Title	**FUNctional molecules designed from IN SIlico EleMEntary reactions**
PI	**Laura Orian**
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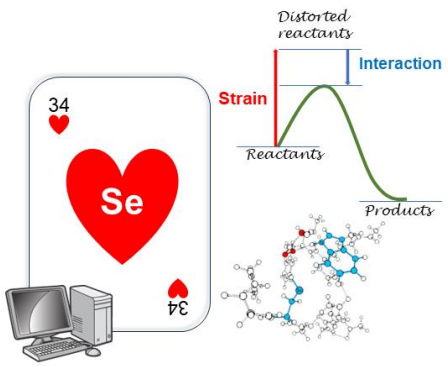
Project description: Nowadays, computational methodologies are well consolidated in a multi-scale range, so that accurate in silico experiments can be carried out on molecules with tenths of atoms as well as on very large systems like biomolecules. An ambitious goal in computational chemistry is the design of functional molecules, i.e. drugs, devices, catalysts, and in many cases inspiration is searched in nature. In this case, a solid and rigorous approach to the design of bio-inspired molecules, i.e. drugs and catalysts, requires investigation of the natural systems as well as a bottom-up approach starting from small model molecules. These studies are intrinsically multi-scale and benefit of data from synthesis and measurements set up by collaborators. Among others, systems of interest for FUN INSIEME are thiol-based enzymes, such as GPx and TrxR, proteins in which the chemistry of chalcogens (selenium and sulfur) is fundamental. In particular, the REDOX state of the catalytic center plays a key-role. The mechanisms of oxidation and reaction with ligands will be studied in biological environment as well as in model systems, to establish the roots of complex redox bio ogy phenomena in elementary chemical reactions. The PhD student will gain experience with advanced computational methodologies, among which quantum chemistry and molecular dynamics approaches, but also machine learning algorithms. In addition, he/she will learn and practice script/programming languages and abilities to work with supercomputers (local and national facilities). Requisites are chemical curiosity, passion for numerical problems and computers and inclination to apply consolidated chemistry background to solve problems.



Publications:

- D. Zeppilli, A. Madabeni, L. Sancineto, L. Bagnoli, C. Santi, L. Orian *Role of Group 12 metals in the reduction of H_2O_2 by Santi's reagent: a computational mechanistic investigation Inorg. Chem.* **62**(42), 17288-17298 (2023)
- Madabeni, L. Orian *The key role of chalcogenurane intermediates in the reduction mechanism of sulfoxides and selenoxides by thiols explored in silico Int. J. Mol. Sc.* **24** 7754 (2023)
- F. B. Omage, A. Madabeni, A. R. Tucci, P. A. Nogara, M. Bortoli, A. dos Santos Rosa, V. N. Ferreira, J. B. T. Rocha, M. Dias Miranda, L. Orian *Diphenyl diselenide and SARS-CoV-2: in silico exploration of the mechanisms of inhibition of Main protease (M^{pro}) and Papain-like protease (PL^{pro}) J. Chem. Inf. Mod.* **63**, 7, 2226-2239 (2023)
- Madabeni, S. Zucchelli, P.A. Nogara, J. B. T. Rocha, L. Orian *In the chalcogenoxide elimination panorama: systematic insight into a key reaction J. Org. Chem.* **87**, 11766−11775 (2022).
- L. Flohé, S. Toppo, L. Orian *The glutathione peroxidase family: discoveries and mechanism Free Rad. Biol. Med.* **187**, 113-122 (2022).

Collaborations/network: Theoretical Chemistry Group VU Amsterdam (The Netherlands) (Prof. F.M. Bickelhaupt and Prof. Célia Fonseca Guerra)