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Department of Pharmacology and Bioinformatics
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SEARCH FOR NEW ANXIOLYTIC SUBSTANCES BY NEURAL NETWORK MODELING USING MULTIPLE DOCKING

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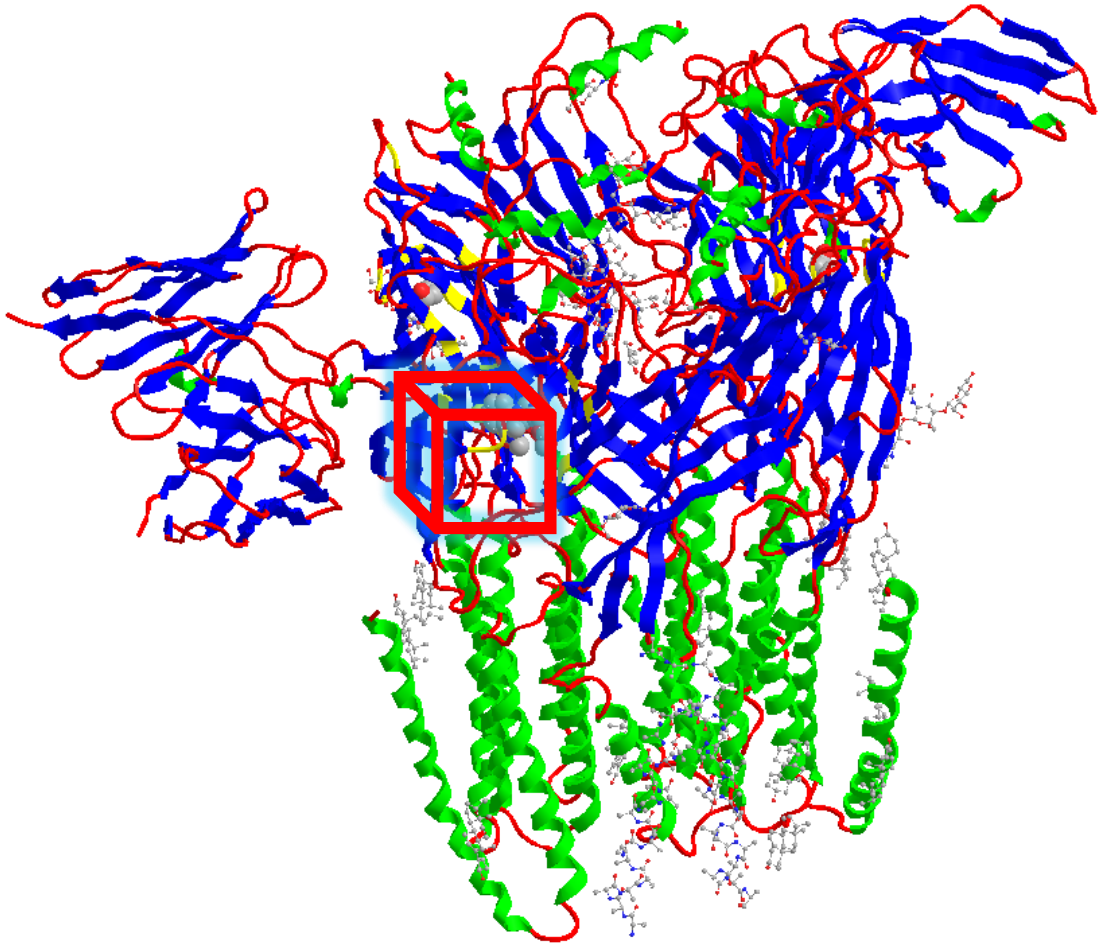
The aim of the study

To provide high efficiency of drug discovery using neural network modeling based on multiple docking methodology.

Tasks

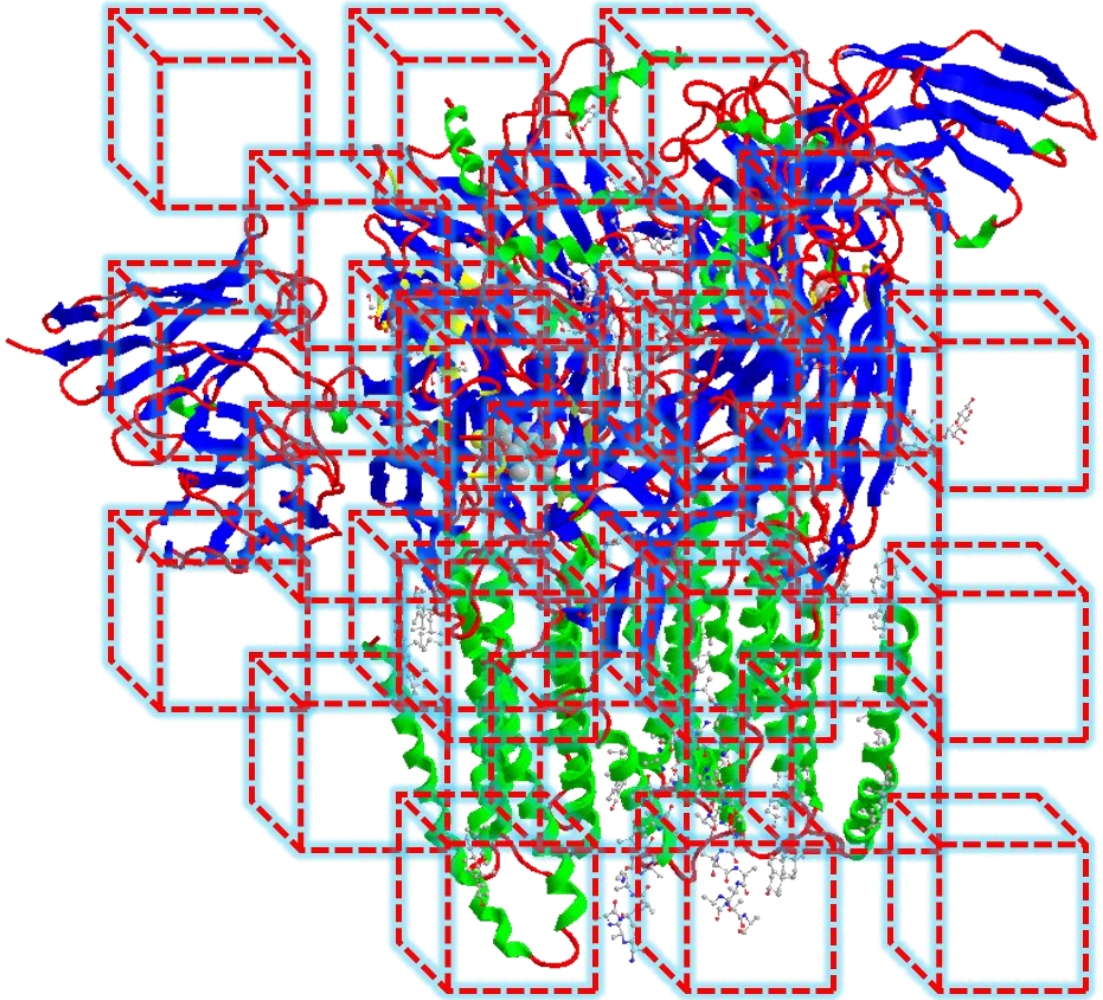
1. Perform multiple docking of new quinazoline-2,4(1*H*,3*H*)-dione derivatives.
2. Predict the activity level of new compounds using a previously built neural network model.
3. Conduct an experiment in behavioral tests to confirm the prediction.
4. Prepare new compounds for future research.

Simple docking



Vassiliev PM et al. VJMS, 2021; 3: 57-61. eLIBRARY ID: 46679171

Multiple docking



Comparison of simple and multiple docking

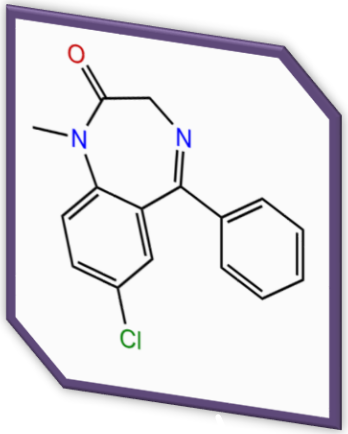
Prediction accuracy indicator	Value for model using	
	ΔE_0	$\Delta E_1 ... \Delta E_{27}$
F_0, %	51,3	94,8
F_a, %	66,7	83,3
F_n, %	49,1	96,4
z_0	0,58	8,73
z_a	1,08	2,23
z_n	0,14	8,45
p_0	0,281	$<1 \cdot 10^{-15}$
p_a	0,139	0,0127
p_n	0,555	$<1 \cdot 10^{-15}$

Примечание.
F_0, F_a, F_n – overall predictive accuracy, sensitivity, specificity
z_0, z_a, z_n – binomial test for F_0, F_a, F_n.
p_0, p_a, p_n – significance F_0, F_a, F_n.

Vassiliev PM, Kochetkov AN, Perfilev MA. JVSMU, 2022; 19(4): 88-93.

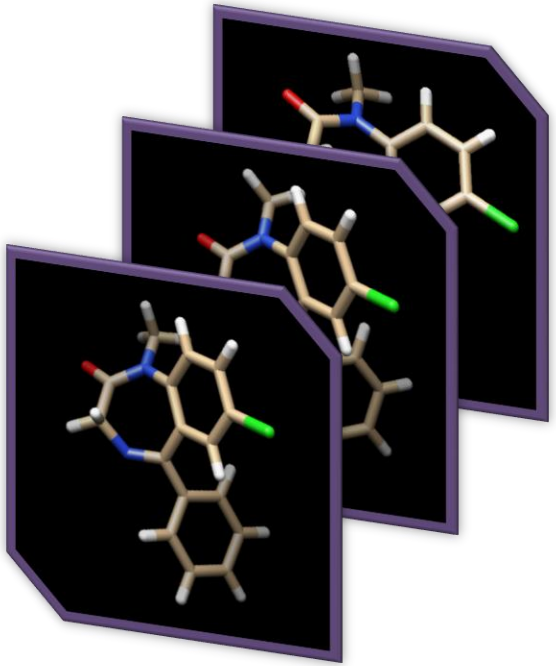
Databases and software

General scheme

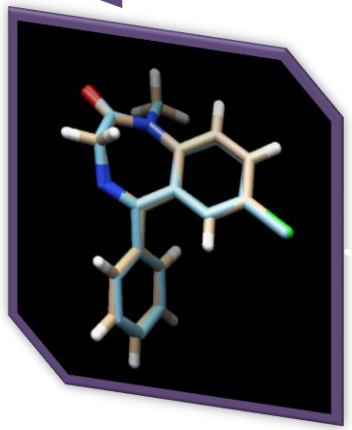


ChemAxon

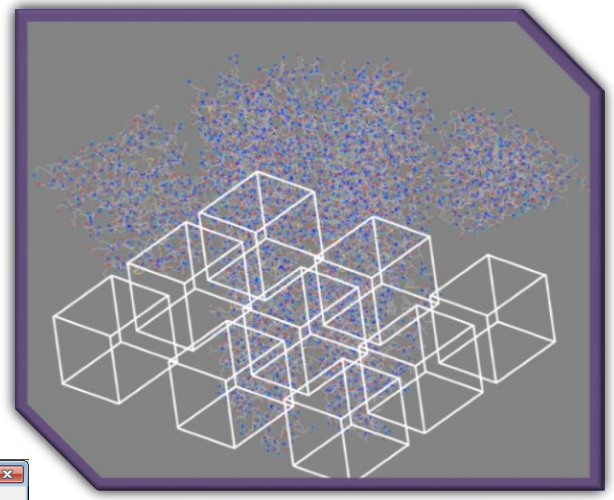
MarvinSketch



MOPAC2012™

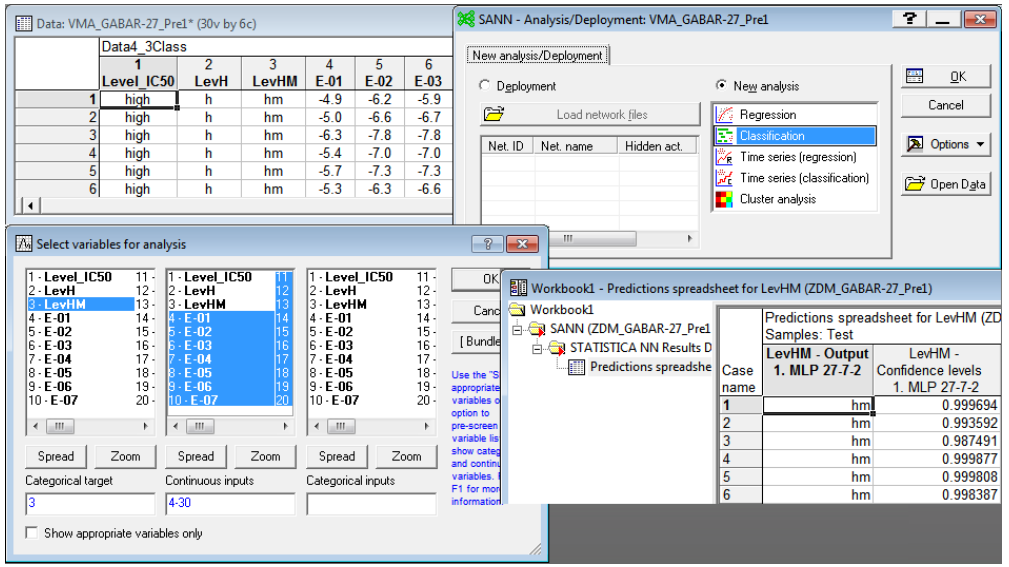


AutoDock Vina



StatSoft®

STATISTICA



Results

Case name	LevHM Target	LevHM - Output 1. MLP 27-7-2	LevHM - Residuals 1. MLP 27-7-2	LevHM - Confidence levels 1. MLP 27-7-2
	Predictions spreadsheet for LevHM (VMA_GABAR-27_Pre1) Samples: Test			
1	hm	nhm	Incorrect	0.978494
2	hm	nhm	Incorrect	0.845162
3	hm	hm	Correct	0.997323
4	hm	nhm	Incorrect	0.999198
5	hm	nhm	Incorrect	0.994857
6	hm	hm	Correct	0.999218

Compound	Level of activity	Membership function F_m
1	nhm	0.978
2	nhm	0.999
3	nhm	0.995
4	nhm	0.845
5	**hm**	**0.997**
Diazepam	**hm**	**0.999**

* hm is the high or moderate level of activity; nhm is the low level of activity or its absence; the data for compounds assigned by the prediction to the class of compounds with pronounced activity are highlighted in bold.

Compound	Latent period	Line crossings	Rearing	Center square entries	Center square duration	Indicator of priming action
1	103±34	−26±25	0±0	−11±40	−25±4	0
2	−80±6[b]	34±20	50±120[b]	−22±0	−89±0	2
3	135±31	28±34	0±0	89±102[c]	197±22[b]	3
4	−74±5	70±21[b]	250±582[c]	111±162[d]	−41±24[b]	4
5	**−75±10**	**101±30[b]**	**217±465[c]**	**200±242[d]**	**9±29[b]**	**7**
Diazepam	**−97±0[d]**	**135±42[d]**	**0±0**	**167±194[c]**	**13±31[b]**	**9**

[a] The values of the indicators are given in percent to the control. The indicators for compounds with very pronounced priming activity are highlighted in bold. Significance of changes according to the Mann—Whitney U-test:
[b] very weak, $0.1 \leqslant p < 0.2$;
[c] weak, statistically insignificant, $0.05 \leqslant p < 0.1$;
[d] statistically significant, $0.01 \leqslant p < 0.05$.

Results

1. We have performed ensemble multiple docking of new acetamide derivatives of quinazolines.
2. We have performed an activity level prediction of new compounds based on a new methodology with consensus ensemble neural network classification model.
3. We tested these compounds in an experiment.
4. We have shown that the developed methodology is effective and can be used for other types of activities.

Thank you for listening