

Tutorial: Membrane protein modeling: Insights into GPCRs

Alejandro Giorgetti (University of Verona)

Introduction:

Human G protein coupled receptors or GPCRs belong to the largest membrane-bound receptor family expressed by humans. This family encompasses 4% of the protein-coding genes in humans. Remarkably, GPCRs participate in about the 80% of the signaling processes in the brain. Thus, a detailed characterization of the molecular mechanisms underlying their function is key to understand molecular processing of perception in human brain and this implies the characterization of the interaction with their natural ligands.

The recent progress in GPCRs crystallography opened an unprecedented venue for receptor–ligand. Indeed, the 2012 Nobel Prize in Chemistry was awarded to Brian Kobilka (Stanford University) and Robert Lefkowitz (Duke University) for their structural work on the GPCRs (http://www.nobelprize.org/nobel_prizes/chemistry/laureates/2012/). However, the lack of structural data for about the 95% of the members of the family, calls upon the development and application of *ad hoc* computational-based approaches to investigate structure, dynamics and function of these GPCRs. Comparative modeling technique is the key tool for obtaining three-dimensional (3D) models of the receptors when experimental structural data is lacking. Functional assays-validated bioinformatics approaches, complemented with molecular docking provide structural insights on agonist–receptors interactions.

This tutorial will introduce the basic elements of bioinformatics aimed at the characterization of structural/functional assessment of GPCRs.

Arguments:

- Introduction to homology modeling
- Template search and alignments using Hidden Markov models
- Protein structure prediction of membrane proteins in particular GPCRs
- Introduction and exercise using GOMoDo server.

Organization:

The day will consist in an introduction of theoretical concepts followed by exercises at the PC. State-of-art methods that will be used are all free, available through web-servers, thus no complex installation of programs is needed.