Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supporting Information

The Protein Environment Restricts the Intramolecular Charge Transfer Character of the Luciferine/Luciferase Complex

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1 Oxyluciferin Parameters for the Classical Molecular Dynamics Simulations

1.1 Atom Types and Charges

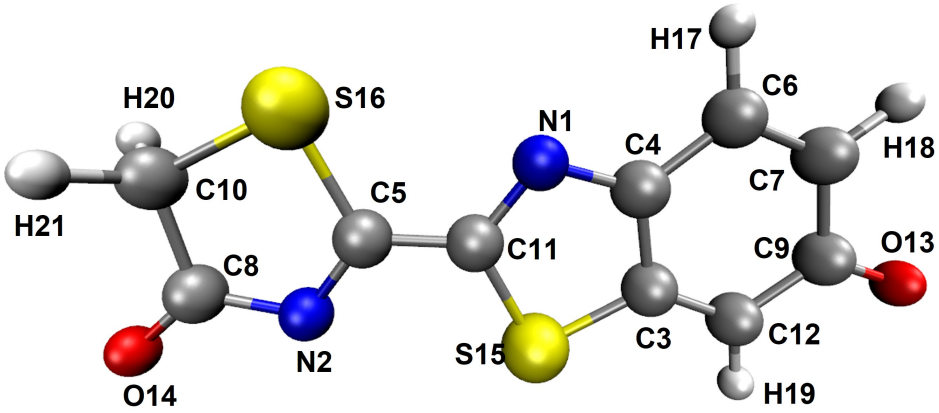

Figure S1: Structure of the OLU with its atoms labeled.

Atom	Atom type	Charge	
		S_0	S_1
N1	NC	-0.318749	-0.507990
N2	NE	-0.323092	-0.522480
C3	CA	-0.187395	0.138902
C4	CA	0.194161	0.238767
C5	CF	-0.004360	0.171311
C6	CA	-0.178360	-0.235721
C7	CA	-0.301687	-0.432107
C8	C	0.335751	0.644779
C9	CA	0.281274	0.600080
C10	C3	-0.682846	0.032659
C11	CD	-0.007420	0.258466
C12	CA	-0.347720	-0.405953
O13	O	-0.445425	-0.618213
O14	O	-0.355803	-0.608688
S15	SS	0.207947	-0.084461
S16	SS	0.141643	-0.254811
H17	HA	0.173894	0.162641
H18	HA	0.162581	0.157964
H19	HA	0.166778	0.197981
H20	H1	0.244164	0.033211
H21	H1	0.244665	0.033664

Table S1: Atom types and charges of the OLU chomophore as represented in Figure S1.

1.2 Stretching

Taking into account the Hamiltonian description of the Amber FF, then the stretching term is described by:

$$E^{stretching} = \sum_{bonds} k_b(r - r_0)^2 \tag{1}$$

where k_b and r_0 represent the stretching force constant in kcal/mol and the bond length in Å, respectively.

Stretching	S_0		S_1	
	k_b	r_0	k_b	r_0
NC-CA	377.701	1.340	236.501	1.380
NC-CD	416.221	1.319	324.665	1.323
NE-CF	458.539	1.309	406.144	1.320
NE-C	294.500	1.379	313.284	1.367
CA-CA	256.038	1.439	277.658	1.412
CA-CA	451.744	1.370	357.402	1.384
CA-SS	158.716	1.756	95.295	1.754
CA-CA	341.153	1.420	342.363	1.414
CF-CD	334.443	1.412	252.306	1.425
CF-SS	119.431	1.786	120.216	1.782
CA-CA	495.168	1.359	444.964	1.374
CA-HA	376.657	1.084	373.389	1.085
CA-CA	241.339	1.465	226.137	1.449
CA-HA	375.522	1.085	377.921	1.084
C -C3	140.708	1.540	131.071	1.544
C -O	746.684	1.218	697.688	1.228
CA-CA	301.545	1.443	256.391	1.457
CA-O	585.278	1.255	553.729	1.257
C3-SS	141.318	1.819	135.249	1.823
C3-H1	359.823	1.090	355.135	1.091
C3-H1	363.312	1.088	357.178	1.090
CD-SS	126.329	1.784	115.780	1.770
CA-HA	378.966	1.083	385.174	1.082

Table S2: Stretching parameters for the OLU chomophore. Force constants appear in kcal/mol and bond lengths in Å.

1.3 Bending

In the case of the bending, the Hamiltonian term is described by:

$$E^{bending} = \sum_{angles} k_\theta(\theta - \theta_0)^2 \tag{2}$$

where k_θ and θ_0 represent the bending force constant in kcal/mol/radian^2 and the equilibrium angle in degrees, respectively.

Bending	S_0		S_1	
	k_θ	θ_0	k_θ	θ_0
NC-CA-CA	127.744	116.106	135.009	115.517
NC-CA-CA	136.731	125.480	160.500	125.852
NC-CD-CF	90.143	123.975	94.941	125.092
NC-CD-SS	87.079	114.374	70.479	115.698
NE-CF-CD	111.777	123.523	111.352	123.935
NE-CF-SS	98.118	117.523	89.791	117.373
NE-C -C3	102.894	113.937	105.649	113.807
NE-C -O	107.507	124.563	112.087	125.332
CA-CA-CA	168.666	118.414	161.108	118.632
CA-CA-CA	139.873	119.977	144.296	119.773
CA-CA-HA	57.373	122.115	57.161	122.396
CA-SS-CD	142.809	88.849	148.032	88.348
CA-NC-CD	125.552	112.442	110.362	110.685
CA-CA-CA	148.626	122.435	131.358	122.426
CA-CA-SS	135.996	108.229	102.784	109.753
CA-CA-CA	150.852	119.751	149.373	120.570
CA-CA-HA	62.076	118.682	61.577	118.572
CF-NE-C	134.402	113.139	142.658	113.465
CF-CD-SS	111.565	121.651	83.053	119.210
CF-SS-C3	120.223	88.975	121.190	88.847
CA-CA-CA	168.734	123.061	160.130	122.228
CA-CA-HA	63.359	120.856	62.997	120.875
CA-CA-HA	64.218	121.567	64.158	120.858
CA-CA-CA	217.531	116.362	217.730	116.369
CA-CA-O	124.901	121.167	122.433	122.962
C -C3-SS	118.433	106.426	118.662	106.507
C -C3-H1	66.861	109.886	66.983	110.297
C -C3-H1	66.273	109.991	66.502	110.372
CA-CA-HA	63.480	116.083	60.755	116.897
CA-CA-HA	60.999	117.908	62.987	117.830
C3-C -O	92.922	121.500	91.674	120.861
CD-CF-SS	117.039	118.955	111.526	118.692
CA-CA-SS	145.301	129.335	121.419	127.821
CA-CA-O	123.460	122.471	114.548	120.669
SS-C3-H1	48.855	110.727	46.200	110.534
SS-C3-H1	48.100	110.794	45.677	110.544
H1-C3-H1	34.684	108.994	33.747	108.587

Table S3: Bending parameters for the OLU chomophore. Force constants appear in kcal/mol/radian^2 and equilibrium angles in degrees.

1.4 Torsion

Torsion movements, both proper and improper are included in the Hamiltonian term by:

$$E^{dihedral} = \sum_{dihedrals} V_n(1 + cos(n\phi - \gamma)] \tag{3}$$

where V_n represents the torsion barrier term (in kcal/mol); γ, the phase (degrees) and n, the periodicity. Additionally, Amber20 employs a divider term that splits the torsion term into individual contributions for each pair of atoms involved in the torsion.

Dihedral	S_0				S_1			
	Divider	V_n	γ	n	Divider	V_n	γ	n
CA-CA-CA-NC	4	14.500	180.000	2.000	4	14.500	180.000	2.000
HA-CA-CA-NC	4	14.500	180.000	2.000	4	14.500	180.000	2.000
NC-CD-SS-CA	2	2.200	180.000	2.000	2	2.200	180.000	2.000
NC-CD-CF-NE	4	4.000	180.000	2.000	4	4.000	180.000	2.000
SS-CD-CF-NE	4	4.000	180.000	2.000	4	4.000	180.000	2.000
NE-CF-SS-C3	2	2.200	180.000	2.000	2	2.200	180.000	2.000
NE-C -C3-SS	6	0.000	180.000	2.000	6	0.000	180.000	2.000
NE-C -C3-H1	6	0.000	180.000	2.000	6	0.000	180.000	2.000
CA-CA-CA-CA	4	14.500	180.000	2.000	4	14.500	180.000	2.000
CA-CA-CA-HA	4	14.500	180.000	2.000	4	14.500	180.000	2.000
CF-CD-NC-CA	2	9.500	180.000	2.000	2	9.500	180.000	2.000
SS-CD-NC-CA	2	9.500	180.000	2.000	2	9.500	180.000	2.000
CA-CA-SS-CD	2	0.800	180.000	2.000	2	0.800	180.000	2.000
C3-C -NE-CF	2	0.400	180.000	2.000	2	0.400	180.000	2.000
O -C -NE-CF	2	0.400	180.000	2.000	2	0.400	180.000	2.000
CF-CD-SS-CA	2	2.200	180.000	2.000	2	2.200	180.000	2.000
CA-CA-CA-O	4	14.500	180.000	2.000	4	14.500	180.000	2.000
CD-CF-NE-C	2	1.600	180.000	2.000	2	1.600	180.000	2.000
SS-CF-NE-C	2	1.600	180.000	2.000	2	1.600	180.000	2.000
C -C3-SS-CF	3	1.000	0.000	3.000	3	1.000	0.000	3.000
CA-CA-NC-CD	2	9.600	180.000	2.000	2	9.600	180.000	2.000
CD-CF-SS-C3	1	1.100	180.000	-2.000	1	1.100	180.000	-2.000
CD-CF-SS-C3	1	0.700	180.000	3.000	1	0.700	180.000	3.000
HA-CA-CA-O	4	14.500	180.000	2.000	4	14.500	180.000	2.000
O -C -C3-SS	6	0.000	180.000	2.000	6	0.000	180.000	2.000
O -C -C3-H1	1	0.800	0.000	-1.000	1	0.800	0.000	-1.000
O -C -C3-H1	1	0.000	0.000	-2.000	1	0.000	0.000	-2.000
O -C -C3-H1	1	0.080	180.000	3.000	1	0.080	180.000	3.000
NC-CA-CA-SS	4	14.500	180.000	2.000	4	14.500	180.000	2.000
CA-CA-CA-SS	4	14.500	180.000	2.000	4	14.500	180.000	2.000
HA-CA-CA-SS	4	14.500	180.000	2.000	4	14.500	180.000	2.000
NC-CD-CF-SS	4	4.000	180.000	2.000	4	4.000	180.000	2.000
SS-CD-CF-SS	4	4.000	180.000	2.000	4	4.000	180.000	2.000
HA-CA-CA-HA	4	14.500	180.000	2.000	4	14.500	180.000	2.000
H1-C3-SS-CF	3	1.000	0.000	3.000	3	1.000	0.000	3.000

Table S4: Dihedral parameters for the OLU chomophore. Torsional barriers and dividers appear in kcal/mol and phases in degrees.

Dihedral	S_0			S_1		
	V_n	γ	n	V_n	γ	n
CA-CA-CA-SS	1.1	180.0	2.0	1.1	180.0	2.0
CA-CA-CA-NC	1.1	180.0	2.0	1.1	180.0	2.0
CD-NE-CF-SS	1.1	180.0	2.0	1.1	180.0	2.0
CA-CA-CA-HA	1.1	180.0	2.0	1.1	180.0	2.0
C3-NE-C -O	10.5	180.0	2.0	10.5	180.0	2.0
CA-CA-CA-O	1.1	180.0	2.0	1.1	180.0	2.0
CF-NC-CD-SS	1.1	180.0	2.0	1.1	180.0	2.0

Table S5: Improper torsional parameters for the OLU chomophore. Torsional barriers and dividers appear in kcal/mol. The torsional barrier height is NOT divided by the divider.

1.5 Non-Bonding Parameters

Finally, for each pair of atoms the non bonding interaction is given by:

$$V_{ij} = \epsilon \left[\left(R_{min}/r_{ij} \right)^{12} - 2 \left(R_{min}/r_{ij} \right)^{6} \right] \tag{4}$$

where ϵ represents the 6-12 potential well depth in kcal/mol and R_{min}, the van der Waals radii in Å.

Atom type	S_0		S_1	
	$R_{min}/2$	ϵ	$R_{min}/2$	ϵ
NC	1.8240	0.1700	1.8240	0.1700
NE	1.8240	0.1700	1.8240	0.1700
CA	1.9080	0.0860	1.9080	0.0860
CF	1.9080	0.0860	1.9080	0.0860
C	1.9080	0.0860	1.9080	0.0860
C3	1.9080	0.1094	1.9080	0.1094
CD	1.9080	0.0860	1.9080	0.0860
O	1.6612	0.2100	1.6612	0.2100
SS	2.0000	0.2500	2.0000	0.2500
HA	1.4590	0.0150	1.4590	0.0150
H1	1.3870	0.0157	1.3870	0.0157

Table S6: Non-bonding parameters for the OLU chomophore. van der Waals radii appear in Åand 6-12 potential well depth in kcal/mol.

2 Absorption and Emission Spectra from the Classical and QM/MM Trajectories and Angle Contributions.

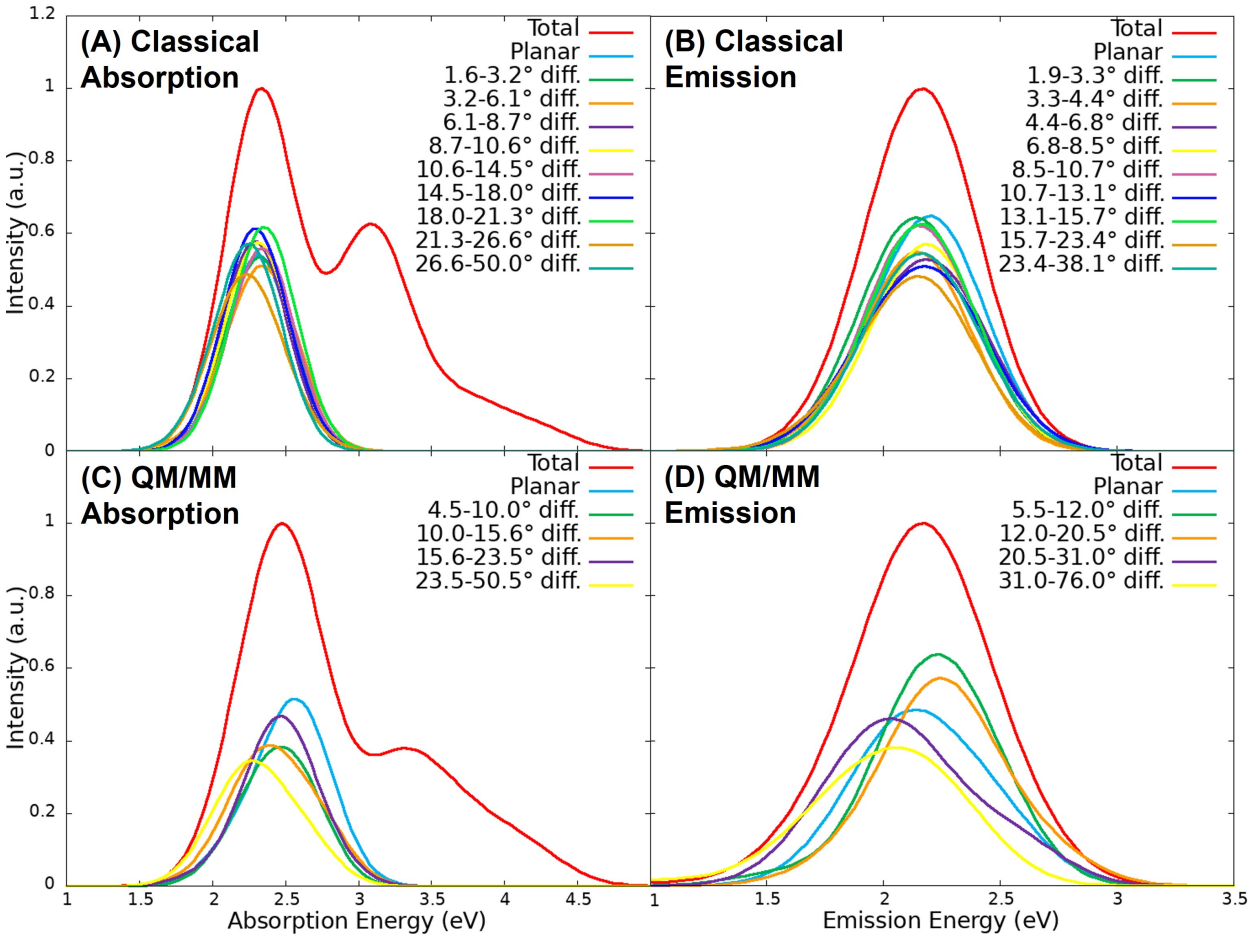

Figure S2: (A,C) Absorption and (B,D) emission spectra computed from the classical (A,B) and QM/MM (C,D) trajectories, together with their respective contributions from the S0 → S1 band depending on the SCCS dihedral angle.

3 Probability Distribution of the SCCS Dihedral Angles for the 500 ns Trajectory

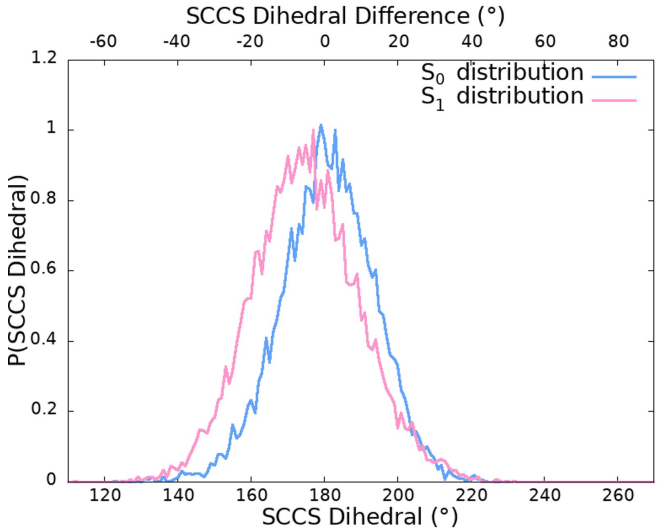

Figure S3: Probability distributions of the SCCS dihedral angles for the S_0 (blue) and the S_1 (pink) trajectories evolved at classical level for 500 ns.

4 Environment of the Two Clusters with the Smallest and Largest CT Number Values from the QM/MM Trajectory of the S_0 State.

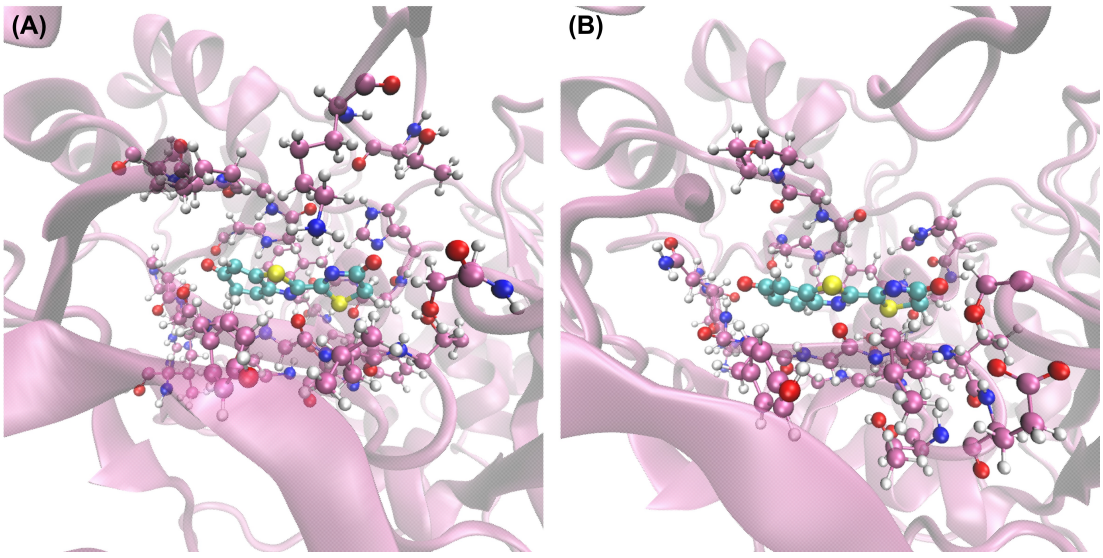

Figure S4: Representative structure with the protein environment of the two clusters with the 20 snapshots with smallest (A) and largest (B) CT number values extracted from the QM/MM trajectory of the S_0 state.

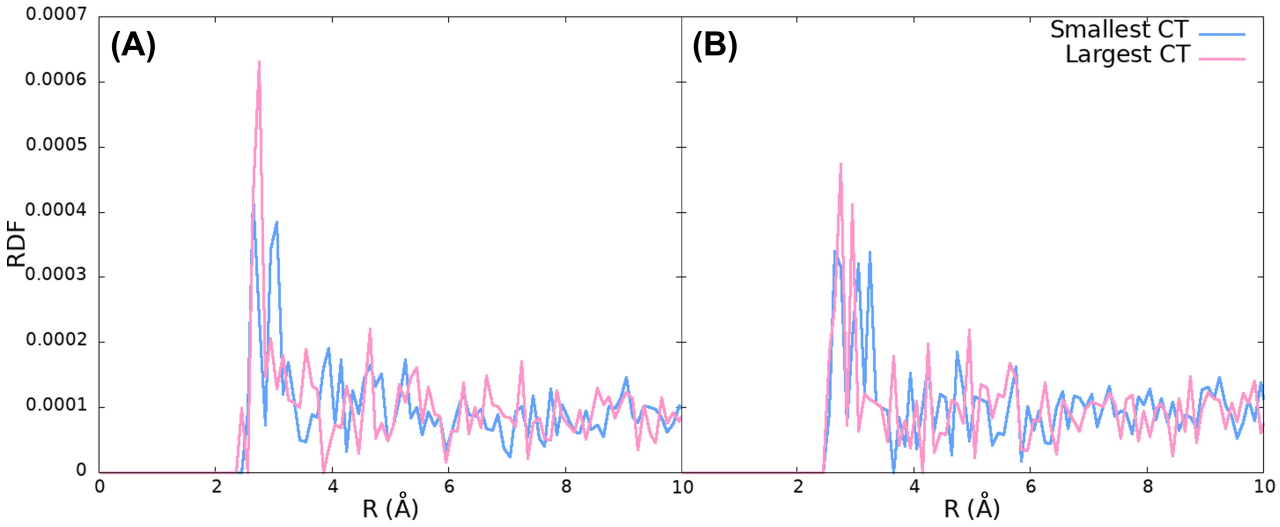

Figure S5: Radial distribution functions (RDF) between (A) the oxygen atom of the thiazole fragment and the oxygen atom of water and (B) the oxygen atom of the benzothiazole fragment and the oxygen atom of water for the two clusters with the 20 snapshots with smallest (blue) and largest (pink) CT number values extracted from the QM/MM trajectory of the S_0 state.

Cluster	<CT>	Protein			H_2O			Protein + H_2O		
		O^{tz}	O^{btz}	Total	O^{tz}	O^{btz}	Total	O^{tz}	O^{btz}	Total
Small	0.45±0.06	0.0±0.0	0.6±1.5	0.6±1.5	0.1±0.3	0.0±0.0	0.1±0.3	0.1±0.3	0.6±1.5	0.7±1.5
Large	0.66±0.06	0.2±0.9	0.4±1.2	0.6±1.5	0.2±0.4	0.3±0.4	0.5±0.6	0.4±0.9	0.7±1.4	1.1±1.6

Table S7: Number of H bonds between the O of the thiazole (tz) and benzothiazole fragments of the OLU and its environment.

5 Total Binding Free Energy per Residue of the Classical S_1 Trajectories Without and With AMP

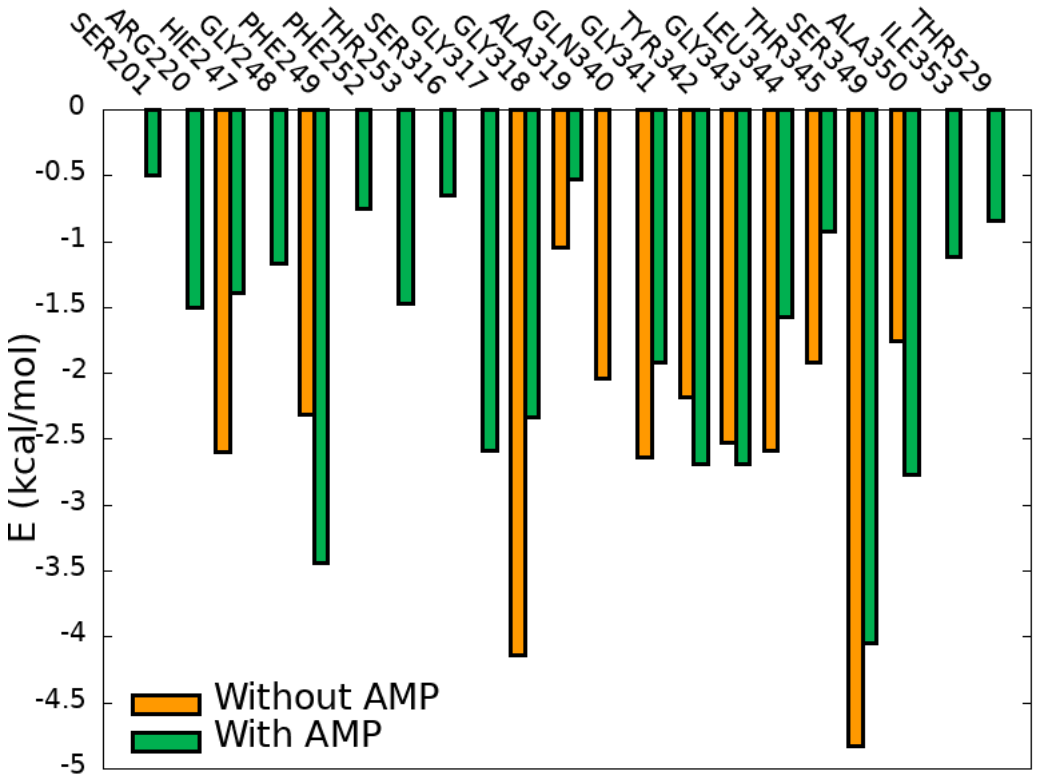

Figure S6: Total binding free energy per residue of the classical S_1 trajectories without (orange) and with AMP (green) for the residues that are closer for at least 1% of the simulation time.

6 Representation of the Three Positions Found for the Analysed Snapshots of the S_0 QM/MM Trajectory

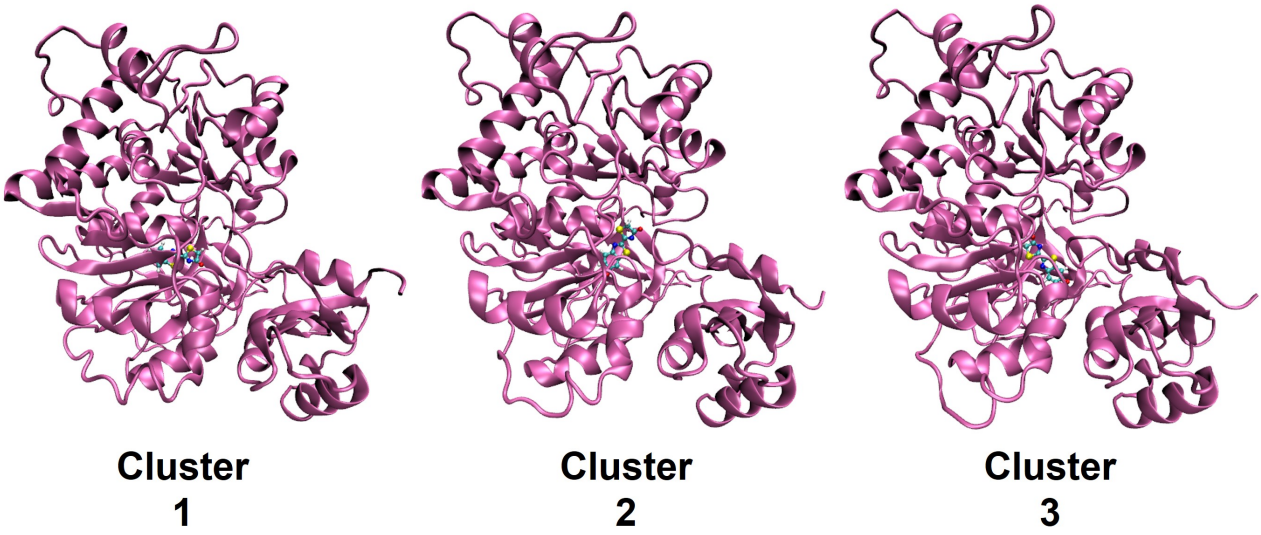

Figure S7: Representation of the three clusters of the analysed snapshots of the S_0 QM/MM trajectory

7 Charge Transfer Number Variation with Respect to the Distance of the Closest Amino-acids of the Protein

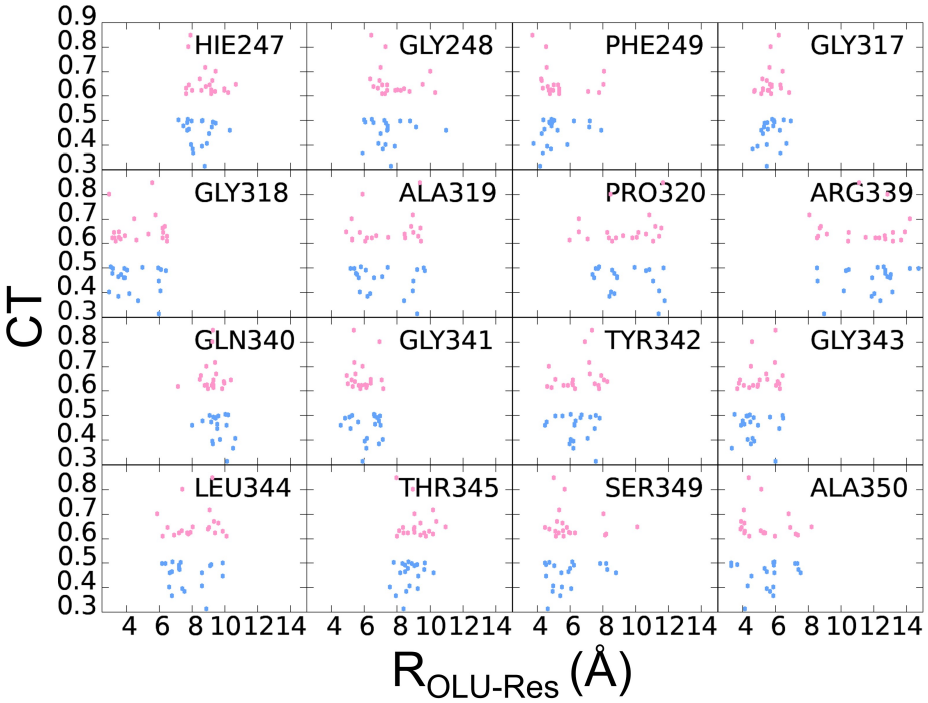

Figure S8: CT number variation with the distance between the centers of mass of the chromophore and different amino-acids for the clusters of the 20 geometries with smallest (blue) and largest (pink) CT number values