BRFAA
BIOMEDICAL RESEARCH FOUNDATION
ACADEMY OF ATHENS

ChemBioServer

- Uploading and Browsing Compounds in 2D and 3D
- Filtering of compounds based on ***physicochemical properties***
- ***Substructure filtering*** of compounds based on custom sdf files
- ***Van der Waals filtering*** using distance and energy tests
- ***Toxicity filtering*** using specific organic toxic roots
- ***Hierarchical clustering*** with 4 different distances
- ***Affinity Propagation clustering***, providing exemplars for each cluster
- Creating custom pipeline filtering
- Visualization of compounds' properties

Athanasiadis, Cournia, Spyrou (2012) Bioinformatics

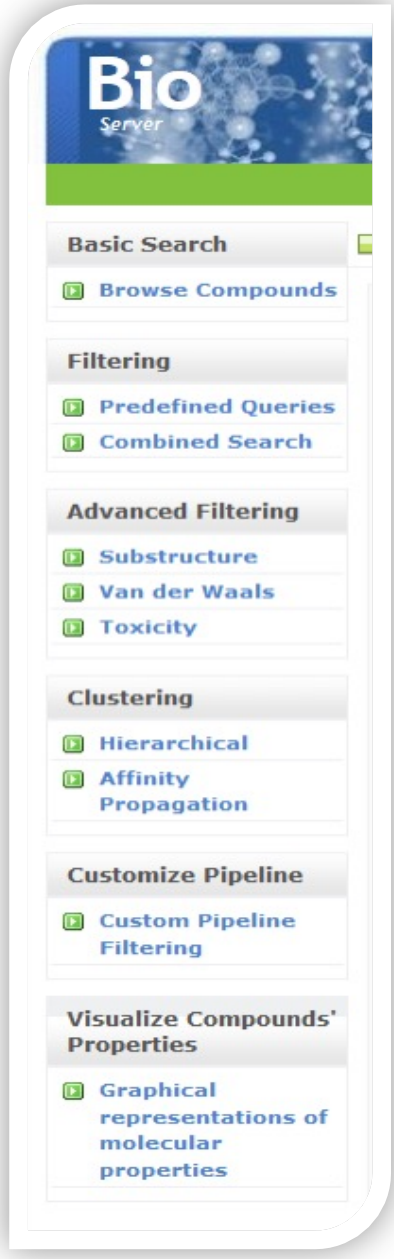
Filtering of chemical compounds

Computational methods can predict important physicochemical properties.

- *LogP*, a lipophilicity measure
- Solubility
- Permeability

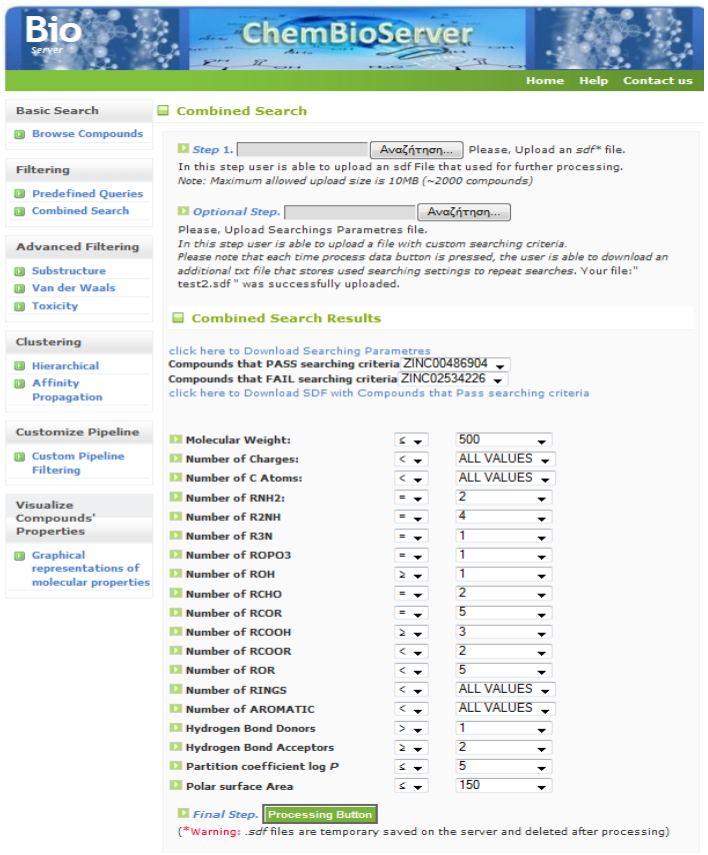
Conformation of ligand inside the protein (e.g. bad van der Waals contacts)

Identification of unwanted or toxic moieties on a compound



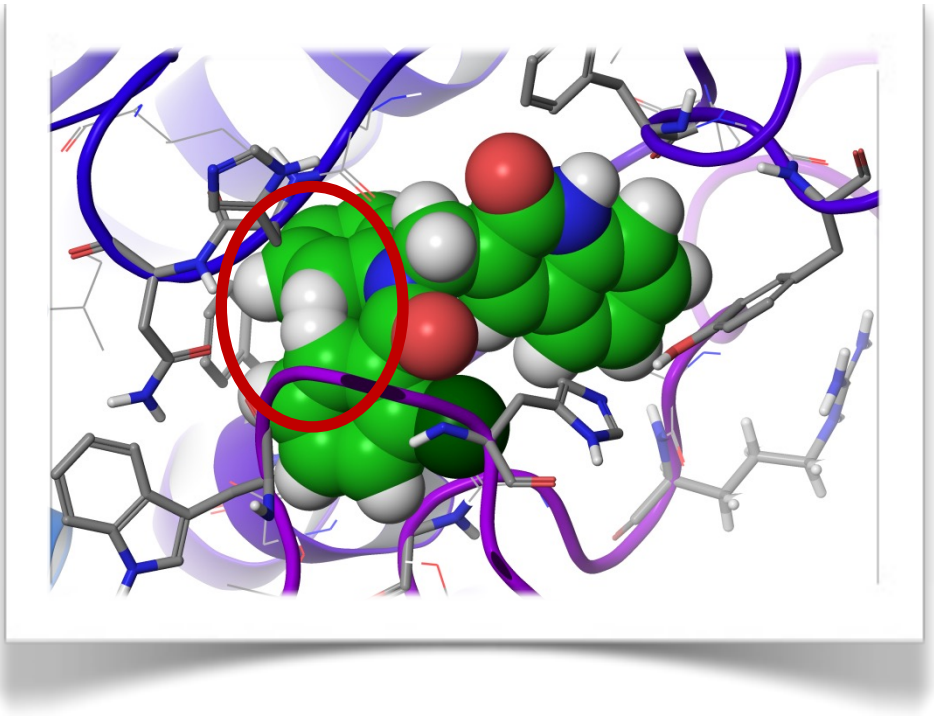
Physicochemical Properties

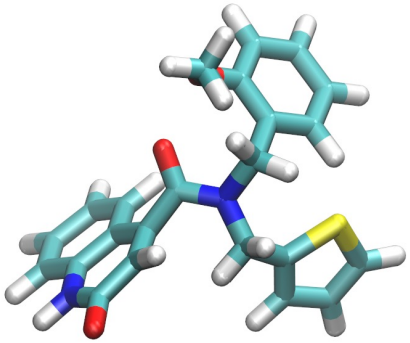
ChemBioServer Performs filtering to discard molecules with undesired physicochemical properties

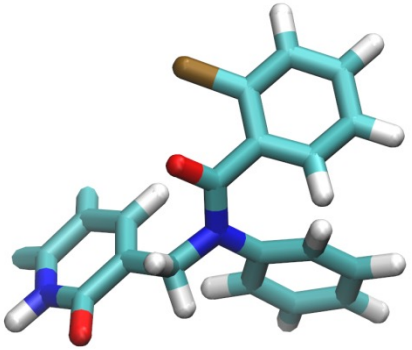


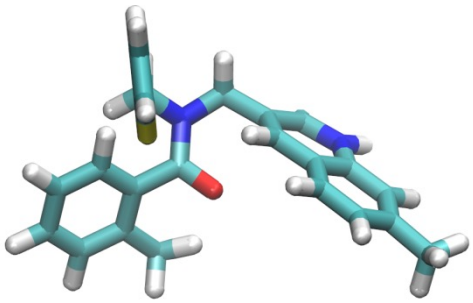
Compound ID	VDW Energy Test	VDW Distance Test
Compound: 1 AW 00785	- PASS AW 00785 - Browse List For Details...	- FAIL AW 00785 - Browse List For Details...
Compound: 2 AW 00788	- PASS AW 00788 - Browse List For Details...	- FAIL AW 00788 - Browse List For Details...
Compound: 3 AW 00785	- PASS AW 00785 - Browse List For Details...	- FAIL AW 00785 - Browse List For Details...
Compound: 4 AW 00939	- PASS AW 00939 - Browse List For Details...	- FAIL AW 00939 - Browse List For Details...
Compound: 5 AW 00694	- PASS AW 00694 - Browse List For Details...	- FAIL AW 00694 - Browse List For Details...
Compound: 6 CD 10205	- PASS CD 10205 - Browse List For Details...	- PASS CD 10205 - Browse List For Details...
Compound: 7 GK 02096	- PASS GK 02096 - Browse List For Details...	- FAIL GK 02096 - Browse List For Details...
Compound: 8 HTS 01561	- PASS HTS 01561 - Browse List For Details...	- FAIL HTS 01561 - Browse List For Details...
Compound: 9 MWP 00404	- PASS MWP 00404 - Browse List For Details...	- FAIL MWP 00404 - Browse List For Details...
Compound: 10 NRB 02577	- PASS NRB 02577 - Browse List For Details...	- FAIL NRB 02577 - Browse List For Details...

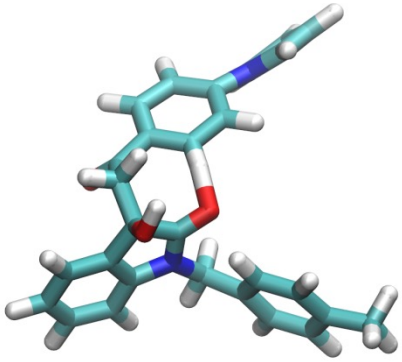
Bad van der Waals contacts





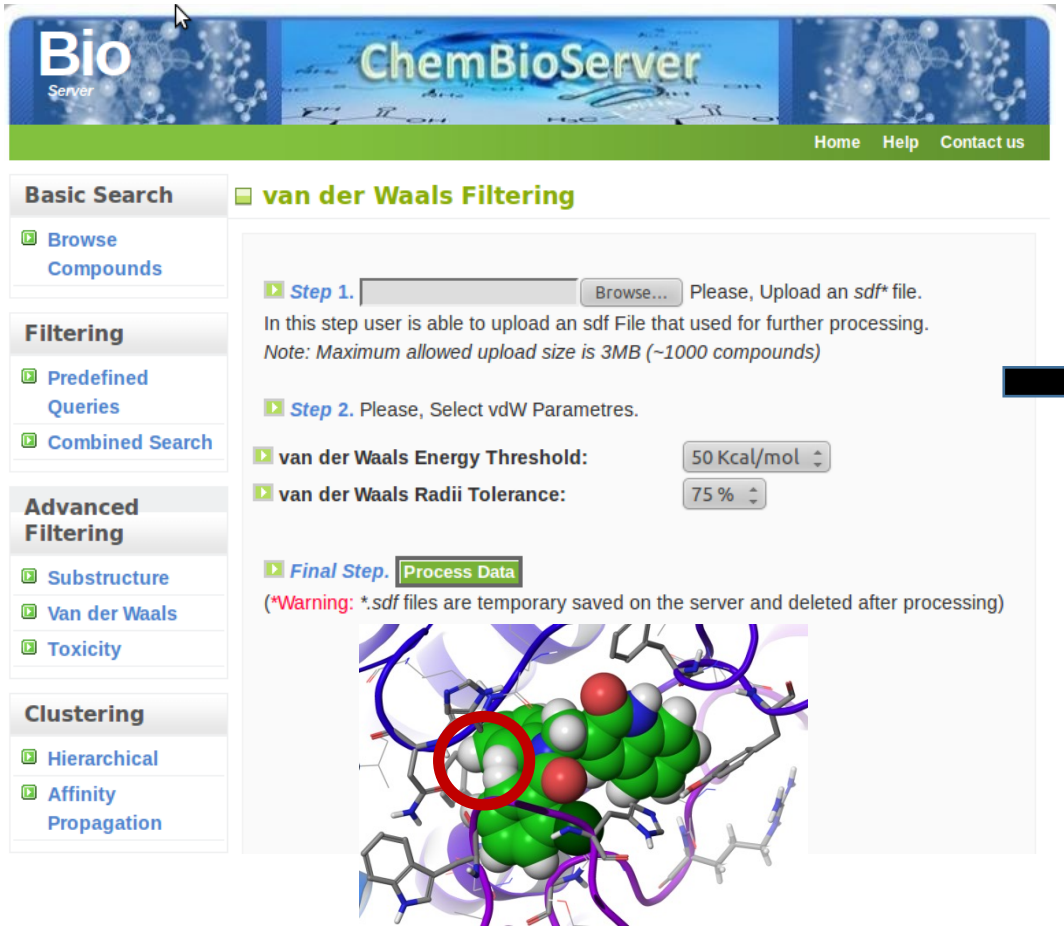






Bad van der Waals contacts

ChemBioServer Performs filtering to discard molecules with steric clashes by means of van der Waals energy and radii tolerance (*OPLS parameters**)

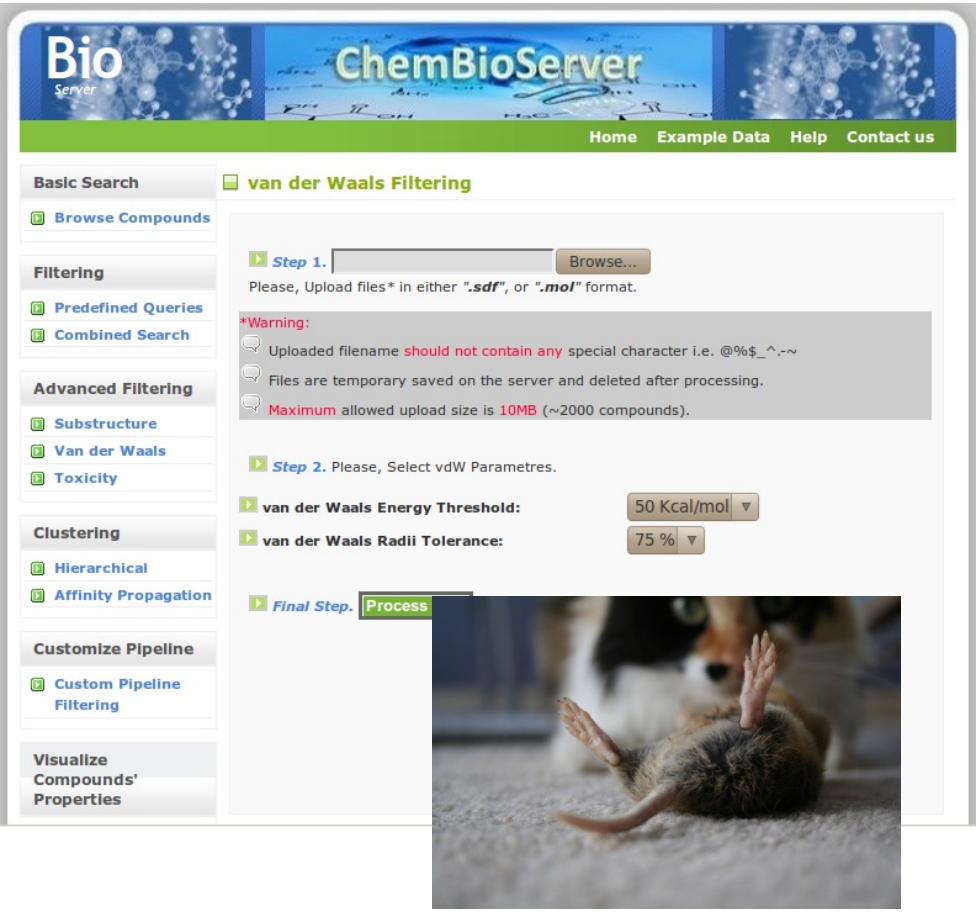


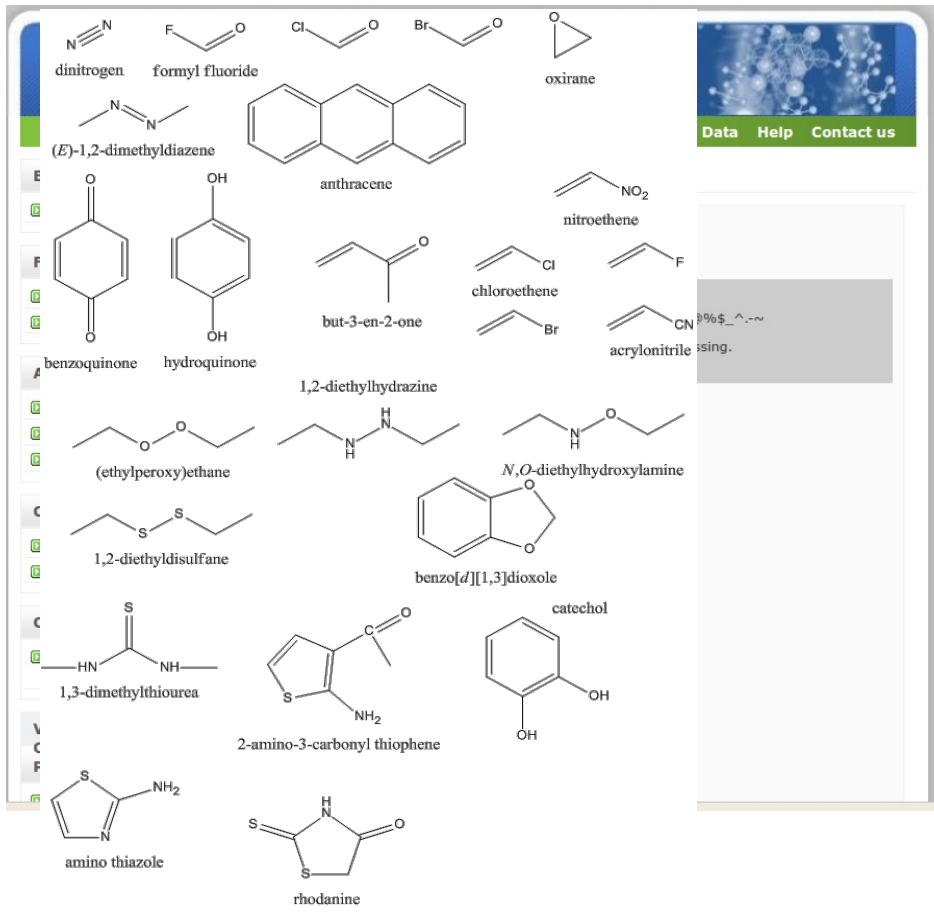
Compound ID	VDW Energy Test	VDW Distance Test
Compound: 1 AW 00785	- PASS AW 00785 - Browse List For Details...	- FAIL AW 00785 - Browse List For Details...
Compound: 2 AW 00788	- PASS AW 00788 - Browse List For Details...	- FAIL AW 00788 - Browse List For Details...
Compound: 3 AW 00785	- PASS AW 00785 - Browse List For Details...	- FAIL AW 00785 - Browse List For Details...
Compound: 4 AW 00939	- PASS AW 00939 - Browse List For Details...	- FAIL AW 00939 - Browse List For Details...
Compound: 5 AW 00694	- PASS AW 00694 - Browse List For Details...	- FAIL AW 00694 - Browse List For Details...
Compound: 6 CD 10205	- PASS CD 10205 - Browse List For Details...	- PASS CD 10205 - Browse List For Details...
Compound: 7 GK 02096	- PASS GK 02096 - Browse List For Details...	- FAIL GK 02096 - Browse List For Details...
Compound: 8 HTS 01561	- PASS HTS 01561 - Browse List For Details...	- FAIL HTS 01561 - Browse List For Details...
Compound: 9 MWP 00404	- PASS MWP 00404 - Browse List For Details...	- FAIL MWP 00404 - Browse List For Details...
Compound: 10 NRB 02577	- PASS NRB 02577 - Browse List For Details...	- FAIL NRB 02577 - Browse List For Details...

* Jorgensen *et al.*, *JACS*, 1996.

Toxicity filtering

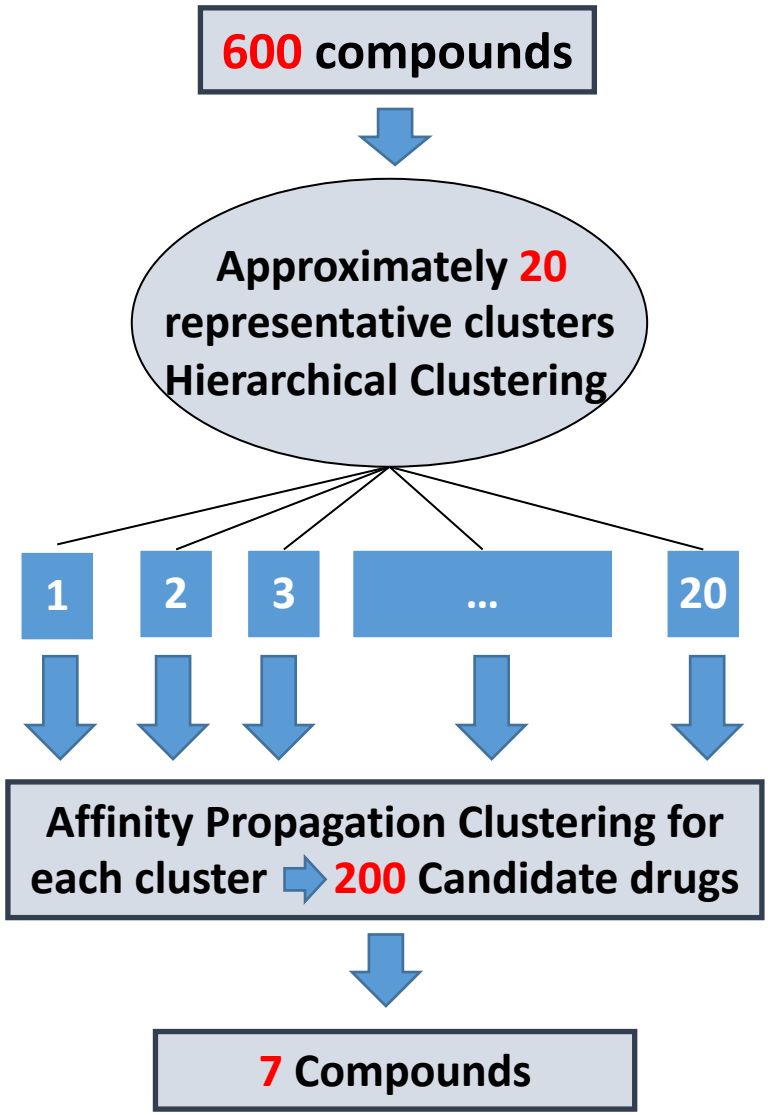
ChemBioServer Performs filtering to discard molecules with undesired toxic moieties



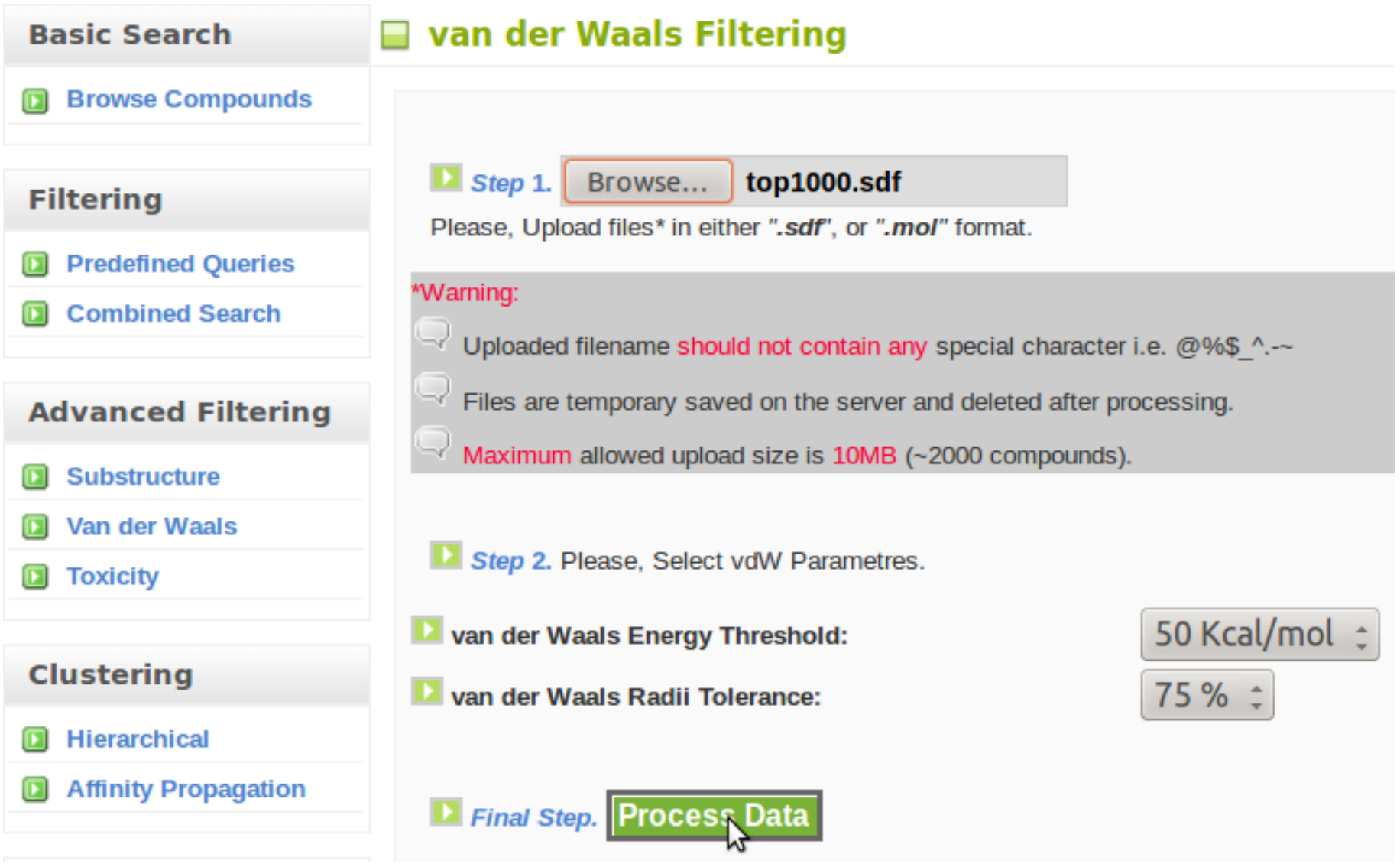


Athanasiadis, Cournia, Spyrou (2012) Bioinformatics

Clustering and molecular similarity



Back to the example….



Compound: 7 HTS 05412	- PASS HTS 05412 - Browse List For Details...	- PASS HTS 05412 - Browse List For Details...
Compound: 8 HTS 05683	- PASS HTS 05683 - Browse List For Details...	- PASS HTS 05683 - Browse List For Details...
Compound: 9 BTB 05835	- PASS BTB 05835 - Browse List For Details...	- PASS BTB 05835 - Browse List For Details...
Compound: 10 BTB 14912	- PASS BTB 14912 - Browse List For Details...	- PASS BTB 14912 - Browse List For Details...
Compound: 11 HTS 07996	- PASS HTS 07996 - Browse List For Details...	- PASS HTS 07996 - Browse List For Details...
Compound: 12 SEW 02809	- PASS SEW 02809 - Browse List For Details...	- PASS SEW 02809 - Browse List For Details...
Compound: 13 HTS 05414	- PASS HTS 05414 - Browse List For Details...	- PASS HTS 05414 - Browse List For Details...
Compound: 14 JFD 00844	- PASS JFD 00844 - Browse List For Details...	- FAIL JFD 00844 - Browse List For Details...
Compound: 15 HTS 05414	- PASS HTS 05414 - Browse List For Details...	- PASS HTS 05414 - Browse List For Details...

Basic Search
- Browse Compounds

Filtering
- Predefined Queries
- Combined Search

Advanced Filtering
- Substructure
- Van der Waals
- Toxicity

Clustering
- Hierarchical
- Affinity Propagation

Customize Pipeline
- Custom Pipeline Filtering

Visualize Compounds' Properties
- Graphical representations of

Toxicity Filtering Toxicophores

Step 1. Browse... **upload_1412609322_vdW_pass.sdf**

Please, Upload files* in either "***.sdf***", or "***.mol***" format.

*Warning:

- Uploaded filename should not contain any special character i.e. @%$_^.-~
- Files are temporary saved on the server and deleted after processing.
- Maximum allowed upload size is 10MB (~2000 compounds).

Custom List of Organic Toxic Compounds

1. N#N dinitrogen
2. C(=O)F formyl fluoride-Michael acceptor
3. C(=O)Cl formyl chloride-Michael acceptor
4. C(=O)Br formyl bromide-Michael acceptor
5. O1CC1 oxirane
6. C/N=N/C diazene
7. c1ccc2c(c1)cc1c(c2)cccc1 anthracene
8. C1=CC(=O)C=CC1=O quinone
9. c1cc(ccc1O)O hydroquinone
10. C=CC(=O)C butenone--Michael acceptor
11. CCOOCC O-O heteroatom
12. CCNNCC hydrazine-N-N heteroatom
13. CCNOCC N-O heteroatom
14. C=CCl chloroethane--Michael acceptor
15. C=CF fuoroethane-Michael acceptor
16. C=CBr bromoethane-Michael acceptor
17. C=CC#N acrylonitrile-Michael acceptor
18. C=C[N+](=O)[O-] nitroethene-Michael acceptor
19. CCSSCC disulfane-S-S heteroatom
20. c1ccc2c(c1)OCO2 benzo-dioxane

TOXIC RESULTS

- Compound with NO Toxic Roots: HTS 05684

- TOXIC Compounds: SPB 08304

click here to Download Results in txt format

click here to Download SDF file with Compounds that pass the Toxic test

CLICK on the NAME for 3D Display using JMOL APPLET

Compounds	Toxicity Results
Compound: 1 HTS 05684	NOT FOUND dinitrogen
Compound: 2 RH 01155	NOT FOUND dinitrogen
Compound: 3 HTS 05414	NOT FOUND dinitrogen
Compound: 4 RH 01155	NOT FOUND dinitrogen
Compound: 5 HTS 05414	NOT FOUND dinitrogen
Compound: 6 SPB 08304	NOT FOUND dinitrogen
Compound: 7 HTS 05412	NOT FOUND dinitrogen
Compound: 8 HTS 05683	NOT FOUND dinitrogen
Compound: 9 BTB 05835	NOT FOUND dinitrogen
Compound: 10 BTB 14912	NOT FOUND dinitrogen
Compound: 11 HTS 07996	NOT FOUND dinitrogen
Compound: 12 SEW 02809	NOT FOUND dinitrogen
Compound: 13 HTS 05414	NOT FOUND dinitrogen

Hierarchical Clustering

Step 1. Browse... **upload_1412609972_tox_pass.sdf**

Please, Upload files* in *".sdf"*, *".mol"*, *or binary fingerptint in ".txt"* format.

*Warning:

- Uploaded filename should not contain any special character i.e. @%$_^.-~
- Files are temporary saved on the server and deleted after processing.
- Maximum number of compounds that can be easily distinguished in the plot area is approximately 1000.
- Maximum allowed upload size is 10MB (~2000 compounds).
- fingerprint .txt format should contain two parts separated by a comma (,) character, the binary fingerprint and the name of the compound i.e:

00000110000001010000111101100000000000001111111111111110, Compound 0001
00111111111111111111000000000000000000011011100000000000, Compound 0002
01011110011001000110100100101011101110000000101111001101, Compound 0003

Binary part should not conatain any space before comma.
(see Example Data set 7. for more information)

- Please notice that a PDF reader program should be installed in order to display clustering results.

Step 2. Please, select Parametres

Distance Selection: 1. Soergel (Tanimoto Coefficient)

Clustering Linkage Selection: 3. Complete

Clustering Threshold: 0.85

Final Step. Process Data

No file selected or the file you attempted to upload is not allowed.

Affinity Propagation Clustering

The affinity propagation algorithm takes as input a set of pairwise similarities among compound fingerprints, considering them as potential representative compounds (exemplars). The clusters and their corresponding representative compounds are calculated by exchanging messages between data points until a maximization process converge. Thus, exemplars for each cluster are proposed to the researcher for further investigation.

Step 1. Browse... **1412668473cluster_1_.sdf**

Please, Upload files* in *".sdf"*, *".mol"*, *or binary fingerptint in ".txt"* format.

*Warning:

- Uploaded filename should not contain any special character i.e. @%$_^.-~
- Files are temporary saved on the server and deleted after processing.
- Maximum allowed upload size is 10MB (~2000 compounds).
- fingerprint .txt format should contain two parts separated by a comma (,) character, the binary fingerprint and the name of the compound i.e:

00000110000001010000111101100000000000001111111111111110, Compound 0001
00111111111111111111000000000000000000011011000000000000, Compound 0002
01011110011001000110100100101011101110000000101111001101, Compound 0003

Binary part should not conatain any space before comma.
(see Example Data set 7. for more information)

Step 2. Please, Select Distance Parametres.

Distance Selection: 1. Soergel (Tanimoto Coefficient)

Final Step. Process Data