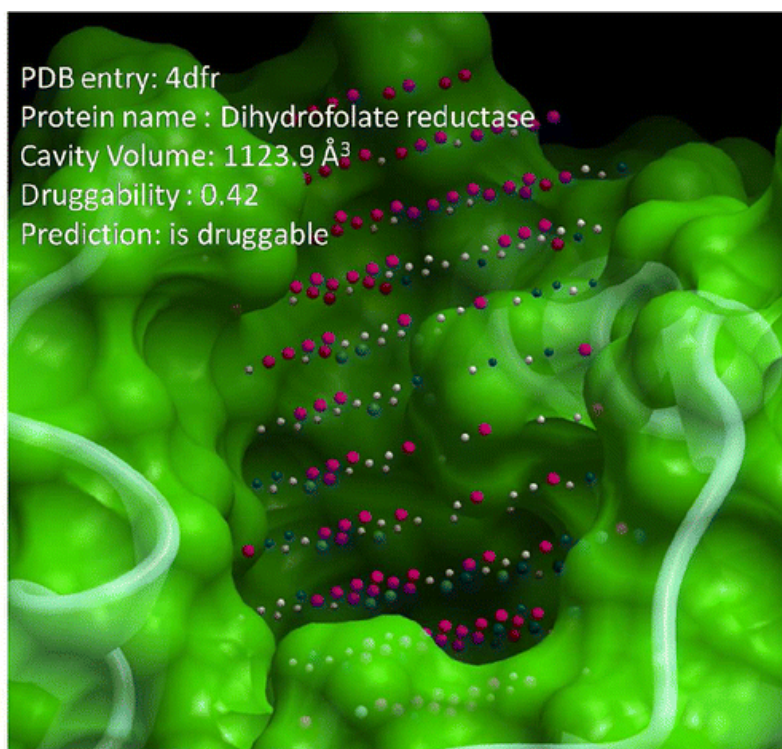


## Comparison and Druggability Prediction of Protein–Ligand Binding Sites from Pharmacophore-Annotated Cavity Shapes

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# Shaper

## How-To use Shaper :

Shaper gives the possibility to align 2 cavities and scores the shape and physico-chemical overlaps.

```
./Shaper -r refcav -c compcav [-f cffFile] [-o output] [- -  
Debug] [-rn refcav_name] [-cn compcav_name] [-s simil]
```

### Minimal Usage:

```
./Shaper -r refcav -c compcav
```

-r	Reference cavity file
-c	Comparison cavity file

### Optional flag :

-f cffFile	ColorForceField file. If not defined, will automatically used the default one.
-o output	Output the aligned comparison cavity. Preferred output file format : PDB.
-rn	Name of the reference cavity. Useful only for the Shape_res.csv file
-cn	Name of the comparison ligand or cavity. Useful only for the Shape_res.csv file
-s simil	If known similarity, set to 1. 0 otherwise. For classification purpose. Useful only for the Shape_res.csv file.
--Debug	Activate the verbose mode

**Note :** For output cavity files, PDB file format is preferred from MOL2 file format because OpenEye output parser will add in MOL2 hydrogens. With PDB it keeps the same atoms order and doesn't add any atoms.

## Scoring and alignment example:

You will find in the archive 2 entries: 1dah and 1a82. To align these cavities, you simply need to specify the path of both “cavity 6” files.

```
../Shaper -rn 1dah -cn 1a82 -r 1dah/1dah_protein_CAVITY_6.mol2 -c  
1a82/1a82_protein_CAVITY_6.mol2 -o output.pdb
```

### Output results:

```
1 Reference file : ../1dah/1dah_protein_CAVITY_6.mol2 ; Num Confs : 1  
2 Comparison file : ../1a82/1a82_protein_CAVITY_6.mol2  
3 _____  
4 Tanim FitTversky RefTversky  
5 COLOR: 0.59 0.717 0.769  
6 FIT: 0.889 0.932 0.889  
7 COMBO: 1.48 1.65 1.48
```

Shaper output 9 different scores. Only two have been kept for classification: Color Tanimoto and Color Ref Tversky. However, it is always interesting to know the fit score (shape overlap) between the two cavities.

Moreover, Shaper also automatically generated a Shape\_res.csv file that gives condensed results of multiple alignments into one single file. If you re-run the execution of Shaper, the same values will be outputted at the end of the file.

### Shape\_res.csv:

Ref	Comp	Simil	ColorTc	ColorRefTversky	ColorFitTversky
1dah	1a82	-1	0.59	0.769	0.717

### Align a protein/ligand complex based on Shaper alignment:

Shaper will only align and score cavities based on their shape and color complementarity. However, it is unable to align the corresponding protein/ligand complex. Therefore, you'll find in this archive a third program, RotaMole, developed in the lab, which allow to retrieve the rotation matrix and the translation vector generated by Shaper and apply it to any given file, i.e the protein and the ligand. The Shaper example above showed an alignment of 1a82 cavity on 1dah cavity. Since we asked for an output file, the 1a82 aligned cavity is outputted as *output.pdb*. We can use RotaMole with this output to align protein/ligand complex, as follow:

```
../RotaMole -r output.pdb -c 1a82/1a82_protein_CAVITY_6.mol2 -a  
1a82/protein.mol2 1a82/ligand.mol2
```

Rotamole will output the aligned protein and ligand of 1a82 protein as *rot\_protein.mol2* and *rot\_ligand.mol2*. If you open your favorite molecular viewer and load *1dah/protein.mol2*, *1dah/ligand.mol2*, *rot\_protein.mol2* and *rot\_ligand.mol2*, you'll see both protein/ligand complex aligned.