Subject: Re: Evolutionary algorithm
Posted by thomas on Thu, 07 Mar 2019 15:25:14 GMT
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When you have a few active molecules on a given target and intend to search a large compound collection for similar compounds in order to find more potential active ones, then the fastest approach is to use chemical(=graph) similarity of some kind, e.g. the SkeletonSpheres descriptor. Very similar compounds often have similar activities. The drawback of this approach is that this won't do scaffold hopping, which mean that you won't find structures with a substantially different structure core or substitution pattern. The idea of the flexophore (https://pubs.acs.org/doi/abs/10.1021/ci700359j addresses this issue. It was designed to compare the representative conformer sets of two molecules concerning their protein-binding potential. It classifies atoms that may contribute to binding using PDB statistics. The flexophore considers molecules similar, if they contains atoms that have similar binding behaviour to protein atoms if these atoms' relative 3D orientations are also similar. Depending on the conformational flexibility of individual molecules and the target you may achieve a significantly higher hit rate compared to random or diverse selection, if you preselect screening candidates by flexophore similarity.