Natural Product-like Compounds Library

Remarkable structural diversity and drug-likeness of molecular scaffolds, identified in natural compounds, provides a basis for the design of novel natural product-derived compound libraries for drug discovery [1-2].

Life Chemicals presents its Natural Product-like Compound Library, containing 2 subsets generated through the following approaches:

- Similarity based search against commercial databases of Timetek, Specnet, Analyticon, Selleck: **900** compounds in stock.
- Superposition of chemoinformatics and substructure search methods, applied to the entire Life Chemicals Compound Collection with the overlapping items selection [1, 3]: **2,000** compounds in stock.

Natural Products-like Compounds Library by Similarity Search

The Library was designed by means of 2D fingerprint similarity filtering of the Life Chemicals HTS Compound Collection using commercial databases of Timetek, Specnet, Analyticon, Selleck as the reference sets. A Tanimoto 85% similarity cut-off was applied to obtain about **900** stock available compounds.

Natural Products-like Compounds Library by Chemoinformatics and Substructure Search

Overlapping both collections obtained after analysis of the Life Chemicals Stock Collection by two different methods - chemical descriptors calculation (7,300 compounds) and natural-likeness scoring (9,700 compounds), a chemical space of about **2,000** compounds with good characteristics in both studies was obtained:

Descriptor-based selection method

The selection has been done in two steps:

1. Substructure search for natural-like scaffolds in the Life Chemicals Stock Collection. About 62,000 were selected from about 380,000 compounds.
2. Validation of the method and calculation of the parameters listed in Table1 for Drugs (COBRA), Pure Natural Products (PNP, MNP), NPs and Derivatives/Analogs (SNP), and NP-Based Combinatorial Compounds (NatDiv).

	COBRA	PNP	MNP	SNP	NatDiv
Molecular mass	414.5 (142.7)	393.9 (196.3)	503.6 (250.1)	409.2 (102.4)	441.3 (74.2)
# heavy atoms	29.1	28.2	34.6	29.1	31.1
SlogP	3.5 (2.2)	2.3 (2.7)	3.9 (2.6)	3.7 (1.7)	2.1 (1.8)
# nitrogen atoms	3.0	0.7	1.2	2.1	3.6
# oxygen atoms	3.4	5.9	6.1	4.3	4.4
ACC	6.4	6.6	7.4	6.4	8.00
DON	2.1	2.7	2.6	1.4	2.26
LipViol ≥ 2	10%	18%	30%	10%	8%
TPSA	90.5 (55.4)	98.9 (82.1)	108.9 (88.4)	83.2 (35.1)	104.7 (35.9)
# aromatic atoms	12.4	5.1	3.5	11.8	9.5
# chiral atoms	1.4	5.5	6.3	1.4	3.3
RGB	18.8	19.5	18.6	19.4	21.4
Rings	3.3	3.6	2.9	3.5	4.0
RTB	6.7	5.2	11.5	6.1	5.3
Globularity	0.10	0.12	0.14	0.08	0.08

Table 1. Mean values of descriptors which play the most important role in characterization of natural products.

Natural product-likeness calculator

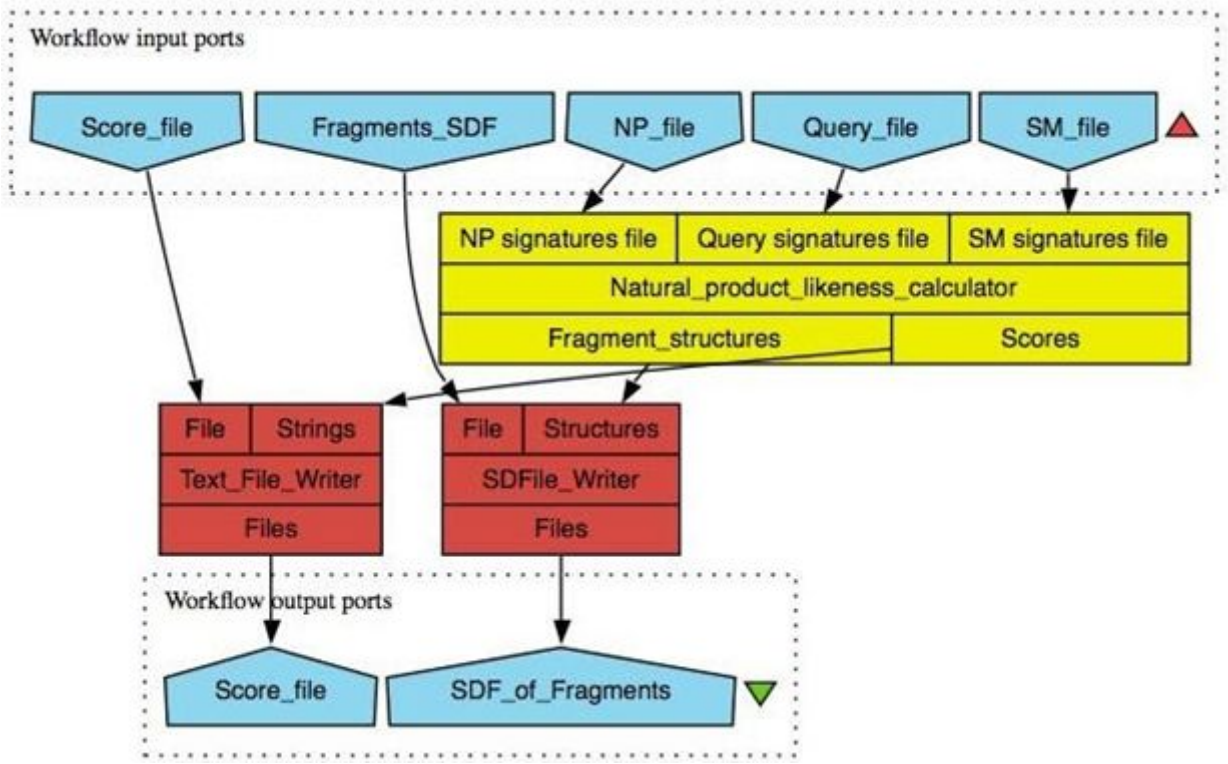

Fig. 1. Standard cross-platform view of Taverna 2.0 software with a schema of connections between template files, natural-product likeness calculator and query file the HTS Compound Library

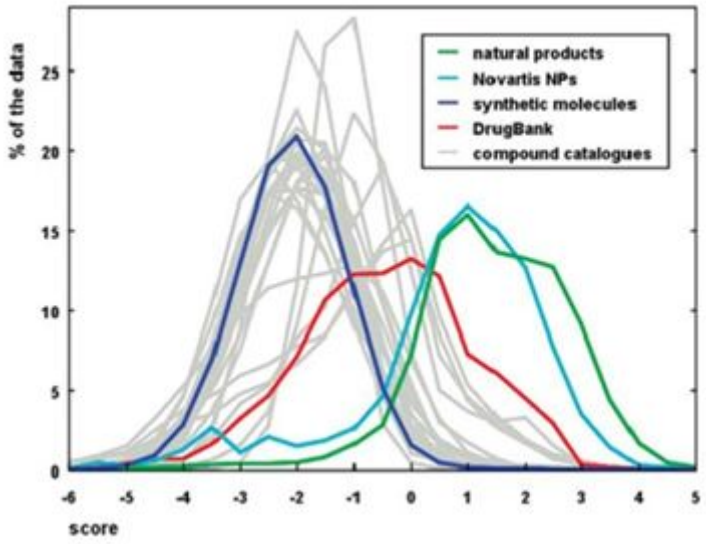

Fig. 2. Natural product-likeness scorer. Distribution of real natural products.

References

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