The class of membrane proteins called G-protein-coupled-receptors (GPCRs) mediate important physiological processes like cell-to-cell communication, and are also implicated in the pathogenesis of many diseases. Thus the subfamily of GPCRs form one of the most prominent drug targets. An understanding of the molecular level interactions of agonists and antagonists to GPCRs would greatly aid drug design of these membrane proteins. GPCRs activate in multiple conformations going from active to inactive states. Hence structure based drug design methods have to take this dynamic aspect into account while understanding the binding site of agonists versus antagonists. I will discuss the developments we have made in predicting various low-energy packing of the transmembrane helices that could lead to active versus inactive states. The results of applying the improved methods to rhodopsin will be discussed. I will also take one example of a GPCR, adrenergic receptor, and discuss the process in going from the structure and function prediction for this receptor, with agonists and antagonists bound, compare subtype selectivity to antagonists binding and also discuss the results of conformational changes that occur on agonist binding tracked with molecular dynamics with explicit lipid/water mixture.

A brief discussion on the progress made in olfactory receptors and overview of the various computational methods integrated together as tools for flexible protein docking will be discussed.