## **POSTER PRESENTATION**



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# The assessment of computationally derived protein ensembles in protein-ligand docking

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*From* 7th German Conference on Chemoinformatics: 25 CIC-Workshop Goslar, Germany. 6-8 November 2011

The inclusion of receptor flexibility in protein-ligand docking experiments has become a major research interest in drug discovery [1,2]. One of the possible methods applied is the use of multiple discrete protein conformations, so called ensemble docking [3,4]. With computational techniques like Molecular Dynamics (MD) a large number of different conformations can be generated, not all of which can or should be included in the docking or virtual screening process [5]. The question arises if and how suitable protein conformations can be selected systematically *a priori* based on quantifiable conformational features.

For neuraminidase and cyclin-dependent kinase II (CDK2), snapshots of MD simulation trajectories have been clustered based on different structural properties using a variety of clustering methods. To establish a possible correlation between docking performance and target conformational attributes the clustered snapshots have been subjected to extensive self- and cross-docking experiments as well as virtual screening using the GOLD docking programme. It is shown that conformationally similar snapshots do not necessarily result in a similar docking or virtual screening performance. The selection of the particular structural property on which to base the clustering appears to be the essential problem.

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Published: 1 May 2012

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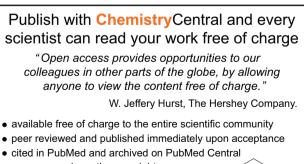


#### References

- 1. Carlson HA: Protein flexibility and drug design: how to hit a moving target. *Curr Opin Chem Biol* 2002, **6**:447-452.
- Durrant JD, McCammon JA: Computer-aided drug-discovery techniques that account for receptor flexibility. Curr Opin Pharmacol 2010, 10:770-774.
- Barril X, Morley DS: Unveiling the full potential of flexible receptor docking using multiple crystallographic structures. J Med Chem 2005, 48:4432-4443.
- Huang S-Y, Zou H: Ensemble docking of multiple protein structures: considering protein structural variations in molecular docking. *Proteins* 2007, 66:399-421.
- Lin J-H, Perryman AL, Schames JR, McCammon JA: Computational drug design accomodating receptor flexibility: the relaxed complex scheme. J Am Chem Soc 2002, 124:5632-5633.

### doi:10.1186/1758-2946-4-S1-P34

**Cite this article as:** Sander *et al.*: **The assessment of computationally derived protein ensembles in protein-ligand docking.** *Journal of Cheminformatics* 2012 **4**(Suppl 1):P34.



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