular cavity following the real structure of the solute + use of a Boundary Element Method to map the surface cavity





Discretization of σ into point-like charges q

$$\mathbf{Tq} = -\mathbf{RV}_{solute}$$

T and **R** are matrices of dimension NXN (N is the number of surface elements) and $\mathbf{V}_{\text{solute}}$ collects the solute electrostatic potential on the surface

E. Cancès, B. Mennucci, J. Tomasi, J. Chem. Phys., 107 (1997) 3032.

The Polarizable QM/MM Model

Solute + all solvent molecules

1. MM description

Solute (ρ) surrounded by classical charges representing the solvent molecules

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2. inclusion of polarizable dipoles

Additional induced dipoles

$$H_{QM/MM} = H^{el}_{\mathrm{QM/MM}} + H^{pol}_{\mathrm{QM/MM}}$$
$$= \sum_m q_m V^{solute}(\mathbf{r}_m) - \frac{1}{2}\sum_a \boldsymbol{\mu}_a^{ind} \cdot \mathbf{E}^{solute}(\mathbf{r}_a)$$

$$\boldsymbol{\mu}_a^{ind} = \alpha_a \left(\mathbf{E}_a^{solute} + \mathbf{E}_a^{solvent}\{\mathbf{q}; \mu^{ind}\}\right)$$

The solvent is described using both charges and polarizabilties

Polarizable QM/MM Model vs PCM

To get a correct QM/MM description a multi-step procedure is required:

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1. Classical MD (or MC) simulation
2. Extraction of solute-solvent clusters from simulation (cut-off)
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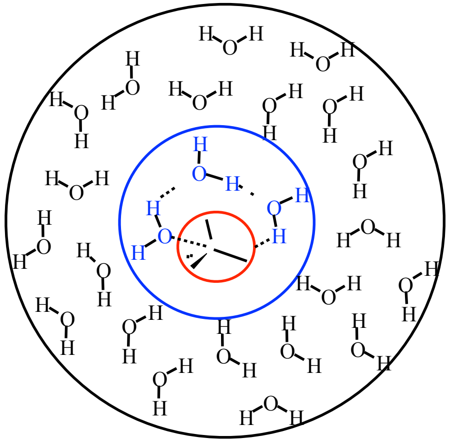
The multi-step procedure reduces to a single step when a continuum approach is used.

The solvent polarization is determined by the macroscopic dielectric constant:

the statistical average is implicitly included!

Polarizable QM/MM Model vs PCM

Macro- and micro-solvation



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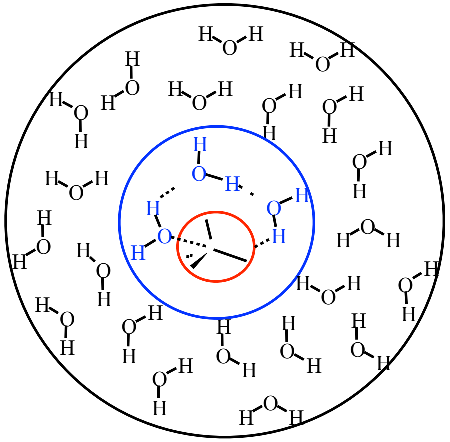

In homogeneous environments not specifically interacting with the solute

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Bulk (averaged) effects:
PCM & MMPol coincides

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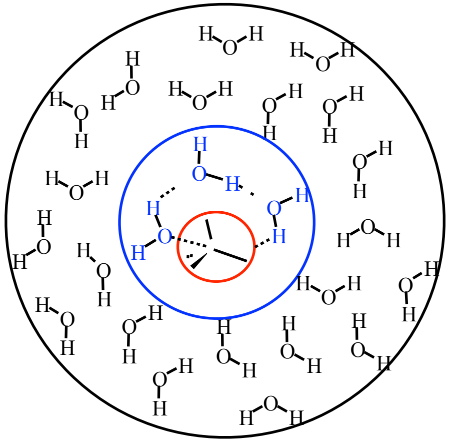


In homogeneous environments not specifically interacting with the solute

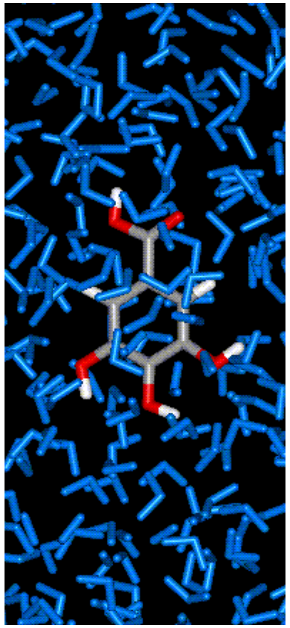
Bulk (averaged) effects: PCM & MMPol coincides

In heterogeneous environments or in the presence of specific & persistent interactions with the solute

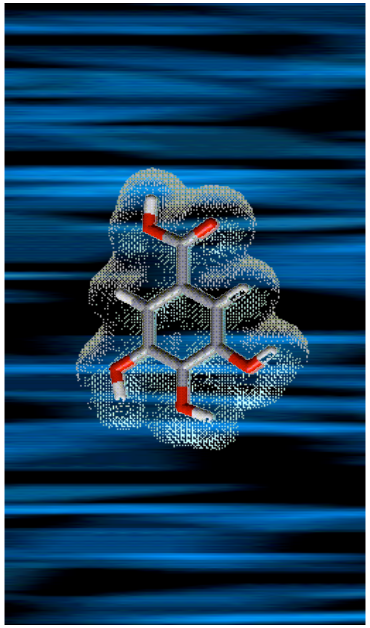
Local (specific) effects: PCM & MMPol can differ

Which model for the environment?

Discrete models



QM/MM



Continuum models

QM/continuum

How can we introduce mutual polarization effects between the QM solute and the classical solvent?

The polarization in the QM equations

Effective Schrödinger equation for the solute

$$H_{eff}\left|\Psi\right\rangle = \left[H_0 + H^{\text{charges}} - \frac{1}{2}\sum_a \boldsymbol{\mu}_a^{ind}\cdot\mathbf{E}^{solute}(\mathbf{r}_a)\right]\left|\Psi\right\rangle = E\left|\Psi\right\rangle$$

$$H_{eff}\left|\Psi\right\rangle = \left[H_0 + \sum_i q_i^{PCM} V_i\right]\left|\Psi\right\rangle = E\left|\Psi\right\rangle$$

MM induced dipoles & PCM charges quadratically depend on the solute wavefunction

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Solute and solvent mutually polarize

BUT

a nonlinearity is introduced

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MM induced dipoles & PCM charges quadratically depend on the solute wavefunction

The nonlinear solvent operator is easily nested in the standard Self-Consistent-Field approaches (Hartree-Fock, DFT):

no need of further iterative schemes

But difficulties appear in post-SCF calculations

Post-SCF methods & Polarization

An example: inclusion of electronic correlation using Moller Plesset perturbation theory (MP2)

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Solvated Hartree-Fock (uncorrelated) reference state: orbitals and orbital energies obtained in the presence of the environment

MP2 correlation correction to the energy for the solvated system:

$$G^{(2)} = \frac{1}{4} \sum_{ijab} t_{ij}^{ab} \langle ij || ab \rangle$$

$$t_{ij}^{ab} = \frac{\langle ij || ab \rangle}{\epsilon_i + \epsilon_j - \epsilon_a - \epsilon_b}$$

antisymmetrized combinations of two-electron integrals on HF orbitals

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antisymmetrized combinations of two-electron integrals on HF orbitals

<u>Unrelaxed scheme</u>

the solvent response is kept frozen at HF level

It includes solvation effects in correlation but not viceversa

MP2: the relaxed scheme

Solvated Hartree-Fock reference state

MP2: the relaxed scheme

Solvated Hartree-Fock reference state

Relaxed MP2 density

$$\mathbf{P}_{relax} = \mathbf{P}_{\mathrm{HF}} + \mathbf{P}^{(2)}$$

MP2 change in the density matrix: orbital relaxation

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Relaxed MM dipoles or PCM charges

$$\mu^{\mathrm{ind}}(\mathbf{P}_{relax}) = \mu^{\mathrm{ind}}(\mathbf{P}_{\mathrm{HF}}) + \mu^{\mathrm{ind}}(\mathbf{P}^{(2)})$$

$$\mathbf{q}^{\mathrm{PCM}}(\mathbf{P}_{relax}) = \mathbf{q}^{\mathrm{PCM}}(\mathbf{P}_{\mathrm{HF}}) + \mathbf{q}^{\mathrm{PCM}}(\mathbf{P}^{(2)})$$

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New reference state in the presence of new dipoles or PCM charges

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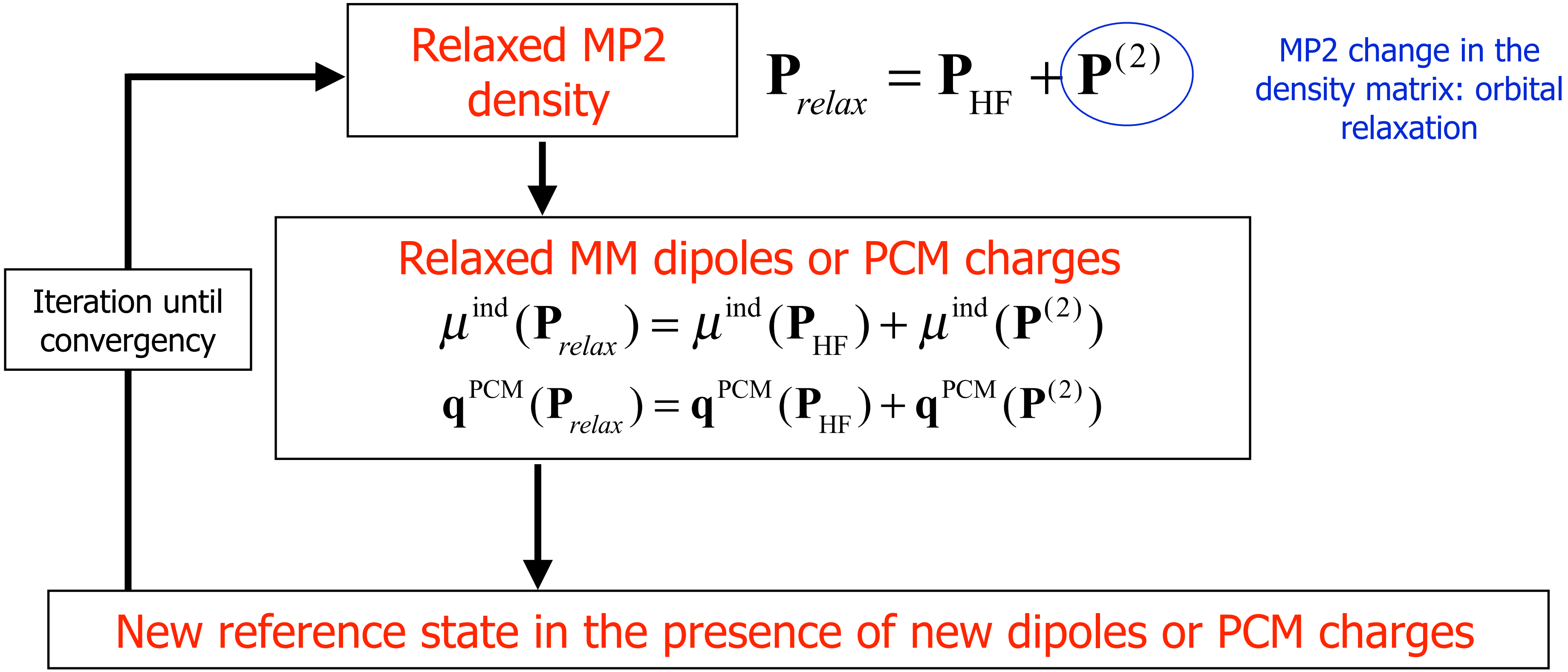

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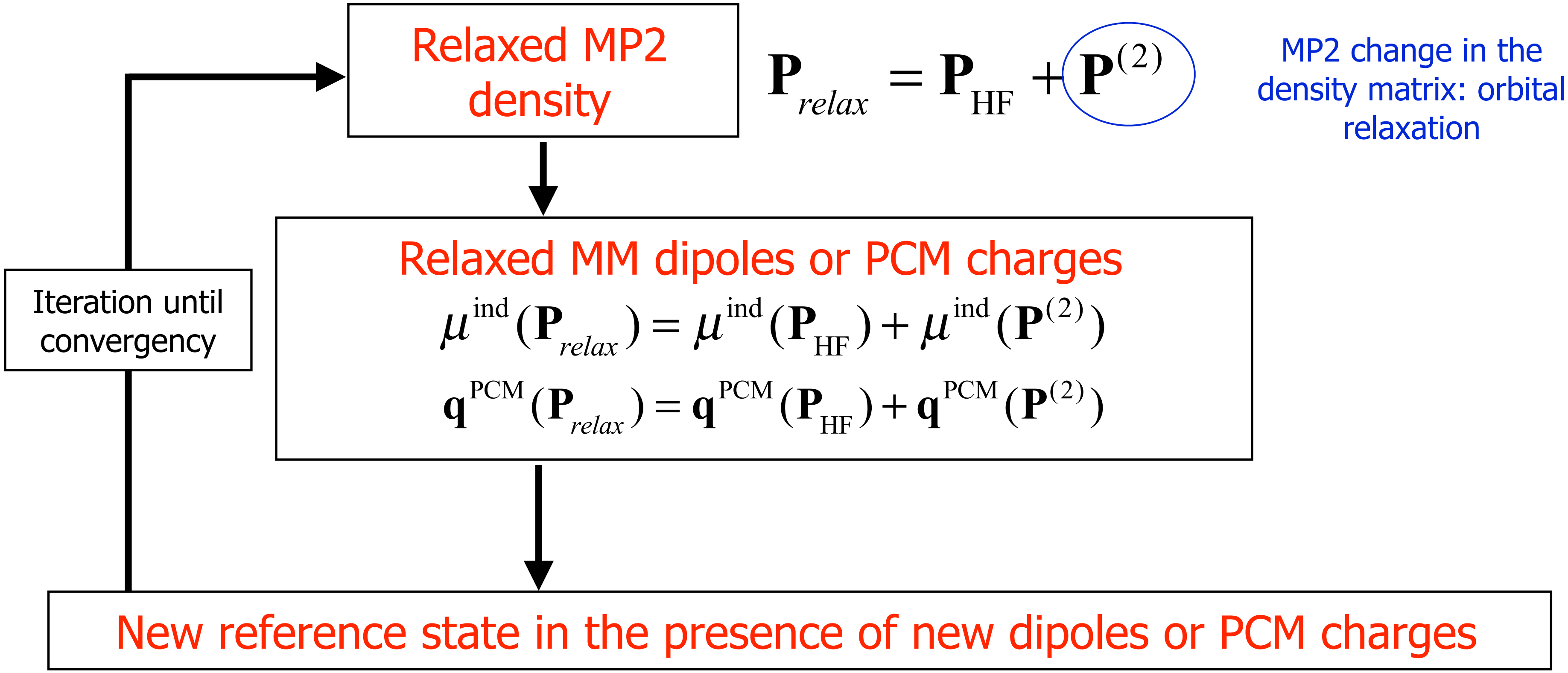

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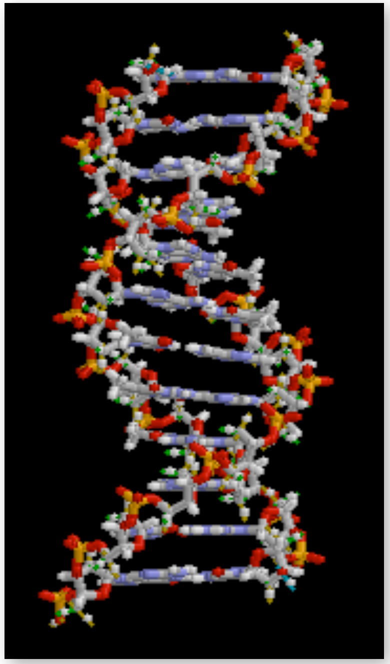
New reference state in the presence of new dipoles or PCM charges

It is a self-consistent approach: starting from an unrelaxed calculation, the correlated density is used to update the solvent response, which is back used to recalculate the correlated density, iterating until self-consistency

Unrelaxed versus relaxed scheme: an example

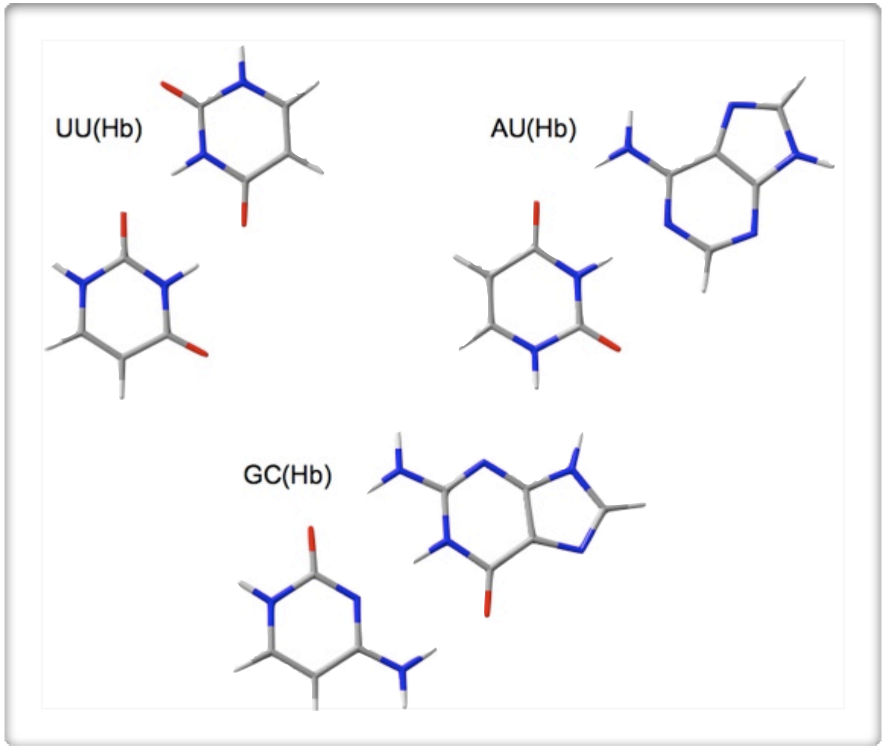
Hydrogen bonding and aromatic stacking in DNA

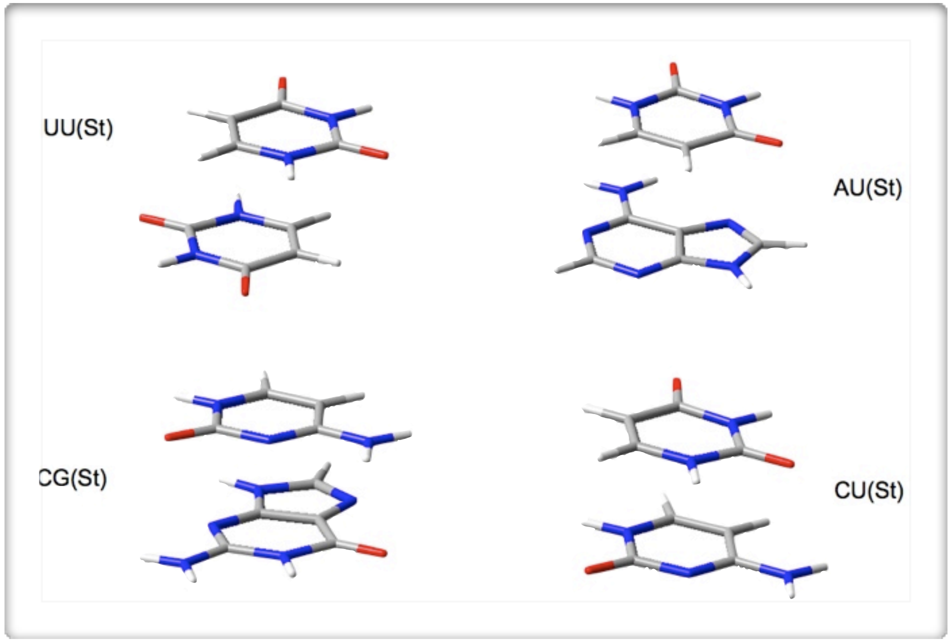


Stability in DNA (RNA) mainly depends on two different non-covalent interactions between bases (hydrogen bonding & stacking).

These are the result of a complex mix of electrostatic and dispersion interactions, and solvent effects.

Hydrogen bonding & stacking





F. Lipparini, G. Scalmani, B. Mennucci, PCCP accepted

Hydrogen bonding & stacking: the importance of electronic correlation

Benchmark interaction energies (kcal/mol) for isolated base-pairs

	E_{int}
UU (Hb)	-12.4
UU (St)	-7.50
GC (Hb)	-27.5
GC (St)	-10.60
AU (Hb)	-13.2
Au (St)	-9.80
CU (St)	-10.40

complete basis set extrapolation of RI-MP2 calculations, corrected for higher order correlation contributions calculated at the CCSD(T) level

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Hydrogen bonding

		BSSE
		E_{int}
UU	B3LYP	**-10.03**
	MP2	**-11.48**
GC	B3LYP	**-28.21**
	MP2	**-26.95**
AU	B3LYP	**-12.13**
	MP2	**-14.19**

Basis set: aug-cc-pVDZ; energies in kcal/mol

HB energies (mostly electrostatic) are accurate at the DFT/B3LYP level of theory

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GC	B3LYP	**-1.04**
	MP2	**-11.05**
AU	B3LYP	**+0.33**
	MP2	**-10.67**
CU	B3LYP	**-1.83**
	MP2	**-10.21**

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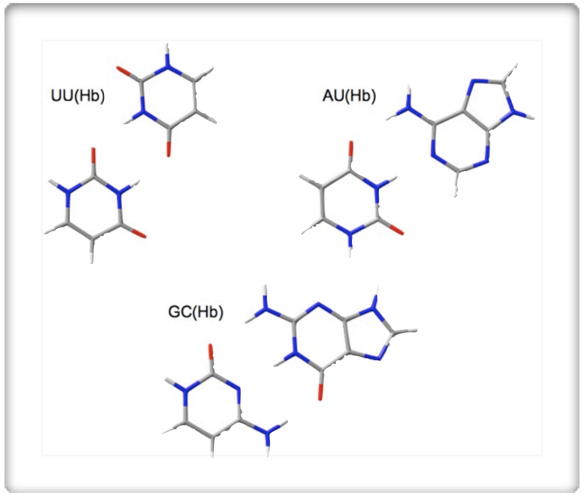
We need to treat correlation at MP2 level !!

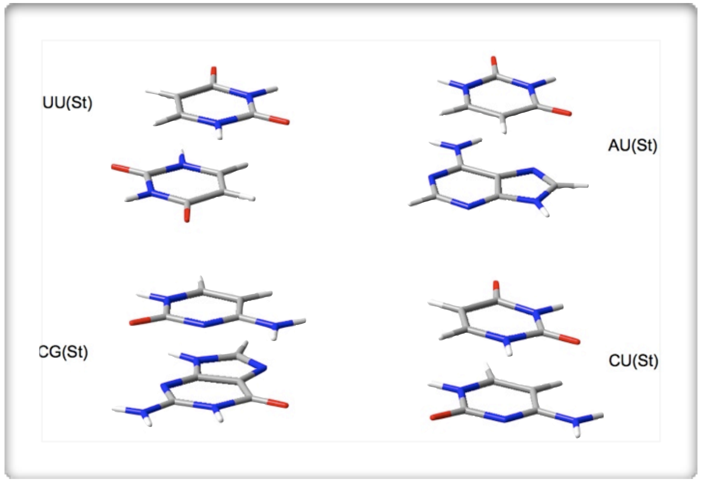
Unrelaxed & Relaxed solvation: solvation free energies



		dipole	ΔG(solv)
UU	UnRelaxed	4.09	-28.92
	Relaxed	3.76	-22.31
GC	UnRelaxed	7.87	-32.40
	Relaxed	7.71	-28.30
AU	UnRelaxed	2.37	-26.93
	Relaxed	2.06	-23.01

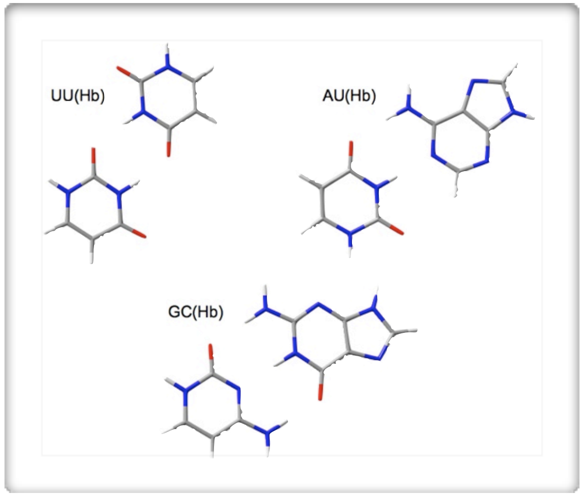
MP2/aug-cc-pVDZ;
dipoles in debye,
energies in kcal/mol

		dipole	ΔG(solv)
CU	UnRelaxed	3.27	-34.93
	Relaxed	3.46	-30.53
UU	UnRelaxed	0	-34.02
	Relaxed	0	-28.20
GC	UnRelaxed	6.16	-43.56
	Relaxed	5.55	-38.36
AU	UnRelaxed	2.47	-31.81
	Relaxed	1.87	-28.11



ΔG_{sol} is less negative in the Relaxed than in the UnRelaxed scheme, BUT.....

Unrelaxed & Relaxed solvation: Interaction energies



Hydrogen bonding interaction energies

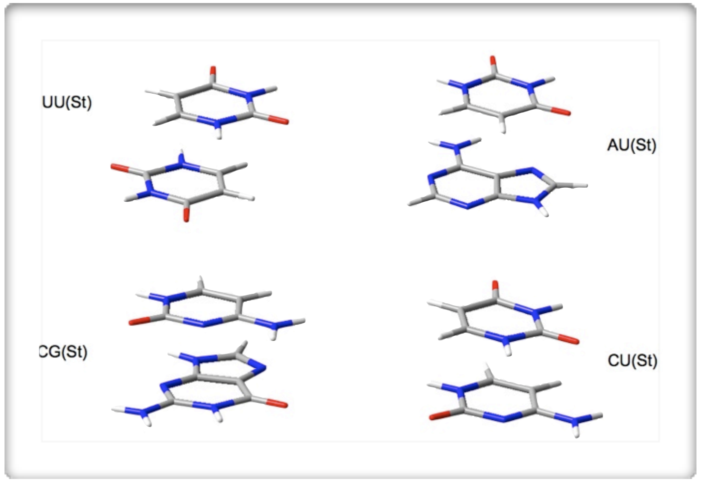
	UnRelaxed	Relaxed	% variation
UU	-1.06	-2.23	-110
GC	-6.73	-9.97	-48
AU	-3.37	-4.65	-38

BSSE MP2/aug-cc-pVDZ; energies in kcal/mol

Stacking interaction energies

	UnRelaxed	Relaxed	% variation
CU	-4.58	-6.85	-50
UU	-4.54	-5.90	-30
GC	-4.92	-6.24	-27
AU	-6.53	-7.68	-18

BSSE MP2/aug-cc-pVDZ; energies in kcal/mol



Relaxed calcs predict more stable pairs: it is due to the coupling the intra-pair interaction and the solvent response

Hydrogen bonding & stacking: the role of solvent polarization

Hydrogen bonding interaction energies

	gas-phase	Relaxed	% variation
UU	-11.48	-2.23	80
GC	-26.95	-9.97	63
AU	-14.19	-4.65	67

Stacking interaction energies

	gas-phase	Relaxed	% variation
CU	-10.21	-6.85	33
UU	-7.73	-5.90	24
GC	-11.05	-6.24	44
AU	-10.67	-7.68	28

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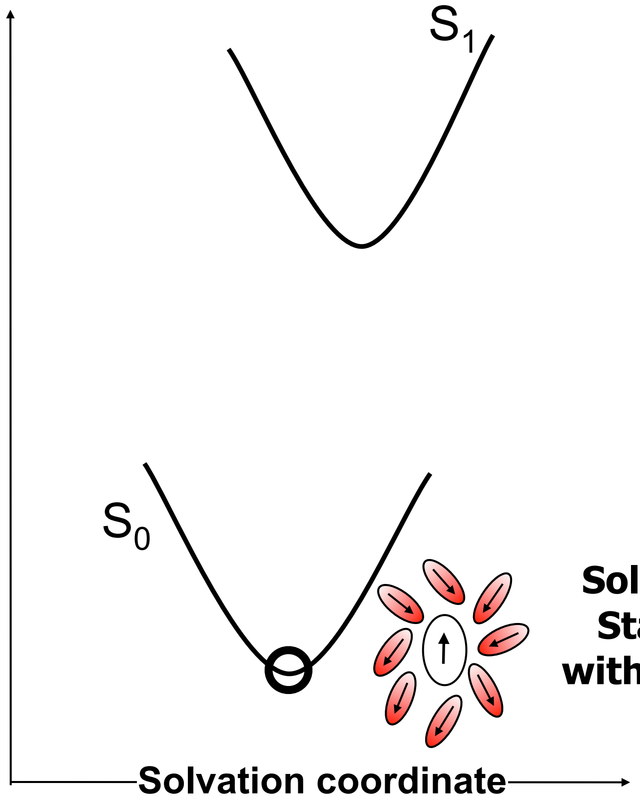
BSSE MP2/aug-cc-pVDZ; energies in kcal/mol

In gas phase H-bonding is much stronger than stacking
BUT
in water stacking & H-bonding become competitive!!

A further example of polarization: electronic excitations in solutions

Polar solvation

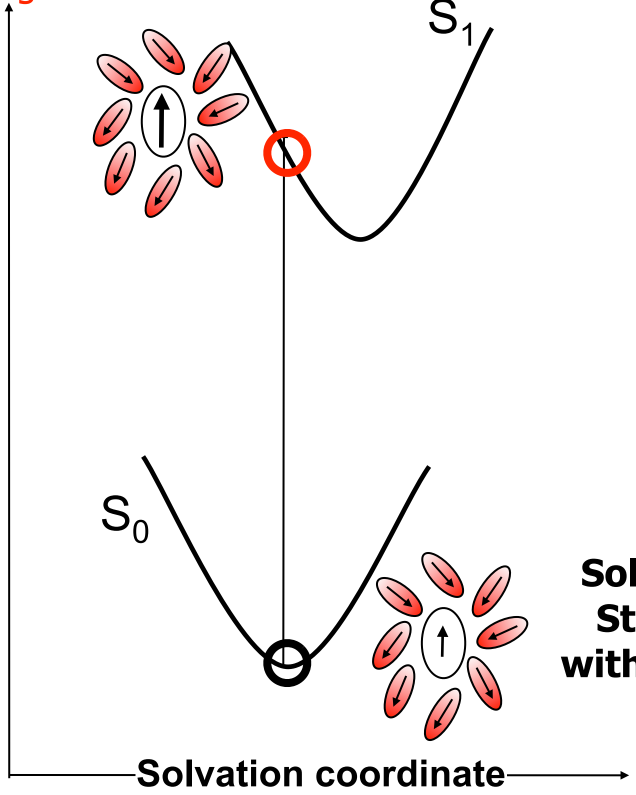


Solute in its ground State equilibrated with the environment (equilibrium)

Polar solvation

Dynamic response
(nonequilibrium)

Only the environment dynamic (electronic) response readjusts: the inertial part is frozen in the initial configuration



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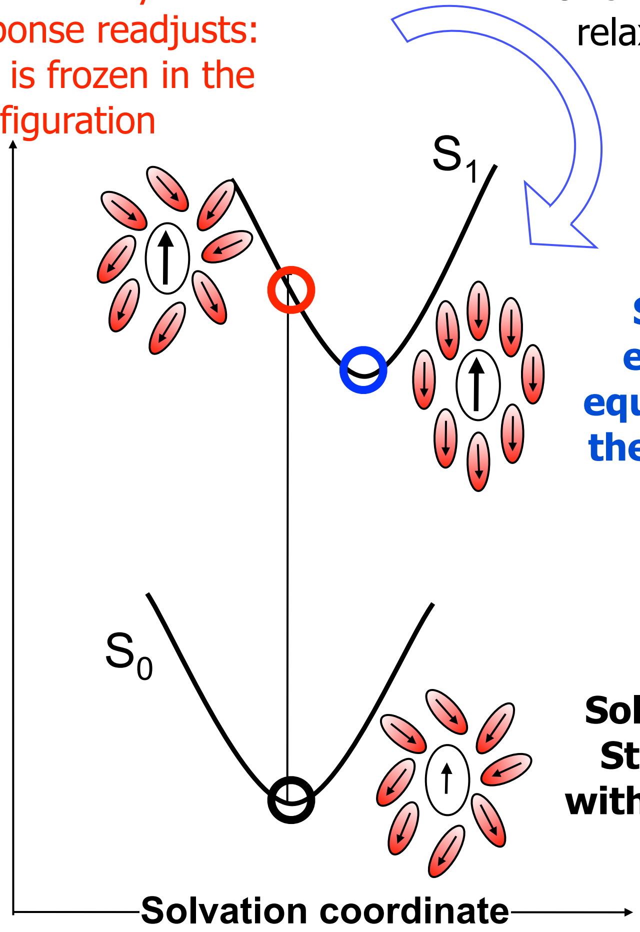

Orientational relaxation

Solute in its excited state equilibrated with the environment

Solute in its ground State equilibrated with the environment (equilibrium)

Polar solvation

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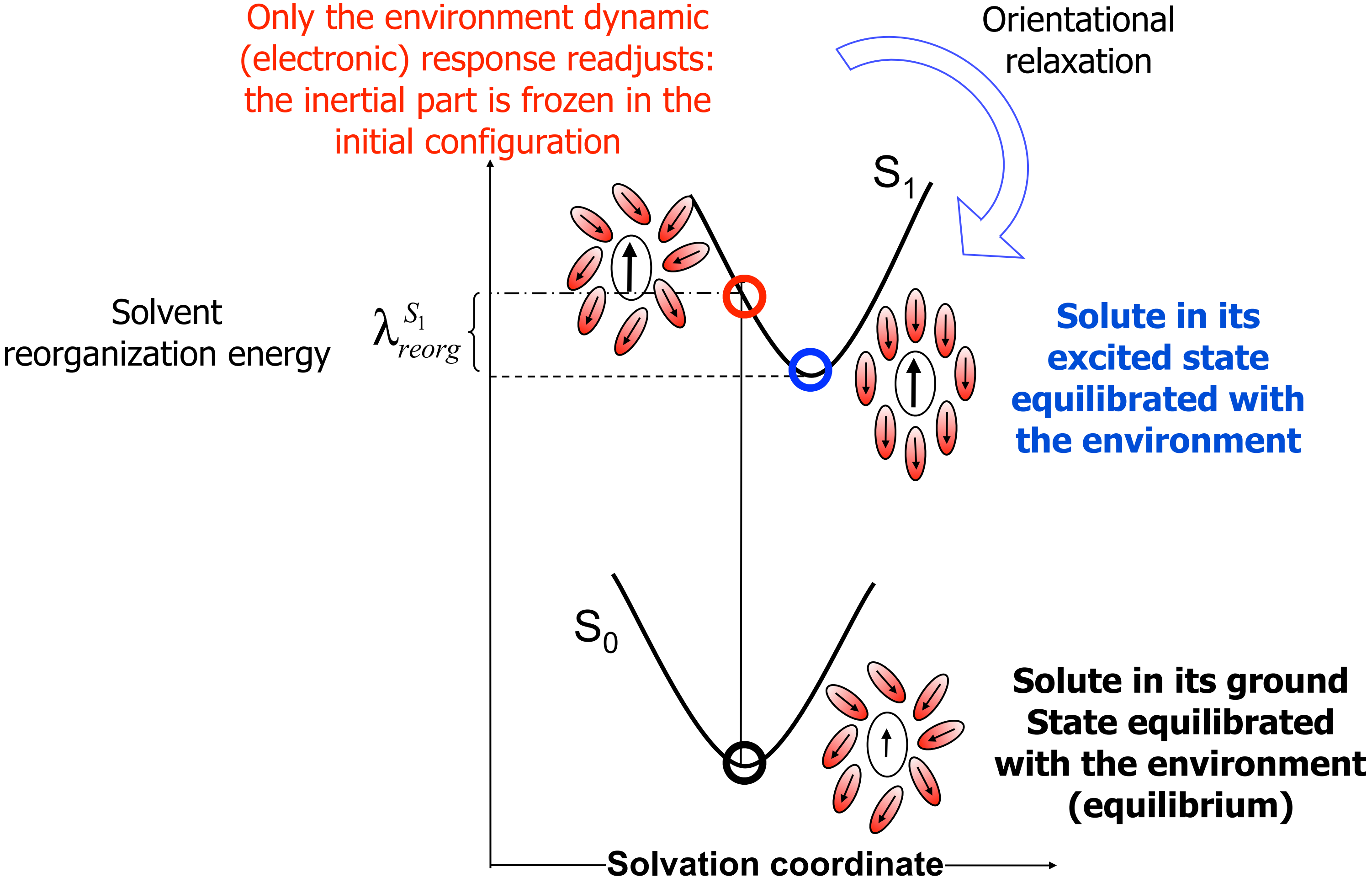

Orientational relaxation

Solvent reorganization energy $\lambda^{S_1}_{reorg}$

Solute in its excited state equilibrated with the environment

Solute in its ground State equilibrated with the environment (equilibrium)

Nonequilibrium

How can we include the correct environment effect (nonequilibrium) in the quantum mechanical calculation of electronic excitations?

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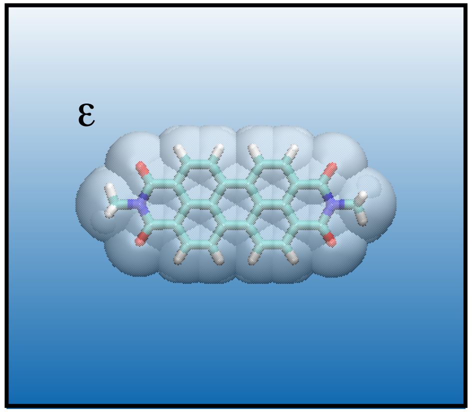

PCM

- Chromophore: QM level
- Environment: continuum level
- nonequilibrium:
  - separation into static (ε_0) and optical dielectric constant (ε_∞)
  - separation of charges into dynamic and inertial components:

$$\mathbf{q}_K^{neq} = \mathbf{q}_{GS}^{in} + \mathbf{q}_K^{dyn}(\varepsilon_\infty)$$

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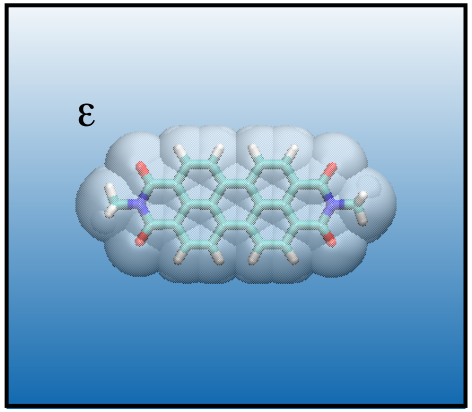

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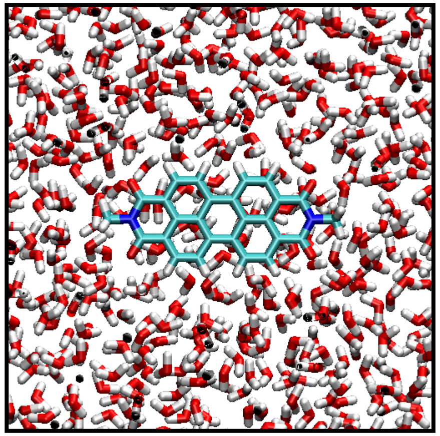
$$\mathbf{q}_K^{neq} = \mathbf{q}_{GS}^{in} + \mathbf{q}_K^{dyn}(\varepsilon_\infty)$$

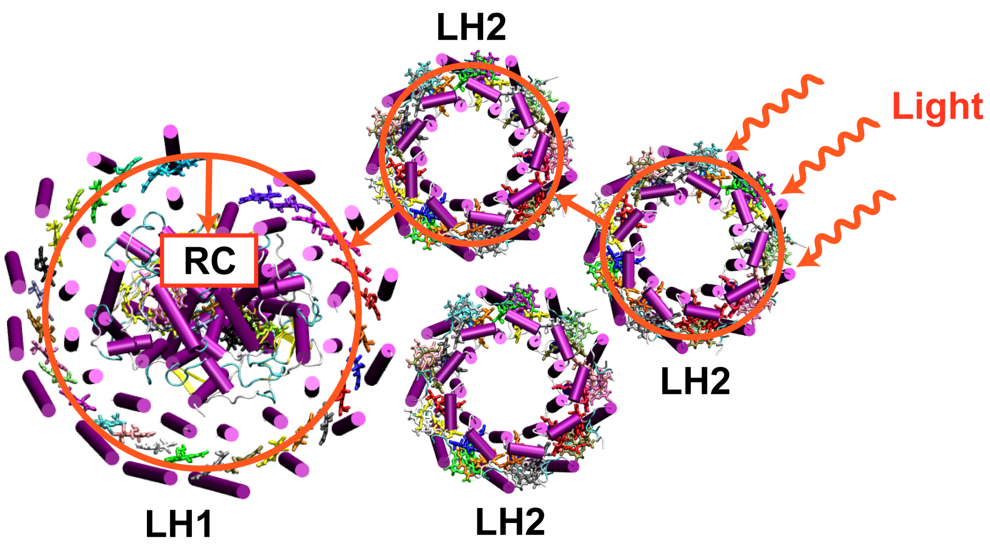
QM/MMpol

- Chromophore: QM level
- Environment: MM level (classical polarizable force field)
- nonequilibrium:
  - induced dipoles for the dynamic component,
  - fixed charges for the inertial one



An “extreme” example of nonequilibrium polarization: excitation energy transfer

Excitation energy transfer

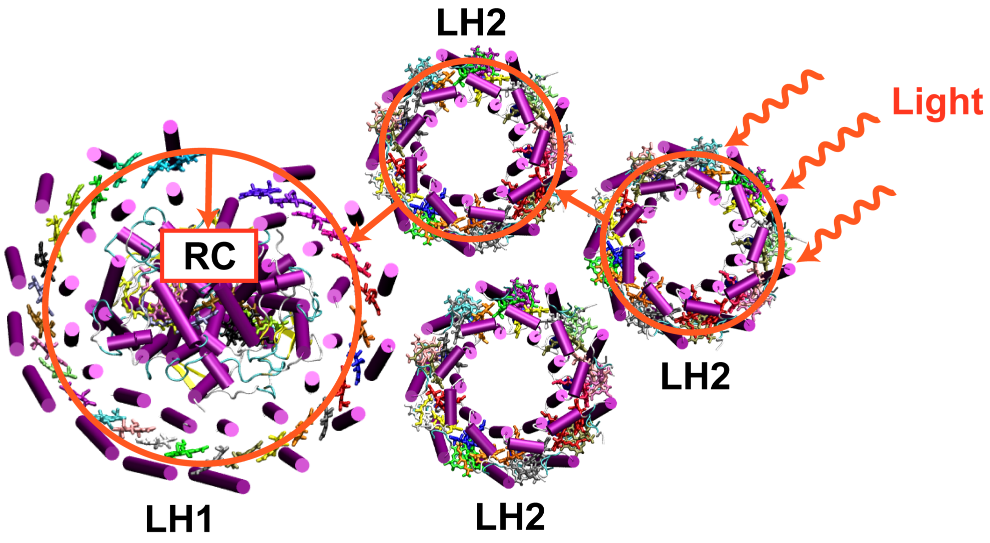


Photosynthesis begins when light is absorbed by antenna pigments.

Light energy is subsequently funnelled (through multiple energy transfers) to reaction centre complexes where it is converted into chemical potential:

almost 100% efficiency!!

Excitation energy transfer



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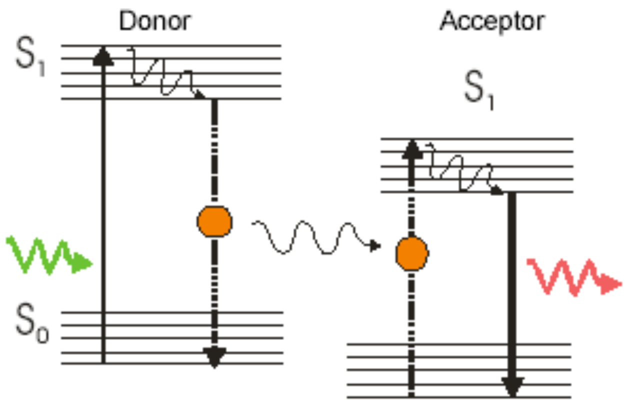
EET

Energy absorbed by a pigment (donor) is transferred to another pigment (acceptor): it is a non-radiative process

$$D^* + A \xrightarrow{k_{EET}} D + A^*$$



Förster theory for EET

In the weak coupling limit:

EET rate $$k_{EET} = \frac{2\pi}{\hbar} \left| s V_s \right|^2 J$$

- spectral overlap, J, between donor emission and acceptor absorption
- electronic coupling, V_s, between donor and acceptor
- environment screening, s

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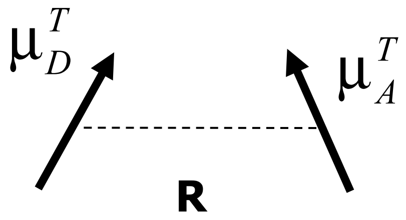
In the dipole-dipole approximation:



Electronic coupling $$sV_s = \frac{1}{n^2}\left[\frac{\vec{\mu}_A^T \cdot \vec{\mu}_D^T}{\mathrm{R}^3} - \frac{3}{\mathrm{R}^5}\left(\vec{\mu}_A^T \cdot \vec{R}\right)\left(\vec{\mu}_D^T \cdot \vec{R}\right) \right]$$

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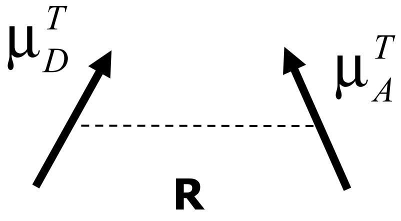


Electronic coupling $$sV_s = \frac{1}{n^2}\left[\frac{\vec{\mu}_A^T \cdot \vec{\mu}_D^T}{R^3} - \frac{3}{R^5}\left(\vec{\mu}_A^T \cdot \vec{R}\right)\left(\vec{\mu}_D^T \cdot \vec{R}\right) \right]$$

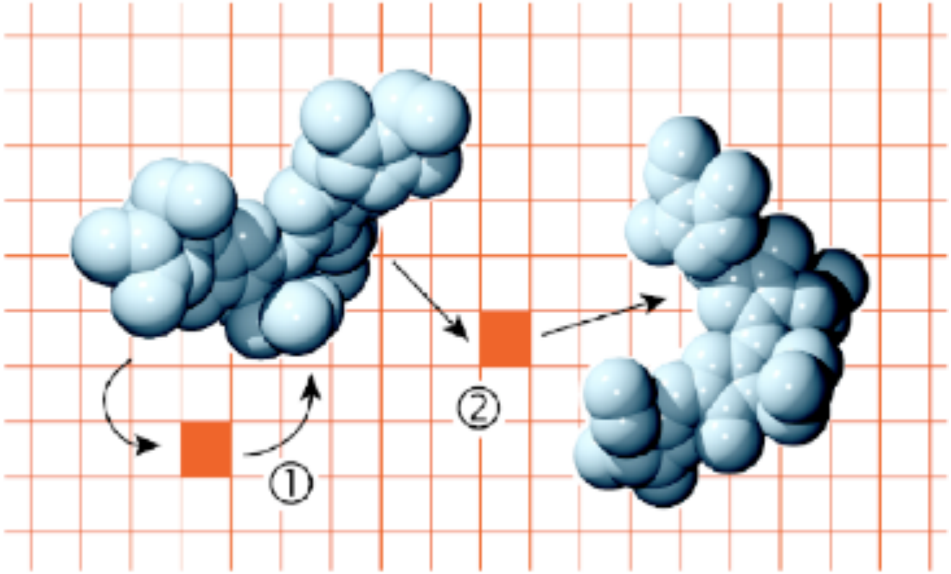
Screening of the solvent

n= refractive index

n ≈1.4

EET rate reduced by a factor of 4 !!

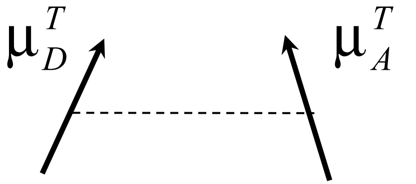
How does the environment control EET ?



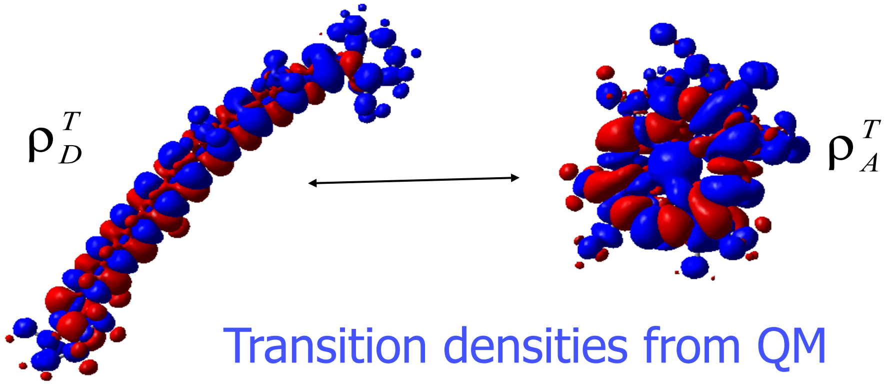
(1) The environment changes donor & acceptor properties, and hence, implicitly, the electronic coupling.

(2) The solvent explicitly screens the donor/acceptor interaction: it is a pure polarization effect

Beyond Förster theory:
a QM electronic coupling

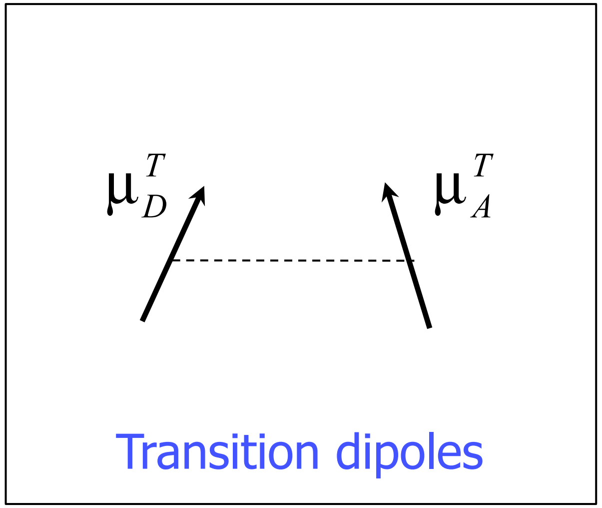


Transition dipoles



Transition densities from QM
(ZINDO, CIS, TDDFT, ...)

Beyond Förster theory: a QM electronic coupling



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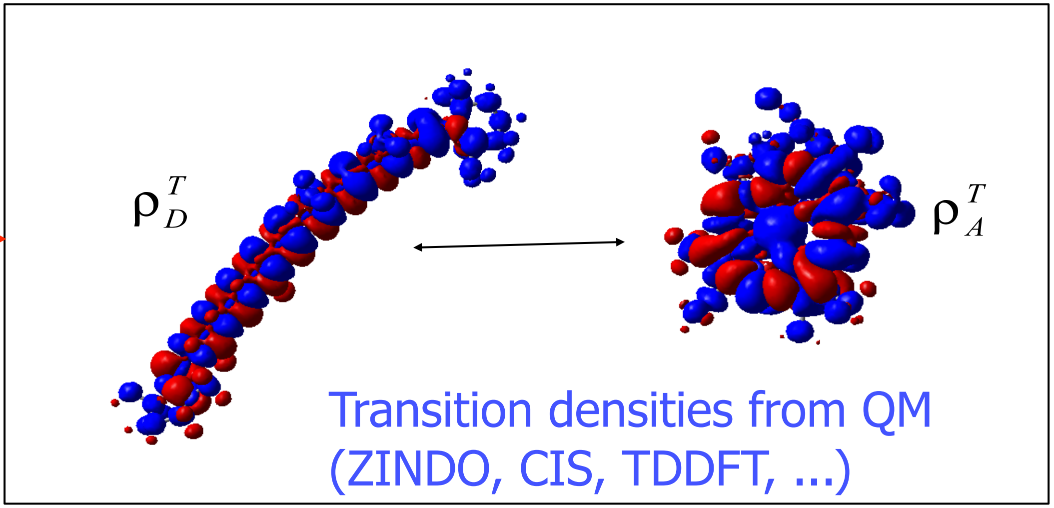

Transition densities from QM (ZINDO, CIS, TDDFT, ...)

$$V_s = \int d\vec{r}\,'\int d\vec{r}\,\rho_A^{T*}(\vec{r}\,')\left[\underbrace{\frac{1}{|\vec{r}-\vec{r}\,'|}}_{\text{Coulomb}} + \underbrace{g_{xc}}_{\text{Exchange-correlation}}\right]\rho_D^T(\vec{r}) - \omega_0 \underbrace{\int d\vec{r}\,'\int d\vec{r}\,\rho_A^{T*}(\vec{r}\,')\rho_D^T(\vec{r})}_{\text{Overlap}}$$

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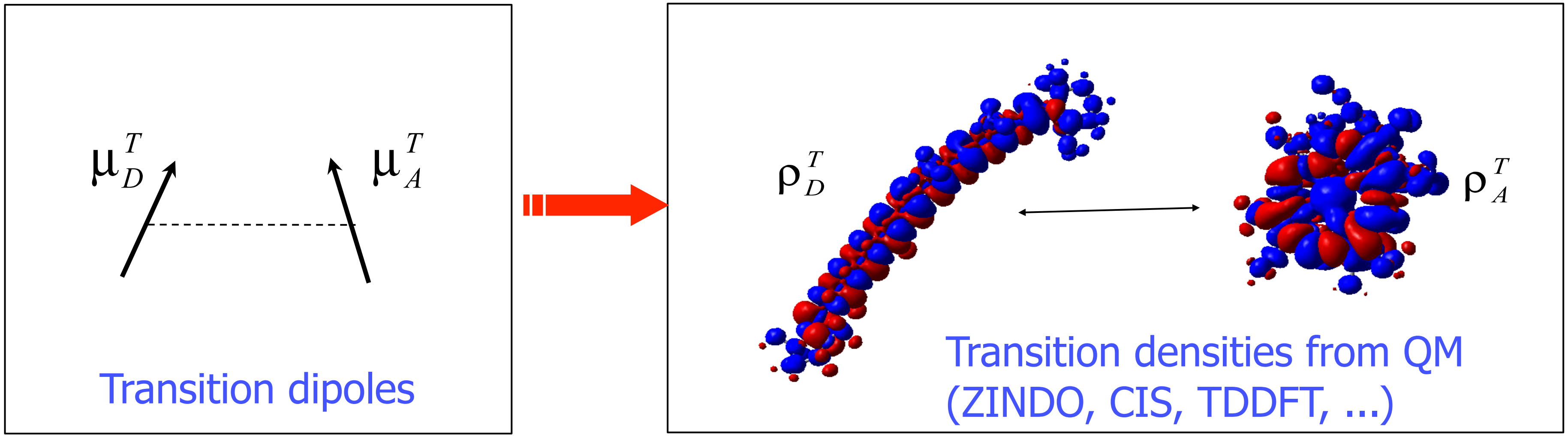

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And what about solvent effects?

1) Implicit Solvent effect

$$V = V_s + V_{\text{explicit}}$$

Implicit solvent effect in general increases the total coupling (enhancing effect)

M.F. Iozzi, B. Mennucci, J. Tomasi, R. Cammi, J. Chem. Phys. 120 (2004) 7029
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Coulomb

Exchange-correlation

Overlap

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The solvent term enters in the QM equations determining the transition densities of each chromophore

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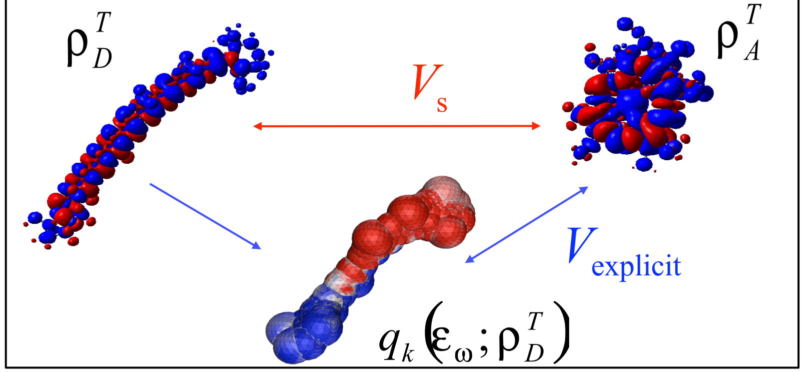

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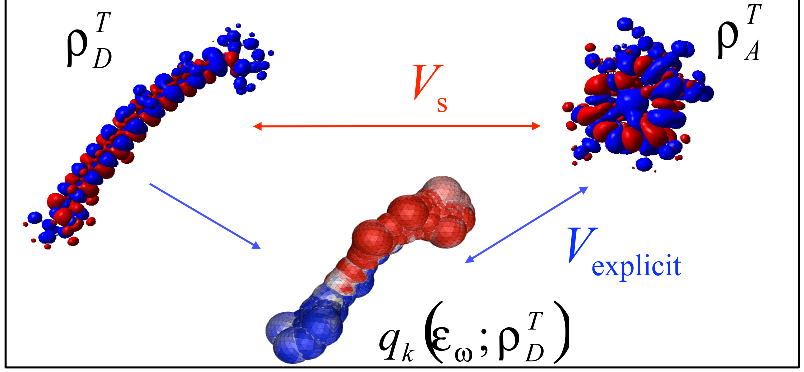
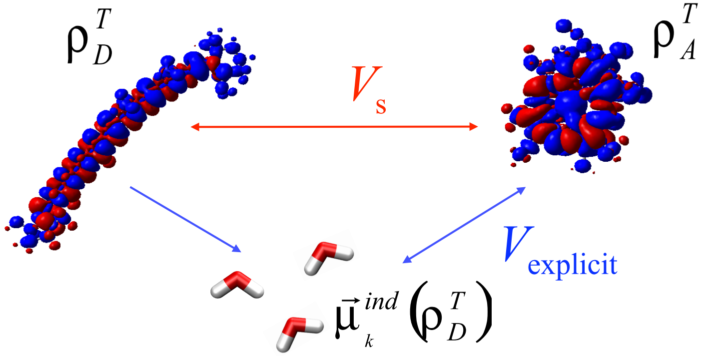


MMpol

$$V_{\text{explicit}} = \sum_k \vec{\mu}_k^{ind}\left(\rho_D^T\right)\int d\vec{r}\,\frac{\rho_A^T(\vec{r})\left(\vec{r}_k-\vec{r}\right)}{\left|\vec{r}_k-\vec{r}\right|^3}$$



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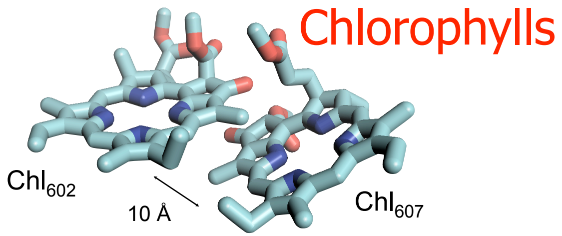
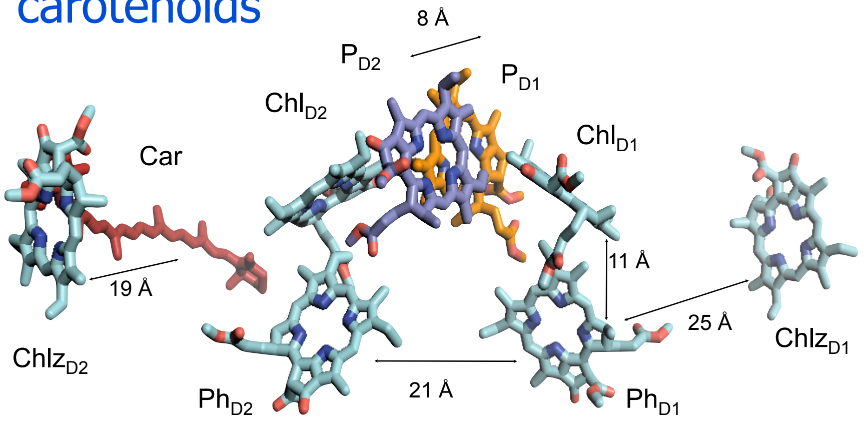
Effect of the environment in light harvesting antennae: the PCM-EET model

Higher plants:
Light harvesting complex II (LHCII)



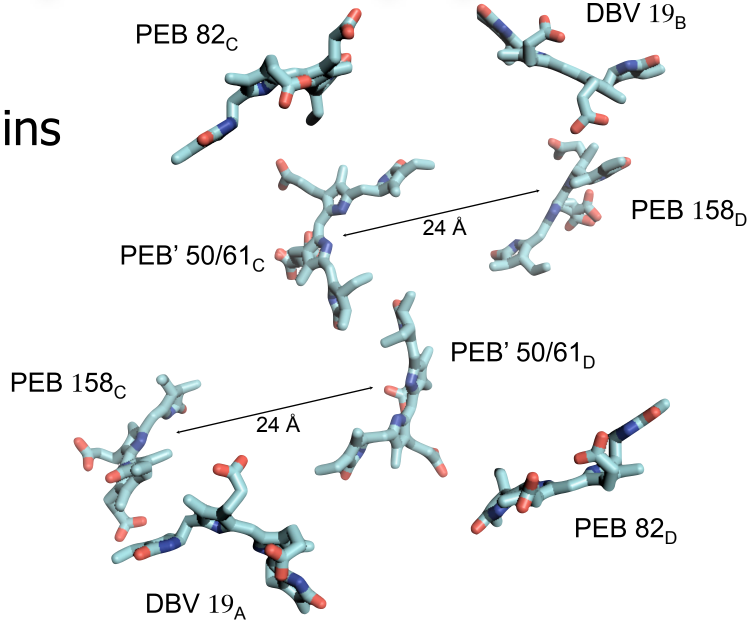
Cyanobacteria:
Photosystem II (PSII)

Chlorophylls &
carotenoids



Algae living in shallow water:
phycoeritrin & phycocianin

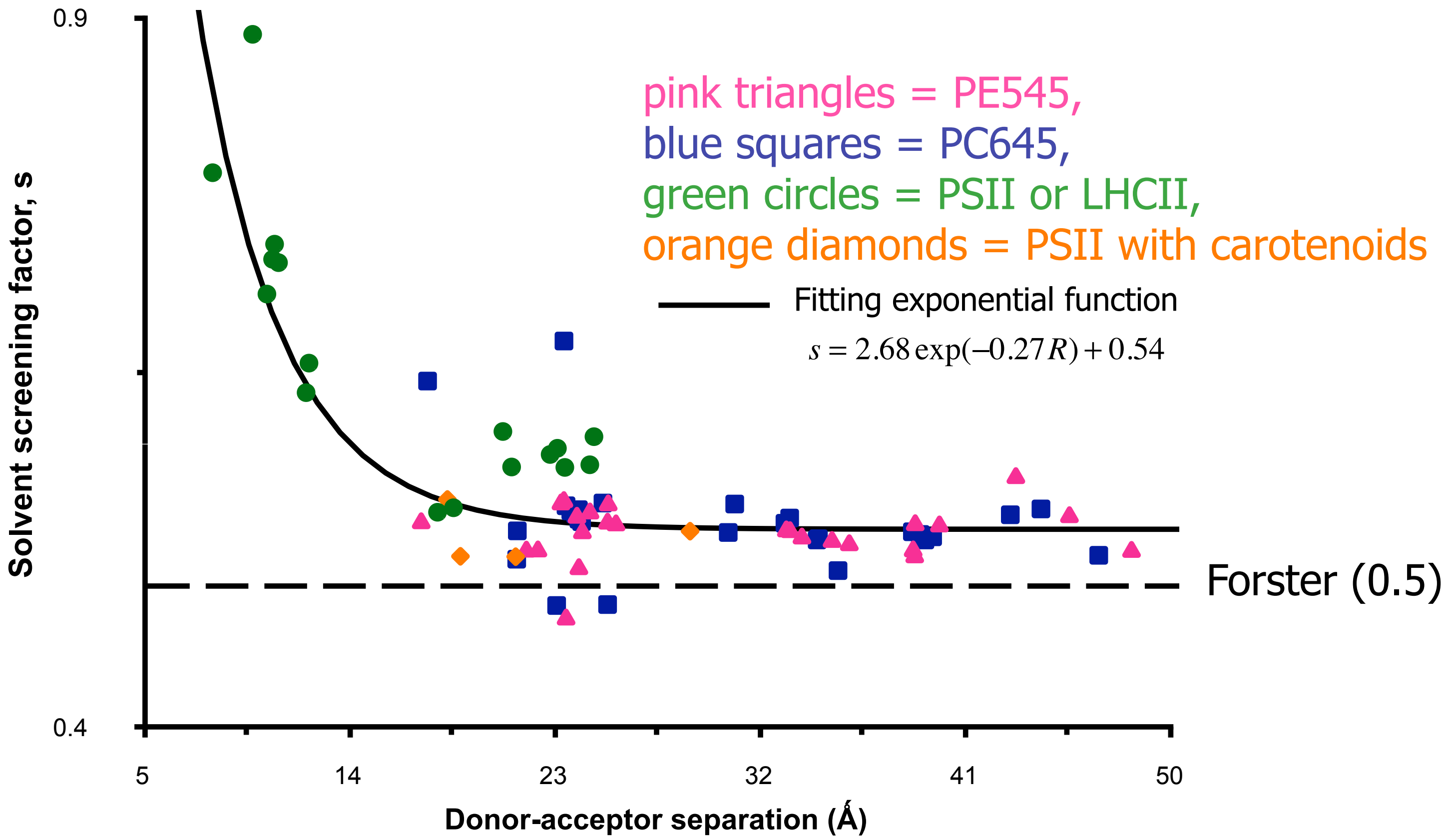
Bilins



How does the environment control EET ?
The screening effect

PCM-EET CIS/6-31G;
protein environment
described with ε=15
and ε∞=2

$$\boxed{s = V_{\text{tot}} / V_s}$$

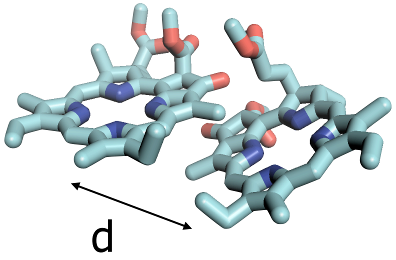


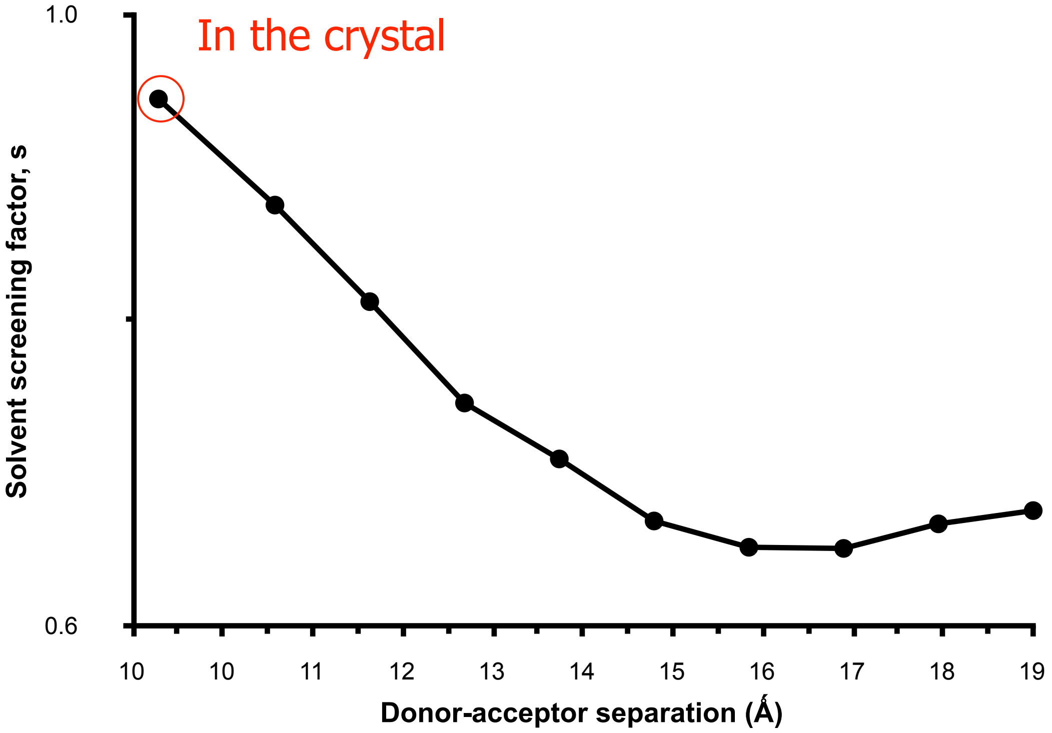
PCM screening is not a simple factor but a function of the donor-acceptor distance

G. D. Scholes, C. Curutchet, B. Mennuci, R. Cammi, J. Tomasi, J. Phys. Chem. B 111 (2007) 6978

Why a distance dependent screening?

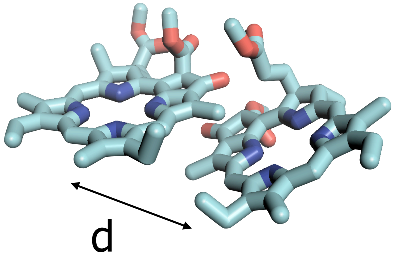
Light harvesting complex II (LHCII)

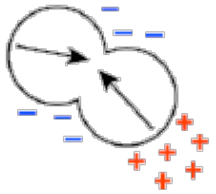



In the crystal

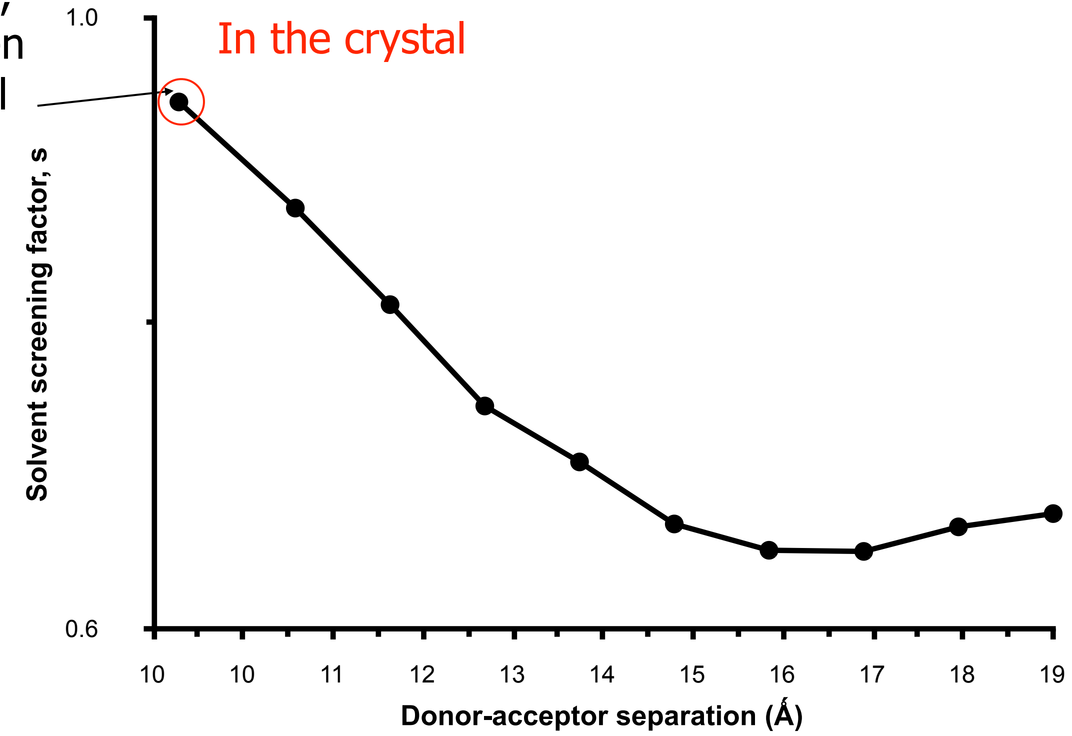
Why a distance dependent screening?

Light harvesting complex II (LHCII)





When the two molecules are close, there is no explicit medium between them: the screening effect is small and **s** approaches unity


In the crystal

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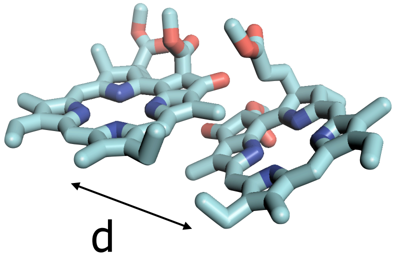
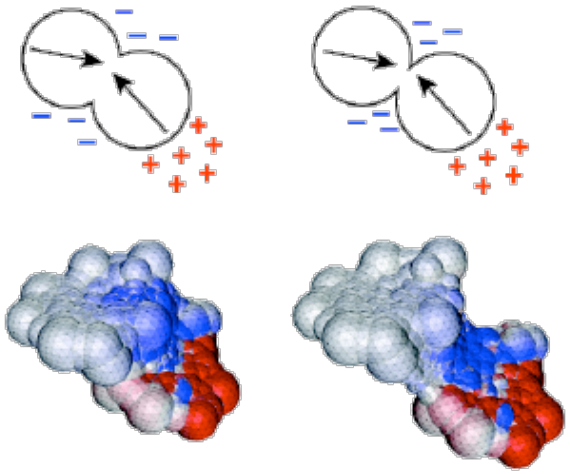
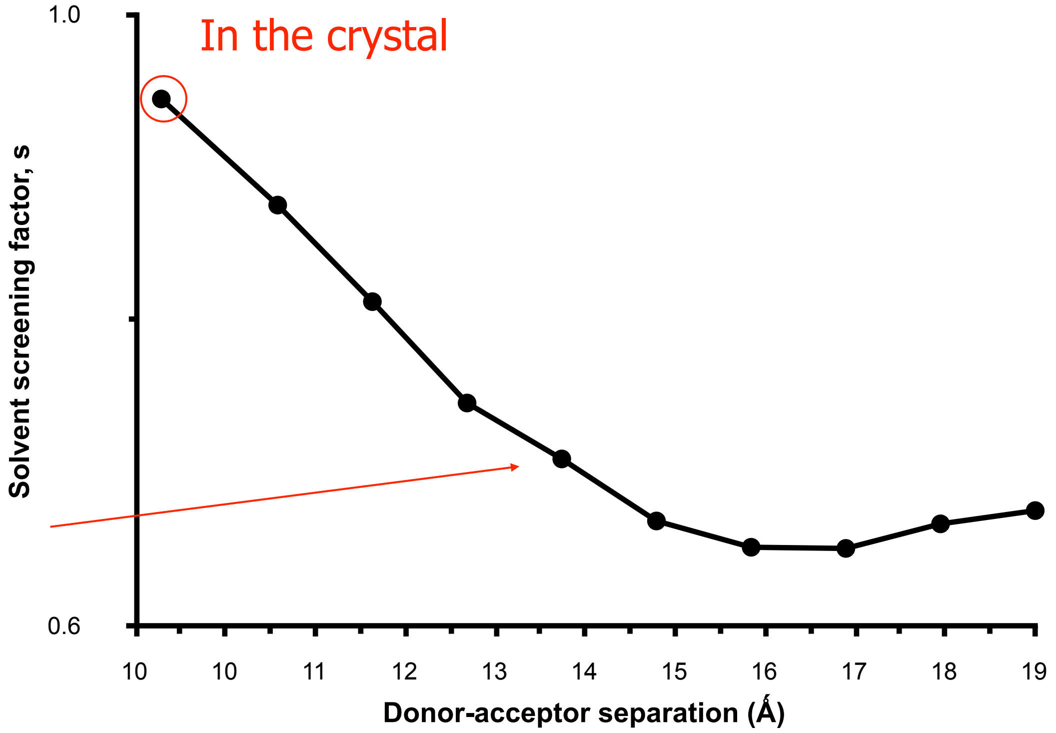


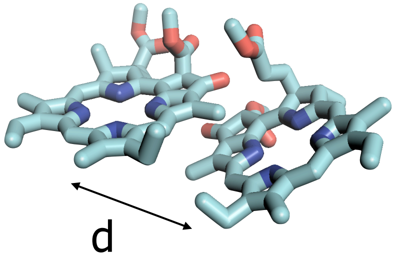


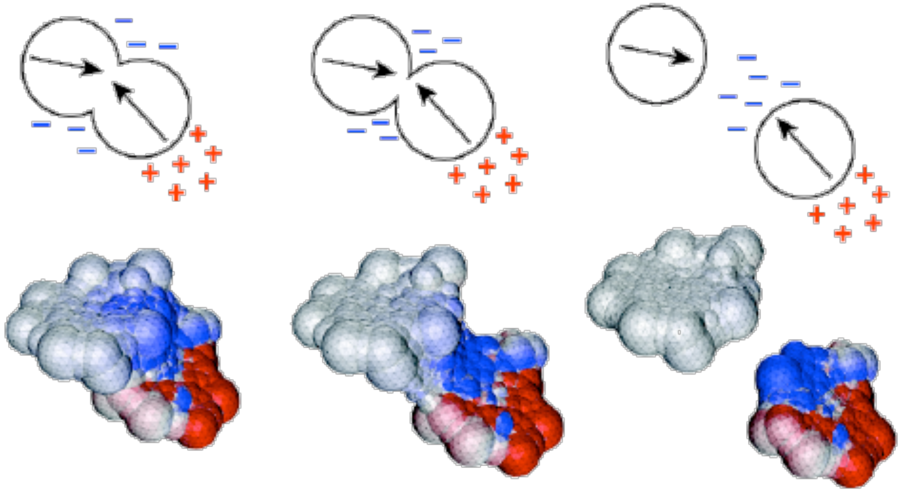


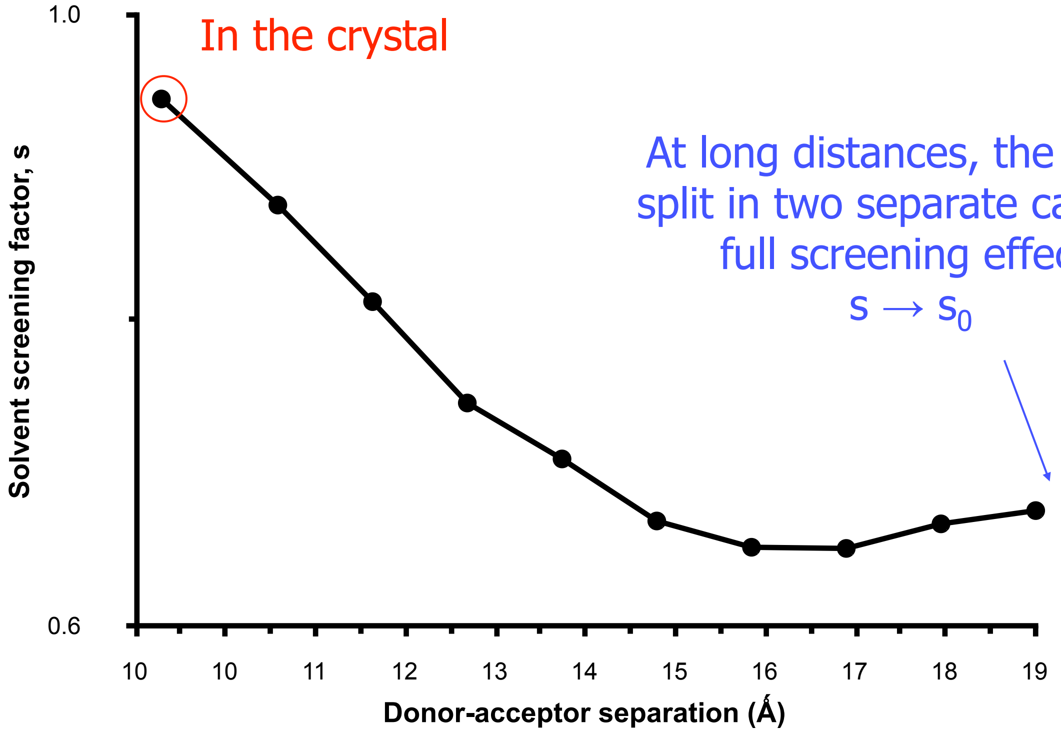
As the molecules go farther, the cavity is progressively stretched and the medium starts to appear between them: the screening increases (**s** < 1)

Why a distance dependent screening?

Light harvesting complex II (LHCII)







In the crystal

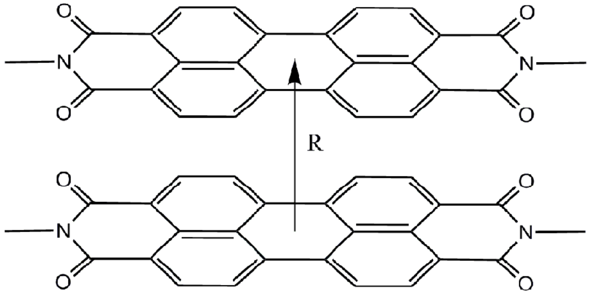
At long distances, the cavity split in two separate cavities: full screening effect.

$s \rightarrow s_0$

But we have simulated a protein environment
with a uniform continuum dielectric !

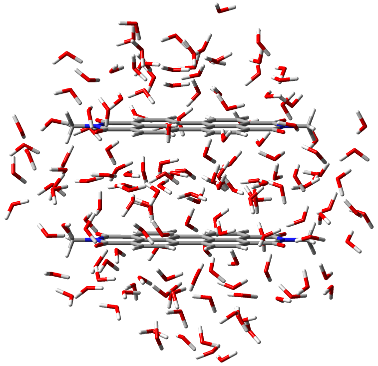
How accurate is such an approximation?

A test on the PCM accuracy on EET: the PDI dimer in water



R = 3.5 Å and 7 Å

Molecular Dynamics simulations (298 K)



- Amber ff02 polarizable force-field:
    water: POL3 parameters
    PDI: B3LYP/cc-pVTZ ESP charges
    and ff02 van der Waals parameters
- Periodic boundary conditions:
    R = 3.5 Å Box of 937 waters
    R = 7 Å Box 1055 waters
- 2 ns run (1fs time step)

A test on the PCM accuracy on EET: the PDI dimer in water

Transition properties of the monomer

CIS/6-31G(d)	ΔE(eV)	Shift	μ^T (Debye)	Shift
Vacuum	**3.31**		**9.88**	
PCM	**3.19**	**-0.12**	**10.60**	**0.72**
QM/MMpol	**3.18**	**-0.13**	**10.67**	**0.79**

QM/MMpol & PCM give the same solvent-induced shifts on transition properties

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EET couplings in the dimers

		V_s	$V_{explicit}$	V_{total}	s
R=3.5	**Vacuum**	**1642**		**1642**	
	PCM	**1813**	**-504**	**1309**	**0.72**
	QM/MMpol	**1805**	**-457**	**1348**	**0.75**
R=7	**Vacuum**	**571**		**571**	
	PCM	**660**	**-228**	**432**	**0.65**
	QM/MMpol	**661**	**-214**	**447**	**0.68**

-0.07

-0.07

The screening factor s behaves very consistently in the two approaches, giving support to the distance-dependent screening function derived from PCM-EET calculations in photosynthetic proteins.

Conclusions

Hybrid QM/Classical models represent a computationally efficient approach to study solvated systems

They can be extended to any QM level and generalized to excited states properties and processes.

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Future developments:

extension of the same formalisms to explicitly time-dependent descriptions

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