

3D Screen

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Introduction

3D Screen is a search tool that offers a new and fast similarity search strategy for three dimensional molecular structures. It helps the top ranking of molecules regarding their 3D structures.

Main Aspects

- 3D Screen tool handles the most common molecular file types.
 - mol, rgf, sdf, smiles, mol2, pdb, cdx, cdxml, etc.
- The alignment process is tuneable according to user interest.
- The results can be presented in MarvinView and MarvinSpace as well.
- Enrichment can be applied for assessing the 3D screening performance and protocol optimization.

Methods

Two different methods are available in 3D Screen to compare molecules according to their three dimensional structure.

- 'Shape' scores full molecular shape similarity. The result of this algorithm derives from the van der Waals volume overlap of molecular pairs.
- 'Match' similarity score is based on calculating the atomic distances within the query and target molecules respectively. Atom type, 3D geometry and conformational flexibility are incorporated in this method.

How to Use

General

3D Screen is a command line tool for three dimensional similarity comparison of molecular pairs in batch mode.

- To run 3D Screen, you need to have JChem 5.5 installed on your computer.
- For information on usage of the tool, launch the command line script `screen3d` without any parameters from `ChemAxon\JChem\bin` folder.
- The practical screening process consists of two separate steps.
 - The first step is the conversion of molecular files to binary files.
 - The second step is the screening of target molecules according to query criteria.
- There are optional commands for special settings e.g., considering the structure flexibility or selecting output file formats.

Input file generation

3D Screen tool works with binary files generated from the molecular files in the first step. This action has to be run once for the query and once for the target molecule during the search process. These binary files are the basis for the virtual screening.

Command

```
screen3d_g [name of molecule file]
```

g: Generates binary file (extension *.ser).
[name of mol. file]: Name of the appropriate molecular file (and its path).
(_: space)

Optional commands

```
screen3d_g [name of molecule file] [-F] [-match] [-oformat parameter] [-pharm]
```

Considers molecule flexible, if possible. (Default setting is rigid.)
-F: Suggestion: Keep targets and query flexible during the preprocessing step. You can freeze the structures later with -frq switch in the screening step.
-match: Generates input data for 'Match' screen method that is also valid for 'Shape' screen method. (Default data generation is for 'Shape' method.)
-oformat: Sets the extension of the viewable output file. (Default setting is mrv but other molecular formats are also available.)
-pharm: Sets the atom coloring according to pharmacophoric properties. (Default setting is extended atom types.)

Virtual screening I.

Perform screen process by using 'Shape' method.

Command

```
screen3d_s -t [binary file of target molecule] -q [binary file of query molecule]
```

s: Starts screening the target and query molecules.
-t *.ser: Adds binary file of the target molecule(s).
-q *.ser: Adds binary file of the query molecule(s).

Optional commands

```
screen3d_s -t [* .ser of target molecule] -q [* .ser of query molecule] [-shape/match] [-c comment] [-conf value] [-accurate/fast] [-frq] [-oformat parameter]
```

-match: Applies 'Match' similarity algorithm. (Default setting is Shape.)
-frq: Forces the structure of query molecule as rigid.
-c comment: Adds comment for a single screen run.
-conf value: Defines the number of generated initial conformers for 'Shape' algorithm, or sets the number of conformers to remember 'Match' algorithm. (Default setting is 2.)
-oformat: Sets the extension of the visual output file. (Default setting is mrv, but other molecular format can also be set.)

- accurate or -fast: Specifies the alignment accuracy in method 'Shape'. The quality can be fast, normal or accurate. (Default setting is normal.)

Virtual screening II.

You can screen through the molecules of an entire molecular file and find similar 3D structures among its entries by 'Shape' or 'Match' algorithm. The calculated alignment matrix contains all the possible alignment pairs.

Command

```
screen3d_s_t_[binary file of molecules]_a_[shape/match]
```

- a shape: Compares entries of the molecular file by shape algorithm.
- a match: Compares entries of the molecular file by match algorithm.

Results

The result of the screening process is obtained in two separate files. One is a text file, containing all the collected data during 3D screening, and an output file, that can be directly loaded to MarvinView or MarvinSpace to visualize the aligned pose.

Evaluation

The evaluation of results after three dimensional screening can be obtained as enrichment plot that serves as a validation of the screening method.

Command

```
screen3d_e_[*.txt, output for active]_[*.txt, output for inactive]
```

- e: Calculates Enrichment of screening.

Example

Preprocessing

```
c:\Program Files\ChemAxon\JChem\bin>screen3d g 1CBX_lig.mol

Calculate distance ranges : 1CBX_lig.mol
2. t: 154 ms
3. t: 5 ms
4. t: 19 ms
5. t: 26 ms
6. t: 26 ms
7. t: 11 ms
8. t: 3 ms
9. t: 8 ms
10. t: 2 ms
...
c:\Program Files\ChemAxon\JChem\bin>screen3d g AMIDES.SDF

Calculate distance ranges : AMIDES.SDF
2. t: 321 ms
3. t: 125 ms
4. t: 48 ms
5. t: 86 ms
6. t: 88 ms
7. t: 30 ms
8. t: 142 ms
9. t: 147 ms
10. t: 59 ms
...

```

Screening

```
c:\Program Files\ChemAxon\JChem\bin>screen3d s -t AMIDES.ser
-q 1CBX_lig.ser
write aligned structures to: AMIDES_aligned.mrv
Mem: 483,4 MB
similarity: chemaxon.marvin.alignment.PairwiseAlignment
seq. 3sim. 3DTanimoto t(ms)
0 -71,52 0.1354383642202589 t: 53
1 -278,14 0.5606163404515209 t: 29
2 -237,14 0.47465295020949655 t: 17
3 -162,02 0.30292976462396587 t: 18
4 -338,26 0.4850445413663752 t: 24
5 -71.51 0.15038703161420217 t: 10

```

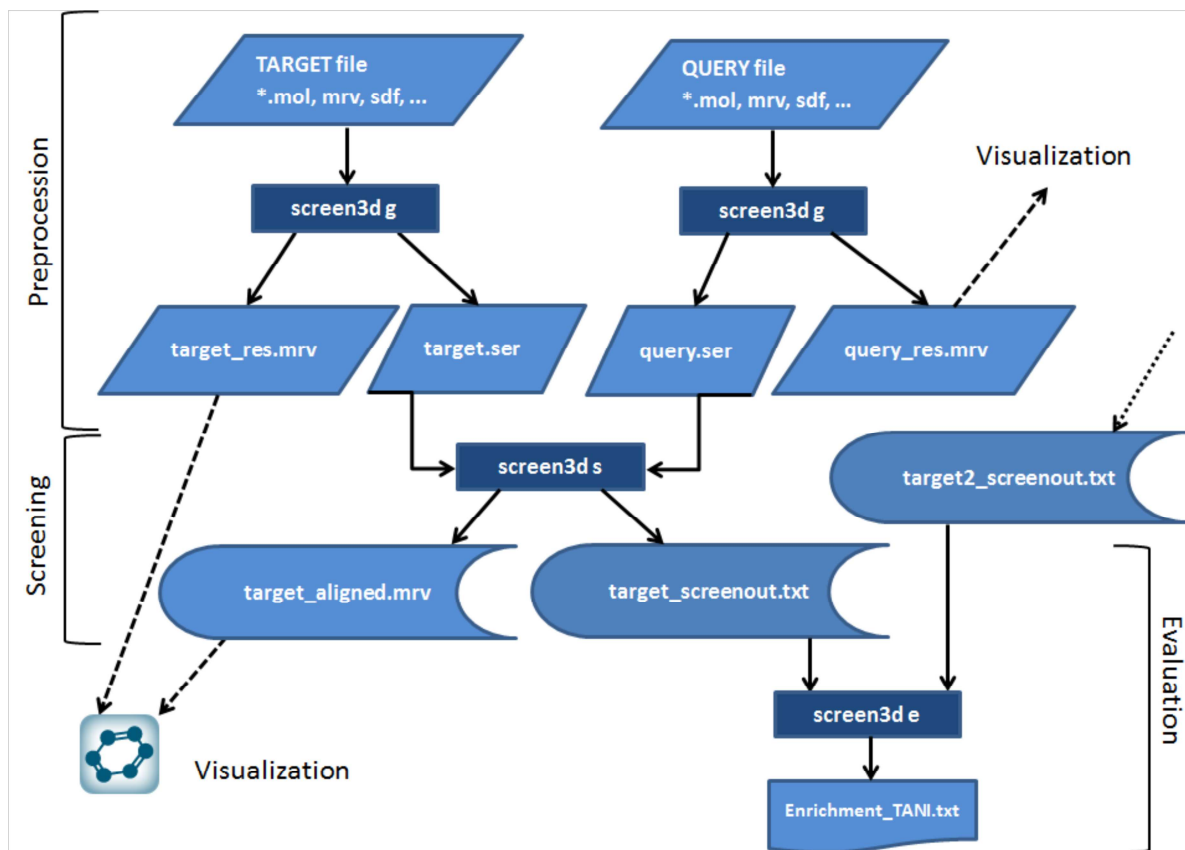


Figure 1 Input and output file formats around screen3d processes