Supporting Material

Design and development of novel antibiotics based on FtsZ inhibition - in silico studies

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1. Applicability domain

When QSAR model is developed molecules from the training set can be used for defining one of its main features, QSAR model applicability domain (AD). AD is defined as biological, structural, or physicochemical space, knowledge, or information on which the developed QSAR model from training set is developed and which can be used further for predicting whether a developed QSPR model can be used on compounds which are not used in the model developing. For these reasons AD can be applied for the assessment of the reliability of a developed QSPR model, because if the application of the AD defines a studied compound as very different in comparison to all compounds from the training set, a reliable prediction of its property/activity is uncertain [1,2]. In presented research the difference between experimental and calculated values for a studied endpoint is used for defining the AD, with the application of $Delta(obs)$, d and $\bar{d}$ as defined with Eq. 1 and 2. For each molecule used in the QSPR study, $Delta(obs)$ is calculated as the difference between experimental and calculated values from a studied endpoint. d and $\bar{d}$ are defined in Eqs. 1 and 2, respectively, where n is the number of studied compounds.

$$\bar{d} = \frac{\sum Delta(obs)}{n} \quad (1)$$

$$d = \frac{\sum [Delta(obs) - Delta(calc)]^2}{n} \quad (2)$$

If $Delta(obs)$ of a studied compound belongs within the range $\bar{d}$ - d and $\bar{d}$ + d, then it falls in the defined model AD, but, if a compound's $Delta(obs)$ does not belong within a defined range, then that compound does not belong in the defined AD. For this reason, the compound is considered as outlier, and it is discarded from the development of a QSPR model. A defined methodology for the determination of the AD was successfully applied in the development of various QSAR models based on the Monte Carlo method[5]. The relation used for defining the AD is given in Eq. 3:

$$Delta(obs) \in \left(\bar{d} - d, \bar{d} + d\right) \quad (3)$$

Table S1. The SMILES notation of the studied molecules, calculated values for the DCW, experimental data (Ac) – expr, the values of Ac calculated with the application of CORAL software – calc, the difference between expr and calc – diff for the built QSPR model.

	SMILES notation	DCW	Ac(expr.)	Ac(calc.)	Diff	Set
1	COc1cc(ccc1)C(N)=O	40.68943	1.868	2.158	-0.29	Training
2	NC(=O)c1c(F)ccc(OCCCCCC)c1F	102.5646	4.507	4.996	-0.489	Training
3	NC(=O)c2c(F)c(OCc1nc(C)cs1)ccc2F	82.97029	4.25	4.0973	0.1527	Training
4	NC(=O)c2c(F)c(OCc1ncc(C)s1)ccc2F	65.3319	3.045	3.2883	-0.2433	Training
5	NC(=O)c3c(F)c(OCc1nc(cs1)c2ccccc2)ccc3F	90.10409	4.973	4.4245	0.5485	Test
6	NC(=O)c2c(F)ccc(OCCn1cccn1)c2F	70.45059	3.018	3.5231	-0.5051	Training
7	NC(=O)c3c(F)ccc(Oc1nc2ccccc2s1)c3F	75.4637	3.077	3.753	-0.676	Training
8	NC(=O)c3c(F)ccc(OCc1nc2ccccc2s1)c3F	79.2083	5.204	3.9248	1.2792	Training
9	NC(=O)c3c(F)ccc(OCc1ccc2ccccc2n1)c3F	80.4635	4.293	3.9823	0.3107	Training
10	NC(=O)c3c(F)ccc(OCc1nc2ccccc2o1)c3F	79.14101	3.376	3.9217	-0.5457	Test
11	Cc2cc(COc1ccc(F)c(C(N)=O)c1F)sc2	75.24137	3.947	3.7428	0.2042	Training
12	NC(=O)c2c(F)ccc(OCc1cccc(C)n1)c2F	77.46416	3.939	3.8448	0.0942	Test
13	NC(=O)c3c(F)ccc(OCc2nc1c(cccc1Cl)s2)c3F	96.69232	4.345	4.7267	-0.3817	Training
14	NC(=O)c3c(F)ccc(OCc1nc2ccc(Cl)cc2s1)c3F	94.15516	4.948	4.6103	0.3377	Training
15	NC(=O)c3c(F)ccc(OCc1nc2cccc(Cl)c2s1)c3F	93.40735	4.948	4.576	0.372	Training
16	NC(=O)c3c(F)ccc(OCc1nc2c(C)cccc2s1)c3F	94.84867	4.32	4.6421	-0.3221	Test
17	NC(=O)c3c(F)ccc(OCc1nc2ccc(C)cc2s1)c3F	95.59648	4.621	4.6764	-0.0554	Training
18	NC(=O)c3c(F)ccc(OCc1nc2c(cccc2s1)OC)c3F	96.16465	4.34	4.7025	-0.3625	Training
19	NC(=O)c3c(F)ccc(OCc1nc2ccc(cc2s1)OC)c3F	96.91246	3.136	4.7368	-1.6008	Training
20	NC(=O)c4c(F)ccc(OCc1nc2c(cccc2s1)c3ccccc3)c4F	88.28479	3.189	4.3411	-1.1521	Training
21	NC(=O)c4c(F)ccc(OCc1nc2ccc(cc2s1)c3ccccc3)c4F	89.0326	3.189	4.3754	-1.1864	Training
22	NC(=O)c4c(F)ccc(OCc1nc2cccc(c2s1)c3ccccc3)c4F	88.28479	3.189	4.3411	-1.1521	Training
24	NC(=O)c3c(F)ccc(OCc1nc2cc(Cl)ccc2s1)c3F	94.15516	5.551	4.6103	0.9407	Training
25	NC(=O)c3c(F)ccc(OCc1nc2cc(C)ccc2s1)c3F	95.59648	4.922	4.6764	0.2456	Training
26	NC(=O)c3c(F)ccc(OCc1nc2cc(ccc2s1)CCC)c3F	117.6633	6.462	5.6886	0.7734	Training

27	NC(=O)c3c(F)ccc(OCc1nc2cc(ccc2s1)OC)c3F	96.91246	5.244	4.7368	0.5072	Training
28	NC(=O)c3c(F)ccc(OCc1nc2cc(ccc2s1)OCC)c3F	108.9121	6.464	5.2872	1.1768	Training
29	NC(=O)c4c(F)ccc(OCc1nc2cc(ccc2s1)c3ccccc3)c4F	89.0326	6.2	4.3754	1.8246	Training
30	NC(=O)c3c(F)ccc(OCc1nc2cc(Br)ccc2s1)c3F	117.5234	6.504	5.6821	0.8219	Test
31	NC(=O)c3c(F)ccc(OCc1nc2cc(ccc2s1)C(F)(F)F)c3F	113.3412	6.191	5.4903	0.7007	Test
32	NC(=O)c3c(F)ccc(OCc1nc2cc(O)ccc2s1)c3F	92.89664	4.021	4.5526	-0.5316	Test
33	NC(=O)c3c(F)ccc(OCc1nc2cc(N)ccc2s1)c3F	85.63922	3.719	4.2197	-0.5007	Training
34	NC(=O)c3c(F)ccc(OCc1nc2cc(ccc2s1)N(C)C)c3F	87.65862	3.754	4.3123	-0.5583	Training
35	NC(=O)c3c(F)ccc(OCc1nc2cc(ccc2s1)C(N)=O)c3F	87.84261	3.754	4.3208	-0.5668	Training
36	NC(=O)c3c(F)ccc(OCc1nc2cc(ccc2s1)C(=O)O)c3F	94.29396	3.755	4.6167	-0.8617	Training
37	NC(=O)c3c(F)ccc(OCc1nc2cc(ccc2s1)C(=O)OC)c3F	97.24277	5.57	4.7519	0.8181	Training
38	NC(=O)c4c(F)ccc(OCc1nc2cc(ccc2s1)c3ncno3)c4F	118.8551	5.89	5.7432	0.1468	Training
39	NC(=O)c4c(F)ccc(OCc1nc2cc(ccc2s1)c3nccn3)c4F	81.86677	3.78	4.0467	-0.2667	Test
40	NC(=O)c3c(F)ccc(OCc1nc2cc(Cl)cnc2s1)c3F	112.1993	5.551	5.4379	0.1131	Training
41	NC(=O)c4c(F)ccc(OCc1nc2cc(cnc2s1)c3ccccc3)c4F	107.0768	5.9	5.203	0.697	Training
42	NC(=O)c3c(F)ccc(OCc1nc2cc(cnc2s1)OCC)c3F	126.9562	6.465	6.1148	0.3502	Training
43	NC(=O)c3c(F)ccc(OCc1nc2cc(Cl)ncc2s1)c3F	94.9643	4.648	4.6474	0.0006	Test
44	NC(=O)c3c(F)ccc(OCc1nc2cc(OC)c(Cl)nc2s1)c3F	108.2252	4.382	5.2557	-0.8737	Training
45	NC(=O)c3c(F)c(OCc1nc(co1)c2ccccc2)ccc3F	87.22225	4.314	4.2923	0.0217	Training
46	NC(=O)c3c(F)c(OCc1nc(co1)c2ccc(O)cc2)ccc3F	100.9106	4.636	4.9202	-0.2842	Test
47	NC(=O)c3c(F)c(OCc1nc(co1)c2ccc(Cl)cc2)ccc3F	102.1691	4.962	4.9779	-0.0159	Training
48	NC(=O)c3c(F)c(OCc1nc(co1)c2ccc(OC)cc2)ccc3F	103.8594	5.255	5.0554	0.1996	Training
49	NC(=O)c3c(F)c(OCc1nc(c(C)o1)c2ccc(Cl)cc2)ccc3F	109.299	5.879	5.3049	0.5741	Test
50	NC(=O)c3c(F)c(OCc1nc(c(Br)o1)c2ccc(Cl)cc2)ccc3F	143.6156	6.869	6.8789	-0.0099	Training
51	NC(=O)c3c(F)c(OCc1nc(c(N)o1)c2ccc(Cl)cc2)ccc3F	90.6516	3.773	4.4496	-0.6766	Training
52	NC(=O)c3c(F)c(OCc1nc(c(o1)[N+]([O-])=O)c2ccc(Cl)cc2)ccc3F	72.65428	3.8	3.6241	0.1759	Training
53	NC(=O)c3c(F)c(OCc1nc(c(OC)o1)c2ccc(Cl)cc2)ccc3F	109.548	5.897	5.3163	0.5807	Training
54	NC(=O)c3c(F)c(OCc1nc(c(CO)o1)c2ccc(Cl)cc2)ccc3F	110.9263	4.693	5.3796	-0.6866	Training
55	NC(=O)c3c(F)c(OCc1nc(c(OCC)o1)c2ccc(Cl)cc2)ccc3F	121.5476	6.835	5.8667	0.9683	Test
56	NC(=O)c3c(F)c(OCc1nc(c(CCC)o1)c2ccc(Cl)cc2)ccc3F	134.0501	7.154	6.4402	0.7138	Training

57	NC(=O)c3c(F)c(OCc1nc(c(CC=C)o1)c2ccc(Cl)cc2)ccc3F	150.6818	6.829	7.203	-0.374	Training
58	NC(=O)c3c(F)c(OCc1nc(c(CCCO)o1)c2ccc(Cl)cc2)ccc3F	129.3658	5.325	6.2253	-0.9003	Training
59	NC(=O)c3c(F)c(OCc1nc(c(CC)o1)c2ccc(OC)cc2)ccc3F	129.3005	6.511	6.2223	0.2887	Test
60	NC(=O)c4c(F)c(OCc1nc(c(o1)C2CC2)c3ccc(OC)cc3)ccc4F	137.0224	6.524	6.5765	-0.0525	Training
61	NC(=O)c4c(F)c(OCc1nc(c(o1)c2ccccc2)c3ccc(OC)cc3)ccc4F	114.483	6.562	5.5427	1.0193	Training
62	NC(=O)c4c(F)ccc(OCc1nc(c(o1)c2cncs2)c3ccc(OC)cc3)c4F	117.658	5.345	5.6883	-0.3433	Training
63	FC(F)(F)c1ccc(cc1)c3nc(COc2ccc(F)c(c2F)C(N)=O)oc3Br	138.5985	6.6	6.6488	-0.0488	Training
64	FC(F)(F)c1ccc(cc1)c3nc(COc2ccc(F)c(c2F)C(N)=O)oc3C#N	108.8656	5.326	5.285	0.041	Training
65	FC(F)(F)Oc1ccc(cc1)c3nc(COc2ccc(F)c(c2F)C(N)=O)oc3Cl	133.6508	6.578	6.4219	0.1561	Training
66	FC(F)(F)Oc1ccc(cc1)c3nc(COc2ccc(F)c(c2F)C(N)=O)oc3Br	141.2232	6.917	6.7692	0.1478	Training
67	FC(F)(F)Oc1ccc(cc1)c3nc(COc2ccc(F)c(c2F)C(N)=O)oc3I	146.4128	6.954	7.0072	-0.0532	Training
68	FC(F)(F)Oc1ccc(cc1)c3nc(COc2ccc(F)c(c2F)C(N)=O)oc3C(F)(F)F~	134.1588	5.987	6.4452	-0.4582	Training
69	O=C(N)c1cc(O)ccc1	91.26327	5.137	4.4777	0.6593	Training
70	NC(=O)c1cc(OCCCCl)ccc1	73.24415	3.523	3.6512	-0.1282	Training
71	NC(=O)c1cc(OCCCCCl)ccc1	79.68399	4.454	3.9466	0.5074	Training
72	NC(=O)c1cc(OCCCCCCl)ccc1	86.12383	5.383	4.2419	1.1411	Training
73	NC(=O)c1cc(OCCCCCCCl)ccc1	92.56367	3.6	4.5373	-0.9373	Training
74	NC(=O)c1cc(OCCBr)ccc1	66.16264	3.28	3.3264	-0.0464	Training
75	NC(=O)c1cc(OCCCBr)ccc1	72.60248	3.6	3.6218	-0.0218	Training
76	NC(=O)c1cc(OCCCCBr)ccc1	79.04232	4.531	3.9171	0.6139	Training
77	NC(=O)c1cc(OCCCCCBr)ccc1	85.48216	4.252	4.2125	0.0395	Test
78	NC(=O)c1cc(OCCCCCCBr)ccc1	91.922	3.671	4.5079	-0.8369	Training
79	NC(=O)c1cc(OCCCCCOCC)ccc1	87.55336	3.594	4.3075	-0.7135	Training
80	NC(=O)c1cc(OCCCCOCCC)ccc1	87.55336	3.918	4.3075	-0.3895	Test
81	NC(=O)c1cc(OCCCOCCCC)ccc1	87.55336	4.844	4.3075	0.5365	Training
82	NC(=O)c2cc(OCCCOc1ccccc1)ccc2	57.02518	3.326	2.9073	0.4187	Training
83	NC(=O)c2cc(OCCCOc1ccc(OC)cc1)ccc2	73.66233	3.18	3.6704	-0.4904	Test
84	Clc2ccc(OCCCOc1cc(ccc1)C(N)=O)cc2	64.70941	3.378	3.2597	0.1183	Training
85	[O-][N+](=O)c1ccc(cc1)OCCCOc2cc(ccc2)C(N)=O	57.81389	3.392	2.9435	0.4485	Training
86	NC(=O)c2cc(OCCCCOc1ccccc1)ccc2	63.46502	3.348	3.2027	0.1453	Training

87	NC(=O)c2cc(OCCCCOc1ccc(OC)cc1)ccc2	80.10217	3.391	3.9658	-0.5748	Test
88	Clc2ccc(OCCCCOc1cc(ccc1)C(N)=O)cc2	71.14925	3.397	3.5551	-0.1581	Training
89	[O-][N+](=O)c1ccc(cc1)OCCCCOc2cc(ccc2)C(N)=O	64.25373	3.411	3.2388	0.1722	Training
90	NC(=O)c2cc(OCCCn1cncn1)ccc2	74.93402	3.284	3.7287	-0.4447	Test
91	NC(=O)c2cc(OCCCCn1cncn1)ccc2	81.37386	3.308	4.0241	-0.7161	Test
92	NC(=O)c2cc(OCCCCn1ccnc1)ccc2	79.39307	3.306	3.9332	-0.6272	Test
93	NC(=O)c1cc(ccc1)OCCCn2c3ccccc3nc2C	73.55311	3.402	3.6654	-0.2634	Test
94	NC(=O)c1cc(ccc1)OCCSc2nc3ccccc3s2	71.20661	3.411	3.5577	-0.1467	Test
95	NC(=O)c1cc(ccc1)OCCCSc2nc3ccccc3s2	77.64645	3.43	3.8531	-0.4231	Test
96	NC(=O)c1cc(ccc1)OCCCSc2nc3ccccc3n2	71.19445	3.407	3.5572	-0.1502	Training
97	NC(=O)c1cc(ccc1)OCCCCSc2nc3ccccc3s2	84.08629	3.447	4.1485	-0.7015	Test

Table S2. The list of SA_ks together with their correlation weights for the three runs of the Monte Carlo optimization

	$CW(SA_k)$		
SA_k	Run 1	Run 2	Run 3
#.....	-0.80818	-1.24613	-1.87344
$10011000000	0.3717	-0.30894	1.99769
$10011000010	1.68322	0.94243	1.49703
$10011000100	-0.06119	0.99702	0.56411
$10011001000	0.62931	0.25447	-0.62012
$10011001001	6.62961	4.74703	4.0669
$10011001010	3.50111	4.74683	2.93972
$10011001100	-0.8142	0.24994	-0.81012
$10011001110	9.00294	6.56144	6.87027
$11011001000	-1.43347	-0.87131	-0.93612
(...(.....	-0.25143	-0.37877	-0.30844
(.....	1.50277	0.81214	0.12999
(...C...(...	-0.31355	-0.24748	-1.00043
(...F...(...	-0.24855	1.62989	1.31257
(...Br..(...	3.93456	4.12281	3.87337
(...Cl..(...	-0.00479	-1.12296	-1.62044
(...N...(...	-0.44207	0.37479	0.18324
(...O...(...	1.24777	4.25096	1.75457
(...c...(...	-2.99915	-4.9339	-5.06318
+.....	-0.62708	-0.49861	-0.24737
+...[...(...	-0.24836	-0.87033	0.99784
-.....	-0.2495	-1.25273	0.562
-...[...(...	-1.87905	-1.31137	-2.12076
1...(.....	0.12062	-0.18608	-0.43792
1.....	7.99659	7.06165	1.68629
1...F...(...	1.1297	-0.43441	1.62204
1...Cl..(...	0.25034	-0.81644	-1.12046
1...c...(...	2.81698	1.24942	3.12228
1...n...(...	0.99508	0.99691	1.00429
1...o...(...	-0.87851	0.37048	0.06214
1...s...(...	-2.37761	-0.50034	-0.99526
2...(.....	-0.00258	-0.74588	-0.18533
2.....	0.00466	0.24586	0.06112
2...C...(...	1.87571	5.06014	5.18969
2...F...(...	3.24954	1.62369	2.93648
2...c...(...	-0.62433	-1.56685	-0.37873
2...n...1...	1.56155	0.18847	2.87566

2...o...1...	1.00144	0.99875	0.99512
2...s...(...	-0.19071	-0.80969	0.12731
2...s...1...	0.62932	0.19081	0.7515
3...(.....	0.31408	2.12139	0.55834
3.....	0.8145	0.49992	-0.5651
3...C...#...	-1.06048	-1.56026	-0.62393
3...C...(...	-6.503	-7.30799	-4.75024
3...c...(...	2.37413	1.56555	1.49736
3...c...2...	0.9981	0.99811	0.99569
3...n...2...	-1.55985	-2.12921	-1.49551
3...s...2...	1.00234	0.99554	0.9991
4.....	0.74513	0.49588	0.24743
4...c...(...	1.24577	0.43528	0.62872
=...(.....	-2.00432	-2.62802	-1.75299
=.....	-0.37261	-0.05989	-0.62155
=...C...(...	9.87221	9.62696	9.49682
=...O...(...	-6.05969	-4.56542	-4.68436
C...#.....	0.00071	0.99678	0.4984
C...(.....	1.8756	2.18626	2.12628
C...(...1...	0.37789	0.18593	1.12352
C...(...2...	0.25023	1.37827	0.31744
C...(...=...	1.87781	1.62604	1.80862
C...(...C...	-6.55788	-6.87483	-5.06687
C.....	2.00399	1.9967	1.49876
C...2...(...	2.81017	3.8743	3.87258
C...2.....	1.19248	-0.00288	0.68958
C...2...C...	4.30896	3.93979	2.49585
C...3.....	-2.62684	-3.37821	-1.06636
C...=.....	6.44149	7.43867	5.93357
C...=...C...	3.05956	1.69061	2.25315
C...C...(...	6.49523	7.00448	5.87359
C...C.....	3.00323	2.00326	2.49731
C...C...2...	1.31467	4.00298	2.87807
C...C...=...	2.12068	2.12426	2.56521
C...C...C...	1.43262	2.06112	0.94073
C...Br..(...	1.56018	2.43899	2.31723
C...Cl..(...	3.9423	3.94189	3.50117
C...O...(...	0.99733	1.87444	1.62245
C...O...C...	-0.87626	-0.50489	-0.18307
C...c...1...	0.62302	1.81347	2.18754
C...c...2...	1.37909	1.81476	1.00263

C...n...1...	2.12898	1.62291	0.93924
C...n...2...	1.00351	0.99709	1.00193
F...(...(...	-0.56119	-0.12575	-0.30888
F...(.....	1.74777	1.68378	1.25053
F...(...C...	1.62343	0.87028	1.99896
F...(...F...	-0.31624	0.68852	1.62024
F.....	1.99877	1.99812	1.93629
F...1.....	-0.68761	-0.81709	1.75268
F...2.....	1.0662	1.49896	0.37181
F...3.....	1.18611	2.74951	1.99843
F...4.....	0.06597	0.12585	0.4963
F...C...(...	2.25281	2.56227	2.37229
F...C.....	2.24874	1.2507	0.18869
Br..(.....	4.00347	2.87463	3.56013
Br.....	5.37821	4.37194	5.18997
Br..3.....	2.62936	3.43747	2.49674
Br..C.....	-0.06268	0.81389	1.62564
Br..C...C...	1.37511	2.62254	0.56391
I.....	4.93408	3.93579	3.87669
I...3.....	3.87656	4.37842	4.62836
Cl..(.....	1.50465	2.81326	2.50093
Cl.....	1.25304	1.99763	1.87669
Cl..1.....	2.87318	0.43557	1.56417
Cl..3.....	6.49976	3.81717	3.31115
Cl..C.....	4.06639	4.24716	4.12174
Cl..C...C...	4.24747	4.62704	3.37537
Cl..c...2...	0.68374	1.75144	0.18462
HALO00000000	1.87868	0.1293	2.2548
HALO00100000	0.5644	1.93755	2.25499
HALO01000000	0.62628	0.31627	0.44177
HALO10000000	-0.37168	0.81676	-0.00483
HALO10010000	6.00423	3.74834	4.68252
HALO10100000	4.18385	4.12041	2.93949
HALO11000000	-0.93614	-0.49576	0.37361
HALO11100000	5.56096	6.31642	6.56584
N...#.....	-1.49755	-0.12717	-0.75355
N...#...C...	-0.12118	-1.18588	-1.18384
N...(.....	0.68684	0.44098	0.49664
N...(...1...	-7.62837	-6.37145	-5.6267
N...(...=...	1.24964	0.87056	0.62218
N...(...C...	1.49565	0.56361	0.55864

N...+.....	-0.50056	-0.68866	0.37559
N.....	-1.56394	-1.75149	-0.99872
N...C...(...	1.06232	2.94189	1.05862
N...C.....	1.87142	1.68778	1.87615
N...[...(...	0.62362	-0.25462	-1.00342
O...(.....	1.93945	0.06428	0.62823
O...(...1...	2.62379	4.18683	3.37741
O...(...F...	2.19178	1.56052	2.87316
O...(...O...	0.93404	1.0614	1.25369
O...-.....	-0.24787	-0.74821	0.12578
O.....	0.6258	-0.99714	-0.31457
O...=...(...	-1.87462	-1.24971	-0.62209
O...=.....	-0.93681	-0.06284	0.56728
O...=...C...	23.74822	26.00449	22.75104
O...C...(...	0.87703	1.81298	0.81711
O...C.....	-1.12326	0.37109	0.49941
O...C...C...	1.3742	1.44023	-0.12071
O...[...(...	-1.75227	-0.31425	-1.68635
O...c...1...	0.55971	0.25107	1.12024
O...c...2...	1.12486	1.18488	-0.06277
S.....	1.18901	1.43581	1.68313
S...C.....	1.31321	0.0607	1.80831
S...C...C...	1.75316	2.00407	1.81681
S...c...2...	0.94176	0.87815	0.44132
[...(.....	-1.37036	-0.99749	-1.12671
[...(...1...	-2.06097	-1.18373	-0.43389
[...(...=...	-0.93664	-1.12196	-1.24722
[...(...[...	-2.00173	-0.87978	-1.3137
[...+.....	-0.43745	-0.44023	-0.49757
[...+...N...	-0.3084	0.0635	0.18791
[...-.....	-0.80771	-0.12243	-1.06443
[...-...O...	0.00147	0.00105	-0.99522
[.....	-0.05851	0.12987	-0.37905
[...N...+...	-1.18364	-0.37661	0.49557
[...N.....	-0.62897	-0.62185	0.06081
[...O...-...	-0.74918	-0.87884	0.50165
[...O.....	-0.31126	0.81296	-0.4406
[...[...-...	-0.25264	0.37766	0.31681
[...[.....	-0.24696	0.93348	-0.62778
[...[...N...	-0.37501	2.49617	-0.12594
c...(.....	1.37505	1.87839	1.81365

c...(...1...	0.74752	2.74859	1.68441
c...(...2...	1.93891	0.24721	1.31599
c...(...3...	0.06653	2.05897	-0.12611
c...(...C...	2.2534	2.1831	2.50316
c...(...F...	1.00062	0.00395	2.12819
c...(...Br..	3.56414	1.8738	1.99606
c...(...Cl..	3.12876	2.50423	2.18498
c...(...N...	0.31175	0.94033	1.06747
c...(...O...	0.74807	1.31132	1.12293
c...(...c...	-0.06119	0.50032	0.31679
c.....	0.31456	0.18335	0.25189
c...1...(...	-1.12509	-1.06051	-0.94153
c...1.....	1.00386	2.62042	1.87546
c...1...F...	1.18288	-0.30861	0.81183
c...1...Cl..	1.8139	-0.93792	0.19002
c...1...c...	0.62316	2.12039	2.00372
c...2...(...	0.87096	1.31499	1.87439
c...2.....	0.43386	0.3767	0.43815
c...2...C...	0.99993	1.00137	1.00132
c...2...F...	0.18289	0.62517	0.81594
c...2...c...	-0.06506	-0.50441	-0.4369
c...3...(...	0.62792	0.44066	1.37413
c...3.....	0.93782	1.18627	1.62783
c...3...C...	-2.87076	-2.81376	-1.74873
c...3...F...	1.93804	2.12726	2.19179
c...3...Br..	3.69102	3.1838	3.12058
c...3...I...	3.12864	4.49577	4.12753
c...3...Cl..	5.80862	2.06588	7.00408
c...3...c...	1.37957	0.06091	-0.49554
c...4.....	0.87401	-0.0048	0.25117
c...4...F...	0.87276	0.06108	0.37951
c...4...c...	0.68851	0.05847	0.87082
c...C.....	0.6209	1.87481	1.06403
c...C...O...	3.68293	0.37838	2.3161
c...Cl.....	1.74712	1.12514	1.74791
c...O...(...	1.50495	1.81345	1.12323
c...O.....	0.99564	0.43771	1.43386
c...O...C...	-0.06641	1.12473	0.12544
c...S.....	1.68622	0.24836	0.8119
c...S...C...	0.18515	0.99742	1.81346
c...c...(...	-0.06383	0.25486	0.50153

c...c.....	0.06174	0.25191	0.4986
c...c...1...	1.62106	2.18844	2.24594
c...c...2...	-0.24945	0.44108	0.50383
c...c...3...	-0.68314	-0.12908	-0.5594
c...c...4...	8.24523	7.24897	7.05873
c...c...c...	-0.43676	0.12175	-0.24988
c...n...(...	-0.05962	-2.05815	-1.56127
c...n...1...	-0.62737	0.25365	-0.30885
c...n...2...	0.7547	0.44035	0.87604
c...n...3...	-0.75131	-2.68602	-3.62766
c...n...c...	7.00095	6.12542	5.87162
c...o...(...	0.62088	1.75474	2.50485
c...o...1...	0.18396	1.93332	1.87147
c...s...(...	3.37056	1.56533	-0.0604
c...s...1...	1.44076	2.87951	2.87692
c...s...2...	-1.12978	-3.25321	-1.19202
n...(.....	2.18923	2.37328	1.81699
n...(...C...	1.00333	0.99768	0.99787
n...(...Cl..	0.12662	-2.18938	-1.74528
n.....	0.6842	2.12017	1.9354
n...1...(...	0.74847	3.99903	2.62657
n...1.....	1.06013	0.5641	0.43988
n...1...c...	0.87092	0.1871	0.37835
n...2.....	-0.06161	0.12144	-0.30842
n...2...c...	1.18477	1.62251	0.62665
n...3...(...	1.00287	0.99825	0.99821
n...3.....	-6.12724	-3.8733	-1.25252
n...3...c...	2.059	1.56189	1.12425
n...C.....	1.81022	-0.0674	2.12254
n...C...C...	1.43707	2.12882	1.43285
n...c...(...	5.99553	3.12957	3.74944
n...c.....	1.6839	3.12792	1.99901
n...c...1...	1.7516	1.68741	2.18715
n...c...2...	0.68364	2.37425	1.37557
n...c...3...	1.25109	0.05978	-0.56365
n...c...c...	0.56432	-0.19049	0.19069
n...c...n...	0.87189	1.80967	3.43599
n...o...3...	7.50441	5.06278	5.24536
o...(.....	-0.8792	-0.31369	0.81327
o...(...C...	1.69042	1.62564	1.49728
o...(...Br..	6.50392	7.87973	6.19226

o...(...N...	-8.94138	-8.87196	-8.06028
o...(...O...	1.56343	-0.50328	0.62002
o...(...c...	-0.62336	0.31075	0.99961
o.....	-1.87234	-0.81178	-1.75146
o...1...(...	0.56727	1.00038	1.18365
o...1.....	1.12023	1.18673	0.87685
o...2.....	1.00002	1.00344	1.00018
o...2...c...	0.99743	0.99779	0.99645
o...3...(...	6.245	5.62651	4.80844
o...3.....	6.06221	4.44164	4.2465
o...c...(...	0.06731	0.93395	1.8168
o...c.....	1.62801	1.05869	0.1281
o...c...3...	1.99888	1.99515	-0.31522
o...n.....	6.80983	6.68269	4.94045
o...n...c...	6.99661	5.1243	6.50195
s...(.....	0.44117	-0.74504	0.8134
s...(...C...	-2.75376	-1.62116	-0.81524
s...(...F...	0.5653	1.06678	1.1295
s...(...Cl..	0.62438	0.49995	-1.99896
s.....	-1.49627	0.18594	-0.62552
s...1...(...	1.75353	1.56708	1.12225
s...1.....	0.4326	0.49531	0.87115
s...2...(...	-0.87139	-0.24557	0.00037
s...2.....	-0.06615	-2.68491	-1.87123
s...2...c...	1.62832	0.12348	1.56115
s...3.....	1.0028	1.00277	1.00177
s...3...c...	1.00378	1.00337	0.99564
s...c...(...	1.31687	2.50309	1.93447
s...c.....	1.1288	3.81191	1.69118
s...c...2...	0.75005	1.43368	3.62084
s...c...n...	-1.37636	-2.62828	-0.62582

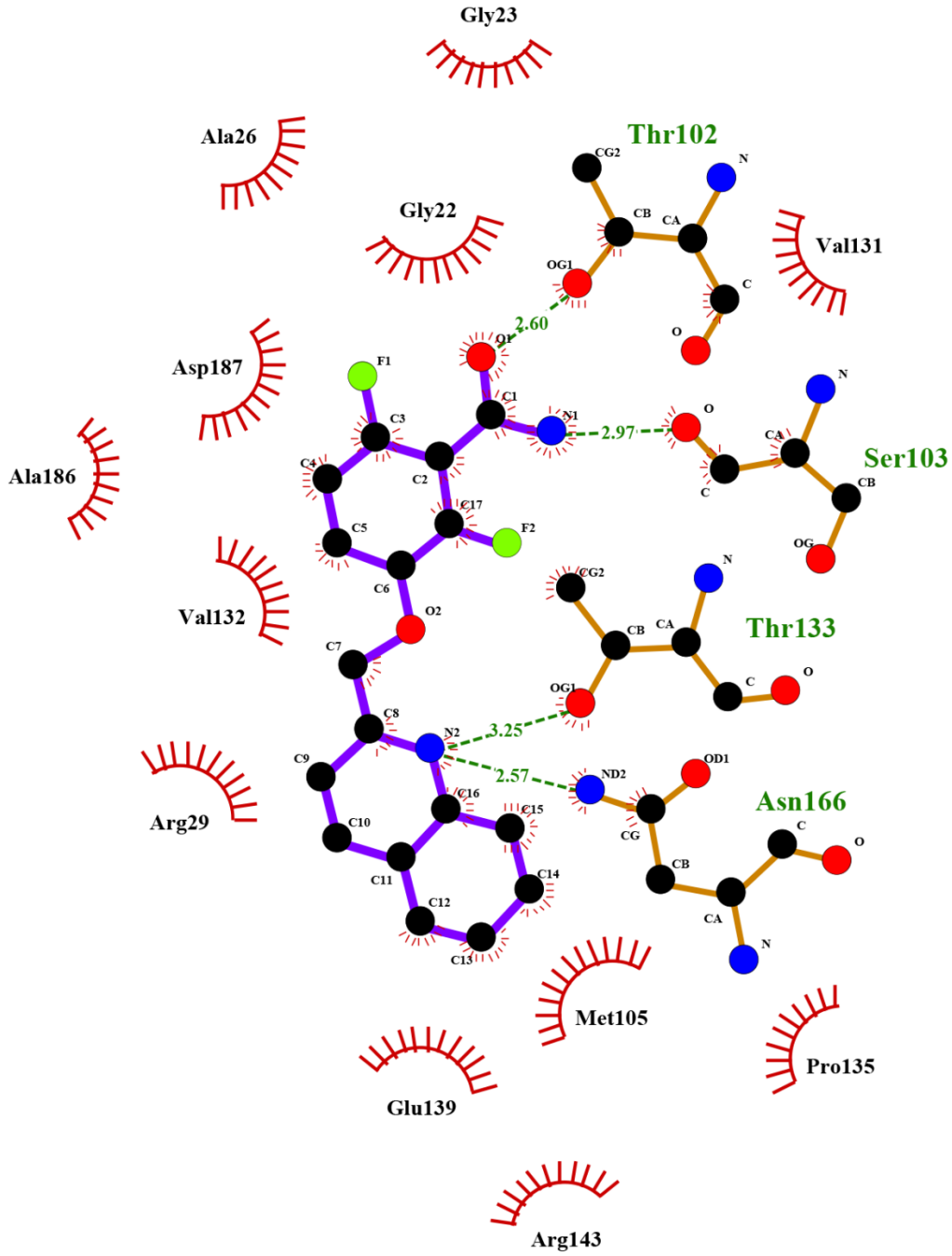

Figure S1. Two-dimensional representation of interaction between molecule A0 and amino acids inside FtsZ binding pocket.

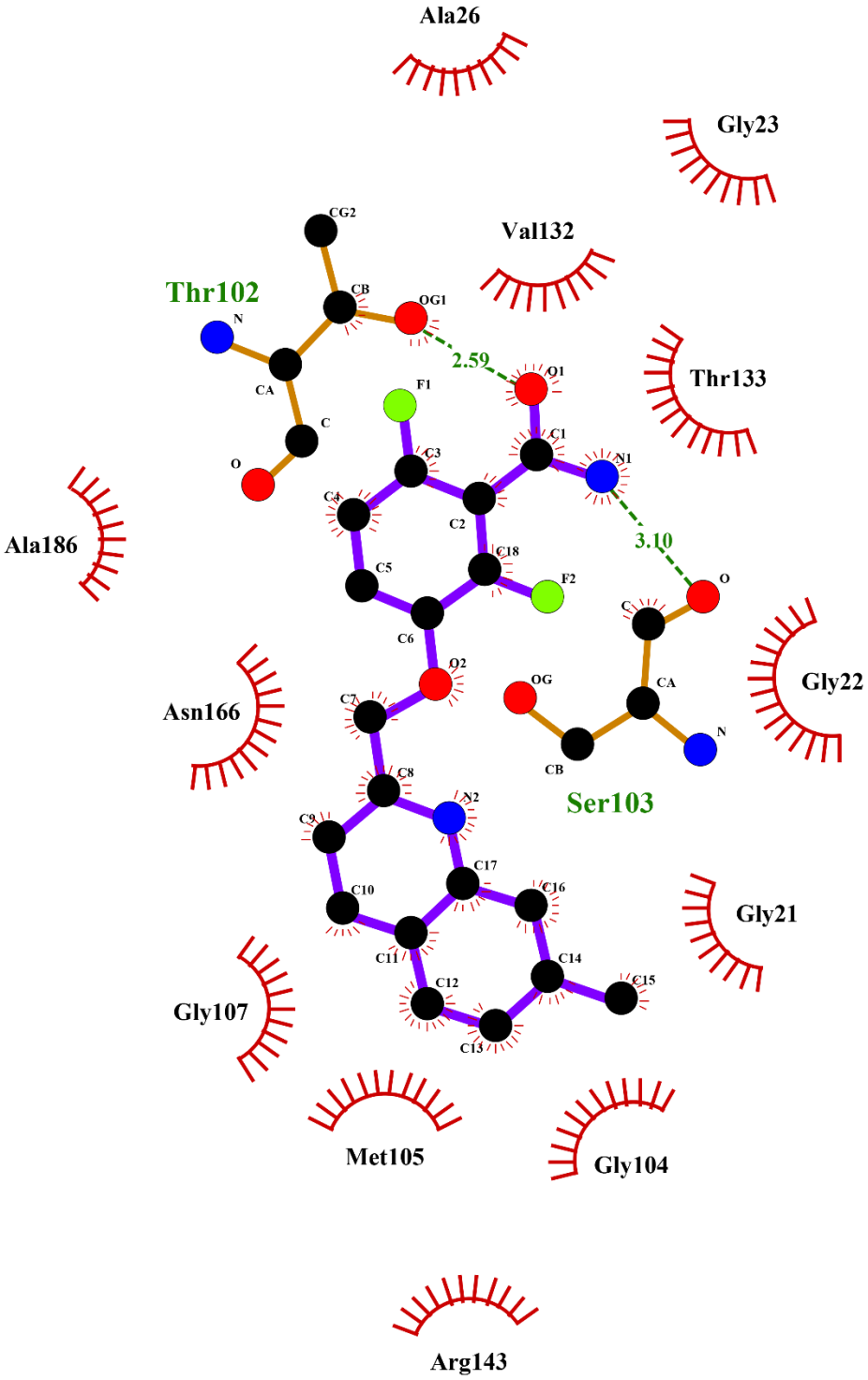

Figure S2. Two-dimensional representation of interaction between molecule A1 and amino acids inside FtsZ binding pocket.

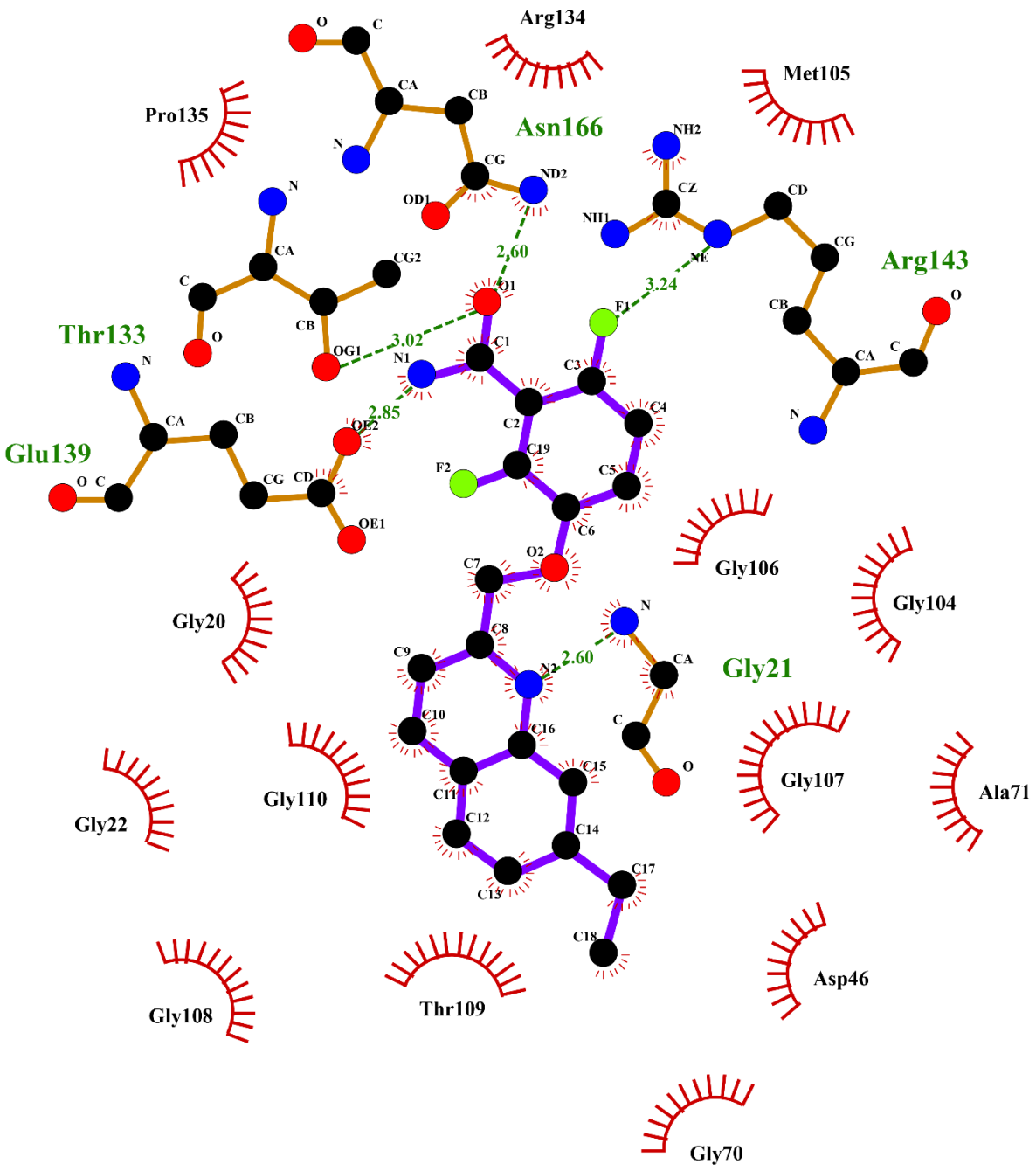

Figure S3. Two-dimensional representation of interaction between molecule A2 and amino acids inside FtsZ binding pocket.

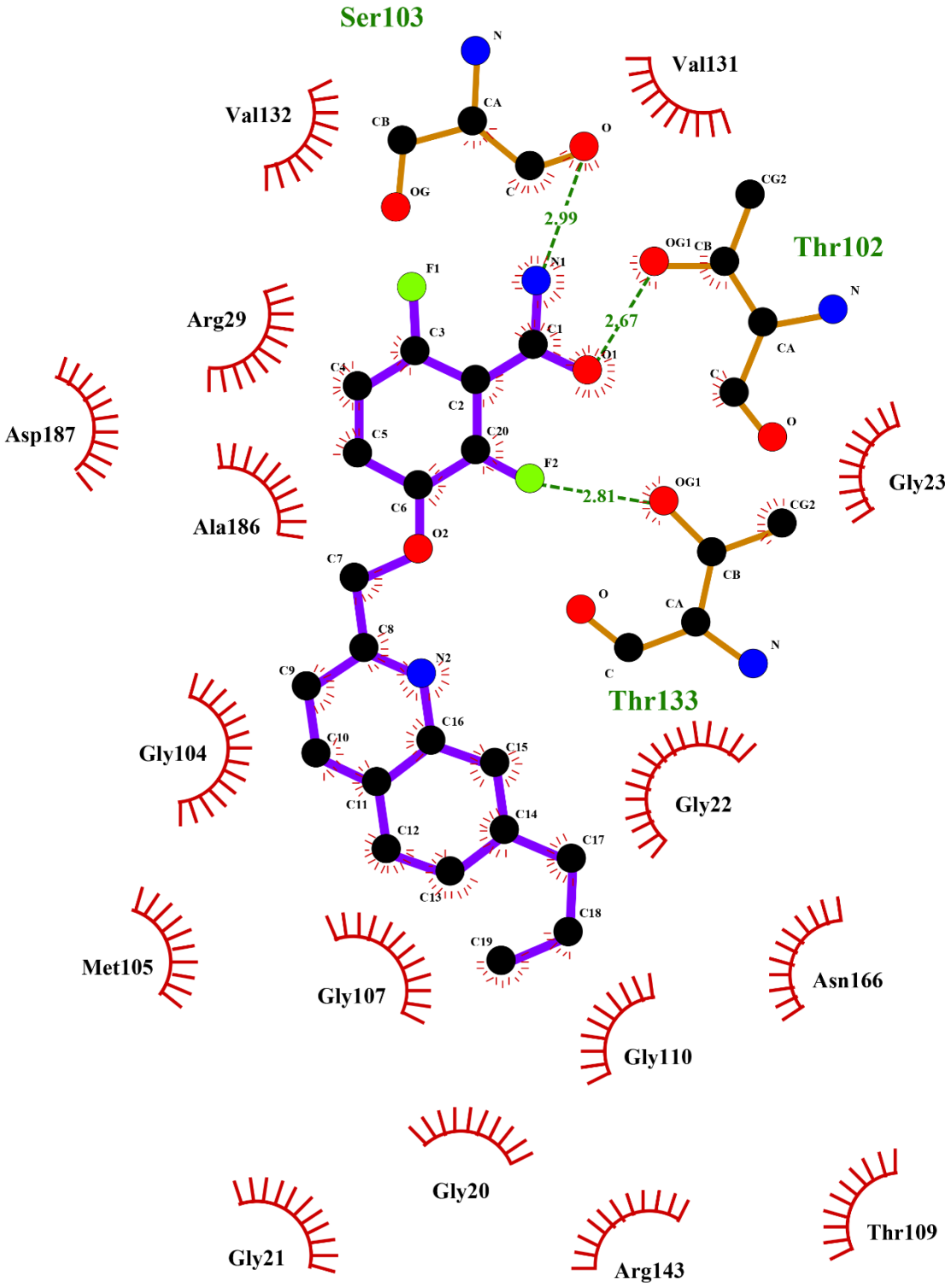

Figure S4. Two-dimensional representation of interaction between molecule A3 and amino acids inside FtsZ binding pocket.

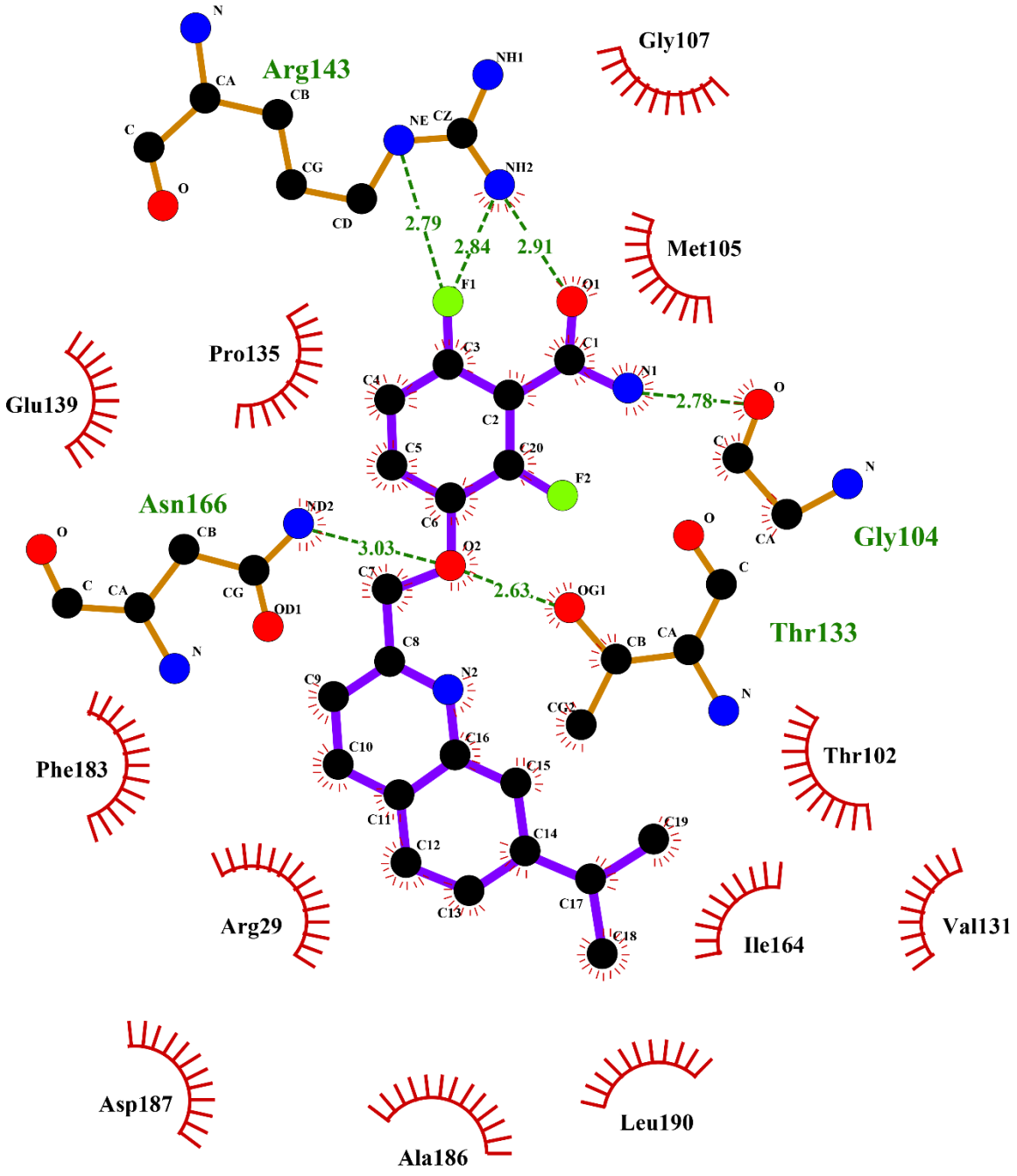

Figure S5. Two-dimensional representation of interaction between molecule A4 and amino acids inside FtsZ binding pocket.

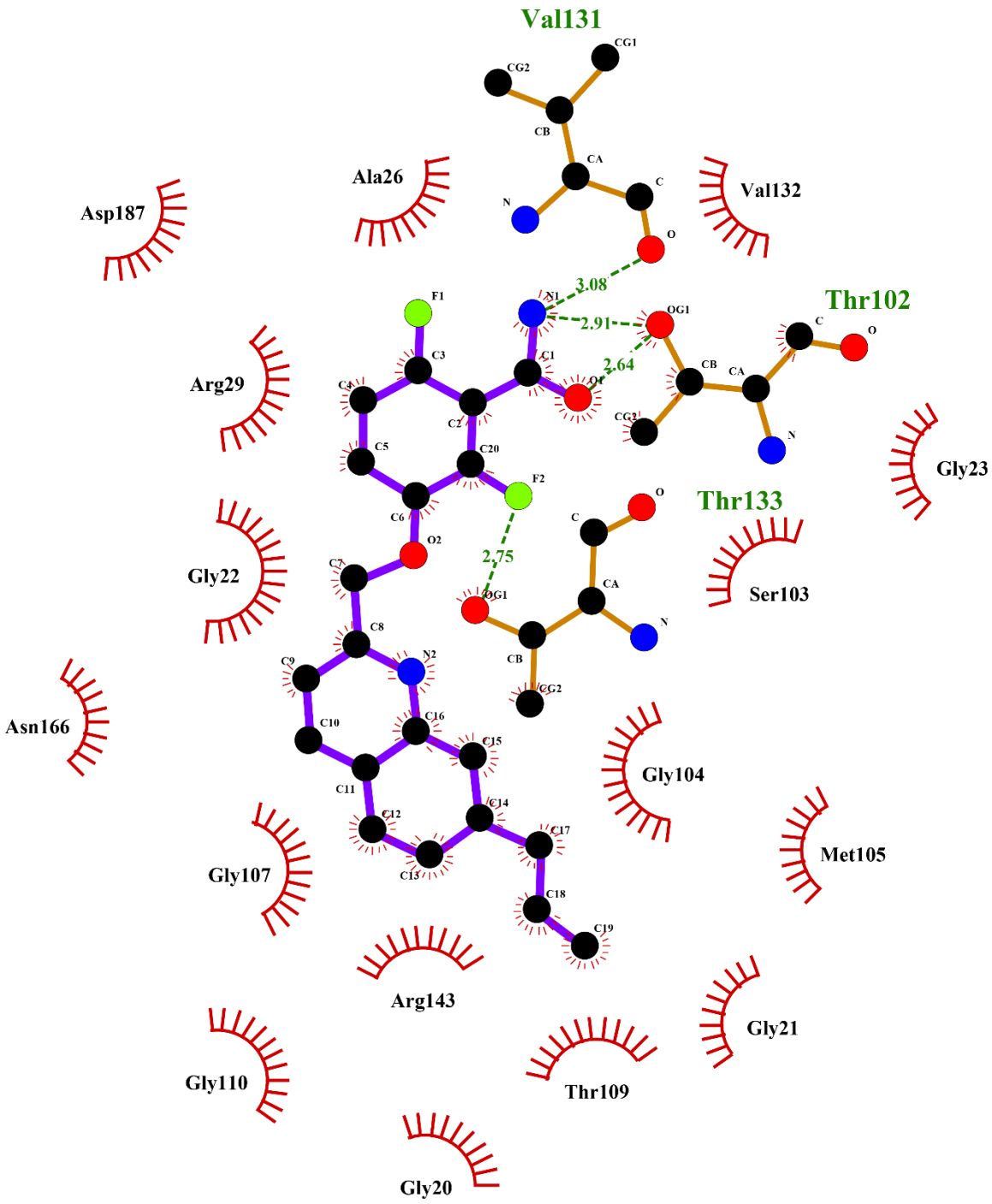

Figure S6. Two-dimensional representation of interaction between molecule A5 and amino acids inside FtsZ binding pocket.

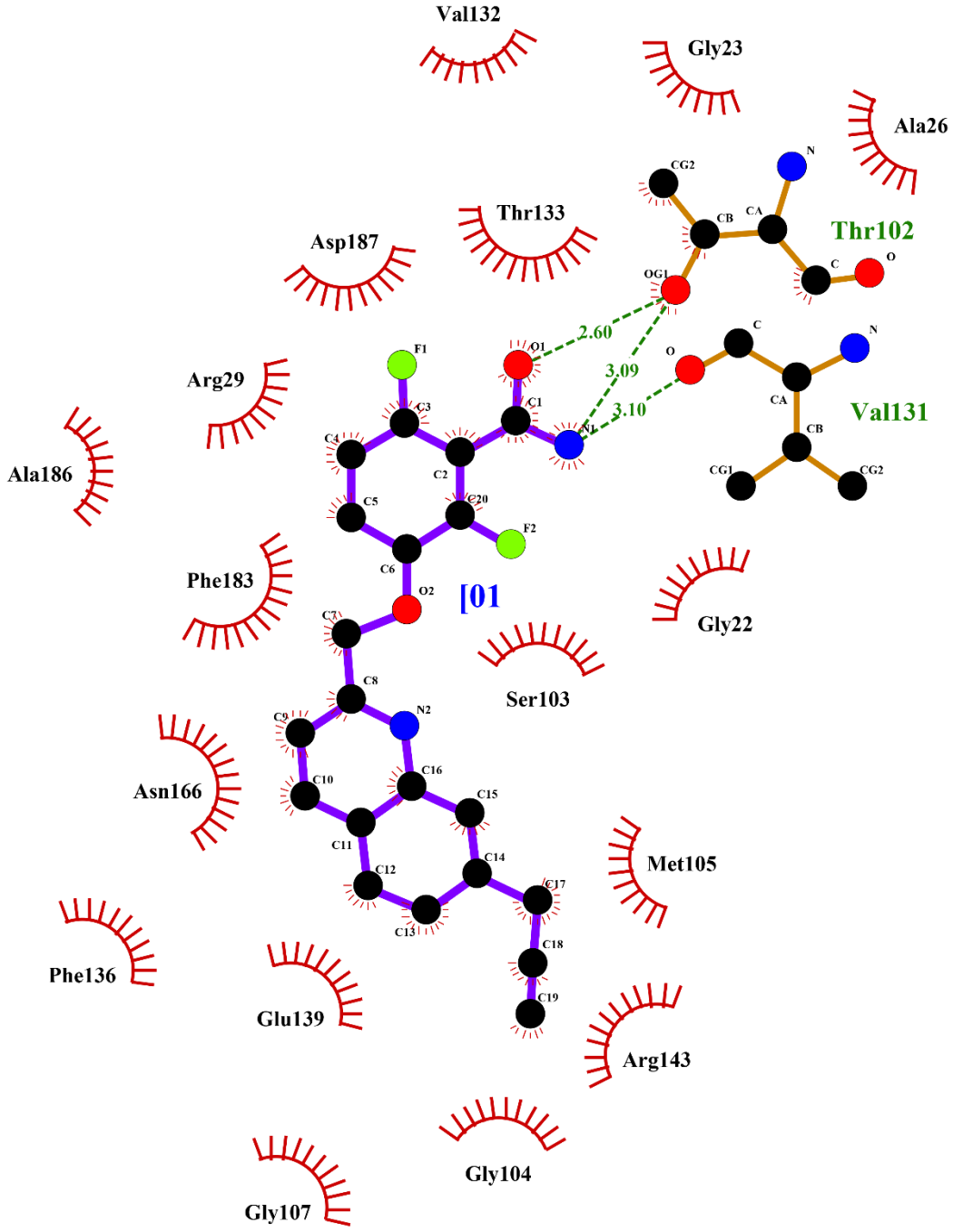

Figure S7. Two-dimensional representation of interaction between molecule A6 and amino acids inside FtsZ binding pocket.

References

1. Gadaleta D, Mangiatordi GF, Catto M, Carotti A, Nicolotti O (2016) Applicability Domain for QSAR Models: Where Theory Meets Reality. IJQSPR 1: 45-63.
2. Gramatica P (2007) Principles of QSAR models validation: internal and external. QSAR Comb Sci 26: 694-701.
3. Roy PP, Leonard JT, Roy K (2008) Exploring the impact of size of training sets for the development of predictive QSAR models. Chemom Intell Lab Syst 90: 31-42.