Accurate Binding Pose Predicton with Induced-Fit Posing (IFP)

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Abstract:

Accurate predicton of binding poses is a fundamental requirement in structure-based design. High accuracy can be easily achieved in lead optimization, where most molecules of interest share significant similarities in shape and chemical features with a known crystallographic ligand. However, in the hit-to-lead stage, multiple chemotypes are often pursued, many of which may not be similar in their 3D pose to known ligands, thus reducing the reliability and accuracy of pose prediction. We have recently introduced Induced-Fit Posing (IFP) to enhance pose prediction accuracy in hit-to-lead scenarios. IFP provides new pose prediction functionality combining docking with Short Trajectory Molecular Dynamics (STMD) to sample both ligand and protein binding site conformations. In this talk, we will present the basic protocol of this method as well as compare its accuracy with standard docking methods.

Keywords: Induced Fit Posing, Short Trajectory Molecular Dynamics, Binding pose