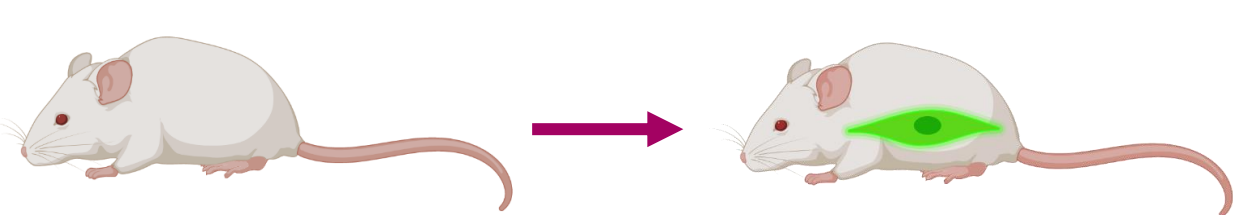# Computational Refinement of the Oxyluciferin/Luciferase System for its Applications in Bioimaging and Biosensing

H. Mateo-delaFuente and J. J. Nogueira
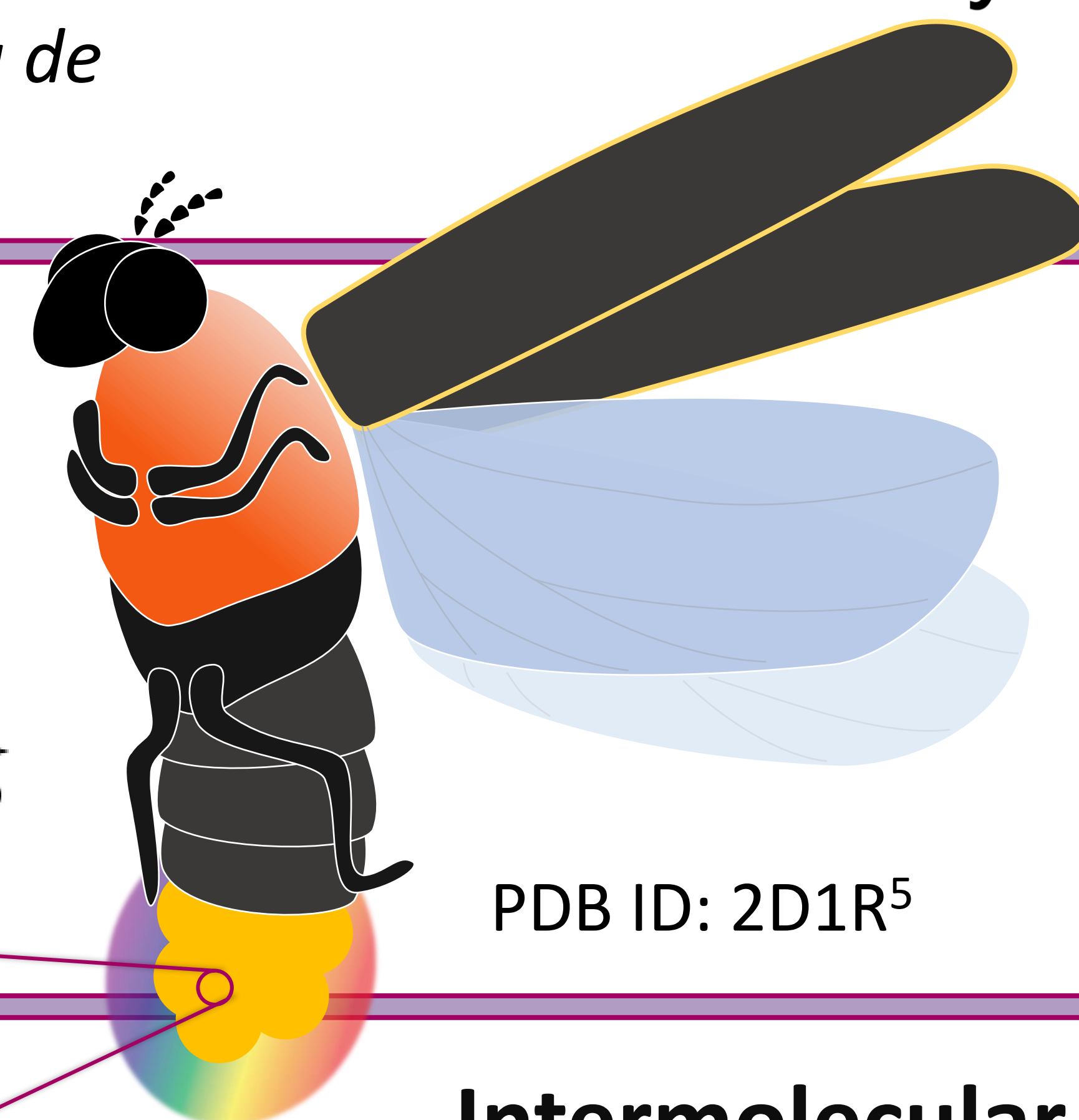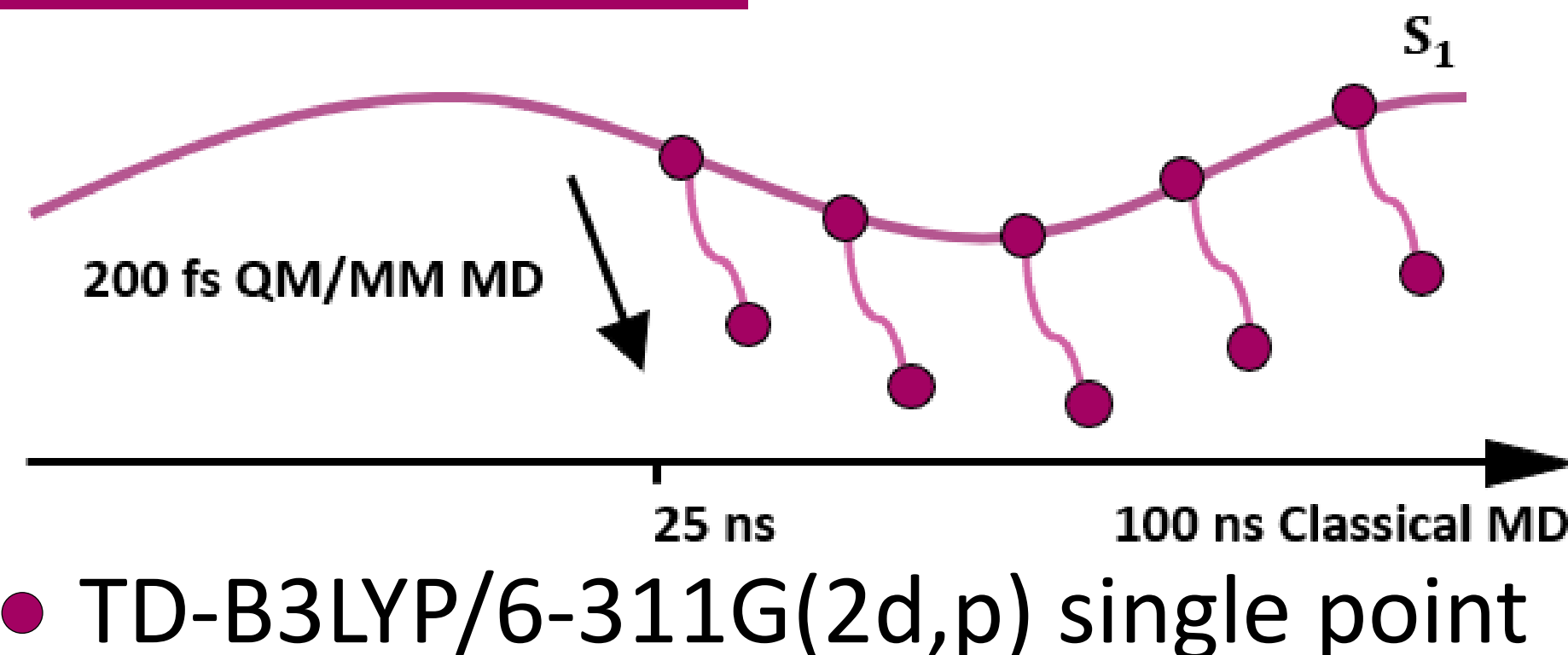
Department of Chemistry, Universidad Autónoma de Madrid, 28049, Madrid, Spain

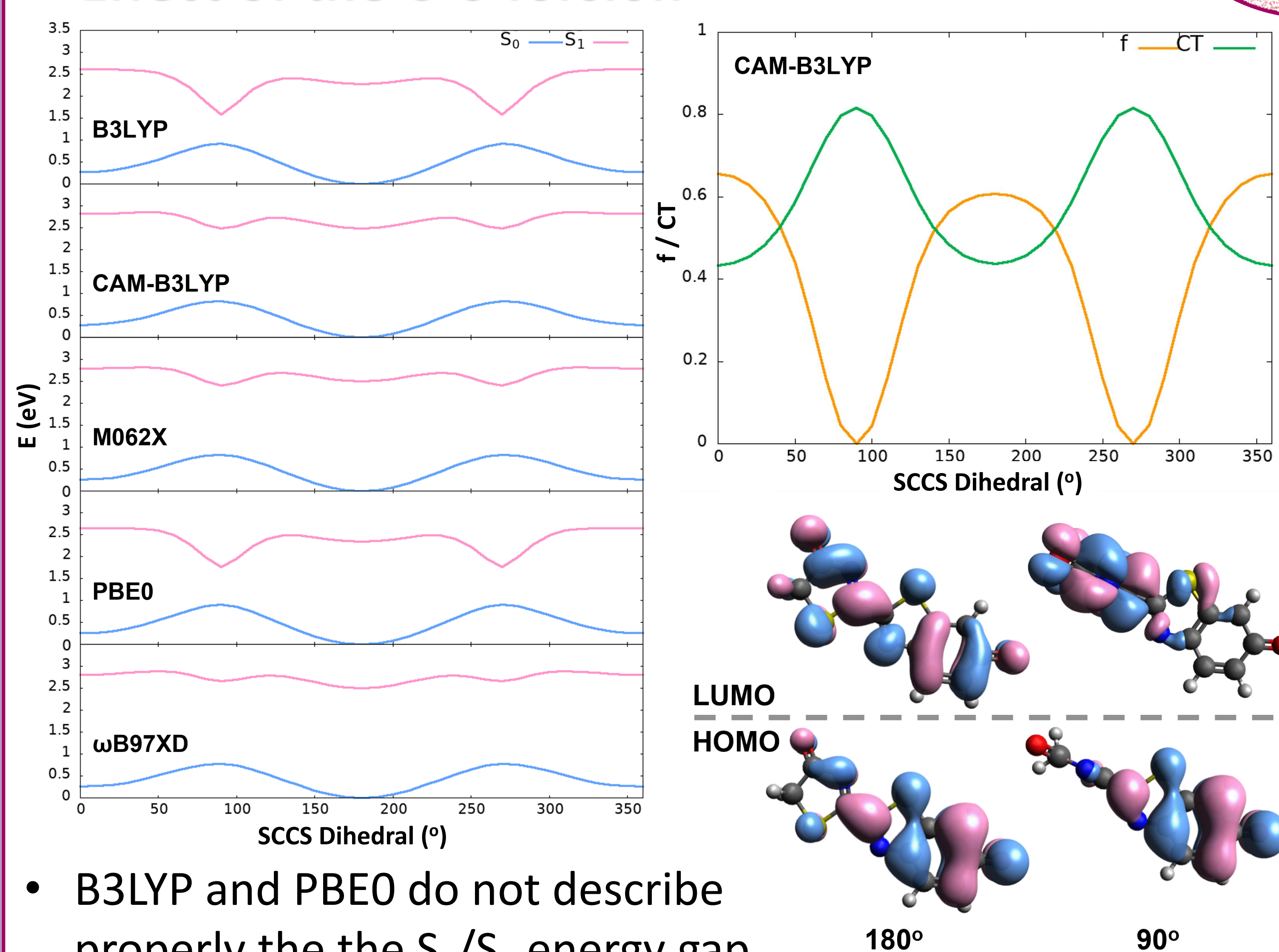**MoBioChem**

Modeling Biology and Chemistry

Motivation

- The oxyluciferin/luciferase complex has may applications in bioimaging[1,2] and biosensing[3,4]
- Goal: determine the structural characteristics that affect the electronic transition properties of the oxyluciferin/luciferase system
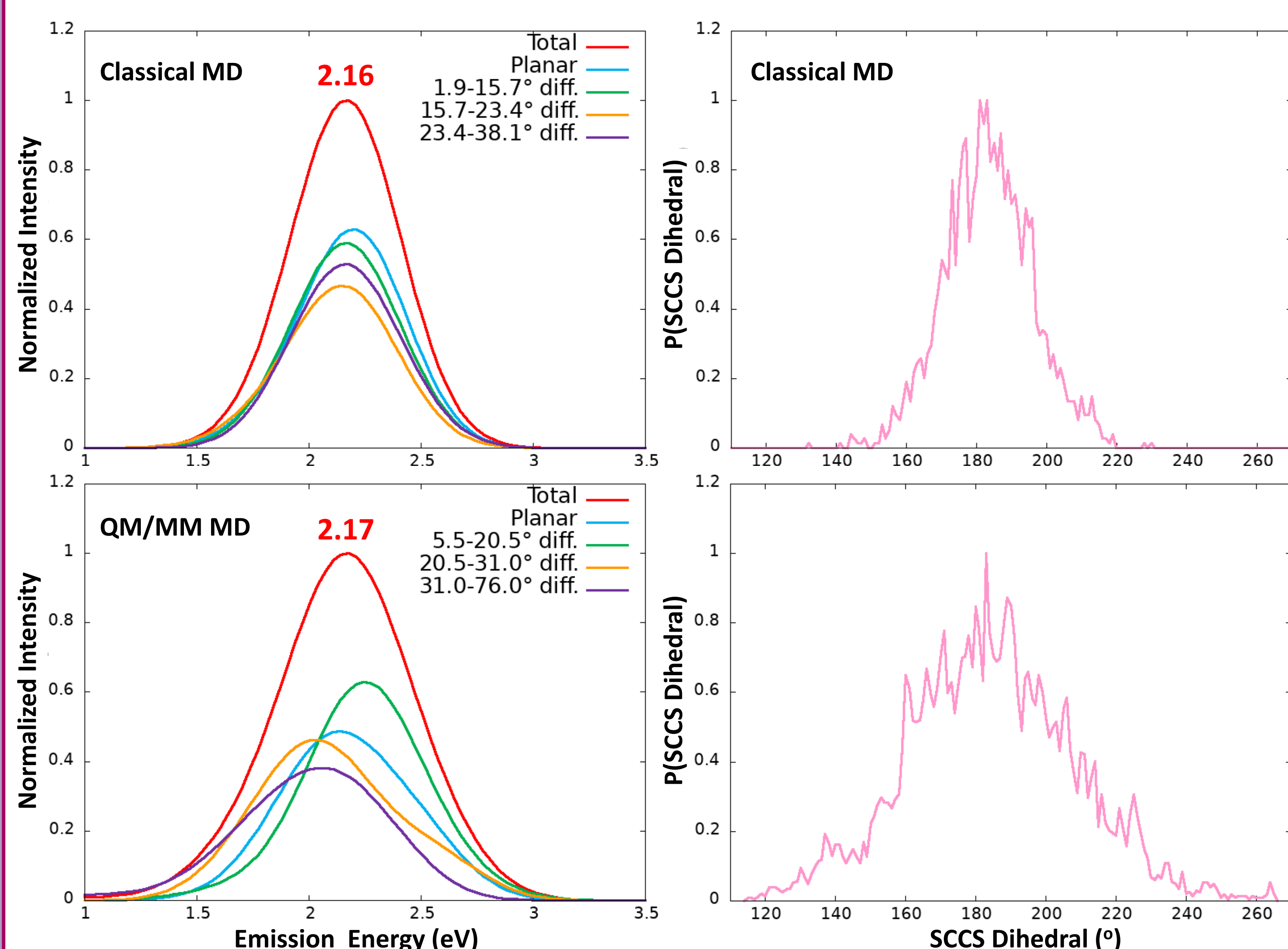
Methodology

S_1

200 fs QM/MM MD

25 ns   100 ns Classical MD

- TD-B3LYP/6-311G(2d,p) single point

PDB ID: 2D1R[5]

Intramolecular Degrees of Freedom

Effect of the C-C Torsion

B3LYP

CAM-B3LYP

M062X

PBE0

ωB97XD

S_0 S_1

E (eV) / SCCS Dihedral (º)

CAM-B3LYP   f / CT

f / CT vs SCCS Dihedral (º)

LUMO
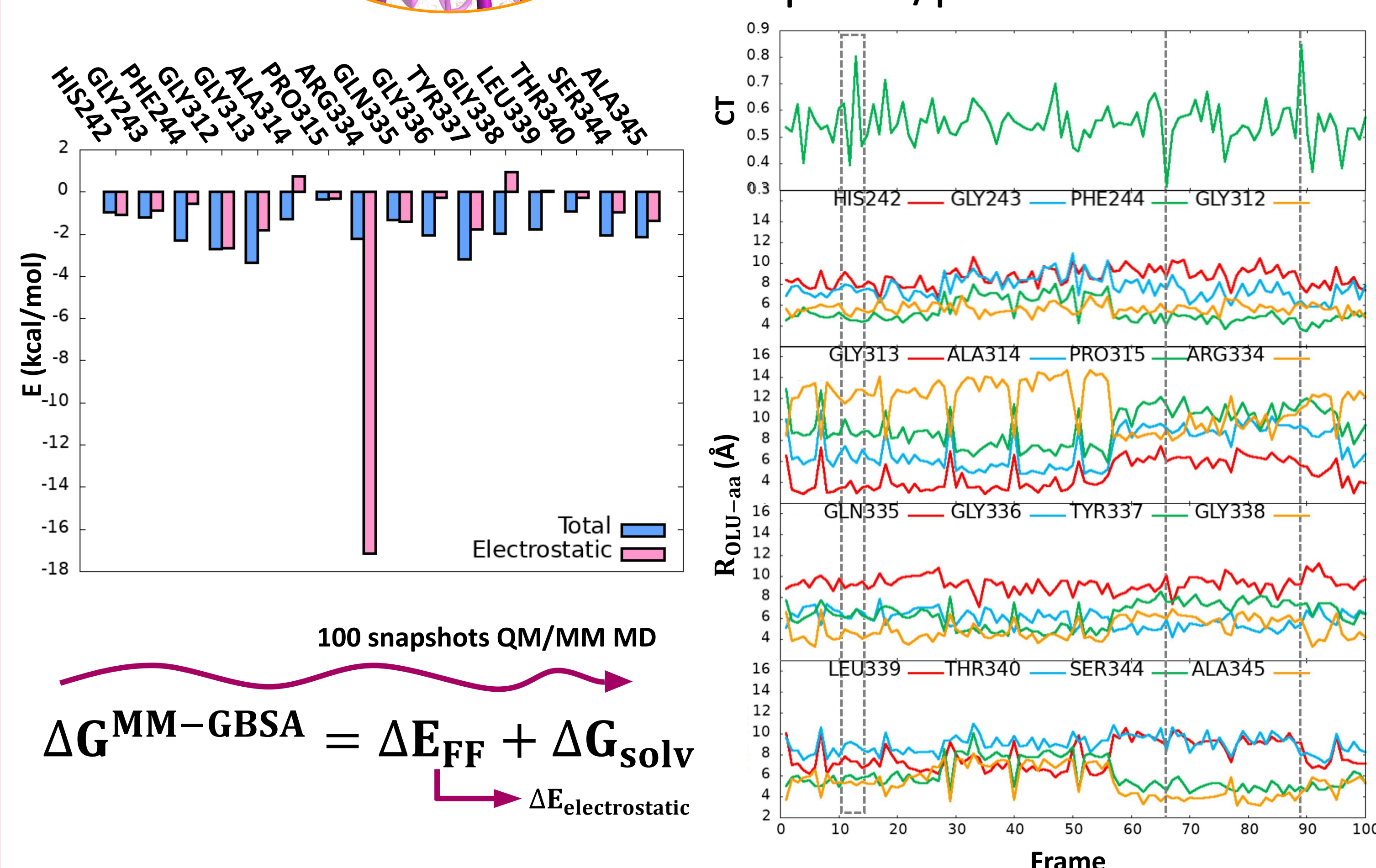HOMO

180º   **90º**

- B3LYP and PBE0 do not describe properly the the S_1/S_0 energy gap
- Torsion produces dark CT states with lower transition E

Dynamic Effect on the Electronic Properties

Classical MD   **2.16**
Total
Planar
1.9-15.7° diff.
15.7-23.4° diff.
23.4-38.1° diff.

Classical MD
P(SCCS Dihedral)

QM/MM MD   **2.17**
Total
Planar
5.5-20.5° diff.
20.5-31.0° diff.
31.0-76.0° diff.

Emission Energy (eV)

SCCS Dihedral (º)

Intermolecular Degrees of Freedom

Modelling the effect of the chromophore/protein interactions

E (kcal/mol)

HIS242 GLY243 PHE244 GLY312 ALA313 GLY313 ARG315 PRO334 GLN335 GLY335 TYR336 GLY337 LEU338 THR339 SER340 ALA344 ALA345

Total
Electrostatic

100 snapshots QM/MM MD

$$\Delta G^{MM-GBSA} = \Delta E_{FF} + \Delta G_{solv}$$

$\Delta E_{electrostatic}$

R_{OLU-aa} (Å) vs Frame

HIS242 GLY243 PHE244 GLY312
GLY313 ALA314 PRO315 ARG334
GLN335 GLY336 TYR337 GLY338
LEU339 THR340 SER344 ALA345

- Strong electrostatic interaction with ARG334
- No CT correlation with any amino acid (aa) closeness

- Both classical and QM/MM spectra present good agreement with the experimental value (2.21 eV)[5]
- QM/MM MD samples a slightly larger region of the space and presents the expected small red-shift and hypochromism

Geometrical Relation with the CT

P(CT)

smaller CT cluster   **larger CT cluster**

CT

| 0.41 ± 0.16 | ← 0.33 → | 0.41 ± 0.17 | **RMSD** |
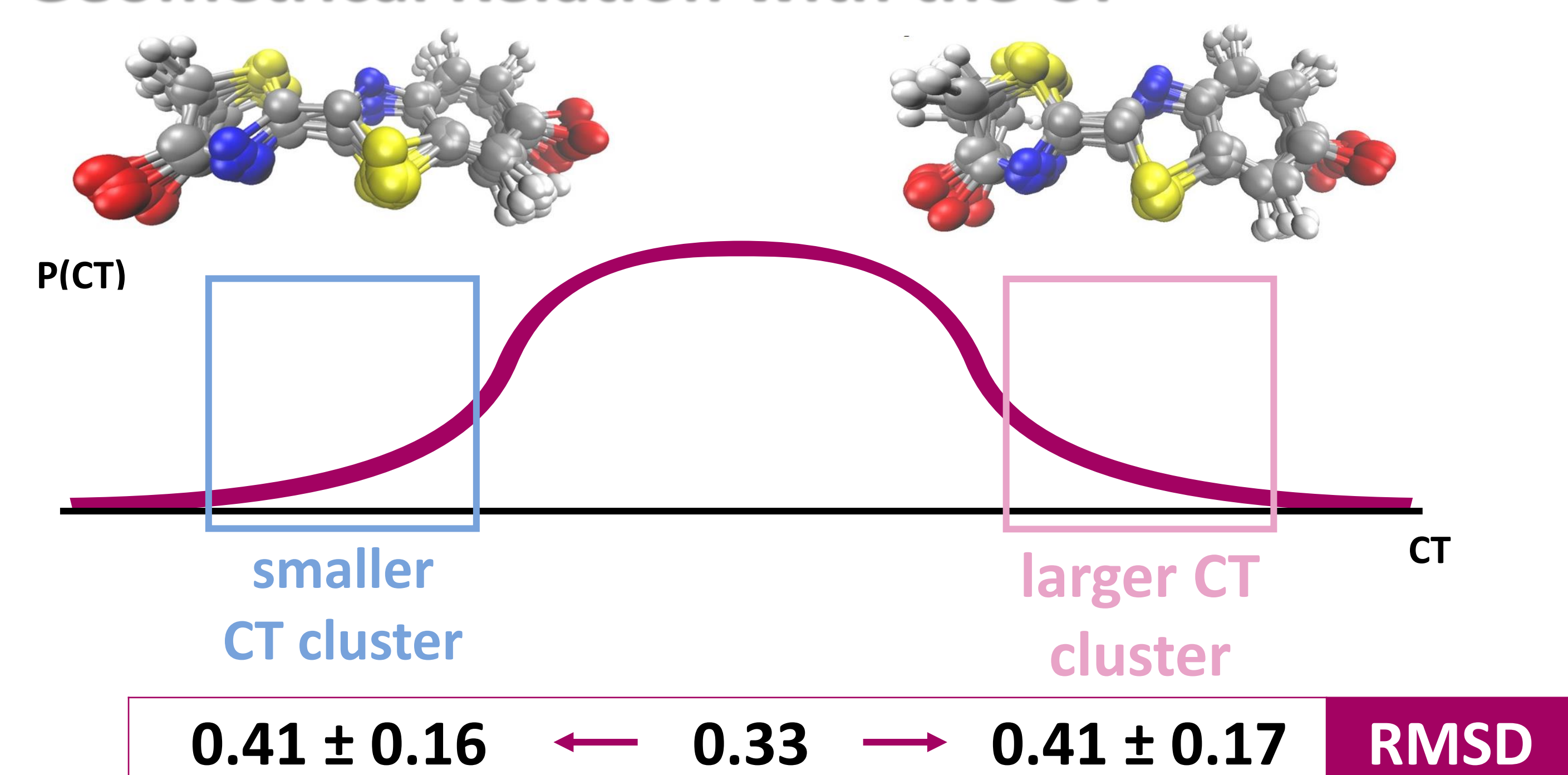
- Differences within each cluster are larger than differences between clusters → no significative differences

Conclusions

- Electronic transition properties highly change around the torsion
- No intramolecular nor intermolecular correlation with the CT values due to a complex combination of different degrees of freedom

1) *Teleman F1000Prime Rep.* **2015**, 7, 1
2) *Free Radic. Biol. Med.* **2015**, 79, 253
3) *J. Microbiol. Methods*, **2001**, 47, 159
4) *Am. J. Infect. Control*, **2015**, 43, 882
5) *Nature*, **2006**, 440, 372