

Supplementary Material

Improving the Performance of the MM/PBSA and MM/GBSA Methods in Recognizing the Native Structure of the Bcl-2 Family using the Interaction Entropy Method

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	Native	Decoy1	Decoy2	Decoy3	Decoy4	Decoy5	Decoy6	Decoy7	Decoy8	Decoy9	Decoy10
4QVX	17487	18789	23157	19515	17919	19200	19665	19422	22320	17097	17919
2O21	24496	22138	23926	21172	23587	26353	22546	30163	23926	23974	20863
4LVT	18562	21367	19246	20701	21115	21112	21367	19246	20701	21115	21151
3ZLR	22047	21852	23022	18942	25530	20787	22191	22548	28848	19977	20703
3ZK6	17379	17223	19113	18834	17319	19686	18240	18678	18897	18945	21171
6O0K	20762	27659	21668	27575	22475	19484	19631	22307	20969	19598	26498
4AQ3	17650	20542	23104	23926	22132	19462	18811	20812	23992	23647	22798
6QGH	25276	24568	32800	27748	37522	39709	34684	24721	31126	42067	35578
6GL8	20831	18053	21809	18737	17084	19097	18236	18818	21884	18713	19430
6O0O	17117	20810	20612	17021	21299	19550	19157	20771	20924	18398	20612
4CIN	28851	26778	27474	31314	21564	27531	25683	29076	28161	28350	28818
1G5J	22128	27480	27597	33930	29994	30357	25545	26058	26724	23295	28398
2XA0	25797	22260	24861	29745	25557	29925	22272	16650	21378	26322	25773
3R85	31068	28695	27471	30339	43023	46428	50457	38316	54258	43851	49566
3PL7	22257	18240	17349	19944	17997	17850	21159	19587	19044	19620	18351
2PON	17031	19077	21087	22332	21423	24783	21120	19362	20835	21456	22122

Table S1

Total population	Native structure	Decoy structure
Predicted native structure	True positive (TP)	False positive (FP)
Predicted decoy structure	False negative (FN)	True negative (TN)

Table S2

4AQ3		ΔE_{ele}	ΔE_{vdw}	ΔG_{np}	$\Delta G_{\text{pb/gb}}$	ΔH	$-T\Delta S$	ΔG_{bind}
Native	PB_IE	-2.32	-64.97	-7.43	27.82	-46.90	11.89	-35.01
	GB ^{HCT} _IE	-2.32	-64.97	-8.65	19.06	-56.88	11.89	-44.99
Decoy1	PB_IE	-15.53	-42.10	-5.70	40.95	-22.38	24.33	1.95
	GB ^{HCT} _IE	-15.53	-42.10	-6.35	31.68	-32.30	24.33	-7.97
Decoy2	PB_IE	-35.55	-49.22	-6.53	59.80	-31.50	26.93	-4.57
	GB ^{HCT} _IE	-35.55	-49.22	-7.45	48.13	-44.09	26.93	-17.16
Decoy3	PB_IE	-16.08	-35.18	-5.01	33.12	-23.15	21.48	-1.67
	GB ^{HCT} _IE	-16.08	-35.18	-5.44	30.36	-26.34	21.48	-4.86
Decoy4	PB_IE	-13.29	-43.90	-5.82	37.73	-25.28	24.28	-1.00
	GB ^{HCT} _IE	-13.29	-43.90	-6.51	32.12	-31.58	24.28	-7.30
Decoy5	PB_IE	-39.20	-38.91	-5.75	63.28	-20.58	32.18	11.60
	GB ^{HCT} _IE	-39.20	-38.91	-6.41	52.56	-31.96	32.18	0.22
Decoy6	PB_IE	-11.62	-36.16	-5.02	28.84	-23.96	19.55	-4.41
	GB ^{HCT} _IE	-11.62	-36.16	-5.44	24.59	-28.63	19.55	-9.08
Decoy7	PB_IE	-3.22	-30.85	-4.65	23.89	-14.83	15.28	0.45
	GB ^{HCT} _IE	-3.22	-30.85	-4.96	19.83	-19.20	15.28	-3.92
Decoy8	PB_IE	-32.04	-44.63	-6.08	51.75	-31.00	25.71	-5.29
	GB ^{HCT} _IE	-32.04	-44.63	-6.85	43.19	-40.33	25.71	-14.62
Decoy9	PB_IE	-58.45	-43.80	-5.98	73.72	-34.51	39.94	5.43
	GB ^{HCT} _IE	-58.45	-43.80	-6.72	66.03	-42.94	39.94	-3.00
Decoy10	PB_IE	0.53	-38.54	-5.71	20.17	-23.55	20.14	-3.41
	GB ^{HCT} _IE	0.53	-38.54	-6.36	14.97	-29.40	20.14	-9.26

Table S3

2PON		ΔE_{ele}	ΔE_{vdw}	ΔG_{np}	$\Delta G_{\text{pb/gb}}$	ΔH	$-T\Delta S$	ΔG_{bind}
Native	PB_IE	-157.65	-103.46	-13.13	185.92	-88.32	67.72	-20.60
	GB^{HCT}_IE	-157.65	-103.46	-16.22	172.78	-104.55	67.72	-36.83
Decoy1	PB_IE	-9.14	-94.03	-12.42	60.01	-55.58	75.89	20.31
	GB^{HCT}_IE	-9.14	-94.03	-15.27	41.07	-77.37	75.89	-1.48
Decoy2	PB_IE	-118.48	-75.08	-11.04	138.68	-65.92	81.19	15.27
	GB^{HCT}_IE	-118.48	-75.08	-13.45	127.71	-79.30	81.19	1.89
Decoy3	PB_IE	-3.52	-44.84	-7.54	23.08	-32.82	42.29	9.47
	GB^{HCT}_IE	-3.52	-44.84	-8.79	21.72	-35.43	42.29	6.86
Decoy4	PB_IE	-107.57	-22.92	-5.42	113.50	-22.41	110.34	87.93
	GB^{HCT}_IE	-107.57	-22.92	-5.98	117.02	-19.45	110.34	90.87
Decoy5	PB_IE	-151.96	-37.42	-7.99	167.44	-29.93	75.93	46.00
	GB^{HCT}_IE	-151.96	-37.42	-9.39	158.99	-39.78	75.93	36.15
Decoy6	PB_IE	23.62	-48.09	-7.66	8.05	-24.08	37.94	28.98
	GB^{HCT}_IE	23.62	-48.09	-8.96	-3.19	-36.62	37.94	1.32
Decoy7	PB_IE	4.79	-42.89	-7.42	29.78	-15.74	89.00	73.26
	GB^{HCT}_IE	4.79	-42.89	-8.64	21.48	-25.26	89.00	63.74
Decoy8	PB_IE	-6.58	-42.54	-7.40	33.19	-23.33	52.89	29.56
	GB^{HCT}_IE	-6.58	-42.54	-8.61	27.46	-30.27	52.89	22.62
Decoy9	PB_IE	106.52	-52.83	-7.36	-78.45	-32.12	218.43	186.31
	GB^{HCT}_IE	106.52	-52.83	-8.56	-82.75	-37.62	218.43	180.81
Decoy10	PB_IE	-86.70	-69.95	-9.73	119.39	-46.99	47.87	0.88
	GB^{HCT}_IE	-86.70	-69.95	-11.71	104.46	-63.90	47.87	-16.03

Table S4

Protein-Ligand	4QVX	2O21	4LVT	3ZLR	3ZK6	6O0K	4AQ3	6QGH	6GL8	6O0O
Decoy1	3.60	3.19	3.80	4.53	0.94	3.85	3.92	2.29	4.62	3.94
Decoy2	3.70	2.51	1.41	5.10	2.48	3.19	3.94	7.18	3.58	2.81
Decoy3	3.00	3.00	3.21	4.11	3.28	3.35	4.56	5.82	3.34	3.64
Decoy4	1.96	2.68	3.05	1.45	3.52	3.48	3.79	5.53	3.59	3.73
Decoy5	3.57	2.76	2.88	4.13	1.92	3.20	4.07	5.78	3.97	4.31
Decoy6	3.37	3.13	3.81	2.07	2.71	2.38	2.63	6.13	2.46	1.31
Decoy7	3.19	2.81	1.38	4.78	3.05	3.29	3.49	5.81	3.74	4.32
Decoy8	3.14	2.47	3.22	2.82	3.48	2.97	3.93	4.05	3.91	3.48
Decoy9	3.38	2.00	2.94	3.86	3.63	2.92	4.19	5.32	3.38	3.47
Decoy10	3.01	2.65	3.42	2.37	3.46	3.62	4.43	5.35	3.52	3.64

Table S5

Protein-Protein	4CIN	1G5J	2XA0	3R85	2PON	3PL7
Decoy1	1.83	2.98	4.87	1.19	2.52	1.96
Decoy2	4.97	3.87	1.41	3.67	3.05	2.82
Decoy3	1.73	3.13	2.52	5.96	2.87	1.78
Decoy4	2.62	2.72	3.16	4.87	2.90	7.73
Decoy5	3.72	3.67	3.58	5.27	2.31	1.84
Decoy6	4.78	1.79	4.88	4.60	2.77	5.70
Decoy7	2.77	3.98	4.94	4.62	4.18	1.90
Decoy8	3.82	4.05	4.24	2.31	4.83	6.04
Decoy9	4.90	1.62	2.77	4.99	5.11	5.30
Decoy10	2.01	3.64	2.79	4.21	4.42	2.85

Table S6

4AQ3		ΔE_{ele}	ΔE_{vdw}	ΔG_{np}	$\Delta G_{\text{pb/gb}}$	ΔH	$-T\Delta S$	ΔG_{bind}
5	PB_IE	-5.22	-63.31	-7.39	33.16	-42.75	13.38	-29.37
	GB^{HCT}_IE	-5.22	-63.31	-8.60	23.22	-53.91	13.38	-40.53
10	PB_IE	-6.32	-62.25	-7.28	32.89	-46.91	11.89	-35.02
	GB^{HCT}_IE	-6.32	-62.25	-8.45	23.34	-56.89	11.89	-45.00
15	PB_IE	-5.41	-62.16	-7.35	32.81	-42.11	19.09	-23.02
	GB^{HCT}_IE	-5.41	-62.16	-8.54	23.18	-52.93	19.09	-33.84

Table S7

2PON		ΔE_{ele}	ΔE_{vdw}	ΔG_{np}	$\Delta G_{\text{pb/gb}}$	ΔH	$-T\Delta S$	ΔG_{bind}
5	PB_IE	-117.80	-110.36	-13.26	158.55	-82.87	89.16	6.29
	GB^{HCT}_IE	-117.80	-110.36	-16.39	143.34	-101.21	89.16	-12.05
10	PB_IE	-116.89	-105.77	-13.18	151.52	-88.32	67.72	-20.60
	GB^{HCT}_IE	-116.89	-105.77	-16.29	138.94	-104.55	67.72	-36.83
15	PB_IE	-104.10	-108.67	-13.65	142.46	-83.95	81.91	-2.04
	GB^{HCT}_IE	-104.10	-108.67	-16.91	127.27	-102.41	81.91	-20.50

Table S8

4AQ3	PB	GB^{HCT}	GB^{OBC1}	GB^{OBC2}	GB^{GBn1}	GB^{GBn2}	PB_{IE}	GB^{HCT}_{IE}	GB^{OBC1}_{IE}	GB^{OBC2}_{IE}	GB^{GBn1}_{IE}	GB^{GBn2}_{IE}
Native	-46.90	-56.88	-51.18	-74.94	-69.71	-470.69	-35.01	-44.99	-39.29	-63.05	-57.82	-458.80
Decoy1	-45.26	-52.10	-47.19	-66.68	-67.03	-249.34	-32.30	-39.14	-34.23	-53.72	-54.07	-236.38
Decoy2	-40.73	-49.74	-43.73	-61.66	-48.40	-370.42	-25.34	-34.35	-28.34	-46.27	-33.01	-355.03
Decoy3	-47.86	-56.33	-50.04	-77.56	-74.95	-436.71	-30.32	-38.79	-32.50	-60.02	-57.41	-419.17
Decoy4	-45.37	-53.09	-46.88	-72.62	-65.75	-462.43	-32.08	-39.80	-33.59	-59.33	-52.46	-449.14
Decoy5	-44.32	-52.22	-46.08	-72.63	-73.30	-463.20	-27.94	-35.84	-29.70	-56.25	-56.92	-446.82
Decoy6	-46.27	-58.14	-51.83	-75.92	-72.14	-370.99	-28.10	-39.97	-33.66	-57.75	-53.97	-352.82
Decoy7	-51.44	-60.00	-53.20	-80.43	-10.52	-629.00	-36.57	-45.13	-38.33	-65.56	-52.64	-614.13
Decoy8	-40.79	-47.70	-41.99	-63.03	-58.74	-251.73	-27.26	-34.17	-28.46	-49.50	-45.21	-238.20
Decoy9	-47.10	-54.52	-48.70	-66.22	-63.24	-369.04	-35.09	-42.51	-36.69	-54.21	-51.23	-357.03
Decoy10	-45.00	-53.33	-46.76	-77.23	-69.76	-486.98	-28.62	-36.95	-30.38	-60.85	-53.38	-470.60

Table S9

2PON	PB	GB^{HCT}	GB^{OBC1}	GB^{OBC2}	GB^{GBn1}	GB^{GBn2}	PB_{IE}	GB^{HCT}_{IE}	GB^{OBC1}_{IE}	GB^{OBC2}_{IE}	GB^{GBn1}_{IE}	GB^{GBn2}_{IE}
Native	-88.32	-104.55	-85.87	-19.98	-157.59	-1161.72	-20.60	-36.83	-18.15	47.74	-89.87	-1094.00
Decoy1	-88.28	-104.80	-84.55	-9.66	-76.77	-837.43	-19.52	-36.04	-15.79	59.11	-8.01	-768.67
Decoy2	-115.55	-140.13	-113.71	-11.87	-166.67	-858.61	-26.50	-51.08	-24.66	77.18	-77.62	-115.55
Decoy3	-98.96	-122.35	-99.65	-6.57	-121.35	-1042.74	-10.39	-33.78	-11.08	82.00	-32.78	-954.17
Decoy4	-104.31	-125.49	-105.39	-25.44	-132.49	-1167.53	-6.25	-27.43	-7.33	72.62	-34.43	-1069.47
Decoy5	-80.71	-104.00	-82.10	19.67	-42.87	-1119.52	-5.85	-29.14	-7.24	94.53	31.99	-1044.66
Decoy6	-84.35	-115.09	-93.95	-7.31	-125.14	-797.66	-5.69	-36.43	-15.29	71.35	-46.48	-719.00
Decoy7	-84.56	-100.80	-73.92	21.97	-10.52	-1029.33	-18.99	-35.23	-8.35	87.54	55.05	-963.76
Decoy8	-81.22	-95.03	-79.12	-4.45	-11.70	-872.61	-6.58	-20.39	-4.48	70.19	62.94	-797.97
Decoy9	-68.97	-86.58	-68.29	18.79	0.13	-803.34	-12.47	-30.08	-11.79	75.30	56.64	-746.84
Decoy10	-89.89	-99.97	-77.90	-29.58	-92.60	-1053.25	-21.40	-31.48	-9.41	38.91	-24.11	-984.76

Table S10

4AQ3	PB	GB ^{HCT}	GB ^{OBC1}	PB_IE	GB ^{HCT} _IE	GB ^{OBC1} _IE	PB_Nmode	GB ^{HCT} _Nmode	GB ^{OBC1} _Nmode	PB_QH	GB ^{HCT} _QH	GB ^{OBC1} _QH
Native	-46.90	-56.88	-51.18	-35.01	-44.99	-39.29	-15.88	-25.86	-20.16	-16.48	-26.46	-20.76
Decoy1	-45.26	-52.10	-47.19	-32.30	-39.14	-34.23	-17.13	-23.97	-19.06	-15.19	-22.03	-17.12
Decoy2	-40.73	-49.74	-43.73	-25.34	-34.35	-28.34	-11.07	-20.08	-14.07	-10.01	-19.02	-13.01
Decoy3	-47.86	-56.33	-50.04	-30.32	-38.79	-32.50	-17.96	-26.43	-20.14	-18.60	-27.07	-20.78
Decoy4	-45.37	-53.09	-46.88	-32.08	-39.80	-33.59	-14.82	-22.54	-16.33	-15.13	-22.85	-16.64
Decoy5	-44.32	-52.22	-46.08	-27.94	-35.84	-29.70	-12.69	-20.59	-14.45	-14.21	-22.11	-15.97
Decoy6	-46.27	-58.14	-51.83	-28.10	-39.97	-33.66	-16.52	-28.39	-22.08	-17.21	-29.08	-22.77
Decoy7	-51.44	-60.00	-53.20	-36.57	-45.13	-38.33	-21.19	-29.75	-22.95	-20.87	-29.43	-22.63
Decoy8	-40.79	-47.70	-41.99	-27.26	-34.17	-28.46	-13.40	-20.31	-14.60	-13.79	-20.70	-14.99
Decoy9	-47.10	-54.52	-48.70	-35.09	-42.51	-36.69	-15.68	-23.10	-17.28	-17.19	-24.61	-18.79
Decoy10	-45.00	-53.33	-46.76	-28.62	-36.95	-30.38	-11.34	-19.67	-13.10	-13.94	-22.27	-15.70
Rank	4	3	3	3	2	1	5	4	3	5	4	4

Table S11

2PON	PB	GB ^{HCT}	GB ^{OBC1}	PB_IE	GB ^{HCT} _IE	GB ^{OBC1} _IE	PB_Nmode	GB ^{HCT} _Nmode	GB ^{OBC1} _Nmode	PB_QH	GB ^{HCT} _QH	GB ^{OBC1} _QH
Native	-88.32	-104.55	-85.87	-20.60	-36.83	-18.15	-31.97	-51.96	-33.28	-43.33	-59.56	-40.88
Decoy1	-88.28	-104.80	-84.55	-19.52	-36.04	-15.79	-29.17	-44.47	-24.22	-33.70	-50.22	-29.97
Decoy2	-115.55	-140.13	-113.71	-26.50	-51.08	-24.66	-59.69	-85.27	-58.85	-57.46	-82.04	-55.62
Decoy3	-98.96	-122.35	-99.65	-10.39	-33.78	-11.08	-34.89	-60.66	-37.96	-44.7	-68.09	-45.39
Decoy4	-104.31	-125.49	-105.39	-6.25	-27.43	-7.33	-40.27	-64.67	-44.57	-45.9	-67.08	-46.98
Decoy5	-80.71	-104.00	-82.10	-5.85	-29.14	-7.24	-39.42	-58.00	-36.10	-33.26	-56.55	-34.65
Decoy6	-84.35	-115.09	-93.95	-5.69	-36.43	-15.29	-26.76	-61.09	-39.95	-34.78	-65.52	-44.38
Decoy7	-84.56	-100.80	-73.92	-18.99	-35.23	-8.35	-29.89	-51.59	-24.71	-32.46	-48.70	-21.82
Decoy8	-81.22	-95.03	-79.12	-6.58	-20.39	-4.48	-32.08	-39.15	-23.24	-26.88	-40.69	-24.78
Decoy9	-68.97	-86.58	-68.29	-12.47	-30.08	-11.79	-7.93	-28.52	-10.23	-25.82	-43.43	-25.14
Decoy10	-89.89	-99.97	-77.90	-21.40	-31.48	-9.41	-51.90	-62.68	-40.61	-48.00	-58.08	-36.01
Rank	5	6	5	3	2	2	7	7	7	6	5	5

Table S12

4QVX	PB	GB^{HCT}	GB^{OBC1}	PB_IE	GB^{HCT}_IE	GB^{OBC1}_IE
Native	-69.45	-86.50	-77.46	-25.06	-42.11	-33.07
Decoy1	-67.74	-82.90	-73.59	-24.47	-39.63	-30.32
Decoy2	-69.84	-80.59	-71.62	-10.60	-21.35	-12.38
Decoy3	-64.16	-79.83	-71.53	-4.50	-20.17	-11.87
Decoy4	-69.02	-85.62	-76.21	-21.75	-38.35	-28.94
Decoy5	-62.59	-80.77	-71.88	-21.09	-39.27	-30.38
Decoy6	-59.15	-74.97	-65.92	-3.45	-19.27	-10.22
Decoy7	-66.22	-82.92	-73.02	-14.41	-31.11	-21.21
Decoy8	-67.68	-86.82	-70.40	-22.17	-41.31	-23.94
Decoy9	-64.85	-79.57	-76.69	-18.39	-33.11	-31.18
Decoy10	-69.20	-84.99	-75.02	-13.93	-29.72	-19.75
Rank	2	2	1	1	1	1

Table S13(A)

2O21	PB	GB^{HCT}	GB^{OBC1}	PB_IE	GB^{HCT}_IE	GB^{OBC1}_IE
native	-34.81	-47.10	-39.82	-12.78	-25.07	-17.79
decoy1	-34.73	-42.05	-35.61	-8.68	-16.00	-9.56
decoy2	-33.20	-47.79	-40.18	-9.54	-24.13	-16.52
decoy3	-42.13	-65.58	-56.13	-1.48	-24.93	-15.48
decoy4	-37.19	-44.30	-37.92	-13.12	-20.23	-13.85
decoy5	-28.91	-42.67	-37.09	-3.54	-17.30	-11.72
decoy6	-42.55	-59.03	-55.60	-6.10	-22.58	-19.15
decoy7	-35.76	-48.58	-41.88	-9.85	-22.67	-15.97
decoy8	-33.69	-48.81	-40.77	-8.78	-23.90	-15.86
decoy9	-36.58	-45.61	-37.77	-2.75	-11.78	-3.94
decoy10	-28.47	-37.27	-31.54	-6.87	-15.67	-9.94
Rank	6	6	6	2	1	2

Table S13(B)

4LVT	PB	GB^{HCT}	GB^{OBC1}	PB_IE	GB^{HCT}_IE	GB^{OBC1}_IE
Native	-56.24	-75.33	-66.13	-25.32	-44.41	-35.21
Decoy1	-43.11	-49.75	-43.56	-16.51	-23.15	-16.96
Decoy2	-56.29	-71.10	-62.71	-17.55	-32.36	-23.97
Decoy3	-50.85	-66.24	-55.59	-11.06	-26.45	-15.80
Decoy4	-52.07	-66.48	-55.82	-9.06	-23.47	-12.81
Decoy5	-52.63	-67.38	-56.57	-21.71	-36.46	-25.65
Decoy6	-44.08	-51.21	-45.54	-9.13	-16.26	-10.59
Decoy7	-54.97	-70.54	-62.22	-7.89	-23.46	-15.14
Decoy8	-50.56	-66.32	-55.41	-9.47	-25.23	-14.32
Decoy9	-51.80	-66.58	-55.71	-15.87	-30.65	-19.78
Decoy10	-41.35	-53.48	-44.72	-5.66	-17.79	-23.45
Rank	2	1	1	1	1	1

Table S13(C)

3ZLR	PB	GB^{HCT}	GB^{OBC1}	PB_{IE}	GB^{HCT}_{IE}	GB^{OBC1}_{IE}
Native	-66.95	-79.00	-67.60	-35.59	-47.64	-36.24
Decoy1	-61.86	-75.48	-65.09	-11.81	-25.43	-15.04
Decoy2	-66.07	-77.41	-67.38	-32.15	-43.49	-33.46
Decoy3	-59.01	-71.29	-62.89	-24.55	-36.83	-28.43
Decoy4	-62.67	-76.11	-66.39	-25.31	-38.75	-29.03
Decoy5	-61.89	-74.04	-64.22	-8.89	-21.04	-11.22
Decoy6	-58.02	-70.99	-61.65	-26.95	-39.92	-30.58
Decoy7	-68.98	-79.88	-70.22	-36.72	-47.62	-37.96
Decoy8	-68.39	-81.33	-70.34	-33.92	-46.86	-35.87
Decoy9	-63.97	-77.11	-66.71	-18.63	-31.77	-21.37
Decoy10	-59.62	-72.18	-65.74	-34.33	-46.89	-40.45
Rank	3	3	3	2	1	3

Table S13(D)

3ZK6	PB	GB^{HCT}	GB^{OBC1}	PB_{IE}	GB^{HCT}_{IE}	GB^{OBC1}_{IE}
Native	-46.03	-55.13	-48.24	-35.07	-44.17	-37.28
Decoy1	-44.42	-53.23	-46.06	-33.58	-42.39	-35.22
Decoy2	-45.95	-56.14	-50.81	-33.90	-44.09	-38.76
Decoy3	-41.79	-51.40	-44.95	-28.22	-37.83	-31.38
Decoy4	-45.79	-55.07	-48.59	-29.35	-38.63	-32.15
Decoy5	-41.81	-50.99	-44.24	-29.22	-38.40	-31.65
Decoy6	-44.91	-53.59	-46.85	-34.22	-42.90	-36.16
Decoy7	-44.07	-56.21	-48.83	-30.52	-42.66	-35.28
Decoy8	-47.05	-57.18	-50.15	-32.42	-42.54	-35.51
Decoy9	-48.96	-59.99	-53.17	-31.04	-42.07	-35.25
Decoy10	-50.72	-61.87	-54.63	-36.54	-47.69	-40.45
Rank	4	6	7	2	2	3

Table S13(E)

600K	PB	GB^{HCT}	GB^{OBC1}	PB_{IE}	GB^{HCT}_{IE}	GB^{OBC1}_{IE}
Native	-45.40	-72.23	-64.68	-23.35	-50.18	-42.63
Decoy1	-45.93	-54.32	-52.54	-8.05	-16.44	-14.66
Decoy2	-48.82	-55.71	-54.16	-4.06	-10.95	-9.40
Decoy3	-51.72	-62.08	-54.33	-22.28	-32.64	-24.89
Decoy4	-52.40	-66.70	-59.70	-16.05	-30.35	-23.35
Decoy5	-45.89	-54.16	-45.84	-23.19	-31.46	-23.14
Decoy6	-53.07	-67.73	-63.54	-9.69	-24.35	-20.16
Decoy7	-55.25	-66.77	-62.91	-23.20	-34.72	-30.86
Decoy8	-48.77	-62.04	-58.26	-24.94	-38.21	-34.43
Decoy9	-41.55	-57.32	-55.20	-8.03	-23.80	-21.68
Decoy10	-42.16	-51.69	-44.12	-21.49	-31.02	-23.45
Rank	9	1	1	2	1	1

Table S13(F)

4AQ3	PB	GB^{HCT}	GB^{OBC1}	PB_{IE}	GB^{HCT}_{IE}	GB^{OBC1}_{IE}
Native	-46.90	-56.88	-51.18	-35.01	-44.99	-39.29
Decoy1	-45.26	-52.10	-47.19	-32.30	-39.14	-34.23
Decoy2	-40.73	-49.74	-43.73	-25.34	-34.35	-28.34
Decoy3	-47.86	-56.33	-50.04	-30.32	-38.79	-32.50
Decoy4	-45.37	-53.09	-46.88	-32.08	-39.80	-33.59
Decoy5	-44.32	-52.22	-46.08	-27.94	-35.84	-29.70
Decoy6	-46.27	-58.14	-51.83	-28.10	-39.97	-33.66
Decoy7	-51.44	-60.00	-53.20	-36.57	-45.13	-38.33
Decoy8	-40.79	-47.70	-41.99	-27.26	-34.17	-28.46
Decoy9	-47.10	-54.52	-48.70	-35.09	-42.51	-36.69
Decoy10	-45.00	-53.33	-46.76	-28.62	-36.95	-30.38
Rank	4	3	3	3	2	1

Table S13(G)

6QGH	PB	GB^{HCT}	GB^{OBC1}	PB_{IE}	GB^{HCT}_{IE}	GB^{OBC1}_{IE}
Native	-47.89	-68.27	-57.22	-37.26	-57.64	-46.59
Decoy1	-48.21	-61.92	-51.48	-35.87	-49.58	-39.14
Decoy2	-57.83	-68.11	-58.47	-41.64	-51.92	-42.28
Decoy3	-51.15	-61.87	-53.31	-30.49	-41.21	-32.65
Decoy4	-51.22	-60.66	-52.53	-33.56	-43.00	-34.87
Decoy5	-51.41	-58.03	-49.74	-35.51	-42.13	-33.84
Decoy6	-48.39	-58.99	-50.16	-33.66	-44.26	-35.43
Decoy7	-55.23	-66.44	-56.95	-36.50	-47.71	-38.22
Decoy8	-42.74	-50.29	-41.27	-25.07	-32.62	-23.60
Decoy9	-55.08	-62.56	-53.14	-40.69	-48.17	-38.75
Decoy10	-52.64	-59.66	-50.23	-32.14	-39.16	-29.73
Rank	10	1	2	3	1	1

Table S13(H)

6GL8	PB	GB^{HCT}	GB^{OBC1}	PB_{IE}	GB^{HCT}_{IE}	GB^{OBC1}_{IE}
Native	-36.06	-41.28	-37.17	-28.99	-34.21	-30.10
Decoy1	-38.00	-41.85	-37.31	-29.83	-33.68	-29.14
Decoy2	-36.17	-40.73	-37.42	-28.51	-33.07	-29.76
Decoy3	-34.62	-38.72	-34.08	-25.96	-30.06	-25.42
Decoy4	-33.43	-39.45	-34.97	-26.44	-32.46	-27.98
Decoy5	-40.11	-45.67	-40.05	-24.75	-30.31	-24.69
Decoy6	-37.90	-42.36	-38.87	-27.76	-32.22	-28.73
Decoy7	-36.45	-41.77	-36.31	-23.26	-28.58	-23.12
Decoy8	-34.34	-40.98	-38.09	-26.16	-32.80	-29.91
Decoy9	-36.99	-40.78	-36.44	-27.76	-31.55	-27.21
Decoy10	-36.03	-41.52	-36.98	-27.18	-32.67	-28.13
Rank	7	6	6	2	1	1

Table S13(I)

6000	PB	GB^{HCT}	GB^{OBC1}	PB_IE	GB^{HCT}_IE	GB^{OBC1}_IE
Native	-35.39	-43.17	-38.71	-25.22	-33.00	-28.54
Decoy1	-21.54	-27.00	-23.09	-8.80	-14.26	-10.35
Decoy2	-20.84	-21.17	-20.12	-10.90	-11.23	-10.18
Decoy3	-18.41	-23.36	-20.13	-3.61	-8.56	-5.33
Decoy4	-26.04	-27.39	-24.79	-6.48	-7.83	-5.23
Decoy5	-25.64	-29.93	-27.26	-3.77	-8.06	-5.39
Decoy6	-36.35	-42.05	-38.76	-25.04	-30.74	-27.45
Decoy7	-27.67	-31.46	-30.09	-9.70	-13.49	-23.18
Decoy8	-30.02	-32.10	-30.46	-18.76	-20.84	-19.20
Decoy9	-20.41	-26.71	-23.70	-9.68	-15.98	-12.97
Decoy10	-22.75	-23.80	-22.48	-7.95	-9.00	-7.68
Rank	2	1	2	1	1	1

Table S13(J)

4CIN	PB	GB^{HCT}	GB^{OBC1}	PB_IE	GB^{HCT}_IE	GB^{OBC1}_IE
Native	-89.67	-109.82	-93.06	-32.04	-52.19	-52.19
Decoy1	-102.50	-121.68	-98.14	-31.06	-50.24	-50.24
Decoy2	-92.67	-114.70	-92.70	-16.48	-38.51	-38.51
Decoy3	-95.36	-106.32	-89.54	-29.36	-40.32	-40.32
Decoy4	-97.68	-122.93	-92.03	-19.80	-45.05	-45.05
Decoy5	-83.94	-109.14	-90.95	-16.91	-42.11	-42.11
Decoy6	-82.19	-91.66	-75.94	-11.13	-20.60	-20.60
Decoy7	-66.04	-84.52	-68.46	-6.84	-25.32	-25.32
Decoy8	-91.29	-114.77	-93.19	-28.69	-52.17	-52.17
Decoy9	-87.54	-104.29	-84.47	-10.91	-27.66	-27.66
Decoy10	-88.22	-105.11	-88.44	-12.30	-29.19	-29.19
Rank	6	5	3	1	1	1

Table S13(K)

1G5J	PB	GB^{HCT}	GB^{OBC1}	PB_IE	GB^{HCT}_IE	GB^{OBC1}_IE
Native	-93.53	-121.90	-98.97	-24.13	-52.50	-29.57
Decoy1	-101.83	-125.16	-100.75	-9.70	-33.03	-8.62
Decoy2	-112.20	-142.48	-115.59	-21.31	-51.59	-24.70
Decoy3	-90.62	-109.65	-96.89	-12.34	-31.37	-18.61
Decoy4	-95.24	-115.43	-96.84	-23.75	-43.94	-25.35
Decoy5	-129.27	-149.50	-124.11	-15.11	-35.34	-9.95
Decoy6	-105.86	-124.91	-105.50	-17.96	-37.01	-17.60
Decoy7	-117.26	-141.57	-116.17	-22.18	-46.49	-21.09
Decoy8	-117.52	-149.42	-122.98	-24.49	-56.39	-29.95
Decoy9	-78.33	-104.94	-85.25	-17.77	-44.38	-24.69
Decoy10	-134.74	-159.28	-129.72	-19.22	-43.76	-14.20
Rank	9	8	8	2	2	2

Table S13(L)

2XA0	PB	GB^{HCT}	GB^{OBC1}	PB_{IE}	GB^{HCT}_{IE}	GB^{OBC1}_{IE}
Native	-122.07	-139.84	-118.19	-23.77	-41.54	-19.89
Decoy1	-110.30	-124.36	-100.75	-17.05	-31.11	-7.50
Decoy2	-101.82	-126.87	-105.32	-5.75	-30.80	-9.25
Decoy3	-100.40	-115.11	-91.33	-17.90	-32.60	-8.82
Decoy4	-112.42	-133.04	-103.08	-13.65	-34.27	-4.31
Decoy5	-106.25	-126.91	-101.99	-14.20	-34.86	-9.94
Decoy6	-90.46	-114.09	-92.59	-4.53	-28.16	-6.66
Decoy7	-117.78	-138.07	-108.32	-19.56	-39.85	-10.10
Decoy8	-101.16	-117.84	-94.48	-12.36	-29.04	-5.68
Decoy9	-92.83	-110.15	-84.46	-15.19	-32.51	-6.82
Decoy10	-115.51	-142.25	-116.21	-9.73	-36.47	-10.43
Rank	1	2	1	1	1	1

Table S13(M)

3R85	PB	GB^{HCT}	GB^{OBC1}	PB_{IE}	GB^{HCT}_{IE}	GB^{OBC1}_{IE}
Native	-90.30	-107.12	-90.64	-21.93	-38.75	-22.27
Decoy1	-119.68	-143.11	-114.83	-11.58	-35.01	-6.73
Decoy2	-77.79	-89.19	-73.97	-7.84	-19.24	-4.02
Decoy3	-58.76	-71.96	-57.13	-10.36	-23.56	-8.73
Decoy4	-109.49	-127.18	-108.15	-14.65	-32.34	-13.31
Decoy5	-76.31	-89.48	-72.81	-7.88	-21.05	-4.38
Decoy6	-83.59	-90.94	-76.41	-11.90	-19.25	-4.72
Decoy7	-80.79	-95.42	-79.32	-17.29	-31.92	-15.82
Decoy8	-79.13	-94.39	-76.73	-11.24	-26.50	-8.84
Decoy9	-76.27	-90.74	-74.80	-19.75	-34.22	-18.28
Decoy10	-72.79	-86.47	-72.33	-4.70	-18.38	-4.24
Rank	3	3	3	1	1	1

Table S13(N)

3PL7	PB	GB^{HCT}	GB^{OBC1}	PB_{IE}	GB^{HCT}_{IE}	GB^{OBC1}_{IE}
Native	-79.34	-96.13	-80.52	-17.45	-34.24	-18.63
Decoy1	-75.51	-89.19	-72.80	-8.46	-22.14	-5.75
Decoy2	-85.19	-90.59	-74.72	-22.72	-28.12	-12.25
Decoy3	-85.42	-101.31	-80.77	-9.02	-24.91	-4.37
Decoy4	-77.15	-100.96	-79.67	-4.29	-28.10	-6.81
Decoy5	-79.76	-94.38	-77.74	-7.18	-21.80	-5.16
Decoy6	-102.23	-130.11	-102.60	-5.71	-33.59	-6.08
Decoy7	-92.86	-104.02	-87.99	-6.94	-18.10	-25.05
Decoy8	-78.94	-95.93	-74.58	-12.88	-29.87	-8.52
Decoy9	-94.57	-136.16	-106.45	-18.19	-59.78	-30.07
Decoy10	-79.59	-87.67	-73.35	-17.14	-25.22	-10.90
Rank	8	6	5	3	2	3

Table S13(O)

2PON	PB	GB^{HCT}	GB^{OBC1}	PB_IE	GB^{HCT}_IE	GB^{OBC1}_IE
Native	-88.32	-104.55	-85.87	-20.60	-36.83	-18.15
Decoy1	-88.28	-104.80	-84.55	-19.52	-36.04	-15.79
Decoy2	-115.55	-140.13	-113.71	-26.50	-51.08	-24.66
Decoy3	-98.96	-122.35	-99.65	-10.39	-33.78	-11.08
Decoy4	-104.31	-125.49	-105.39	-6.25	-27.43	-7.33
Decoy5	-80.71	-104.00	-82.10	-5.85	-29.14	-7.24
Decoy6	-84.35	-115.09	-93.95	-5.69	-36.43	-15.29
Decoy7	-84.56	-100.80	-73.92	-18.99	-35.23	-8.35
Decoy8	-81.22	-95.03	-79.12	-6.58	-20.39	-4.48
Decoy9	-68.97	-86.58	-68.29	-12.47	-30.08	-11.79
Decoy10	-89.89	-99.97	-77.90	-21.40	-31.48	-9.41
Rank	5	6	5	3	2	2

Table S13(P)

Figure

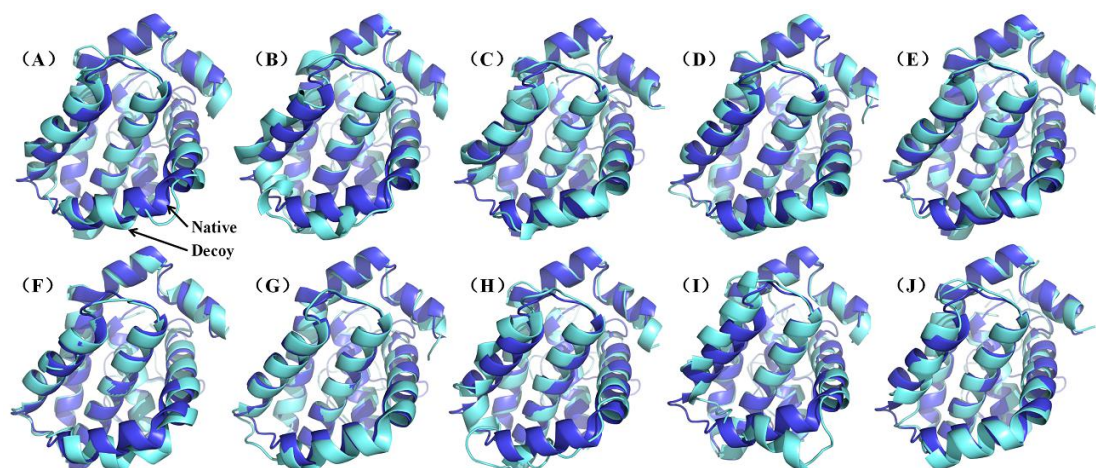


Figure S1 The structure comparison of protein between native structure and 10 decoys of 4AQ3 system.

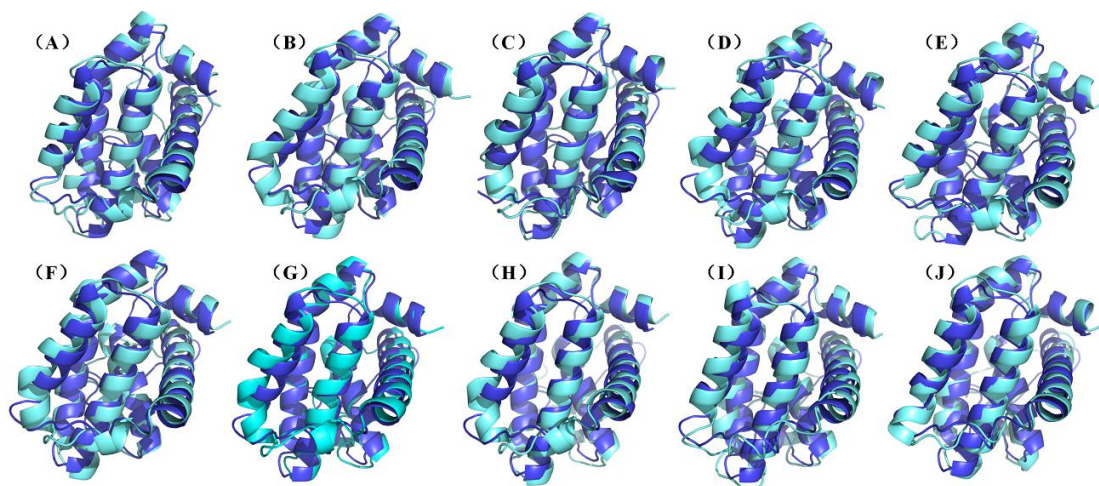


Figure S2 The structure comparison of protein between native structure and 10 decoys of 2PON system.

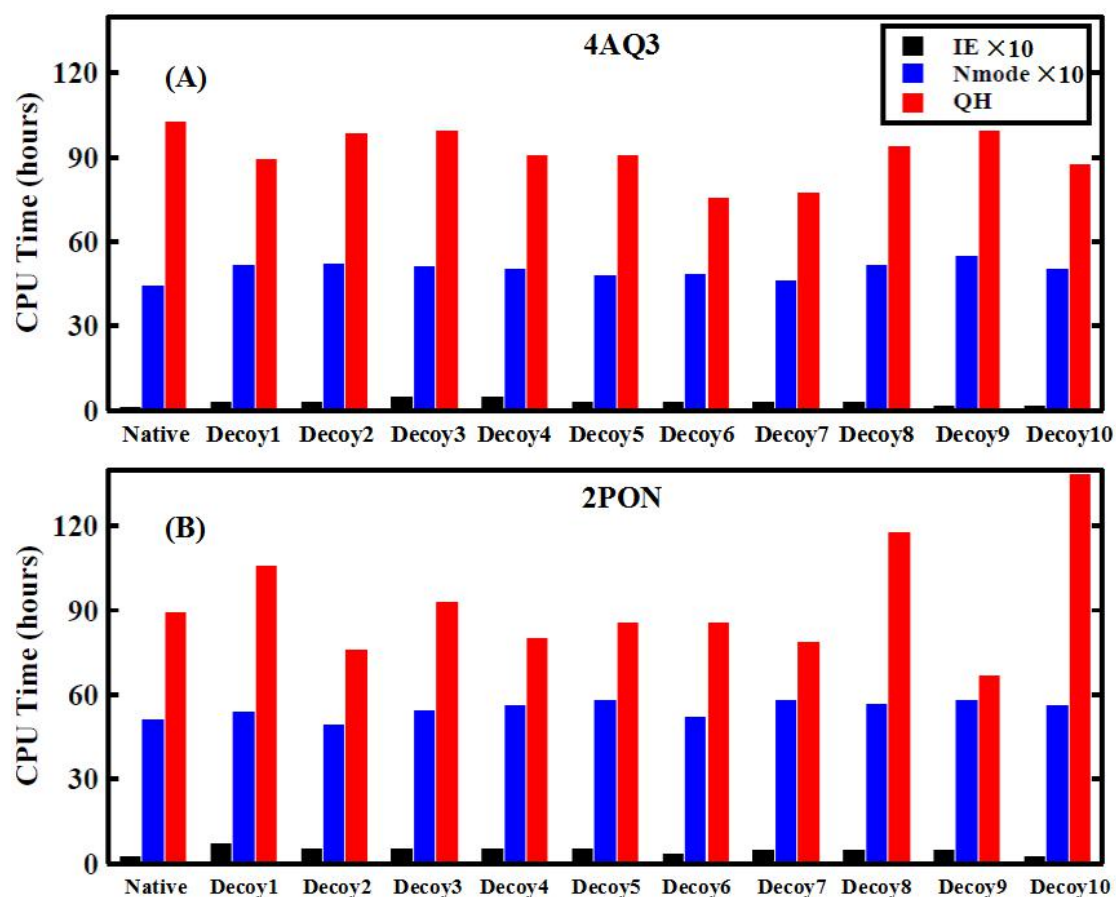


Figure S3 Computation cost (core hours) of IE, Nmode, and QH methods to calculate entropic contribution for 100 000, 30, and 30 configurations (snapshots) of the native and decoy structures of 4AQ3 and 2PON systems, respectively. The $\times 10$ in the table represents that the required time of IE and Nmode methods are multiplied by a factor of 10 before they were plotted.

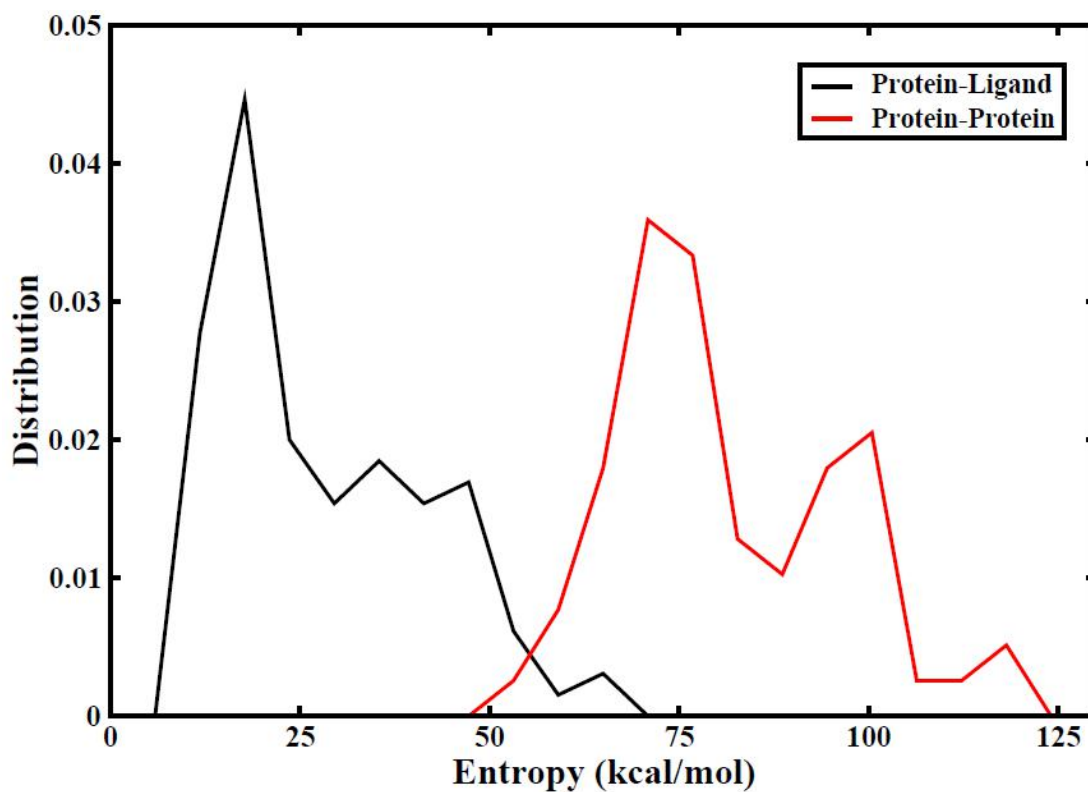


Figure S4 The distribution of entropic contribution for all native and decoy structures of protein-ligand and protein-protein systems calculated by IE method.

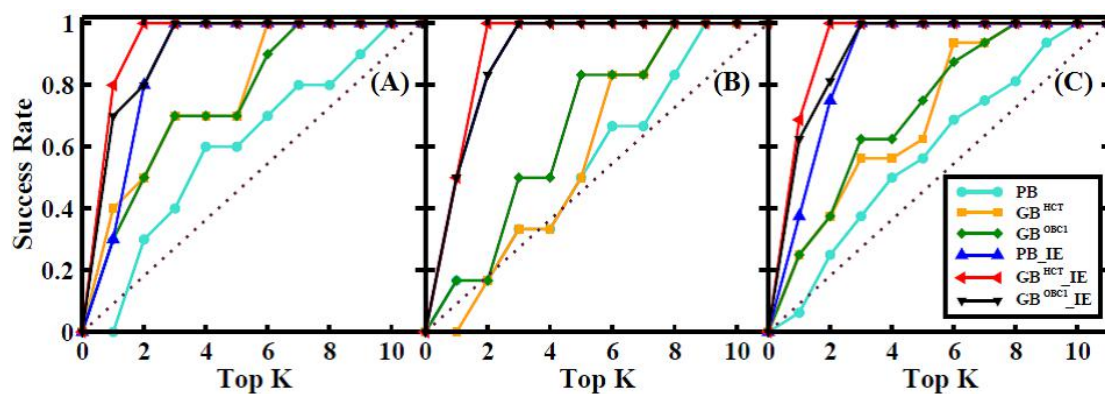


Figure S5 The success-rate curves (the proportion of the case in which the native structure could be found in the top K predictions) of (A) the 10 protein-ligand systems, (B) the 6 protein-protein systems and (C) all the 16 systems.

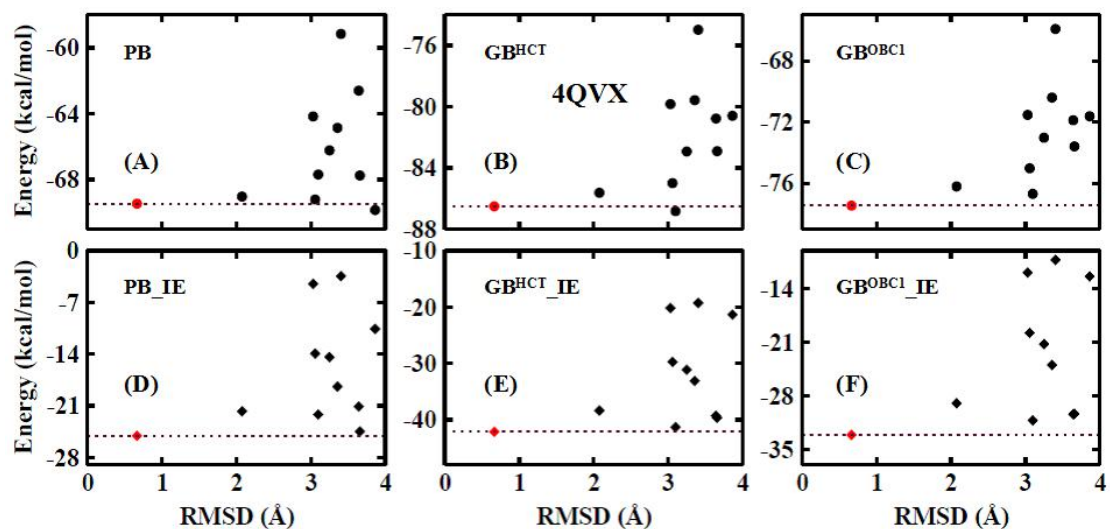


Figure S6 The binding free energy plotted against the average RMSD value of protein backbone responding to the initial native structure during the MD simulation of six methods for 4QVX system.

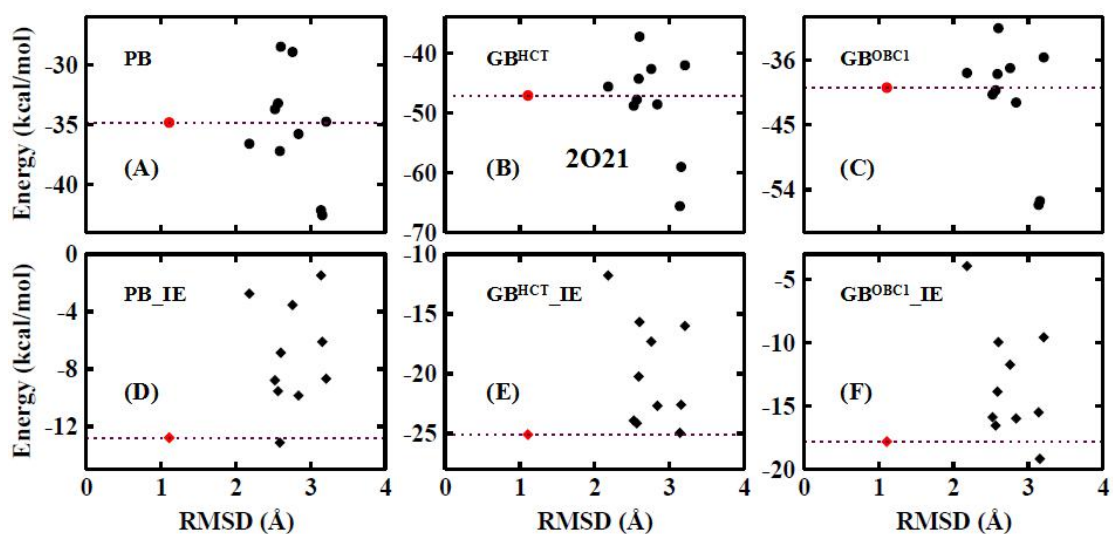


Figure S7 The same as Figure S6, but for 2O21 system.

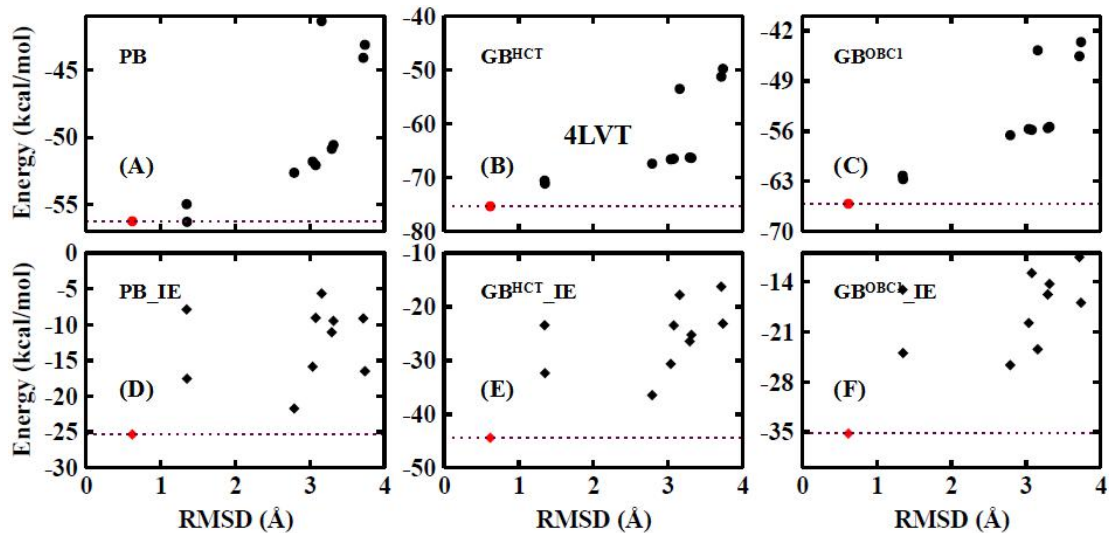


Figure S8 The same as Figure S6, but for 4LVT system.

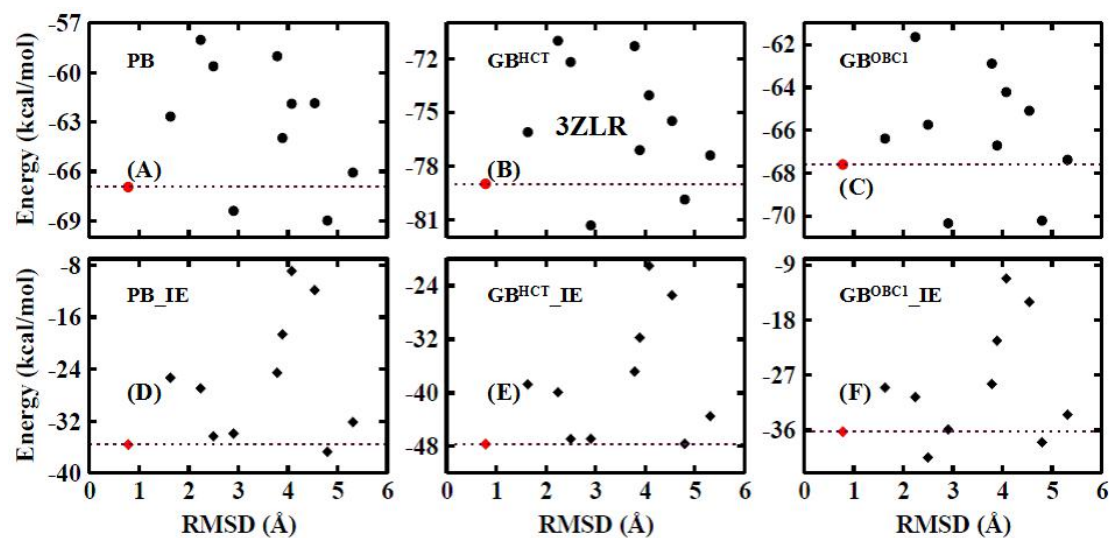


Figure S9 The same as Figure S6, but for 3ZLR system.

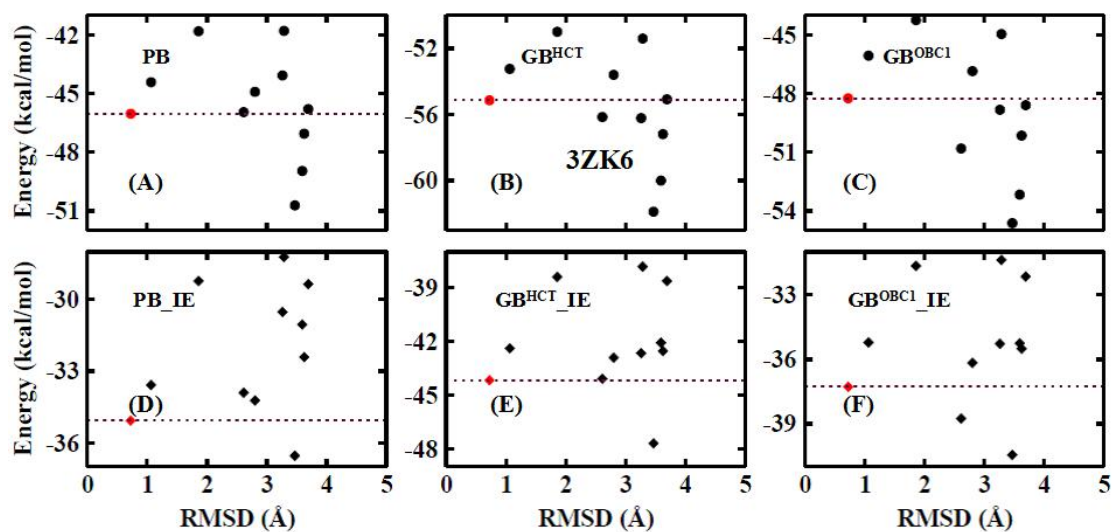


Figure S10 The same as Figure S6, but for 3ZK6 system.

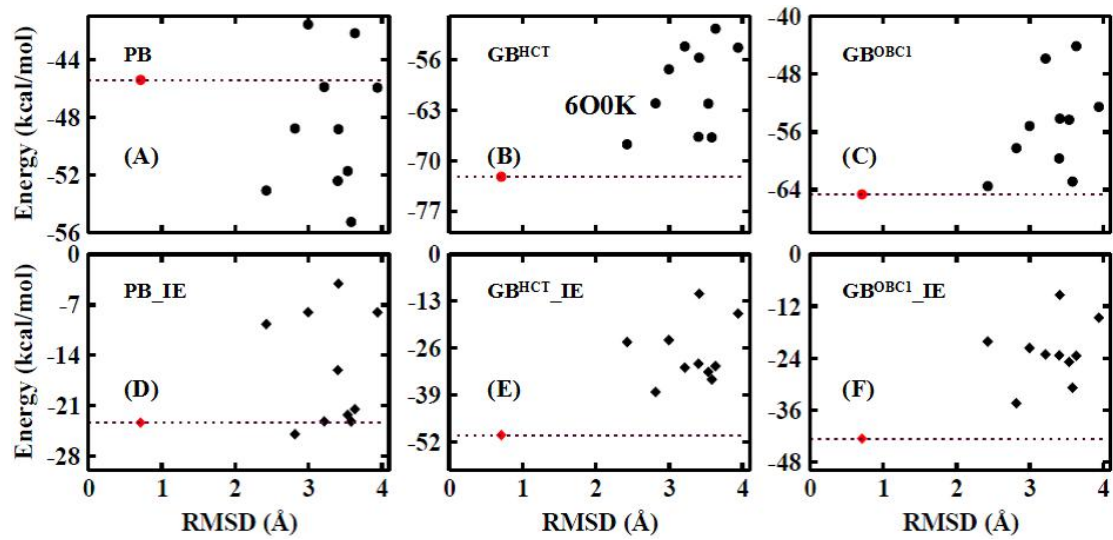


Figure S11 The same as Figure S6, but for 600K system.

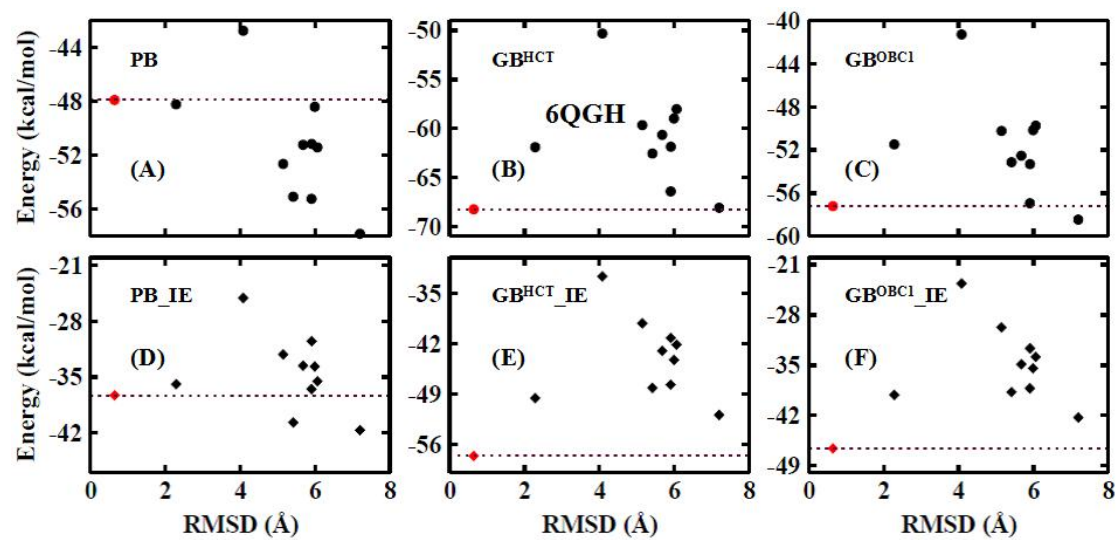


Figure S12 The same as Figure S6, but for 6QGH system.

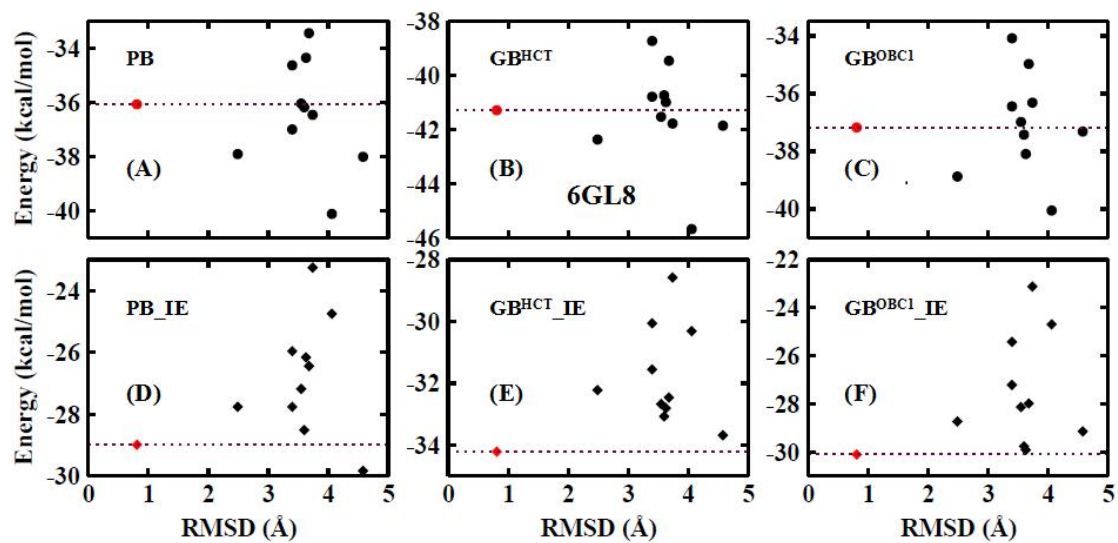


Figure S13 The same as Figure S6, but for 6GL8 system.

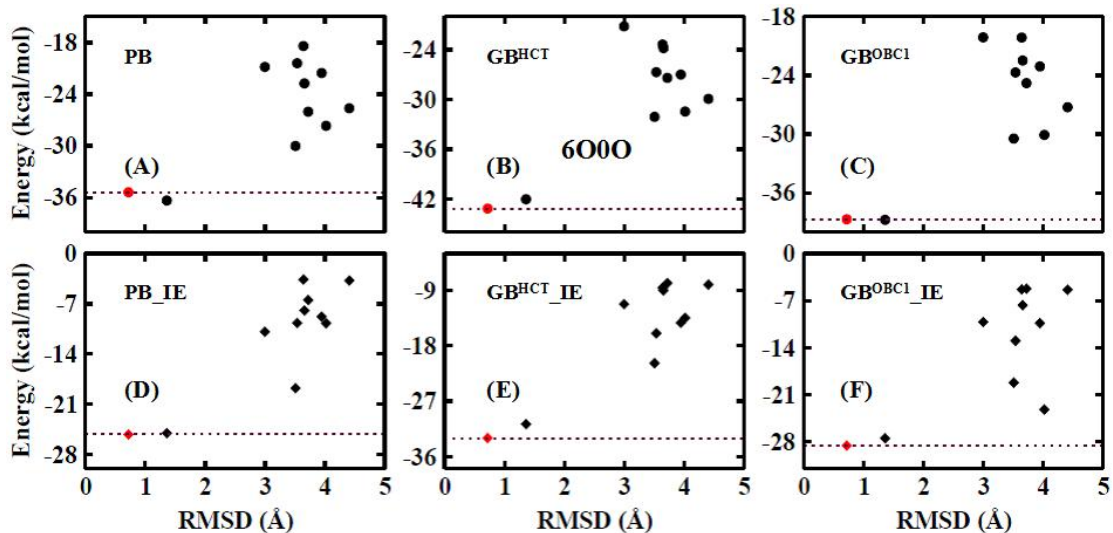


Figure S14 The same as Figure S6, but for 6000 system.

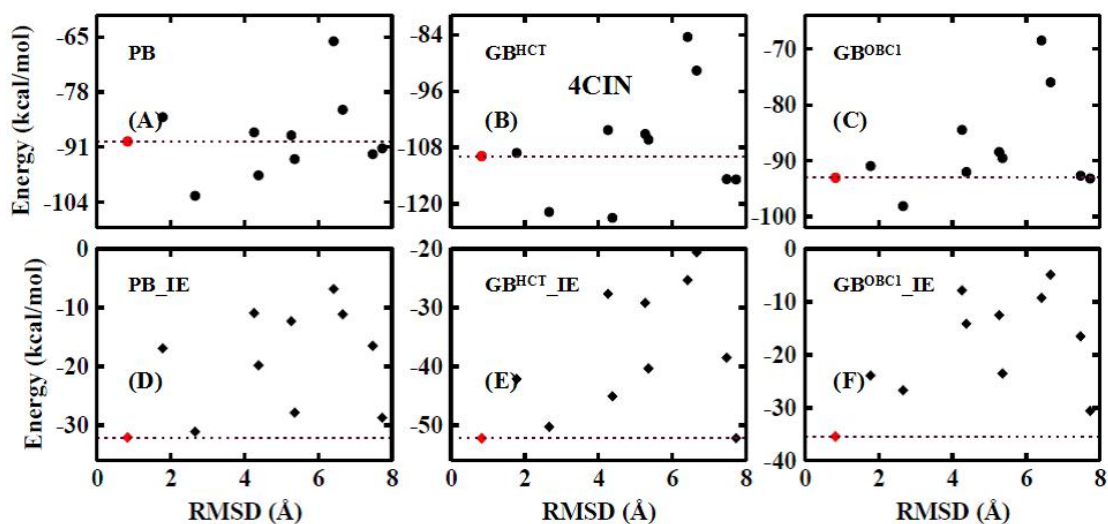


Figure S15 The same as Figure S6, but for 4CIN system.

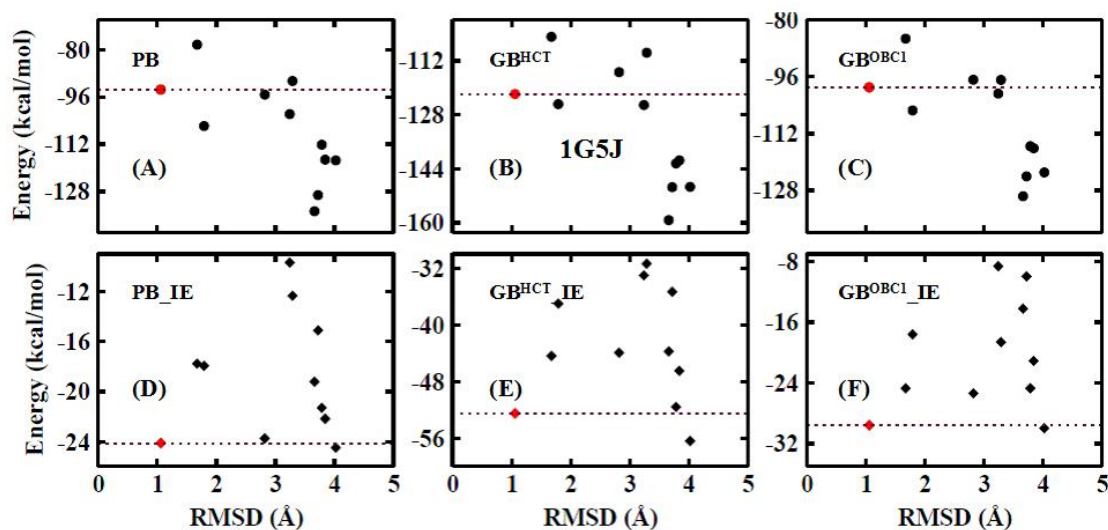


Figure S16 The same as Figure S6, but for 1G5J system.

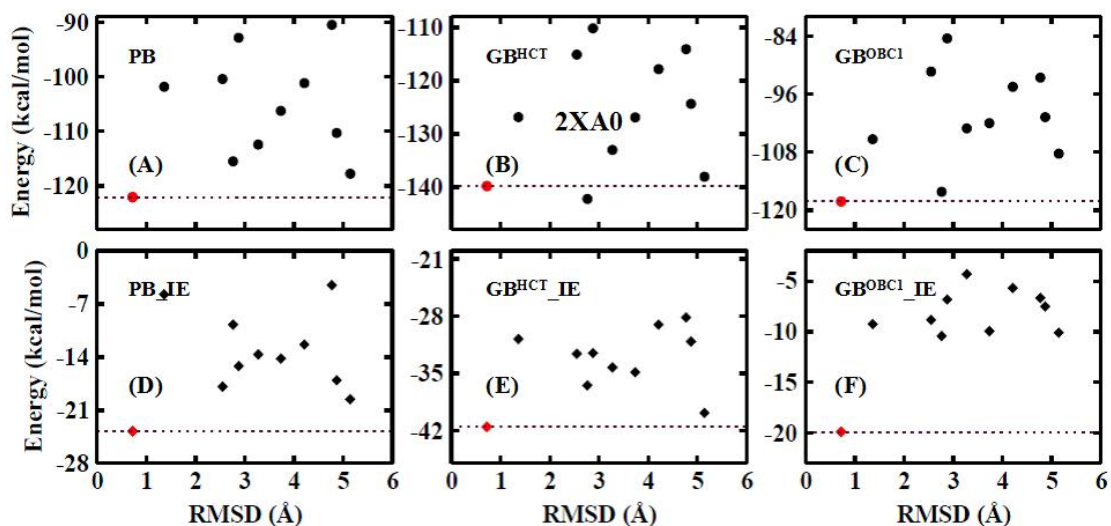


Figure S17 The same as Figure S6, but for 2XA0 system.

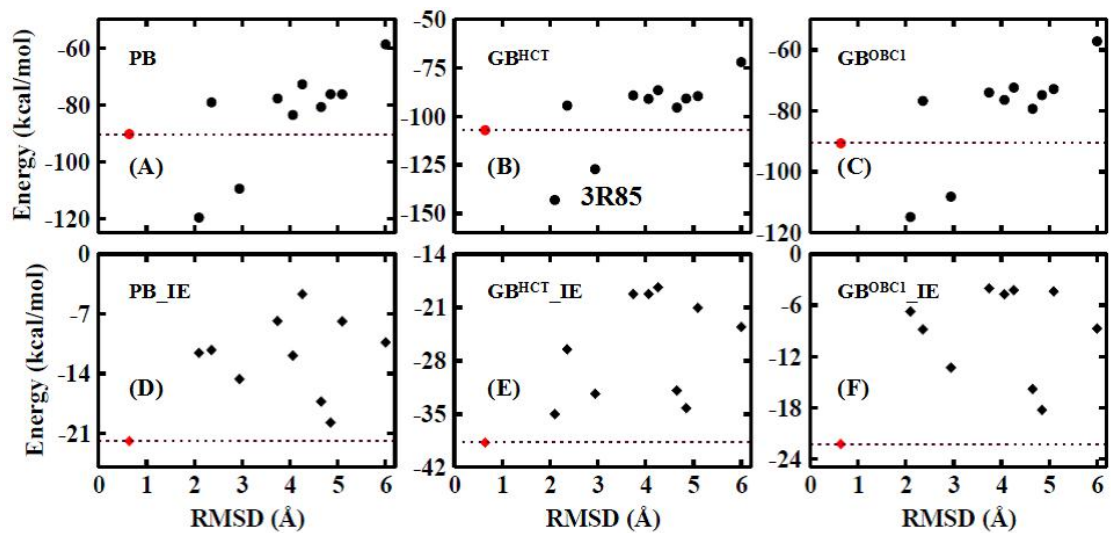


Figure S18 The same as Figure S6, but for 3R85 system.

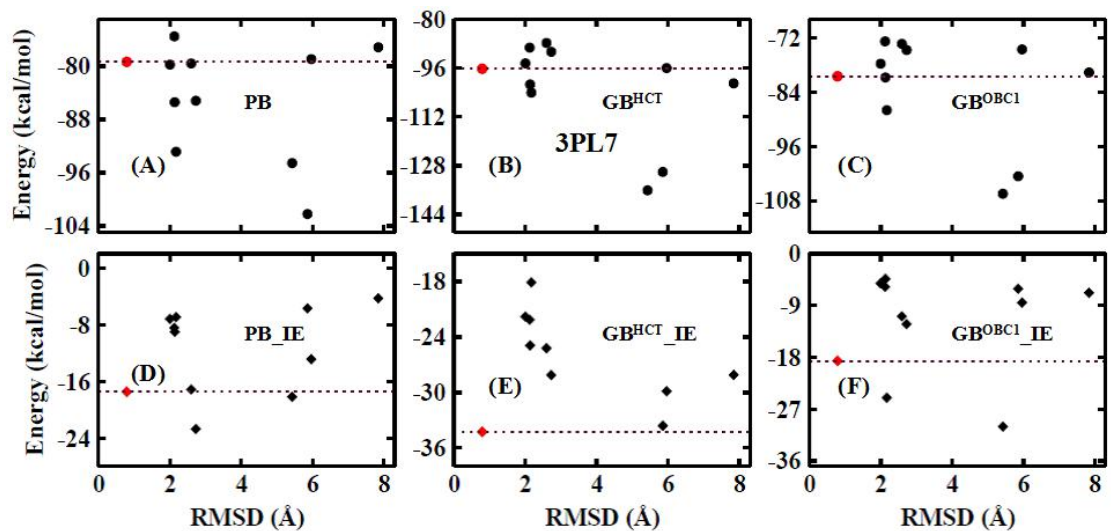


Figure S19 The same as Figure S6, but for 3PL7 system.