Supporting Information

Multiscale Modeling of Two-Photon Probes for Parkinson's Diagnostics Based on Monoamine Oxidase B Biomarker

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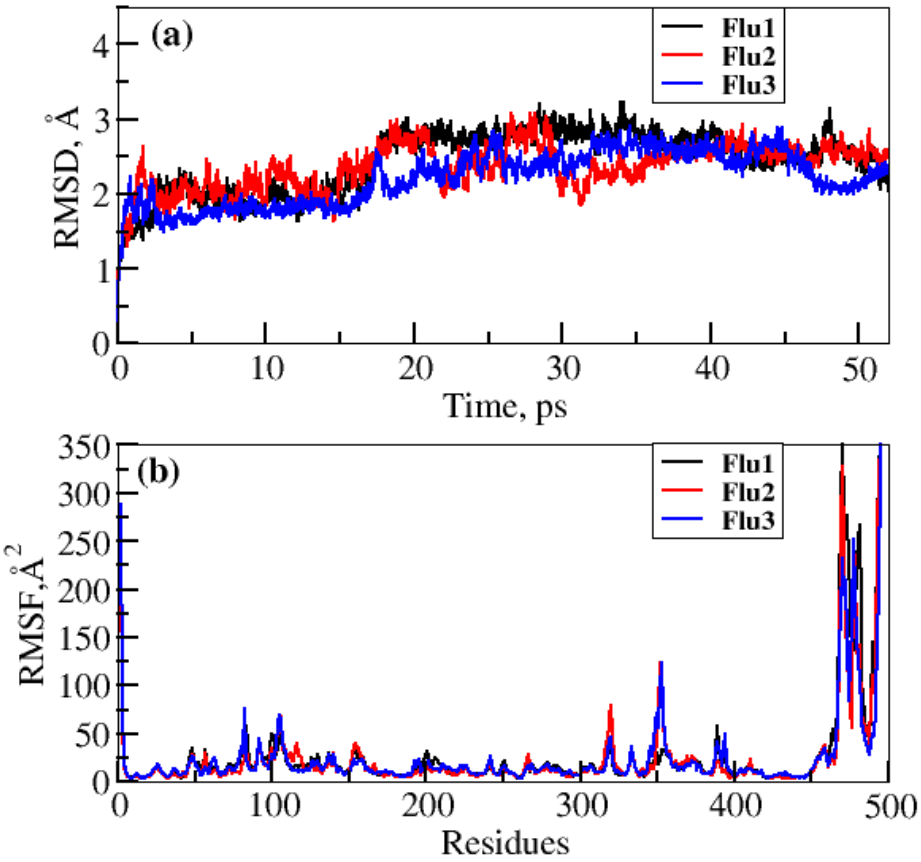


Figure S1: (a) RMSD computed for MAO-B protein when bound to ligands Flu1-Flu3 using the reference configuration from the production run, (b) RMSF calculated for MAO-B backbone carbons.

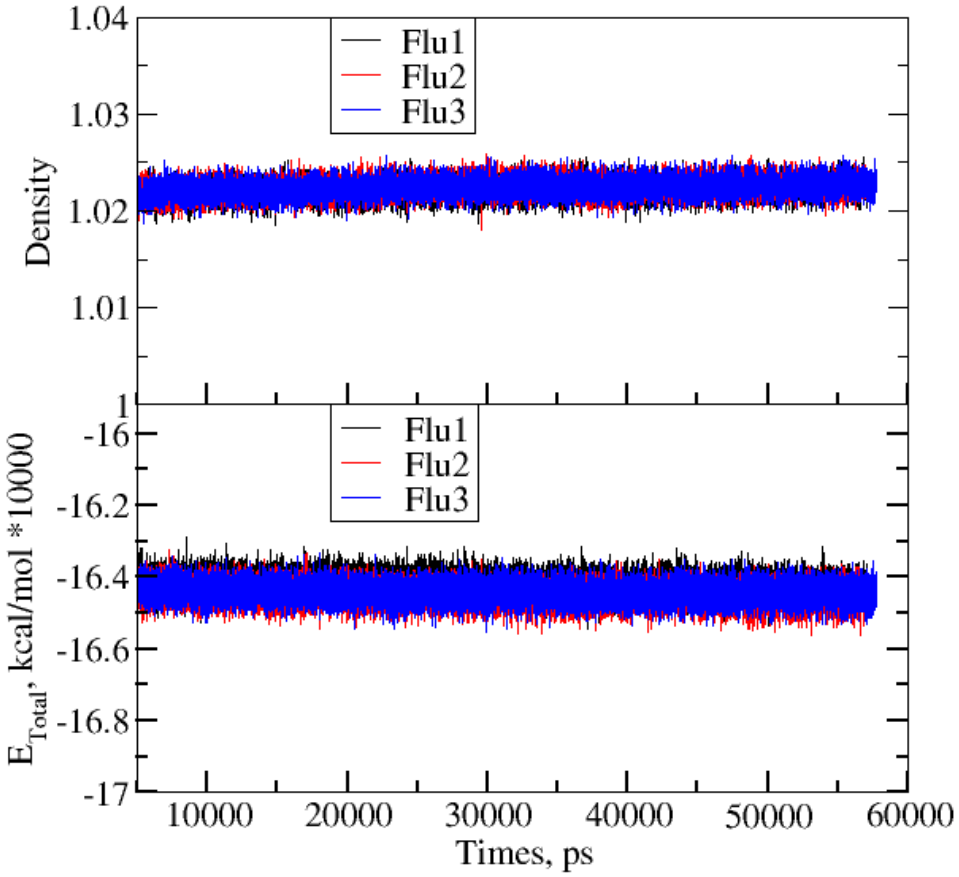


Figure S2: Time evolution of density and total energies in the three complexes of MAO-B with the ligands Flu1-Flu3.

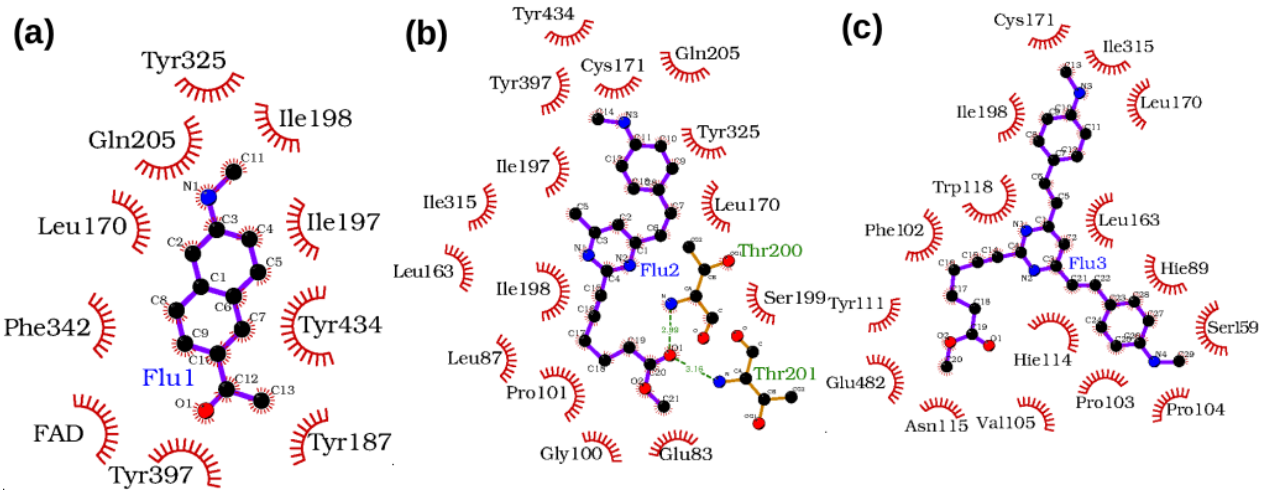


Figure S3: Protein-ligand interaction diagram computed using Ligplus software for the three complexes of Flu1 (a), Flu2 (b) and Flu3 (c) with MAO-B. In the case of Flu1 and Flu3, C-methyl is labelled as C13, while in the case of Flu-2, C-methyl group is labelled as C14.

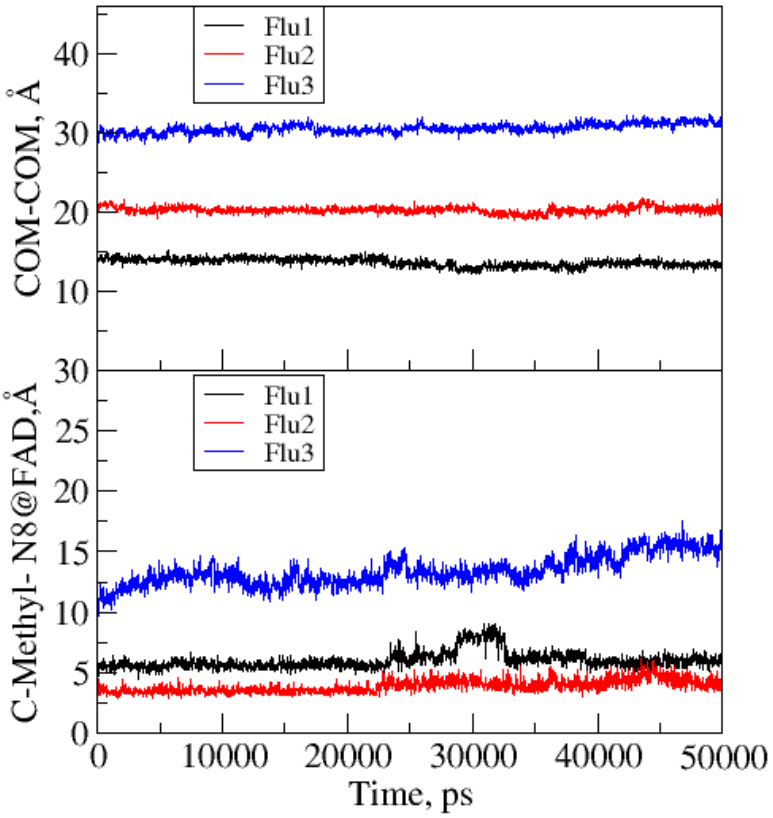
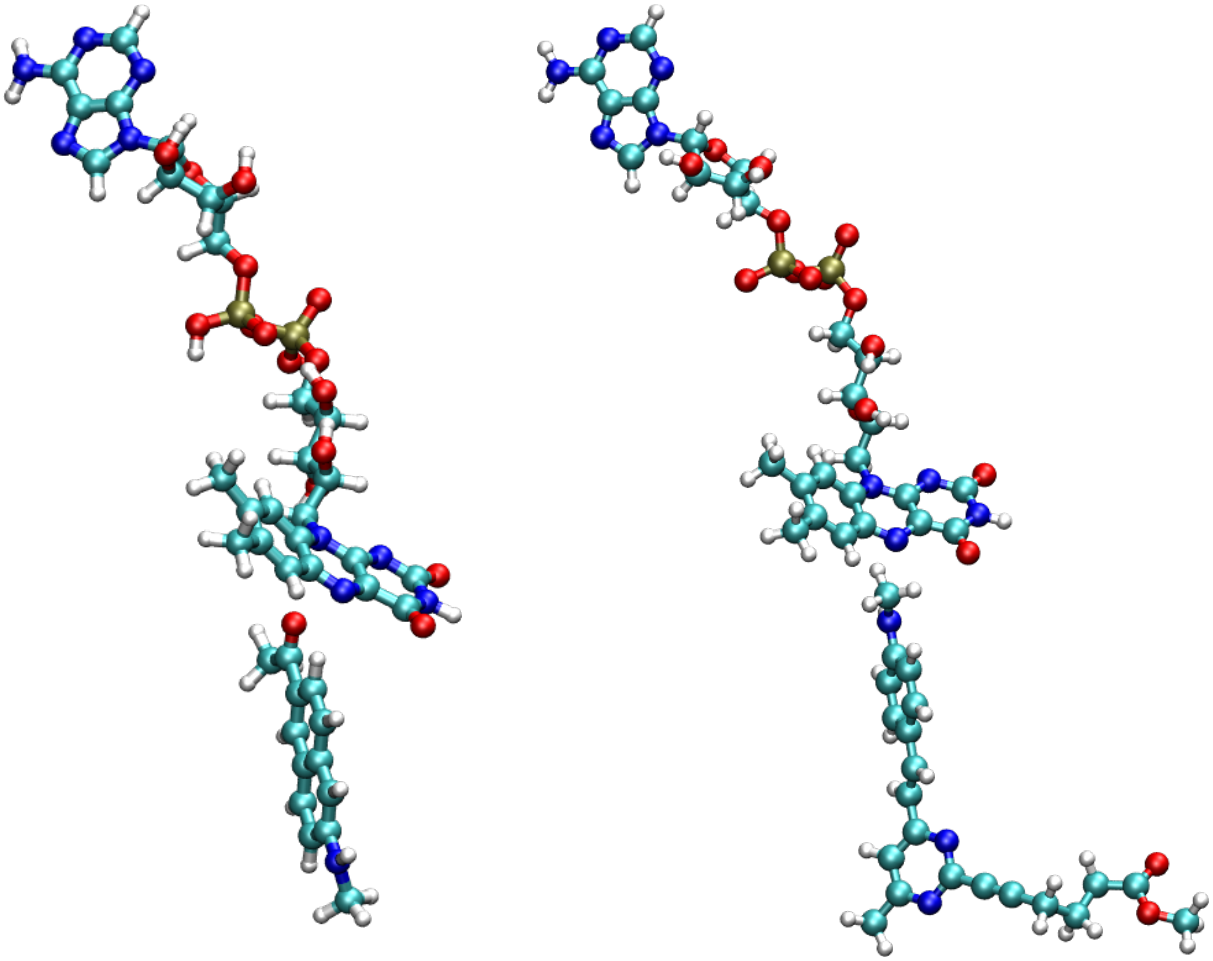


Figure S4: (a) The time evolution of center of mass distance between the protein and ligands for Flu1-Flu3, (b) the time evolution of distance between the C-methyl group of ligands and terminal N of FAD cofactor.



a) **b)**

Figure S5: (a) The representative structure of Flu1-FAD used in the two-photon spectra calculation to estimate the effect of cofactor on the two-photon absorption cross sections of Flu1. The FAD orientation is kept as it is in the crystal structure while the relative orientation of Flu1 is based on the docking result, (b) the representative structure of Flu2-FAD used in the two-photon absorption calculation to estimate the effect of cofactor on the two-photon absorption cross sections of Flu2.

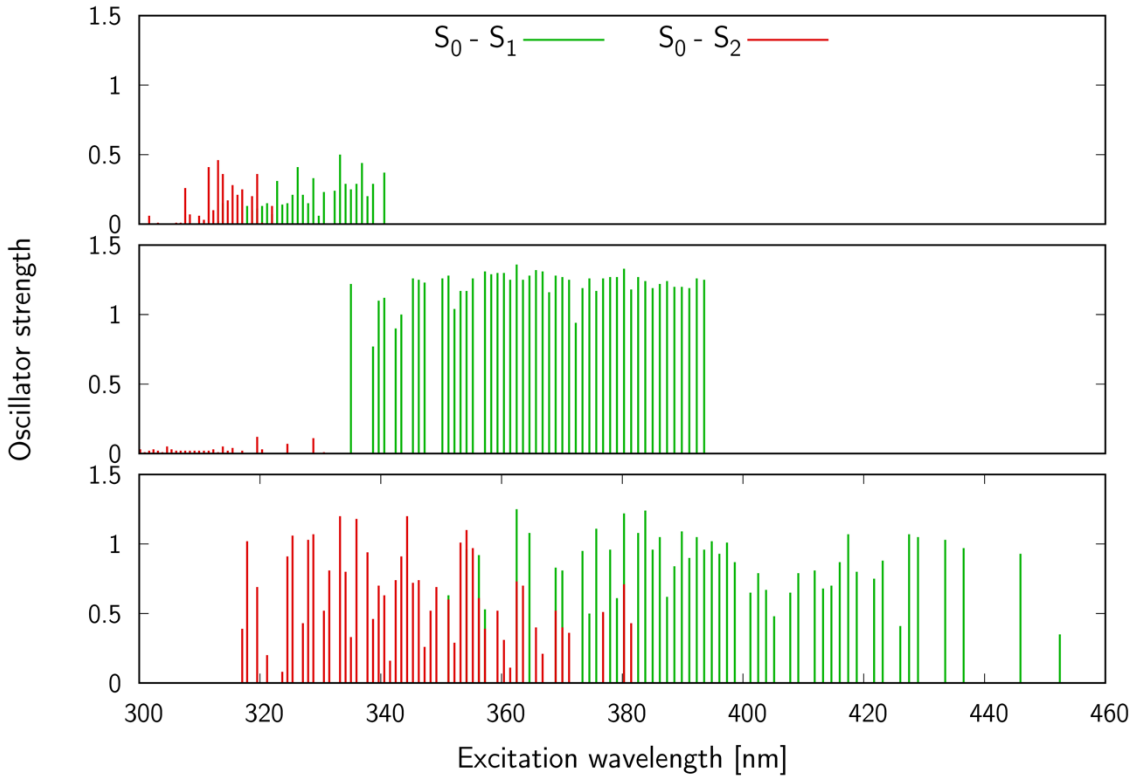


Figure S6: One-photon absorption spectra for Flu1 (top), Flu2 (middle) and Flu3 (bottom) computed at the CC2 level of theory.

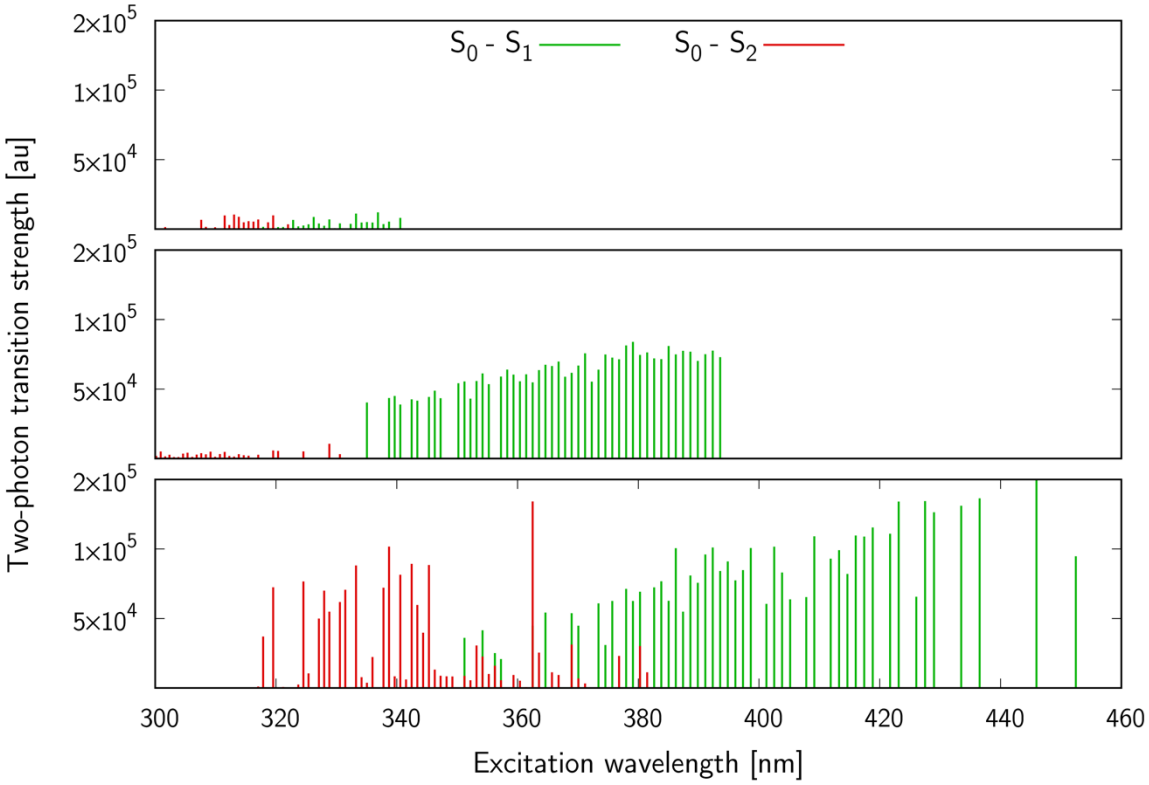


Figure S7: Two-photon absorption spectra for Flu1 (top), Flu2 (middle) and Flu3 (bottom) computed at the CC2 level of theory.

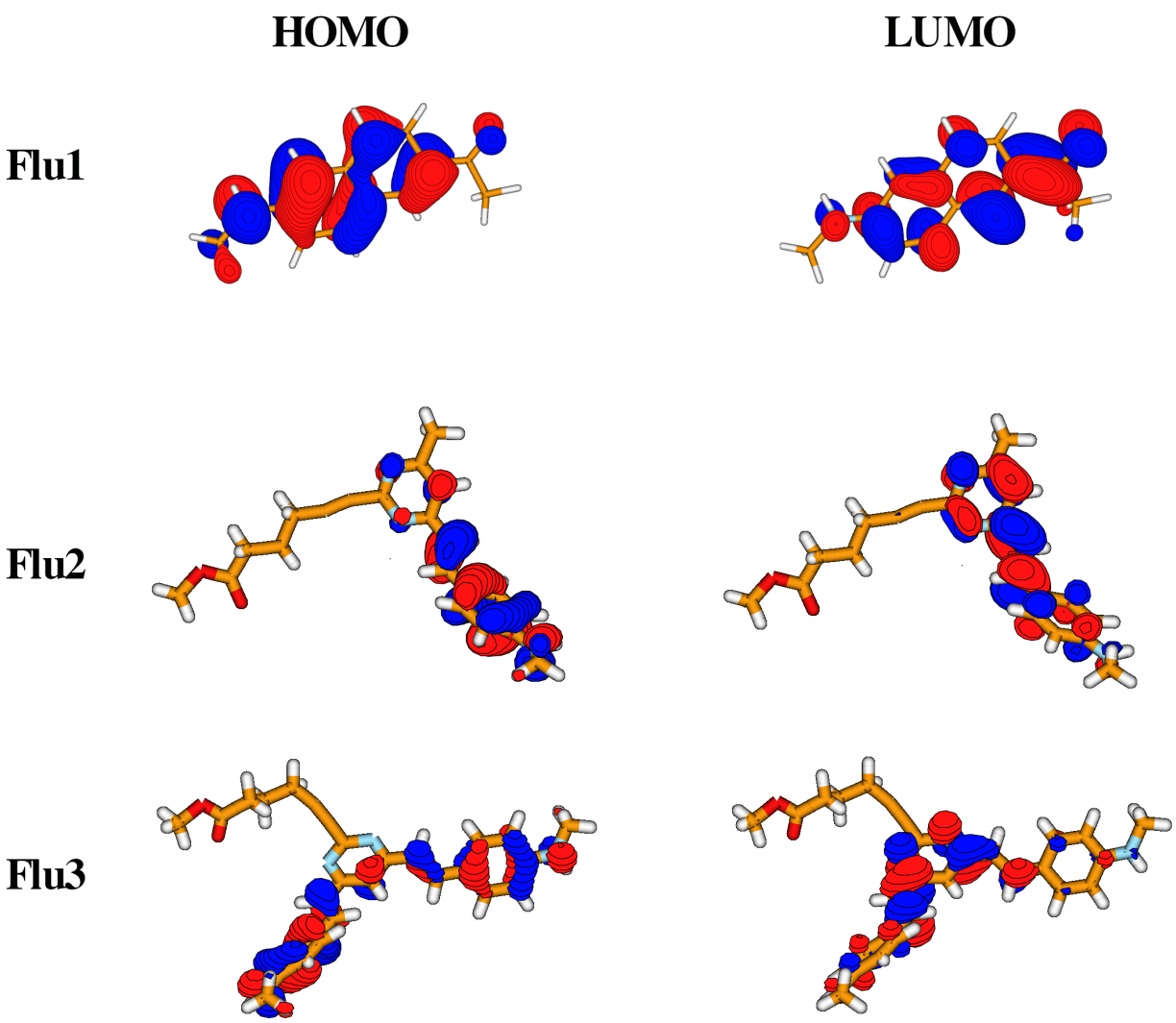


Figure S8: Frontier orbitals involved in large-intensity electronic excitations. The calculations were performed at the CAM-B3LYP/TZVP level of theory.

Table S1: Excitations with significant two-photon absorption cross sections (in GM) and the corresponding absorption wavelength (in nm). The input structure for FAD as in crystal structure while that of Flu1 or Flu2 based on the docking. The calculations for free probe carried out by including 10 excitations while for the case with the neutral form of FAD, the calculations were carried out by including 30 low energy excitations. All data were obtained using B3LYP functional.

System	**Excited state**	**Two-photon absorption wavelength, nm**	**Two-photon absorption cross section, GM**
Flu1	1	693	37
Flu1-FADH2	15	683	39
Flu2	1	732	186
Flu2-FADH2	20	729	230