Subject: Skelspheres descriptor
Posted by ECG93 on Fri, 04 Mar 2022 13:23:37 GMT
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It is reported that Skelspheres considers stereochemistry, but how much is the threedimensionality considered? For example when dealing with a library of molecules with high sp3 fraction.

Probably flexophore descriptor would be more appropriate for "Analyse similarity cliffs", but for PCA Skelspheres can't be used as it is not a vector.

Subject: Re: Skelspheres descriptor
Posted by thomas on Sat, 02 Apr 2022 15:15:06 GMT
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The SkelSpheres based similarity is basically a measure of how many circular fragments match between two molecules in regard to both molecules' total count of circular fragments (up to a radius of 5 atoms). Since these fragments largely overlap and since stereo centers within these fragments need to match, a high similarity implicitly goes along with similar 3D-shape of at least a large part of the molecule.

In regard to ligand-to-target binding similarity, the Flexophore is certainly more appropriate than the SkelSpheres, because it allows for scaffold hopping. Even better would be the PheSA shape and pharmacophore similarity, but that requires conformers and is computationally more demanding. Therefore, PheSA similarity is not implemented as standard descriptor and only accessible as 'Superpose conformers...' and as fitness criterion in the evolutionary library creation. The same is true for ligand-to-protein docking.