Absorption spectra of protein chromophores

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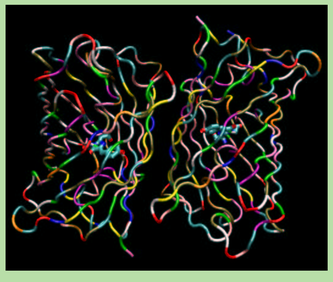
Abstract

Not surprisingly, the theoretical understanding of biophysical processes is a very active field of research. In particular, there have been spectacular advances in the characterisation of structural and dynamical properties of complex biomolecules by a combination of quantum-mechanical and classical-molecular mechanics methods (QM-MM). However, and in spite of the large amount of experimental work in photo-active molecules, the theoretical description of the interaction of these molecules with external time-dependent fields is very much in its infancy. Photo-active molecules relevant for biology include retinal (responsible for the process of vision), the green fluorescent protein (GFP), chlorophyll, etc. On the other hand, time dependent density functional (TDDFT) theory has proved to be an invaluable tool for the calculation of excitation spectra of molecules. We will present a way to combined QM-MM methods (for the ground state) with TDDFT (for the description of the excited states) to calculate optical absorption spectra. Our first test case, the GFP, yielded remarkably good results.

Starting point

X-ray diffraction

Aequorea Victoria



But...

- The experimental resolution is only **1.9 Å**, which is clearly not enough to study the optical properties of the chromophore.
- Several water molecules are identified by the X-rays.
- Hydrogen atoms are completely absent in the experimental structure.

Solution...

- Eliminate useless crystalographic water molecules.
- Add hydrogen atoms to the structure (there may be some ambiguity with some residues that may appear in more than one protonation state).
- Minimize the resulting structure

Structure optimized in 3 steps.

- An initial optimization was performed with all backbone and chromophore atoms fixed at their crystallographic positions.
- In a second step we allowed relaxation only of the coordinates of the chromophore. These first two steps were done using empirical potentials to model the interaction between the atoms.
- The geometry of the chromophore is futher optimized by using a **QM/MM** method.

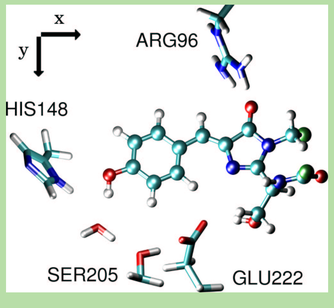
QM/MM Methods

Most proteins are clearly too large to be handle in our current DFT codes. However, only a small part of the protein – the chromophore – is responsible for the optical absoprtion in the lower end of the spectrum.

QM/MM is an approximate framework that allows us to treat the important part of large biological molecules using quantum mechanics, while the rest is handle with empirical potentials.

- The QM part sees the MM atoms as if they were external point charges.
- The QM/MM boundary sometimes has to run through a bond. In this case a hydrogen atom (H-link) is added to the QM system in order to saturate the bonds.

The final geometry of the (QM) chromophore of the GFP (together with the closest MM residues) was



Time-Dependent DFT

Time-dependent density functional theory has proved to be a very reliable technique to calculate optical absorption spectra of finite systems. This quantity can be calculated using two possible routes: either by using linear response theory, or by solving the time-dependent Kohn-Sham equation. In this work we used this latter path.
The time-dependent Kohn-Sham equation reads

$$\mathrm{i}\frac{\partial}{\partial t}\psi_i(\boldsymbol{r},t) = \left[-\frac{\nabla^2}{2} + v(\boldsymbol{r},t) + \int \mathrm{d}^3r' \, \frac{n(\boldsymbol{r}',t)}{|\boldsymbol{r}-\boldsymbol{r}'|} + v_{\mathrm{xc}}(\boldsymbol{r},t)\right]\psi_i(\boldsymbol{r},t)\,.$$

To approximate the exchange-correlation potential we used the adiabatic LDA

$$v_{\mathrm{xc}}^{\mathrm{ALDA}}[n](\boldsymbol{r},t) = \frac{\mathrm{d}}{\mathrm{d}n}\epsilon_{\mathrm{xc}}^{\mathrm{HEG}}(n)\Big|_{n=n(\boldsymbol{r},t)}\,.$$

Our starting point for the time-dependent propagation we use the ground-state Kohn-Sham wave-functions, $\tilde{\psi}_i(\boldsymbol{r})$, excited by a small perturbation of the form $-\boldsymbol{\kappa}_0\cdot\boldsymbol{r}\delta(t)$.
The dynamical polarizability can be obtained from

$$\alpha_{ij}(\omega) = \frac{1}{\kappa_{0i}}\int \mathrm{d}^3r\, \boldsymbol{r}_j \delta n(\boldsymbol{r},\omega)\,,$$

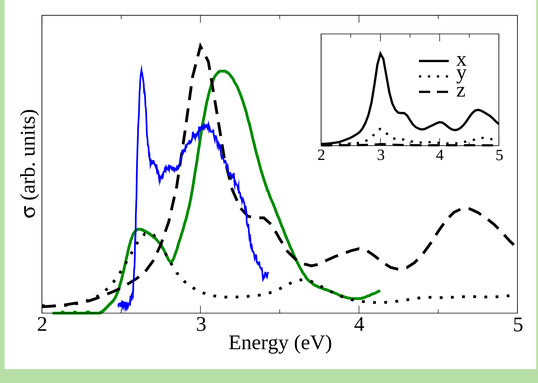
where $\delta n(\boldsymbol{r},\omega)$ is the Fourier transform of $n(\boldsymbol{r},t)-n(\boldsymbol{r},t=0)$. The photo-absorption cross-section is then proportional to the imaginary part of the dynamical polarizability

$$\sigma(\omega) = \frac{4\pi\omega}{c}\frac{1}{3}\mathrm{Tr}\;\alpha$$

Our Tool

`http://www.tddft.org/programs/octopus`

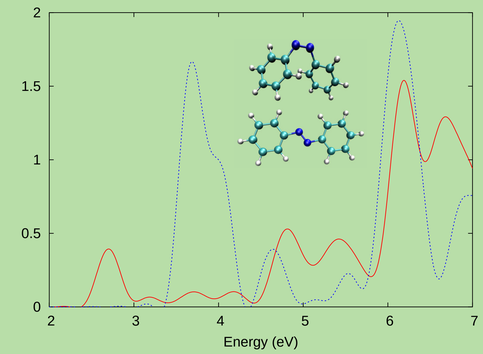
Results - GFP



The dashed line corresponds to the neutral chromphore, the dotted line to the anionic, whereas the green and blue curves are the experimental results of Nielson *et al* [PRL **87**, 228102 (2001)] and of Creemers*et al* [PNAS **97**, 2974 (2000)] respectively. For comparative purposes, we divided the anionic results by 4 with respect to the neutral results. Inset: decomposition of the computed spectra of the neutral species in the three directions, showing the inherent anysotropy of the GFP molecule.

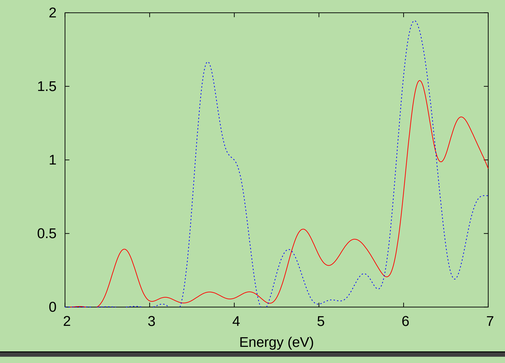
Under Construction

Azobenzene



Calculated optical absorption spectra of azobenzene. The red curve corresponds to the cis conformation (upper image), and the blue to the trans conformation (lower image).

DNA Basis



The Future

- Include the influence of the MM part also in the calculation of the linear response.
- Perform similar calculations for other systems of biological interest, like retinal, chlorophill, etc.
- Include the (coupled QM/MM) dynamics of the nuclei to study, e.g., photo-isomerization processes.