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Ligand binding modes for serotonin receptors

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The first 3D structure of the G protein-coupled receptor (bovine rhodopsin) was published in 2000 [1]; since then, it has served as a template for the homology modeling of hundreds of other GPCRs, including the numerous subtypes of serotonin receptors. Homology models are tools for the structure-based drug design, virtual screening of compound libraries, and they also enable an investigation of the phenomena involved in receptor activation at the atomic detail level using molecular dynamics simulations.

The lecture focuses on summarizing the available rhodopsin-based serotonin receptors models. First, different approaches used in their construction, in a context of recent advances in modeling methodologies are presented. Next, the experimental site-directed mutagenesis data on serotonin receptors is shortly reviewed and its application in the process of receptor modeling and ligand binding mode prediction is discussed. The differences in amino acid composition of all the binding sites are then emphasized, concentrating on their possible influence on ligands selectivity. Finally, the binding modes proposed by different authors are compared and discussed in details. Special attention is paid to arylpiperazine type of ligands due to their importance, multireceptoral profile and authors own experience [2,3].

References

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