

Volgograd State Medical University, Volgograd, Russia
Department of Pharmacology and Bioinformatics
Research Center for Innovative Medicines

THE CONSENSUS ENSEMBLE NEURAL NETWORK MULTITARGET MODEL OF ANXIOLYTIC ACTIVITY

M.A. Perfilev, P.M. Vassiliev,
A.A. Spasov, A.N. Kochetkov

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.

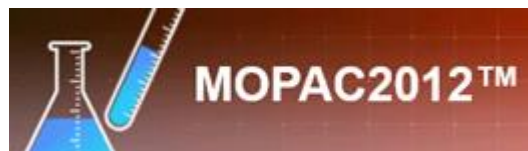
Databases and software



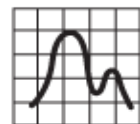
ChemAxon



MarvinSketch



AutoDock Vina



StatSoft®



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

The screenshot displays the SANN software interface. The main window shows a data table with columns 1-11. A 'Data5' window is open, showing a list of variables for analysis. A 'SANN - Results' window is also open, displaying a table of active neural networks with their performance metrics.

Data5

1	2	3	4	5	6	7	8	9	10	11
Code	Levels	LevH	LevHM	LevA	ADRA1A	ADRA1E	ADRA2A			
						-8.9	-10.7			
						-8.8	-9.3			

Select variables for analysis

1 - Code	1	21 - NMDA-Ca	1	1 - Code	1
2 - Levels	1	22 - SLC18A2	1	2 - Levels	1
3 - LevH	1	23 - Sample1	1	3 - LevH	1
4 - LevHM	1	24 - Sample2	1	4 - LevHM	1
5 - LevA	1	25 - Sample3	1	5 - LevA	1
6 - ADRA1A	1	26 - Sample4	1	6 - ADRA1A	1
7 - ADRA1B	1	27 - Sample5	1	7 - ADRA1B	1
8 - ADRA2A	1	28 - Sample6	1	8 - ADRA2A	1
9 - ADRA2B	1	29 - Sample7	1	9 - ADRA2B	1
10 - AGTR1	2			10 - AGTR1	2

SANN - Results: NetWorks ChEMBL_Anxiolitic-Correct_All v03

Net. ID	Net. name	Training perf.	Test perf.	Validation ...	Algorithm	Error funct.
1	MLP 17-10-2	86.286920	88.297872	86.170213	BFGS 8	CE
2	MLP 17-6-2	86.497890	88.297872	86.170213	BFGS 11	CE
3	MLP 17-8-2	87.341772	88.297872	85.106383	BFGS 15	CE
4	MLP 17-11-2	86.708861	88.297872	87.234043	BFGS 17	CE
5	MLP 17-6-2	85.864979	88.297872	85.106383	BFGS 10	CF

Results of training and selection of neural networks

LevH (Classification summary) (NetWorks ChEMBL_Anxiolytic-Correct_All v03-H4) Samples: Train, Test, Validation			LevH (Classification summary) (NetWorks ChEMBL_Anxiolytic-Correct_All v03-H4) Samples: Train, Test, Validation				
	LevH-h	LevH-nh		LevH-h	LevH-nh	Level	%
Total	95.0000	567.0000					
Correct	15.0000	564.0000					
Incorrect	80.0000	3.0000					
Correct (%)	15.0000	99.0000	Incorrect (%)	86.0000	1.0000		
Incorrect (%)	84.0000	0.0000	Total	95.0000	567.0000		
Total	95.0000	567.0000	Correct	76.0000	544.0000	F(High)	89.5
Correct	17.0000	557.0000	Incorrect	19.0000	23.0000		
Incorrect	78.0000	10.0000	Correct (%)	80.0000	95.0000	F(Moderate)	96.7
Correct (%)	17.0000	98.0000	Incorrect (%)	20.0000	4.0000		
Incorrect (%)	82.0000	1.0000	Total	95.0000	567.0000	F(Low)	97.3
Total	95.0000	567.0000	Correct	66.0000	546.0000		
Correct	12.0000	559.0000	Incorrect	29.0000	21.0000		
Incorrect	83.0000	8.0000	Correct (%)	69.0000	96.0000	F(General)	92.6
Correct (%)	12.0000	98.0000	Incorrect (%)	30.0000	3.0000		
Incorrect (%)	87.0000	1.0000	Total	95.0000	567.0000		
Total	95.0000	567.0000	Correct	39.0000	552.0000		
Correct	18.0000	556.0000	Incorrect	56.0000	15.0000		
Incorrect	77.0000	11.0000	Correct (%)	41.0000	97.0000		
Correct (%)	18.0000	98.0000	Incorrect (%)	58.0000	2.0000		
Incorrect (%)	81.0000	1.0000	Total	95.0000	567.0000		
Total	95.0000	567.0000	Correct	67.0000	548.0000		
Correct	6.0000	564.0000	Incorrect	28.0000	19.0000		
Incorrect	89.0000	3.0000	Correct (%)	70.0000	96.0000		
Correct (%)	6.0000	99.0000	Incorrect (%)	29.0000	3.0000		
Incorrect (%)	93.0000	0.0000	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		
						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