The possibility to attach dyes at distinct positions in biomolecules led to a rebirth of Förster / Fluorescence Resonance Energy Transfer (FRET) Experiments. The successful use in experiments is a consequence of the RET theory developed by Theodor Förster in the late 40s [1]. Försters assumptions resulted into a simple formula, in principle allowing direct measurement of the dye-to-dye distance and thus the retrieval of information about the underlying system [2]. Although widely used in experiments, the simple formula of T. Förster includes assumptions which can lead to a significant loss of accuracy [3]. In this context, theoretical consideration of the underlying process and its structures can aid in the interpretation of experiments and provide insight into the biological processes.

Excited state calculations were performed in the Pople 6-31+G* basis set and the Gaussian99 package. As can be seen from the transition electron densities in the left picture, the two Alexa dyes mainly show dipolar transition characteristics. Additionally, the density is weakly influenced by the sulf groups providing solubility and the linker. This allows the use of fractions for the actual coupling calculations.

On the right, a comparison between different excited state methods is shown. The overall shape of the transition density is recovered by all three methods. Yet the transition dipole moment is best recovered by CIS calculations while TD-DFT accurately reproduces the excitation energies (B. P. Krueger, unpublished results).

Simulations were performed with the GROMACS 4.0 MD package [4] and a modified version of the OPLS/AA force field including parameters for the two dyes and their linkers. Trajectories for all trans and single cis prolines of 50-150 ns were collected.

The Coulombic coupling was sampled in 3 ps steps. Here, an advantage of the TDC method is transformability of the densities (green boxes). Thus, only the Coulombic sum has to be evaluated every step while the transition density can be evaluated once.

Open Questions

- How does the dye environment (e.g. protein) influence the resonance energy transfer process?
- Can multiple expansion centers partially recover the spatial extension of the density?
- How can we efficiently model the short range (Dexter) energy transfer process?
- Can we make suggestions about specific dye and linker usage in experiments?

References


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Results and Comparison:

The coulombic coupling of the dyes in polyproline 15 is dominated by the dipole - dipole term. At separations of 3 nm, TDC shows no improvement over a multipole expansion. Yet, a significant difference between the coupling potentials is visible in the case of polyproline 20 with a cisco bond located at residue 10. Here the multipole coupling overestimates the coulombic coupling between the two dyes. In this case, the Transition Density Cube method provides an improvement of the coupling treatment, assuming that the two electronic systems can still be considered as separated (weak coupling limit).