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

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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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References

1. Carlson HA: **Protein flexibility and drug design: how to hit a moving target.** *Curr Opin Chem Biol* 2002, **6**:447-452.
2. Durrant JD, McCammon JA: **Computer-aided drug-discovery techniques that account for receptor flexibility.** *Curr Opin Pharmacol* 2010, **10**:770-774.
3. Barril X, Morley DS: **Unveiling the full potential of flexible receptor docking using multiple crystallographic structures.** *J Med Chem* 2005, **48**:4432-4443.
4. Huang S-Y, Zou H: **Ensemble docking of multiple protein structures: considering protein structural variations in molecular docking.** *Proteins* 2007, **66**:399-421.
5. 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.

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