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# Pseudoreceptor-based pocket selection in a molecular dynamics simulation of the histamine H4 receptor

T Werner*, T Geppert, Y Tanrikulu, E Proschak and G Schneider

Address: Johann Wolfgang Goethe-University, Siesmayerstr. 70, D-60323 Frankfurt, Germany
* Corresponding author

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There is a renewed interest in pseudoreceptor models which enable computational chemists to bridge the gap of ligand- and receptor-based drug design [1]. We developed a pseudoreceptor model for the histamine H4 receptor (H4R) based on five potent antagonists representing different chemotypes. Here we present the selection of potential ligand binding pockets that occur during molecular dynamics (MD) simulations of a homology-based receptor model. We present a method for prioritizing receptor models according to their match with the consensus ligand-binding mode represented by the pseudoreceptor. In this way, ligand information can be transferred to receptor-based modelling.

We use Geometric Hashing to match three-dimensional points in Cartesion space [2]. This allows for the rapid translation- and rotation-free comparison of atom coordinates, which also permits partial matching. The only prerequisite is a hash table, which uses distance triplets as hash keys. Each time a distance triplet occurring in the candidate point set which corresponds to an existing key, the match is represented by a vote of the respective key. Finally, the global match of both point sets can be easily extracted by selection of voted distance triplets.

The results revealed a preferred ligand-binding pocket in H4R, which would not have been identified using an unrefined homology model of the protein. The key idea was to rely on ligand information by pseudoreceptor modelling.

## References

1. Tanrikulu Y, Schneider G: *Nature Rev Drug Discov* 2008, **7**:667.
2. Wolfson HJ, Rigoutsos I: *IEEE Comp Sci Engin* 1997, **11**:263.