

Table S1: Results of competing methods under pair prediction in the subsampled test sets .

Dataset	Combination	Pairs	
		AUPR	
NR	[SPEC-k4]-[AERS-freq] †	0.7616	(±0.0205)
	[SPEC-k4]-[GIP] *	0.8389	(±0.0176)
	BLM-KA	0.5069	(±0.0198)
	BLM-MEAN	0.5070	(±0.0251)
	KBMF2MKL	0.6344	(±0.0163)
	KRONRLS-KA	0.8124	(±0.0281)
	KRONRLS-MEAN	0.8088	(±0.0275)
	KRONRLS-MKL	0.8197	(±0.0290)
	LAPRLS-KA	0.6993	(±0.0421)
	LAPRLS-MEAN	0.6891	(±0.0504)
	NETLAPRLS-KA	0.7075	(±0.0402)
	NETLAPRLS-MEAN	0.7033	(±0.0453)
	PKM-KA	0.7012	(±0.0416)
	PKM-MAX	0.5551	(±0.0263)
	PKM-MEAN	0.6982	(±0.0468)
SITAR	0.7990	(±0.0442)	
WANG-MKL	0.7390	(±0.0317)	
GPCR	[SPEC-k4]-[MINMAX] †	0.8703	(±0.0084)
	[SW]-[GIP] *	0.9249	(±0.0028)
	BLM-KA	0.6416	(±0.0195)
	BLM-MEAN	0.6234	(±0.0125)
	KBMF2MKL	0.8637	(±0.0098)
	KRONRLS-KA	0.9417	(±0.0039)
	KRONRLS-MEAN	0.9398	(±0.0046)
	KRONRLS-MKL	0.9440	(±0.0040)
	LAPRLS-KA	0.8204	(±0.0086)
	LAPRLS-MEAN	0.8206	(±0.0083)
	NETLAPRLS-KA	0.8593	(±0.0069)
	NETLAPRLS-MEAN	0.8604	(±0.0069)
	PKM-KA	0.8679	(±0.0083)
	PKM-MAX	0.7602	(±0.0167)
	PKM-MEAN	0.8631	(±0.0073)
SITAR	0.9470	(±0.0065)	
WANG-MKL	0.9122	(±0.0067)	
IC	[PPI]-[GIP] †	0.9372	(±0.0049)
	[SW]-[GIP] *	0.9815	(±0.0006)
	BLM-KA	0.7154	(±0.0122)
	BLM-MEAN	0.7049	(±0.0096)
	KBMF2MKL	0.9558	(±0.0020)
	KRONRLS-KA	0.9790	(±0.0011)
	KRONRLS-MEAN	0.9799	(±0.0008)
	KRONRLS-MKL	0.9810	(±0.0008)
	LAPRLS-KA	0.8721	(±0.0090)
	LAPRLS-MEAN	0.8756	(±0.0086)
	NETLAPRLS-KA	0.9218	(±0.0035)
	NETLAPRLS-MEAN	0.9252	(±0.0032)
	PKM-KA	0.9459	(±0.0057)
	PKM-MAX	0.8134	(±0.0080)
	PKM-MEAN	0.9501	(±0.0051)
SITAR	0.9779	(±0.0021)	
WANG-MKL	0.9630	(±0.0027)	
E	[GO]-[GIP] †	0.9632	(±0.0007)
	[SW]-[GIP] *	0.9777	(±0.0012)
	BLM-KA	0.7481	(±0.0066)
	BLM-MEAN	0.7431	(±0.0077)
	KBMF2MKL	0.9511	(±0.0019)
	KRONRLS-KA	0.9767	(±0.0007)
	KRONRLS-MEAN	0.9777	(±0.0005)
	KRONRLS-MKL	0.9804	(±0.0007)
	LAPRLS-KA	0.9106	(±0.0032)
	LAPRLS-MEAN	0.9068	(±0.0034)
	NETLAPRLS-KA	0.9187	(±0.0035)
	NETLAPRLS-MEAN	0.9158	(±0.0037)
	PKM-KA	0.9450	(±0.0040)
	PKM-MAX	0.8648	(±0.0027)
	PKM-MEAN	0.9412	(±0.0040)
SITAR	0.9885	(±0.0012)	
WANG-MKL	0.9749	(±0.0014)	

†best on training *best on testing

Table S2: AUPR results of predicted scores against new interactions found on current release of KEGG, Matador, Drugbank and ChEMBL databases.

Dataset	Combination	KEGG	MATADOR	DRUGBANK	ChEMBL
NR	SINGLE [†]	0.4122	0.0149	0.0442	0.2537
	SINGLE*	0.2533	0.0227	0.0389	0.2245
	BLM-KA	0.0069	0.0063	0.0108	0.1249
	BLM-MEAN	0.0048	0.0028	0.0079	0.1267
	KBMF2MKL	0.0394	0.0075	0.0128	0.2208
	KRONRLS-KA	0.0599	0.0095	0.0499	0.3246
	KRONRLS-MEAN	0.0410	0.0097	0.0469	0.3238
	KRONRLS-MKL	0.1235	0.0091	0.0472	0.3139
	LAPRLS-KA	0.0133	0.0104	0.0245	0.2949
	LAPRLS-MEAN	0.0133	0.0153	0.0297	0.3135
	NETLAPRLS-KA	0.0182	0.0130	0.0290	0.3071
	NETLAPRLS-MEAN	0.0176	0.0126	0.0277	0.3041
	NRWRH-KA	0.7600	0.0105	0.0351	0.1739
	NRWRH-MEAN	0.7600	0.0109	0.0365	0.1762
	PKM-MEAN	0.0094	0.0056	0.0358	0.2875
	PKM-KA	0.0132	0.0113	0.0183	0.2748
	PKM-MAX	0.0064	0.0053	0.0120	0.1728
WANG-MKL	0.3403	0.0056	0.0430	0.3429	
SITAR	0.5204	0.0068	0.0618	0.2513	
GPCR	SINGLE [†]	0.0912	0.0179	0.1481	0.2121
	SINGLE*	0.0912	0.0179	0.1481	0.2121
	BLM-KA	0.0118	0.0055	0.0423	0.1551
	BLM-MEAN	0.0116	0.0066	0.0447	0.1499
	KBMF2MKL	0.0586	0.0084	0.0831	0.1690
	KRONRLS-KA	0.0867	0.0230	0.1769	0.2489
	KRONRLS-MEAN	0.0746	0.0249	0.1880	0.2544
	KRONRLS-MKL	0.1085	0.0231	0.2191	0.2256
	LAPRLS-KA	0.0164	0.0129	0.0641	0.2508
	LAPRLS-MEAN	0.0182	0.0116	0.0656	0.2526
	NETLAPRLS-KA	0.0260	0.0199	0.0975	0.2606
	NETLAPRLS-MEAN	0.0269	0.0205	0.1004	0.2606
	NRWRH-KA	0.1555	0.0110	0.1871	0.2000
	NRWRH-MEAN	0.1527	0.0109	0.1861	0.1947
	PKM-MEAN	0.0214	0.0377	0.0639	0.2446
	PKM-KA	0.0252	0.0085	0.0792	0.2361
	PKM-MAX	0.0159	0.0134	0.0360	0.1682
WANG-MKL	0.0691	0.0249	0.1651	0.2469	
SITAR	0.1536	0.0097	0.2289	0.1997	
IC	SINGLE [†]	0.0905	0.0234	0.0557	0.0409
	SINGLE*	0.0905	0.0234	0.0557	0.0409
	BLM-KA	0.0125	0.0131	0.0184	0.0219
	BLM-MEAN	0.0126	0.0127	0.0174	0.0171
	KBMF2MKL	0.0419	0.0255	0.0457	0.0421
	KRONRLS-KA	0.0714	0.0348	0.0472	0.0399
	KRONRLS-MEAN	0.0618	0.0275	0.0369	0.0363
	KRONRLS-MKL	0.0723	0.0261	0.0462	0.0403
	LAPRLS-KA	0.0105	0.0258	0.0151	0.0315
	LAPRLS-MEAN	0.0106	0.0256	0.0152	0.0316
	NETLAPRLS-KA	0.0221	0.0261	0.0217	0.0301
	NETLAPRLS-MEAN	0.0231	0.0257	0.0223	0.0300
	NRWRH-KA	0.1585	0.0255	0.0987	0.0272
	NRWRH-MEAN	0.1646	0.0254	0.1063	0.0271
	PKM-MEAN	0.0285	0.0238	0.0275	0.0455
	PKM-KA	0.0228	0.0218	0.0239	0.0631
	PKM-MAX	0.0080	0.0095	0.0134	0.0140
WANG-MKL	0.0941	0.0438	0.0441	0.0595	
SITAR	0.0983	0.0264	0.0599	0.0319	
E	SINGLE [†]	0.0058	0.0621	0.0513	0.0422
	SINGLE*	0.0058	0.0621	0.0513	0.0422
	BLM-KA	0.0047	0.0451	0.0116	0.0272
	BLM-MEAN	0.0049	0.0456	0.0118	0.0273
	KBMF2MKL	0.0034	0.0570	0.0311	0.0556
	KRONRLS-KA	0.0084	0.0666	0.0325	0.0385
	KRONRLS-MEAN	0.0063	0.0652	0.0376	0.0432
	KRONRLS-MKL	0.0106	0.0638	0.0445	0.0335
	LAPRLS-KA	0.0008	0.0041	0.0183	0.0599
	LAPRLS-MEAN	0.0007	0.0038	0.0179	0.0581
	NETLAPRLS-KA	0.0070	0.0354	0.0247	0.0641
	NETLAPRLS-MEAN	0.0070	0.0351	0.0241	0.0620
	NRWRH-KA	0.0125	0.0121	0.0268	0.0402
	NRWRH-MEAN	0.0098	0.0123	0.0247	0.0419
	PKM-MEAN	0.0001	0.0013	0.0024	0.0155
	PKM-KA	0.0001	0.0012	0.0028	0.0156
	PKM-MAX	0.0001	0.0009	0.0028	0.0180
WANG-MKL	0.0001	0.0011	0.0025	0.0137	
SITAR	0.0006	0.0045	0.0322	0.0403	

[†]best on training *best on testing

Table S3: Average memory (MB) usage during training and testing of competing methods.

Dataset	Combination	Pairs	Targets	Drugs
NR	BLM-KA	383.00	359.80	356.80
	BLM-MEAN	380.00	363.20	362.00
	KBMF2MKL	358.40	362.00	372.20
	KRONRLS-KA	367.00	355.60	356.60
	KRONRLS-MEAN	356.40	360.00	363.80
	KRONRLS-MKL	388.20	383.20	385.60
	LAPRLS-KA	367.60	367.00	360.80
	LAPRLS-MEAN	358.60	364.00	359.60
	NETLAPRLS-KA	384.67	365.80	359.80
	NETLAPRLS-MEAN	360.20	359.80	360.60
	NRWRH-KA	-	358.60	358.60
	NRWRH-MEAN	-	357.00	361.60
	PKM-KA	359.40	358.00	355.60
	PKM-MAX	358.20	355.00	360.80
	PKM-MEAN	358.80	358.60	358.60
SITAR	370.40	373.20	369.20	
WANG-MKL	381.20	384.80	383.40	
GPCR	BLM-KA	584.80	488.00	542.40
	BLM-MEAN	581.20	514.20	462.40
	KBMF2MKL	372.80	497.00	507.20
	KRONRLS-KA	370.40	563.20	570.80
	KRONRLS-MEAN	365.60	484.40	417.60
	KRONRLS-MKL	397.60	512.40	577.00
	LAPRLS-KA	415.40	403.20	512.60
	LAPRLS-MEAN	499.60	440.00	454.40
	NETLAPRLS-KA	370.60	382.40	381.20
	NETLAPRLS-MEAN	368.60	386.20	376.20
	NRWRH-KA	-	438.80	473.20
	NRWRH-MEAN	-	465.60	462.40
	PKM-KA	541.80	496.80	545.20
	PKM-MAX	512.60	635.80	600.40
	PKM-MEAN	525.60	617.80	522.00
SITAR	450.40	428.80	490.60	
WANG-MKL	550.60	576.60	525.40	
IC	BLM-KA	946.00	575.80	552.00
	BLM-MEAN	879.40	502.60	612.60
	KBMF2MKL	517.80	521.40	522.40
	KRONRLS-KA	476.20	469.80	469.00
	KRONRLS-MEAN	457.60	459.00	580.00
	KRONRLS-MKL	565.40	547.40	654.00
	LAPRLS-KA	497.00	417.00	544.80
	LAPRLS-MEAN	484.20	491.20	467.20
	NETLAPRLS-KA	384.40	382.40	381.20
	NETLAPRLS-MEAN	380.00	386.20	376.20
	NRWRH-KA	-	376.00	487.80
	NRWRH-MEAN	-	375.80	504.60
	PKM-KA	813.40	677.60	723.80
	PKM-MAX	788.80	680.20	855.40
	PKM-MEAN	805.40	695.60	861.00
SITAR	540.40	384.80	567.80	
WANG-MKL	809.20	863.20	855.60	
E	BLM-KA	3411.00	921.40	1021.20
	BLM-MEAN	3604.20	915.40	996.40
	KBMF2MKL	861.80	716.80	834.00
	KRONRLS-KA	734.80	675.60	784.80
	KRONRLS-MEAN	661.40	818.20	698.20
	KRONRLS-MKL	844.40	816.80	717.40
	LAPRLS-KA	641.20	705.60	709.40
	LAPRLS-MEAN	668.20	701.20	668.60
	NETLAPRLS-KA	562.60	567.80	576.80
	NETLAPRLS-MEAN	542.60	549.40	575.60
	NRWRH-KA	-	645.60	642.80
	NRWRH-MEAN	-	691.60	728.20
	PKM-KA	4899.20	4985.20	5220.20
	PKM-MAX	5048.20	4997.00	5195.40
	PKM-MEAN	4976.80	4891.60	5194.20
SITAR	789.80	598.00	741.40	
WANG-MKL	4990.40	5090.60	5121.60	

Table S4: Average computing time in minutes for training and testing the model in all four datasets (ranking of each method is given in parenthesis).

METHOD	PAIRS	TARGETS	DRUGS
BLM-KA	340.32 (15)	54.25 (13)	24.68 (10)
BLM-MEAN	299.60 (14)	39.95 (12)	16.24 (5)
KBMF-MKL	105.17 (11)	110.34 (15)	114.30 (15)
KRONRLS-KA	21.17 (7)	21.53 (6)	21.39 (8)
KRONRLS-MEAN	20.39 (6)	21.51 (5)	21.34 (7)
KRONRLS-MKL	74.00 (10)	92.82 (14)	93.25 (14)
LAPRLS-KA	27.11 (8)	33.82 (9)	33.80 (13)
LAPRLS-MEAN	30.28 (9)	33.40 (8)	33.37 (12)
NETLAPRLS-KA	135.20 (13)	134.64 (17)	134.98 (17)
NETLAPRLS-MEAN	132.16 (12)	132.65 (16)	132.75 (16)
NRWRH-KA	-	39.90 (11)	30.09 (11)
NRWRH-MEAN	-	38.36 (10)	23.03 (9)
PKM-KA	0.63 (3)	0.95 (4)	0.64 (3)
PKM-MAX	0.55 (2)	0.93 (3)	0.61 (2)
PKM-MEAN	0.54 (1)	0.84 (2)	0.54 (1)
SITAR	15.54 (5)	22.59 (7)	16.30 (6)
WANG-MKL	0.82 (4)	0.80 (1)	0.68 (4)