

DEELIG: A docking-free deep learning-based approach to predict protein-ligand binding affinity

Supplementary Document: Appendix File

List of appendices:

Appendix A: List of ligand features calculated for DEELIG

Appendix B: (1) Network layout for modules and (2) Hyperparameters in Composite model

Appendix C: Training curve for Composite model

Appendix D: DEELIG performance on Kinases dataset

Appendix A

List of Ligand features calculated for DEELIG

Following properties were calculated using PADEL:

- Basic Group Count
- Carbon Type
- Hybridization Ratio
- Manhold LogP (The Ratio of carbon to hetero atoms)
- Number of Aromatic bonds
- MACCS Key
- Klehotaroth fingerprints (Types and Counts)
- AtomPair2D fingerprints (Types and Counts)

Following ADMET properties were calculated using PADEL:

- *donorHB*
- *accptHB*
- *Constitutional (Electronegativity)*
- *rotatableBondCounts (#ringatoms)*
- *RuleofFive*
- *VABC (Volume)*
- *Weight (mol_MW)*

Following ADMET properties were calculated using OikProp:

- Amine
- Amidine
- Acid
- Amide
- Rotor
- rtvFG (reactive functional groups)
- mol_MW, dipole
- Volume
- donorHB
- accptHB

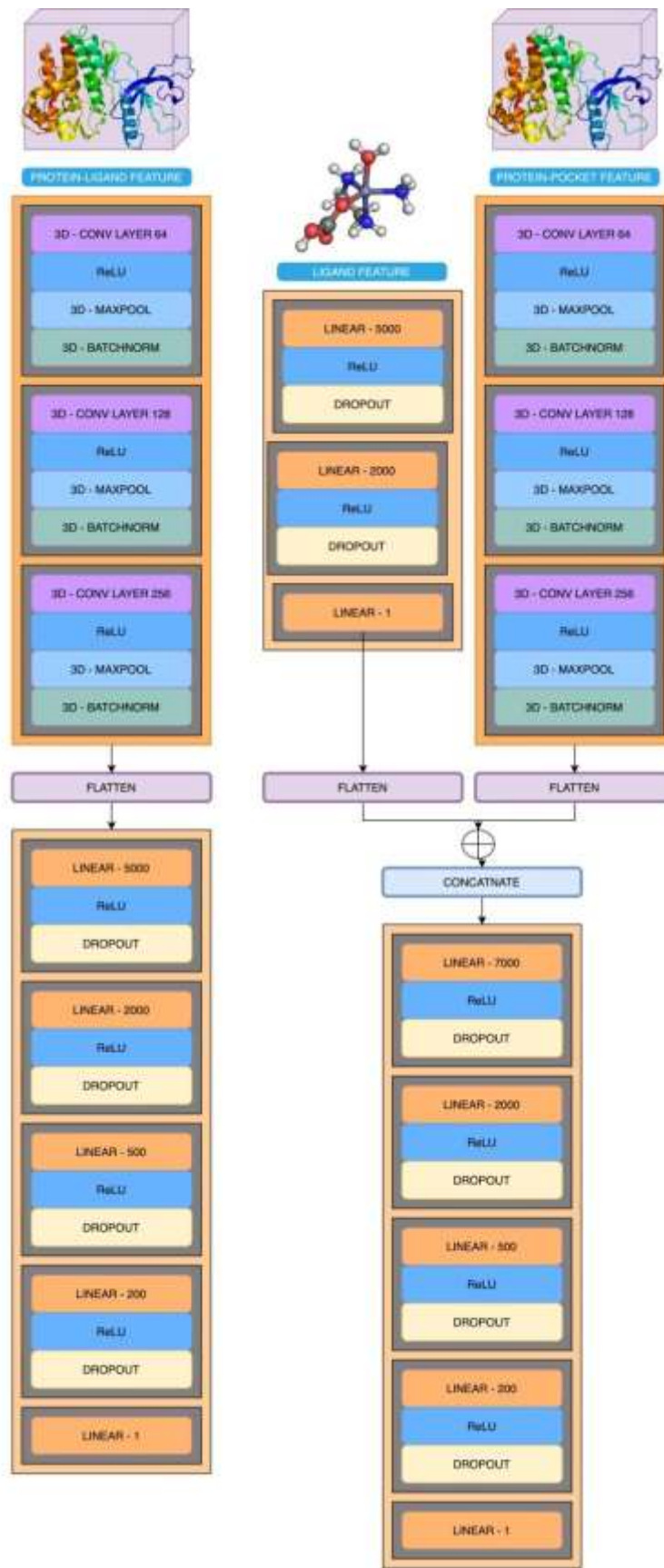
- QPpolrz (polarizability)
- SASA
 - SASA (probe of 1.4Å)
 - FOSA (hydrophobic component of SASA)
 - FISA (hydrophilic component of SASA)
 - PISA (pi of SASA)
 - WPSA (polar of SASA)
 - SAFluorine
 - SAamideO
- **Partition coefficients =>**
 - QPlogPC16
 - QPlogPoct
 - QPlogPw
 - QPlogPo/w
- CIQPlogS (**Conformation indie aqueous solubility**)
- IP (ev) (ionization potential)
- EA (eV) (electron affinity)
- #metab (likely metabolic reactions)
- PSA (van der waals SA of polar N and O atoms)
- #NandO, #ringatoms (number of atoms in rings)
- #in34 (number of atoms in 3 or 4 membered rings)
- #in56 (number of atoms in 5 or 6 membered rings)
- #noncon (ring atoms cannot form conjugated aromatic bonds)
- #nonHatm (heavy atoms- nonhydrogen atoms)
- RuleOfThree
- RuleOfFive (lipinski violations)
- QPlogKhsa (binding to human serum albumin)
- PercentHuman-OralAbsorption
- Globular nature index

Appendix B

1. Network Layout for modules

Following is the detailed layout of the modules Atomic Model and Composite Model that have been referenced in the main article in **Sections 4.4.1** and **4.4.2** respectively.

Hyperparameters of the Composite Model have also been provided here.



(a) Atomic Model Network

(b) Complex Model Network

Appendix_Figure A1: Network layout for models.

Appendix_Table B1: Hyperparameters in Composite Model

Hyper Parameter			
Protein Layer	Channels	Filter size	Padding
Conv3D	64	5	3
ReLU	0	0	0
MaxPool3D	0	3	1
Conv3D	128	5	3
ReLU	0	0	0
MaxPool3D	0	3	1
BatchNorm3D	128	0	0
Conv3D	256	3	1
ReLU	0	0	0
MaxPool3D	0	3	1
BatchNorm3D	256	0	0
Ligand Layer			
Layers	Neurons		
Linear	7000		
ReLU	0		
Dropout	0.5		
Linear	5000		
ReLU	0		
Dropout	0.5		
Linear	2000		
ReLU	0		
Regressor layer			
Layers	Neurons		
Linear	7000		
ReLU	0		
Dropout	0.5		
Linear	2000		
ReLU	0		
Dropout	0.5		
Linear	500		
ReLU	0		
Dropout	0.5		
Linear	200		
ReLU	0		
Dropout	0.5		
Linear	1		
Optimizer Parameters			
Optimizer	Learning Rate	Momentum	
Adam	0.001	0.99	
Batch Size	28	-	

Appendix C

Training curve of composite model:

Mean Square Error vs Epochs

Training curve for 20 epochs



Appendix_Figure C1: Hyperparameters in Composite Model

Appendix D

DEELIG performance on Kinases dataset

Protein-ligand complexes used have been presented in the format ‘\$PDB-ID_\$Ligand-ID_\$Chain-ID_\$Atom-number’. Here, the ligand ID (Ligand-ID) is as obtained from PDB and ‘Atom-number’ indicates the atom number at which ligand is bound to the protein structure.

Appendix_Table D1: Performance of DEELIG on kinases

PDB ID	Ground Truth (-log (kd/ki))	Predicted (-log (kd/ki))	Set
1ATP_ATP_E_355	14.33	10.162511	training
1B38_ATP_A_381	12.89	11.011607	training
1B39_ATP_A_381	13.64	10.672279	training
1BX6_BA1_A_351	16.88	17.481277	training
1KV1_BMU_A_391	11.34	11.811321	training
1PXJ_CK2_A_500	8.11	8.140871	training
1Q8T_Y27_A_930	9.22	8.202146	training
1Q8U_H52_A_961	12.6	14.963462	training
1Q8U_H52_A_962	12.6	12.837863	training
1Q8W_M77_A_960	11.05	13.436903	training
1R0E_DFN_A_702	20.73	18.322815	training
1R0E_DFN_B_501	20.73	20.813835	training
1TVO_FRZ_A_1001	11.68	14.313412	training
1UNL_RRC_A_1293	3.97	5.2938104	training
1UU3_LY4_A_1374	4.97	12.5554905	training
1XH4_R69_A_351	14.9	10.410368	training
1XH5_R68_A_1001	10.29	11.608167	training
1XWS_BI1_A_1001	16.12	15.265529	training
1YDT_IQB_E_351	14.51	11.634923	training
2BAK_AQZ_A_401	14.81	13.099378	training
2C5O_CK2_A_1297	8.11	4.862343	training
2C5O_CK2_C_1298	8.11	5.131049	training

2EWA_SB2_A_361	15.98	13.587485	training
2F2U_M77_A_501	14.07	10.874512	training
2F2U_M77_B_1501	14.07	12.677324	training
2J2I_LY4_B_1307	5.92	9.034196	training
2NPQ_BOG_A_1000	10.39	10.77333	training
2NPQ_BOG_A_2000	10.39	9.395628	training
2O3P_QUE_A_501	15.21	11.99402	training
2O63_MYC_A_501	11.77	10.327488	training
2O64_MYU_A_501	12.6	15.132906	training
2QHM_7CS_A_500	11.93	15.419877	training
2RIO_ADP_A_1101	8.5	8.839855	training
2RIO_ADP_B_2101	8.5	8.12286	training
2RKU_R78_A_500	17.33	17.202715	training
2UZT_SS3_A_1351	13.93	10.50961	training
2VU3_LZE_A_1299	15.02	11.712693	training
2WTV_ZZL_A_1390	16.48	14.356284	training
2WTV_ZZL_B_1390	16.48	14.618113	training
2XJ2_985_A_1001	14.24	13.576728	training
2Y7J_B49_A_1294	9.74	8.980873	training
2Y7J_B49_B_1294	9.74	10.673288	training
2Y7J_B49_C_1294	9.74	8.560607	training
2Y7J_B49_D_1294	9.74	5.335432	training
2YIW_YIW_A_1353	19.34	12.520471	training
2YIX_YIX_A_1355	17.23	14.783937	training
2ZB1_GK4_A_361	12.25	11.635828	training
3AMA_SKE_A_351	9.22	6.7474203	training
3AMB_VX6_A_351	9.22	11.450221	training
3AT4_CCK_A_336	17.61	16.972866	training
3BWJ_ARX_A_352	12.66	10.589522	training
3D0E_G93_A_1	17.04	12.532833	training

3D0E_G93_B_2	17.04	17.183178	training
3DDQ_RRC_A_299	12.9	8.297859	training
3DDQ_RRC_C_299	12.9	7.178257	training
3E5A_VX6_A_500	17.73	12.699175	training
3EQG_4BM_A_1	14.99	9.964328	training
3FC1_52P_X_362	10.49	10.373807	training
3FLS_FLS_A_361	18.24	13.88539	training
3FLW_FLW_A_361	18.16	16.465137	training
3FSK_RO6_A_450	14.96	13.170166	training
3GCP_SB2_A_361	15.72	12.1016035	training
3GCS_BAX_A_401	5.6	6.2856894	training
3GCU_R48_B_401	13.32	12.8222475	training
3GCV_SS6_A_361	14.12	12.847186	training
3GNI_ATP_B_1	15.43	9.653784	training
3GP0_NIL_A_1	14.84	18.384321	training
3HEC_STI_A_1	9.22	8.287979	training
3HEG_BAX_A_1	5.6	7.008605	training
3HMO_STU_A_1	15.01	12.163776	training
3HP5_52P_A_401	10.49	10.918285	training
3HV6_R39_A_361	12.72	9.466206	training
3IW5_DF3_A_362	11.69	9.562438	training
3IW6_PP0_A_361	10.33	7.345064	training
3IW8_HIZ_A_361	8.92	9.450232	training
3JVS_AGY_A_900	13.44	14.485944	training
3L8S_BFF_A_361	13.83	12.68417	training
3L8X_N4D_A_361	16.12	14.4477	training
3LFA_1N1_A_361	8.22	9.860175	training
3MYG_EML_A_1	22.34	17.777912	training
3NPC_B96_A_365	9.53	10.554703	training
3NPC_B96_B_365	9.53	8.5307665	training

3O8P_BMU_A_361	11.34	10.370246	training
3O8U_BMU_A_361	11.34	9.472248	training
3OBJ_BMU_A_361	11.34	11.657911	training
3PG3_DG7_A_362	11.01	13.260027	training
3PXF_2AN_A_304	7.91	8.43764	training
3PXQ_2AN_A_300	7.91	8.458857	training
3PXQ_2AN_A_301	7.91	7.9644737	training
3PXQ_2AN_A_302	7.91	7.834199	training
3PXZ_2AN_A_299	7.91	6.5781374	training
3PXZ_JWS_A_301	9.74	7.590602	training
3PY1_2AN_A_301	7.91	6.6630545	training
3PY1_2AN_A_302	7.91	7.0281353	training
3PY1_SU9_A_300	13.56	13.19573	training
3RGF_BAX_A_465	5.78	8.478868	training
3SW7_19K_A_299	9.76	12.033982	training
3TZM_085_A_1	6.27	13.889732	training
3UBD_SL0_A_400	10.45	11.020773	training
3UO4_0C0_A_1	12.73	12.905641	training
3UOL_0C7_A_2	15.54	13.293035	training
3UOL_0C7_B_1	15.54	14.602809	training
3VQH_IQB_A_401	15.29	15.187998	training
3VVH_4BM_B_503	14.99	13.505534	training
3VVH_4BM_C_503	14.99	15.487566	training
3ZSH_469_A_400	19.12		training
3ZSI_52P_A_1000	10.49	7.871111	training
4BCQ_TJF_C_1295	13.44	12.84407	training
4BTK_DTQ_A_1337	12.95	9.336148	training
4CRL_C1I_A_1360	20.06	15.915939	training
4DLI_IRG_A_401	10.64	9.909659	training
4DLI_IRG_A_402	10.64	11.62527	training

4EK6_10K_A_301	9.92	10.227652	training
4EZ7_2AN_A_302	7.91	7.93563	training
4EZ7_2AN_A_303	7.91	6.879238	training
4F9Y_GG5_A_401	12.03	14.077505	training
4F9Y_GG5_A_402	12.03	12.441417	training
4F9Y_LM3_A_403	13.21	10.422124	training
4FKI_09K_A_301	7.45	10.119772	training
4FKL_CK2_A_300	8.11	7.9371223	training
4FKO_20K_A_301	7.84	8.178918	training
4FKU_60K_A_301	12.39	9.98849	training
4FKU_60K_A_303	12.39	14.65224	training
4GUE_QCT_A_401	9.76	10.720871	training
4I3Z_ADP_A_301	0.67	5.0668316	training
4I3Z_ADP_C_301	0.67	6.001342	training
4I5M_R78_A_401	18.65	21.034546	training
4JBQ_VX6_A_501	17.73	14.951972	training
4KS8_B49_A_701	3.73	7.098278	training
4L9I_8PR_A_601	8.95	12.205049	training
4L9I_8PR_B_601	8.95	10.86388	training
4LOO_SB4_A_401	16.48	16.590876	training
4LOP_SB4_A_401	16.48	16.209667	training
4LOP_SB4_B_401	16.48	14.673704	training
4LOP_SB4_C_401	16.48	14.650061	training
4LOP_SB4_D_401	16.48	14.583004	training
4LOQ_SB4_A_401	16.48	15.305688	training
4LOQ_SB4_B_401	16.48	12.504713	training
4LOQ_SB4_C_401	16.48	13.820618	training
4OTI_MI1_A_1001	13.13	12.5323515	training
4QMN_DB8_A_401	11.62	14.84667	training
4QMZ_B49_A_401	5.69	6.55925	training

4QP2_36R_A_401	4.67	7.273883	training
4QTA_38Z_A_411	15.86	13.754637	training
4QTB_38Z_A_418	13.99	12.003158	training
4QTB_38Z_B_412	13.99	11.510162	training
4QTE_390_A_430	17.73	13.258313	training
4QYY_3G7_A_401	14.51	10.219946	training
4TXC_38G_A_301	12.95	11.588561	training
4U43_3D8_A_401	7.65	5.3566923	training
4X21_3WH_A_501	14.84	11.492774	training
4X21_3WH_B_501	14.84	13.035936	training
4XX9_RF4_A_402	9.44	8.770052	training
4Y8D_49J_A_401	16.24	11.525299	training
4Y8D_49J_B_401	16.24	15.099169	training
4ZJI_40Q_B_601	7.83	7.283536	training
4ZJI_40Q_C_601	7.83	9.089074	training
4ZJI_40Q_D_601	7.83	6.8545666	training
4ZJJ_40R_A_601	7.83	7.0933084	training
4ZJJ_40R_B_601	7.83	8.350812	training
4ZJJ_40R_C_601	7.83	5.1687207	training
4ZJJ_40R_D_601	7.83	7.2560215	training
5AJQ_DB8_A_800	16.48	14.70757	training
5AJQ_DB8_B_800	16.48	14.7908	training
5AUT_2AN_A_301	9.62	8.227689	training
5CS6_K82_A_404	5.07	4.468193	training
5CS6_K82_A_405	5.07	5.1155643	training
5CS6_K82_A_406	5.07	4.588729	training
5CS6_K82_A_407	5.07	4.937118	training
5CSH_54E_A_401	5.92	5.2921076	training
5CSH_54E_A_402	5.92	7.947792	training
5CSH_54E_B_403	5.92	5.49813	training

5CSH_54E_B_404	5.92	6.6865587	training
5CSP_54G_A_401	7.46	6.192384	training
5CU3_54S_A_404	12.66	16.073565	training
5CU3_54S_B_403	12.66	9.69426	training
5CU4_54S_A_404	12.66	12.544091	training
5DN3_5DN_A_402	10.19	7.8209085	training
5DR9_SKE_A_401	6	7.5168114	training
5DRB_5FJ_A_501	17.11	14.781893	training
5DT0_SKE_A_401	6	5.988515	training
5JQ5_I74_A_302	10.67	13.649733	training
5L4Q_LKB_A_401	14.46	12.602347	training
5L4Q_LKB_B_401	14.46	14.451378	training
5MO8_C98_A_404	11.02	11.826718	training
5MO8_C98_B_401	11.02	11.957595	training
5MOD_86L_A_404	5.81	5.3589926	training
5MOE_OQC_A_409	5.3	4.6797047	training
5MOE_OQC_A_410	5.3	5.384391	training
5MOE_OQC_A_411	5.3	6.2392187	training
5MOE_OQC_B_409	5.3	6.606739	training
5MRB_C5N_A_901	12.27	16.349714	training
5MTX_FJI_A_401	15.55	13.412746	training
5MTY_HB9_A_401	18.16	13.793211	training
5TBE_78L_A_401	16.94	19.41852	training
5TE0_XIN_A_401	14.28	14.470296	training
5TF9_7AV_A_501	10.04	7.720195	training
5VC3_DB8_A_601	14.08	16.318983	training
5VC4_XZN_A_601	14.65	10.742605	training
5VC5_96M_A_601	16.03	12.171665	training
5VC6_P48_A_601	15.82	14.553338	training
5VCV_1N1_A_404	15.72	9.767446	training

5VCW_93J_A_401	4.51	5.9813185	training
5VCW_93J_B_401	4.51	4.4235907	training
5VCZ_XZN_A_401	12.33	13.311826	training
5VD0_8X7_A_401	12.64	13.869585	training
5VD1_P48_A_401	11.53	17.269943	training
5VD3_H8H_A_401	10.48	12.441893	training
1PY5_PY1_A_700	16.82	14.969334	validation
1XH7_R96_A_351	13.42	14.521075	validation
1XH9_R69_A_351	15.59	11.105695	validation
2A4L_RRC_A_300	3.39	6.7256346	validation
2FVD_LIA_A_299	19.12	15.857263	validation
2UZW_SS4_E_1351	16.82	13.931561	validation
2WTV_ZZL_D_1390	16.48	16.501717	validation
3BWJ_ARX_A_351	12.66	10.008118	validation
3GCQ_1BU_A_401	12.59	17.14584	validation
3GCU_R48_A_401	13.32	11.107234	validation
3GI3_B10_A_391	17.84	15.133845	validation
3HMP_CX4_A_1	10.34	7.4939575	validation
3HUB_469_A_361	19.12	14.843432	validation
3HUC_G97_A_362	11.49	10.609373	validation
3LFF_Z83_A_362	13.15	12.004912	validation
3O8T_BMU_A_361	11.34	10.189346	validation
3PXF_2AN_A_305	7.91	9.076647	validation
3PXZ_2AN_A_300	7.91	6.3745623	validation
3SW4_18K_A_299	9.95	14.080001	validation
3U9N_09H_A_301	13.82	11.017376	validation
3UVQ_FS8_A_361	15.59	11.264186	validation
3VVH_4BM_A_703	14.99	12.857493	validation
4BCQ_TJF_A_1296	13.44	12.502231	validation
4BTJ_ATP_B_1338	8.3	10.083336	validation

4KKH_1RQ_A_501	14.6	17.964321	validation
4LOQ_SB4_D_401	16.48	22.440546	validation
4NJ3_2KD_A_301	12.72	11.144922	validation
4QMS_1N1_A_401	3.97	8.428536	validation
4QMU_SKE_A_401	5.63	5.1778917	validation
4ZJI_4OQ_A_601	7.83	5.5979853	validation
5DIJ_56H_A_4000	14.79	12.7819	validation
5DPV_SKE_A_402	6	7.86001	validation
5LVL_537_A_401	11.29	10.439565	validation
5MOE_OQC_B_408	5.3	6.949047	validation
5V5Y_8X7_A_601	15.83	15.258941	validation
5VCY_DB8_A_401	12.83	14.903077	validation
1KE9_LS5_A_299	10.95	10.35851	test
1XH6_R94_A_351	14.55	14.093109	test
2BAJ_1PP_A_401	17.04	12.874502	test
2BAL_PQA_A_401	12.23	12.644074	test
2WTV_ZZL_C_1392	16.48	13.081798	test
2XJ1_XJ1_A_1307	15.09	12.160637	test
3FLN_3FN_C_361	20.04	13.301807	test
3HRF_P47_A_1374	9.19	9.049356	test
3HV7_1AU_A_361	15.94	10.493131	test
3LFE_Z84_A_361	12.05	12.960303	test
3TI1_B49_A_299	9.22	9.492598	test
4EK8_16K_A_301	10.04	11.950938	test
4FKP_LS5_A_301	10.95	11.706519	test
4FKW_62K_A_301	13.95	14.523321	test
5TCO_79Q_A_401	17.28	12.303295	test
5TF9_7AV_B_501	10.04	10.4065275	test