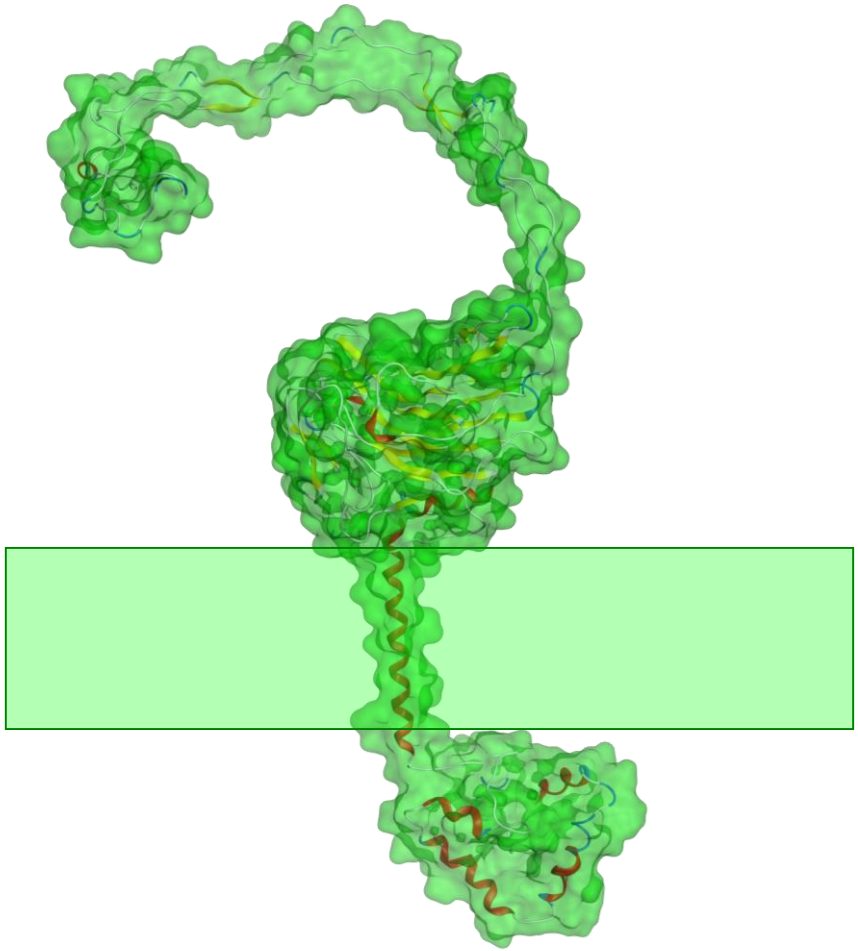
MMRO-2019

Ранжирование и анализ моделей белок-белкового докинга онлайн метасервером QASDOM

Кузнецов Е.Н., Кравацкий Ю.В., Туманян В.Г., Аджубей А.А.,

Анашкина Анастасия Андреевна

Motivation



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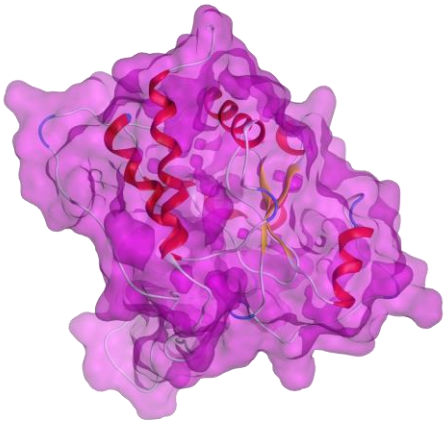
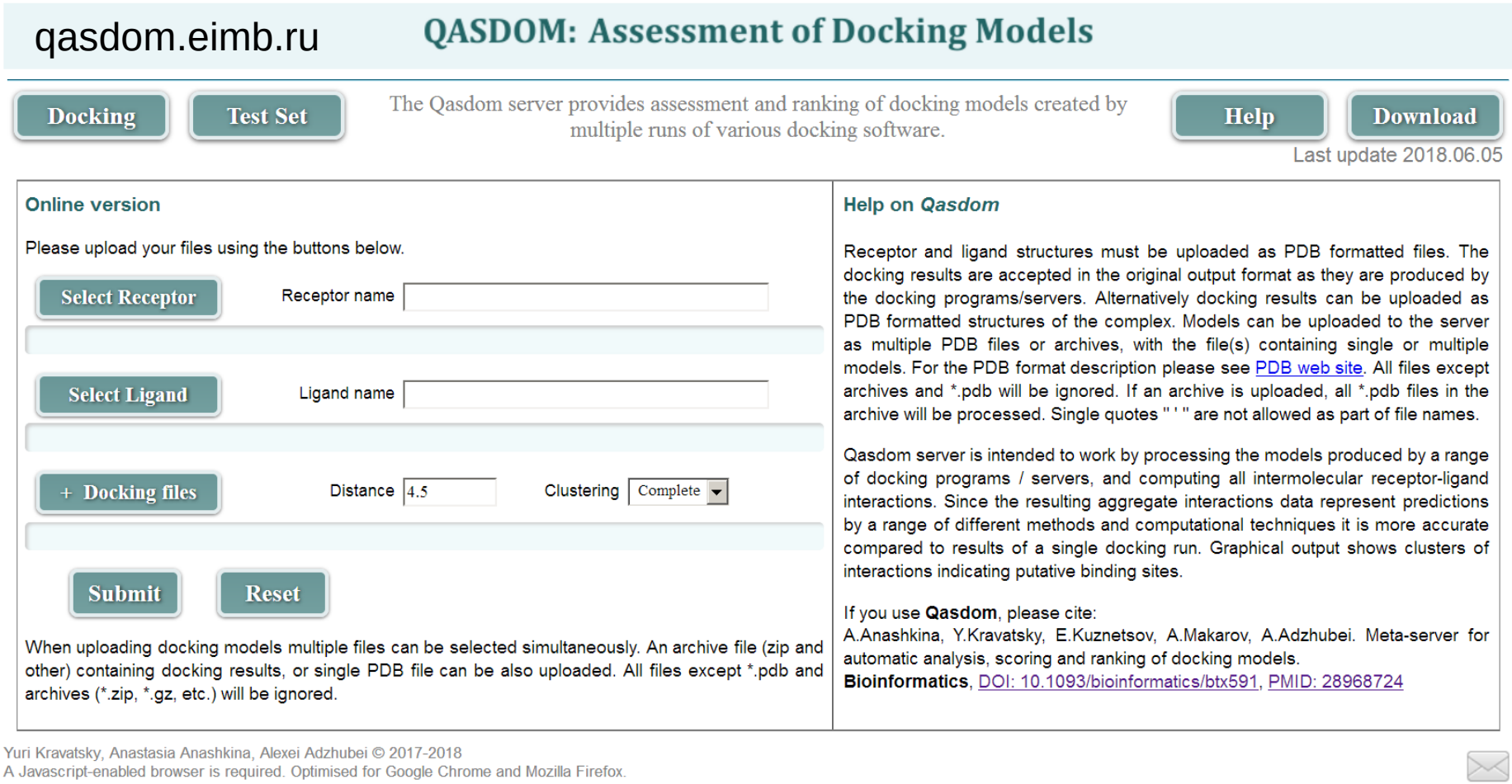


Protein-Protein Docking Servers

- Hex (Macindoe et al., 2010)
- SwarmDock (Torchala et al., 2013)
- ClusPro (Comeau et al., 2004)
- Gramm-X (Tovchigrechko and Vakser, 2006)
- Zdock (Pierce et al., 2014).

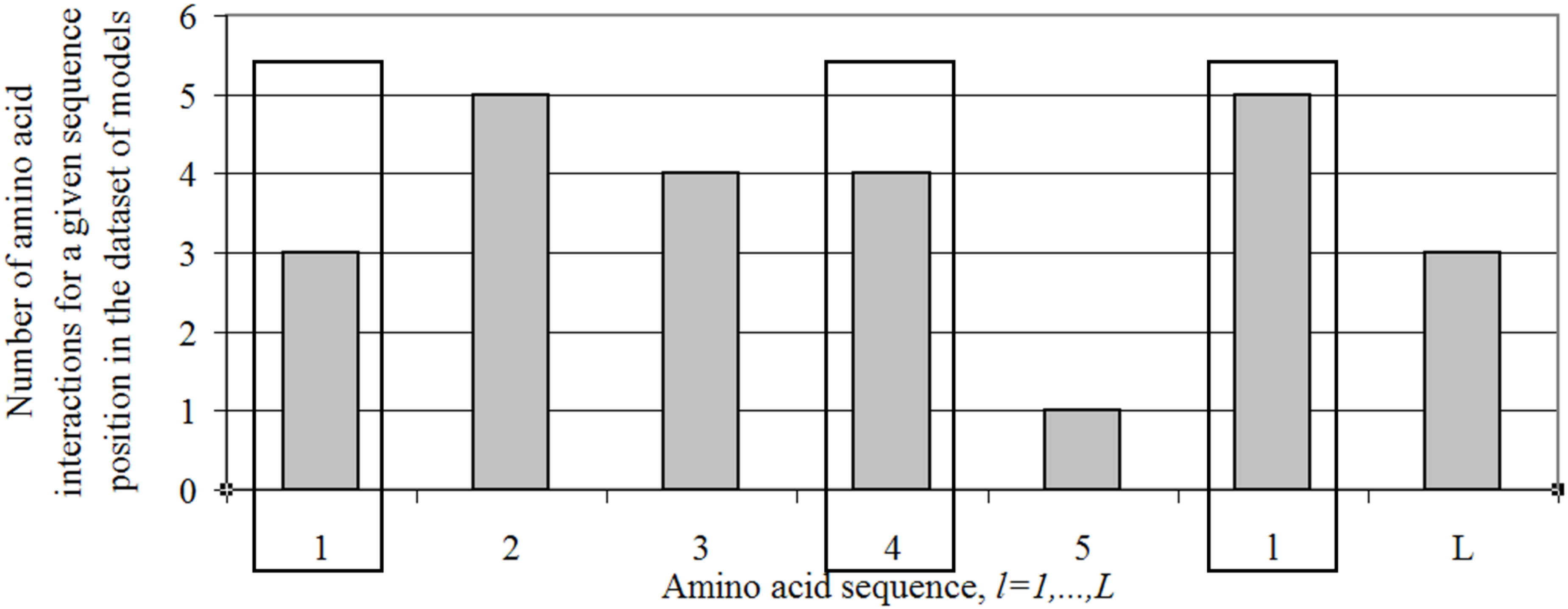


A.Anashkina et al. Meta-server for automatic analysis, scoring and ranking of docking models. **Bioinformatics**, 2018

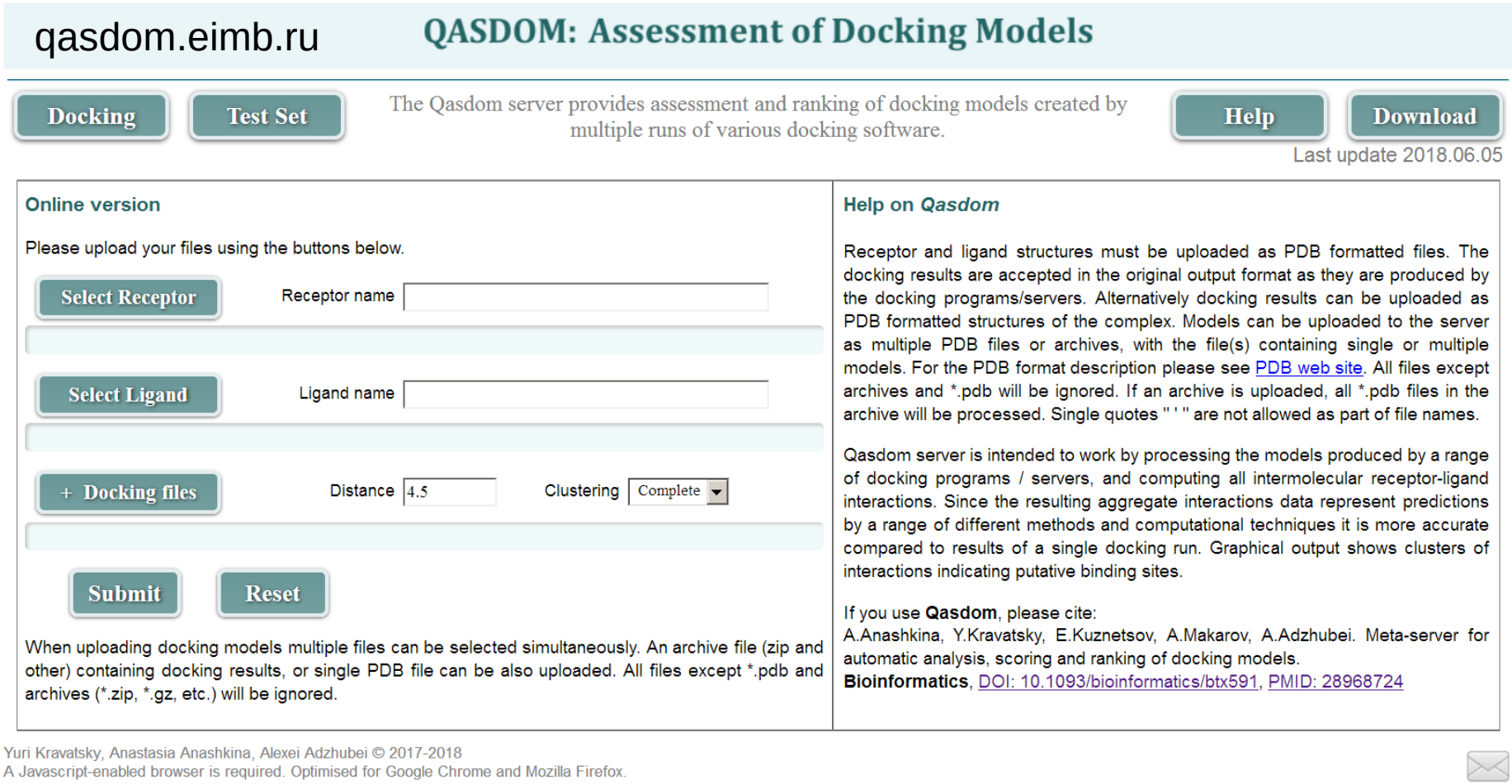
Ranking scores

		Amino acid sequence $l=1,\ldots,L$							
		1	**2**	**3**	**4**	**5**	***l***	***L***	Σ
Dataset of models $m=1,\ldots,M$	**1**		●	●	●			●	RC_1^{mod}
	2	●		●		●	●		RC_2^{mod}
	3		●	●			●	●	RC_3^{mod}
	4		●		●		●		RC_4^{mod}
	5	●	●		●			●	RC_5^{mod}
	m	●			●		●		RC_m^{mod}
	M		●	●			●		RC_M^{mod}
	Σ	RC_1^{aa}	RC_2^{aa}	RC_3^{aa}	RC_4^{aa}	RC_5^{aa}	RC_l^{aa}	RC_L^{aa}	

Ranking scores



$$S_m = \frac{1}{C_{total}} \sum_{l=1}^{L} C_{ml} R_l$$



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qasdom.eimb.ru

QASDOM: Assessment of Docking Models

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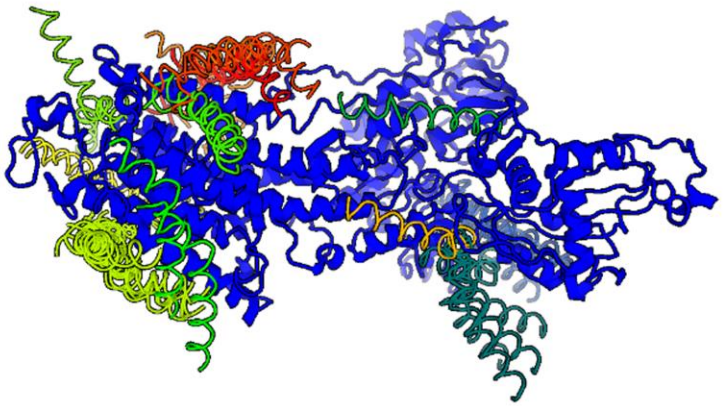
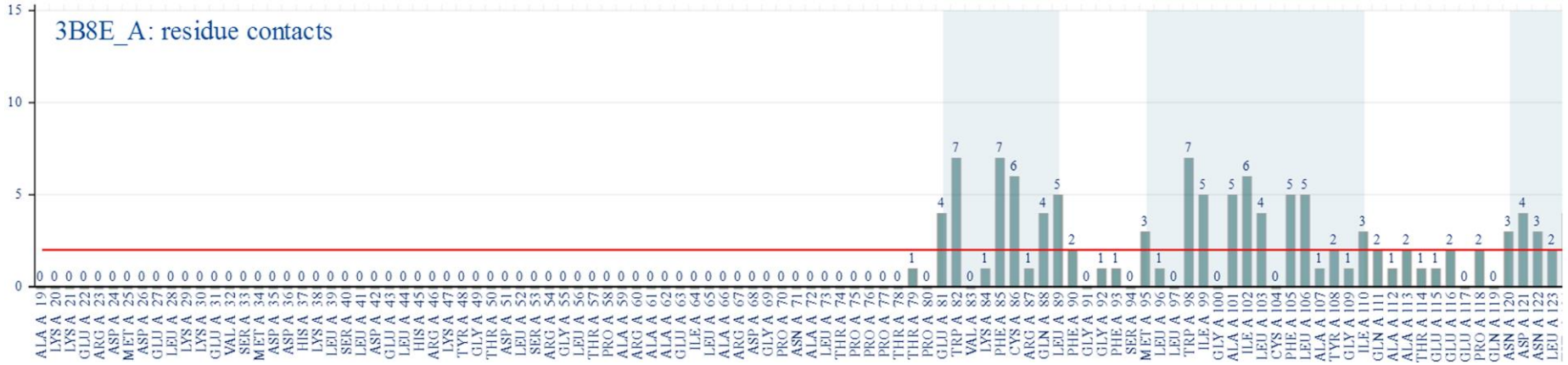
Permalink: http://qasdom.eimb.ru/results/eIO5jrUdAXgkogze/results.html

Model	S	S Atomic	RC	RC Atomic	Cluster		
complex.10	0.2114	0.3800	26	519	7	R	>
complex.8	0.2040	0.3781	24	469	7	R	>
complex.7	0.2040	0.3075	23	388	7	R	>
cluspro_model3	0.1928	0.1074	28	173	7	R	>
complex.2	0.1842	0.3091	23	423	7	R	>
complex.1	0.1718	0.2688	26	455	7	R	>
gramm_x_model5	0.1693	0.1770	20	258	7	R	>
gramm_x_model2	0.1656	0.2028	16	263	7	R	>
cluspro_model4	0.1619	0.0922	16	125	7	R	>
complex.3	0.1397	0.3067	27	616	12	W	>
complex.9	0.1286	0.2312	14	296	7	R	>
gramm_x_model10	0.1248	0.1493	40	541	9	T	>
complex.5	0.1224	0.2331	25	475	12	W	>
complex.6	0.1187	0.2430	22	527	12	W	>
cluspro_model7	0.1100	0.0735	20	170	11	V	>
cluspro_model1	0.1088	0.0560	19	125	11	V	>
cluspro_model0	0.1051	0.1270	18	262	11	V	>
gramm_x_model1	0.1051	0.1080	24	284	2	M	>
gramm_x_model7	0.1026	0.1483	31	485	5	P	>
cluspro_model8	0.1014	0.0761	25	274	5	P	>
hex_model8	0.1001	0.0810	18	173	2	M	>
gramm_x_model8	0.0964	0.1056	22	338	4	O	>
cluspro_model2	0.0964	0.0774	22	227	8	S	>
cluspro_model5	0.0927	0.0762	14	148	10	U	>

Ligand	2mlt_A.pdb
Receptor	3B8E_A.pdb
All Models	All models

Allmodels





Clustering: ***Linear clusters***

Clustering: ***Structural clusters***

QASDOM: Assessment of Docking Models

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Permalink: http://qasdom.eimb.ru/results/eIO5jrUdAXgkogze/results.html

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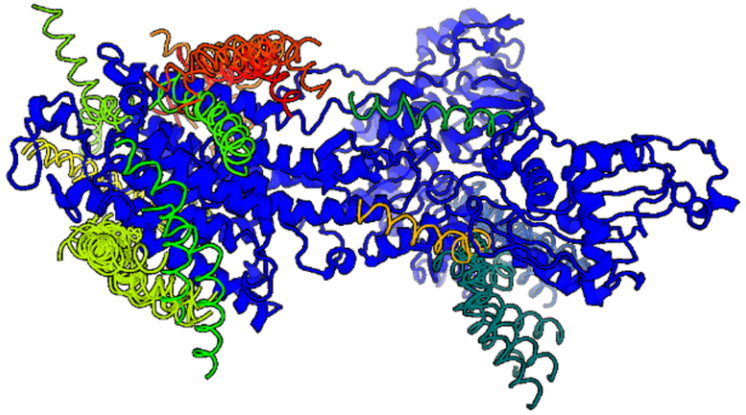
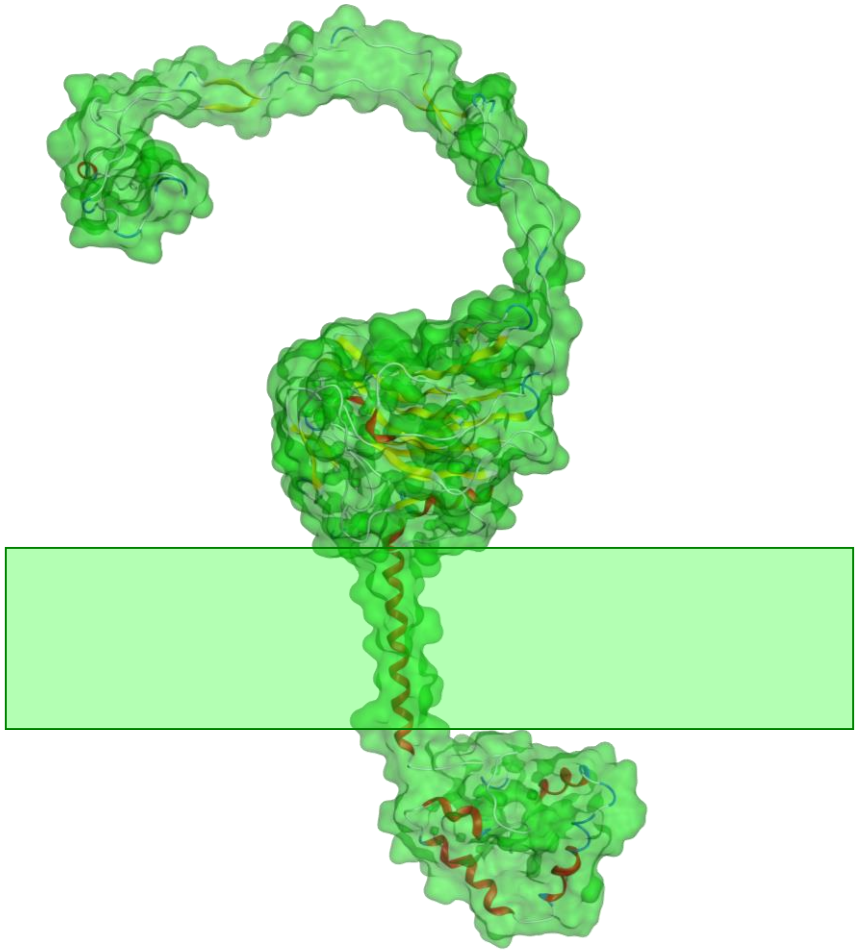
All Models	All models

Allmodels



Nef-Calnexin interaction



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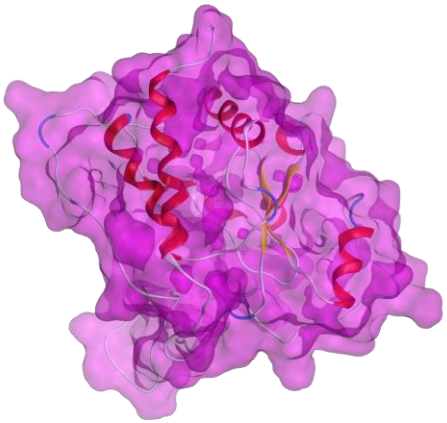
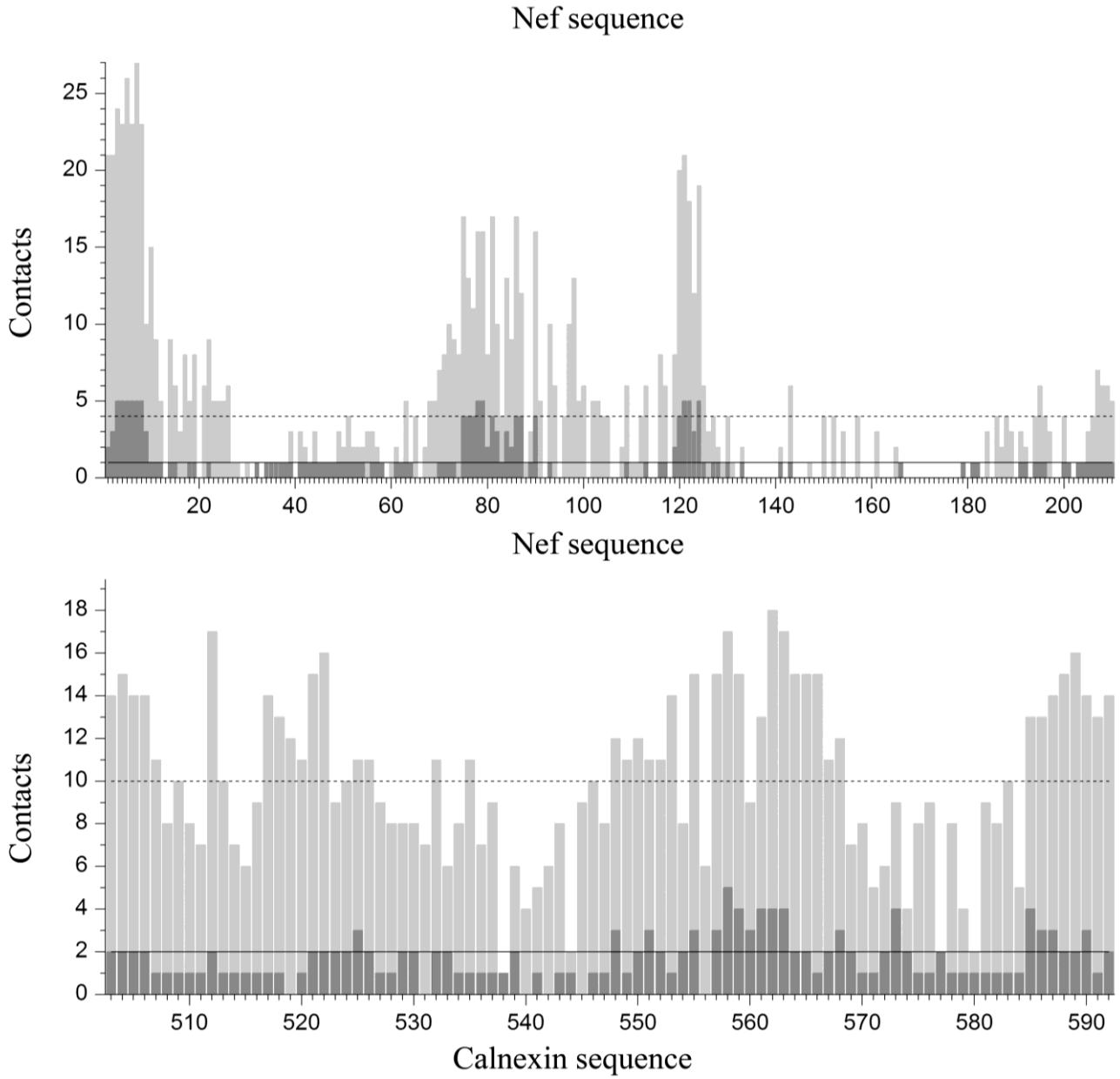
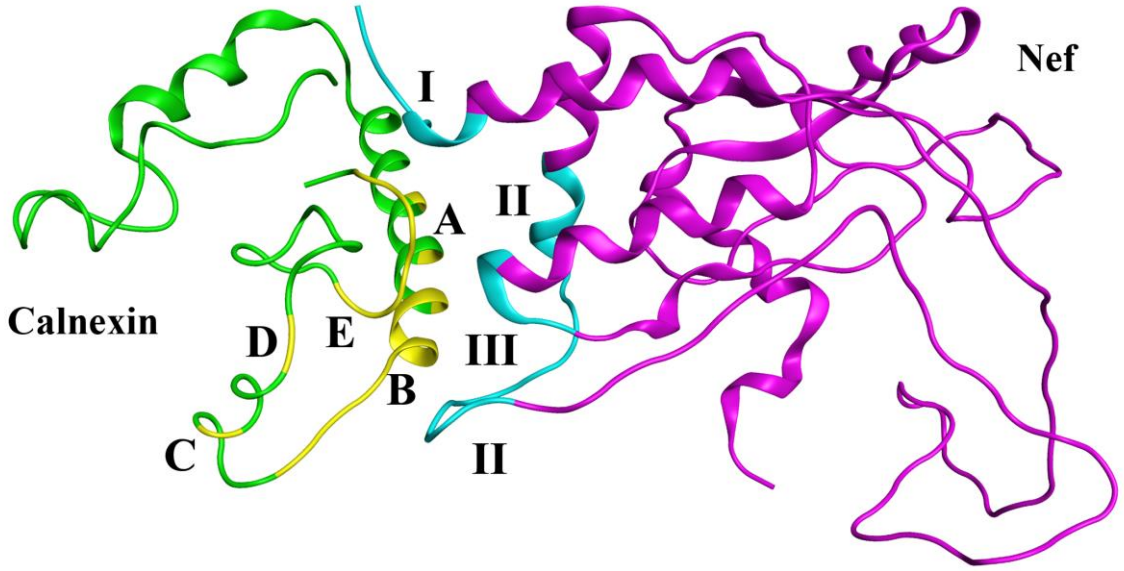
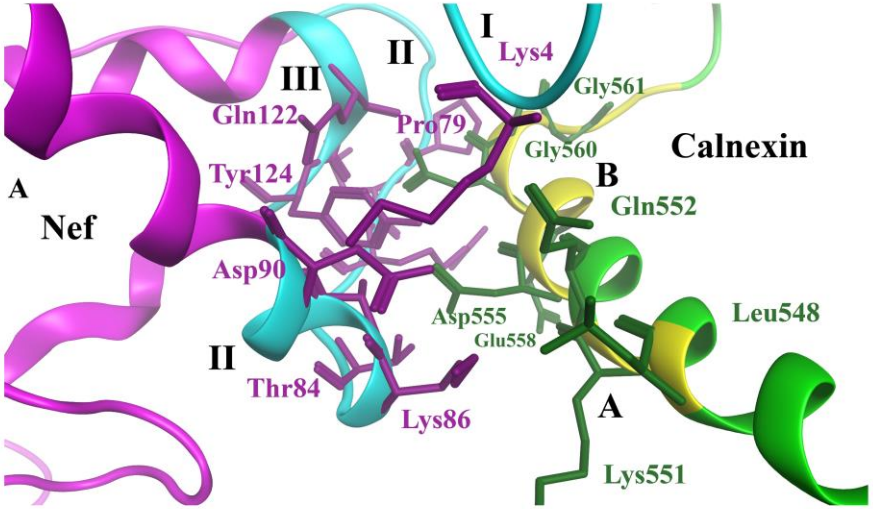
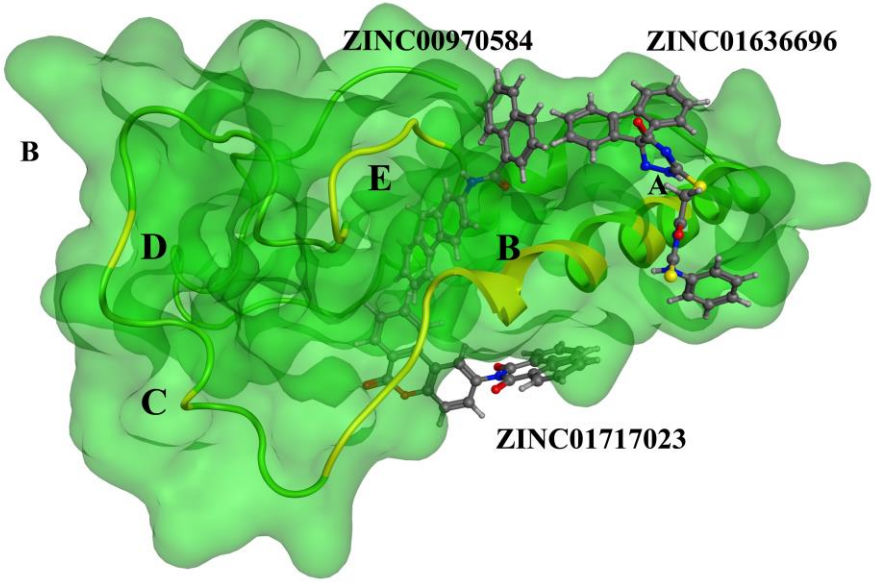



Nef sequence
Contacts
0
5
10
15
20
25
20
40
60
80
100
120
140
160
180
200
Nef sequence
Contacts
0
2
4
6
8
10
12
14
16
18
510
520
530
540
550
560
570
580
590
Calnexin sequence



			Nef interaction sites		
			I	II	III
			1-MGGKWSKRS-9	75-RPQVPLRPMTYKAALD-90	121-TQGY-124
Calnexin interaction sites	A	548L, 551K	**75**	**7**	**10**
	B	555-DAEEDGGTV-563	**90**	**314**	**131**
	C	568E	**0**	**14**	**0**
	D	573K	**13**	**12**	**0**
	E	585-RNRKPR-590	**113**	**60**	**47**


I
II
III
Lys4
Gly561
Gln122
Pro79
Gly560
Calnexin
Tyr124
B
A
Nef
Gln552
Asp90
Asp555
Leu548
Glu558
II
Thr84
A
Lys86
Lys551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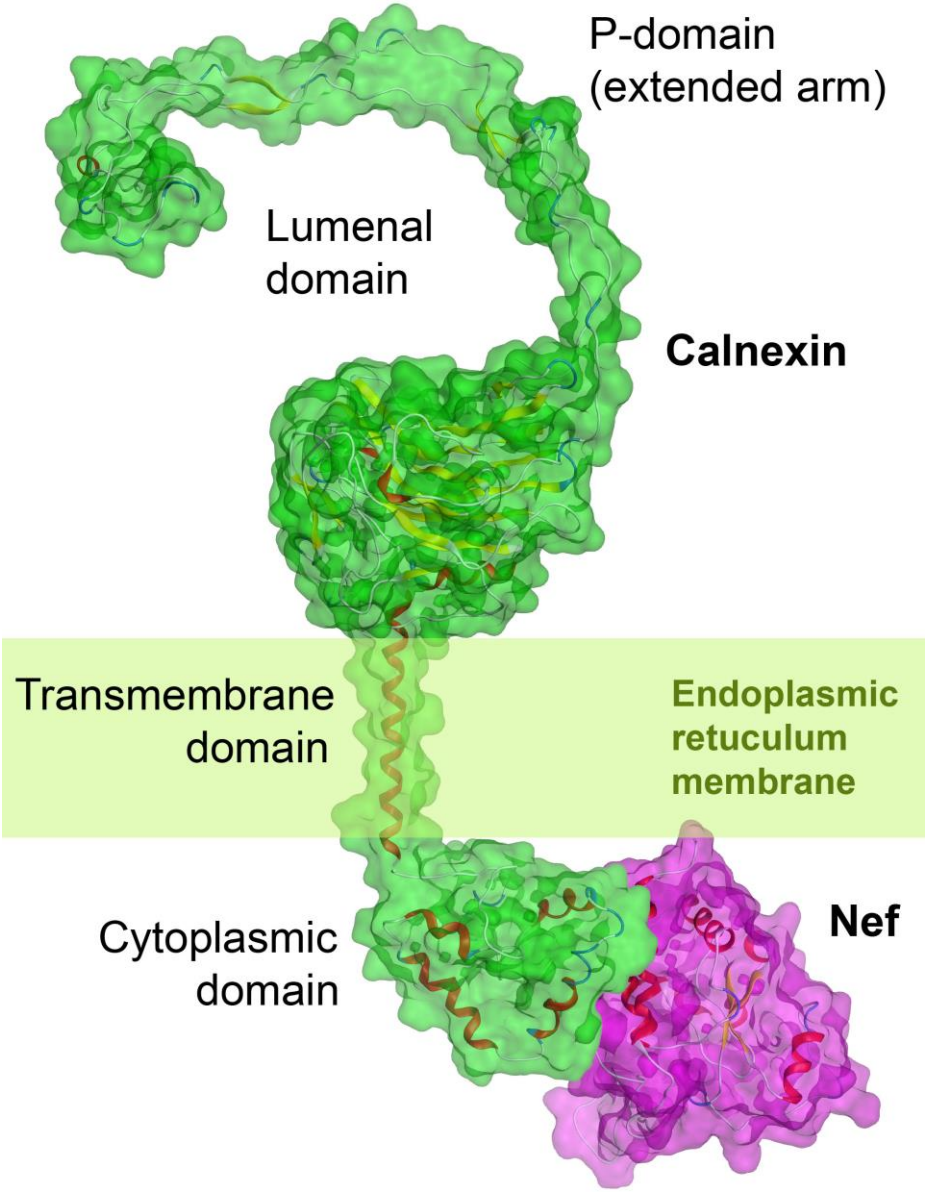
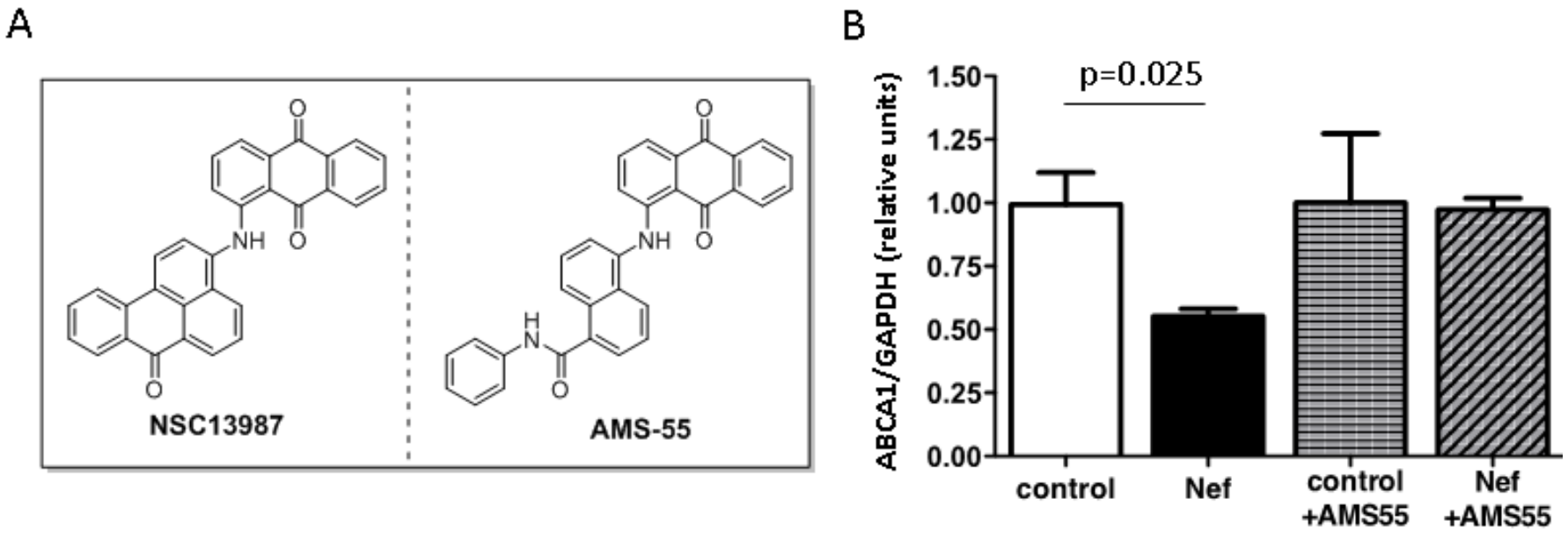
ZINC01636696
B
E
A
D
B
C
ZINC01717023

Hunegnaw, R., Vassylyeva, M., Dubrovsky, L., Pushkarsky, T., Sviridov, D., Anashkina, A.A., Üren, A., Brichacek, B., Vassylyev, D.G., Adzhubei, A.A. and Bukrinsky, M., 2016. Interaction between HIV-1 Nef and calnexin: From modeling to small molecule inhibitors reversing HIV-induced lipid accumulation. *Arteriosclerosis, thrombosis, and vascular biology*, *36*(9), pp.1758-1771.





Adzhubei AA, Anashkina AA, Tkachev YV, Kravatsky YV, Pushkarsky T, Kulkarni A, Makarov AA, Bukrinsky MI. *Modelling interaction between HIV-1 Nef and calnexin*. **AIDS**. 2018.

Thank you for attention!

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