SUPPLEMENTARY MATERIAL

Fusing Docking Scoring Functions Improves the Virtual Screening Performance for Discovering Parkinson's Disease Dual Target Ligands

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SI_File_1: Dataset of known dual ligands and DUD-E decoys.

SI_File_2: Dataset of known dual ligands and desirability-based decoys.

SI_File_3: File containing the tables with the VS performance of each single scoring function as well as the performance of the assayed FS at different selection sizes of the ranked list.

Table TS1. VS performance of each individual scoring function in each target (DUD-E decoys).

Scoring Function	EF %[a]			BEDROC Alpha[b]			ROC[c]
	1	**5**	**8**	**160.9**	**32**	**20**	
A2A							
Grid Score	0.00	0.00	2.49	0.00	0.04	0.09	0.73
PB/SA Score	0.00	2.49	1.87	0.00	0.08	0.12	0.72
GB/SA Score	5.67	3.73	3.73	0.20	0.18	0.21	0.73
SA_Descriptor Score	0.00	1.24	0.62	0.00	0.03	0.05	0.50
Continuous Score	0.00	1.24	1.87	0.00	0.05	0.09	0.71
Amber Score, everything rigid	0.00	0.00	0.00	0.00	0.00	0.02	0.54
Amber Score, flexible ligand	0.00	0.00	1.24	0.00	0.02	0.05	0.56
MAO-B							
Grid Score	11.33	6.22	4.98	0.15	0.28	0.35	0.85
PB/SA Score	5.67	6.22	4.98	0.09	0.22	0.31	0.85
GB/SA Score	5.67	3.73	4.98	0.07	0.15	0.22	0.83
SA_Descriptor Score	0.00	1.24	1.24	0.00	0.04	0.08	0.73
Continuous Score	5.67	7.46	4.98	0.08	0.28	0.37	0.86
Amber Score, everything rigid	0.00	1.24	3.73	0.00	0.07	0.13	0.80
Amber Score, flexible ligand	0.00	0.00	3.11	0.00	0.04	0.10	0.79

[a]Enrichment factor of the model at selection sizes of 1%, 5% and 8% of screened data. [b]BEDROC for values of the α parameter of 160.9, 32.2 and 20. [c]Area under the ROC curve.

Table TS2. VS performance of each individual scoring function in each target (desirability-based decoys).

Scoring Function	EF %[a]			BEDROC Alpha[b]			ROC[c]
	1	5	8	160.9	32	20	
A2A							
Grid Score	0.00	2.50	3.12	0.00	0.07	0.15	0.83
PB/SA Score	6.23	1.25	3.75	0.02	0.08	0.14	0.77
GB/SA Score	6.23	5.00	4.37	0.07	0.18	0.24	0.83
SA_Descriptor Score	0.00	0.00	0.62	0.00	0.01	0.02	0.53
Continuous Score	0.00	2.50	3.12	0.00	0.07	0.15	0.83
Amber Score, everything rigid	0.00	1.25	2.50	0.00	0.03	0.07	0.66
Amber Score, flexible ligand	0.00	2.50	1.87	0.00	0.05	0.09	0.68
MAO-B							
Grid Score	6.23	3.75	4.37	0.02	0.13	0.20	0.83
PB/SA Score	0.00	3.75	3.12	0.01	0.11	0.18	0.82
GB/SA Score	6.23	2.50	5.00	0.02	0.10	0.17	0.83
SA_Descriptor Score	0.00	2.50	1.25	0.01	0.06	0.09	0.71
Continuous Score	0.00	5.00	5.00	0.01	0.16	0.24	0.84
Amber Score, everything rigid	0.00	1.25	1.87	0.00	0.04	0.09	0.78
Amber Score, flexible ligand	0.00	0.00	3.12	0.00	0.03	0.09	0.80

[a]Enrichment factor of the model at selection sizes of 1%, 5% and 8% of screened data. [b]BEDROC for values of the α parameter of 160.9, 32.2 and 20. [c]Area under the ROC curve.

Table TS3. Virtual screening performance of the assayed FS for the DUD-E decoys.

FS Method[a]	EF[b]	BEDROC[c]	AUAC[d]	Fused Scoring Functions[e]
Selection Size 1% of the ranked list				
FS1.1	11.33	0.23	0.83	$A_{2A}AR$: 3 7 MAO-B:1 3 4
FS1.2	11.33	0.20	0.90	$A_{2A}AR$: 3 7 MAO-B:1 3 4
FS1.3	11.33	0.10	0.81	$A_{2A}AR$: 3 7 MAO-B: 1 2 3 4 5
FS1.4	11.33	0.12	0.87	$A_{2A}AR$: 3 7 MAO-B: 1 2 3 4 5
FS1.5	5.67	0.06	0.85	$A_{2A}AR$: 3 MAO-B:1 3 4
FS1.6	0.00	0.02	0.89	$A_{2A}AR$: 3 MAO-B:1 3 4
FS1.7	0.00	0.00	0.83	$A_{2A}AR$: 3 MAO-B: 1 3 4 5
FS1.8	0.00	0.00	0.85	$A_{2A}AR$: 3 MAO-B: 1 3 4 5
FS2.1	22.67	0.22	0.87	$A_{2A}AR$: 2, 3, 7 MAO-B: 1, 4, 5
FS2.2	17.00	0.19	0.83	$A_{2A}AR$: 3, 7 MAO-B: 5
FS2.3	5.67	0.19	0.75	$A_{2A}AR$: 4 MAO-B: 3
FS2.4	5.67	0.09	0.82	$A_{2A}AR$: 1, 2, 3 MAO-B: 4
Selection Size 5% of the ranked list				
FS1.1	8.71	0.34	0.83	$A_{2A}AR$: 3 7 MAO-B: 1 2 3 4 5
FS1.2	8.71	0.34	0.89	$A_{2A}AR$: 3 7 MAO-B: 1 2 3 4 5
FS1.3	6.22	0.27	0.85	MAO-B: 1, 5 $A_{2A}AR$: 2, 3, 7
FS1.4	11.20	0.33	0.89	MAO-B: 1, 5 $A_{2A}AR$: 2, 3, 7
FS1.5	4.98	0.19	0.85	$A_{2A}AR$: 3 MAO-B: 1 3 4
FS1.6	6.22	0.19	0.89	$A_{2A}AR$: 3 MAO-B: 1 3 4
FS1.7	2.49	0.10	0.84	MAO-B: 3, 4 $A_{2A}AR$: 3
FS1.8	2.49	0.09	0.85	MAO-B: 3, 4 $A_{2A}AR$: 3
FS2.1	13.68	0.37	0.90	MAO-B: 1, 2, 4, 5 $A_{2A}AR$: 2, 3
FS2.2	12.44	0.31	0.87	MAO-B: 1, 5 $A_{2A}AR$: 3, 6
FS2.3	7.46	0.33	0.88	MAO-B: 1, 3, 4
FS2.4	4.98	0.15	0.83	MAO-B: 3 4
Selection Size 8% of the ranked list				
FS1.1	4.35	0.36	0.87	MAO-B: 1 3 4 5 $A_{2A}AR$: 3
FS1.2	6.84	0.46	0.92	MAO-B: 1 3 4 5 $A_{2A}AR$: 3
FS1.3	4.98	0.33	0.87	MAO-B: 3 4 5 $A_{2A}AR$: 3
FS1.4	6.22	0.37	0.91	MAO-B: 3 4 5 $A_{2A}AR$: 3
FS1.5	3.73	0.21	0.79	MAO-B: 1 2 3 4 5 $A_{2A}AR$: 3, 7
FS1.6	3.73	0.22	0.85	MAO-B: 1 2 3 4 5 $A_{2A}AR$: 3, 7
FS1.7	3.73	0.17	0.84	MAO-B: 1 3 4 $A_{2A}AR$: 3
FS1.8	3.73	0.16	0.86	MAO-B: 1 3 4 $A_{2A}AR$: 3
FS2.1	8.09	0.51	0.91	MAO-B: 1, 2, 3, 4, 5 $A_{2A}AR$: 1, 2, 3
FS2.2	8.71	0.38	0.93	MAO-B: 1, 3, 5 $A_{2A}AR$: 1, 2, 3
FS2.3	7.46	0.37	0.87	MAO-B: 1, 2, 3, 4, 5
FS2.4	4.98	0.24	0.85	MAO-B:1 3 4

[a]Employed fusion method. See Tables **2** and **3** for the detailed setup of each method. [b]Enrichment Factor for the best scoring scheme. [c]BEDROC for the best scoring scheme. Alpha value is set to 160.9. [d]Area Under the Accumulative Curve for the best scoring scheme. [e]Scoring functions fused in the best scoring scheme. The following numbering is employed for scoring functions: 1) Grid Score; 2) PB/SA Score; 3) GB/SA Score; 4) SA_Descriptor Score; 5) Continuous Score; 6) Amber Score, everything rigid and 7) Amber Score, flexible ligand.

Table TS4. Virtual screening performance of the assayed FS for the DUD-E decoys.

FS Method[a]	EF[b]	BEDROC[c]	AUAC[d]	Fused Scoring Functions[e]
Selection Size 1% of the ranked list				
FS1.1	0.00	0.02	0.88	$A_{2A}AR$: 3 7 MAO-B: 1 3
FS1.2	12.47	0.05	0.90	$A_{2A}AR$: 3 7 MAO-B: 1 3
FS1.3	6.23	0.03	0.91	$A_{2A}AR$: 2 3 MAO-B: 1 3
FS1.4	6.23	0.06	0.90	$A_{2A}AR$: 2 3 MAO-B: 1 3
FS1.5	0.00	0.00	0.76	$A_{2A}AR$: 3 4 6 7 MAO-B: 1 3
FS1.6	0.00	0.00	0.77	$A_{2A}AR$: 3 4 6 7 MAO-B: 1 3
FS1.7	0.00	0.00	0.82	$A_{2A}AR$: 3 MAO-B: 1 3
FS1.8	0.00	0.00	0.81	$A_{2A}AR$: 3 MAO-B: 1 3
FS2.1	31.17	0.11	0.87	$A_{2A}AR$: 3, 5, 6 ,7 MAO-B: 3, 4
FS2.2	18.70	0.10	0.86	$A_{2A}AR$: 2, 3, 7 MAO-B: 3
FS2.3	6.23	0.07	0.84	$A_{2A}AR$: 3 MAO-B: 4
FS2.4	6.23	0.05	0.76	$A_{2A}AR$: 3 MAO-B: 4
Selection Size 5% of the ranked list				
FS1.1	10.00	0.28	0.92	MAO-B: 1 3 4 5 $A_{2A}AR$: 1, 3, 7
FS1.2	11.25	0.28	0.92	MAO-B: 1 3 4 5 $A_{2A}AR$: 1, 3, 7
FS1.3	3.75	0.17	0.88	MAO-B: 1 4 $A_{2A}AR$: 2, 3, 7
FS1.4	5.00	0.19	0.88	MAO-B: 1 4 $A_{2A}AR$: 2, 3, 7
FS1.5	5.00	0.15	0.86	MAO-B: 3 4 $A_{2A}AR$: 3, 7
FS1.6	5.00	0.11	0.85	MAO-B: 3 4 $A_{2A}AR$: 3, 7
FS1.7	3.75	0.10	0.83	MAO-B: 3 4 $A_{2A}AR$: 3, 7
FS1.8	1.25	0.07	0.81	MAO-B: 3 4 $A_{2A}AR$: 3, 7
FS2.1	15.00	0.32	0.92	MAO-B: 4, 5, 7 $A_{2A}AR$: 3, 5
FS2.2	10.00	0.26	0.93	MAOB: 3, 5 A2A: 3, 5
FS2.3	6.25	0.18	0.90	MAO-B: 3, 4 $A_{2A}AR$: 3
FS2.4	3.75	0.09	0.85	MAOB: 3, 4
Selection Size 8% of the ranked list				
FS1.1	8.75	0.48	0.93	MAO-B: 1 3 4 5 $A_{2A}AR$: 3, 5
FS1.2	8.12	0.41	0.93	MAO-B: 1 3 4 5 $A_{2A}AR$: 3, 5
FS1.3	8.75	0.41	0.93	MAO-B: 1 3 4 5 7 $A_{2A}AR$: 3, 5
FS1.4	7.50	0.34	0.92	MAO-B: 1 3 4 5 7 $A_{2A}AR$: 3, 5
FS1.5	3.12	0.12	0.83	MAO-B: 1 3 4 5 $A_{2A}AR$: 3, 7
FS1.6	2.50	0.12	0.84	MAO-B: 1 3 4 5 $A_{2A}AR$: 3, 7
FS1.7	2.50	0.16	0.83	MAO-B: 3 4 $A_{2A}AR$: 3, 7
FS1.8	1.87	0.12	0.81	MAO-B: 3 4 $A_{2A}AR$: 3, 7
FS2.1	8.75	0.48	0.93	MAO-B: 3, 7 $A_{2A}AR$: 1, 3, 5
FS2.2	8.75	0.32	0.92	MAOB: 1, 2, 3, 4, 5 A2A: 1, 3, 5, 6
FS2.3	6.87	0.23	0.89	MAO-B: 3, 4, 7 $A_{2A}AR$: 3
FS2.4	3.75	0.16	0.85	MAOB: 3, 4

[a]Employed fusion method. See Tables 2 and 3 for the detailed setup of each method. [b]Enrichment Factor for the best scoring scheme. [c]BEDROC for the best scoring scheme. Alpha value is set to 160.9. [d]Area Under the Accumulative Curve for the best scoring scheme. [e]Scoring functions fused in the best scoring scheme. The following numbering is employed for scoring functions: 1) Grid Score; 2) PB/SA Score; 3) GB/SA Score; 4) SA_Descriptor Score; 5) Continuous Score; 6) Amber Score, everything rigid and 7) Amber Score, flexible ligand.