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Drugscore^{Maps} visualizing similarities in protein-ligand interactions

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A new approach will be presented that graphical evaluate Drugscore Fingerprints [1] using emergent self-organizing maps (ESOMs) [2] for clustering of binding geometries to identify similarities among protein-ligand interactions in data sets of protein-ligand poses. The result of the clustering shows a landscape of valleys and mountains and is easy to interpret. Similar binding geometries are clustered together within a valley surrounded by mountains. Colouring of the data points based on Drugscore^{CSD} ranks [3] or known affinity data reveals additional information.

A survey of the Wang [4] and the Astex Diverse Dataset [5] exhibits that Drugscore^{Maps} is useful for the evaluation of docking poses and it supports the search for the correct low energy binding mode. Drugscore^{Maps} combines the information about similar protein-ligand poses with the information about interaction patterns (represented by Drugscore). Clearly separated clusters with high-ranked docking poses are an indication of good binding geometries and, in contrast, a lack of clustering seems to indicate a failing of the docking procedure. Additionally, bad geometries with a high rank and situations were the scoring function fails can be identified. Furthermore, an analysis of a successfully used QSAR dataset reveals a first indication that Drugscore^{Maps} is also useful for visualization of structure-activity landscape within this dataset. Compared to other fingerprint based methods, Drugscore^{Maps} (using Drugscore^{FP}) integrates protein information for creating these structure-activity landscapes.

Drugscore^{Maps} benefits by ease of visualization. Protein-ligand similarity is included in one image that gives you a direct overview of the used dataset. One gains information about similar high-ranked docking poses and dissimilar docking poses or an overview over the structure-activity landscape without looking at all docking solutions or protein-ligand poses.

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