Internship Topic: **Virtual Screening of Chemosensory Receptors (TAS2R)**

Host Laboratory: Institut de Chimie de Nice (ICN) - UMR7272 CNRS – UniCA

Contacts: Dr. Sébastien Fiorucci et Dr. Jérémie Topin (UniCA)
sebastien.fiorucci@univ-cotedazur.fr ; jeremie.topin@univ-cotedazur.fr

Internship Funding: Stipend of approximately 630 euros per month

Duration: 6 months starting from early 2025

Scientific Description: Our brain perceives our olfactory and gustatory environment thanks to chemosensory receptors, particularly those of the G Protein-Coupled Receptor (GPCR) family. From a pharmacological perspective, a molecule responsible for bitter taste must bind to a sensory receptor of the TAS2R family according to the lock-and-key principle. We have 25 bitterness receptors, and recent experimental structures of the TAS2R14 receptor [1,2] open the way for virtual screening of this receptor family to identify new ligands. The ChemSenSim group has a solid expertise in understanding chemical senses using computational approaches ranging from artificial intelligence [3] to molecular dynamics simulations [4] to decipher the molecular basis of olfaction and taste. They have made significant advances in describing mammalian olfactory and gustatory receptors [5,6] and identifying ligands for insect ORs [7,8]. The goal of the internship will be to identify new potential ligands of the TAS2R receptor family through virtual screening, and predictions can be validated by functional characterization with our partners in charge of *in vitro* experiments.

References:

[1] *Bitter taste receptor activation by cholesterol and an intracellular tastant*. Kim, Y., Gumpper, R.H., Liu, Y. et al. Nature, **2024**, 628, 664–671.
[2] *Bitter taste TAS2R14 activation by intracellular tastants and cholesterol*. Hu, X., Ao, W., Gao, M. et al. Nature, **2024**, 631, 459–466.
[3] Matching receptor to odorant with protein language and graph neural networks. M. Hladiš, M. Lalis, S. Fiorucci, J. Topin. International Conference on Learning Representation (ICLR), **2023**, https://openreview.net/forum?id=q9VherQJd8_
[4] *Odorant receptor 7D4 activation dynamics.* C.A. de March, **J. Topin**, E. Bruguera, G. Novikov, K. Ikegami, H. Matsunami, J. Golebiowski. Angew. Chem. Int. Ed., **2018**, 57, 4554-4558
[5] *Novel scaffold of natural compound eliciting sweet taste revealed by machine learning.* C. Bouysset, C. Belloir, S. Antonczak, L. Briand, **S. Fiorucci**. Food Chem., **2020**, 324, 126864.
[6] *Functional Molecular Switches of Mammalian G Protein-Coupled Bitter-Taste Receptors.* **J. Topin**, C. Bouysset, J. Pacalon, Y. Kim, M. Rhyu, **S. Fiorucci**, J. Golebiowski. Cell. Mol. Life Sci., **2021**, 78, 7605-7615
[7] *Reverse chemical ecology in a moth: machine learning on odorant receptors identifies new behaviorally active agonists.* G. Caballero-Vidal, C. Bouysset, J. Gévar, H. Mbouzid, C. Nara, J. Delaroche, J. Golebiowski, N. Montagné, **S. Fiorucci**, E. Jacquin-Joly. Cell. Mol. Life Sci., **2021**, 78, 6593-6603
[8] *Accelerating Ligand Discovery for Insect Odorant Receptors.* A. Comte, M. Lalis, L. Brajon, R. Moracci, N. Montagné, **J. Topin**, E. Jacquin-Joly, **S. Fiorucci**. submitted. BioRxiv, **2024**, doi : 10.1101/2024.09.12.612620v1

Keywords: GPCR, TAS2R, IA, virtual screening.

Methodology: docking, homology modeling, machine learning.

Skills sought: The candidate should have a degree in physical chemistry, physics, or biochemistry and have a strong interest in biomolecular simulations. Knowledge of structural biology is essential to understand the systems being studied. Experience with Linux environments and Python programming will be a clear advantage.