Structural studies of G protein coupled receptors by using Molecular dynamics simulation and docking studies

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G protein coupled receptors (GPCRs) represent one of the largest proteins in mammals that play a key role in the transmission of external signals to the cell interior. GPCRs can be activated by ligands, hormones, light, as many others. GPCRs play a key role in an incredible array of functions in the human body, and increased understanding of these receptors has greatly affected modern medicine. In fact, researchers estimate that about 50% of all the marketed drugs act binding to GPCRs.

As their name implies, GPCRs interact with G proteins in the plasma membrane. When an external signaling molecule binds to a GPCR, it causes a conformational change in the membrane protein. Then, this change triggers the interaction the GPCR and a nearby G protein.

Nowadays, computational techniques such as Molecular dynamics (MD) simulations represent a powerful tool to detect these conformational changes that occur in the membrane proteins as result of ligand binding. On the other side, docking analysis permit to predict not only the affinity of the ligands of interest on the membrane proteins but also to identify the residues that are involved in the molecular recognition in the binding process.

Our works presents some examples of MD simulations of GPCRs by using NAMD Program. In this process, we have employed the following force fields, CHARMM22 for protein and CHARMM27 for lipids, and TIP3 model for water molecules. Specific server (OPM) was used to orient the membrane proteins in the lipid bilayer. Structural analysis was carried out by using Carma Program. From these results we were able to investigate the stability of the proteins, identification of most flexible residues, and residues which could be involved in the molecular recognition process. Moreover, our results permitted to get some insights about the design of known or new drugs that target these important receptors.