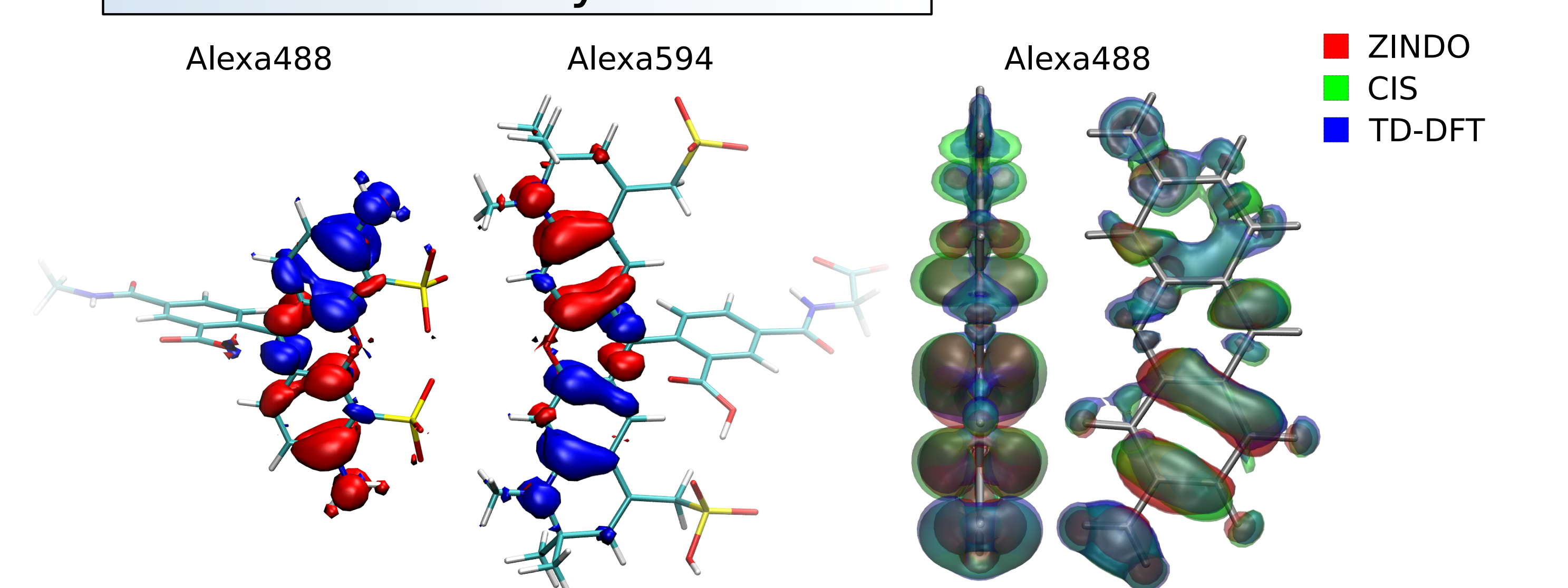


Introduction

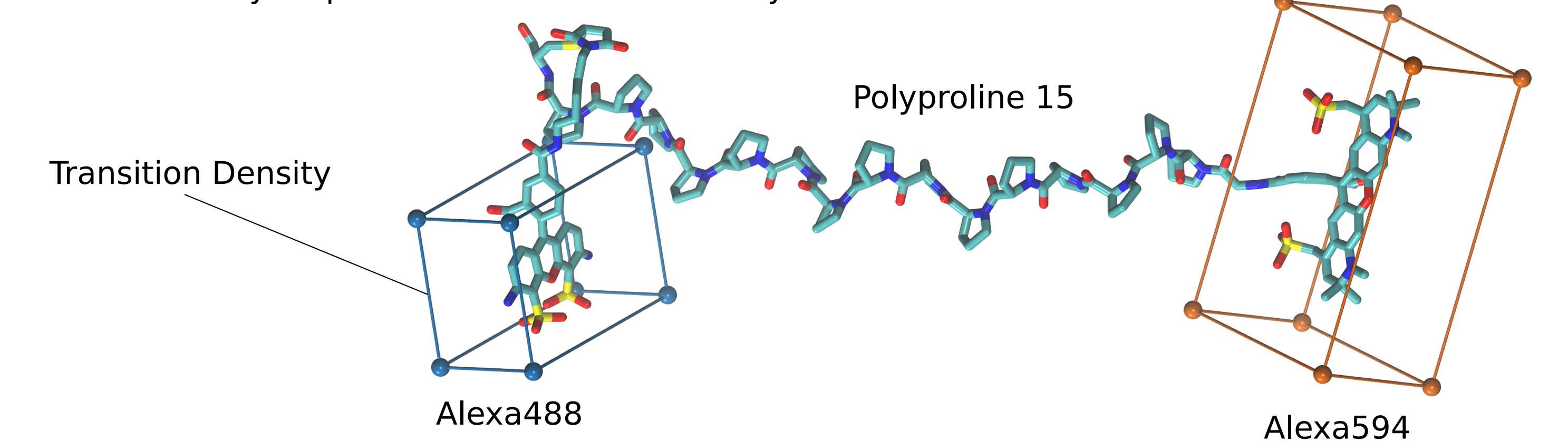
The possibility to attach dyes at distinct positions in biomolecules led to a rebirth of Förster / Fluorescence Resonance Energy Transfer (FRET) Experiments. The successful use in experiments is a consequence of the RET theory developed by Theodor Förster in the late 40s [1]. Förster's assumptions resulted 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 structures can aid in the interpretation of experiments and provide insight into the biological processes.

Transition Density Calculation

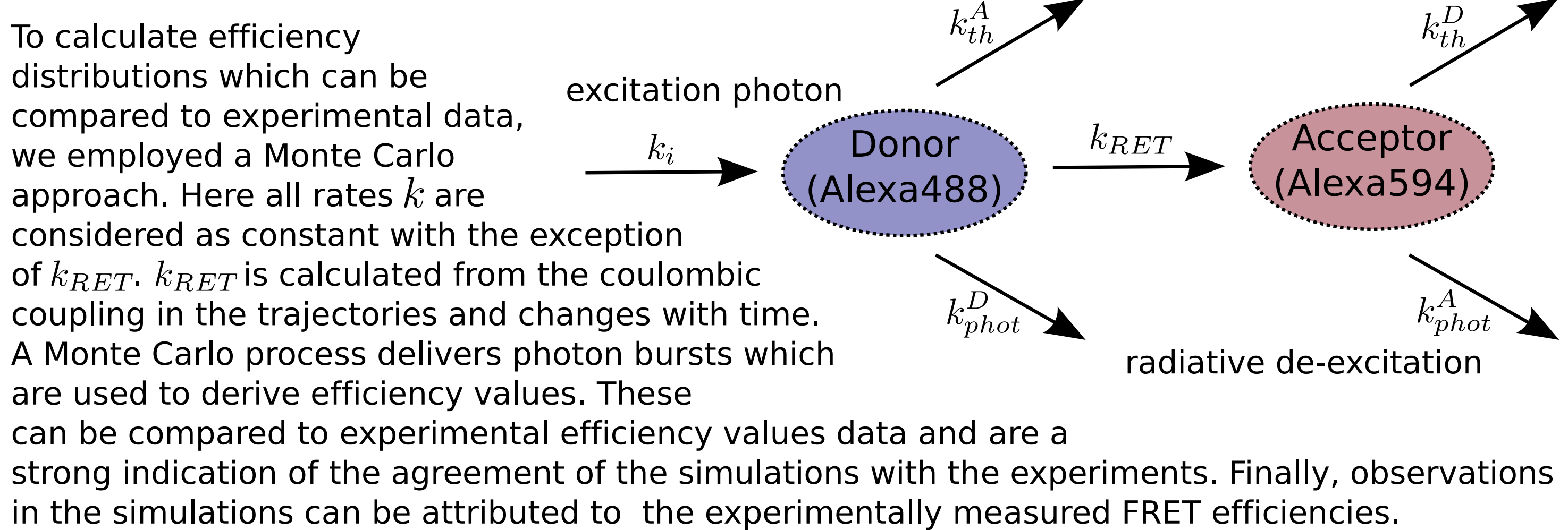


Simulations & Coupling Calculations

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 calculated. The coulombic coupling was sampled in 1 ps steps. Here, an advantage of the TDC method is transformability of the densities (green boxes). Thus, only the coulombic sum has to be re-evaluated every step while the transition density can be evaluated once.



Monte Carlo Approach



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?

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Acknowledgments

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Förster Resonance Energy Transfer

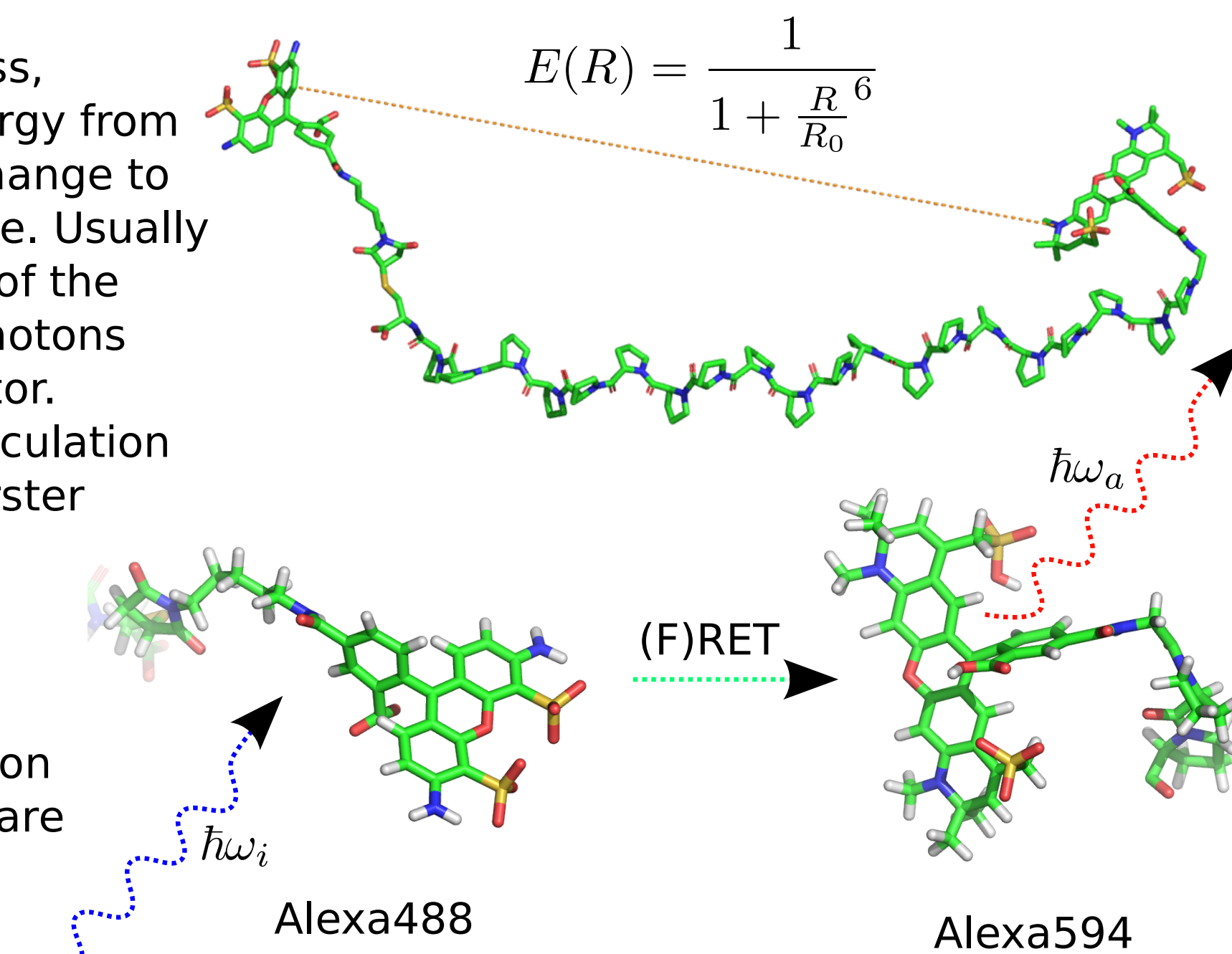
The radiationless energy transfer process, described by Förster is transmitting energy from an excited donor via virtual photon exchange to an acceptor molecule in the ground state. Usually the measured quantity is the efficiency of the RET, $E(R)$, defined e.g. by the ratio of photons collected from the donor and the acceptor. Förster's formula then allows a direct calculation of the distance R , assuming that the Förster Radius R_0 is known:

$$R_0 = \frac{c\kappa^2\phi_D}{n^4} \int d\omega f_D(\omega)\epsilon_A(\omega)\omega^4$$

Here, κ^2 contains the averaged orientation while the transition dipole moments are contained in c . ϕ_D is the excited state lifetime of the donor in absence of the acceptor molecule.

The integral over ω accounts for the spectral overlap and n is the dielectricity of the surrounding media. In order to obtain the above formula and constant, several assumptions are made:

- The transition densities are approximated as dipoles (Ideal Dipole Approximation).
- The (dipole - dipole) orientation is isotropically sampled and thus the orientation factor κ^2 is 2/3.
- The surrounding medium is isotropic and homogeneous.
- The electronic structures of donor and acceptor can be treated separately (Weak coupling limit).



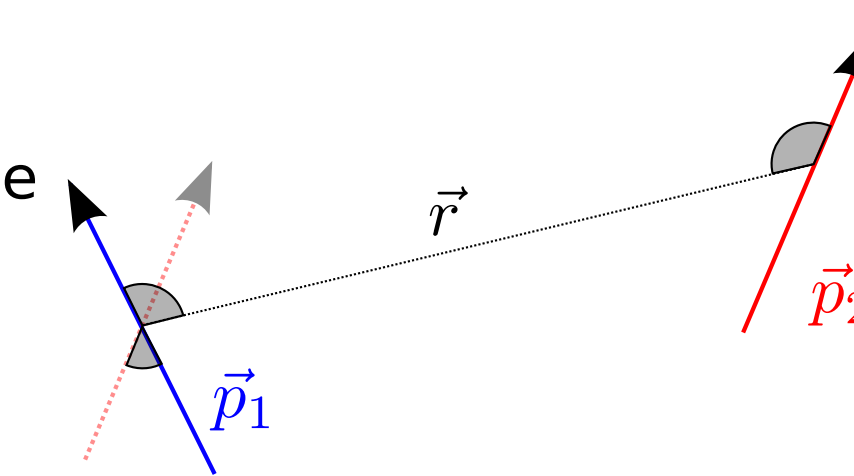
Coulombic Coupling

The rate of the RET process follows a "Golden Rule" like scheme: $k_{ret} = \frac{2\pi}{\hbar} |V|^2 \cdot J$. V is the coupling potential (Transition matrix element) while the Franck-Condon overlap J accounts for the density of final states. We tested several methods to determine the coulombic coupling potential from simulated dye conformations.

Dipole - Dipole: cartesian dipole interaction

The dipole-dipole interaction energy, as used by T. Förster to derive the RET formula can be seen as a special case of the multipole expansion. In cartesian coordinates, it takes the simple form:

$$V(\vec{r}) = \frac{\vec{p}_1 \vec{p}_2 - 3(\hat{r} \vec{p}_1 \cdot \hat{r} \vec{p}_2)}{r^3}$$

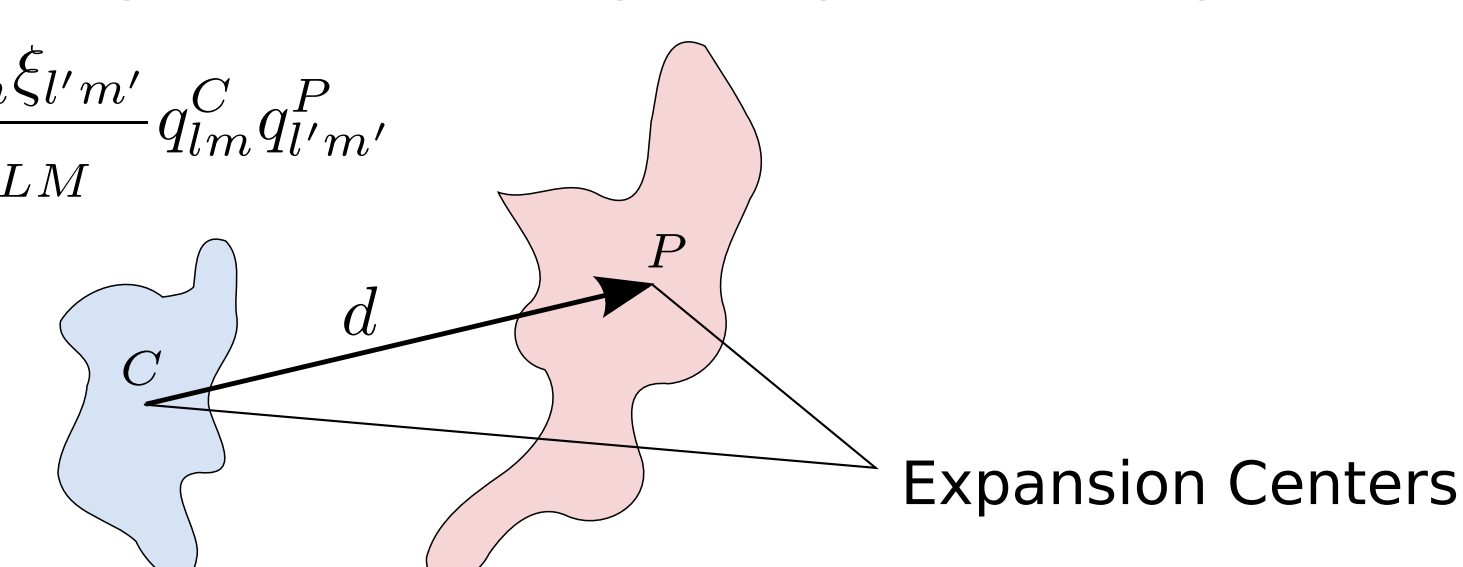


Multipole - Multipole: expansion of the densities to the order n

In general, the interaction of two charge distributions can be evaluated by multipole expansion. The $1/r$ potential is evaluated in a Laplace expansion. From each charge distribution, multipole moments are calculated. Below, the convoluted multipole momentum according to Ref. [5] and the corresponding potential calculation are shown. The order L in the convoluted form denotes the total momentum: 0 for monopole-monopole, 1 for monopole-dipole, 2 for dipole-dipole, ...

$$Q_{LM}^{CP} = \sum_{l+l'=L} (-1)^l \frac{4\pi(2L+1)}{(2l+1)(2l'+1)} \sum_{m+m'=M} \frac{\xi_{lm}\xi_{l'm'}}{\xi_{LM}} q_{lm}^C q_{l'm'}^P$$

$$V_{mp} = \sum_{L,M} \frac{4\pi}{2L+1} Q_{LM}^{CP} \frac{Y_{LM}(\hat{d})}{|d|^{L+1}}$$

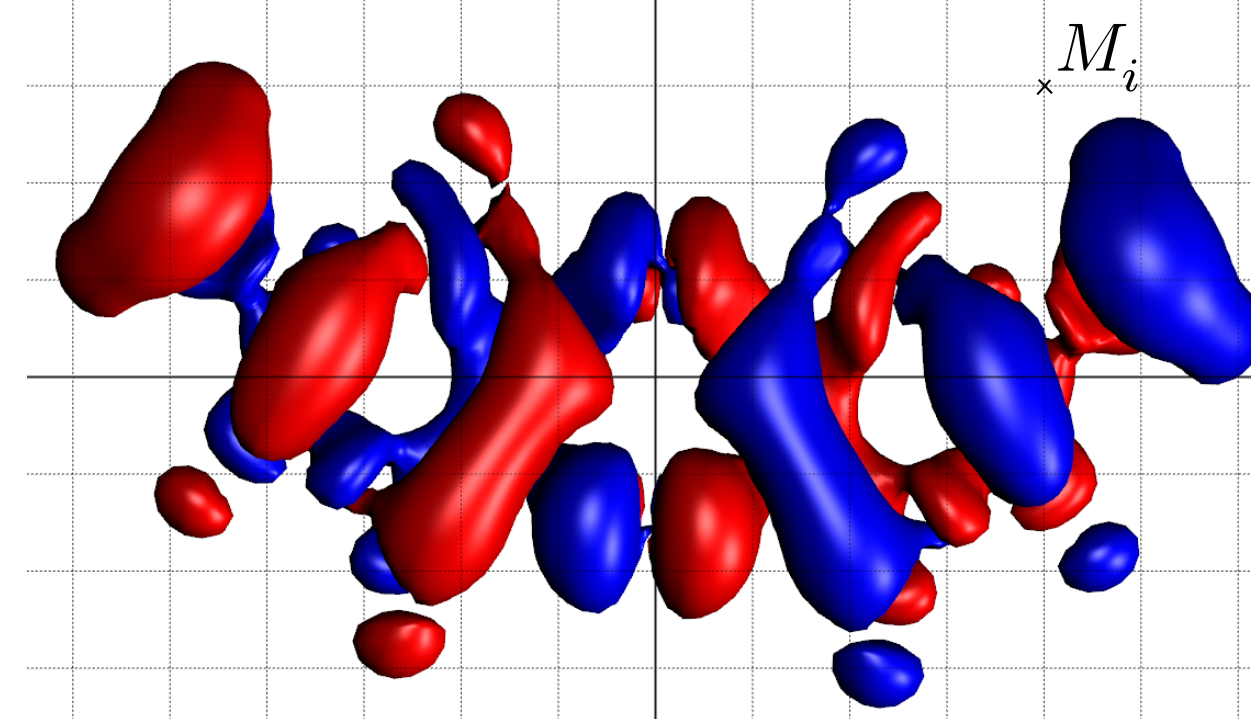


Transition Density Cube: Direct coulombic sum of the densities

At small dye separations or in large resonating structures, the size of the system cannot be neglected. B. P. Krueger et al. [6] developed a method which allows the direct coupling of transition densities via discrete mapping on a grid:

$$M(r) = \int_s \Psi_g \Psi_e^* ds dr$$

$$V_{coul} = \sum_{i,j} \frac{M_i \cdot M_j}{d_{ij}}$$



Results and Comparison:

