# Supporting Material for
# Fretting about FRET: Failure of the Ideal Dipole Approximation

Aurora Muñoz-Losa[†], Carles Curutchet[‡], Brent P. Krueger[§], Lydia R. Hartsell[§], Benedetta Mennucci[†]

[†]Dipartimento di Chimica e Chimica Industriale, Università degli Studi di Pisa

Via Risorgimento 35

56126 Pisa (Italy)

[‡]Department of Chemistry, University of Toronto

80 St. George Street

M5S 3H6 Toronto (Canada)

[§]Hope College, Department of Chemistry

Holland, MI 49423 (USA)

## 1  Effects of Model Chemistry

Recently, some of the authors presented a study on the effect of the QM method in evaluating coupling strengths.(1) In this study, we introduced a benchmark QM description (SAC-CI) to compare with in order to quantify both the reliability in describing excited states and the accuracy in evaluating transition properties and couplings of the other QM methods. The same type of analysis is repeated here for three dyes (AMCA, Fluorescein, and Cy3) which can be seen as representative cases of all the studied systems. Due to the high computational cost of the SAC-CI calculation, a single relative orientation (10-90-270-180-0, a 10 Å anti-parallel side-by-side arrangement) will be considered. Such an orientation has been chosen to amplify the donor-acceptor interactions and consequently the possible differences among QM descriptions. The results are given in Table 1.

### Table 1

As already found in the previous study, the semi-empirical ZINDO/s method gives quite erratic results for the fluorophores examined here. In AMCA the excitation energy is quite accurate and in fluorescein the coupling strength is quite accurate when compared to the SAC-CI results. However, none of the three molecules give consistent results for both quantities. In contrast, the CIS method

is very uniform in its behavior: in all cases it strongly overestimates the excitation energy (by 30-70%) yet gives excellent results for the transition dipole magnitude ($\pm 3\%$) and the coupling ($\pm 2\%$).

The TD-DFT results can be classified into three types of behavior depending on the molecule studied. These will be discussed beginning with AMCA, which is representative of the behavior seen for the dyes without strong charge transfer character (PB, AMCA). For these 'typical' molecules, the TD-DFT methods perform exactly opposite to CIS, yielding excellent excitation energies ($\pm 5\%$) and strongly underestimating the transition dipole magnitude ($-13$ to $-20\%$) and coupling ($-23$ to $-40\%$). Note that for both the CIS and TD-DFT methods the error in the coupling strength (relative to SAC-CI) is what one would expect based on the error in the transition dipole magnitude. Thus, for molecules that behave like AMCA, all of the QM methods (aside from ZINDO/s) appear to accurately describe the detailed shape of the transition densities. In the cases of fluorescein and Cy3, the excited states show significant charge-transfer character, which is known to be problematic for TD-DFT methods (2). The excitation energies are not as well described for these dyes (though still significantly better than CIS) being overestimated by 20 and 30%, respectively. The transition dipole magnitudes and coupling strengths behave quite differently in the two cases, being very strongly underestimated for fluorescein and quite well described for Cy3.

Note that the state of interest remains the first excited state for Cy3, but becomes state 4 or 5 for fluorescein depending on the basis set. This poor performance for fluorescein is due to interactions between the $\pi$ structure of the aromatic portion of the molecule with the nearby $COO^-$ group which leads to artificially low-lying charge transfer states. These states have little or no oscillator strength and their mixing with the desired excited state reduces the magnitude of the transition moment and, therefore, the coupling strength. Increasing the size of the basis set leads to unpredictable results as it generally improves the description of the wavefunctions, but also leads to increased mixing between the aromatic and anionic portions of the molecules, exacerbating the charge transfer effect. Calculations performed with the CAM-B3LYP functional, which is designed for excited states with charge-transfer character(3), are significantly better, returning the state of interest as the first excited state and resulting in errors in the transition dipole magnitudes and coupling strengths that are comparable to AMCA, though the excitation energies are still overestimated. Again, note that the error in the coupling is, for the most part, consistent with the error in the transition dipole magnitude suggesting that the shapes of the transition densities are still reasonably represented by the TD-DFT results even for these challenging molecules.

Note also that the effects of basis set appear to be quite small both for CIS and for TD-DFT, consistent with the recent work by Muñoz-Losa et al.(1).

The effect of the QM method was further investigated here to calculate the average Coulombic coupling for all 196 relative orientations at a separation of 15 Å as shown in Table 2. Such a separation is the smallest one which allows a complete isotropic average; at R=10 Å there are orientations which bring the molecules into contact with each other.

**Table 2**

Here, the analysis is extended to Pacific Blue and AlexaFluor488 providing a larger window of different molecules to estimate the relative performance of ZINDO, CIS and TD-DFT descriptions. Note that reference SAC-CI calculations were not performed as they were computationally too expensive. We also begin to examine the performance of the IDA, reporting the relative error in the IDA, given by

$$\text{Err}_{\text{IDA}} = \frac{\langle V_{dip-dip}^2 \rangle - \langle V_{LR}^2 \rangle}{\langle V_{LR}^2 \rangle} \tag{1}$$

The results found in Table 1 for a single orientation are also valid here. In fact, if we consider CIS as the most stable approach to estimate coupling strengths, it is evident that TD-B3LYP performs nearly as well with regard to $\text{Err}_{\text{IDA}}$. TD-B3LYP behavior is comparable to CIS for PB and AMCA, and slightly less accurate ($-7$-15 % for TD-B3LYP compared to $-6$-12 % for CIS) for fluorescein, Alexa488, and Cy3. As before, moving to CAM-B3LYP improves the description in the difficult cases.

As the primary goal of this work is to identify situations in which the IDA performs poorly, we conclude this Supplement by analyzing the relative error in the IDA (Eq. 1) which is of foremost importance to the discussion in the paper itself. Its value shows minimal dependence on QM method or basis set (aside from the ZINDO/s results). This shows that non-coulombic contributions ($V_{Ex-Corr}$ and $V_{Ovlp}$) do not significantly affect $V_{LR}$ and it suggests that the shape of the transition densities are well-determined by both CIS and TD-DFT regardless of basis-set. Thus, the conclusions reached in the manuscript are reasonably independent of the QM model chemistry chosen (at least for CIS and TD-DFT with modest-sized basis sets). That said, results for two model chemistries (CIS/6-31G(d), and TD-B3LYP/6-31(d)) have been utilized in the present study.

## References

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**Table 1.** Dependence of the desired excited state ($n$), excitation energy ($\Delta E$), transition dipole magnitude ($\mu$) and coupling ($V_{LR}$) as a function of QM model chemistry. The percent error with respect to the SAC-CI method is given in parenthesis for the $\Delta E$, $\mu$, and $V_{LR}$ values. Results for one relative orientation for three dyes are presented: AMCA, fluorescein, and Cy3. The relative orientation is 10-90-270-180-0, which is an anti-parallel side-by-side arrangement with a separation of 10 Å.

| Method | Basis Set | $n$ | $\Delta E$ (eV) | $\mu$ (D) | $V_{LR}$ (cm$^{-1}$) |
|---|---|---|---|---|---|
| | | | **AMCA** | | |
| ZINDO/s | | 1 | 3.82 (1%) | 5.2 (-16%) | 127.4 (-12%) |
| CIS | 6-31G(d) | 1 | 5.00 (32%) | 6.2 (0%) | 144.9 (0%) |
| CIS | 6-31+G(d,p) | 1 | 4.91 (30%) | 6.2 (0%) | 146.2 (1%) |
| B3LYP | 6-31G(d) | 1 | 3.82 (1%) | 5.2 (-16%) | 102.3 (-29%) |
| B3LYP | 6-31+G(d,p) | 1 | 3.77 (0%) | 5.4 (-13%) | 111.3 (-23%) |
| CAM-B3LYP | 6-31+G(d,p) | 1 | 4.11 (9%) | 5.7 (-8%) | 122.1 (-16%) |
| SAC-CI | 6-31G(d) | 1 | 3.81 (1%) | 5.9 (-5%) | 135.3 (-7%) |
| SAC-CI | 6-31+G(d,p) | 1 | 3.78 | 6.2 | 144.8 |
| | | | **Fluorescein** | | |
| ZINDO/s | | 1 | 2.53 (4%) | 10.0 (9%) | 285.1 (0%) |
| CIS | 6-31G(d) | 1 | 3.83 (57%) | 9.3 (1%) | 288.7 (1%) |
| CIS | 6-31+G(d,p) | 1 | 3.74 (53%) | 9.3 (1%) | 291.2 (2%) |
| B3LYP | 6-31G(d) | 5 | 2.94 (20%) | 6.6 (-28%) | 144.3 (-49%) |
| B3LYP | 6-31+G(d,p) | 4 | 2.88 (18%) | 7.3 (-21%) | 172.8 (-39%) |
| CAM-B3LYP | 6-31+G(d,p) | 1 | 3.02 (24%) | 8.1 (-12%) | 208.5 (-27%) |
| SAC-CI | 6-31+G(d,p) | 1 | 2.44 | 9.2 | 284.8 |
| | | | **Cy3** | | |
| ZINDO/s | | 1 | 2.53 (21%) | 11.9 (7%) | 376.8 (7%) |
| CIS | 6-31G(d) | 1 | 3.62 (73%) | 11.4 (3%) | 351.0 (0%) |
| B3LYP | 6-31G(d) | 1 | 2.72 (30%) | 11.2 (1%) | 329.3 (-6%) |
| SAC-CI | 6-31G(d) | 1 | 2.09 | 11.1 | 352.0 |

**Table 2.** The coupling ($V_{LR}$) and relative error of the IDA (Err$_{\text{IDA}}$, see Eq. 1) as a function of QM model chemistry. Unlike Table 1, results here are averaged over the complete set of 196 relative orientations. The intermolecular separation ($R_{DA}$) is 15 Å for all calculations. Results are presented for PB, AMCA, Fluorescein, AlexaFluor488, and Cy3.

| Method | Basis Set | $\langle V_{LR}^2 \rangle$ (cm$^{-2}$) | Err$_{\text{IDA}}$ (%) |
|---|---|---|---|
| **Pacific Blue** | | | |
| ZINDO/s | | 1503 | -33.7 |
| CIS | 6-31G(d) | 2007 | -7.1 |
| B3LYP | 6-31G(d) | 889 | -7.5 |
| B3LYP | 6-31+G(d,p) | 1081 | -7.3 |
| CAM-B3LYP | 6-31+G(d,p) | 1179 | -7.8 |
| **AMCA** | | | |
| ZINDO/s | | 1810 | -37.1 |
| CIS | 6-31G(d) | 2230 | -3.5 |
| B3LYP | 6-31G(d) | 1121 | -2.9 |
| B3LYP | 6-31+G(d,p) | 1308 | -2.6 |
| CAM-B3LYP | 6-31+G(d,p) | 1568 | -2.8 |
| **Fluorescein** | | | |
| ZINDO/s | | 10930 | -34.2 |
| CIS | 6-31G(d) | 11645 | -6.3 |
| B3LYP | 6-31G(d) | 3071 | -7.3 |
| B3LYP | 6-31+G(d,p) | 4669 | -7.9 |
| CAM-B3LYP | 6-31+G(d,p) | 6808 | -8.1 |
| **AlexaFluor488** | | | |
| ZINDO/s | | 4055 | -35.7 |
| CIS | 6-31G(d) | 7844 | -7.3 |
| B3LYP | 6-31G(d) | 779 | -10.1 |
| B3LYP | 6-31+G(d,p) | 309 | -11.0 |
| CAM-B3LYP | 6-31+G(d,p) | 2995 | -9.2 |
| **Cy3** | | | |
| ZINDO/s | | 24015 | -24.2 |
| CIS | 6-31G(d) | 28459 | -11.5 |
| B3LYP | 6-31G(d) | 27515 | -15.1 |
| B3LYP | 6-31+G(d,p) | 27796 | -13.1 |
| CAM-B3LYP | 6-31+G(d,p) | 28924 | -11.8 |