

## **Supporting Information**

### **Comparison of Several Molecular Docking Programs: Pose Prediction and Virtual Screening Accuracy**

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**Table 1.** Analysis of the mean RMSDs for the top scoring poses from cognate ligand docking. The upper triangles contain the mean differences and the lower triangles contain the correlation corrected 95% confidences. Examples of modified parameter settings are shaded.

	DOCK	FlexX	GLIDE SP	GLIDE XP	ICM	PhDOCK	Surflex	GLIDE HTVS	Surflex Ringflex
<i>Input Ligand Conformation from X-ray Complex</i>									
<b>DOCK</b>		0.94	1.26	1.49	0.88	0.055	0.64	0.25	0.58
<b>FlexX</b>	0.91		1.97	2.20	1.65	0.80	1.43	0.80	1.26
<b>GLIDE SP</b>	0.79	0.91		0.22	0.37	1.21	0.61	1.12	0.71
<b>GLIDE XP</b>	0.77	0.89	0.26		0.59	1.43	0.83	1.19	0.93
<b>ICM</b>	0.79	0.92	0.58	0.59		0.83	0.24	0.64	0.34
<b>PhDOCK</b>	0.80	0.95	0.83	0.78	0.83		0.58	0.14	0.52
<b>Surflex</b>	0.69	0.79	0.54	0.50	0.53	0.76		0.49	0.097
<b>GLIDE HTVS</b>	0.80	0.98	0.54	0.58	0.73	0.85	0.71		0.24
<b>Surflex Ringflex</b>	0.73	0.93	0.60	0.57	0.70	0.88	0.55	0.76	
<i>Input Ligand Conformation from CORINA</i>									
<b>DOCK</b>		1.16	1.07	1.16	1.41	1.29	0.33	0.59	1.01
<b>FlexX</b>	1.24		2.16	2.29	2.43	0.20	1.38	1.51	2.04
<b>GLIDE SP</b>	0.79	1.23		0.11	0.24	2.36	0.81	0.76	0.14
<b>GLIDE XP</b>	0.77	1.11	0.50		0.14	2.62	0.96	0.79	0.26
<b>ICM</b>	0.77	1.17	0.48	0.50		2.70	1.07	0.74	0.39
<b>PhDOCK</b>	1.11	5.56	0.84	0.90	0.97		1.62	1.22	2.30
<b>Surflex</b>	0.79	1.17	0.59	0.63	0.61	0.88		0.14	0.68
<b>GLIDE HTVS</b>	0.78	1.10	0.57	0.47	0.56	0.77	0.71		0.51
<b>Surflex Ringflex</b>	0.76	1.19	0.44	0.64	0.53	0.91	0.47	0.70	

**Table 2.** Analysis of the mean RMSDs for the top scoring poses from cognate ligand docking for the kinase and nuclear receptor subsets using the CORINA ligand conformations. The upper triangles contain the mean differences and the lower triangles contain the correlation corrected 95% confidences. Examples of modified parameter settings are shaded.

	DOCK	FlexX	GLIDE SP	GLIDE XP	ICM	PhDOCK	Surflex	GLIDE HTVS	Surflex Ringflex
<i>Kinase Subset</i>									
<b>DOCK</b>		0.47	1.14	1.63	1.16	0.86	1.22	1.00	0.56
<b>FlexX</b>	3.66		1.61	2.11	1.64	0.38	1.70	1.47	1.04
<b>GLIDE SP</b>	2.60	2.90		0.49	0.02	2.00	0.08	0.14	0.58
<b>GLIDE XP</b>	2.37	2.60	0.65		0.47	2.49	0.41	0.63	1.07
<b>ICM</b>	2.36	2.93	1.55	2.48		2.02	0.06	0.16	0.60
<b>PhDOCK</b>	2.65	2.05	1.70	1.21	1.98		2.08	1.86	1.42
<b>Surflex</b>	2.36	2.53	1.10	0.72	1.72	1.36		0.22	0.66
<b>GLIDE HTVS</b>	1.32	2.91	1.95	1.75	1.41	1.89	1.70		0.43
<b>Surflex Ringflex</b>	2.58	2.53	0.99	0.96	0.98	1.68	1.11	1.79	
<i>Nuclear Receptor Subset</i>									
<b>DOCK</b>		3.69	1.90	1.16	1.77	2.01	0.09	0.33	1.60
<b>FlexX</b>	3.75		5.37	4.67	5.01	1.67	3.45	3.50	4.87
<b>GLIDE SP</b>	2.36	4.31		0.68	0.02	3.54	1.66	1.77	0.16
<b>GLIDE XP</b>	1.62	4.08	0.89		0.67	2.80	0.98	1.08	0.52
<b>ICM</b>	2.17	4.01	0.25	1.02		3.79	1.56	1.67	0.15
<b>PhDOCK</b>	3.56	4.44	3.38	3.24	3.23		2.11	0.40	3.61
<b>Surflex</b>	2.06	4.26	1.47	1.32	1.42	3.68		0.13	0.41
<b>GLIDE HTVS</b>	1.41	3.87	1.47	1.14	1.43	2.17	1.93		1.69
<b>Surflex Ringflex</b>	2.26	3.96	0.23	0.94	0.38	2.98	1.40	1.51	

**Table 3.** DUD composition and docking success rates. Examples of modified parameter settings are shaded.

Target	DUD dataset		DOCK		FlexX		GLIDE HTVS		ICM		PhDOCK		Surflex		GLIDE SP		Surflex Ringflex	
	Actives	Decoys	Actives	Decoys	Actives	Decoys	Actives	Decoys	Actives	Decoys	Actives	Decoys	Actives	Decoys	Actives	Decoys	Actives	Decoys
Nuclear Hormone Receptors																		
AR	74	2628	72	2499	71	2577	45	992	71	2628	67	1861	74	2628	49	1625	74	2628
ER <sub>agonist</sub>	67	2355	67	2293	64	2301	58	1665	67	2355	64	1500	67	2355	63	2240	67	2355
ER <sub>antagonist</sub>	39	1395	39	1341	39	1376	29	1086	25	1276	39	1040	39	1395	37	1358	39	1395
GR	78	2797	77	2710	67	2753	22	445	77	2797	78	2114	78	2797	29	1309	78	2797
MR	15	535	15	534	14	519	4	92	14	535	12	343	15	535	7	207	15	535
PPAR <sub>g</sub>	81	2906	78	2630	81	2853	37	1106	6	61	80	1833	81	2906	77	2404	81	2906
PR	27	967	27	958	24	958	15	618	27	967	26	615	27	967	22	807	27	967
RXR <sub>a</sub>	20	708	19	684	20	688	14	99	20	690	18	397	20	708	17	328	20	708
Kinases																		
CDK2	50	1779	50	1651	50	1770	46	1649	44	1777	50	1244	50	1779	50	1751	50	1779
EGFr	444	14894	444	14545	444	14825	444	14334	410	14892	444	10866	444	14894	444	14733	444	14894
FGFr1	118	4205	116	3802	118	4185	114	3986	92	949	118	3051	118	4205	118	4125	118	4205
HSP90	24	860	24	820	24	852	19	812	23	859	24	548	24	860	24	847	24	860
P38 MAP	256	8387	254	8256	256	8290	225	6991	244	8387	92	1095	256	8387	254	8189	256	8387
PDGFr <sub>b</sub>	157	5614	150	5368	157	5583	77	3672	135	5614	157	4610	157	5614	104	4965	157	5614
SRC	155	5793	152	5531	155	5773	152	5559	129	5750	155	4140	155	5792	155	5702	155	5793
TK	22	784	22	783	22	764	19	644	20	749	21	459	22	784	22	749	22	784
VEGFr2	74	2641	69	2456	71	2634	71	2492	63	2641	73	1919	74	2641	73	2564	74	2640
Serine Proteases																		
FXa	142	5095	137	4594	142	5075	141	4937	29	778	49	3127	142	5095	142	5025	142	5095
Thrombin	65	2292	63	2014	65	2281	63	2128	18	816	65	1372	65	2292	65	2251	65	2292

<b>Trypsin</b>	44	1544	44	1371	44	1537	42	1452	6	384	43	945	44	1544	44	1508	44	1544
<b>Metalloenzymes</b>																		
<b>ACE</b>	49	1727	48	1684	49	1723	46	1666	40	1701	49	1308	49	1727	47	1715	49	1727
<b>ADA</b>	23	821	23	804	23	813	20	622	18	804	22	455	23	821	23	811	23	821
<b>COMT</b>	11	430	10	430	11	430	11	415	8	390	10	243	11	430	11	426	11	430
<b>PDE5</b>	51	1809	51	1748	51	1796	47	1650	32	1766	47	1475	51	1809	51	1774	51	1809
<b>Folate Enzymes</b>																		
<b>DHFR</b>	201	7145	201	6966	146	7110	200	6267	190	6986	201	4608	201	7145	201	6985	201	7145
<b>GART</b>	21	753	21	725	21	737	21	545	0	20	21	548	21	753	21	740	21	753
<b>Other Enzymes</b>																		
<b>AChE</b>	105	3714	99	3525	104	3667	105	3610	97	3712	101	2412	105	3714	105	3677	105	3714
<b>ALR2</b>	26	918	26	910	26	916	23	855	26	918	26	683	26	918	24	904	26	918
<b>AmpC</b>	21	732	21	732	21	730	21	714	21	732	21	518	21	732	21	725	21	732
<b>COX-1</b>	25	849	25	843	25	826	14	367	25	849	22	632	25	849	19	570	25	849
<b>COX-2</b>	348	12464	348	12174	346	12378	223	1925	344	8610	291	8266	348	12464	297	5628	348	12464
<b>GPB</b>	52	1850	51	1798	52	1828	44	743	34	1331	50	1054	52	1850	49	1237	52	1850
<b>HIVPR</b>	53	1885	52	1743	53	1879	44	1683	7	35	52	1195	53	1885	52	1857	53	1885
<b>HIVRT</b>	40	1437	40	1393	40	1428	24	848	39	1437	33	1090	40	1437	33	1238	40	1437
<b>HMGR</b>	35	1241	35	1201	35	1234	18	1194	21	1072	35	802	35	1241	18	1224	35	1241
<b>InhA</b>	85	3035	83	2918	78	3006	82	2917	70	3035	85	2526	85	3035	84	2999	85	3035
<b>NA</b>	49	1745	47	1687	49	1728	46	1679	37	1479	49	910	49	1745	46	1722	49	1745
<b>PARP</b>	33	1176	32	1167	33	1167	33	1151	33	1176	33	822	33	1176	33	1166	33	1176
<b>PNP</b>	25	882	25	878	25	871	7	136	21	817	22	481	25	882	11	295	25	882
<b>SAHH</b>	33	1159	33	1129	33	1145	29	235	3	942	30	550	33	1159	30	427	33	1159

**Table 4.** Mean enrichment factors and mean relative enrichments for the DUD.

Program	Mean Enrichment Factor					Mean Relative Enrichment				
	0.5%	1.0%	2.0%	5.0%	10.0%	0.5%	1.0%	2.0%	5.0%	10.0%
<b>DOCK</b>	14.9	10.8	7.6	4.6	2.9	0.41	0.30	0.21	0.23	0.29
<b>FlexX</b>	7.7	7.1	5.7	4.1	2.9	0.21	0.20	0.16	0.20	0.29
<b>GLIDE HTVS</b>	13.3	11.5	9.2	5.9	3.8	0.36	0.31	0.25	0.30	0.38
<b>ICM</b>	10.4	9.0	6.4	3.8	2.5	0.28	0.25	0.17	0.19	0.25
<b>PhDOCK</b>	11.9	9.5	7.3	4.3	2.9	0.32	0.26	0.20	0.21	0.29
<b>Surflex</b>	9.3	8.6	7.1	4.6	3.3	0.26	0.24	0.19	0.23	0.33
<i>Tuned Parameters</i>										
<b>GLIDE SP</b>	14.0	11.5	10.1	6.7	4.6	0.38	0.31	0.28	0.34	0.46
<b>Surflex Ringflex</b>	12.6	11.7	9.7	6.4	4.2	0.34	0.32	0.27	0.32	0.42

**Table 5.** Analysis of the mean ROC AUCs for the DUD dataset. The upper triangle contains the mean differences and the lower triangle contains the correlation corrected 95% confidences. Examples of modified parameter settings are shaded.

	<b>DOCK</b>	<b>FlexX</b>	<b>GLIDE HTVS</b>	<b>ICM</b>	<b>PhDOCK</b>	<b>Surflex</b>	<b>GLIDE SP</b>	<b>Surflex Ringflex</b>
<b>DOCK</b>		0.057	0.17	0.088	0.038	0.11	0.22	0.17
<b>FlexX</b>	0.059		0.12	0.029	0.019	0.050	0.16	0.11
<b>GLIDE HTVS</b>	0.065	0.067		0.093	0.14	0.067	0.044	0.0038
<b>ICM</b>	0.059	0.061	0.053		0.037	0.021	0.14	0.085
<b>PhDOCK</b>	0.062	0.071	0.058	0.057		0.069	0.18	0.13
<b>Surflex</b>	0.050	0.054	0.047	0.047	0.053		0.11	0.064
<b>GLIDE SP</b>	0.062	0.069	0.031	0.059	0.067	0.048		0.048
<b>Surflex Ringflex</b>	0.046	0.053	0.051	0.085	0.058	0.029	0.045	