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THE CONSENSUS ENSEMBLE NEURAL NETWORK MULTITARGET MODEL OF ANXIOLYTIC ACTIVITY

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The aim of the study

To provide evidence concerning the universality of the consensus ensemble neural network multitarget approach taken as exemplified by anxiolytic activity.

Tasks

1. Choice and search for valid 3D models of target proteins that probable have a significant role in the treatment of anxiety disorders.
2. Optimization of ligand 3D structures by methods of molecular mechanics and quantum chemistry.
3. Ensemble docking into binding sites.
4. Training of the neural networks for consensus ensemble multitarget model.
5. Estimation of recognition and prediction accuracy of the obtained neural network models.

Databases and software

ChEMBL

UniProt

RCSB PDB PROTEIN DATA BANK

IUPHAR/BPS Guide to PHARMACOLOGY

ChemAxon

MarvinSketch

MOPAC2012™

AutoDock Vina

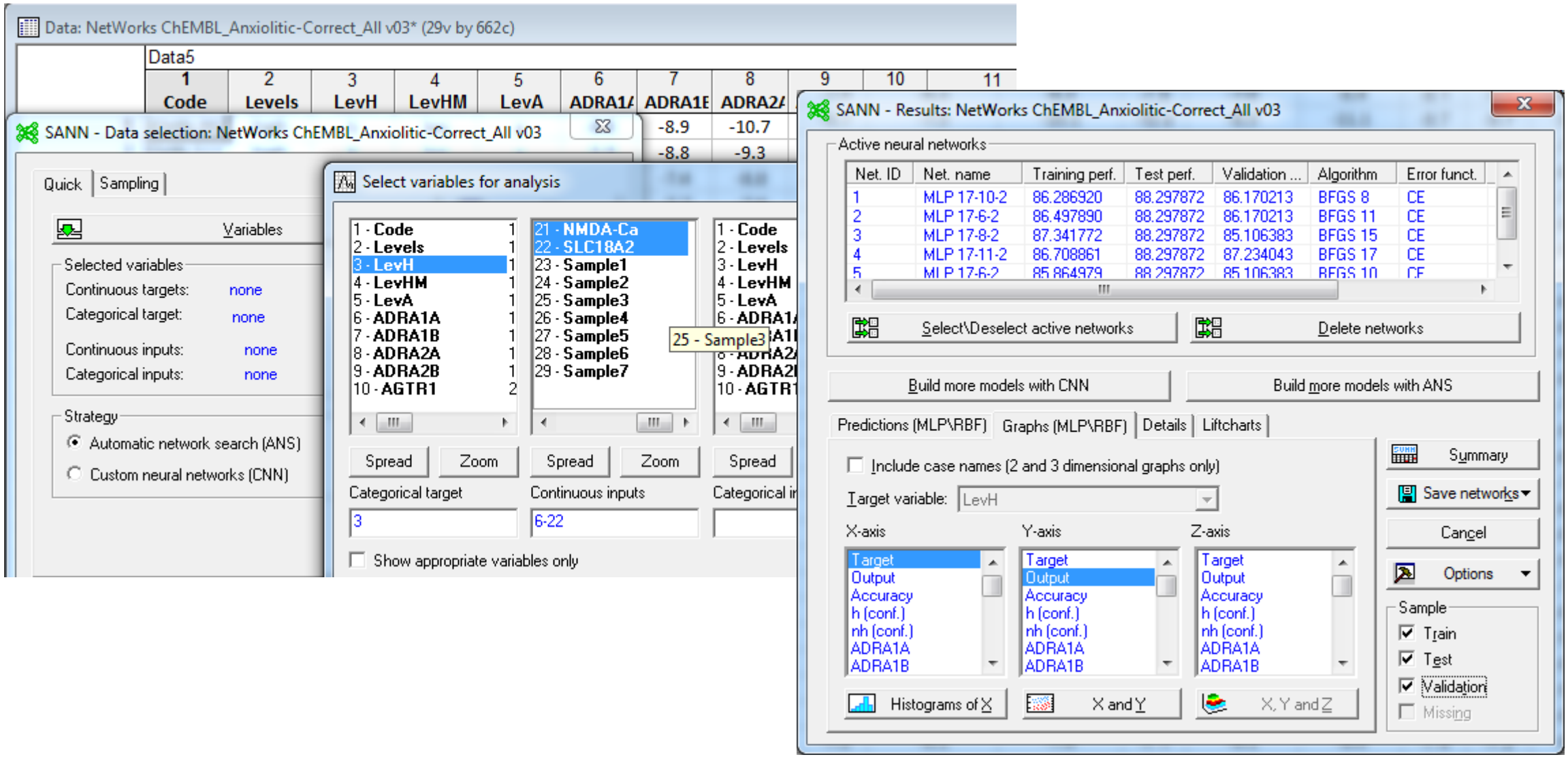
StatSoft®

STATISTICA

Training set

	A	B	C	D	E	F	G	H	I	J	K	L
1	Mol_ID	Code	Levels	LevH	LevHM	LevA	ADRA1A	ADRA1B	ADRA2A	ADRA2B	AGTR1	GABA-A-GABA
2	1	CHEMBL99259	high	h	hm	a	-8.8	-8.9	-10.7	-6.6	-9.1	-7.7
3	2	CHEMBL513136	high	h	hm	a	-5.9	-8.8	-9.3	-7.0	-9.8	-8.0
4	3	CHEMBL3410223	high	h	hm	a	-7.6	-7.4	-8.8	-6.6	-9.8	-7.4
5	4	CHEMBL323519	high	h	hm	a	-6.4	-7.7	-7.6	-5.6	-8.8	-6.6
6	5	CHEMBL204240	high	h	hm	a	-7.5	-7.1	-7.6	-5.1	-7.8	-6.4
7	6	CHEMBL314608	high	h	hm	a	-6.4	-7.3	-7.8	-5.6	-7.9	-6.3
8	7	CHEMBL319178	high	h	hm	a	-8.1	-8.7	-10.4	-6.5	-9.7	-7.5
9	8	CHEMBL101045	high	h	hm	a	-6.8	-7.2	-8.1	-5.2	-8.2	-6.7
10	9	CHEMBL543621	high	h	hm	a	-6.5	-7.4	-7.4	-5.3	-8.0	-6.4
11	10	CHEMBL545731	high	h	hm	a	-6.5	-7.2	-6.8	-5.4	-8.0	-6.4
12	11	CHEMBL3409256	high	h	hm	a	-8.1	-8.1	-9.6	-7.6	-9.8	-7.7
13	12	CHEMBL153823	high	h	hm	a	-7.7	-7.0	-8.2	-9.2	-8.1	-6.5
14	13	CHEMBL466847	high	h	hm	a	-6.9	-7.9	-9.2	-7.0	-9.1	-7.8
15	14	CHEMBL3084529	high	h	hm	a	-6.8	-9.6	-9.3	-5.7	-10.3	-7.8
16	15	CHEMBL3410224	high	h	hm	a	-7.3	-8.0	-8.7	-6.3	-8.8	-6.9
17	16	CHEMBL13662	high	h	hm	a	-9.1	-7.8	-9.4	-8.5	-9.4	-7.7
18	17	CHEMBL3246317	high	h	hm	a	-8.3	-8.2	-8.5	-8.1	-8.9	-7.7
19	18	CHEMBL3808873	high	h	hm	a	-6.7	-7.5	-7.5	-5.3	-7.9	-6.3
20	19	CHEMBL67100	high	h	hm	a	-8.1	-7.6	-8.9	-7.0	-8.5	-7.0

Multilayer Perceptron Neural Networks



Results of training and selection of neural networks

	LevH (Classification summary) (NetWorks ChEMBL_Anxiolitic-Correct_All v03-H4) Samples: Train, Test, Validation	
	LevH-h	LevH-nh
Total	95.0000	567.0000
Correct	15.0000	564.0000
Incorrect	80.0000	3.0000
Correct (%)	15.0000	99.0000
Incorrect (%)	84.0000	0.0000
Total	95.0000	567.0000
Correct	17.0000	557.0000
Incorrect	78.0000	10.0000
Correct (%)	17.0000	98.0000
Incorrect (%)	82.0000	1.0000
Total	95.0000	567.0000
Correct	12.0000	559.0000
Incorrect	83.0000	8.0000
Correct (%)	12.0000	98.0000
Incorrect (%)	87.0000	1.0000
Total	95.0000	567.0000
Correct	18.0000	556.0000
Incorrect	77.0000	11.0000
Correct (%)	18.0000	98.0000
Incorrect (%)	81.0000	1.0000
Total	95.0000	567.0000
Correct	6.0000	564.0000
Incorrect	89.0000	3.0000
Correct (%)	6.0000	99.0000
Incorrect (%)	93.0000	0.0000

	LevH (Classification summary) (NetWorks ChEMBL_Anxiolitic-Correct_All v03-H4) Samples: Train, Test, Validation	
	LevH-h	LevH-nh
Incorrect (%)	86.0000	1.0000
Total	95.0000	567.0000
Correct	76.0000	544.0000
Incorrect	19.0000	23.0000
Correct (%)	80.0000	95.0000
Incorrect (%)	20.0000	4.0000
Total	95.0000	567.0000
Correct	66.0000	546.0000
Incorrect	29.0000	21.0000
Correct (%)	69.0000	96.0000
Incorrect (%)	30.0000	3.0000
Total	95.0000	567.0000
Correct	39.0000	552.0000
Incorrect	56.0000	15.0000
Correct (%)	41.0000	97.0000
Incorrect (%)	58.0000	2.0000
Total	95.0000	567.0000
Correct	67.0000	548.0000
Incorrect	28.0000	19.0000
Correct (%)	70.0000	96.0000
Incorrect (%)	29.0000	3.0000
Total	95.0000	567.0000
Correct	64.0000	547.0000
Incorrect	31.0000	20.0000
Correct (%)	67.0000	96.0000
Incorrect (%)	32.0000	3.0000

Level	%
F(High)	89.5
F(Moderate)	96.7
F(Low)	97.3
F(General)	92.6
Consensus recognition accuracy for references	**100%**

Results

1. We have found the most significant targets associated with anxiolytic activity, and selected their valid 3D models.
2. Molecular mechanical and quantum chemistry approaches were used to optimize 3D models of ligand structures.
3. We have performed ensemble docking into binding sites.
4. More than 136,000 neural networks have been trained.
5. We constructed a consensus ensemble neural network multitarget classification model of anxiolytic activity of chemical compounds.
6. There was evaluated the recognition and prediction accuracy of the resulting model.

Thank you for listening