

## Applications of the simplified time-dependent density functional theory (sTD-DFT) and the new eXact integral – sTD-DFT (XsTD-DFT) to evaluate two-photon absorption of large systems

The evaluation of the two-photon (2P) absorption (2PA) of large systems is beyond the reach of current *ab initio* methods. We recently overcome this limit by implementing the ultra-fast evaluation of 2PA cross-sections ( $\sigma_{2PA}$ ) with the simplified time-dependent density functional theory (sTD-DFT) as well as by introducing a more accurate scheme: the eXact integral - sTD-DFT (XsTD-DFT). In this PhD project, we will apply both methods to characterize the 2PA of two types of large and challenging systems: fluorescent proteins (FPs) and cocrystals, targeting applications in bio-imaging and 3D optical data storage. A new all-atom quantum chemistry (QC) methodology will be established and design guidelines to improve the experiment will be proposed.

### Context

Two-photon absorption is a nonlinear optical (NLO) phenomenon in which a compound absorbs simultaneously two photons. The molecule may reemit one photon at half of the excitation wavelength. It is used in 2P-excited near-infrared-emitting materials (2P-Ms) for applications in bio-imaging, optical data storage, microfabrication, and photodynamic therapy.

2P excitation microscopy (TPEM)<sup>1,2</sup> provides high resolution deep tissue imaging. FPs<sup>3</sup> can be used as genetically encoded fluorescent tags. A rainbow of FPs with enhanced/tuned biochemical and optical properties are available.<sup>4</sup> FP engineering aims to develop bright FPs, with varying color, and providing images with sufficient contrast with respect to the auto-fluorescent background.<sup>4</sup>

As 2P-excited near-infrared-emitting materials (2P-Ms), organic cocrystals have lately gained attention.<sup>5,6</sup> Cocrystallization is an elegant way to fine-tune properties of organic molecules by non-covalent interactions. Usually, large  $\sigma_{2PA}$  are obtained by increasing electron delocalization and changing donor-acceptor groups to produce charge transfer (CT) states. In cocrystals, CT states with large  $\sigma_{2PA}$  can be obtained via supramolecular architecture.<sup>6</sup>

### Objectives

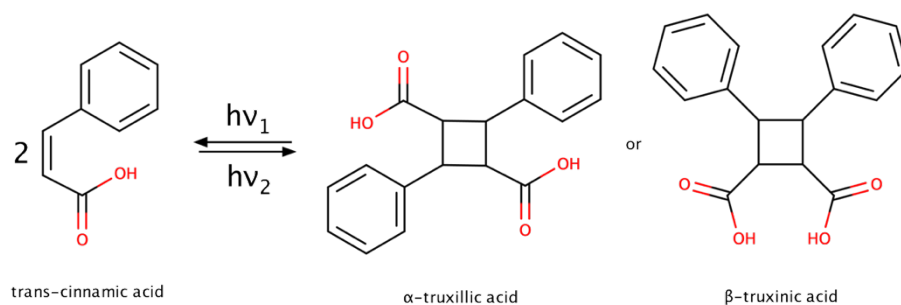
The main objective of this project is for a PhD student to develop an expertise in the determination of 2PA especially with both sTD-DFT and XsTD-DFT methods for two applications:

#### WP1: All-atom QC characterization of the 2PA of FPs

Recently, we proposed a new all-atom QC methodology to compute the second harmonic generation of FPs.<sup>7</sup> This was the first time that a NLO property of a system as big as a protein

was characterized fully quantum mechanically, thanks to our sTD-DFT implementation.<sup>8,9</sup> This study was the first step towards extension to other NLO properties. **WP1** aims at investigating the 2PA of FPs by both sTD-DFT and XsTD-DFT methods and at developing a new all-atom QC methodology. We will be able to understand their structure/property relationship to provide new insights in order to improve their  $\sigma_{2PA}$  for applications in TPDM.

**WP2:** 2P-induced reversible photodimerization of trans-cinnamic acid, chalcone, and coumarin derivatives cococrystals



**Figure 4:** The photodimerizations of trans-cinnamic acid.

In the solid state, the [2+2] photodimerizations of trans-cinnamic acid<sup>10</sup> (tCA), coumarin<sup>11</sup> and chalcone derivatives<sup>12</sup> are reversible and can be triggered by 2PA<sup>11,13</sup> that increases the yield and the penetration of the light. The reaction cross-section ( $\Omega_{2P}$ ) is proportional to  $\sigma_{2PA}$ . For tCA (**Fig.4**), two products are formed: the  $\alpha$ -truxillic and  $\beta$ -truxinic acids. By using cococrystal of tCA with dichlororesorcinol or urea, only  $\beta$ -truxinic acid is formed. With the possible application as 3D optical data storage, we propose to use both sTD-DFT and XsTD-DFT methods to screen different types of cococrystals to enhance  $\sigma_{2PA}$  by manufacturing intermolecular CT states, which increase  $\Omega_{2P}$ . Comparisons with experiment will be done in collaboration with Prof. Tom Leysens at UCLouvain for the experimental part.

Other applications will be considered according to the progress in the field.

<b>PhD supervisor:</b>	Marc de Wergifosse
<b>Where:</b>	Theoretical chemistry group, Institute of Condensed Matter and Nanosciences, Université Catholique de Louvain, Belgium
<b>Duration:</b>	4 years
<b>Starting date:</b>	October 2022
<b>Funding:</b>	Seedfund FSR 2022 grant at UCLouvain
<b>Contact:</b>	<a href="mailto:mdewergifosse@gmail.com">mdewergifosse@gmail.com</a>

## References:

- <sup>1</sup> R.K.P. Benninger and D.W. Piston, *Curr. Protoc. Cell Biol.* **59**, 4.11.1 (2013).
- <sup>2</sup> H. Myung Kim and B. Rae Cho, *Chem. Rev.* **115**, 5014 (2015).
- <sup>3</sup> M. Drobizhev, N.S. Makarov, S.E. Tillo, T.E. Hughes, and A. Rebane, *Nat. Methods* **2011** **85**, 393 (2011).
- <sup>4</sup> E.A. Rodriguez, R.E. Campbell, J.Y. Lin, M.Z. Lin, A. Miyawaki, A.E. Palmer, X. Shu, J. Zhang, and R.Y. Tsien, *Trends Biochem. Sci.* **42**, 111 (2017).
- <sup>5</sup> Y. Wang, H. Wu, P. Li, S. Chen, L.O. Jones, M.A. Mosquera, L. Zhang, K. Cai, H. Chen, X.-Y. Chen, C.L. Stern, M.R. Wasielewski, M.A. Ratner, G.C. Schatz, and J.F. Stoddart, *Nat. Commun.* **2020** **111** **11**, 1 (2020).
- <sup>6</sup> C. Dai, Z. Wei, Z. Chen, X. Liu, J. Fan, J. Zhao, C. Zhang, Z. Pang, and S. Han, *Adv. Opt. Mater.* **7**, 1900838 (2019).
- <sup>7</sup> P. Beaujean, B. Champagne, S. Grimme, and M. de Wergifosse, *J. Phys. Chem. Lett.* **12**, 9684 (2021).
- <sup>8</sup> M. de Wergifosse and S. Grimme, *J. Chem. Phys.* **149**, 024108 (2018).
- <sup>9</sup> M. de Wergifosse and S. Grimme, *J. Phys. Chem. A* **125**, 3841 (2021).
- <sup>10</sup> G.M.J. Schmidt, *J. Chem. Soc.* **2014** (1964).
- <sup>11</sup> T. Buckup, A. Southan, H.C. Kim, N. Hampp, and M. Motzkus, *J. Photochem. Photobiol. A Chem.* **210**, 188 (2010).
- <sup>12</sup> J. Träger, S. Härtner, J. Heinzer, H.C. Kim, and N. Hampp, *Chem. Phys. Lett.* **455**, 307 (2008).
- <sup>13</sup> J. B. Benedict and P. Coppens, *J. Phys. Chem. A* **113**, 3116 (2009).