Supplementary Data

Figure caption

S1 RMSD versus MD simulation time (30 ns) of AChE and BuChE-ligand complexes. The conformation was recorded every 2 fs. RMSD values were calculated by comparing each of those conformations with the original conformation.

S2 RMSD versus MD simulation time (30 ns) of $A\beta_{1-40}$ peptide free dimer and $A\beta_{1-40}$ peptide dimer-ligand complexes at sites I and II. The conformation was recorded every 2 fs. RMSD values were calculated by comparing each of those conformations with the original conformation.

S3 3D representations of initial minimised $A\beta_{1-40}$ peptide dimer structure without ligand (left) and final 30 ns of MD simulations without ligand (right).

Table caption

S1 Contributions of various energy components to the binding free energy (kcal mol^{-1}) of AChE-Compound 2 complex (26–30 ns).

S2 Contributions of various energy components to the binding free energy (kcal mol^{-1}) of AChE-Tacrine complex (26–30 ns).

S3 Contributions of various energy components to the binding free energy (kcal mol^{-1}) of BuChE-Compound 2 complex (26–30 ns).

S4 Contributions of various energy components to the binding free energy (kcal mol^{-1}) of BuChE-Tacrine complex (26–30 ns).

S5 Docking study of compound 2 with the NMR structure of an $A\beta_{1-40}$ (PDB ID: 2LMN). Number of distinct conformational clusters found = 28, out of 100 runs, using rmsd-tolerance of 2.0 Å for amyloidogenic sites I and II.

S6 Docking study of myricetin with the NMR structure of an $A\beta_{1-40}$ (PDB ID: 2LMN). Number of distinct conformational clusters found = 22, out of 100 runs, using rmsd-tolerance of 2.0 Å for amyloidogenic sites I and II.

S7 Contributions of various energy components to the binding free energy (kcal $mol^{-1)}$ of $A\beta_{1-40}$ peptide dimer-compound 2 complex at Site I (20−25 ns).

S8 Contributions of various energy components to the binding free energy (kcal mol^{-1}) of $A\beta_{1-40}$ peptide dimer-myricetin complex at Site I (26−30 ns).

S9 Contributions of various energy components to the binding free energy (kcal mol^{-1}) of $A\beta_{1-40}$ peptide dimer-compound 2 complex at Site II (15−20 ns).

S10 Contributions of various energy components to the binding free energy (kcal mol^{-1}) of $A\beta_{1-40}$ peptide dimer–myricetin complex at Site II (26−30 ns).

S11 The interchain (chains A and B) binding free energy (kcal mol^{-1}) of $A\beta_{1-40}$ peptide free dimer (26−30 ns).

S12 The interchain (chains A and B) binding free energy (kcal mol^{-1}) of $A\beta_{1-40}$ peptide dimer-compound 2 complex at Site I (20−25 ns).

S13 The interchain (chains A and B) binding free energy (kcal mol^{-1}) of $A\beta_{1-40}$ peptide dimer-myricetin complex at Site I (26−30 ns).

S14 The interchain (chains A and B) binding free energy (kcal mol^{-1}) of $A\beta_{1-40}$ peptide dimer-compound 2 complex at Site II (15−20 ns).

S15 The interchain (chains A and B) binding free energy (kcal mol^{-1}) of $A\beta_{1-40}$ peptide dimer-myricetin complex at Site II (26−30 ns).

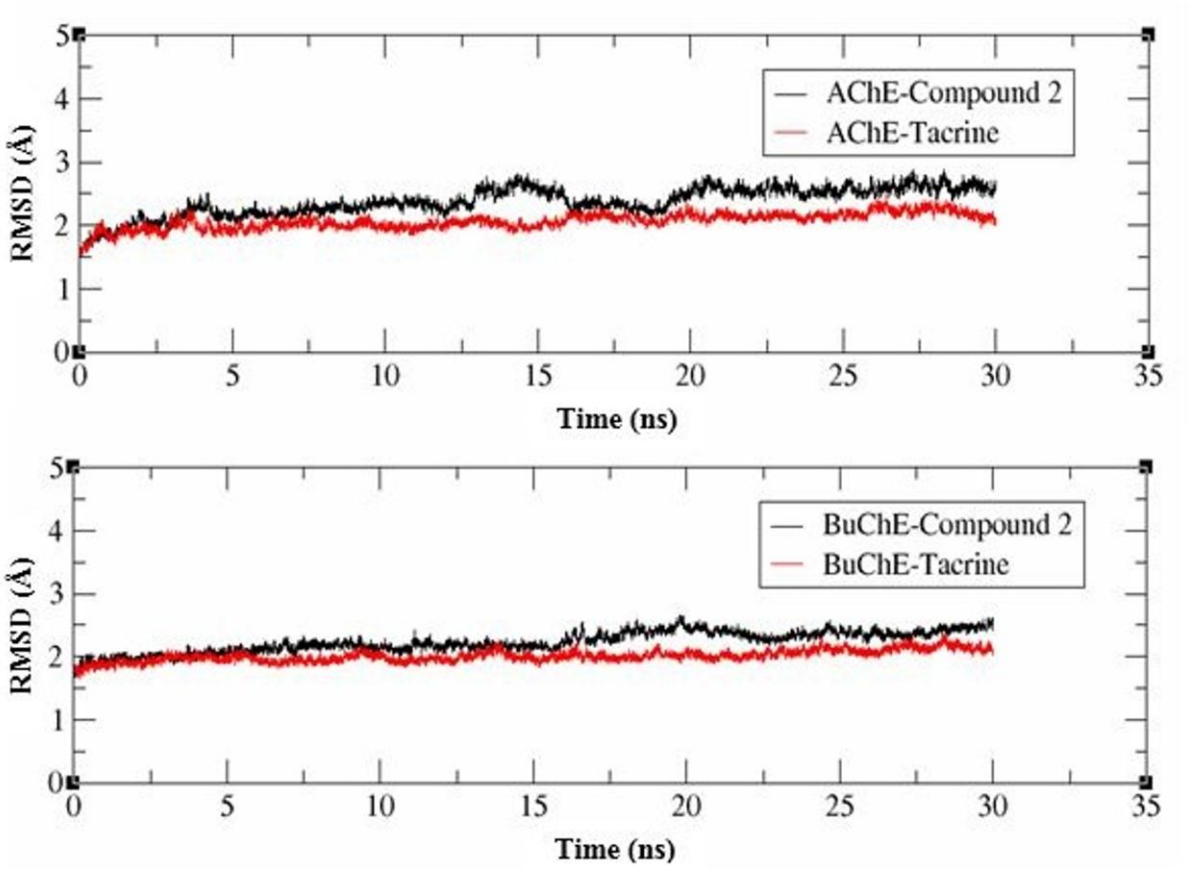
AChE-Compound 2
AChE-Tacrine
RMSD (Å)
Time (ns)
BuChE-Compound 2
BuChE-Tacrine
RMSD (Å)
Time (ns)

Figure S1

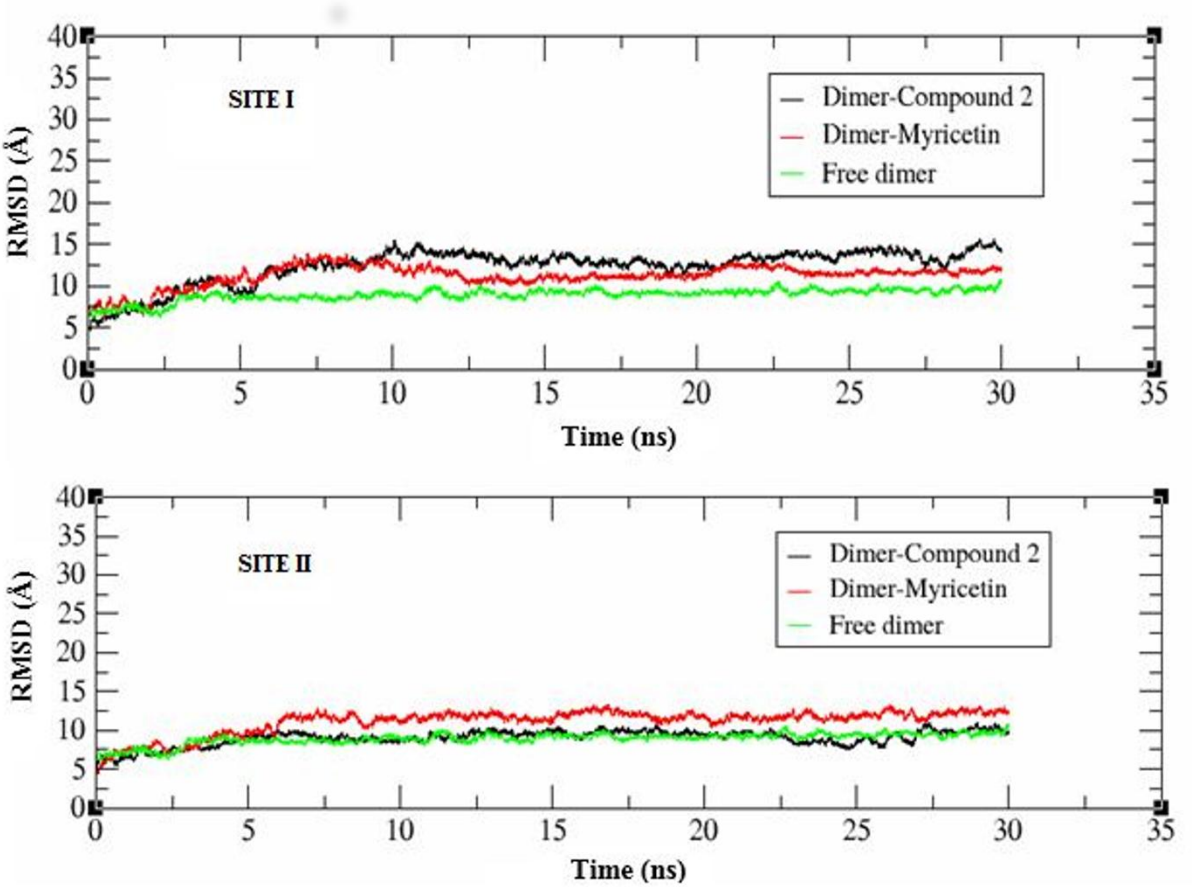

Figure S2

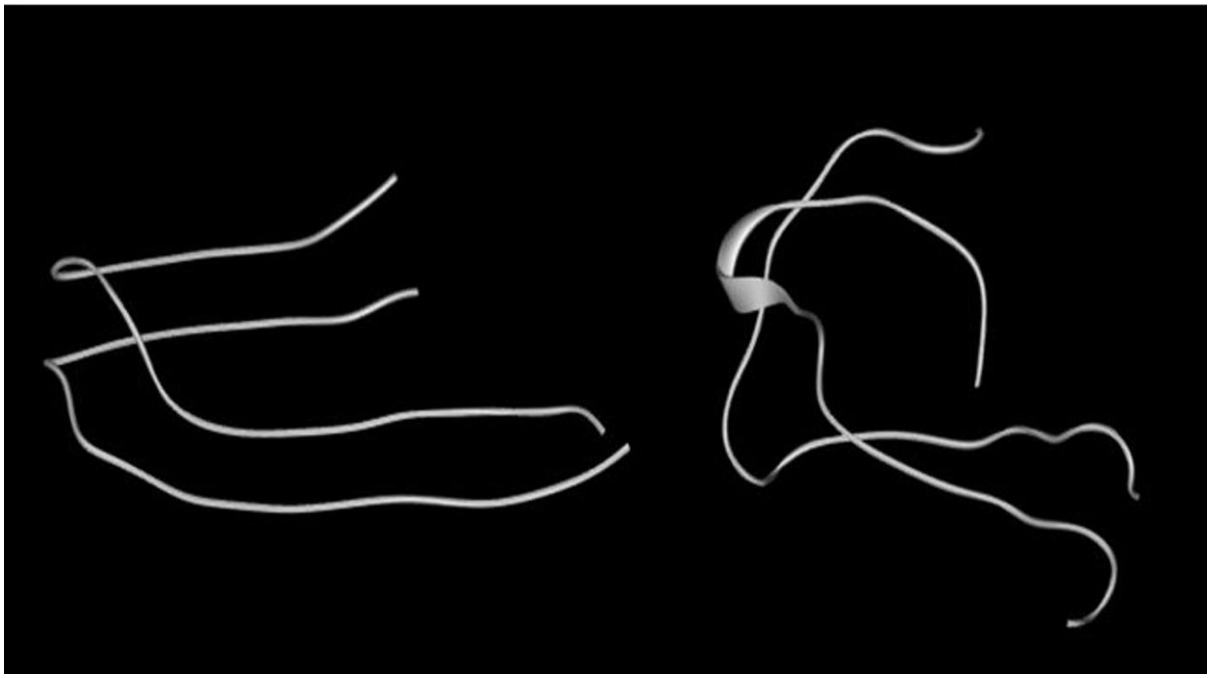

Figure S3

Table S1

PARAMETER	COMPLEX		RECEPTOR		LIGAND		DELTA	
	MEAN	STD	MEAN	STD	MEAN	STD	MEAN	STD
ELE	-17224.42	68.64	-17182.16	68.35	-21.74	0.67	-20.53	2.76
VDW	-2524.49	34.04	-2491.67	33.96	14.93	1.69	-47.75	2.37
INT	15074.78	63.50	15035.66	63.73	39.12	4.80	0.00	0.00
GAS	-4674.13	90.26	-4638.16	89.90	32.31	4.70	-68.28	3.16
PBSUR	146.89	1.16	149.43	1.17	4.65	0.05	-7.19	0.10
PBCAL	-4741.80	60.04	-4776.37	60.64	-27.69	0.51	62.25	5.12
PBSOL	-4594.91	59.39	-4626.93	60.00	-23.04	0.51	55.07	5.13
PBELE	-21966.22	43.01	-21958.52	42.80	-49.43	0.62	41.73	5.55
PBTOT	-9269.03	71.40	-9265.09	70.95	9.27	4.71	-13.21	5.09
GBSUR	104.91	1.24	106.77	1.23	2.54	0.03	-4.41	0.11
GB	-5015.12	59.41	-5028.91	59.26	-30.32	0.57	44.11	2.24
GBSOL	-4910.21	58.89	-4922.14	58.73	-27.78	0.56	39.71	2.20
GBELE	-22239.54	35.54	-22211.07	35.51	-52.06	0.53	23.59	1.53
GBTOT	-9584.34	66.42	-9560.30	66.23	4.53	4.72	-28.57	2.25

Table S2

PARAMETER	COMPLEX		RECEPTOR		LIGAND		DELTA	
	MEAN	STD	MEAN	STD	MEAN	STD	MEAN	STD
ELE	-17412.69	85.74	-17163.06	85.47	14.70	0.47	-264.34	11.94
VDW	-2503.88	34.67	-2485.36	34.58	10.87	1.19	-29.39	1.75
INT	15045.84	68.54	15010.93	68.51	34.91	3.74	-0.00	0.00
GAS	-4870.73	97.34	-4637.48	96.99	60.48	3.61	-293.73	12.00
PBSUR	147.62	1.16	148.70	1.17	3.04	0.02	-4.11	0.09
PBCAL	-4631.68	70.72	-4841.46	69.90	-60.94	0.45	270.73	10.58
PBSOL	-4484.05	70.15	-4692.76	69.32	-57.91	0.45	266.62	10.61
PBELE	-22044.37	42.81	-22004.52	42.52	-46.24	0.44	6.39	4.84
PBTOT	-9354.79	69.46	-9330.25	69.35	2.57	3.58	-27.11	4.67
GBSUR	105.28	1.23	106.04	1.22	1.44	0.01	-2.20	0.07
GB	-4876.48	69.28	-5087.54	69.11	-60.15	0.57	271.21	9.43
GBSOL	-4771.20	68.85	-4981.49	68.71	-58.72	0.57	269.01	9.39
GBELE	-22289.17	36.60	-22250.60	36.58	-45.45	0.61	6.88	3.25
GBTOT	-9641.93	67.35	-9618.98	67.38	1.76	3.57	-24.72	3.19

Table S3

PARAMETER	COMPLEX		RECEPTOR		LIGAND		DELTA	
	MEAN	STD	MEAN	STD	MEAN	STD	MEAN	STD
ELE	-15026.67	77.59	-14995.66	77.55	-26.64	1.33	-4.37	2.97
VDW	-2492.60	35.87	-2459.98	35.73	14.62	1.82	-47.25	2.49
INT	15307.41	67.16	15267.22	66.98	40.19	4.89	0.00	0.00
GAS	-2211.86	95.41	-2188.42	95.20	28.17	5.05	-51.62	4.10
PBSUR	151.51	1.05	153.77	1.06	4.60	0.05	-6.85	0.12
PBCAL	-5516.83	65.44	-5528.31	65.63	-26.82	0.98	38.30	4.77
PBSOL	-5365.31	65.35	-5374.54	65.56	-22.22	0.99	31.45	4.76
PBELE	-20543.49	39.81	-20523.97	39.31	-53.46	0.99	33.93	3.81
PBTOT	-7577.17	66.43	-7562.96	65.70	5.95	4.86	-20.17	3.97
GBSUR	100.10	1.31	101.71	1.34	2.52	0.02	-4.13	0.14
GB	-5767.87	65.08	-5768.03	65.05	-29.27	0.91	29.42	2.98
GBSOL	-5667.77	64.92	-5666.32	64.88	-26.75	0.91	25.30	2.92
GBELE	-20794.54	35.03	-20763.69	35.02	-55.90	0.89	25.05	1.40
GBTOT	-7879.63	65.06	-7854.74	64.69	1.43	4.92	-26.32	2.36

Table S4

PARAMETER	COMPLEX		RECEPTOR		LIGAND		DELTA	
	MEAN	STD	MEAN	STD	MEAN	STD	MEAN	STD
ELE	-15086.80	83.92	-14988.21	84.92	14.65	0.48	-113.23	9.55
VDW	-2503.23	34.38	-2485.87	34.43	10.91	1.22	-28.27	2.08
INT	15298.30	66.01	15263.26	65.78	35.04	3.98	-0.00	0.00
GAS	-2291.73	100.27	-2210.82	99.97	60.59	3.96	-141.50	9.78
PBSUR	150.88	1.13	152.03	1.13	3.04	0.02	-4.19	0.10
PBCAL	-5498.83	70.62	-5557.15	71.46	-60.84	0.46	119.17	6.86
PBSOL	-5347.94	70.23	-5405.12	71.07	-57.80	0.46	114.98	6.85
PBELE	-20585.62	39.13	-20545.36	39.04	-46.19	0.44	5.94	5.02
PBTOT	-7639.67	66.68	-7615.94	66.04	2.79	3.89	-26.52	5.32
GBSUR	98.22	1.38	98.89	1.36	1.44	0.01	-2.10	0.08
GB	-5709.25	72.34	-5772.39	73.48	-60.01	0.56	123.15	7.41
GBSOL	-5611.03	71.87	-5673.50	73.07	-58.57	0.56	121.04	7.40
GBELE	-20796.05	34.20	-20760.60	34.10	-45.36	0.66	9.91	3.20
GBTOT	-7902.76	65.80	-7884.32	65.32	2.02	3.93	-20.46	3.52

Table S5

Cluster Rank	Lowest Binding Energy	Run	Mean Binding Energy	Num in Clus	Histogram 5 10 15 20 25 30 35
1	-5.97	27	-5.69	24	######################### A(16-21) AMYLOIDOGENIC REGION 1 (SITE I:[Chain A(16-21)]
2	-5.41	55	-4.95	13	############A(16-21)
3	-5.07	61	-4.79	6	######AB(16-21)
4	-5.06	51	-4.71	2	##A(16-21)
5	-5.06	86	-4.98	8	########A(16-21)
6	-5.03	14	-4.57	2	##A(16-21)
7	-4.99	48	-4.65	2	##A(16-21)
8	-4.98	39	-4.90	3	###A(16-21)
9	-4.92	21	-4.92	1	#A(16-21)
10	-4.90	78	-4.67	2	##A(16-21)
11	-4.83	95	-4.83	1	#A(16-21)
12	-4.71	73	-4.71	1	# B(32-36) AMYLOIDOGENIC REGION 2 (SITE II:[Chain B(32-36)]
13	-4.66	20	-4.66	1	#
14	-4.64	2	-4.64	1	#
15	-4.61	65	-4.46	3	###
16	-4.60	96	-4.35	3	###
17	-4.57	10	-4.30	12	############
18	-4.51	23	-4.51	1	#
19	-4.31	7	-4.31	1	#
20	-4.10	97	-4.06	4	####
21	-4.00	43	-4.00	1	#
22	-3.99	4	-3.99	1	#
23	-3.95	69	-3.95	1	#
24	-3.94	91	-3.93	2	##
25	-3.88	99	-3.88	1	#
26	-3.85	56	-3.85	1	#
27	-3.79	17	-3.79	1	#
28	-3.59	19	-3.59	1	#

Table S6

Cluster Rank	Lowest Binding Energy	Run	Mean Binding Energy	Num in Clus	Histogram 5 10 15 20 25 30 35
1	-3.95	30	-3.64	7	#######
2	-3.92	20	-3.49	11	###########
3	-3.90	22	-3.90	1	#
4	-3.89	28	-3.58	29	############################ A(16-21) AMYLOIDOGENIC REGION 1 (SITE I):[Chain A(16-21)]
5	-3.80	97	-3.80	1	#
6	-3.73	89	-3.66	4	####
7	-3.66	70	-3.65	3	### B(32-36) AMYLOIDOGENIC REGION 2 (SITE II:[Chain B(32-36)]
8	-3.66	54	-3.48	2	##
9	-3.58	64	-3.47	19	##################
10	-3.56	47	-3.41	4	####
11	-3.52	79	-3.50	2	##
12	-3.49	16	-3.49	1	#
13	-3.46	88	-3.43	2	##
14	-3.44	81	-3.42	2	##
15	-3.27	69	-3.27	1	#
16	-3.26	78	-3.17	3	###
17	-3.25	35	-3.25	1	#
18	-3.14	37	-3.10	2	##
19	-3.02	63	-3.02	1	#
20	-2.68	40	-2.68	1	#
21	-2.61	41	-2.59	2	##
22	-2.59	75	-2.59	1	#

Table S7

PARAMETER	COMPLEX		RECEPTOR		LIGAND		DELTA	
	MEAN	STD	MEAN	STD	MEAN	STD	MEAN	STD
ELE	-998.15	32.40	-960.95	31.53	-28.01	1.32	-9.18	3.25
VDW	-100.61	11.05	-80.32	10.84	14.54	1.62	-34.83	2.46
INT	1729.48	24.24	1691.43	23.32	38.05	4.85	0.00	0.00
GAS	630.72	38.86	650.16	38.16	24.57	4.93	-44.01	4.31
PBSUR	44.89	0.92	45.62	0.99	4.75	0.05	-5.47	0.22
PBCAL	-1265.27	32.15	-1256.27	31.51	-33.91	0.97	24.92	3.47
PBSOL	-1220.37	31.95	-1210.65	31.28	-29.17	0.97	19.45	3.37
PBELE	-2263.42	12.53	-2217.22	11.94	-61.93	0.91	15.73	2.57
PBTOT	-589.65	24.30	-560.49	23.64	-4.60	4.77	-24.56	2.73
GBSUR	28.60	0.56	29.38	0.56	2.64	0.03	-3.42	0.17
GB	-1307.34	31.14	-1293.68	30.28	-37.04	0.99	23.38	3.60
GBSOL	-1278.74	30.97	-1264.30	30.10	-34.40	0.98	19.96	3.56
GBELE	-2305.49	10.13	-2254.63	10.04	-65.05	0.77	14.19	1.14
GBTOT	-648.02	24.42	-614.14	23.71	-9.83	4.82	-24.05	2.26

Table S8

PARAMETER	COMPLEX		RECEPTOR		LIGAND		DELTA	
	MEAN	STD	MEAN	STD	MEAN	STD	MEAN	STD
ELE	-984.59	29.08	-887.98	28.91	-37.92	2.04	-58.68	5.11
VDW	-130.27	13.65	-118.05	12.79	20.74	2.42	-32.97	3.98
INT	1729.84	23.06	1691.77	22.44	38.07	4.53	-0.00	0.00
GAS	614.98	34.54	685.74	33.89	20.89	4.41	-91.65	4.72
PBSUR	37.26	1.26	38.61	1.30	3.43	0.02	-4.78	0.10
PBCAL	-1259.39	25.82	-1284.20	25.91	-45.55	1.34	70.36	3.42
PBSOL	-1222.13	25.66	-1245.59	25.78	-42.12	1.34	65.58	3.42
PBELE	-2243.97	13.82	-2172.18	12.60	-83.47	1.26	11.68	4.40
PBTOT	-607.14	23.55	-559.85	22.88	-21.23	4.17	-26.07	3.67
GBSUR	23.77	0.88	25.25	0.92	2.03	0.01	-3.51	0.13
GB	-1305.73	25.77	-1326.73	25.87	-50.44	1.62	71.44	3.25
GBSOL	-1281.96	25.81	-1301.48	25.90	-48.41	1.62	67.93	3.21
GBELE	-2290.31	10.13	-2214.71	9.53	-88.36	1.21	12.76	3.29
GBTOT	-666.97	23.11	-615.74	22.63	-27.52	4.34	-23.72	3.17

Table S9

PARAMETER	COMPLEX		RECEPTOR		LIGAND		DELTA	
	MEAN	STD	MEAN	STD	MEAN	STD	MEAN	STD
ELE	-1116.43	28.44	-1106.53	26.94	-5.78	1.79	-4.11	3.92
VDW	-118.95	13.62	-113.24	14.44	14.09	1.65	-19.80	2.56
INT	1727.68	23.22	1688.69	23.14	38.99	4.85	-0.00	0.00
GAS	492.30	36.81	468.92	36.13	47.30	5.05	-23.91	4.22
PBSUR	42.65	0.89	41.55	1.05	4.76	0.04	-3.65	0.30
PBCAL	-1089.99	29.53	-1070.30	28.20	-29.14	1.77	9.45	4.12
PBSOL	-1047.34	29.03	-1028.76	27.54	-24.38	1.76	5.80	4.13
PBELE	-2206.42	12.94	-2176.84	13.32	-34.92	1.01	5.34	1.47
PBTOT	-555.04	22.15	-559.84	21.79	22.92	4.86	-18.12	2.21
GBSUR	26.58	0.67	26.03	0.78	2.61	0.02	-2.06	0.25
GB	-1141.52	27.71	-1120.75	26.44	-31.73	1.62	10.97	3.81
GBSOL	-1114.94	27.35	-1094.72	25.98	-29.13	1.61	8.91	3.84
GBELE	-2257.94	9.89	-2227.29	10.01	-37.51	0.86	6.86	0.97
GBTOT	-622.64	22.21	-625.80	22.01	18.17	4.92	-15.01	2.21

Table S10

PARAMETER	COMPLEX		RECEPTOR		LIGAND		DELTA	
	MEAN	STD	MEAN	STD	MEAN	STD	MEAN	STD
ELE	-1183.52	49.43	-1137.29	49.16	-42.96	3.84	-3.26	3.37
VDW	-127.02	12.90	-115.08	12.37	21.20	2.35	-33.14	2.37
INT	1735.39	22.44	1698.72	21.82	36.68	4.44	-0.00	0.00
GAS	424.85	54.42	446.34	54.16	14.91	5.55	-36.40	3.83
PBSUR	38.78	0.93	39.94	1.09	3.42	0.03	-4.59	0.30
PBCAL	-1097.53	48.32	-1075.97	48.34	-42.88	2.86	21.32	3.61
PBSOL	-1058.76	47.73	-1036.03	47.54	-39.45	2.86	16.73	3.55
PBELE	-2281.05	13.46	-2213.27	13.14	-85.84	1.32	18.06	2.32
PBTOT	-633.91	24.55	-589.69	23.90	-24.54	4.23	-19.67	2.55
GBSUR	24.36	0.63	25.31	0.62	2.03	0.01	-2.98	0.19
GB	-1143.08	45.34	-1118.42	46.27	-47.17	3.15	22.51	3.94
GBSOL	-1118.73	44.95	-1093.11	45.84	-45.14	3.14	19.53	3.90
GBELE	-2326.60	11.20	-2255.72	10.67	-90.14	1.24	19.25	2.18
GBTOT	-693.88	24.03	-646.77	23.22	-30.24	4.39	-16.87	2.31

Table S11

PARAMETER	DIMER		CHAIN A		CHAIN B		DELTA	
	MEAN	STD	MEAN	STD	MEAN	STD	MEAN	STD
ELE	-1077.91	35.25	-530.68	15.42	-499.13	25.07	-48.09	18.44
VDW	-115.00	10.94	3.38	7.60	8.86	6.81	-127.24	6.20
INT	1683.32	22.32	840.51	15.86	842.80	16.46	-0.00	0.00
GAS	490.41	38.79	313.22	21.51	352.53	27.56	-175.34	20.11
PBSUR	41.35	0.66	29.25	0.69	31.67	0.30	-19.57	0.60
PBCAL	-1133.05	31.16	-594.05	13.40	-620.06	22.28	81.05	17.04
PBSOL	-1091.70	30.89	-564.79	13.35	-588.39	22.19	61.48	16.77
PBELE	-2210.95	12.01	-1124.72	7.05	-1119.19	6.55	32.96	6.38
PBTOT	-601.29	21.97	-251.57	16.36	-235.86	15.87	-113.86	7.60
GBSUR	25.54	0.46	17.78	0.40	19.02	0.19	-11.27	0.44
GB	-1171.16	32.14	-612.85	13.51	-643.54	22.84	85.23	16.97
GBSOL	-1145.63	31.97	-595.07	13.41	-624.52	22.82	73.96	16.78
GBELE	-2249.07	9.49	-1143.53	6.15	-1142.67	5.79	37.13	4.80
GBTOT	-655.22	21.15	-281.85	15.98	-271.99	16.04	-101.38	6.63

Table S12

PARAMETER	DIMER		CHAIN A		CHAIN B		DELTA	
	MEAN	STD	MEAN	STD	MEAN	STD	MEAN	STD
ELE	-960.95	31.53	-434.27	33.76	-500.47	23.06	-26.21	21.87
VDW	-80.32	10.84	12.65	7.51	2.74	7.43	-95.70	6.13
INT	1691.43	23.32	843.07	15.91	848.36	16.37	-0.00	0.00
GAS	650.16	38.16	421.45	33.37	350.63	29.55	-121.92	21.19
PBSUR	45.62	0.99	32.01	0.53	29.87	0.79	-16.26	0.82
PBCAL	-1256.26	31.51	-679.96	29.67	-622.91	22.64	46.61	20.81
PBSOL	-1210.64	31.27	-647.95	29.81	-593.03	22.27	30.35	20.88
PBELE	-2217.21	11.93	-1114.24	7.64	-1123.37	7.63	20.40	5.66
PBTOT	-560.48	23.64	-226.50	16.19	-242.41	16.74	-91.57	6.30
GBSUR	29.38	0.56	19.52	0.32	18.66	0.48	-8.80	0.57
GB	-1293.68	30.28	-704.35	30.08	-643.90	22.27	54.58	20.18
GBSO	-1264.30	30.10	-684.84	30.17	-625.24	22.02	45.78	20.29
GBELE	-2254.63	10.04	-1138.63	6.74	-1144.37	6.59	28.37	4.53
GBTOT	-614.14	23.71	-263.39	16.24	-274.61	16.56	-76.14	5.53

Table S13

PARAMETER	DIMER		CHAIN A		CHAIN B		DELTA	
	MEAN	STD	MEAN	STD	MEAN	STD	MEAN	STD
ELE	-887.98	28.91	-430.82	17.62	-477.85	18.63	20.69	23.01
VDW	-118.86	12.80	-11.67	7.06	1.53	7.29	-108.72	7.02
INT	1691.42	22.31	848.38	16.13	843.03	15.48	0.00	0.00
GAS	684.57	33.66	405.89	22.98	366.71	22.69	-88.03	25.24
PBSUR	38.61	1.30	27.08	0.56	29.25	0.86	-17.72	0.85
PBCAL	-1284.21	25.90	-670.75	14.31	-637.98	15.65	24.52	21.60
PBSOL	-1245.60	25.77	-643.67	14.32	-608.74	15.81	6.81	21.44
PBELE	-2172.19	12.60	-1101.57	7.81	-1115.84	6.66	45.22	6.59
PBTOT	-561.02	22.81	-237.78	16.61	-242.03	15.48	-81.22	7.81
GBSUR	25.25	0.92	16.95	0.26	18.05	0.45	-9.74	0.59
GB	-1326.73	25.87	-694.11	15.13	-659.08	16.56	26.46	20.73
GBSOL	-1301.48	25.90	-677.16	15.11	-641.03	16.60	16.72	20.50
GBELE	-2214.71	9.53	-1124.93	6.30	-1136.93	5.75	47.15	4.82
GBTOT	-616.91	22.60	-271.27	16.31	-274.32	15.62	-71.31	8.12

Table S14

PARAMETER	DIMER		CHAIN A		CHAIN B		DELTA	
	MEAN	STD	MEAN	STD	MEAN	STD	MEAN	STD
ELE	-1106.53	26.94	-509.88	18.01	-585.78	14.61	-10.87	17.94
VDW	-113.24	14.44	15.57	7.11	2.96	8.54	-131.76	7.69
INT	1688.69	23.14	842.15	16.12	846.5	16.05	0.00	0.00
GAS	468.92	36.13	347.84	23.44	263.71	19.18	-142.63	21.45
PBSUR	41.55	1.05	32.82	0.40	29.14	0.61	-20.42	0.85
PBCAL	-1070.37	28.20	-606.96	15.81	-532.78	12.08	69.37	20.17
PBSOL	-1028.82	27.54	-574.14	15.62	-503.64	11.91	48.96	19.69
PBELE	-2176.90	13.32	-1116.85	6.11	-1118.56	7.24	58.50	9.45
PBTOT	-559.90	21.79	-226.30	15.46	-239.92	14.92	-93.68	8.38
GBSUR	26.03	0.78	19.72	0.24	18.11	0.48	-11.80	0.56
GB	-1120.75	26.44	-631.39	16.79	-552.33	12.88	62.97	17.51
GBSOL	-1094.72	25.98	-611.67	16.68	-534.22	12.77	51.16	17.22
GBELE	-2227.29	10.01	-1141.27	5.69	-1138.11	6.43	52.10	5.28
GBTOT	-625.80	22.01	-263.83	15.46	-270.51	15.16	-91.47	6.98

Table S15

PARAMETER	DIMER		CHAIN A		CHAIN B		DELTA	
	MEAN	STD	MEAN	STD	MEAN	STD	MEAN	STD
ELE	-1137.29	49.16	-457.79	14.47	-574.44	43.32	-105.06	20.28
VDW	-115.77	12.34	-5.86	7.75	-0.20	7.59	-109.71	5.10
INT	1697.96	21.92	850.85	15.76	847.10	15.66	-0.00	0.00
GAS	444.90	54.25	387.20	20.84	272.46	45.67	-214.77	19.33
PBSUR	39.94	1.09	28.46	0.74	28.26	0.49	-16.78	0.37
PBCAL	-1075.99	48.33	-662.32	12.29	-547.60	40.19	133.93	17.21
PBSOL	-1036.04	47.52	-633.86	12.02	-519.33	39.98	117.15	17.20
PBELE	-2213.28	13.16	-1120.11	6.83	-1122.04	7.89	28.87	8.85
PBTOT	-591.15	24.13	-246.65	16.04	-246.87	16.52	-97.62	9.09
GBSUR	25.31	0.62	17.74	0.37	17.43	0.35	-9.87	0.27
GB	-1118.42	46.27	-683.68	12.54	-572.15	40.95	137.41	17.50
GBSOL	-1093.11	45.84	-665.94	12.40	-554.72	40.72	127.54	17.49
GBELE	-2255.72	10.67	-1141.47	6.46	-1146.59	6.51	32.34	5.63
GBTOT	-648.22	23.48	-278.74	16.18	-282.25	16.28	-87.23	5.76

STD = Standard deviation; ELE = Electrostatic energy as calculated by the Molecular Mechanics (MM) force field; VDW = Van der Waals contribution from MM; INT = Internal energy arising from bond, angle, and dihedral terms in the MM force field (this term always amounts to zero in the single trajectory approach); GAS = Total gas phase energy (sum of ELE, VDW, and INT); PBSUR/GBSUR = Non-polar contribution to the solvation free energy calculated by an empirical model; PBCAL/GB = The electrostatic contribution to the solvation free energy calculated by PB or GB, respectively; PBSOL/GBSOL = Sum of non-polar and polar contributions to solvation; PBELE/GBELE = Sum of the electrostatic solvation free energy and MM electrostatic energy; PBTOT/GBTOT = Final estimated binding free energy calculated from the terms above (kcal mol^{-1}); DELTA = Equal to mean (complex) − [mean (ligand) + mean (receptor)]