Indian Journal of Biochemistry & Biophysics
Vol. 59, June 2022, pp.

Identification of potential AChE inhibitors through combined machine-learning and structure-based design approaches

Ankit Ganeshpurkar[1], Ravi Singh[1], Ravi Bhushan Singh[2], Devendra Kumar[3], Ashok Kumar[1] & Sushil Kumar Singh[1]*

[1]Pharmaceutical Chemistry Research Laboratory I, Department of Pharmaceutical Engineering & Technology, Indian Institute of Technology (Banaras Hindu University), Varanasi-221 005, Uttar Pradesh, India

[2]Institute of Pharmacy, Harish Chandra Post Graduate College, Varanasi-221 001, Uttar Pradesh, India

[3]Faculty of Pharmacy, DIT University, Dehradun-248 009, Uttarakhand, India

Received 18 March 2022; *revised 25 June 2022*

Supplementary Data

Table S1 — Protocol for energy minimisation carried out before molecular dynamics simulation in AMBER2018.

Stage	Maximum number of steps (steepest descent) *	Maximum number of steps (conjugate gradient) *	Weight for the positional restraints. (in kcal/mol-Å^2)	Restrained elements
1	2000	3000	500	Protein
2	1000	4000	500	Protein except their hydrogens
3	1000	4000	500	Backbone of the protein
4	1000	4000	50	Protein except their hydrogens
5	1000	4000	50	Backbone of the protein
6	1000	4000	5	Protein except their hydrogens
7	1000	4000	5	Backbone of the protein
8	1000	4000	0.5	Backbone of the protein
9	1000	4000	0.1	Backbone of the protein
10	1000	4000	0.01	Backbone of the protein

* Represent a maximum number of minimisation steps. If the system converges before reaching the maximum number of steps, then the corresponding stage is terminated and the system enters the next stage of energy minimisation.

Table S2 — LGA parameters for virtual screening and precision docking

Docking	Number of GA run	Population size	Maximum number of generations	Maximum number of evaluations	Rate of Gene mutation	Rate of crossing over
Virtual screening	10	150	27000	250000	0.02	0.8
Precision docking	100	150	27000	2500000	0.02	0.8

Table S3 — Protocol for energy minimisation carried out before molecular dynamics simulation in AMBER2018

Stage	Maximum number of steps (steepest descent) *	Maximum number of steps (conjugate gradient) *	Weight for the positional restraints. (in kcal/mol-Å^2)	Restrained elements
1	2000	3000	500	Protein
2	1000	4000	500	Protein except their hydrogens
3	1000	4000	500	Backbone of the protein
4	1000	4000	50	Protein except their hydrogens
5	1000	4000	50	Backbone of the protein
6	1000	4000	5	Protein except their hydrogens

7	1000	4000	5	Backbone of the protein
8	1000	4000	0.5	Backbone of the protein

Table S4 — Details of protocol for Molecular dynamics

Heating					
Number of steps	Intial temperature(K)	Final temperature(K)	Temperature regulation	collision frequency (in ps^{-1})	Ensemble
50000	100.0	310.15	Langevin dynamics	2	NVT
Density equilibration					
Number of steps	Temperature(K)	Temperature regulation	Pressure regulation	SHAKE bond length constraints	Ensemble
50000	310.15	Langevin dynamics	Berendsen	bonds involving hydrogen	NPT
Equilibration					
Number of steps	Temperature(K)	Temperature regulation	Pressure regulation	SHAKE bond length constraints	Ensemble
100000	310.15	Langevin dynamics	Berendsen	bonds involving hydrogen	NPT
MD run					
Number of steps	Temperature(K)	Temperature regulation	Pressure regulation	SHAKE bond length constraints	Ensemble
25000000	310.15	Langevin dynamics	Berendsen	bonds involving hydrogen	NPT

Table S5 — Summary of the datasets used for ML model development

S. No.	Dataset	Type	Descriptors	Remark
1	D1	Structure	Smiles	1988 inhibitors
2	D2	Structure	Smiles	1092 inhibitors
3	D1a	Descriptors	SlogP, SMR, LabuteASA, TPSA, AMW, ExactMW, FractionCSP3, Chi0v, Chi1v, Chi2v, Chi3v, Chi4v, Chi1n, Chi2n, Chi3n, Chi4n, HallKierAlpha, kappa1, kappa2, kappa3, slogp_VSA1, slogp_VSA2, slogp_VSA3, slogp_VSA4, slogp_VSA5, slogp_VSA6, slogp_VSA7, slogp VSA8, slogp VSA10, slogp VSA11, slogp VSA12, smr_VSA1, smr_VSA2, smr_VSA3, smr_VSA4, smr_VSA5, smr VSA6, smr VSA7, smr VSA9, smr VSA10, peoe VSA1, peoe_VSA2, peoe_VSA3, peoe_VSA4, peoe_VSA5, peoe_VSA6, peoe_VSA7, peoe_VSA8, peoe_VSA9, peoe_VSA10, peoe_VSA11, peoe_VSA12, peoe_VSA13, peoe_VSA14, MQN1, MQN2, MQN3, MQN4, MQN5, MQN6, MQN7, MQN8, MQN9, MQN10, MQN11, MQN12, MQN13, MQN14, MQN15, MQN16, MQN17, MQN19, MQN20, MQN21, MQN22, MQN23, MQN24, MQN25, MQN26, MQN27, MQN28, MQN29, MQN30, MQN31, MQN32, MQN33, MQN34, MQN35, MQN36, MQN37, MQN38, MQN39, MQN40, MQN41, MQN42	Obtained from D1, 95 features
4	D1b	Descriptors	SlogP, TPSA, FractionCSP3, HallKierAlpha, slogp_VSA1, slogp VSA2, slogp VSA3, slogp VSA4, slogp VSA5, slogp VSA6, slogp_VSA7, slogp_VSA8, slogp_VSA10, slogp_VSA11, slogp_VSA12, smr_VSA1, smr_VSA2, smr_VSA3, smr_VSA4, smr_VSA10, peoe_VSA1, peoe_VSA2, peoe_VSA3, peoe_VSA4, peoe_VSA5, peoe_VSA6, peoe_VSA7, peoe_VSA8, peoe_VSA9, peoe VSA10, peoe VSA11, peoe VSA12, peoe VSA13, peoe_VSA14, MQN2, MQN4, MQN5, MQN6, MQN7, MQN8, MQN9, MQN10, MQN11, MQN14, MQN15, MQN16, MQN22, MQN24, MQN25, MQN26, MQN28, MQN29, MQN30, MQN31, MQN32, MQN33, MQN34, MQN35, MQN36, MQN37, MQN38, MQN39, MQN40, MQN41	Obtained from D1a, after applying correlation and variance filter, 64 features were obtained
5	D1c	Descriptors	SlogP, SMR, LabuteASA, TPSA, AMW, ExactMW, FractionCSP3, Chi0v, Chi1v, Chi2v, Chi3v, Chi4v, Chi1n, Chi2n, Chi3n, Chi4n, HallKierAlpha, kappa1, kappa2, kappa3, slogp_VSA1, slogp_VSA2, slogp_VSA3, slogp_VSA4, slogp_VSA5, slogp_VSA6, slogp_VSA7, slogp_VSA8, slogp_VSA10, slogp_VSA11, slogp_VSA12, smr_VSA1, smr_VSA2, smr_VSA3, smr_VSA4, smr_VSA5,	Obtained from D1a, after normalisation, 95 features

			smr_VSA6, smr_VSA7, smr_VSA9, smr_VSA10, peoe_VSA1, peoe_VSA2, peoe_VSA3, peoe_VSA4, peoe_VSA5, peoe_VSA6, peoe_VSA7, peoe_VSA8, peoe_VSA9, peoe_VSA10, peoe_VSA11, peoe_VSA12, peoe_VSA13, peoe_VSA14, MQN1, MQN2, MQN3, MQN4, MQN5, MQN6, MQN7, MQN8, MQN9, MQN10, MQN11, MQN12, MQN13, MQN14, MQN15, MQN16, MQN17, MQN19, MQN20, MQN21, MQN22, MQN23, MQN24, MQN25, MQN26, MQN27, MQN28, MQN29, MQN30, MQN31, MQN32, MQN33, MQN34, MQN35, MQN36, MQN37, MQN38, MQN39, MQN40, MQN41, MQN42	
6	D1d	Descriptors	SlogP, TPSA, FractionCSP3, HallKierAlpha, slogp_VSA1, slogp_VSA2, slogp_VSA3, slogp_VSA4, slogp_VSA5, slogp_VSA6, slogp_VSA7, slogp_VSA8, slogp_VSA10, slogp_VSA11, slogp_VSA12, smr_VSA1, smr_VSA2, smr_VSA3, smr_VSA4, smr VSA10, peoe VSA1, peoe VSA2, peoe VSA3, peoe VSA4, peoe_VSA5, peoe_VSA6, peoe_VSA7, peoe_VSA8, peoe_VSA9, peoe VSA10, peoe VSA11, peoe VSA12, peoe VSA13, peoe_VSA14, MQN2, MQN4, MQN5, MQN6, MQN7, MQN8, MQN9, MQN10, MQN11, MQN14, MQN15, MQN16, MQN22, MQN24, MQN25, MQN26, MQN28, MQN29, MQN30, MQN31, MQN32, MQN33, MQN34, MQN35, MQN36, MQN37, MQN38, MQN39, MQN40, MQN41	Obtained from D1b, after normalisation, 64 features
4	D2a	Descriptors	SlogP, SMR, LabuteASA, TPSA, AMW, ExactMW, FractionCSP3, Chi0v, Chi1v, Chi2v, Chi3v, Chi4v, Chi1n, Chi2n, Chi3n, Chi4n, HallKierAlpha, kappa1, kappa2, kappa3, slogp_VSA1, slogp_VSA2, slogp VSA3, slogp VSA4, slogp VSA5, slogp VSA6, slogp VSA7, slogp_VSA8, slogp_VSA10, slogp_VSA11, slogp_VSA12, smr VSA1, smr VSA2, smr VSA3, smr VSA4, smr VSA5, smr_VSA6, smr_VSA7, smr_VSA9, smr_VSA10, peoe_VSA1, peoe_VSA2, peoe_VSA3, peoe_VSA4, peoe_VSA5, peoe_VSA6, peoe_VSA7, peoe_VSA8, peoe_VSA9, peoe_VSA10, peoe_VSA11, peoe_VSA12, peoe_VSA13, peoe_VSA14, MQN1, MQN2, MQN3, MQN4, MQN6, MQN8, MQN9, MQN10, MQN11, MQN12, MQN13, MQN14, MQN15, MQN16, MQN17, MQN19, MQN20, MQN21, MQN22, MQN23, MQN24, MQN25, MQN26, MQN27, MQN28, MQN29, MQN30, MQN31, MQN32, MQN33, MQN35, MQN36, MQN37, MQN38, MQN41, MQN42	Obtained from D2, 90 features
5	D2b	Descriptors	SlogP, TPSA, FractionCSP3, HallKierAlpha, slogp_VSA1, slogp VSA2, slogp VSA3, slogp VSA4, slogp VSA5, slogp VSA6, slogp_VSA7, slogp_VSA8, slogp_VSA10, slogp_VSA11, slogp_VSA12, smr_VSA1, smr_VSA2, smr_VSA3, smr_VSA4, smr_VSA10, peoe_VSA2, peoe_VSA3, peoe_VSA4, peoe_VSA5, peoe_VSA6, peoe_VSA7, peoe_VSA8, peoe_VSA9, peoe_VSA10, peoe VSA11, peoe VSA12, peoe VSA13, peoe VSA14, MQN2, MQN4, MQN6, MQN8, MQN9, MQN11, MQN14, MQN16, MQN22, MQN24, MQN25, MQN26, MQN28, MQN29, MQN30, MQN31, MQN32, MQN35, MQN36, MQN37, MQN38, MQN41	Obtained from D2a, after applying correlation and variance filter, 55 features
6	D2c	Descriptors	SlogP, SMR, LabuteASA, TPSA, AMW, ExactMW, FractionCSP3, Chi0v, Chi1v, Chi2v, Chi3v, Chi4v, Chi1n, Chi2n, Chi3n, Chi4n, HallKierAlpha, kappa1, kappa2, kappa3, slogp VSA1, slogp VSA2, slogp_VSA3, slogp_VSA4, slogp_VSA5, slogp_VSA6, slogp_VSA7, slogp VSA8, slogp VSA10, slogp VSA11, slogp VSA12, smr_VSA1, smr_VSA2, smr_VSA3, smr_VSA4, smr_VSA5, smr_VSA6, smr_VSA7, smr_VSA9, smr_VSA10, peoe_VSA1, peoe_VSA2, peoe_VSA3, peoe_VSA4, peoe_VSA5, peoe_VSA6, peoe_VSA7, peoe_VSA8, peoe_VSA9, peoe_VSA10, peoe_VSA11, peoe VSA12, peoe VSA13, peoe VSA14, MQN1, MQN2, MQN3, MQN4, MQN6, MQN8, MQN9, MQN10, MQN11, MQN12, MQN13, MQN14, MQN15, MQN16, MQN17, MQN19, MQN20, MQN21, MQN22, MQN23, MQN24, MQN25, MQN26, MQN27, MQN28, MQN29, MQN30, MQN31, MQN32, MQN33, MQN35, MQN36,	Obtained from D2a, after normalisation, 90 features

			MQN37, MQN38, MQN41, MQN42	
7	D2d	Descriptors	SlogP, TPSA, FractionCSP3, HallKierAlpha, slogp_VSA1, slogp_VSA2, slogp_VSA3, slogp_VSA4, slogp_VSA5, slogp_VSA6, slogp_VSA7, slogp_VSA8, slogp_VSA10, slogp_VSA11, slogp VSA12, smr VSA1, smr VSA2, smr VSA3, smr VSA4, smr_VSA10, peoe_VSA2, peoe_VSA3, peoe_VSA4, peoe_VSA5, peoe_VSA6, peoe_VSA7, peoe_VSA8, peoe_VSA9, peoe_VSA10, peoe_VSA11, peoe_VSA12, peoe_VSA13, peoe_VSA14, MQN2, MQN4, MQN6, MQN8, MQN9, MQN11, MQN14, MQN16, MQN22, MQN24, MQN25, MQN26, MQN28, MQN29, MQN30, MQN31, MQN32, MQN35, MQN36, MQN37, MQN38, MQN41	Obtained from D2b, after normalisation, 55 features

- Datasets staring with D1 were used for first sets of models
- Datasets staring with D2 were used for second sets of models

Table S6 — Comparison of the models developed from datasets D1a – D1d for identification of Kernel.

			Training set*				Validation set			
Model	Dataset	Method	Accuracy	Precision	Recall	ROC_AUC	Accuracy	Precision	Recall	ROC_AUC
1.01	D1a	linear	77.41 ± 3.42	78.88 ± 3.01	80.21 ± 7.56	83.4 ± 1.77	77.52	80.71	80.23	77.52
1.02	D1a	rbf	65.55 ± 5.93	64.84 ± 4.04	86.45 ± 5.35	70.95 ± 4.67	68.73	70.27	84.36	68.73
1.03	D1a	poly	57.3 ± 1.79	58.22 ± 1.03	95.48 ± 0.92	66.25 ± 5.34	57.33	60.78	96.46	57.33
1.04	D1a	sigmoid	51.2 ± 4.45	55.19 ± 3.97	57.89 ± 3.78	52.1 ± 4.79	46.45	53.63	52.21	46.45
1.05	D1b	linear	75.75 ± 1.7	77.81 ± 3.7	77.82 ± 4.95	82.25 ± 2.88	76.86	81.3	76.99	76.86
1.06	D1b	rbf	73.14 ± 3.21	74.05 ± 1.31	78.89 ± 7.78	81.08 ± 2.69	74.42	76.66	81.41	74.42
1.07	D1b	poly	71.76 ± 2.17	70.46 ± 3.22	86.46 ± 8.74	82.27 ± 4.72	71.12	71.99	86.43	71.12
1.08	D1b	sigmoid	55.22 ± 4.73	58.74 ± 4.32	61.22 ± 6.16	56.97 ± 4.79	48.61	55.58	55.75	48.61
1.09	D1c	linear	71.83 ± 3.05	72.13 ± 3.13	80.34 ± 2.56	79.3 ± 3.08	75.97	78.84	80.23	75.97
1.1	D1c	rbf	80.97 ± 4.05	81.78 ± 4.59	84.2 ± 8.49	87.71 ± 1.02	78.92	80	86.13	78.92
1.11	D1c	poly	80.63 ± 2.01	82.07 ± 4.1	82.74 ± 6.51	87.35 ± 0.98	80.61	81.84	86.43	80.61
1.12	D1c	sigmoid	49.76 ± 2.38	53.93 ± 2.18	54.7 ± 7.18	46.69 ± 3.94	46.56	53.82	53.98	46.56
1.13	D1d	linear	70.5 ± 4.16	71.17 ± 3.79	78.61 ± 4.35	78.59 ± 3.58	74.66	77.42	79.94	74.66
1.14	D1d	rbf	80.76 ± 3.14	81.66 ± 4.97	83.93 ± 6.72	88.41 ± 1.08	78.47	79.83	85.25	78.47
1.15	D1d	poly	81.18 ± 2.13	82.81 ± 4.32	82.73 ± 3.51	87.74 ± 1.04	80.02	81.63	85.25	80.02
1.16	D1d	sigmoid	51.33 ± 1.77	55.29 ± 1.63	59.09 ± 1.65	48.15 ± 2.04	48.23	55.3	56.93	48.23

* K-Fold validation (K = 4)

Table S7 — Comparison of hyperparameter tuned models selected from initial models developed

					Training set*				Validation Set			
Model	C	Dataset	Kernel	gamma	Accuracy	Precision	Recall	ROC_AUC	Accuracy	Precision	Recall	ROC_AUC
1.17	1	D1c	rbf	auto	55.4 ± 1.32	57.01 ± 0.93	98.27 ± 2.4	72.08 ± 3.29	62.37	63.86	96.46	62.37
1.18	1	D1c	rbf	scale	80.97 ± 4.05	81.78 ± 4.59	84.2 ± 8.49	87.71 ± 1.02	78.92	80	86.13	78.92
1.19	1	D1c	rbf	0.001	50 ± 0	54.13 ± 0.24	100 ± 0	70.89 ± 3.96	50	56.78	100	50
1.2	1	D1c	rbf	0.0001	50 ± 0	54.13 ± 0.24	100 ± 0	70.94 ± 4.33	50	56.78	100	50
1.21	10	D1c	rbf	auto	71.17 ± 3.51	71.55 ± 3	79.81 ± 4.12	77.45 ± 3.42	73.84	76.03	81.41	73.84
1.22	10	D1c	rbf	scale	83.2 ± 1.65	84.15 ± 4.09	85.52 ± 4.02	89.75 ± 1.83	82.16	83.71	86.43	82.16
1.23	10	D1c	rbf	0.001	53.32 ± 2.78	55.86 ± 1.54	98.8 ± 1.73	70.94 ± 3.99	60.39	62.59	96.75	60.39
1.24	10	D1c	rbf	0.0001	50 ± 0	54.13 ± 0.24	100 ± 0	70.76 ± 4	50	56.78	100	50
1.25	100	D1c	rbf	auto	79.46 ± 1.94	80.86 ± 1.55	81.8 ± 6.79	85.08 ± 1.08	79.46	82.63	81.41	79.46
1.26	100	D1c	rbf	scale	82.14 ± 2.3	83.86 ± 4.71	83.4 ± 7.08	88.63 ± 2.12	83.05	83.98	88.2	83.05
1.27	100	D1c	rbf	0.001	69.31 ± 2.93	69.62 ± 2.65	79.68 ± 2.69	76.18 ± 3.99	73.7	75.96	81.12	73.7
1.28	100	D1c	rbf	0.0001	53.16 ± 3.09	55.78 ± 1.71	98.8 ± 1.73	70.81 ± 4.03	60	62.35	96.75	60
1.29	1000	D1c	rbf	auto	82.37 ± 2.78	82.73 ± 4.6	86.05 ± 4.26	88.26 ± 2.5	80.78	83.63	82.89	80.78
1.3	1000	D1c	rbf	scale	80.57 ± 2.31	82.49 ± 3.2	81.67 ± 5.9	87.17 ± 3.18	81.71	84.11	84.36	81.71

1.31	1000	D1c	rbf	0.001	74.74 ± 3.05	75.58 ± 4.01	80.21 ± 5.86	81.38 ± 2.37	77.33	80	81.41	77.33
1.32	1000	D1c	rbf	0.0001	69.06 ± 3.13	69.33 ± 2.76	79.81 ± 3.13	75.96 ± 4.22	73.6	75.68	81.71	73.6
1.33	1	D1c	poly	auto	50 ± 0	54.13 ± 0.24	100 ± 0	64.2 ± 4.73	50	56.78	100	50
1.34	1	D1c	poly	scale	80.63 ± 2.01	82.07 ± 4.1	82.74 ± 6.51	87.35 ± 0.98	80.61	81.84	86.43	80.61
1.35	1	D1c	poly	0.001	50 ± 0	54.13 ± 0.24	100 ± 0	52.18 ± 3.78	50	56.78	100	50
1.36	1	D1c	poly	0.0001	50 ± 0	54.13 ± 0.24	100 ± 0	52.18 ± 3.78	50	56.78	100	50
1.37	10	D1c	poly	auto	50 ± 0	54.13 ± 0.24	100 ± 0	63.94 ± 4.91	50	56.78	100	50
1.38	10	D1c	poly	scale	81.95 ± 0.9	83.4 ± 4.75	83.8 ± 7.31	88.05 ± 1.7	81.97	83.47	86.43	81.97
1.39	10	D1c	poly	0.001	50 ± 0	54.13 ± 0.24	100 ± 0	52.18 ± 3.78	50	56.78	100	50
1.4	10	D1c	poly	0.0001	50 ± 0	54.13 ± 0.24	100 ± 0	52.18 ± 3.78	50	56.78	100	50
1.41	100	D1c	poly	auto	52.62 ± 0.63	55.47 ± 0.55	99.6 ± 0.88	72.81 ± 2.72	53.58	58.6	99.41	53.58
1.42	100	D1c	poly	scale	81.52 ± 2.17	83.95 ± 3.57	81.54 ± 6.1	86.38 ± 2.19	82.94	84.68	86.43	82.94
1.43	100	D1c	poly	0.001	50 ± 0	54.13 ± 0.24	100 ± 0	60.39 ± 5.79	50	56.78	100	50
1.44	100	D1c	poly	0.0001	50 ± 0	54.13 ± 0.24	100 ± 0	52.18 ± 3.78	50	56.78	100	50
1.45	1000	D1c	poly	auto	71.42 ± 3.65	69.4 ± 5.23	90.31 ± 11.05	82.92 ± 3.98	74.87	74.69	89.67	74.87
1.46	1000	D1c	poly	scale	79.28 ± 5.78	81.82 ± 5.8	79.41 ± 6.94	84.31 ± 3.51	81.52	83.87	84.36	81.52
1.47	1000	D1c	poly	0.001	50 ± 0	54.13 ± 0.24	100 ± 0	64.28 ± 4.65	50	56.78	100	50
1.48	1000	D1c	poly	0.0001	50 ± 0	54.13 ± 0.24	100 ± 0	52.18 ± 3.78	50	56.78	100	50
1.49	1	D1d	rbf	auto	57.45 ± 2.22	58.2 ± 1.56	98.14 ± 1.17	71.1 ± 5.55	61.79	63.49	96.46	61.79
1.5	1	D1d	rbf	scale	80.76 ± 3.14	81.66 ± 4.97	83.93 ± 6.72	88.41 ± 1.08	78.47	79.83	85.25	78.47
1.51	1	D1d	rbf	0.001	50 ± 0	54.13 ± 0.24	100 ± 0	70.27 ± 5.76	50	56.78	100	50
1.52	1	D1d	rbf	0.0001	50 ± 0	54.13 ± 0.24	100 ± 0	70.28 ± 6.24	50	56.78	100	50
1.53	10	D1d	rbf	auto	70.39 ± 1.43	70.71 ± 1.47	79.81 ± 1.89	78.41 ± 3.93	73.74	76.11	80.82	73.74
1.54	10	D1d	rbf	scale	83.97 ± 1.83	85.64 ± 4.63	84.86 ± 4.22	89.96 ± 1.88	83.48	84.65	87.9	83.48
1.55	10	D1d	rbf	0.001	50.72 ± 1.73	54.5 ± 0.98	99.73 ± 0.53	70.26 ± 5.69	54.25	58.97	98.82	54.25
1.56	10	D1d	rbf	0.0001	50 ± 0	54.13 ± 0.24	100 ± 0	70.23 ± 5.74	50	56.78	100	50
1.57	100	D1d	rbf	auto	78.78 ± 1.79	80.52 ± 1.78	80.61 ± 5.1	85.33 ± 0.9	79.41	82.97	80.53	79.41
1.58	100	D1d	rbf	scale	82.43 ± 2.28	84.64 ± 4.75	82.74 ± 5.67	89.49 ± 1.7	81.72	83.57	85.54	81.72
1.59	100	D1d	rbf	0.001	68.8 ± 2.34	68.38 ± 1.37	82.74 ± 5.19	75.74 ± 4.93	70.91	72.33	84.07	70.91
1.6	100	D1d	rbf	0.0001	50.72 ± 1.73	54.5 ± 0.98	99.73 ± 0.53	70.19 ± 5.67	54.25	58.97	98.82	54.25
1.61	1000	D1d	rbf	auto	82.17 ± 2.57	82.7 ± 5.13	85.66 ± 3.11	88.51 ± 2.91	82.02	83.66	86.13	82.02
1.62	1000	D1d	rbf	scale	81.68 ± 2.75	83.19 ± 3.61	83.26 ± 3.86	87.4 ± 2.86	81.36	84.38	82.89	81.36
1.63	1000	D1d	rbf	0.001	71.89 ± 1.31	72.92 ± 1.1	77.95 ± 4.75	79.92 ± 2.27	75.17	78.8	77.87	75.17
1.64	1000	D1d	rbf	0.0001	68.48 ± 2.21	68.08 ± 1.24	82.74 ± 5.19	75.59 ± 5.04	70.76	72.26	83.77	70.76
1.65	1	D1d	poly	auto	50 ± 0	54.13 ± 0.24	100 ± 0	70.42 ± 5.7	50	56.78	100	50
1.66	1	D1d	poly	scale	81.18 ± 2.13	82.81 ± 4.32	82.73 ± 3.51	87.74 ± 1.04	80.02	81.63	85.25	80.02
1.67	1	D1d	poly	0.001	50 ± 0	54.13 ± 0.24	100 ± 0	59.96 ± 6.69	50	56.78	100	50
1.68	1	D1d	poly	0.0001	50 ± 0	54.13 ± 0.24	100 ± 0	59.95 ± 6.69	50	56.78	100	50
1.69	10	D1d	poly	auto	50 ± 0	54.13 ± 0.24	100 ± 0	70.79 ± 6.16	50	56.78	100	50
1.7	10	D1d	poly	scale	82.6 ± 1.16	84.42 ± 4.29	83.53 ± 5.24	88.7 ± 0.85	81.97	83.47	86.43	81.97
1.71	10	D1d	poly	0.001	50 ± 0	54.13 ± 0.24	100 ± 0	59.96 ± 6.69	50	56.78	100	50
1.72	10	D1d	poly	0.0001	50 ± 0	54.13 ± 0.24	100 ± 0	59.95 ± 6.69	50	56.78	100	50
1.73	100	D1d	poly	auto	51.8 ± 0.93	55.04 ± 0.57	100 ± 0	75.92 ± 2.92	51.16	57.36	100	51.16
1.74	100	D1d	poly	scale	82.24 ± 2.14	84.53 ± 3.06	82.34 ± 6.99	87.39 ± 1.21	81.52	83.87	84.36	81.52
1.75	100	D1d	poly	0.001	50 ± 0	54.13 ± 0.24	100 ± 0	59.96 ± 6.69	50	56.78	100	50
1.76	100	D1d	poly	0.0001	50 ± 0	54.13 ± 0.24	100 ± 0	59.95 ± 6.69	50	56.78	100	50
1.77	1000	D1d	poly	auto	72.24 ± 3.2	70.09 ± 2.69	89.78 ± 8.71	83.39 ± 4.11	75.58	75.95	87.61	75.58
1.78	1000	D1d	poly	scale	80.55 ± 3.98	82.83 ± 4.91	81.01 ± 6.14	85.28 ± 1.54	81.18	83.57	84.07	81.18
1.79	1000	D1d	poly	0.001	50 ± 0	54.13 ± 0.24	100 ± 0	68.76 ± 6.31	50	56.78	100	50
1.8	1000	D1d	poly	0.0001	50 ± 0	54.13 ± 0.24	100 ± 0	59.95 ± 6.69	50	56.78	100	50

* K-Fold validation (K = 4)

Table S8 — Comparison of the models developed from datasets D2a – D2d for identification of Kernel

			Training Set				Validation Set			
Model	Dataset	Method	Accuracy	Precision	Recall	ROC_AUC	Accuracy	Precision	Recall	ROC_AUC
2.01	D2a	linear	71.68 ± 6.85	76.41 ± 9.05	78.07 ± 3.96	78.02 ± 4.58	74.19	79.29	79.69	74.19
2.02	D2a	rbf	49.77 ± 0.78	58.39 ± 0.83	99.54 ± 6.54	68.95 ± 1.56	50	60.06	100	50
2.03	D2a	poly	50.4 ± 1.18	58.7 ± 0.86	99.55 ± 14.33	68.19 ± 1.54	50.38	60.24	100	50.38
2.04	D2a	sigmoid	43.56 ± 2.86	53.36 ± 2.52	55.25 ± 2.75	40.42 ± 3.25	47.51	58.03	56.85	47.51
2.05	D2b	linear	70.74 ± 6.13	75.3 ± 7.14	78.08 ± 5.35	76.84 ± 5.9	72.16	77.5	78.68	72.16
2.06	D2b	rbf	66.7 ± 2.33	71.56 ± 2.69	76.3 ± 4.81	75.17 ± 9.55	68.08	72.76	82.74	68.08
2.07	D2b	poly	68.27 ± 2.26	72.74 ± 2.85	77.86 ± 6.29	75.42 ± 9.06	69.87	74.88	80.2	69.87
2.08	D2b	sigmoid	43.43 ± 2.25	53.33 ± 1.78	55.93 ± 1.58	41.14 ± 4.9	47.38	58	58.88	47.38
2.09	D2c	linear	66.15 ± 3.98	70.41 ± 4.74	80.55 ± 6.14	73.82 ± 14.85	68.33	72.34	86.29	68.33
2.1	D2c	rbf	71.41 ± 3.47	74.76 ± 5.32	82.55 ± 1.51	81.85 ± 8.82	76.22	79.62	85.27	76.22
2.11	D2c	poly	73.18 ± 3.58	77.77 ± 6.57	78.52 ± 2.94	82.07 ± 10.16	77.5	81.59	83.24	77.5
2.12	D2c	sigmoid	45.81 ± 4.18	55.09 ± 3.05	55.03 ± 7.53	38.78 ± 3.88	50.3	60.3	60.91	50.3
2.13	D2d	linear	66.44 ± 3.69	70.72 ± 3.97	79.88 ± 6.78	73.46 ± 14.9	66.81	71.36	84.77	66.81
2.14	D2d	rbf	71.84 ± 2.24	75.93 ± 4.16	79.64 ± 2.41	81.77 ± 11.77	75.46	79.32	83.75	75.46
2.15	D2d	poly	73.15 ± 2.37	77.42 ± 5.58	79.42 ± 3.05	82.53 ± 9.83	77.88	81.46	84.77	77.88
2.16	D2d	sigmoid	48.48 ± 8.83	57.48 ± 6.46	66.66 ± 12.62	44.55 ± 5.1	51.18	60.86	71.06	51.18

Table S9 — Comparison of the hyperparameter tuned models and selected models in second set of model development

					Training Set				Validation Set			
Model	Dataset	Kernel	C	gamma	Accuracy	Precision	Recall	ROC_AUC	Accuracy	Precision	Recall	ROC_AUC
2.17	D2d	rbf	1	auto	51.98 ± 1.55	59.49 ± 0.47	99.55 ± 1.54	71.99 ± 4.37	53.18	61.63	99.49	53.18
2.18	D2d	rbf	1	scale	71.84 ± 2.24	75.93 ± 4.16	79.64 ± 11.77	81.77 ± 2.41	75.46	79.32	83.75	75.46
2.19	D2d	rbf	1	0.001	50 ± 0	58.5 ± 0.45	100 ± 0	71.51 ± 4.44	50	60.06	100	50
2.2	D2d	rbf	1	0.0001	50 ± 0	58.5 ± 0.45	100 ± 0	71.86 ± 3.93	50	60.06	100	50
2.21	D2d	rbf	10	auto	63.98 ± 4.1	68.22 ± 5.01	83.46 ± 16.64	74.37 ± 5.09	69.35	72.54	89.84	69.35
2.22	D2d	rbf	10	scale	79.42 ± 5.13	83.14 ± 9.36	83.44 ± 8.44	85.6 ± 1.93	80.42	84	85.27	80.42
2.23	D2d	rbf	10	0.001	50 ± 0	58.5 ± 0.45	100 ± 0	71.49 ± 4.5	50	60.06	100	50
2.24	D2d	rbf	10	0.0001	50 ± 0	58.5 ± 0.45	100 ± 0	71.54 ± 4.57	50	60.06	100	50
2.25	D2d	rbf	100	auto	68.87 ± 4.09	73.23 ± 4.7	78.75 ± 12	77.61 ± 6.13	72.79	76.36	85.27	72.79
2.26	D2d	rbf	100	scale	77.72 ± 7.54	82.05 ± 9.46	80.99 ± 3.75	83.42 ± 3.02	79.15	83	84.26	79.15
2.27	D2d	rbf	100	0.001	63 ± 4.6	67.28 ± 4.33	84.35 ± 14.27	73.21 ± 4.99	66.04	69.92	90.86	66.04
2.28	D2d	rbf	100	0.0001	50 ± 0	58.5 ± 0.45	100 ± 0	71.51 ± 4.59	50	60.06	100	50
2.29	D2d	rbf	1000	auto	75.62 ± 5.38	79.08 ± 8.45	82.77 ± 6.19	82.6 ± 1.65	77.37	80.76	85.27	77.37
2.3	D2d	rbf	1000	scale	77.02 ± 5.07	81.16 ± 5.21	80.54 ± 4.73	79.34 ± 3.24	79.53	84.02	82.74	79.53
2.31	D2d	rbf	1000	0.001	67.07 ± 4.93	71.53 ± 4.15	78.31 ± 11.98	73.81 ± 5.92	68.46	72.8	84.26	68.46
2.32	D2d	rbf	1000	0.0001	62.95 ± 4.5	67.22 ± 4.31	84.58 ± 14.7	73.19 ± 5.03	66.04	69.92	90.86	66.04
2.33	D2c	poly	1	auto	50 ± 0	58.5 ± 0.45	100 ± 0	75.98 ± 3.94	50	60.06	100	50
2.34	D2c	poly	1	scale	73.18 ± 3.58	77.77 ± 6.57	78.52 ± 10.16	82.07 ± 2.94	77.5	81.59	83.24	77.5
2.35	D2c	poly	1	0.001	50 ± 0	58.5 ± 0.45	100 ± 0	54.83 ± 6.48	50	60.06	100	50
2.36	D2c	poly	1	0.0001	50 ± 0	58.5 ± 0.45	100 ± 0	54.83 ± 6.48	50	60.06	100	50
2.37	D2c	poly	10	auto	50 ± 0	58.5 ± 0.45	100 ± 0	76.02 ± 3.62	50	60.06	100	50
2.38	D2c	poly	10	scale	76.67 ± 2.98	80.6 ± 6.17	81.43 ± 7.72	83.63 ± 2.51	79.66	83.75	83.75	79.66
2.39	D2c	poly	10	0.001	50 ± 0	58.5 ± 0.45	100 ± 0	54.83 ± 6.48	50	60.06	100	50
2.4	D2c	poly	10	0.0001	50 ± 0	58.5 ± 0.45	100 ± 0	54.83 ± 6.48	50	60.06	100	50
2.41	D2c	poly	100	auto	50 ± 0	58.5 ± 0.45	100 ± 0	75.98 ± 3.48	50.38	60.24	100	50.38
2.42	D2c	poly	100	scale	76.87 ± 3.25	80.21 ± 4.52	82.77 ± 5.81	81.69 ± 1.96	79.28	82.75	85.27	79.28
2.43	D2c	poly	100	0.001	50 ± 0	58.5 ± 0.45	100 ± 0	62.16 ± 6.4	50	60.06	100	50

2.44	D2c	poly	100	0.0001	50 ± 0	58.5 ± 0.45	100 ± 0	54.83 ± 6.48	50	60.06	100	50
2.45	D2c	poly	1000	auto	66.25 ± 3.67	70 ± 5.23	83.91 ± 15.47	78.34 ± 4.1	69.35	72.8	88.32	69.35
2.46	D2c	poly	1000	scale	75.8 ± 2.22	79.84 ± 3.03	80.31 ± 6.51	78.79 ± 2.74	79.15	83.58	82.74	79.15
2.47	D2c	poly	1000	0.001	50 ± 0	58.5 ± 0.45	100 ± 0	75.85 ± 3.11	50	60.06	100	50
2.48	D2c	poly	1000	0.0001	50 ± 0	58.5 ± 0.45	100 ± 0	54.83 ± 6.48	50	60.06	100	50
2.49	D2d	poly	1	auto	50 ± 0	58.5 ± 0.45	100 ± 0	77.35 ± 2.21	50	60.06	100	50
2.5	D2d	poly	1	scale	73.15 ± 2.37	77.42 ± 5.58	79.42 ± 9.83	82.53 ± 3.05	77.88	81.46	84.77	77.88
2.51	D2d	poly	1	0.001	50 ± 0	58.5 ± 0.45	100 ± 0	64.62 ± 10.97	50	60.06	100	50
2.52	D2d	poly	1	0.0001	50 ± 0	58.5 ± 0.45	100 ± 0	64.62 ± 10.97	50	60.06	100	50
2.53	D2d	poly	10	auto	50 ± 0	58.5 ± 0.45	100 ± 0	77.35 ± 2.39	50	60.06	100	50
2.54	D2d	poly	10	scale	77.14 ± 3.39	80.57 ± 6.73	82.99 ± 7.57	84.28 ± 1.14	78	81.77	84.26	78
2.55	D2d	poly	10	0.001	50 ± 0	58.5 ± 0.45	100 ± 0	64.62 ± 10.97	50	60.06	100	50
2.56	D2d	poly	10	0.0001	50 ± 0	58.5 ± 0.45	100 ± 0	64.62 ± 10.97	50	60.06	100	50
2.57	D2d	poly	100	auto	50 ± 0	58.5 ± 0.45	100 ± 0	77.25 ± 2.45	50.76	60.42	100	50.76
2.58	D2d	poly	100	scale	77.16 ± 3.31	80.79 ± 4.79	82.1 ± 4.58	81.53 ± 1.66	78.13	82.08	83.75	78.13
2.59	D2d	poly	100	0.001	50 ± 0	58.5 ± 0.45	100 ± 0	64.62 ± 10.97	50	60.06	100	50
2.6	D2d	poly	100	0.0001	50 ± 0	58.5 ± 0.45	100 ± 0	64.62 ± 10.97	50	60.06	100	50
2.61	D2d	poly	1000	auto	66.46 ± 7.98	70.64 ± 9.21	83.69 ± 19.54	79.15 ± 3.94	70.88	74.34	86.8	70.88
2.62	D2d	poly	1000	scale	75.14 ± 2.6	79.34 ± 3.19	79.64 ± 3.88	77.27 ± 3.35	78.14	83.24	80.71	78.14
2.63	D2d	poly	1000	0.001	50 ± 0	58.5 ± 0.45	100 ± 0	73.8 ± 4.11	50	60.06	100	50
2.64	D2d	poly	1000	0.0001	50 ± 0	58.5 ± 0.45	100 ± 0	64.62 ± 10.97	50	60.06	100	50
2.65	D2c	rbf	1	auto	50 ± 0	58.5 ± 0.45	100 ± 0	71.82 ± 4.62	50	60.06	100	50
2.66	D2c	rbf	1	scale	71.41 ± 3.47	74.76 ± 5.32	82.55 ± 8.82	81.85 ± 1.51	76.22	79.62	85.27	76.22
2.67	D2c	rbf	1	0.001	50 ± 0	58.5 ± 0.45	100 ± 0	71.45 ± 5.02	50	60.06	100	50
2.68	D2c	rbf	1	0.0001	50 ± 0	58.5 ± 0.45	100 ± 0	71.68 ± 4.51	50	60.06	100	50
2.69	D2c	rbf	10	auto	64.96 ± 3.39	68.72 ± 3.89	84.8 ± 16.03	74.51 ± 4.58	67.31	70.91	90.35	67.31
2.70	D2c	rbf	10	scale	79.87 ± 4.94	83.91 ± 8.98	82.77 ± 7.63	86 ± 1.67	81.06	84.5	85.78	81.06
2.71	D2c	rbf	10	0.001	50 ± 0	58.5 ± 0.45	100 ± 0	71.42 ± 5.25	50	60.06	100	50
2.72	D2c	rbf	10	0.0001	50 ± 0	58.5 ± 0.45	100 ± 0	71.4 ± 5.02	50	60.06	100	50
2.73	D2c	rbf	100	auto	68.42 ± 4.15	72.59 ± 3.93	79.43 ± 13.29	77.11 ± 4.53	73.43	77.61	82.74	73.43
2.74	D2c	rbf	100	scale	78.57 ± 4.41	82.12 ± 6.84	83 ± 4.82	83.77 ± 1.75	81.18	84.84	85.27	81.18
2.75	D2c	rbf	100	0.001	65.2 ± 2.87	68.73 ± 3.63	85.92 ± 14.16	73.66 ± 4.98	64.51	69.01	89.34	64.51
2.76	D2c	rbf	100	0.0001	50 ± 0	58.5 ± 0.45	100 ± 0	71.38 ± 5.26	50	60.06	100	50
2.77	D2c	rbf	1000	auto	75.34 ± 2.87	78.71 ± 5.63	82.55 ± 6.93	82.4 ± 1.39	80.17	83.33	86.29	80.17
2.78	D2c	rbf	1000	scale	76.72 ± 6.24	80.66 ± 6.65	81.21 ± 7.49	79.54 ± 4.21	79.28	83.93	82.23	79.28
2.79	D2c	rbf	1000	0.001	67.77 ± 5.33	72.17 ± 4.92	78.76 ± 14.34	74.87 ± 4.96	68.72	73.51	81.72	68.72
2.8	D2c	rbf	1000	0.0001	65.43 ± 3.33	68.89 ± 4.38	86.36 ± 13.88	73.6 ± 4.94	64.51	69.01	89.34	64.51
2.81	D2a	linear	1	auto	71.68 ± 6.85	76.41 ± 9.05	78.07 ± 4.58	78.02 ± 3.96	74.19	79.29	79.69	74.19
2.82	D2a	linear	1	scale	71.68 ± 6.85	76.41 ± 9.05	78.07 ± 4.58	78.02 ± 3.96	74.19	79.29	79.69	74.19
2.83	D2a	linear	1	0.001	71.68 ± 6.85	76.41 ± 9.05	78.07 ± 4.58	78.02 ± 3.96	74.19	79.29	79.69	74.19
2.84	D2a	linear	1	0.0001	71.68 ± 6.85	76.41 ± 9.05	78.07 ± 4.58	78.02 ± 3.96	74.19	79.29	79.69	74.19
2.85	D2a	linear	10	auto	72.03 ± 6.32	76.39 ± 8.57	79.41 ± 6.64	76.41 ± 6.69	73.3	77.77	81.72	73.3
2.86	D2a	linear	10	scale	72.03 ± 6.32	76.39 ± 8.57	79.41 ± 6.64	76.41 ± 6.69	73.3	77.77	81.72	73.3
2.87	D2a	linear	10	0.001	72.03 ± 6.32	76.39 ± 8.57	79.41 ± 6.64	76.41 ± 6.69	73.3	77.77	81.72	73.3
2.88	D2a	linear	10	0.0001	72.03 ± 6.32	76.39 ± 8.57	79.41 ± 6.64	76.41 ± 6.69	73.3	77.77	81.72	73.3
2.89	D2a	linear	100	auto	68.06 ± 4.86	72.84 ± 7.78	78.07 ± 11.75	73.63 ± 8.24	73.3	78.68	78.68	73.3
2.9	D2a	linear	100	scale	68.06 ± 4.86	72.84 ± 7.78	78.07 ± 11.75	73.63 ± 8.24	73.3	78.68	78.68	73.3
2.91	D2a	linear	100	0.001	68.06 ± 4.86	72.84 ± 7.78	78.07 ± 11.75	73.63 ± 8.24	73.3	78.68	78.68	73.3
2.92	D2a	linear	100	0.0001	68.06 ± 4.86	72.84 ± 7.78	78.07 ± 11.75	73.63 ± 8.24	73.3	78.68	78.68	73.3
2.93	D2a	linear	1000	auto	67.95 ± 11.85	73.15 ± 9.4	74.73 ± 10.33	74.01 ± 9.97	73.43	78.04	81.21	73.43
2.94	D2a	linear	1000	scale	67.95 ± 11.85	73.15 ± 9.4	74.73 ± 10.33	74.01 ± 9.97	73.43	78.04	81.21	73.43

2.95	D2a	linear	1000	0.001	67.95 ± 11.85	73.15 ± 9.4	74.73 ± 10.33	74.01 ± 9.97	73.43	78.04	81.21	73.43
2.96	D2a	linear	1000	0.0001	67.95 ± 11.85	73.15 ± 9.4	74.73 ± 10.33	74.01 ± 9.97	73.43	78.04	81.21	73.43

Table S10 — Ramachandran parameter for developed homology model calculated by using PROCHECK and Molprobity

	Residues in allowed region(%)	Residues in outlier region(%)
PROCHECK	99.5	0.5
Molprobity	99.4	0.6

Table S11 — Validation parameters for molecular docking protocol

S.No.	IC_{50} Threshold (nM)	Energy Threshold (Kcal/mol)	True Positive	True Negative	False Positive	False Negative	Accuracy	Precision	Recall/True positive rate	F1 Score	True Negative Rate
1	10	−12.05	2	250	0	77	76.60	100.00	2.53	4.94	100.00
2	100	−9.05	82	137	43	67	66.57	65.60	55.03	59.85	76.11
3	500	−8.05	147	86	61	35	70.82	70.67	80.77	75.38	58.50
4	750	−8.05	156	83	52	38	72.64	75.00	80.41	77.61	61.48
5	1000	−8.05	161	82	47	39	73.86	77.40	80.50	78.92	63.57
6	2000	−8.05	161	81	47	40	73.56	77.40	80.10	78.73	63.28
7	5000	−8.05	161	81	47	40	73.56	77.40	80.10	78.73	63.28
8	10000	−8.05	161	81	47	40	73.56	77.40	80.10	78.73	63.28
9	20000	−8.05	161	81	47	40	73.56	77.40	80.10	78.73	63.28
10	40000	−8.05	161	81	47	40	73.56	77.40	80.10	78.73	63.28
11	80000	−7.8	179	60	44	46	72.64	80.27	79.56	79.91	57.69
12	80000	−7.55	183	56	48	42	72.64	79.22	81.33	80.26	53.85
13	100000	−7.55	191	53	40	45	74.16	82.68	80.93	81.80	56.99
14	500000	−1.3	287	0	39	3	87.23	88.04	98.97	93.18	0.00
15	500000	−1.05	287	0	39	3	87.23	88.04	98.97	93.18	0.00
16	500000	−0.8	287	0	39	3	87.23	88.04	98.97	93.18	0.00
17	500000	−0.55	287	0	39	3	87.23	88.04	98.97	93.18	0.00
18	1000000	−1.3	295	0	31	3	89.67	90.49	98.99	94.55	0.00
19	1000000	−1.05	295	0	31	3	89.67	90.49	98.99	94.55	0.00
20	1000000	−0.8	295	0	31	3	89.67	90.49	98.99	94.55	0.00
21	1000000	−0.55	295	0	31	3	89.67	90.49	98.99	94.55	0.00

Table S12 — Protein-ligand contact analysis.

Residue	Donepezil	AAM13201183	ART21232619	LMG16204648
GLN71	0	96.4	94.6	99.8
TYR72	100	88.6	98.5	100
VAL73	34.6	100	90.9	100
ASP74	100	100	98.7	100
THR75	99.6	97.7	59.1	100
LEU76	100	96.2	39.2	88.9
TYR77	0	96.2	47.5	98
PRO78	0	0	15.2	90.4
GLY79	0	0	15.6	83.4
PHE80	0	11.5	18.2	34.6
GLY82	94.8	98.3	54.4	61.1
THR83	100	100	99.8	100
GLU84	0	100	57.1	99.9
MET85	87	100	99	99.7
TRP86	100	100	100	100

ASN87	100	100	98	100
PRO88	35.8	100	84.6	100
TRP117	100	73.4	38.1	95.8
ILE118	0	0	0	32.2
TYR119	100	77.5	62.2	97.9
GLY120	100	100	99.6	100
GLY121	100	100	100	100
GLY122	100	100	100	99.8
PHE123	98	0	33.9	0
TYR124	100	100	99.9	100
SER125	100	100	100	100
GLY126	100	99.7	100	100
ALA127	99.6	45.7	47.1	54.9
LEU130	100	98.9	96.9	81.2
VAL132	89.9	77.7	49.4	54.5
TYR133	100	100	93.8	98.9
GLH202	100	100	96.7	100
SER203	100	100	97.2	100
ALA204	90.8	92.5	82.4	91.2
GLY205	86.1	54.3	13	61.1
ALA206	0	0	0	23.1
SER229	94.2	67	68.8	24.7
TRP286	100	22.5	13.5	56.3
HID287	49.7	0	0	0
LEU289	94.2	0	0	0
GLN291	41.5	0	0	0
GLU292	89.9	0	0	0
SER293	99.2	0	0	0
VAL294	99.9	0	0	0
PHE295	100	0	0	0
ARG296	100	0	0	0
PHE297	100	100	66.4	51.9
SER298	53.3	0	0	0
GLH334	59.7	0	0	0
TYR337	100	100	100	100
PHE338	100	100	100	67.5
LEU339	42.3	0	0	0
VAL340	89.6	42.1	0	0.6
TYR341	100	100	93.3	99.5
GLY342	98.2	0	0	0
TRP439	99.9	98.1	62.4	57.8
PRO446	83.1	38.3	73	0
HID447	100	100	100	100
GLY448	100	100	92.9	99.9
TYR449	99.3	94.3	90	41.1
GLU450	87.3	56.9	67.6	11.6
ILE451	100	99.6	73	97.6