

Exploring an accurate ligand-binding pose: ensemble-based docking study

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Molecular docking explores the binding modes of interacting molecules. The technique is increasingly popular for a ligand screening and drug design. However molecular docking is still not sufficient method for these purposes. This is due to that the conventional docking method does not take into account the structural flexibility of receptor. Poor scoring function to estimate the ligand-receptor affinity should be also responsible for a low computational accuracy. The introduce of the structural flexibility and the improving the estimation of intermolecular interaction are required to find the appropriate compounds which have better affinity with the target protein. In this study, we thus first carry out molecular dynamics simulations of apo protein system to sample the flexible protein structure and then dock the ligands to the binding pocket of those protein structures. By estimating the binding free energies and ranking those, we find the appropriate compounds and binding pose for the target protein. The developed method (calculation procedure) and application to accrual system are discussed.