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pharmACOphore: multiple flexible ligand alignment based on ant colony optimization

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Molecular alignment of biologically active compounds is a key technique in ligand-based drug design. Such alignments can be used for similarity-based identification of new compounds by using known active template structures as seeds. Furthermore, alignments allow for the identification of potential pharmacophoric features in a set of chemically divers, biologically active molecules.

Here, pharmACOphore is presented, a new approach for pairwise as well as multiple flexible alignments of ligands based on ant colony optimization (ACO) [1]. Translational, rotational and torsional degrees of freedom of all ligand structures are encoded on a pheromone vector (Figure 1). The artificial ant colony uses this representation to mark favourable values for each degree of freedom by depositing a pheromone trail onto the corresponding pheromone vector. The amount of pheromone deposited directly depends on the solution quality, assessed by the scoring function.

The scoring function was parameterized by reproducing reference alignments taken from four different proteins. The performance of the new alignment algorithm will be demonstrated by pairwise alignments obtained for examples from the FlexS data set [2] and by an additional example for multiple flexible alignment.

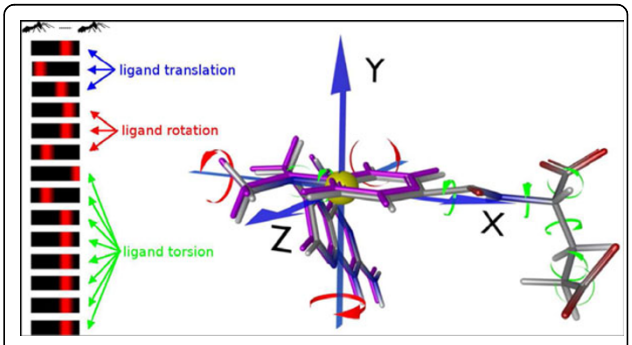

Figure 1

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