Chemistry Central Journal

Poster presentation

Adrenoceptors: ligand-activated molecular dynamics

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from 3rd German Conference on Chemoinformatics
Goslar, Germany. 11-13 November 2007

Published: 26 March 2008

Chemistry Central Journal 2008, **2**(Suppl 1):P36 doi:10.1186/1752-153X-2-S1-P36

This abstract is available from: http://www.journal.chemistrycentral.com/content/2/S1/P36

Adrenoceptors [1] belong to class A of the superfamily of G protein coupled receptors (GPCRs) that transduce signals across the cell membrane, thus initiating a variety of intracellular biochemical events. The adrenoceptors subtypes (α_{1A}, α_{1B} and α_{1D}) are of particular therapeutic interest due to their important role in benign prostatic hyperplasia, a medical condition associated with old age.

Our knowledge of the structure of GPCRs and particularly in adrenoceptors is limited. The only available GPCR crystal structure is that of bovine rhodopsin, which has been characterised with different resolutions, being the most refined 2.2 Å (pdb: 1U19[fig 1]). Utilising the structural data from this structure we were able to produce homology models of the different subtypes α_{1A}- α_{1B}- and α_{1D}-adrenoceptor.

An optimisation and protonation state determination of a selection of ligands has been performed using B3LYP with a 6-31G* basis set. This allowed us to determine the nitrogen of the ligand which is most likely to be protonated. This plays a significant part in ligand-protein interaction.

Molecular dynamics (using the AMBER 9.0 package) has been used to simulate the structural movements of the adrenoceptors due to the influence of the ligands [2]. This results in structures that can possibly represent the active form of the receptor.

References

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2. Kinsella G, Rozas I, Watson G: *J Med Chem* 2006, **49:**501-510.