# Local Interaction Density (LID) in ligand/protein docking

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Scoring functions in molecular docking often fail to select the correct pose in a set of generated conformations [1]. An efficient post-processing approach uses similarity to reference binding modes to filter irrelevant poses [2]. The success of rescoring depends on the coverage of binding modes by the reference molecules. In a recent study of the PDB binding mode, we showed that 10 ligands well cover all interactions of the target site [3]. Therefore, we propose to merge binding information of all reference ligands into a consensus map. We name the scoring method Local Interaction Density (LID) [4]. LID performance is compared to that of a state-of-the-art similarity-based method, GRIM [5], in pose prediction and virtual screening.

LID was evaluated in pose prediction on 19 targets from a high quality dataset [6] (http://bioinfo-pharma.u-strasbg.fr/labwebsite/downloads/Fragdock.zip) and in virtual screening on 8 targets of the DUD-E dataset [7] and 1 target of a challenging dataset based on experimental data [8]. A ligand was docked into all available protein structures except the one it was co-crystallized with (pose prediction) or into several representative protein structures (virtual screening) with PLANTS and ChemPLP scoring function [9]. Interactions were detected using GRIM module of IChem [10]. LID is coded in Python3 and will be implemented in IChem.

In pose prediction, GRIM and LID significantly increase the proportion of correct poses as compared to ChemPLP scoring. In virtual screening the two methods improve by ≈15% the AUC and the enrichment factor at 5% by 6 fold. Overall Grim and LID show similar performance with a slight advantage for GRIM rescoring of large ligand poses. However, LID is 40 to 230 times faster than GRIM.

In conclusion, rescoring using binding mode is as successful when taking binding information as a whole (LID) as when considering references separately (GRIM). LID is suitable to big data analyses (typically docking of many ligands in multiple structures of the target site).

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