Applications of TDDFT to Chemistry and Biochemistry II

Joaquim Jornet-Somoza

j.jornet.somoza@gmail.com

[1] Nano-Bio Spectroscopy Group and ETSF Scientific Development Center, Departamento de Física de Materiales, Centro de Física de Materiales CSIC-UPV/EHU and DIPC, University of the Basque Country UPV/EHU, Avenida Tolosa 72, 20018 Donostia/San Sebastián, Spain

[2] Theory Department, The Max Planck Institute for the Structure and Dynamics of Matter (MPSD), Bldg. 99 (CFEL) , Luruper Chaussee 149 , 22761 Hamburg

Universidad del País Vasco
Euskal Herriko Unibertsitatea

nano-bio spectroscopy group

mpsd
Max-Planck-Institut für Struktur und Dynamik der Materie

MAX-PLANCK-GESELLSCHAFT

- Biochemist's Interests

  - Photobiology

- Mixed Method: QM /MM:

  - QM/MM Schemes + QM/MM Energy Formulation.

  - Boundary Schemes

  - TDDFT in Mixed Methods

- Fragment-density analysis in Real-time TDDFT

  - Fragment-density and AIM theory

  - Local Dipole Analysis in real-time TDDFT

  - Application to LHC-II

- Fundamentals of Subsystem TDDFT

  - Fundamentals of Subsystem DFT

  - Frozen Density Embedding Theory

  - Subsystem TDDFT

Outline

- **Biochemist's Interests**

  - Photobiology

- Mixed Method: QM /MM:

  - QM/MM Schemes + QM/MM Energy Formulation.

  - Boundary Schemes

  - TDDFT in Mixed Methods

- Fragment-density analysis in Real-time TDDFT

  - Fragment-density and AIM theory

  - Local Dipole Analysis in real-time TDDFT

  - Application to LHC-II

- Fundamentals of Subsystem TDDFT

  - Fundamentals of Subsystem DFT

  - Frozen Density Embedding Theory

  - Subsystem TDDFT

Biochemist's Interests

From Wikipedia:

Biochemistry, sometimes called biological chemistry, is the **study of chemical processes** within and relating to **living organisms**.[...]
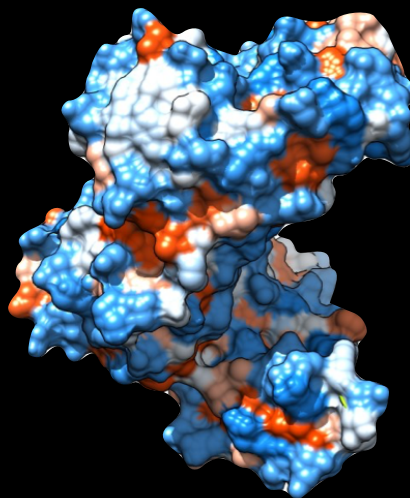
Over the last decades of the 20th century, *biochemistry* has become *so successful at explaining living processes* that now almost all areas of the life sciences from *botany* to *medicine* to *genetics* are engaged in **biochemical research**.

Today, the main focus of pure biochemistry is on understanding how biological molecules give rise to the processes that occur within living cells.
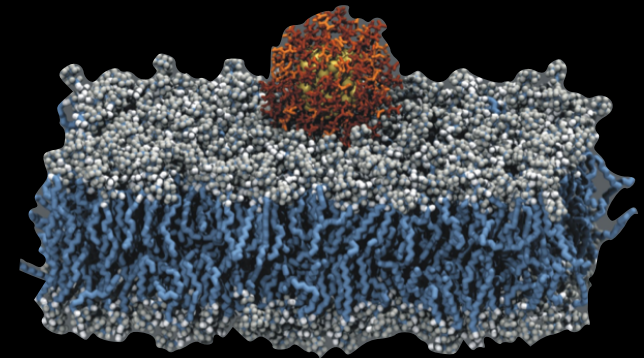

Nucleic Acid (DNA, RNA)   Aminoacid (Proteins)   Lipides (Membrane)
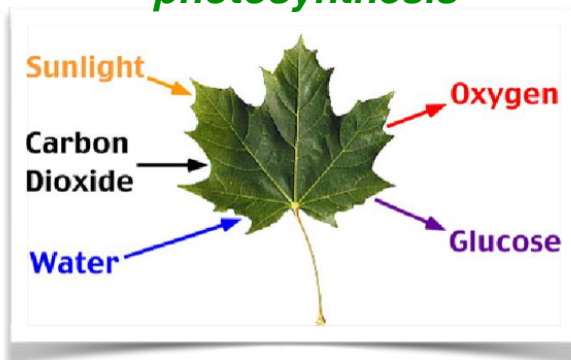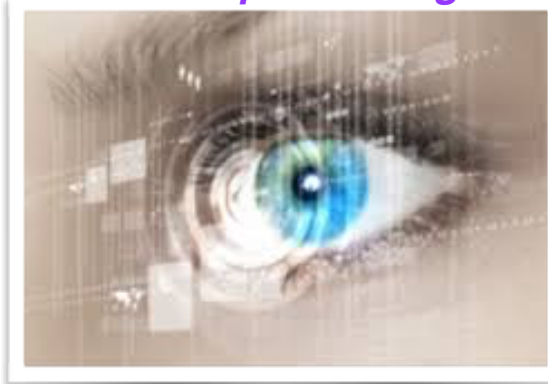
Biochemist's Interests

From Wikipedia:

Photobiology is the scientific study of the **interactions of light** (technically, non-ionizing radiation, typically <10 eV, the energy required to ionize an oxygen atom) and *living organisms*.

The field includes the study of *photosynthesis*, *visual processing*, *circadian rhythms*, *bioluminescence*, and *ultraviolet radiation effects*.

photosynthesis

visual processing

circadian rhythms

ultraviolet radiation effects

bioluminescence

Biochemist's Interests

From Wikipedia:

Photobiology is the scientific study of the **interactions of light** (technically, non-ionizing radiation) and *living organisms*. The field includes the study of *photosynthesis*, *visual processing*, *circadian rhythms*, *biolu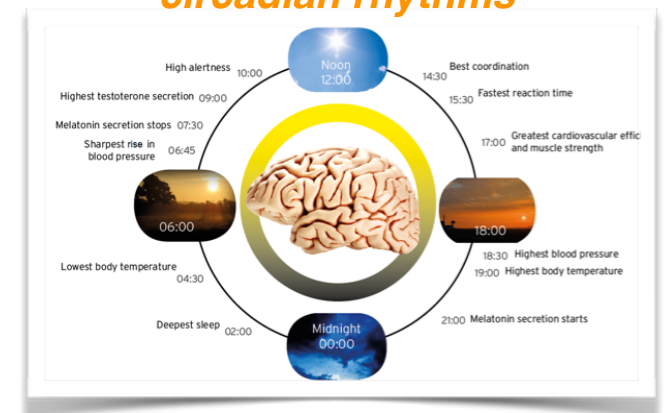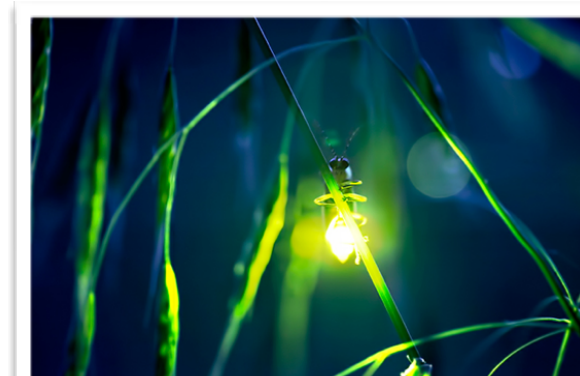minescence*, and *ultraviolet radiation effects*. The division between ionizing radiation and nonionizing radiation is typically considered to be 10 eV, the energy required to ionize an oxygen atom.

All this processes start or take place at the **nano-scale** (i.e. **macromolecular size**, from 10 to 100s nm).

A theoretical/computational approach will therefore need:

- theoretical model for matter in the energy range [0 to few tens of eV]
- *description of the interaction with the environment (condensed phase)*
- description of chemical reactions (structural changes)

Biochemist's Interests

From Wikipedia:

Photobiology is the scientific study of the **interactions of light** (technically, non-ionizing radiation) and *living organisms*. The field includes the study of *photosynthesis*, *visual processing*, *circadian rhythms*, *bioluminescence*, and *ultraviolet radiation effects*. The division between ionizing radiation and nonionizing radiation is typically considered to be 10 eV, the energy required to ionize an oxygen atom.

All this processes start or take place at the nano-scale (i.e. macromolecular size, from 10 nm to several hundred nanometers).

… which translates into:

• electronic structure theory and ways to solve the corresponding equations
• *approximate solutions for the description of the interaction with the environment.*
• solution of the equations of motion for atoms and electrons + statistical mechanics (from the microcanonical to the canonical ensemble)

Biochemist's Interests

From Wikipedia:

Photobiology is the scientific study of the **interactions of light** (technically, non-ionizing radiation) and *living organisms*. The field includes the study of *photosynthesis*, *visual processing*, *circadian rhythms*, *bioluminescence*, and *ultraviolet radiation effects*. The division between ionizing radiation and nonionizing radiation is typically considered to be 10 eV, the energy required to ionize an oxygen atom.

All this processes start or take place at the nano-scale (i.e. macromolecular size, from 10 nm to several hundred nanometers).

… and in practice:

- HF, CI, MPn, CAS, ..., DFT and corresponding theories for excited states —> TDDFT
- *periodic boundary conditions (PBC) for homogeneous systems &*
  hybrid schemes, for inhomogeneous systems: QM/MM, coarse grained, hydrodynamics, …
- time dependent theories for adiabatic and non adiabatic dynamics of atoms and electrons: mixed-quantum classical molecular dynamics

Outline

- Biochemist's Interests
    - Photobiology

- Mixed Method: QM /MM:
    - QM/MM Schemes + QM/MM Energy Formulation.
    - Boundary Schemes
    - TDDFT in Mixed Methods

- Fragment-density analysis in Real-time TDDFT
    - Fragment-density and AIM theory
    - Local Dipole Analysis in real-time TDDFT
    - Application to LHC-II

- Fundamentals of Subsystem TDDFT
    - Fundamentals of Subsystem DFT
    - Frozen Density Embedding Theory
    - Subsystem TDDFT

Mixed Methods QM/MM
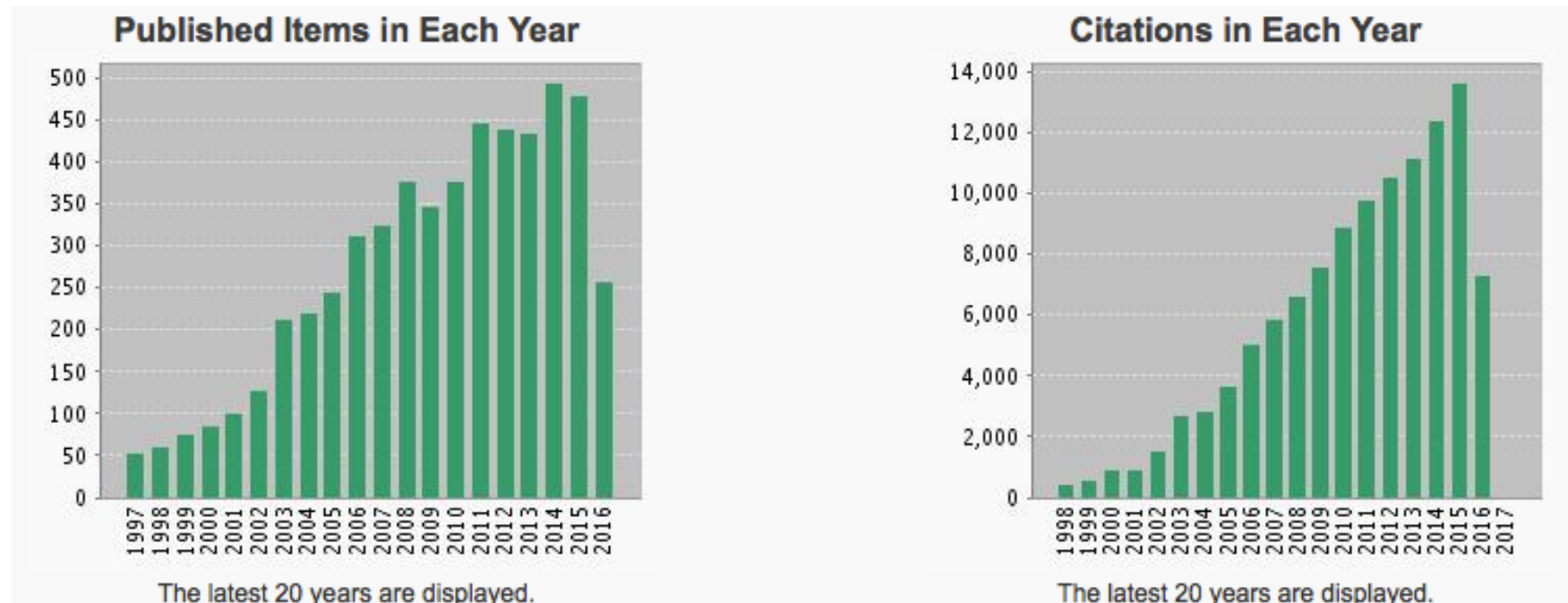
Motivation

Green Fluorescent Protein (mPlum)
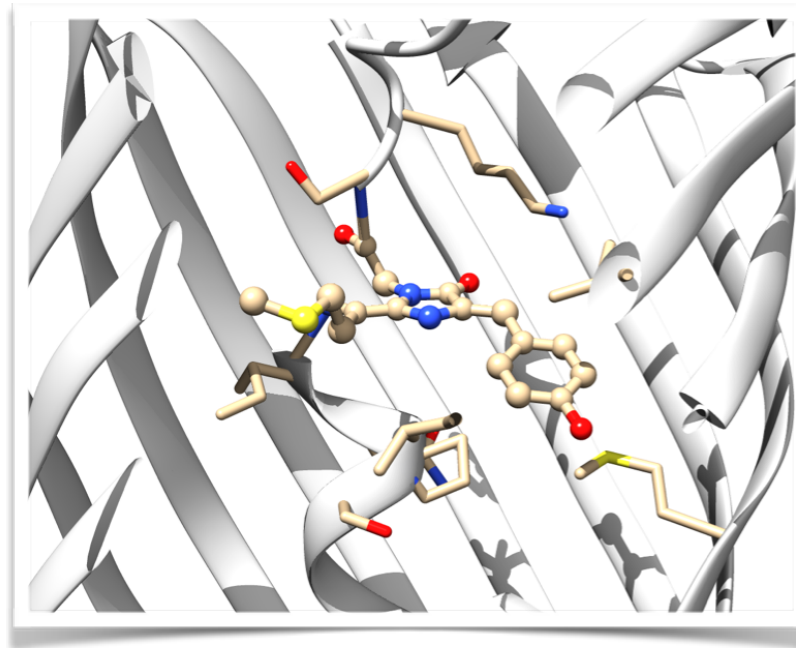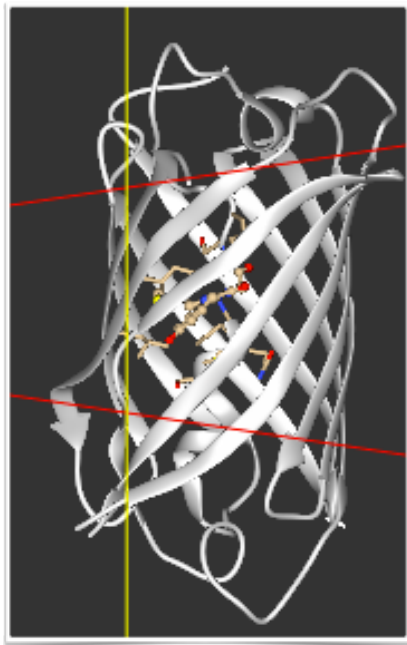
Quantum-mechanical (QM) methods are required for describing chemical reactions and other **electronic processes**, such as charge transfer or electronic excitation, but they are restricted to systems of up to a few hundred atoms.

However, the size and conformational complexity of biomolecules calls for methods capable of treating up to several 100 000 atoms and allowing for simulations over time scales of tens of nanoseconds.

This is achieved by highly efficient, **force-field-based molecular mechanics** (**MM**) methods.

Mixed Methods QM/MM

The **wide success of QM/MM methods** can be visualised in terms of the number of publication and citations in the last years.

Published Items in Each Year

The latest 20 years are displayed.

Citations in Each Year

The latest 20 years are displayed.

Mixed Methods QM/MM

Historical Aspects

The Nobel Prize in Chemistry 2013

Photo: A. Mahmoud
Martin Karplus
Prize share: 1/3

Photo: A. Mahmoud
Michael Levitt
Prize share: 1/3

Photo: A. Mahmoud
Arieh Warshel
Prize share: 1/3

The Nobel Prize in Chemistry 2013 was awarded jointly to Martin Karplus, Michael Levitt and Arieh Warshel *"for the development of multiscale models for complex chemical systems"*.

Theoretical Studies of Enzymic Reactions:

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

A. WARSHEL AND M. LEVITT

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

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 include the quantum mechanical energies associated with bond cleavage and charge redistribution of the substrate and the classical energies of steric and electrostatic interactions between the substrate and the enzyme. The electrostatic

1976 - Introduction, for the first time, a semiempirical QM/MM approach to describe an enzymatic reaction.

Calculation of Ground and Excited State Potential Surfaces of Conjugated Molecules.[1] I. Formulation and Parametrization

A. Warshel and M. Karplus*

Contribution from the Department of Chemistry, Harvard University, Cambridge, Massachusetts 02138. *Received January 31, 1972*

1972 - Method of GS and ExS calculation of conjugated molecules. Different mechanical treatment of σ and π electrons.

account of all bond length and bond angle variations. To permit rapid determination of the potential surfaces, the σ potential function and SCF–MO–CI energy of the π electrons are expressed as analytic functions of the molecular coordinates from which the first and second derivatives can be obtained. Illustrative applications to 1,3-butadiene, 1,3,5-hexatriene, α,ω-diphenyloctatetraene, and 1,3-cyclohexadiene are given.
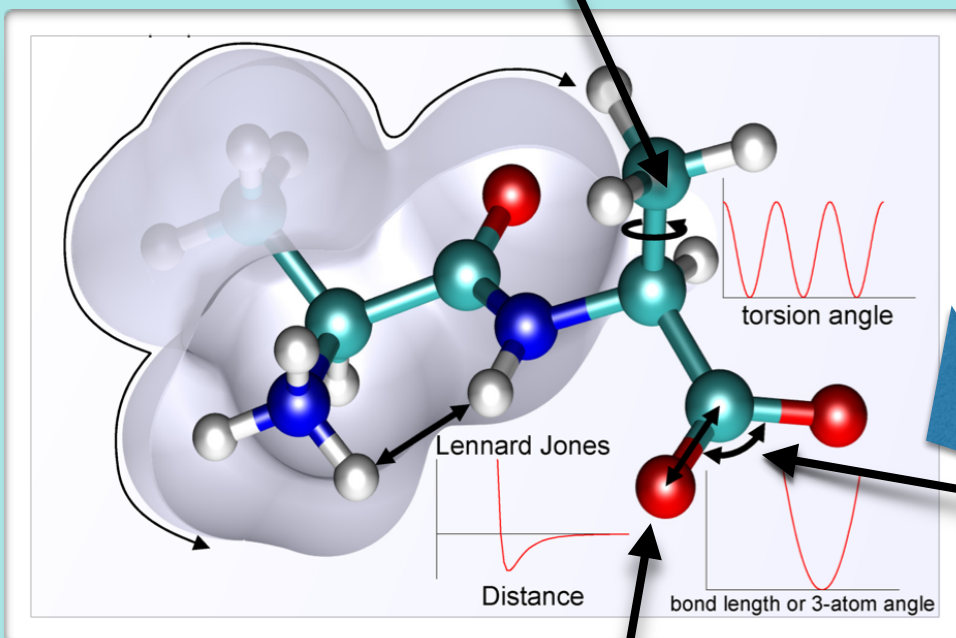
Mixed Methods QM/MM

General Remark

The entire **system is partitioned** into an inner region (QM-treatment), and outer part (MM-treatment).

Biological System

MM ForceField Expressions

$$E_{rotation} = k_{\phi} \cdot [1 + \cos{(n\phi + \phi_0)}]$$

torsion angle

Lennard Jones

Distance

bond length or 3-atom angle

QM

$$\hat{H}\Psi_n = \epsilon_n \Psi_n$$

$$-i\hbar\frac{\partial}{\partial t}\Psi_n = \hat{H}\Psi_n$$

Interaction

$$E_{bending} = k_{\theta} \cdot (\theta - \theta_0)^2$$

$$E_{streching} = k_{bond} \cdot (d - d_0)^2$$

BUT, **due to the (strong) QM-MM interaction**, the total energy of the entire system **cannot** be written as the *sum of the energies of the subsystems*.
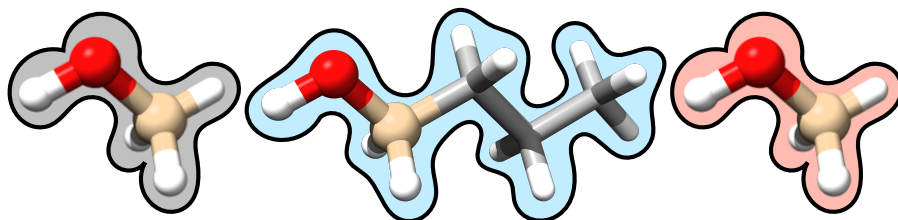
Mixed Methods QM/MM

Mixed Methods Schemes: *How can we "cut" our system ?*

Most of the current QM/MM methods use either a **subtractive** or an **additive** QM/MM scheme for the description of the energy of the full system.

Subtractive Scheme

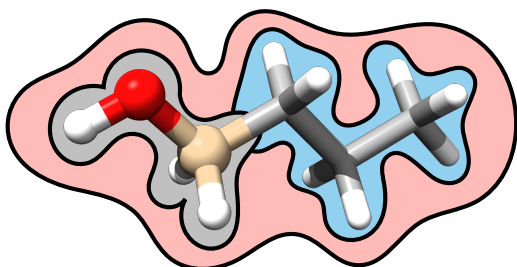$$E_{QM/MM} = E_{QM}(QM) + E_{MM}(QM + MM) - E_{MM}(QM)$$

Advantage: Simplicity and Straightforward implementation.

Drawback: Require a complete set of MM parameters for the inner subsystem. The QM/MM coupling is treated at MM level.

Additive Scheme

$$E_{QM/MM} = E_{QM}(QM) + E_{MM}(MM) + E_{QM/MM}$$

Advantage: very different levels of theory can be used to describe the QM, MM and QM-MM regions.

Drawback: the creation of an abrupt quantum/classical boundary. The electrons cease to exist when crossing from QM to MM.

Most of the QM/MM methods use and additive scheme.

Mixed Methods QM/MM

QM/MM Energy Formulation

In the additive scheme, one assume that the electron density can be partitioned into two regions:

$$\rho(\boldsymbol{r}) = \rho_{QM}(\boldsymbol{r}) + \rho_{MM}(\boldsymbol{r})$$

BUT, due to the (strong) QM-MM interaction, the total energy of the entire system cannot be written only as the sum of the energies of the subsystems:

$$E_{QM/MM} = E_{QM}(QM) + E_{MM}(MM) + E_{QM/MM}$$

QM Energy Expression

In this embedding scheme, any *ab-initio* method from quantum mechanics can be applied to obtain the energy of the "inner" region.

As it concerns us, we can write the energy expression obtained from Density Functional Theory
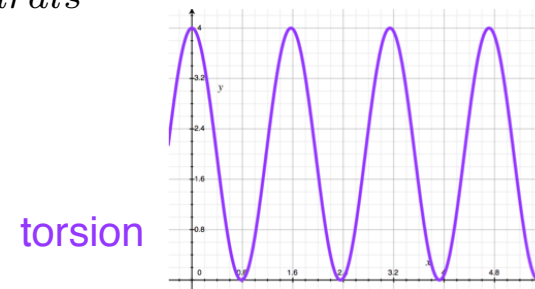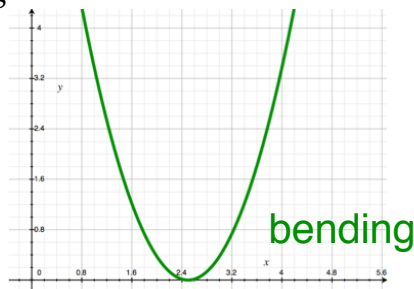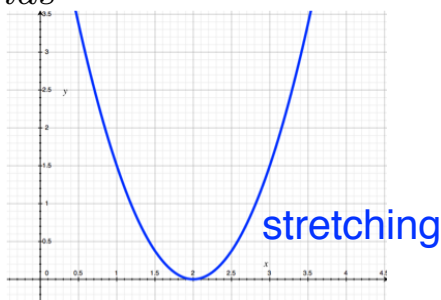
$$E_{QM}^{DFT} = T_s[\rho] - \sum_I \int d\boldsymbol{r}\, \rho(\boldsymbol{r}) \frac{Z_I}{|\boldsymbol{R}_I - \boldsymbol{r}|} + \frac{1}{2} \int \int \frac{\rho(\boldsymbol{r})\rho(\boldsymbol{r}')}{|\boldsymbol{r} - \boldsymbol{r}'|} d\boldsymbol{r} d\boldsymbol{r}'$$

$$+ E_{xc}[\rho] + \frac{1}{2} \sum_I \sum_J \frac{Z_I Z_J}{|\mathbf{R_I} - \mathbf{R_J}|}$$
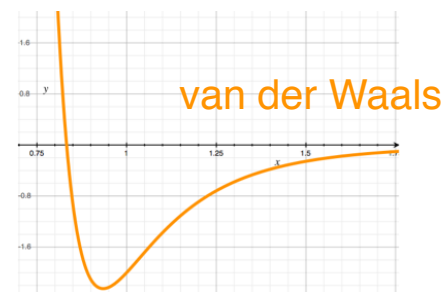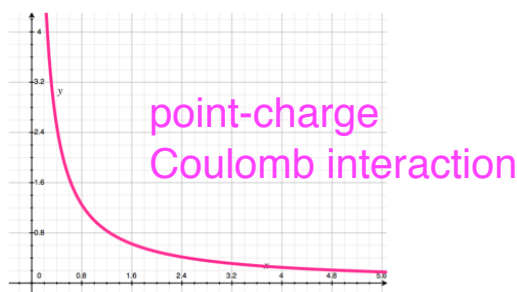
Mixed Methods QM/MM

MM Energy Expression

in the same manner, the potential energy function of the outer regions are described by **classical mechanics** (the "force-field") containing *bonded terms*:

$$E_{MM}^{bonded} = \sum_{bonds} \frac{1}{2} k_d (d_{IJ} - d_0)^2 + \sum_{angles} \frac{1}{2} k_\theta (\theta_{IJK} - \theta_0)^2 + \sum_{dihedrals} k_\phi [1 + \cos(n\phi_{IJKL} + \delta)]$$

stretching   bending   torsion

and *non-bonded terms*

$$E_{MM}^{nonbonded} = \frac{1}{2} \sum_{I \in MM} \sum_{J \in MM} \frac{q_I q_J}{R_{IJ}} + \frac{1}{2} \sum_{I \in MM} \sum_{J \in MM} 4\epsilon_{IJ} \left(\left(\frac{\sigma_{IJ}}{R_{IJ}} \right)^{12} - \frac{\sigma_{IJ}}{R_{IJ}} \right)^6 \right)$$

point-charge Coulomb interaction   van der Waals

where the **kinetic energy contribution has been considered constant**, due to the "frozen" character of the MM electronic density.

QM-MM Energy Expression

The exact form of the QM–MM coupling term $E_{QM\text{-}MM}$ defines a particular QM/MM method. In accordance with the interactions considered in the force field, it **includes** bonded, van der Waals, and electrostatic interactions between QM and MM atoms

$$E_{QM-MM} = E_{QM_M M}^{bond} + E_{QM_M M}^{vdW} + E_{QM_M M}^{el}$$

The **electrostatic coupling** between the QM charge density and the charge model used in the MM region can be handled at **different levels of sophistication**, characterised essentially by the extent of mutual polarisation :

- Mechanical embedding

- Electrostatic embedding

- Polarised embedding

Mixed Methods QM/MM

Mechanical Embedding (unpolarized)

- The QM-MM interaction is treated on the same footing as in the MM part.

$$E_{QM/MM} = \frac{1}{2} \sum_{I \in QM} \sum_{J \in MM} \frac{Q_I q_J}{R_{IJ}}$$

Advantage: Conceptually straightforward and computationally efficient.
Drawback: (1) MM charge **do not interact** with the QM density (no direct polarised by the environment)
(2) Derivation of appropriate Q_I **charges is not trivial** (it has to take into account electrons+nuclei).

Electrostatic Embedding (QM polarized)

- Include QM-MM electrostatic interactions in the QM calculation.

$$\hat{H}^{el}_{QM-MM} = - \sum_{i \in QM}^{N} \sum_{J \in MM}^{L} \frac{q_J}{|r_i - R_J|} + \sum_{\alpha \in QM}^{M} \sum_{J \in MM}^{L} \frac{Q_\alpha q_J}{|R_\alpha - R_J|}$$

Advantage: The electronic structure of the QM part can adapt to changes in the charge distributions of the
MM part (important when doing MD, or geometry optimisations).
Attention: Special care have to be done on the boundaries of the QM/MM, where the **MM part can cause**
overpolarisation.

Polarized Embedding (Fully Polarised)

- Include a flexible MM region polarised by the QM charge distribution. (direct polarised or fully self-
consistent polarisation formalism)

Attention: The inclusion of all polarisable effects seriously increases the computational cost.

Mixed Methods QM/MM

Other contributions

In addition to the electrostatic contributions there are also the van der Waals and bonded contributions to the QM-MM coupling term.

Their treatment is considerably simpler as they are **handled purely at the MM level**, irrespective of the class (subtractive or additive) of QM/MM scheme.

$$E_{QM-MM}^{bonded} = \sum_{bonds} \frac{1}{2} k_d (d_{II'} - d_0)^2 + \sum_{angles} \frac{1}{2} k_\theta (\theta_{I''J''K''} - \theta_0)^2$$

$$+ \sum_{dihedrals} k_\phi [1 + \cos(n\phi_{I''J''K''L''} + \delta)]$$

$$E_{QM-MM}^{vdW} = \frac{1}{2} \sum_{I \in QM} \sum_{J \in MM} 4\epsilon_{IJ'} \left(\left(\frac{\sigma_{IJ'}}{R_{IJ'}} \right)^{12} - \frac{\sigma_{IJ'}}{R_{IJ'}} \right)^6 \right)$$

where I refers to an atom on the QM regions, I' runs over MM atoms, and I'' refers to a set of atoms where a least one atoms belongs to the QM region.

Are good enough the standard MM parameters when covalent bonds crosses the QM-MM boundaries ?

Mixed Methods QM/MM

Boundary Schemes

Several approaches have been devised to treat with **covalent bonds crossing the QM-MM** boundaries.
Then three issues have to be dealt with: **1)** The dangling bond of the QM atom must be capped; **2)** For electrostatic or polarized embedding, overpolarization of the QM density by the MM charges **has to be prevented**, **3)**The bonded MM terms involving atoms from both subsystems have to be selected such that double-counting of interactions is avoided.

Link Atom
An additional atom centre L (usually H-atom) is covalently bound to the Q1 and saturates its free valency.

Boundary Atoms

the first MM atom is replaced by a special boundary atom that appears in both QM and MM calculation. On the QM side, it mimics the cut bond and possibly also the electronic character of the MM moiety attached to Q; in the MM calculation, it behaves as a normal MM atom.

Frozen Localised Orbitals

Hybrid orbitals at the boundary and keep some of them frozen. They serve to cap the QM region, replacing the cut bond.

TDDFT in Mixed methods

Mixed TDDFT/MM schemes are mostly used to **compute excitation energies** influenced by the electrostatic potential of the environment.

The implementation of a QM/MM scheme for the calculation of excitation energies **within LR-TDDFT** and a nonpolarizable MM environment **is straightforward.** Because all excited-state properties are calculated solely as functionals of the ground-state electron density.

All that is needed is to include the effect of the MM part into an additional contribution to the external potential

$$v_{ext}(\boldsymbol{r}, \boldsymbol{R}^{QM}, \boldsymbol{R}^{MM}) = \sum_{I \in QM} \frac{Z_I}{|\boldsymbol{R}_I - \boldsymbol{r}|} + \sum_{m \in MM} \frac{q_m}{|\boldsymbol{R}_m - \boldsymbol{r}|}$$

The new external potential generates a **new (polarized) ground-state density** (and KS orbitals), and its linear response to a frequency-dependent perturbation yields the new excitations energies ω'n via Casida's equations

$$\begin{pmatrix} \mathbb{A} & \mathbb{B} \\ \mathbb{B}^* & \mathbb{A}^* \end{pmatrix} \begin{pmatrix} \mathbf{X} \\ \mathbf{Y} \end{pmatrix} = \Omega \begin{pmatrix} -\mathbb{I} & 0 \\ 0 & \mathbb{I} \end{pmatrix} \begin{pmatrix} \mathbf{X} \\ \mathbf{Y} \end{pmatrix}$$

Mixed Methods QM/MM

Practical Issues

The QM part

Choice of the QM Method:

The QM/MM formalism houses for all types of QM methods.
- **Semiempirical methods**: large QM regions and large times scales (100ps-1ns), but it performance has to be carefully evaluated.
- **DFT-based methods**: ~100 atoms and comprise 10-100ps.
- **MC-CASSCF/CASPT2** and higher: limited to static QM/MM application, for a limited number of configuration.

Choice of the QM Region:
- It is always **based in previous information**.
- Ideally the density of the QM subsystem should match the density of the full QM system within the region of interest — **fairly large QM systems** are needed for quantitative results.

The MM part

Commonly used Force Fields in Biochemistry
Force fields parametrise most of the **biological molecules**: proteins and nucleic acids, and less frequently carbohydrates or lipids.
- AMBER, CHARMM, GROMOS, OPLS-AA,

Other types of molecular interactions have to be previously fitted or treated from ab-initio methods.

Mixed Methods QM/MM

Extended reviews

- Hans Martin Senn and Walter Thiels,
  "QM/MM Methods for Bimolecular Systems"
  Angew. Chem. Int. Ed. **2009**, *48*, 1198-1229

- Elizabeth Brunk and Ursula Rothlisberger,
  "Mixed Quantum Mechanical/Molecular Mechanical Molecular Dynamics
  Simulations of Biological Systems in Ground and Electronically Excited States.
  Chem. Rev. **2015**, 115, 6217-6263

MM ForceField Expressions

torsion angle

Lennard Jones

Distance

bond length or 3-atom angle
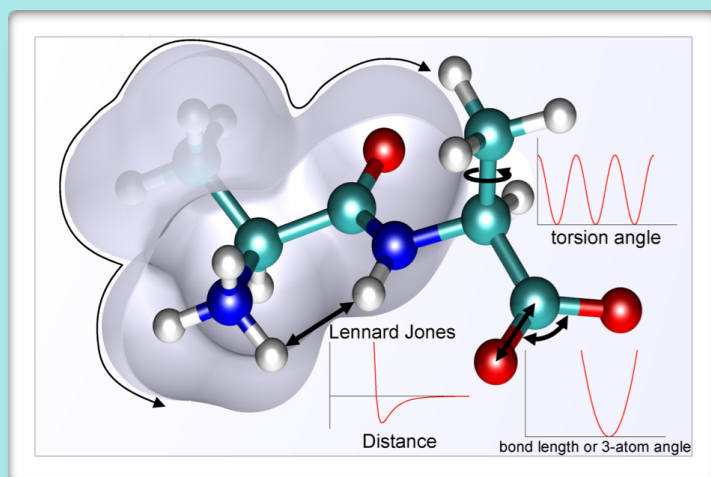
QM

$$\hat{H}\Psi_n = \epsilon_n \Psi_n$$

$$-i\hbar\frac{\partial}{\partial t}\Psi_n = \hat{H}\Psi_n$$

**Need of Force Field
Parametrisation
for each kind of atom
combination !!**

What about complex systems with more than one active centre?

Outline

- Biochemist's Interests
  - Photobiology

- Mixed Method: QM /MM:
  - QM/MM Schemes + QM/MM Energy Formulation.
  - Boundary Schemes
  - TDDFT in Mixed Methods

- **Fragment-density analysis in Real-time TDDFT**
  - Fragment-density and AIM theory
  - Local Dipole Analysis in real-time TDDFT
  - Application to LHC-II

- **Fundamentals of Subsystem TDDFT**
  - Fundamentals of Subsystem DFT
  - Frozen Density Embedding Theory
  - Subsystem TDDFT

Outline

- Biochemist's Interests

  - Photobiology

- Mixed Method: QM /MM:

  - QM/MM Schemes + QM/MM Energy Formulation.

  - Boundary Schemes

  - TDDFT in Mixed Methods

- **Fragment-density analysis in Real-time TDDFT**

  - Fragment-density and AIM theory

  - Local Dipole Analysis in real-time TDDFT

  - Application to LHC-II

- Fundamentals of Subsystem TDDFT

  - Fundamentals of Subsystem DFT

  - Frozen Density Embedding Theory

  - Subsystem TDDFT

Objective: to compute the contribution of the individual chromophores for any observable on complex systems.

Hohenberg-Kohn theorem (1964)
Every observable quantity of a quantum system can be calculated **from the electron density** of the system ALONE !

Principle: split the global density on fragments belonging to each subsystem.
Compute the expectation value on the local domain.

$$\rho(\boldsymbol{r}) = \rho_{tot}(\boldsymbol{r}) = \sum_I \rho_I(\boldsymbol{r});$$

Strong Approximation:
The non-additive terms can be assumed negligible.
Reasonable, since the global density are computed taking into account also interacting terms between fragments

Fragment-density and AIM theory

The **local electronic densities** are obtained by performing a division of the ground-state density based on the **Bader charge-topological approach**.

$$\rho(\boldsymbol{r}) = \rho_{tot}(\boldsymbol{r}) = \sum_I \rho_I(\boldsymbol{r});$$

Bader partitioning scheme: Atoms in Molecules theory.
(Richard F. W. Bader, "Atoms in Molecules: A Quantum Theory")
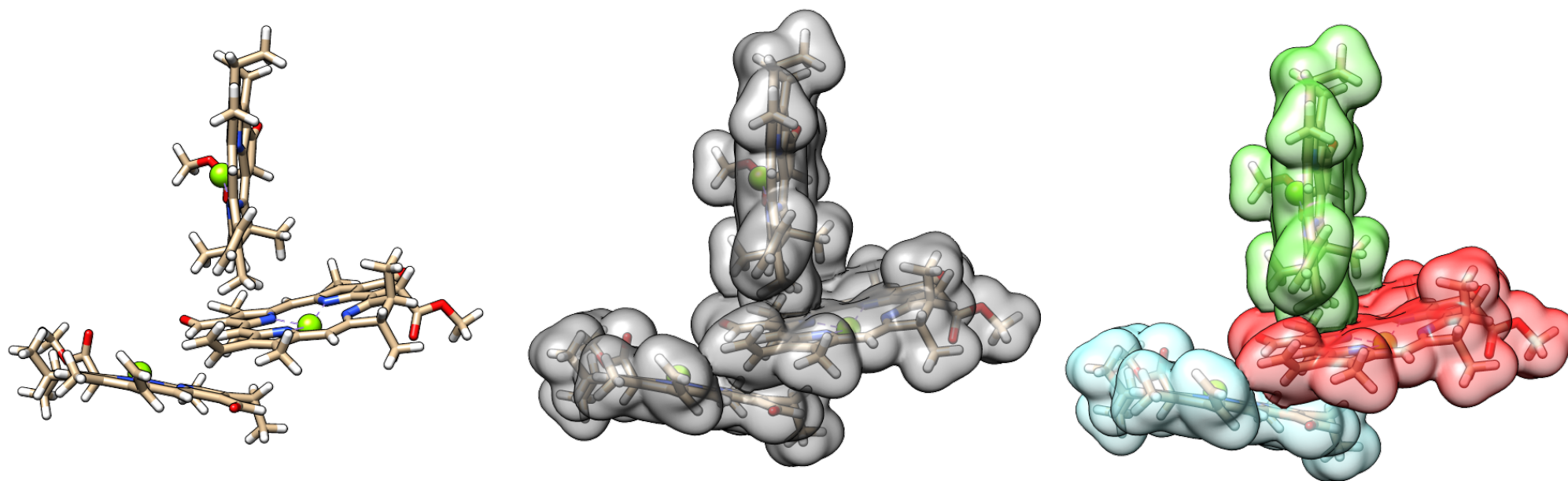
Local Dipole Analysis in real-time TDDFT

- 1 Do a ground state Kohn-Sham calculation: obtain $\{\varphi_i\}$

$$\hat{H}_{KS}[n](\boldsymbol{r}, t)\varphi_i(\boldsymbol{r}, t) = \epsilon_i \varphi_k(\boldsymbol{r}, t)$$

- 2 Time propagation of the KS orbitals (in 3 orthogonal directions)
  - Apply a short perturbative field (usually and instantaneous perturbation).
  - Propagate the KS orbitals for a long time (the longer the propagation, the higher the energy resolution.

- 3 Sample the dipole moment in time series.

$$\mu_\gamma(t) = \int \mathrm{r}_\gamma \cdot n(\boldsymbol{r}, t)d\boldsymbol{r}$$

- 4 Fourier transform to obtain the dynamic polarisability

$$\alpha_{\gamma\delta}(\omega) = \frac{1}{K_\delta} \int_0^\infty dt[\mu_\gamma(t) - \mu_\gamma(0)]e^{-i\omega t}$$

- 5 Spectrum can be obtained from the photo absorption cross-section:

$$\sigma(\omega) = \frac{4\pi\omega}{3c}\Im\mathrm{m}[\alpha(\omega)]$$

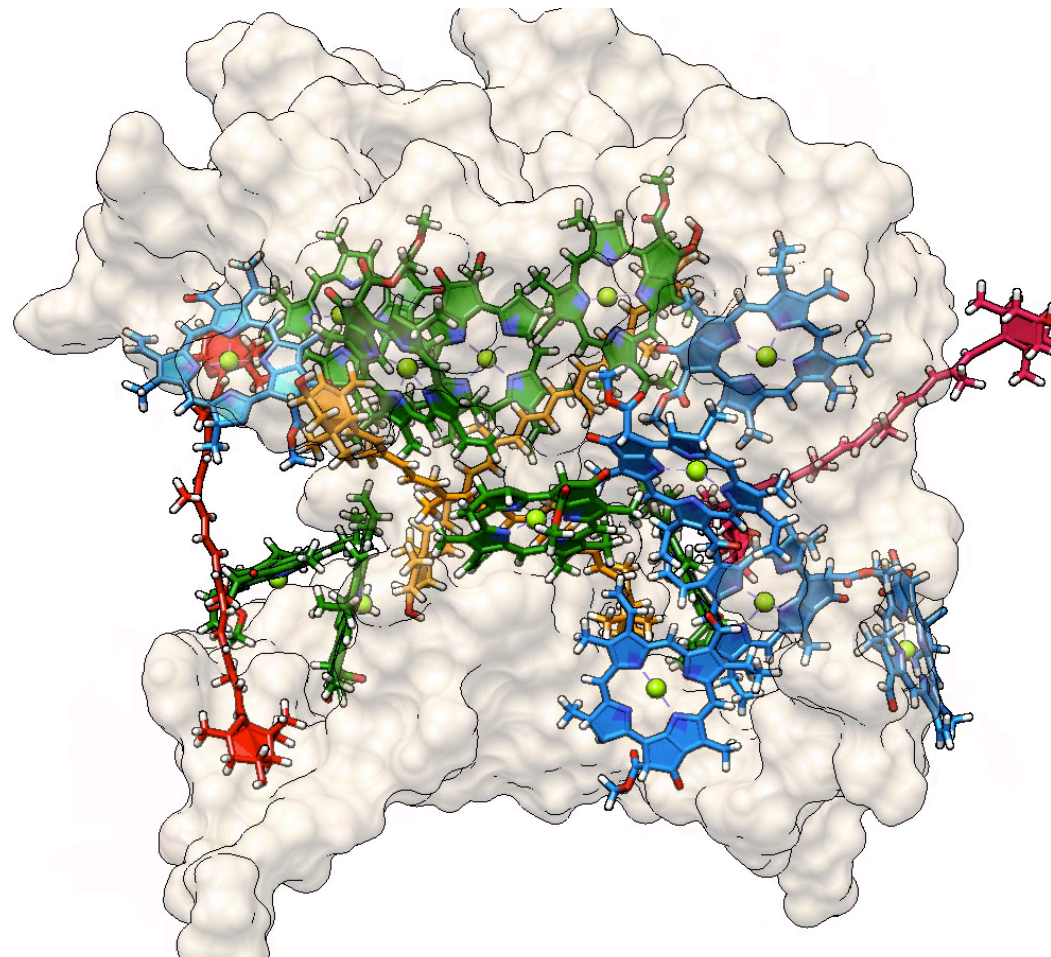## Local Dipole Analysis in real-time TDDFT
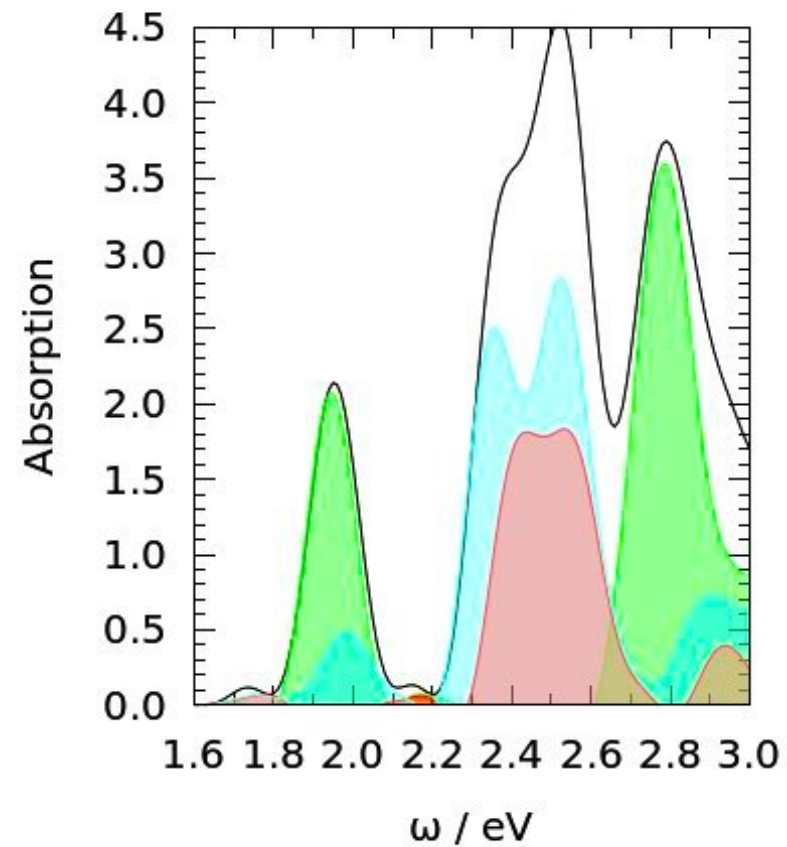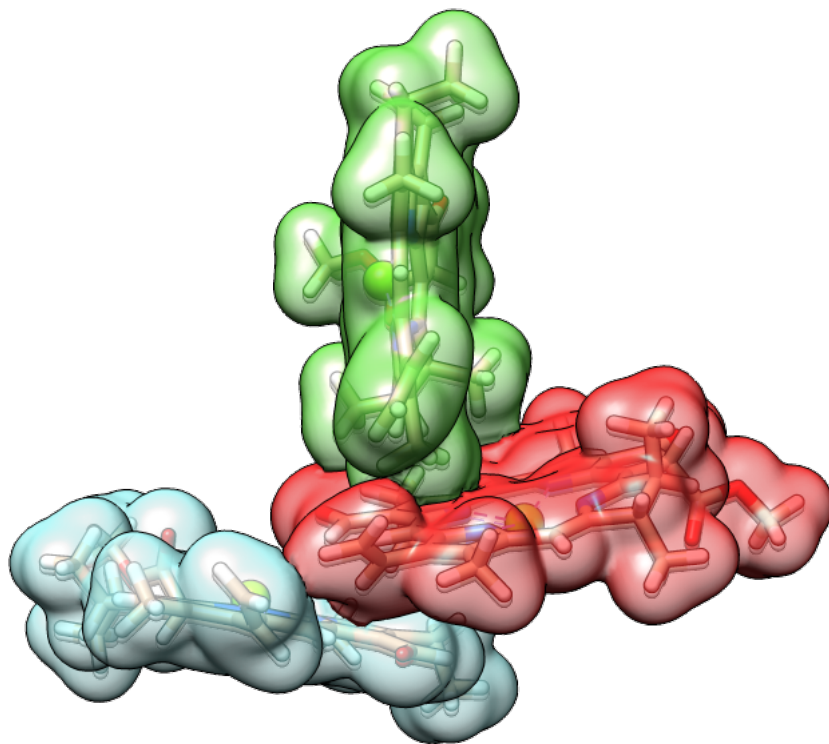
Fragment-density analysis in real-time TDDFT

LHC-II Complex: ~17000 atoms

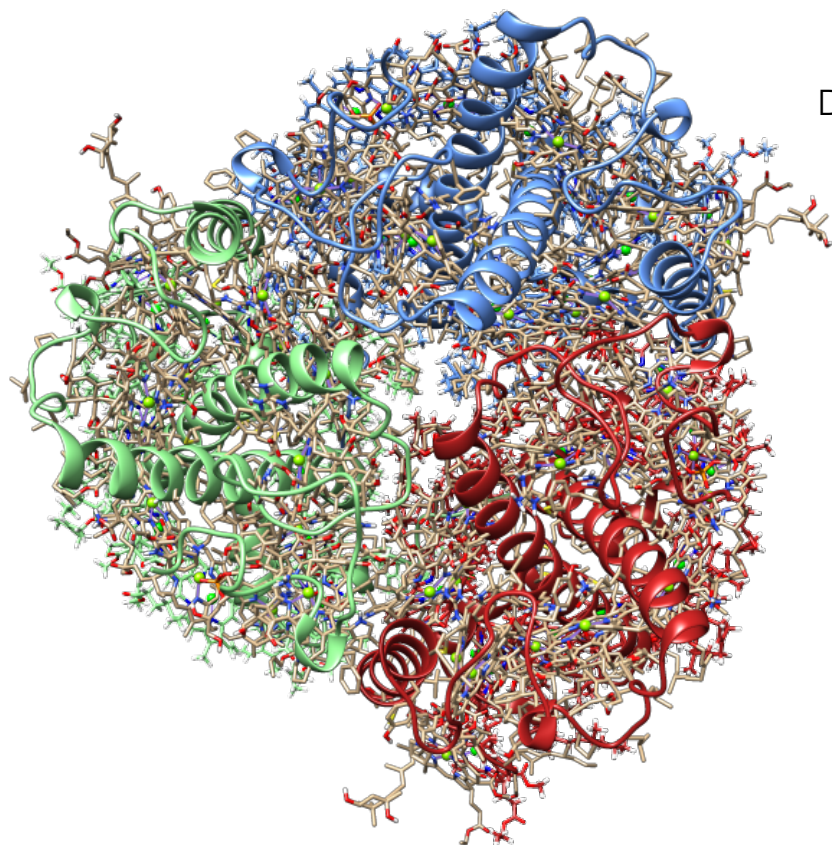Chromophore Network

Stroma

Lumen

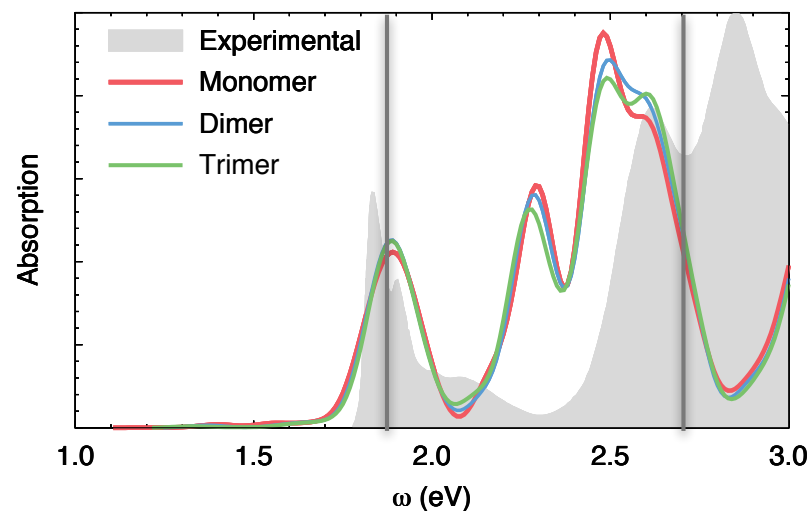6 Chlorophyll b: *3 Stroma + 3 Lumen*

8 Chlorophyll *a: 5 Stroma + 3 Lumen*

4 Carotenoids: Photoprotection Role

Absorption Spectra Chlorophyll's Network

D.Siefermann-Hamms, *Biochim. Biophys. Acta, 1985,* **811**, 325

Q-band   *Soret-band*

Monomer Chl's Network
(2025 atoms, ~2600 states,1440 CPUs, 11s/iter, 20000 iter = 40fs)

Aggregated Chl's Network
(6075 atoms, ~8000 states, 5120 CPUs, 30s/iter, 20000 iter = 40fs)

Good agreement on Q-band. ($\Delta E \sim 0.05$eV)
Red shifted Soret-band ($\Delta E \sim 0.35$ eV)

Only minor inter-monomer perturbations. Absorption process is governed by intra-monomer interactions.

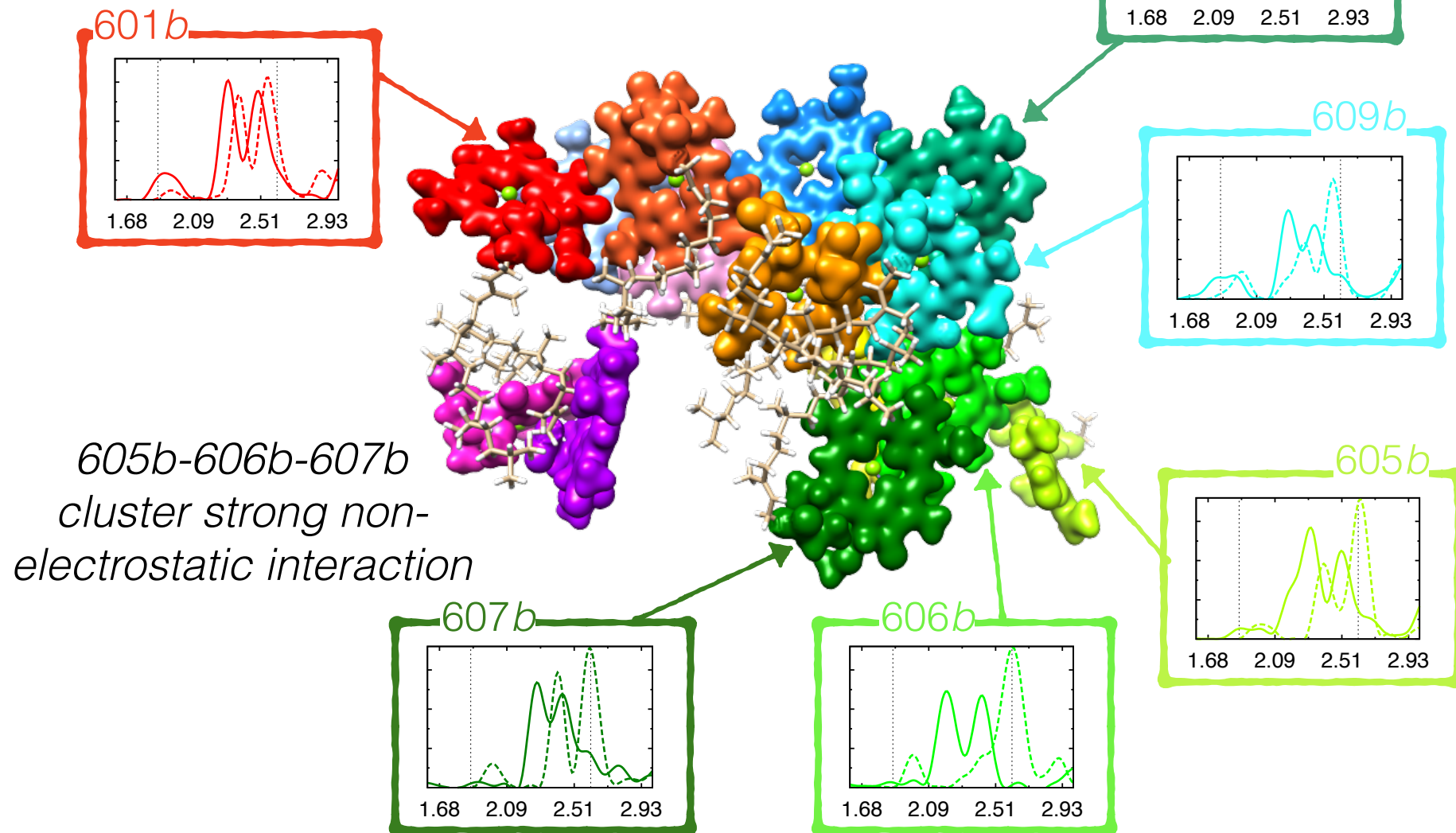# Fragment-density analysis in real-time TDDFT

Chlorophyll *a (LHCII)*

.... Isolated Chl + ligand
Chl's inside Chromophore Network

611*a*

610*a*

612*a*

602*a*

604*a*

614*a*

613*a*

603*a*
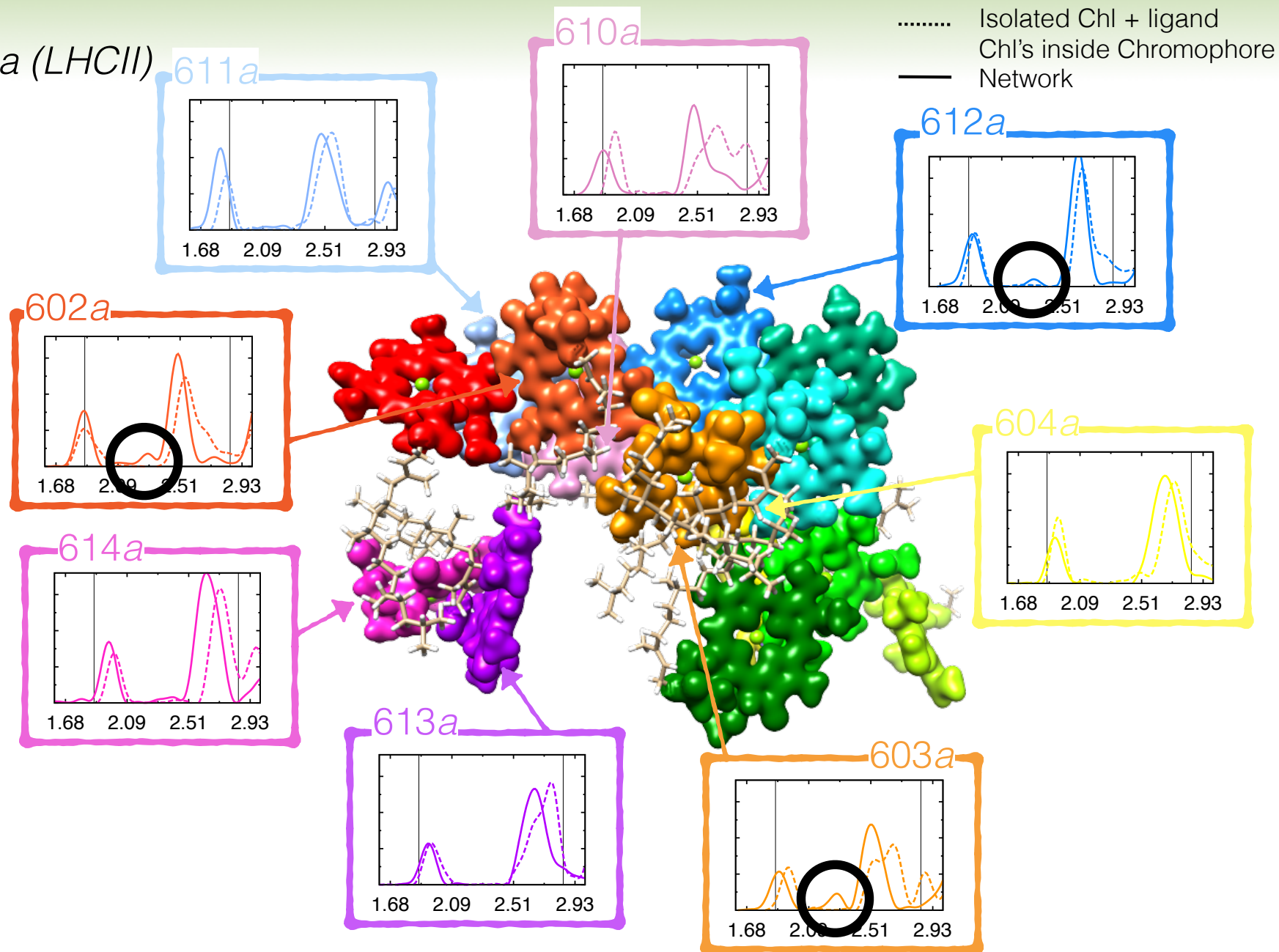
General red-shift due to electrostatic effect
"Hidden peak" apparition attributed to oscillator strength transfer

Fragment-density analysis in real-time TDDFT

Chlorophyll *b* (LHCII)

Low interacting Chlb: enhancement of Q-band peak

605b-606b-607b cluster strong non-electrostatic interaction

608*b*

601*b*

609*b*

605*b*

607*b*

606*b*

..... Isolated Chl + ligand

— Chl's inside Chromophore Network **Insights into colour-tuning of chlorophyll optical response in green plants**

JJornet-Somoza, *Phys.Chem.Chem.Phys.*, 2015, 17, 26599

Outline

- Biochemist's Interests
  - Photobiology

- Mixed Method: QM /MM:
  - QM/MM Schemes + QM/MM Energy Formulation.
  - Boundary Schemes
  - TDDFT in Mixed Methods

- **Fragment-density analysis in Real-time TDDFT**
  - Fragment-density and AIM theory
  - Local Dipole Analysis in real-time TDDFT
  - Application to LHC-II

- Fundamentals of Subsystem TDDFT
  - Fundamentals of Subsystem DFT
  - Frozen Density Embedding Theory
  - Subsystem TDDFT

Objective: to compute the exciton coupling between to chromophores from the analysis of the real-time TDDFT results. Required properties: *transition dipoles* and *transition densities*.

Frenkel Exciton Hamiltonian
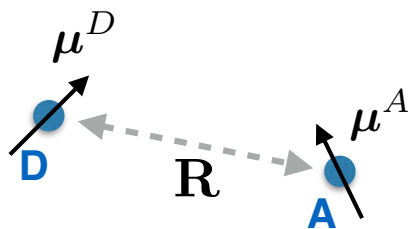
$$\hat{H} = \sum_n \epsilon_n |n\rangle\langle n| + \sum_{n,m} V_{nm} |m\rangle\langle n|$$

Classical Scheme

$|n\rangle \qquad |m\rangle$
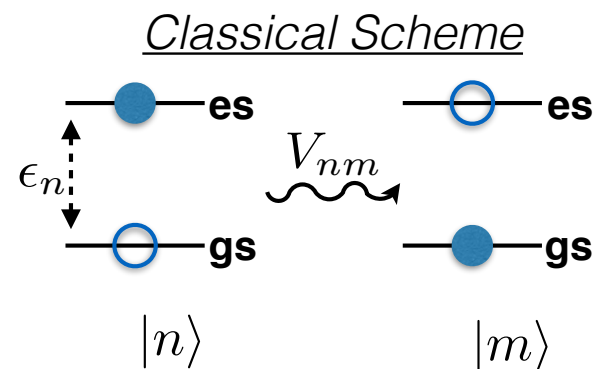
Exciton Coupling

Dipole approximation

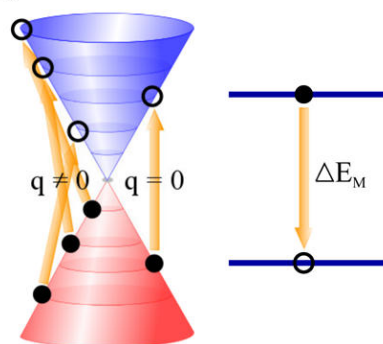$$V^{FRET} = \kappa^{DA} \frac{|\boldsymbol{\mu}^A||\boldsymbol{\mu}^D|}{|\mathbf{R}|^3}$$

$$V_s = \int d\mathbf{r} \int d\mathbf{r}' \rho_A^{T*}(\mathbf{r}') \left(\frac{1}{|\mathbf{r}' - \mathbf{r}|} + g_{xc}(\mathbf{r}',\mathbf{r}) \right) \rho_D^T(\mathbf{r})$$
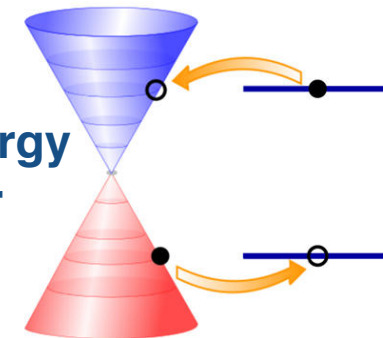
Förster Resonant Energy Transfer

Coulombic term   **Exchange term**

(a) Foerster transfer

$q \neq 0 \quad q = 0 \qquad \Delta E_M$

Dexter Energy Transfer

Objective: to compute the exciton coupling between to chromophores from the analysis of the real-time TDDFT results. Required properties: *transition dipoles* and *transition densities.*

Remember: *Optical response from real-time TDDFT*
The first order density response is related to the applied perturbation by

$$\delta\rho(\boldsymbol{r}, t) = \int_{t_0}^{t} dt' \int d\boldsymbol{r}' \chi(\boldsymbol{r}, \boldsymbol{r}', t - t') \delta v_{ext}(\boldsymbol{r}', t')$$

Impulsive electric field: case of an external field that has the shape of a delta impulse in time.

$$v_{ext}(\boldsymbol{r}, t) = -e\boldsymbol{r} \cdot \boldsymbol{K} \delta(t) = -e\boldsymbol{r} \cdot \boldsymbol{K} \frac{1}{2\pi} \int_{-\infty}^{+\infty} d\omega \exp(i\omega t)$$

An electric field with intensity $\boldsymbol{K}$ and polarised in $\boldsymbol{r}$.

And the photo-absorption cross-section can be obtained from

$$\sigma(\omega) = \frac{4\pi\omega}{3c} \Im m[\alpha(\omega)]$$

$$\alpha_{\gamma\delta}(\omega) = \frac{1}{K_\delta} \int_0^\infty dt [\mu_\gamma(t) - \mu_\gamma(0)] e^{-i\omega t} \qquad \mu_\gamma(t) = \int \mathrm{r}_\gamma \cdot n(\boldsymbol{r}, t) d\boldsymbol{r}$$

Oscillator strength and transition dipoles are related with the dynamic polarisation matrix:

$$\frac{2\omega}{3\pi}\text{Tr}(\Im m \boldsymbol{\alpha}) = \frac{2\Omega_n}{3}\sum_{\nu=1}^{3}|\langle\Psi_0|\hat{r}_\nu|\Psi_n\rangle|^2\delta(\omega - \Omega_n) = f_n\delta(\omega - \Omega_n) = S(\omega)$$

transition dipole moment   **oscillator strength**

Since we have done three different time propagation on three orthogonal directions, the *transition dipole vector direction* can be obtained from the eigenvalues of the **diagonalization** of the dynamic polarisability tensor.

Practical Issue

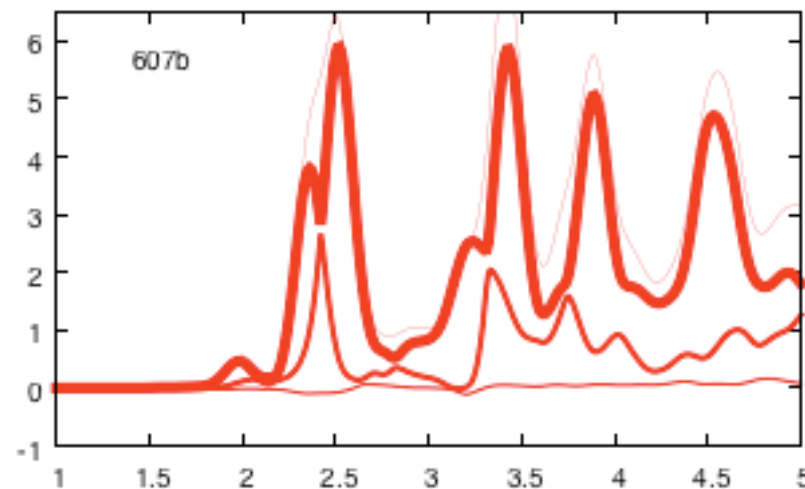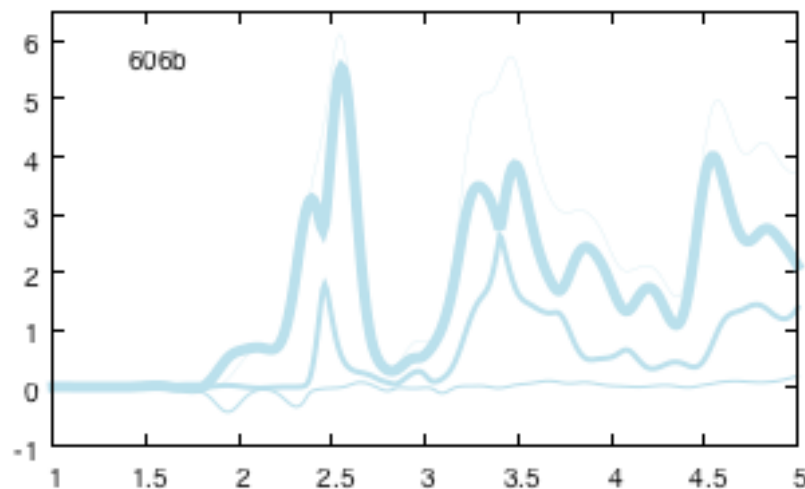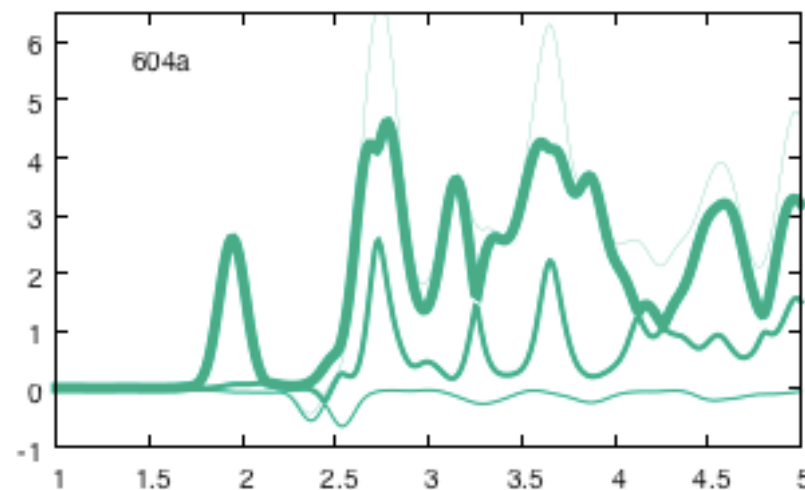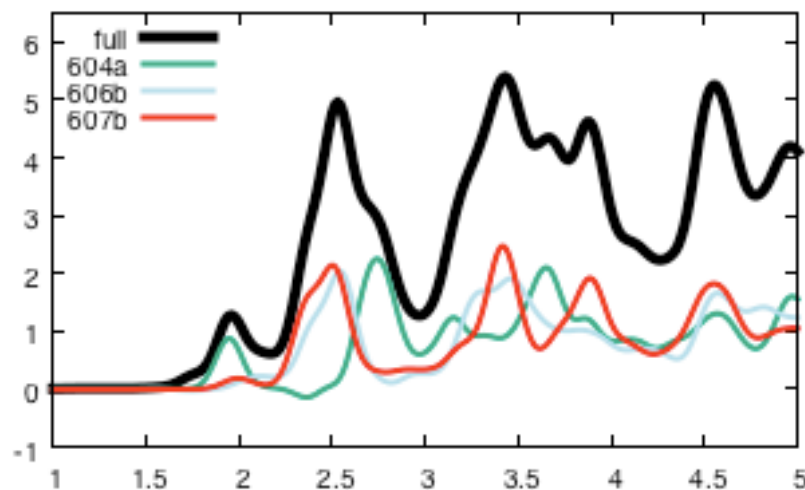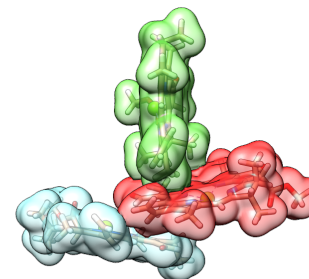$$\alpha_{\nu\lambda}(\omega) = \frac{1}{k_\lambda}\int_0^T dt[\mu_\nu(t) - \mu_\nu(0)]e^{-i\omega t}e^{-\eta t}$$

damping term included as artificial lifetime to decay all excitations to ground state

This term is the responsible of the broadened peaks in the cross-section absorption spectra.

The *oscillator strength* can be then computed by computing the **area under each peak**.

Fragment-density analysis in real-time TDDFT

Local domains analysis

$$\rho(\boldsymbol{r}) = \rho_{tot}(\boldsymbol{r}) = \sum_{I} \rho_{I}(\boldsymbol{r});$$
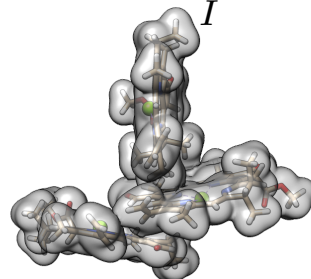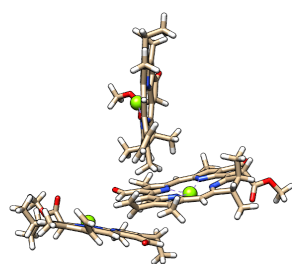
Cross-section photoabsortption diagonalization

Analogously, we can deduce an **analytical expression for the transition density** based on the linear response theory:

$$\delta\rho(\boldsymbol{r},t) = \int_{t_0}^{t} dt' \int d\boldsymbol{r}' \chi(\boldsymbol{r},\boldsymbol{r}',t-t')\delta v_{ext}(\boldsymbol{r}',t')$$

Following the fluctuation-dissipation theorem:

$$\Im\chi_{nn}(\mathbf{r},\mathbf{r}',\omega) = -\pi\big(S_{nn}(\mathbf{r},\mathbf{r}',\omega) - S_{nn}(\mathbf{r}',\mathbf{r},-\omega)\big)$$

Where the dynamical structure factor can be written as;

$$S_{nn}(\mathbf{r},\mathbf{r}',\omega) = n_0(\mathbf{r})n_0(\mathbf{r}')\delta(\omega) + \sum_{n=1}^{\infty}\langle\Psi_0|\hat{n}(\mathbf{r})|\Psi_n\rangle\langle\Psi_0|\hat{n}(\mathbf{r}')|\Psi_n\rangle\delta(\omega - \Omega_n)$$

Physical interpretation: - for ω > 0 —> determines the absorption spectrum.
                    - for ω < 0 —> determines the stimulated-emission spectrum.

The imaginary part of the induced density can be written as:

$$\Im\delta\rho(\mathbf{r},\omega) = \int d\mathbf{r}' \pi S_{nn}(\mathbf{r},\mathbf{r}',\omega)e\mathbf{r}' \cdot \mathbf{K}\delta(\omega - \Omega_n)$$

The imaginary part of the induced density can be written as:

$$\Im \delta\rho(\mathbf{r}, \omega) = \int d\mathbf{r}' \pi S_{nn}(\mathbf{r}, \mathbf{r}', \omega) e\mathbf{r}' \cdot \mathbf{K} \delta(\omega - \Omega_n)$$

Since, the **component of the transition dipole** at the direction of the external field, can be computed from

$$\int \mathbf{r} \cdot \mathbf{K} \langle \Psi_0 | \hat{n}(\mathbf{r}) | \Psi_n \rangle d\mathbf{r} = \mu_k \cdot k$$

Then, the **transition density** can be expressed from

$$\langle \Psi_0 | \hat{n}(\mathbf{r}) | \Psi_n \rangle \delta(\omega - \Omega_n) = \frac{\Im \delta\rho(\mathbf{r}, \omega)}{\pi \mu_k \cdot k}$$

Practical Issue

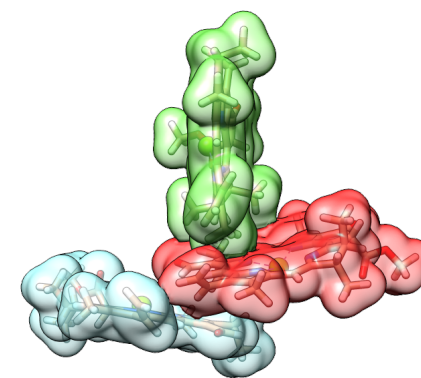Since a damping factor has been used, the **response density is also broadened.**

Using a **gaussian damping** function, and integrating around **Ω**n, then

$$\langle \Psi_0 | \hat{n}(\mathbf{r}) | \Psi_n \rangle = \frac{\sigma}{\mu_k k \sqrt{\pi \ln 2}} \Im \delta\rho(\mathbf{r}, \Omega_n)$$

where σ is the half-width at half-maxima of the Fourier transform gaussian damping function.

Fragment-density analysis in real-time TDDFT

Local domains analysis $\quad \rho(\boldsymbol{r}) = \rho_{tot}(\boldsymbol{r}) = \sum_I \rho_I(\boldsymbol{r});$

$$\langle \Psi_0 | \hat{n}(\mathbf{r}) | \Psi_n \rangle = \frac{\sigma}{\mu_k k \sqrt{\pi \ln 2}} \Im \delta\rho(\mathbf{r}, \Omega_n)$$

1.94eV

Qy   Soret

2.80eV

2.56eV

1.98eV   2.07eV

2.52eV
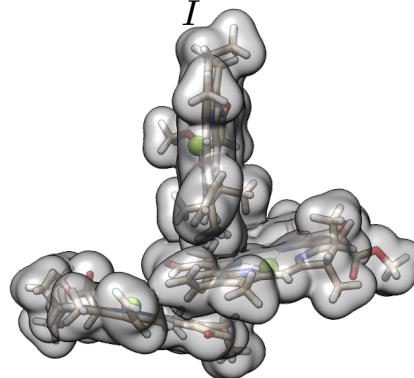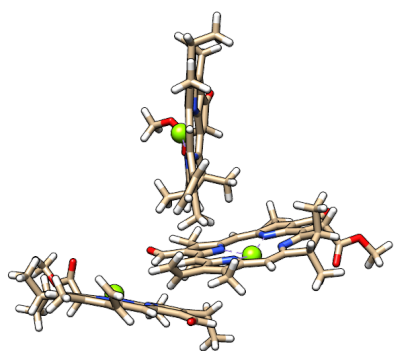
iso = 0.001

Fragment-density analysis in real-time TDDFT

Local domains analysis $\rho(\boldsymbol{r}) = \rho_{tot}(\boldsymbol{r}) = \sum_I \rho_I(\boldsymbol{r});$

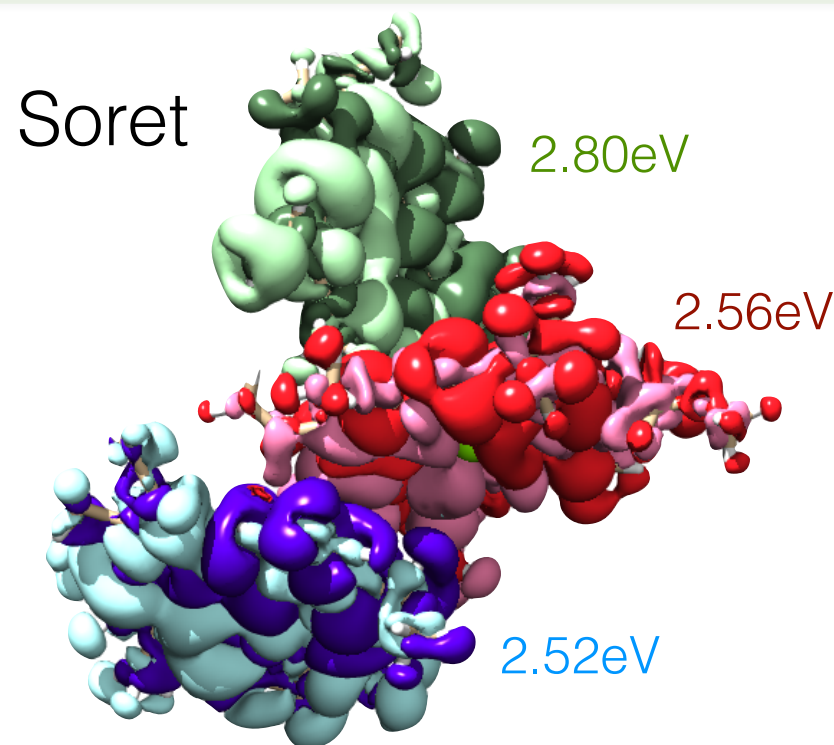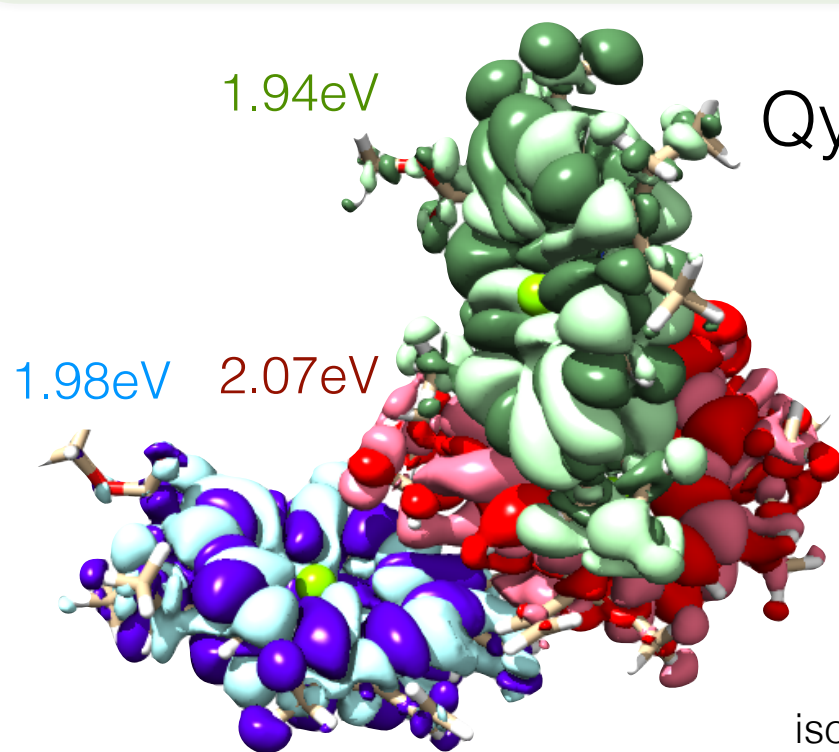**Transition dipole moments**   **Exciton Couplings (IDA & TDCM)**

Qy
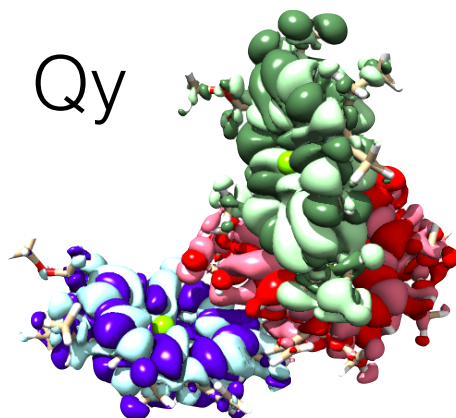
trip / A	x	y	z	f
606b	0.6664	0.0450	0.0087	0.0808
607b	0.0491	-0.3851	0.1311	0.0291
604a	0.2816	0.7520	0.4323	0.1412

V/cm⁻¹	606b-607b	606b-604a	607b-604a
IDA	7.93	39.84	19.23
TDCM (h)	-2.25	32.43	-15.93
TDCM (xc)	0.37	-0.04	0.03

Soret

trip / A	x	y	z	f
606b	1.0183	-0.5544	-0.0213	0.3012
607b	0.9415	-0.7646	-0.0542	0.3250
604a	0.3298	0.8302	0.4877	0.2538

V/cm⁻¹	606b-607b	606b-604a	607b-604a
IDA	-262.01	50.95	20.92
TDCM	**-140.44**	-15.26	-38.22
TDCM (xc)	0.34	0.04	0.06
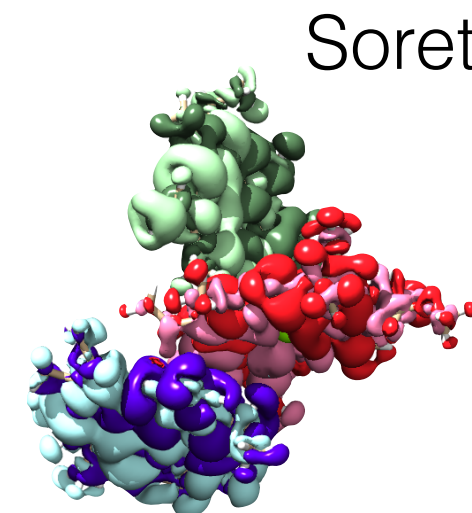
Fragment-density analysis in real-time TDDFT

Excitonic Dynamics: rt-TDDFT

Propagation Time = 0.000 a.u. = 0.000 fs
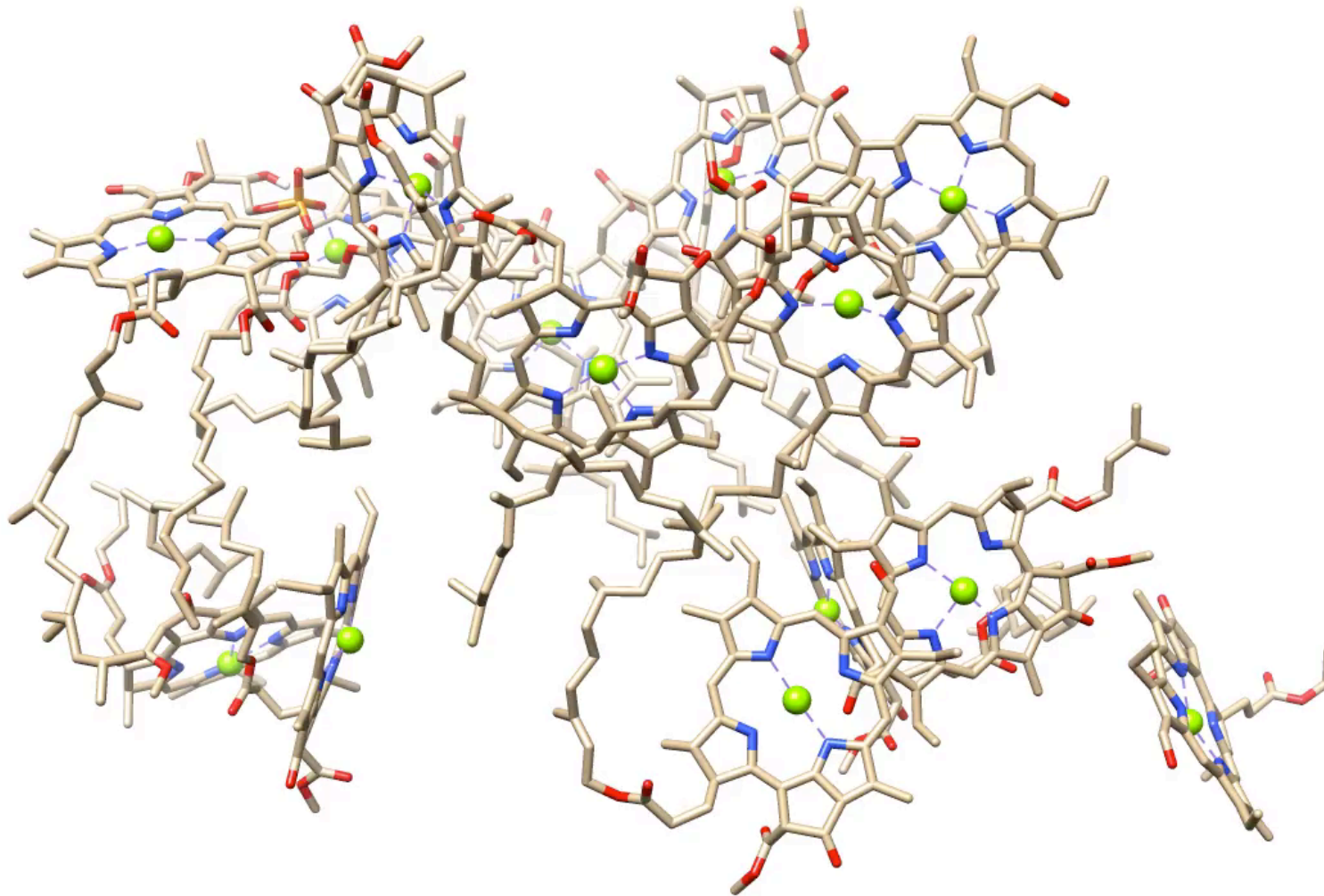
Fragment-density analysis in real-time TDDFT

Excitonic Dynamics: rt-TDDFT

Fourier transform of induced dimples for the chl's network (*solid line*) vs Absorption spectra (*dashed lines*)
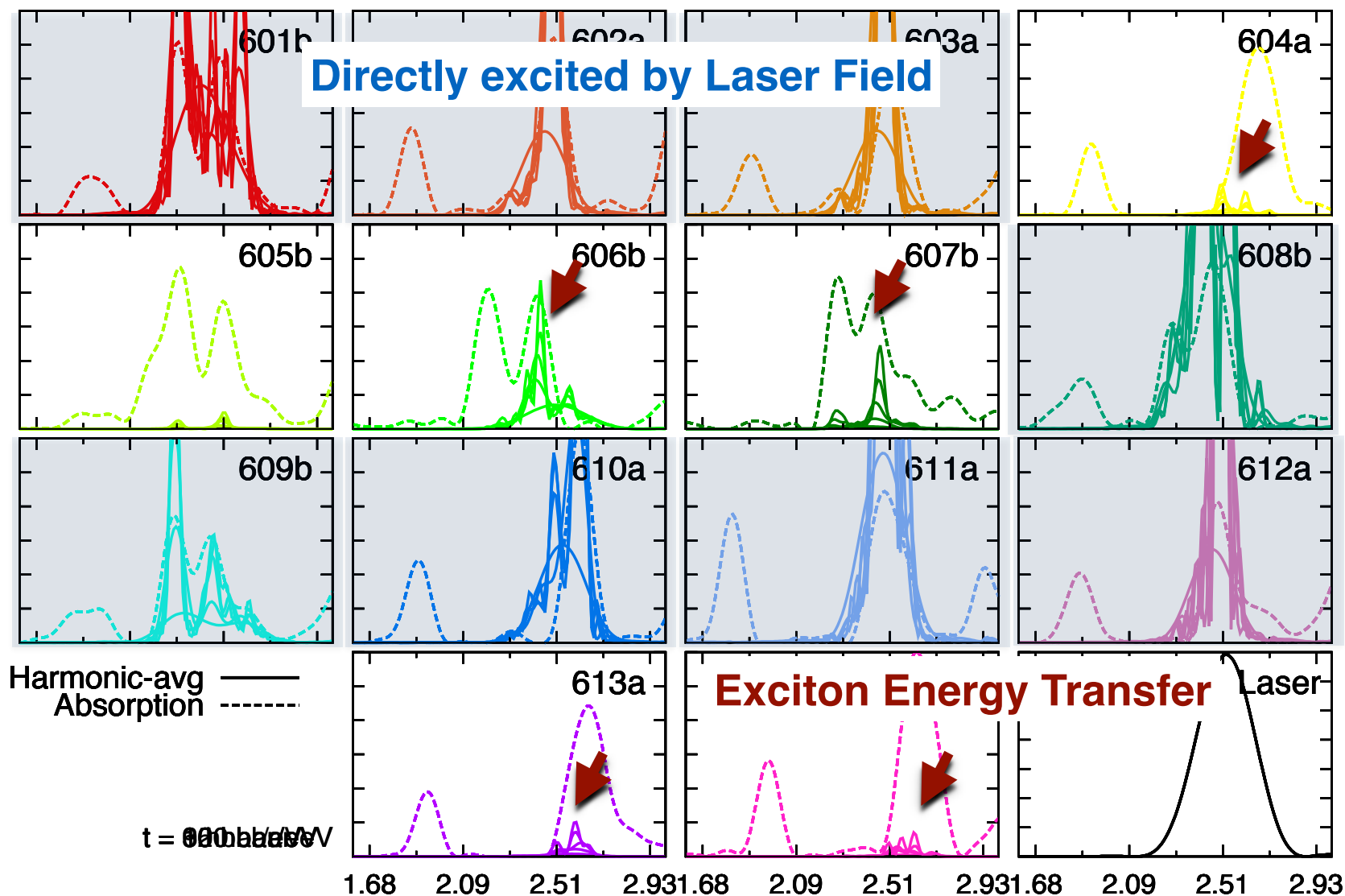
Outline

- Biochemist's Interests

  - Photobiology

- Mixed Method: QM /MM:

  - QM/MM Schemes + QM/MM Energy Formulation.

  - Boundary Schemes

  - TDDFT in Mixed Methods

- Fragment-density analysis in Real-time TDDFT

  - Fragment-density and AIM theory

  - Local Dipole Analysis in real-time TDDFT

  - Application to LHC-II

- **Fundamentals of Subsystem TDDFT**

  - Fundamentals of Subsystem DFT

  - Frozen Density Embedding Theory

  - Subsystem TDDFT

The Kohn-Sham Formalism

The total energy in the KS DFT is usually written as

$$E[\rho] = T_s[\rho] + V_{nuc}[\rho] + J[\rho] + E_{xc}[\rho] + V_{nn}$$

The **kinetic energy term** for the non-interacting system are in general not known as functionals of the electronic density, and can be **approximated to a functional of the non-interacting orbitals**

$$E[\{\psi_i\}] = T_s[\{\psi_i\}] + V_{nuc}[\rho] + J[\rho] + E_{xc}[\rho] + V_{nn}$$

$$T_s[\{\psi_i\}] = \sum_i^n \langle \psi_i | - \nabla^2/2 | \psi_i \rangle$$

Minimisation of the energy with respect to the KS orbitals leads to the *single-particle Kohn-Sham equations*

$$\left(-\frac{\nabla^2}{2} + v_{eff}[\rho](\boldsymbol{r}) \right) \psi_i(\boldsymbol{r}) = \epsilon_i \psi_i(\boldsymbol{r})$$

Subsystem DFT

Starting point: partitioning of the electron density

$$\rho(\boldsymbol{r}) = \rho_{tot}(\boldsymbol{r}) = \sum_I \rho_I(\boldsymbol{r}); \qquad \rho_I(\boldsymbol{r}) = \sum_{i_I}^{n_I} |\psi_{i_I}(\boldsymbol{r})|^2$$

The essential difference is that we are no longer able to use the non-interacting $T_s[\{\psi_i\}]$

Instead, we can define the subsystem kinetic energies :

$$T_s[\{\psi_{i_I}\}] = \sum_{i_I}^{n_I} \langle \psi_{i_I}| -\nabla^2/2 |\psi_{i_I}\rangle \qquad \longrightarrow \qquad T_s[\{\psi_i\}] = \sum_I T_s[\{\psi_{i_I}\}] + T_s^{nad}[\{\psi_i\}, \{\psi_{i_I}\}]$$

subsystem kinetic energy   **non-additive kinetic energy term**

The non-additive kinetic energy term can be formulated in terms of the electronic densities of each subsystem

$$T_s^{nad}[\rho_I] = T_s[\rho_i] - \sum_I T_s[\rho_I] \qquad T_s[\rho_I] = \min_{\{\psi_{i_I}\} \to \rho_I} \sum_i^{n_I} \langle \psi_{i_I}| -\nabla^2/2 |\psi_{i_I}\rangle$$

Fundamentals of Subsystem TDDFT

The total energy expression for the Subsystem DFT becomes:

$$E[\{\psi_{i_I}\}] = \sum_I T_s[\{\psi_{i_I}\}] + V_{nuc}[\rho] + J[\rho] + E_{xc}[\rho] + T_s^{nad}[\{\rho_I\}] + V_{nn}$$

Minimisation of this expression with respect to the **KS-like orbitals {ψ_{iK}} of subsystem K,** *under the constraint that the subsystem orbitals are orthonormal and the electron densities of the other subsystems are fixed, leads to the KS equation with constrained electron density (KSCED)*

contains all terms of KS potential for the isolated subsystem K.

$$\left(-\frac{\nabla^2}{2} + v_{eff}^{(K)}[\rho_K](\boldsymbol{r}) + v_{emb}^{(K)}[\rho_K, \rho_{tot}](\boldsymbol{r})\right)\psi_{i_K}(\boldsymbol{r}) = \epsilon_{i_K}\psi_{i_K}(\boldsymbol{r})$$

depends on the nuclear potential of other subsystems and includes *non-additive terms* for the **kinetic energies** and the **exchange-correlation functionals**.

$$v_{emb}^{(K)}[\rho_K, \rho_{tot}](\boldsymbol{r}) = \sum_{I, I\neq K} v_{nuc}^{(I)}(\boldsymbol{r}) + v_{Coul}[\rho_{tot} - \rho_K] + \left(\frac{\delta T_s[\rho_{tot}]}{\delta\rho_{tot}(\boldsymbol{r})} - \frac{\delta T_s[\rho_K]}{\delta\rho_K(\boldsymbol{r})}\right) + \left(\frac{\delta E_{xc}[\rho_{tot}]}{\delta\rho_{tot}(\boldsymbol{r})} - \frac{\delta E_{xc}[\rho_K]}{\delta\rho_K(\boldsymbol{r})}\right)$$

the coupled equations have to be solved self-consistently with respect to the other subsystems

Fundamentals of Subsystem TDDFT

Original reformulation (disconnected from subsystem DFT) done by Wesolowski and Warshel (*J.Phys.Chem*, **1993**, 97, 8050) define the **target/active density** as the density that **minimise the total energy of the total system**.

$$E_{\text{FDE}}[\{\psi_{i_A}\}, \rho_e^{frozen}] = T_s[\{\psi_{i_A}\}] + T_s[\rho_e^{frozen}] + T_s^{nad}[\rho_A, \rho_e^{frozen}]$$
$$+ V_{nuc}[\rho] + J[\rho] + E_{xc}[\rho] + V_{nn}$$

The solution can be obtained analogously to the KS equation :

$$\left(-\frac{\nabla^2}{2} + v_{eff}^{FDE}[\rho_A, \rho_e^{frozen}](\boldsymbol{r}) \right) \psi_{i_A}(\boldsymbol{r}) = \epsilon_{i_A} \psi_{i_A}(\boldsymbol{r})$$

$$v_{eff}^{FDE}[\rho_A, \rho_e^{frozen}](\boldsymbol{r}) = v_{eff}^{KS}[\rho_{total}] + \frac{\delta T_s^{nad}[\rho_A, \rho_e^{frozen}]}{\delta \rho_A}$$

As a consequence **FDE is no longer able to lead to the exact GS** energy and density of the whole system, but yield an upper bond for the energy.

Practical Issues

The embedding potential has important properties:

$$v_{emb}^{(K)}[\rho_K, \rho_{tot}](\boldsymbol{r}) = \sum_{I, I \neq K} v_{nuc}^{(I)}(\boldsymbol{r}) + v_{Coul}[\rho_{tot} - \rho_K] + \left(\frac{\delta T_s[\rho_{tot}]}{\delta \rho_{tot}(\boldsymbol{r})} - \frac{\delta T_s[\rho_K]}{\delta \rho_K(\boldsymbol{r})} \right) + \left(\frac{\delta E_{xc}[\rho_{tot}]}{\delta \rho_{tot}(\boldsymbol{r})} - \frac{\delta E_{xc}[\rho_K]}{\delta \rho_K(\boldsymbol{r})} \right)$$

- Is exact in the limits of the exact functionals.
- The main contribution are usually the electrostatic potentials (nuclei and coulomb)
- The exchange-correlation effects can be treated as in KS-DFT calculations.
- Includes polarisation effects.

- Electron-leak problem: electrons can be unphysical localised at the nuclei of the frozen environment if no additional contribution are added.
- This effect can be corrected on the approximation of the non-additive kinetic energy.

Subsystem TDDFT

The first assumption of the Subsystem TDDFT is that the response density can also be partitioned into subsystems contributions

$$\delta\rho_{tot}(\boldsymbol{r}) = \sum_I \delta\rho_I(\boldsymbol{r}) \qquad \delta\rho_I(\boldsymbol{r}_1,\omega) = \sum_{(ia)_I} 2\delta P_{(ia)_I}(\omega)\varphi_{i_I}(\boldsymbol{r}_1)\varphi_{a_I}(\boldsymbol{r}_1)$$

It assumes that can be expanded ONLY in terms of intrasubsystem orbital transition.
No Charges Transfer between subsystems.

And also, the external perturbational potential will include non-additive terms.

$$\delta v_{ai}^{(I)}(\omega) = \delta v_{ai}^{ext(I)}(\omega) + \delta v_{ai}^{el(I)}(\omega)$$

where

$$\delta v_I^{el}(\boldsymbol{r}_1) = \sum_K \int \left(\frac{\delta v_{eff}^{(I)}(\boldsymbol{r}_1)}{\delta\rho_K(\boldsymbol{r}_2)} + \frac{\delta v_{emb}^{(I)}(\boldsymbol{r}_1)}{\delta\rho_K(\boldsymbol{r}_2)} \right) \delta\rho_K(\boldsymbol{r}_2) d\boldsymbol{r}_2$$

After some algebra, we can see that the matrix elements of the induced potential are given:

$$\delta v^{el}_{(bj)_I} = 2 \sum_{(ia)_J} K^{eff}_{(jb)_I(ia)_J} \delta P_{(ia)_J}$$

where instead of the kernel for the isolated subsystem, we have an **effective kernel**, which take into account the non-additive terms.

$$K^{eff}_{(jb)_I(ia)_J} = \int d\boldsymbol{r}_1 \varphi_j(\boldsymbol{r}_1)\varphi_b(\boldsymbol{r}_1) \times \int d\boldsymbol{r}_2 \Big(\frac{1}{|\boldsymbol{r}_1 - \boldsymbol{r}_2|} + \frac{\delta^2 E_{xc}[\rho_{tot}]}{\delta \rho_{tot}^2}$$

$$+ \frac{\delta^2 T_s[\rho_{tot}]}{\delta \rho_{tot}^2} - \frac{\delta^2 T_s[\rho_{tot}]}{\delta \rho_{tot}^2}\Big|_{\rho_I} \delta_{IJ} \Big) \varphi_a(\boldsymbol{r}_2)\varphi_i(\boldsymbol{r}_2) \Big]$$

Similar to super molecular case we arrive

$$\delta P_{(jb)_I} = \chi^s_{(jb)_I} \Big[\delta v^{ext}_{(bj)_I} + 2 \sum_{(ia)_J} K^{eff}_{(jb)_I(ia)_J} \delta P_{(ia)_J} \Big]$$

Analogously to the TDDFT formalism, we can set up an eigenvalue problem to determine the excitation energies:

$$[\boldsymbol{\Omega}^{sub} - \omega_k^2]\mathbf{F}^{sub}_k = 0$$

Fundamentals of Subsystem TDDFT

where the matrix **can be divided into intrasubsystems** (diagonal terms) and **intersubsystems** (off-diagonal) blocks.

$$
\left[
\begin{pmatrix}
\Omega_{AA} & \Omega_{AB} & \cdots & \Omega_{AZ} \\
\Omega_{BA} & \Omega_{BB} & \cdots & \Omega_{BZ} \\
\vdots & \vdots & \ddots & \vdots \\
\Omega_{ZA} & \Omega_{BZ} & \cdots & \Omega_{ZZ}
\end{pmatrix}
- \omega_k^2
\begin{pmatrix}
1_{AA} & 0_{AB} & \cdots & 0_{AZ} \\
0_{BA} & 1_{BB} & \cdots & 0_{BZ} \\
\vdots & \vdots & \ddots & \vdots \\
0_{ZA} & 0_{BZ} & \cdots & 1_{ZZ}
\end{pmatrix}
\right]
\begin{pmatrix}
\mathbf{F}_k^A \\
\mathbf{F}_k^B \\
\vdots \\
\mathbf{F}_k^Z
\end{pmatrix}
=
\begin{pmatrix}
0_k^A \\
0_k^B \\
\vdots \\
0_k^Z
\end{pmatrix}
$$

Main differences with respect to the isolated formulation:
· The intersystem coupling blocks.
· The matrix elements carry **xc and kinetic-energy contribution from all subsystems**.
· The orbitals and energies are obtained from GS subsystem calculation, i.e. the **non-additive kinetic contribution are also present**.

Two main approximation to solve the above eigenvalue equations:
1. FDEu (uncoupled) - ONLY the response of the embedded systems itself has to be taken into account (off-diagonal blocks are zero).
2. FDEc (coupled) - starting from the FDEu eigenvectors, a unitary transformation can be done that enable a numerical evaluation of the off-diagonal blocks elements and solve the truncated eigenvalue problem.

Detailed derivation are extended in :

- Christoph R. Jacob and Johannes Neugebauer
  "Subsystem density-functional theory"
  WIREs Comput. Mol. Sci. **2013**, *00*: 1-34 doi: 10.1002/wcms.1175

- Johannes Neugebauer
  "Couplings between electronic transitions in a subsystem formulation of time-dependent density functional theory"
  J. Chem. Phys. **2007**, *126*, 134116