

Supplementary Materials

Computational insights into the fluconazole-resistance by the suspected mutations in lanosterol 14 α -demethylase (Erg11p) of *Candida albicans*

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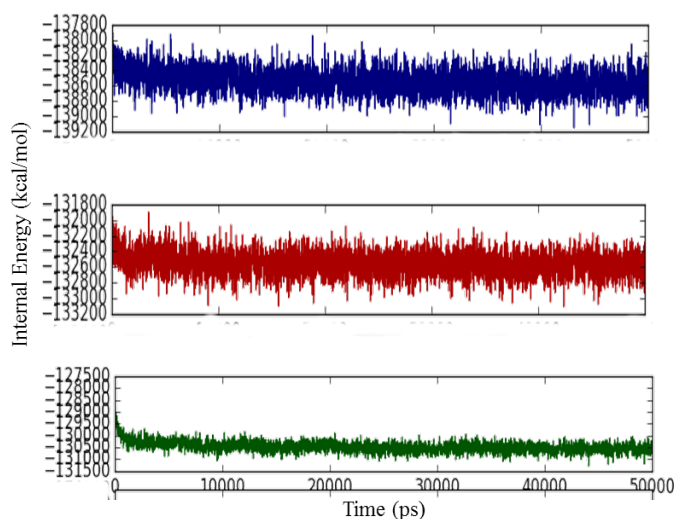
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(A)

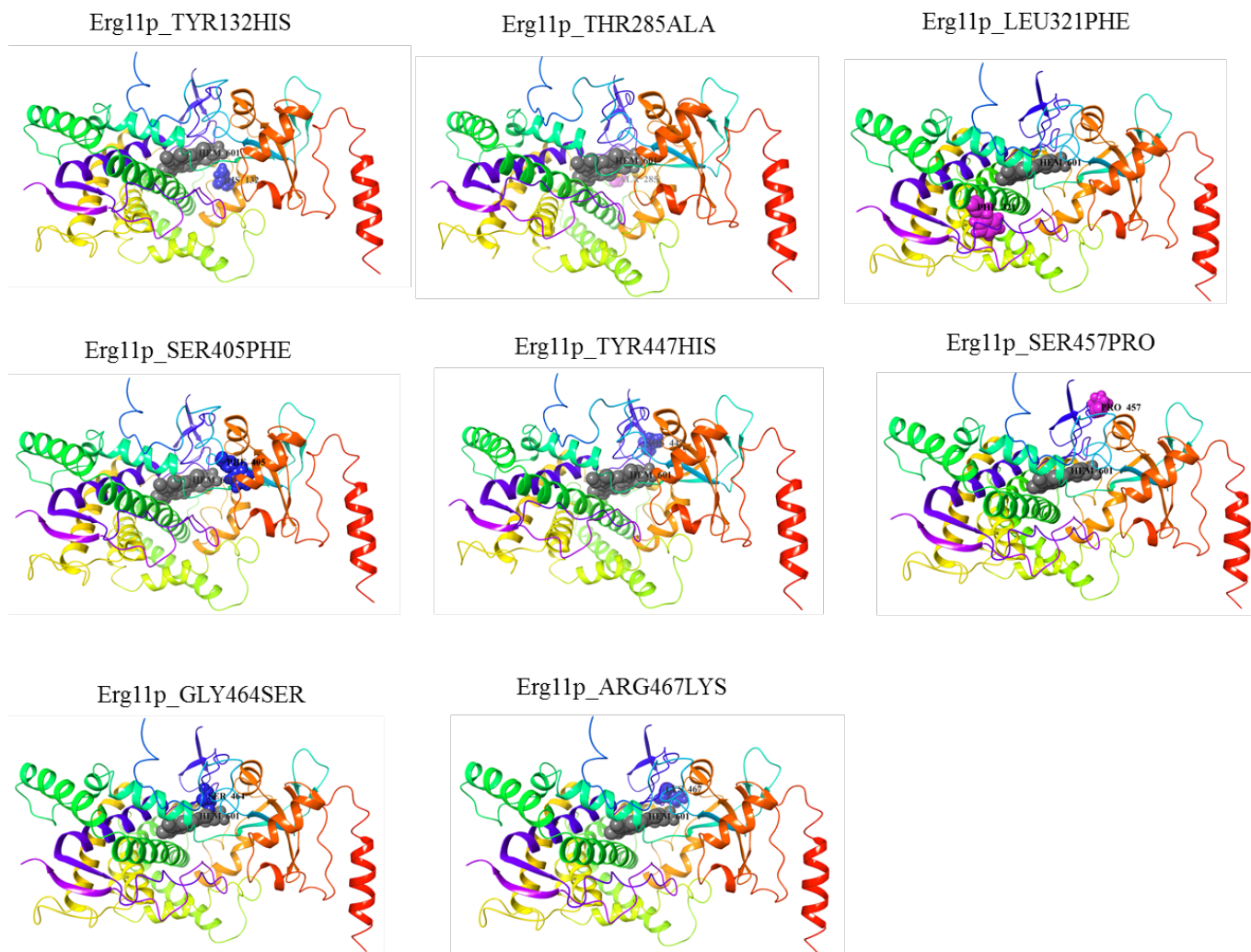
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5Tz1	-----KTPLVVYLPWFQGS	16
CaErg11p	MAIVE TVIDGHHYFLSLVTDQISLLGVPPVYHLVWQVLYSLRKRDRAPLVFVYLPWFQGS	60
5V5Z	-----ILGVPPVYHLVWQVLYSLRKRDRAPLVFVYLPWFQGS	36
SFSa	AASYGQPPVEFFESCRCQYGDVFSFRLGKIDTVLVLPKQHEVFVFAKLSQVSAEAYKH	76
5Tz1	AASYGQPPVEFFESCRCQYGDVFSFRLGKIDTVLVLPKQHEVFVFAKLSQVSAEAYKH	76
CaErg11p	AASYGQPPVEFFESCRCQYGDVFSFRLGKIDTVLVLPKQHEVFVFAKLSQVSAEAYKH	120
5V5Z	AASYGQPPVEFFESCRCQYGDVFSFRLGKIDTVLVLPKQHEVFVFAKLSQVSAEAYKH	96
SFSa	LTPVFGQVYVDCPHSRLNEQKFAKALTTDSFKRVYKIREELHVFVYVDESFLKKE	136
5Tz1	LTPVFGQVYVDCPHSRLNEQKFAKALTTDSFKRVYKIREELHVFVYVDESFLKKE	136
CaErg11p	LTPVFGQVYVDCPHSRLNEQKFAKALTTDSFKRVYKIREELHVFVYVDESFLKKE	180
5V5Z	LTPVFGQVYVDCPHSRLNEQKFAKALTTDSFKRVYKIREELHVFVYVDESFLKKE	156
SFSa	KTHGVANVRKIQEITTFATSRSLFGDEHRRIFDRSFAQLYSDLDKGFTPINVFPHLPL	196
5Tz1	KTHGVANVRKIQEITTFATSRSLFGDEHRRIFDRSFAQLYSDLDKGFTPINVFPHLPL	196
CaErg11p	KTHGVANVRKIQEITTFATSRSLFGDEHRRIFDRSFAQLYSDLDKGFTPINVFPHLPL	240
5V5Z	KTHGVANVRKIQEITTFATSRSLFGDEHRRIFDRSFAQLYSDLDKGFTPINVFPHLPL	216
SFSa	PHYHRDAQKKSATYWKELRERGGIDPDRDLIDSLLSHSYKDVQVHTQEQEIAHL	256
5Tz1	PHYHRDAQKKSATYWKELRERGGIDPDRDLIDSLLSHSYKDVQVHTQEQEIAHL	256
CaErg11p	PHYHRDAQKKSATYWKELRERGGIDPDRDLIDSLLSHSYKDVQVHTQEQEIAHL	300
5V5Z	PHYHRDAQKKSATYWKELRERGGIDPDRDLIDSLLSHSYKDVQVHTQEQEIAHL	276
SFSa	LIGLGGQHTSASTSANFLHLLGKPHLQVIVQEVVLLKEKGGDLIDLTYEDLQKLP	316
5Tz1	LIGLGGQHTSASTSANFLHLLGKPHLQVIVQEVVLLKEKGGDLIDLTYEDLQKLP	316
CaErg11p	LIGLGGQHTSASTSANFLHLLGKPHLQVIVQEVVLLKEKGGDLIDLTYEDLQKLP	360
5V5Z	LIGLGGQHTSASTSANFLHLLGKPHLQVIVQEVVLLKEKGGDLIDLTYEDLQKLP	336
SFSa	SVNITIKETLRNRRPLHSIFRKYVTPLRLEPETHYLVKGGHYLVSPQVAMTSERYFDNPE	376
5Tz1	SVNITIKETLRNRRPLHSIFRKYVTPLRLEPETHYLVKGGHYLVSPQVAMTSERYFDNPE	376
CaErg11p	SVNITIKETLRNRRPLHSIFRKYVTPLRLEPETHYLVKGGHYLVSPQVAMTSERYFDNPE	420
5V5Z	SVNITIKETLRNRRPLHSIFRKYVTPLRLEPETHYLVKGGHYLVSPQVAMTSERYFDNPE	396
SFSa	DFDPTBMTAAAKANSVFSRSDDEVYFGQVSKGVSSPPLFGGGRRCIGEQAVYQL	436
5Tz1	DFDPTBMTAAAKANSVFSRSDDEVYFGQVSKGVSSPPLFGGGRRCIGEQAVYQL	436
CaErg11p	DFDPTBMTAAAKANSVFSRSDDEVYFGQVSKGVSSPPLFGGGRRCIGEQAVYQL	480
5V5Z	DFDPTBMT-----SDEVYFGQVSKGVSSPPLFGGGRRCIGEQAVYQL	444
SFSa	GTILTFVYHLRNTIDQVYVDPDYSNVLPTPAEILMEKRETCHE	484
5Tz1	GTILTFVYHLRNTIDQVYVDPDYSNVLPTPAEILMEKRETCHE	484
CaErg11p	GTILTFVYHLRNTIDQVYVDPDYSNVLPTPAEILMEKRETCHE	528
5V5Z	GTILTFVYHLRNTIDQVYVDPDYSNVLPTPAEILMEKRETCHE	488

(B)

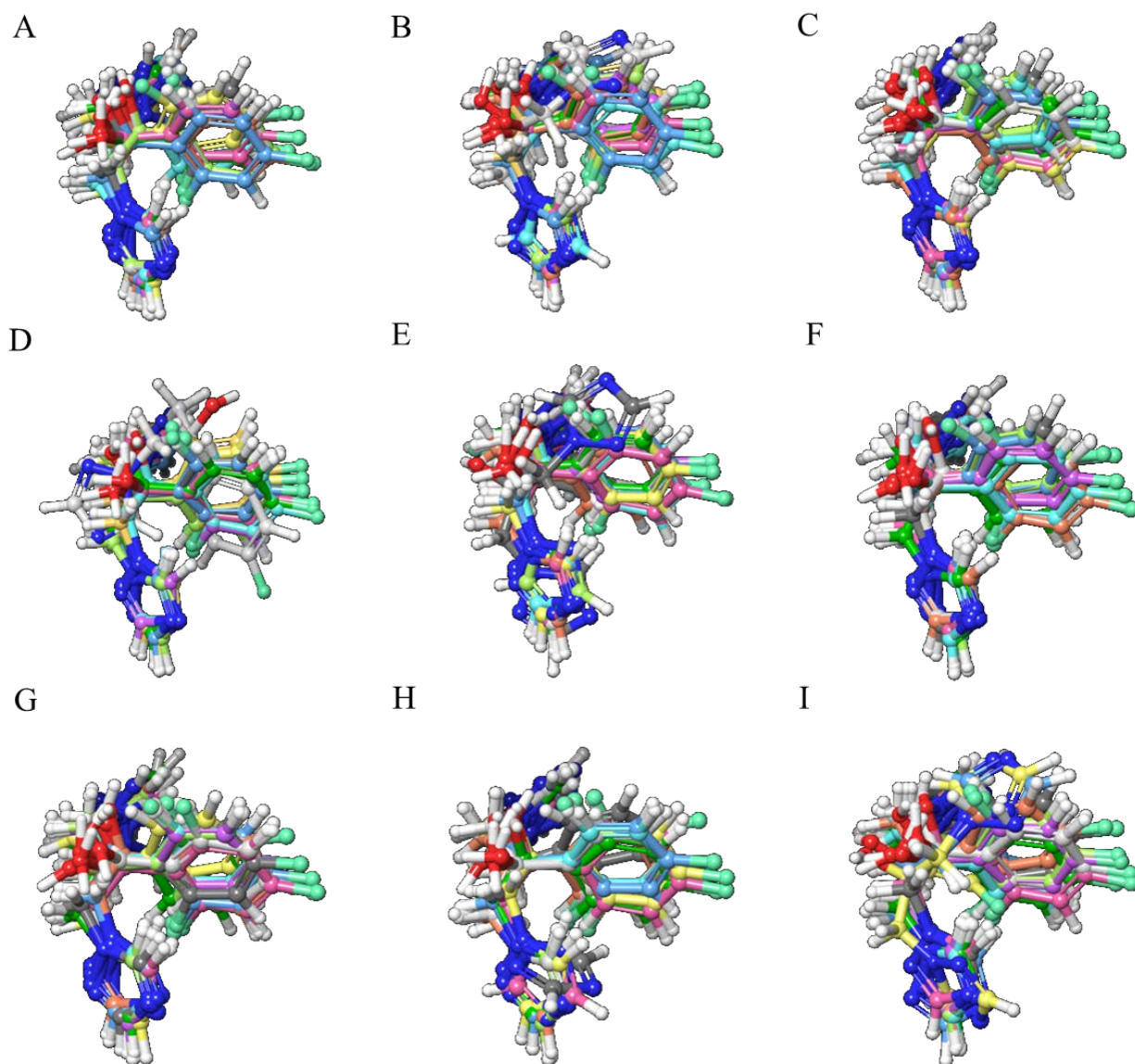


Supplement Figure 1 (A) The multiple sequence alignment of the Erg11 protein (*Candida albicans*) with its available crystal structures 5FSA, 5Tz1, and 5V5Z (Yellow highlights – mutations). (B) Internal energy of all the Erg11p crystal structures from the molecular dynamics simulations analysis (Colour representation: Blue-5FSA, Red- 5Tz1 and Green-5V5Z)

The Erg1p residue mutations incorporated using the mutation tool and processed using the protein preparation tool in the Schrodinger suite. All the mutations along with heme are labeled and showed below respectively.

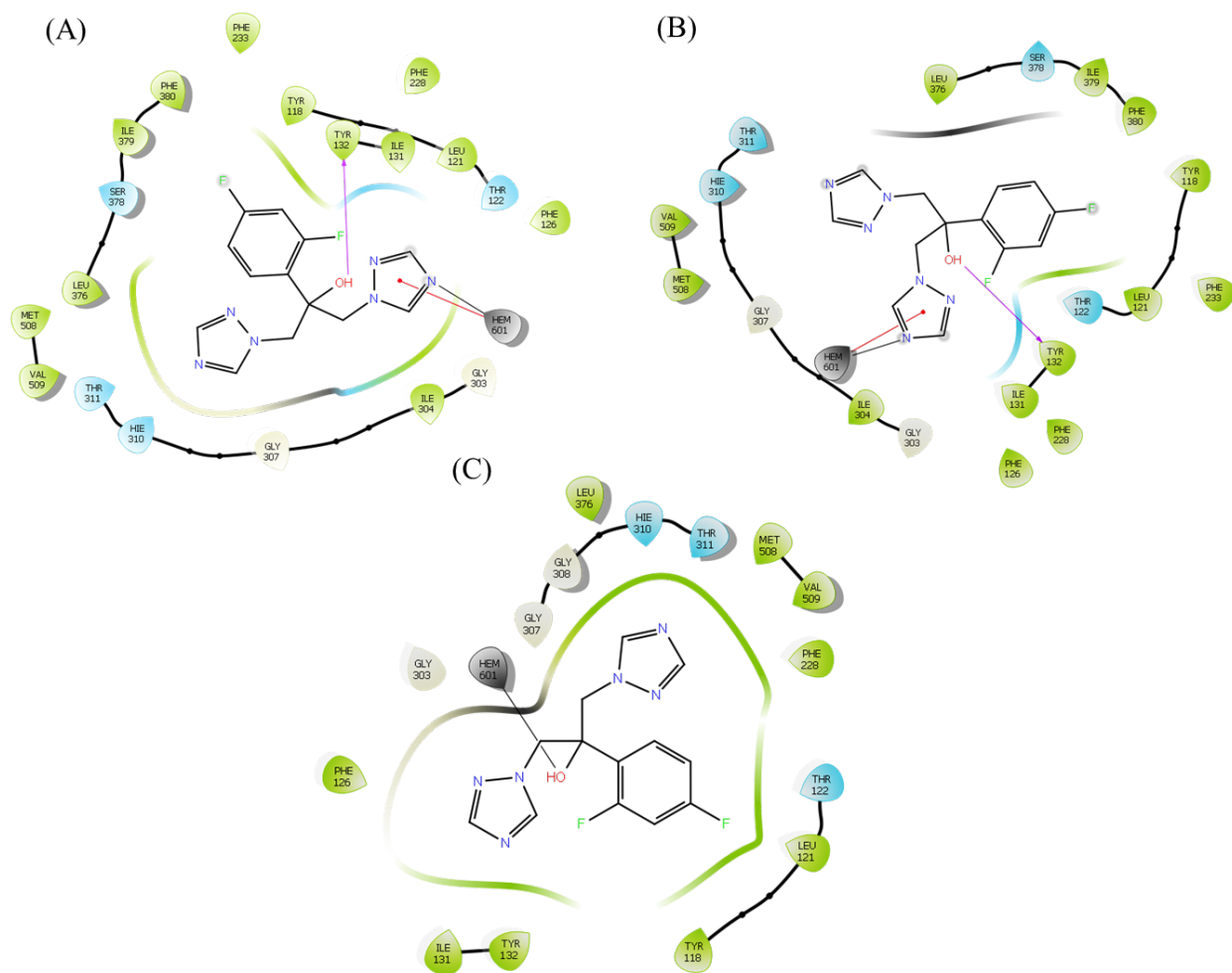


Supplement Figure 2. The crystal structure representation of developed mutations



Supplement Figure 3. The superimpose of the top eight fluconazole docking poses with (A) Erg11p_WT (B) Erg11p_TYR132HIS (C) Erg11p_THR285ALA (D) Erg11p_LEU321PHE (E) Erg11p_SER405PHE (F) Erg11p_TYR447HIS (G) Erg11p_SER457PRO (H) Erg11p_GLY464SER and (I) Erg11p_ARG467LYS

Erg11p mutant structures interactions with the fluconazole after docking.



Supplement Figure 4. The interaction of Erg11p mutants with the fluconazole after docking: (A) Erg11p_SER405PHE (B) Erg11p_GLY464SER and (C) Erg11p_ARG467LYS. (The fluconazole resides in the middle, surrounded by the residues. Residues & interaction types: Light green spheres – hydrophobic; Light blue spheres – Polar; Grey spheres – heme; White spheres – glycine; Purple arrows – Backbone hydrogen bonds; Dotted purple arrows – Side chain hydrogen bonds; Green lines – Pi-pi stacking; Red lines – Pi-pi cation; Black lines – Metal coordination).

Supplement Table 1. The RMSD values of the top eight poses of fluconazole aligned with reference to the first pose of respective Erg11p-fluconazole docked complexes

S.no	WILD_TYPE	TYR132HIS	TYR447HIS	THR285ALA	LEU321PHE	SER405PHE	SER457PRO	GLY464SER	ARG467LYS
1	0.2589	1.9033	1.8832	0.1974	2.2100	1.8546	1.3736	2.4575	1.7844
2	2.0195	1.8995	2.3544	1.0583	2.0443	1.9007	2.2035	2.1113	1.0707
3	2.3071	1.9570	2.1529	1.1061	2.0449	1.9538	2.3895	2.2442	2.1788
4	2.1552	2.1355	0.9964	2.1569	2.0300	2.3314	2.3667	2.4699	1.3556
5	1.4812	2.2099	2.2465	2.3155	2.2410	1.7937	0.2755	1.9654	2.3552
6	0.9457	1.8686	0.3092	0.9879	2.0852	2.2695	2.3402	1.9185	1.7968
7	0.2287	2.1188	1.0195	2.3800	1.9433	2.2094	2.2704	2.4330	2.3953
8	2.2154	1.9243	1.0747	0.3254	2.0038	2.3724	0.4129	2.3973	2.4013

Supplement Table S2. The MM-GBSA calculations for each frame of the docked Erg11p-fluconazole complexes after 50ns MDS

Time (ns)	Erg11p_SER457PRO	Erg11p_LEU321PHE	Erg11p_TYR447HIS	Erg11p_WILD_TYPE
0	0	0	0	0
0.16	-14.054	-25.1035	-31.39	-37.382
0.33	-20.126	-25.8702	-38.171	-37.694
0.5	-15.153	-37.0619	-37.037	-36.33
0.66	-19.516	-31.3656	-33.726	-30.251
0.83	-14.933	-30.4137	-23.691	-37.403
1	-18.4	-24.0108	-14.568	-41.206
1.16	-10.879	-26.019	-16.351	-40.712
1.33	-15.881	-32.8209	-13.9	-36.766
1.5	-23.019	-27.3907	-23.658	-36.869
1.66	-22.482	-30.0523	-19.274	-35.239
1.83	-16.884	-28.3038	-25.848	-40.232
2	-15.312	-24.1527	-19.401	-37.23
2.16	-14.624	-32.6069	-32.06	-41.529
2.33	-24.671	-25.1553	-29.786	-33.281
2.5	-17.952	-36.027	-10.458	-40.052
2.66	-23.245	-30.5228	-14.226	-35.854
2.83	-21.15	-23.3804	-17.279	-38.779
3	-18.786	-31.6197	-16.663	-31.965
3.16	-21.192	-24.4141	-12.093	-37.192
3.33	-16.233	-28.743	-10.506	-36.264
3.5	-21.545	-22.3708	-11.734	-31.155
3.66	-26.785	-27.1715	-14.358	-40.4
3.83	-18.707	-31.3787	-23.14	-36.966
4	-23.336	-31.347	-15.736	-43.023
4.16	-22.512	-32.818	-14.766	-45.459
4.33	-21.545	-27.4527	-10.995	-47.327
4.5	-19.626	-32.823	-12.098	-31.249
4.66	-13.01	-30.666	-15.723	-47.823
4.83	-17.694	-25.0335	-32.361	-29.149
5	-17.867	-30.6383	-22.833	-42.883
5.16	-15.189	-37.9962	-26.393	-38.133
5.33	-8.0839	-37.1058	-11.09	-38.605
5.5	-8.0636	-32.2334	-13.536	-35.322

5.66	-15.668	-27.5312	-19.829	-38.313
5.83	-17.448	-35.1791	-14.156	-40.001
6	-8.8681	-24.7406	-16.477	-33.829
6.16	-9.5076	-30.3046	-13.503	-46.5
6.33	-13.213	-30.3785	-20.638	-41.734
6.5	-18.225	-33.998	-11.844	-37.643
6.66	-7.9767	-30.1802	-16.921	-35.103
6.83	-12.636	-27.9617	-12.081	-34.684
7	-8.8804	-22.6894	-13.502	-35.42
7.16	-12.458	-31.1869	-17.676	-39.119
7.33	-6.9152	-27.9122	-11.017	-40.522
7.5	-16.22	-25.141	-8.0073	-37.059
7.66	-9.6703	-28.1717	-10.779	-38.599
7.83	-5.5177	-25.923	-17.501	-39.617
8	-13.432	-29.2708	-16.808	-44.965
8.16	-13.163	-24.985	-12.834	-41.536
8.33	-11.914	-30.4419	-5.9938	-35.259
8.5	-9.7639	-21.8919	-20.299	-34.492
8.66	-7.6226	-32.7684	-17.744	-44.598
8.83	-9.88	-28.903	-15.625	-48.157
9	-10.977	-29.3536	-14.128	-41.571
9.16	-11.085	-29.4345	-5.3399	-39.805
9.33	-14.084	-26.6423	-8.5761	-36.971
9.5	-23.321	-30.9805	-10.017	-41.505
9.66	-10.438	-31.4102	-9.7462	-41.717
9.83	-10.032	-32.5185	-14.716	-36.279
10	-8.9889	-31.9177	-10.063	-41.123
10.16	-9.1479	-37.5624	-17.17	-48.966
10.33	0.32995	-32.7087	-15.968	-41.134
10.5	-12.819	-33.9876	-12.382	-40.243
10.66	-12.827	-29.2996	-20.491	-48.577
10.83	-7.4805	-28.0309	-19.976	-34.924
11	-15.127	-29.2059	-8.2278	-46.674
11.16	-18.546	-35.9255	-11.677	-36.385
11.33	-14.145	-29.2026	-14.174	-41.977
11.5	-11.666	-29.4215	-16.443	-44.911
11.66	-14.994	-23.6129	-8.1698	-46.198
11.83	-11.649	-2.29091	-15.139	-42.567
12	-11.69	-13.0909	-15.746	-38.716
12.16	-6.2332	-20.2921	-20.495	-42.725
12.33	-12.048	-25.1733	-12.842	-38.37
12.5	-14.682	-23.9321	-10.12	-37.995
12.66	-8.0243	-13.0894	-10.317	-41.967

12.83	-15.4	-7.29737	-12.002	-39.57
13	-4.6979	-15.9171	-13.78	-34.168
13.16	-2.5243	-17.3619	-14.512	-39.493
13.33	-2.4319	-6.14527	-11.772	-32.046
13.5	-10.971	-12.3846	-10.428	-39.601
13.66	-19.394	-19.8446	-15.186	-42.141
13.83	-20.467	-23.6018	-11.205	-37.827
14	-11.289	-14.2049	-14.846	-33.846
14.16	-24.889	-31.4545	-12.795	-36.908
14.33	-18.673	-21.0236	-16.835	-32.928
14.5	-14.814	-17.3557	-9.1379	-28.496
14.66	-6.0605	-20.313	-11.851	-35.696
14.83	-19.629	-20.6939	-11.45	-37.139
15	-25.646	-28.7238	-16.719	-36.158
15.16	-21.54	-32.9452	-10.198	-48.598
15.33	-18.831	-16.3107	-9.4273	-33.702
15.5	-22.914	-10.4985	-14.221	-40.304
15.66	-19.305	-28.5842	-4.3688	-37.337
15.83	-16.646	-27.913	-19.536	-46.555
16	-6.6455	-12.2041	-17.474	-34.659
16.16	-13.253	-25.9002	-16.331	-42.787
16.33	-7.5761	-23.7754	-11.876	-34.927
16.5	-14.821	-25.8586	-20.256	-37.764
16.66	-11.034	-25.2734	-13.314	-37.066
16.83	-17.42	-29.8164	-13.832	-35.562
17	-9.6513	-11.2309	-11.784	-40.16
17.16	-18.03	-31.8767	-21.82	-45.037
17.33	-14.872	-29.6459	-9.0032	-37.377
17.5	-9.6721	-10.8015	-13.934	-45.984
17.66	-22.075	-18.6424	-9.1477	-33.651
17.83	-16.2	-10.8648	-12.633	-46.087
18	-18.009	-9.7224	-10.831	-40.138
18.16	-21.242	-13.921	-15.189	-43.437
18.33	-13.826	-7.9657	-10.079	-33.382
18.5	-9.5571	-16.1466	-13.474	-32.615
18.66	-13.144	-10.158	-16.278	-43.8
18.83	-8.6932	-15.323	-9.4216	-47.467
19	-13.439	-5.17769	-15.667	-41.234
19.16	-6.7214	-7.78406	-18.543	-45.407
19.33	-9.7021	-14.8288	-13.193	-40.047
19.5	-0.9965	-9.69666	-14.146	-36.59
19.66	-16.74	-12.532	-7.488	-48.404
19.83	-13.519	-15.4803	-9.0389	-47.855

20	-16.756	-11.3068	-8.1965	-47.523
20.16	-10.451	-13.0154	-17.754	-44.713
20.33	-12.069	-7.67868	-9.0283	-42.577
20.5	-9.2307	-14.6479	-10.585	-42.587
20.66	-22.163	-9.24799	-13.411	-37.134
20.83	-15.473	-9.39941	-11.872	-43.62
21	-15.815	-30.1848	-9.1635	-48.29
21.16	-13.247	-32.4105	-16.65	-42.257
21.33	-15.694	-33.2984	-16.281	-41.001
21.5	-14.566	-29.6802	-3.4868	-44.657
21.66	-6.9531	-28.9754	-19.801	-40.448
21.83	-15.566	-26.039	-15.151	-41.47
22	-11.141	-23.1185	-7.1876	-37.985
22.16	-11.918	-30.4183	-21.835	-43.344
22.33	-11.172	-39.6622	-15.839	-37.987
22.5	-16.521	-23.2138	-11.525	-38.336
22.66	-24.988	-25.0191	-4.2087	-33.03
22.83	-17.546	-8.39756	-12.625	-38.25
23	-17.301	-19.539	-13.621	-31.582
23.16	-12.953	-32.3578	-21.394	-44.331
23.33	-17.828	-40.8531	-16.996	-50.886
23.5	-17.483	-29.6439	-11.322	-37.494
23.66	-18.387	-39.377	-17.775	-43.926
23.83	-17.009	-33.6269	-18.988	-43.442
24	-7.7154	-26.7465	-14.116	-41.606
24.16	-16.637	-29.7882	-14.125	-47.49
24.33	-22.242	-15.8088	-15.89	-39.555
24.5	-10.699	-21.2689	-12.53	-44.722
24.66	-16.239	-12.6734	-18.378	-37.802
24.83	-20.64	-18.6206	-17.488	-42.486
25	-11.033	-21.3286	-13.894	-39.348
25.16	-20.941	-29.6281	-21.06	-38.593
25.33	-16.234	-25.7355	-17.048	-42.936
25.5	-20.496	-24.1772	-14.537	-44.15
25.66	-11.066	-27.7293	-10.065	-38.033
25.83	-18.167	-27.8313	-16.233	-38.138
26	-20.565	-26.5561	-12.661	-42.29
26.16	-15.79	-23.2694	-24.159	-39.021
26.33	-16.876	-22.7137	-36.306	-34.225
26.5	-11.24	-17.174	-18.523	-27.998
26.66	-18.194	-19.9513	-18.384	-36.806
26.83	-13.92	-16.2093	-14.779	-34.986
27	-13.998	-22.2737	-22.121	-35.34

27.16	-18.614	-20.5097	-20.808	-43.907
27.33	-18.092	-20.592	-13.505	-38.375
27.5	-11.795	-21.2654	-18.566	-32.115
27.66	-11.76	-23.0181	-11.539	-36.798
27.83	-16.64	-19.2547	-11.458	-34.257
28	-10.848	-22.0587	-11.644	-37.6
28.16	-20.192	-15.3253	-21.464	-35.905
28.33	-20.993	-22.3247	-19.82	-36.699
28.5	-12.163	-14.744	-23.761	-37.182
28.66	-8.7273	-21.7551	-18.901	-36.23
28.83	-17.195	-21.396	-18.884	-34.904
29	-7.5142	-20.7094	-21.629	-34.223
29.16	-13.924	-19.7537	-16.034	-35.344
29.33	-13.053	-24.4978	-23.205	-34.496
29.5	-14.733	-24.6709	-12.136	-34
29.66	-9.2841	-17.9561	-18.253	-34.389
29.83	-10.788	-26.873	-11.812	-35.229
30	-11.475	-29.0666	-15.477	-35.105
30.16	-7.7049	-27.1845	-15.871	-42.529
30.33	-13.073	-32.8761	-10.003	-33.648
30.5	-8.9064	-27.1856	-14.847	-34.198
30.66	-15.58	-25.0475	-8.6328	-43.199
30.83	-15.551	-25.8207	-12.091	-41.766
31	-10.06	-30.4278	-14.651	-29.92
31.16	-18.127	-28.1991	-15.19	-36.794
31.33	-18.194	-27.6213	-18.334	-38.36
31.5	-16.78	-25.8784	-17.969	-37.913
31.66	-11.795	-34.5418	-14.748	-43.54
31.83	-14.205	-20.5919	-9.8404	-32.714
32	-11.167	-36.4181	-13.861	-40.836
32.16	-7.9891	-22.7647	-13.202	-34.963
32.33	-16.658	-25.0298	-11.139	-22.648
32.5	-13.072	-25.1061	-26.04	-36.034
32.66	-17.105	-30.3365	-8.8131	-44.252
32.83	-13.729	-30.5429	-10.128	-36.779
33	-17.061	-34.8781	-14.194	-42.369
33.16	-18.718	-19.7668	-9.4966	-35.857
33.33	-16.936	-34.2886	-17.961	-29.498
33.5	-25.744	-13.4771	-24.985	-39.704
33.66	-15.227	-9.78206	-13.811	-45.685
33.83	-17.097	-24.0362	-22.244	-40.94
34	-18.236	-4.17957	-11.132	-32.544
34.16	-14.465	-14.0717	-12.837	-34.435

34.33	-19.71	-11.7592	-8.5004	-32.789
34.5	-18.046	-10.4455	-8.7959	-37.031
34.66	-21.879	-11.3039	-14.816	-33.994
34.83	-22.683	-15.335	-16.36	-41.922
35	-14.246	-9.54008	-14.161	-41.024
35.16	-18.207	-19.2753	-26.611	-36.218
35.33	-19.844	-10.2019	-9.3284	-31.965
35.5	-16.724	-16.1819	-9.6679	-32.79
35.66	-13.83	-6.23702	-11.709	-33.194
35.83	-6.617	-9.78982	-14.999	-30.817
36	-19.317	-10.3693	-15.347	-27.676
36.16	-15.667	-18.0082	-23.907	-33.105
36.33	-15.309	-19.2815	-18.999	-31.26
36.5	-20.798	-21.0096	-20.651	-24.993
36.66	-12.655	-14.4565	-13.998	-31.86
36.83	-10.512	-19.4886	-7.08	-36.828
37	-6.5731	-21.6684	-11.893	-38.092
37.16	-9.1097	-18.6944	-12.554	-33.96
37.33	-12.271	-19.6775	-18.266	-35.742
37.5	-14.214	-21.2558	-16.739	-26.592
37.66	-5.9923	-16.5891	-16.295	-26.843
37.83	-8.1331	-20.942	-17.969	-31.395
38	-7.3017	-19.9789	-15.219	-32.61
38.16	-13.484	-20.1391	-19.234	-28.924
38.33	-6.1732	-18.7585	-11.272	-34.938
38.5	-15.391	-16.0409	-11.703	-30.679
38.66	-3.0432	-10.6166	-19.325	-23.898
38.83	-4.9453	-10.8994	-5.6677	-31.033
39	-9.6196	-34.2584	-27.09	-26.803
39.16	-10.761	-27.3569	-14.709	-29.843
39.33	-8.0114	-14.3597	-16.804	-33.017
39.5	-8.3756	-22.4753	-7.1813	-35.479
39.66	-20.083	-18.4712	-16.773	-31.788
39.83	-14.549	-13.8584	-26.666	-34.798
40	-10.356	-10.9007	-15.39	-28.688
40.16	-13.929	-11.9638	-8.4273	-36.981
40.33	-10.306	-16.5113	-12.902	-29.465
40.5	-21.47	-13.9505	-13.094	-38.67
40.66	-14.455	-13.1755	-12.41	-27.297
40.83	-15.609	-23.6189	-11.415	-36.682
41	-11.892	-16.9379	-14.496	-38.769
41.16	-13.266	-21.7903	-12.552	-23.191
41.33	-18.516	-19.6294	-12.867	-37.761

41.5	-10.705	-16.7764	-12.508	-32.887
41.66	-17.629	-16.4824	-12.401	-40.999
41.83	-16.322	-10.6366	-13.952	-40.087
42	-6.0075	-17.727	-11.239	-36.457
42.16	-14.22	-15.8029	-19.521	-38.739
42.33	-11.21	-18.6623	-7.9422	-26.986
42.5	-19.568	-17.9691	-15.863	-34.576
42.66	-22.067	-17.3639	-9.6098	-37.84
42.83	-18.441	-16.7934	-8.7883	-33.693
43	-12.596	-13.7494	-11.378	-28.34
43.16	-10.045	-11.2646	-8.6135	-33.145
43.33	-18.432	-5.59195	-10.982	-33.843
43.5	-18.598	-8.05922	-11.755	-38.774
43.66	-9.1372	-16.3094	-7.5656	-28.299
43.83	-20.336	-9.56882	-13.658	-39.452
44	-18.842	-13.4337	-14.641	-38.489
44.16	-14.289	-12.7741	-14.974	-41.598
44.33	-0.2988	-14.075	-9.6962	-38.289
44.5	-18.106	-20.1218	-15.811	-35.088
44.66	-10.913	-13.5257	-14.524	-40.213
44.83	-13.53	-11.8552	-4.6183	-41.266
45	-16.497	-16.419	-9.9341	-36.431
45.16	-20.669	-10.0691	-9.311	-30.844
45.33	-13.082	-19.6302	-13.629	-30.719
45.5	-16.549	-15.9269	-15.239	-35.018
45.66	-19.882	-16.1302	-15.442	-34.592
45.83	-16.07	-18.2088	-13.229	-38.401
46	-13.719	-23.454	-5.8824	-38.657
46.16	-12.912	-23.4365	-22.463	-35.742
46.33	-9.491	-15.7309	-9.877	-35.289
46.5	-12.29	-13.4183	-16.568	-30.424
46.66	-13.203	-18.4799	-8.9813	-32.198
46.83	-16.687	-19.5457	-12.012	-36.037
47	-12.259	-7.27889	-10.303	-35.761
47.16	-8.104	-12.7213	-11.159	-23.869
47.33	-7.6693	-14.1833	-15.106	-36.521
47.5	-6.041	-16.6531	-13.6	-35.759
47.66	1.2087	-15.0065	-9.8262	-33.062
47.83	-12.006	-17.0846	-21.021	-32.67
48	-8.2553	-15.7684	-13.839	-27.786
48.16	-16.069	-23.4141	-13.408	-32.655
48.33	-18.047	-25.2262	-14.821	-30.01
48.5	-8.3946	-14.1231	-16.441	-33.649

48.66	-9.8072	-19.7887	-15.508	-36.184
48.83	-10.077	-18.4615	-11.734	-37.676
49	-5.0271	-26.6381	-5.6119	-30.032
49.16	-11.558	-16.7695	-12.799	-35.26
49.33	-7.5244	-20.4639	-7.308	-32.139
49.5	-11.198	-23.431	-12.487	-33.233
49.66	-12.46	-23.5053	-14.866	-33.139
49.83	-9.1996	-21.9881	-17.261	-41.048
50	-7.0515	-15.6457	-19.632	-33.508
