Supplemental Information

Table S1: The performance (Pearson) of finetune_pearson, finetune_mse and LumiNet on the CASF-2016 and FEP datasets.

Model	CASF-2016	FEP2	FEP1
finetune_pearson	0.818	0.517	0.543
finetune_mse	0.809	0.445	0.486
LumiNet	0.848	0.463	0.646

Table S2: The performance of the LumiNet model versus baseline model on the FEP1 dataset.[a]

Model		BACE	CDK2	JNK1	MCL	p38	PTP1B	Thrombin	TYK	Averag
	No.	**36**	**16**	**21**	**42**	**34**	**23**	**11**	**16**	**25**
LumiNet	R	0.44	0.53	0.45	0.81	0.6	0.79	0.91	0.6	0.65
	ρ	0.42	0.57	0.50	0.80	0.6	0.70	0.89	0.5	0.64
	RMS	1.7	1.39	0.75	0.83	1.0	1.16	1.05	1.1	1.13
PIGNET2[1]	R	0.42	0.77	0.36	0.78	0.6	0.76	0.83	0.6	0.64
	ρ	0.42	0.67	0.43	0.75	0.6	0.77	0.78	0.5	0.63
	RMS	0.83	1.45	1.14	0.82	1.1	1.03	0.44	2.4	1.16
PBCNET[2]	R	0.61	0.66	0.41	0.72	0.56	0.75	0.84	0.64	0.65
	ρ	0.52	0.66	0.47	0.73	0.56	0.71	0.82	0.61	0.64
	RMS	0.91	1.35	1.21	1.11	1.15	1.23	0.42	1.54	1.11
FEP+	R	0.78	0.48	0.85	0.77	0.65	0.8	0.71	0.89	0.74
	ρ	0.74	0.41	0.9	0.78	0.64	0.82	0.62	0.87	0.72
	RMSE	1.03	1.11	1	1.41	1.03	1.22	0.93	0.93	1.08
Glide-SP	R	0	-0.56	0.24	0.59	0.14	0.55	0.53	0.79	0.29
	ρ	0.11	-0.36	0.27	0.5	-0.24	0.23	0.49	0.79	0.23
	RMSE	1.4	2.63	2.16	1.54	3.24	2.8	0.92	2.06	2.09
MM-GB/SA	R	-0.4	-0.53	0.65	0.42	0.66	0.67	0.93	0.79	0.4
	ρ	-	-	-	-	-	-	-	-	-
	RMSE	-	-	-	-	-	-	-	-	-
DeltaDelta[3]	R	0.13	0.24	0.55	0.4	0.37	0.47	0.05	0.31	0.32
	ρ	-	-	-	-	-	-	-	-	-
	RMSE	-	-	-	-	-	-	-	-	-
Default2018[4]	R	0.14	0.95	0.31	0.29	0.34	0.38	0.27	0.33	0.38
	ρ	-	-	-	-	-	-	-	-	-
	RMSE	-	-	-	-	-	-	-	-	-
Dense[4]	R	0.37	0.96	-0.1	0.22	0.14	0.63	0.01	0.25	0.31
	ρ	-	-	-	-	-	-	-	-	-
	RMSE	-	-	-	-	-	-	-	-	-

[a] RMSEs are reported in kcal·mol^{-1}.

Table S3: The performance of the LumiNet model versus baseline model on the FEP2 dataset.[a]

Model		CDK8	c-Met	Eg5	HIF-2α	PFKFB3	SHP-2	SYK	TNKS2	Average
	No.	33	24	28	42	40	26	44	27	33
LumiNet	R	0.32	0.75	0.5	0.39	0.47	0.39	0.35	0.52	0.46
	ρ	0.26	0.73	0.2	0.43	0.50	0.46	0.42	0.41	0.43
	RM	1.74	1.43	2.0	1.12	0.96	1.09	1.10	1.08	1.32
Glide SP	R	0	0	0	0.4	0.47	0.44	0.24	0.37	0.24
	ρ	0.13	0.13	-	0.42	0.51	0.44	0.21	0.32	0.26
	RM	2.49	3.01	1.9	1.51	1.57	1.52	1.27	1.35	1.83
PBCNET	R	0.55	0.7	0.64	0.19	0.43	0.4	0.47	0.36	0.47
	ρ	0.63	0.76	0.58	0.3	0.47	0.56	0.48	0.32	0.51
	RM	1.61	1.88	1.11	1.57	1.4	1.57	1.08	1.71	1.49
FEP+	R	0.62	0.9	0.71	0.61	0.79	0.71	0.5	0.4	0.66
	ρ	0.74	0.88	0.72	0.59	0.79	0.78	0.42	0.41	0.67
	RMSE	2.09	1.43	1.23	1.6	1.78	1.39	1.61	2.2	1.67
MM-GB/SA	R	0.77	0.6	0.14	0.54	0.5	0.6	0	0.26	0.43
	ρ	0.82	0.64	0.1	0.48	0.54	0.5	-0.12	0.22	0.4
	RMSE	7.03	5.96	10.09	11.69	6.99	8.76	15.81	7.9	9.28

[a] RMSEs are reported in kcal·mol^{-1}.

Table S4: The performance of LumiNet on the PDE10A dataset based on four partitioning methods of time splits and random splits.[a]

Method	Random split		Temporal split 2011		Temporal split 2012		Temporal split 2013	
	ρ	RMSE	ρ	RMSE	ρ	RMSE	ρ	RMSE
Mean of train. and val.	–	1.19	–	1.03	–	1.18	–	1.22
Vanilla GOLD.PLP[6]	0.31	–	0.20	–	0.29	–	0.54	
Template GOLD.PLP[6]	0.45	–	0.31	–	0.56	–	0.66	–
RF-PLP[7]	0.56	1.10	0.40	1.05	0.62	0.97	0.61	0.99
AttentiveFP[8]	0.70	0.86	0.40	1.07	0.32	1.74	0.44	1.16
2D3D hybrid	0.72	0.85	0.57	0.81	0.56	1.25	0.61	0.95
ACNN[9]	0.65	1.00	0.37	1.45	0.08	1.60	0.54	1.02
PotentialNet[10]	0.55	1.68	0.34	2.53	0.45	2.22	0.67	1.90
AttentiveFP extended	–	–	0.41	1.12	0.51	1.08	0.60	1.07
2D3D hybrid extended	–	–	0.57	0.82	0.68	0.90	0.66	0.90
LumiNet	0.80	0.76	0.55	0.91	0.74	0.82	0.68	1.14

[a] RMSEs are reported in kcal·mol^{-1}.

Table S5: The performance of LumiNet on the PDE10A dataset based on three partitioning methods of structural binding models.[a]

Method	aminohetaryl_c1_a		c1_hetaryl_alkyl_c2_		aryl_c1_amide_c2_	
	ρ	**RMSE**	**ρ**	**RMSE**	**ρ**	**RMSE**
Mean of train. and val	–	1.18	–	1.14	–	1.24
Vanilla GOLD.PLP	0.20	–	0.38	–	0.25	–
Template GOLD.PLP	0.33	–	0.49	–	**0.59**	–
RF-PLP	0.40	1.48	0.42	1.09	0.52	1.18
AttentiveFP	0.40	1.28	0.11	2.04	0.24	1.25
2D3D hybrid	0.47	1.04	0.31	1.36	0.50	1.05
LumiNet	0.56	-	0.64	-	0.49	

[a] RMSEs are reported in kcal·mol^{-1}.

Table S6: Semi-supervised learning for the best effect of the first strategy optimization on the FEP1 dataset.[a]

No. iter		BACE	CDK2	JNK1	MCL1	p38	PTP1B	Thrombin	TYK2	Average
	No.	**36**	**16**	**21**	**42**	**34**	**23**	**11**	**16**	**25**
LumiNet	R	0.44	0.53	0.45	0.81	0.6	0.79	0.91	0.60	0.65
	ρ	0.42	0.57	0.50	0.80	0.6	0.70	0.89	0.59	0.64
	RMSE	1.7	1.39	0.75	0.83	1.0	1.16	1.05	1.16	1.13
iteration 1	R	0.48	0.66	0.61	0.62	0.65	0.75	0.86	0.72	0.67
	ρ	0.50	0.72	0.64	0.63	0.68	0.75	0.85	0.73	0.69
	RMSE	-	-	-	-	-	-	-	-	1.23
iteration 2	R	0.47	0.67	0.68	0.75	0.65	0.73	0.92	0.69	0.70
	ρ	0.48	0.73	0.73	0.76	0.67	0.71	0.87	0.68	0.70
	RMSE	-	-	-	-	-	-	-	-	1.48

[a] MAEs and RMSEs are reported in kcal·mol^{-1}.

Table S7: Semi-supervised learning for the best effect of the first strategy optimization on the FEP2 dataset.[a]

No. iter		CDK8	c-Met	Eg5	HIF-2α	PFKFB3	SHP-2	SYK	TNKS2	Average
	No.	**33**	**24**	**28**	**42**	**40**	**26**	**44**	**27**	**33**
LumiNet	R	0.32	0.7	0.50	0.39	0.47	0.39	0.35	0.52	0.46
	ρ	0.26	0.7	0.22	0.43	0.50	0.46	0.42	0.41	0.43
	RMS	1.74	1.4	2.05	1.12	0.96	1.09	1.PI	1.08	1.32
iteration 1	R	0.34	0.89	0.60	0.40	0.38	0.50	0.40	0.51	0.50
	ρ	0.27	0.85	0.38	0.48	0.44	0.55	0.41	0.47	0.48
	RMSE	-	-	-	-	-	-	-	-	1.23
iteration 2	R	0.44	0.81	0.70	0.41	0.36	0.57	0.45	0.49	0.53
	ρ	0.44	0.77	0.51	0.50	0.45	0.59	0.43	0.40	0.51
	RMSE	-	-	-	-	-	-	-	-	1.21

[a] RMSEs are reported in kcal·mol^{-1}.

Table S8: Semi-supervised learning for the average effect of the second strategy optimization on the FEP1 dataset.[a]

Repeat	No. 2			No. 6		
	R	**ρ**	**RMSE**	**R**	**ρ**	**RMSE**
1	0.67	0.64	0.89	0.75	0.75	0.81
2	0.69	0.71	0.95	0.71	0.72	0.81
3	0.67	0.66	1.05	0.74	0.75	0.81
4	0.66	0.65	1.00	0.72	0.73	0.87
5	0.70	0.69	0.93	0.74	0.71	0.81
Average	0.68	0.67	0.96	0.73	0.73	0.82

[a] RMSEs are reported in kcal·mol^{-1}.

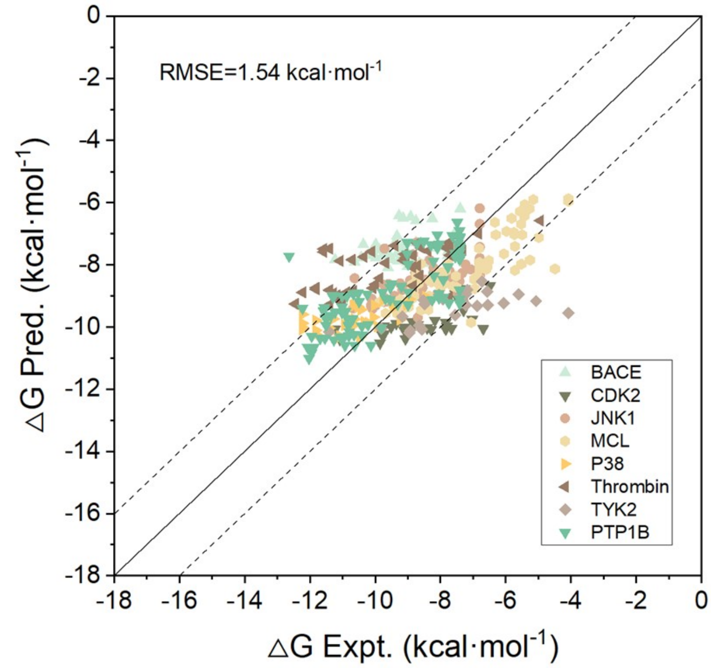

Figure S1: The performance of LumiNet on the extended FEP1 dataset[5], which includes 8 targets and 407 ligands.

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