Supporting Information

Predicting Relative Binding Affinity Using Non-equilibrium QM/MM Simulations

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Table S1: Calculated $\Delta G_{\mathrm{L,s}}^{\mathrm{MM}\rightarrow\mathrm{QM/MM}}$ for the bound and free states. Precisions in brackets in the second last column ($N_{\mathrm{trj}} = 100$) were obtained by bootstrapping.

L_i	state	N_{trj}										ref.[a]
		10	20	30	40	50	60	70	80	90	100	
Bz	Free	-554.9±1.3	-554.1±0.9	-554.4±0.7	-554.1±0.6	-553.8±0.6	-553.5±0.5	-553.6±0.5	-553.6±0.4	-553.6±0.4	-553.8±0.4(0.4)	-554.2±0.3
	Bound	-554.4±0.7	-554.0±0.5	-554.4±0.4	-554.3±0.3	-554.3±0.3	-554.4±0.3	-554.4±0.2	-554.2±0.2	-554.1±0.2	-554.0±0.2(0.2)	-554.8±0.3
MeBz	Free	-477.1±0.4	-477.6±0.3	-477.7±0.2	-478.0±0.3	-478.2±0.3	-478.4±0.3	-478.4±0.2	-478.3±0.2	-478.3±0.2	-478.6±0.3(0.3)	-478.8±0.3
	Bound	-478.0±0.7	-478.3±0.6	-478.1±0.5	-478.2±0.4	-477.9±0.3	-478.1±0.3	-478.2±0.3	-478.3±0.3	-478.4±0.2	-478.5±0.2(0.2)	-479.2±0.3
EtBz	Free	-677.4±0.4	-678.8±0.5	-679.6±0.7	-679.6±0.6	-679.6±0.5	-679.3±0.5	-679.5±0.4	-679.4±0.4	-679.3±0.4	-679.3±0.3(0.3)	-679.3±0.2
	Bound	-676.7±0.5	-676.3±0.4	-676.1±0.3	-676.2±0.3	-677.0±0.5	-676.9±0.4	-676.9±0.4	-677.0±0.3	-677.0±0.3	-676.9±0.3(0.3)	-677.4±0.3
pClBz	Free	-634.3±0.5	-635.2±0.6	-634.9±0.5	-635.0±0.4	-635.2±0.3	-635.1±0.3	-635.2±0.3	-635.1±0.3	-635.1±0.2	-635.2±0.2(0.3)	-635.9±0.3
	Bound	-640.0±0.4	-640.7±0.5	-640.7±0.4	-640.6±0.3	-640.3±0.3	-640.2±0.3	-640.2±0.2	-640.2±0.2	-640.2±0.2	-640.2±0.2(0.2)	-640.9±0.2
mClBz	Free	-557.2±0.6	-558.4±0.6	-559.8±0.8	-559.8±0.6	-559.8±0.5	-559.7±0.5	-559.5±0.4	-559.6±0.4	-559.6±0.4	-559.6±0.3(0.3)	-559.9±0.3
	Bound	-561.9±0.6	-561.8±0.5	-563.3±0.7	-563.4±0.5	-563.4±0.5	-563.4±0.4	-563.2±0.4	-563.1±0.4	-563.8±0.5	-563.7±0.4(0.4)	-564.0±0.3
Hx	Free	-698.9±0.4	-698.7±0.3	-698.5±0.2	-698.4±0.2	-698.3±0.2	-698.3±0.2	-698.4±0.1	-698.4±0.1	-698.4±0.1	-698.4±0.1(0.1)	-699.1±0.2
	Bound	-694.6±0.2	-695.2±0.2	-695.3±0.2	-695.2±0.2	-695.4±0.2	-695.7±0.2	-695.7±0.2	-695.7±0.2	-695.7±0.1	-695.8±0.1(0.1)	-696.1±0.2
MeHx	Free	-600.9±0.5	-601.6±0.3	-601.5±0.3	-601.4±0.2	-601.4±0.2	-601.3±0.2	-601.4±0.2	-601.5±0.1	-601.6±0.1	-601.6±0.1(0.1)	-602.0±0.3
	Bound	-602.3±0.5	-602.5±0.3	-602.5±0.3	-602.3±0.2	-602.4±0.2	-602.4±0.2	-602.3±0.2	-602.3±0.2	-602.2±0.2	-602.1±0.1(0.2)	-602.7±0.2
Pen	Free	-750.2±0.9	-749.9±0.5	-749.6±0.4	-749.5±0.3	-749.5±0.3	-749.6±0.2	-749.7±0.2	-749.6±0.2	-749.6±0.2	-749.6±0.2(0.2)	-749.7±0.2
	Bound	-746.8±0.5	-747.3±0.3	-747.2±0.2	-747.0±0.2	-746.9±0.2	-747.0±0.2	-746.9±0.2	-746.9±0.1	-746.9±0.1	-747.0±0.1(0.1)	-746.8±0.2
Hep	Free	-767.7±0.3	-767.7±0.2	-767.7±0.2	-767.7±0.2	-767.9±0.2	-768.0±0.2	-768.1±0.1	-768.1±0.1	-768.0±0.1	-768.0±0.1(0.1)	-768.5±0.3
	Bound	-767.3±0.4	-767.0±0.3	-766.6±0.3	-766.6±0.3	-766.6±0.3	-766.6±0.2	-766.6±0.2	-766.6±0.2	-766.6±0.2	-766.8±0.2(0.2)	-766.5±0.2

[a] Ref. 28, Table S1, four Λ values; for Bz and Hx averaged over four entries and for MeBz averaged over two entries.

Convergence criteria

In the main article, we selected the $\Delta\lambda$ and $N_{\rm ts}$ parameters by comparing with the previous RPQS results. However, in a typical application of this approach, such reference values are not available. Then other methods need to be used to determine whether the results are converged and reliable. Toward this end, we have tested five measures that has previously been used to check the convergence of MM and MM→QM/MM FEP calculations,[1–4] viz., the standard deviation of the non-equilibrium work distribution σ, the reweighting entropy S_w,[5] the maximum weight $w_{\rm max}$, Kish's effective sampling size Q' and Wu and Kofke's bias metrics (Π).[6] S_w, $w_{\rm max}$ and Q' range from 0 to 1. The larger S_w, Q' and Π are, the more reliable the results will be, whereas for $w_{\rm max}$ and σ, smaller values are better.

The values of these quantities are listed in Table S2 for MeBz in the free state with $N_{\rm trj} = 100$. They clearly show that with fixed $\Delta\lambda$, increasing $N_{\rm ts}$ makes the calculations more reliable, with σ and $w_{\rm max}$ decreasing and S_w, Q' and Π increasing. With a fixed total simulation time, in general, the smaller $\Delta\lambda$ is better. For instance, $\Delta\lambda = 0.01/N_{\rm ts} = 300$ has the same computational expense as $\Delta\lambda = 0.005/N_{\rm ts} = 150$, but the latter combination gave a better result with larger S_w, Q' and Π, and smaller σ and $w_{\rm max}$. Likewise, comparing $\Delta\lambda = 0.01/N_{\rm ts} = 500$ with $\Delta\lambda = 0.005/N_{\rm ts} = 250$, the advantage of a small $\Delta\lambda$ is also obvious. However, for small $N_{\rm ts}$ ($N_{\rm ts} = 200/\Delta\lambda = 0.01$ and $N_{\rm ts} = 100/\Delta\lambda = 0.005$), the advantage of small $\Delta\lambda$ is less clear (σ is smaller, but $w_{\rm max}$ is larger and Q' is smaller). Moreover, it is hard to select proper values for the mClBz simulation based on the values in Table S3, as the simulation with $N_{\rm ts} = 500$ seems to give worse results than that with $N_{\rm ts} = 200$.

Finally, Table S4 shows the convergence measures for the $\Delta G_{\rm L,s}^{\rm MM\rightarrow QM/MM}$ calculations for all the other ligands. It can be seen that the results for the non-aromatic ligands are appreciably better converged than for the aromatic ligands. Among the aromatic ligands, the convergence is better for MeBz and pClBz than for Bz and EtBz. Moreover, the result converges faster for the ligands in the free state and that in the bound state. The correlation

of the various measures are shown in Figure S2. For a general use, some indication of proper parameters seem to obtained with the following criteria: $\sigma < 0.8\ RT$, $S_w > 0.9$, $Q' > 0.4$ and $\Pi > 1.3$.

References

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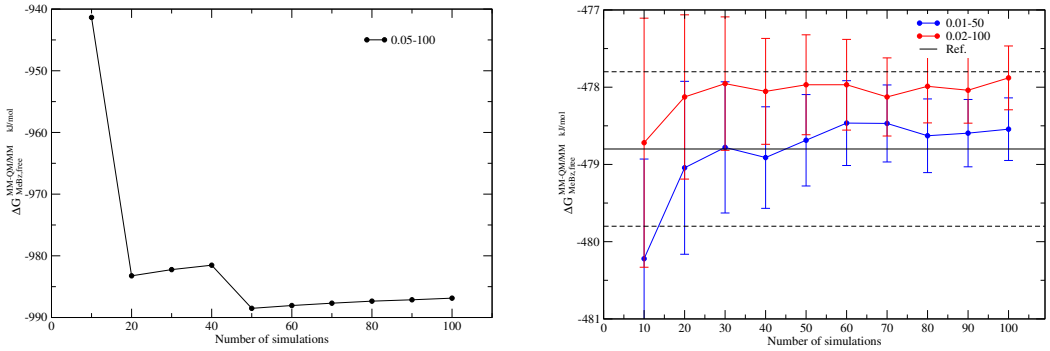

Figure S1: Calculated $\Delta G^{\mathrm{MM}\rightarrow\mathrm{QM/MM}}_{\mathrm{MeBz,free}}$ with $\Delta\lambda = 0.05$ and $\mathrm{N_{ts}} = 100$.

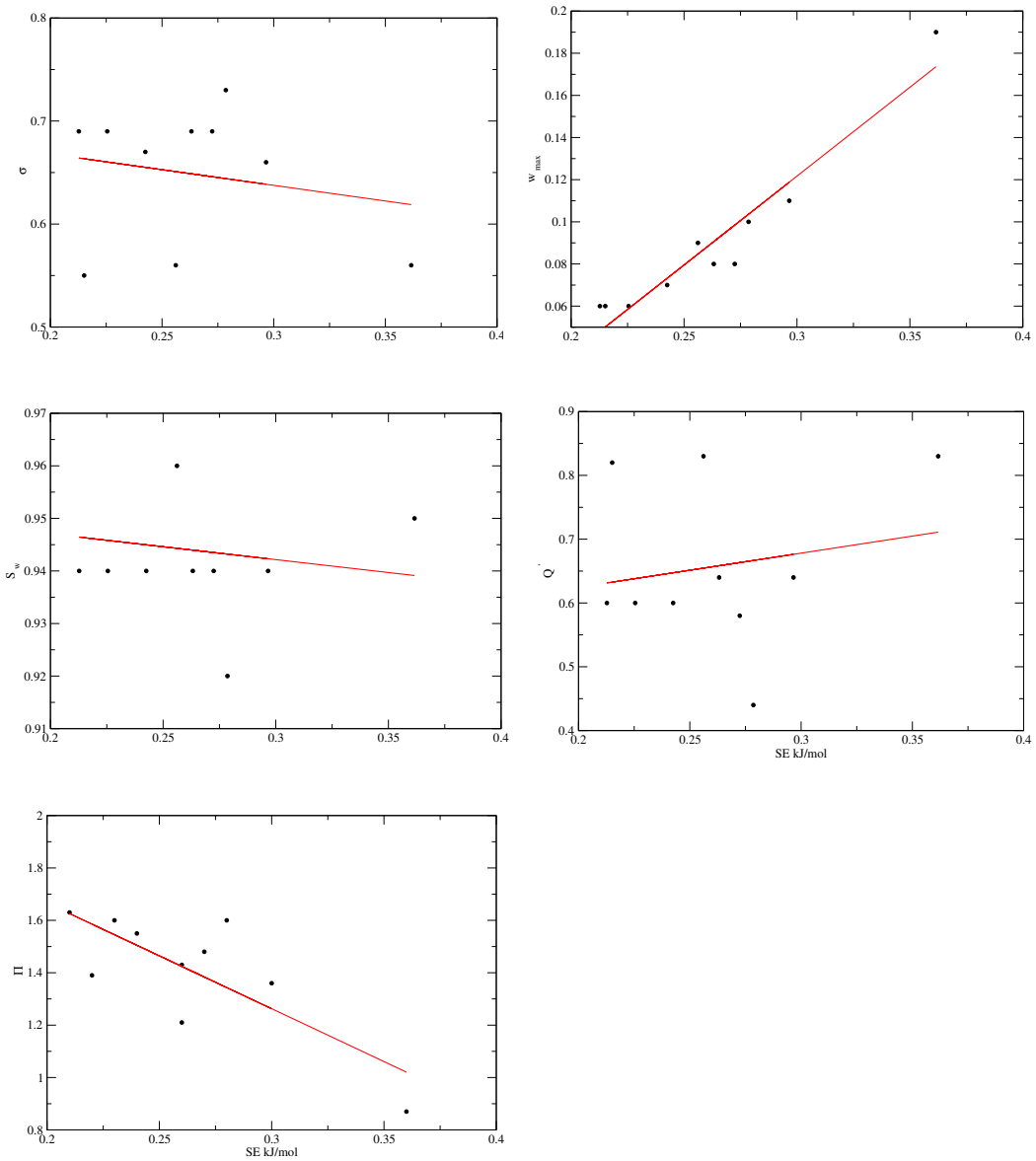

Figure S2: The correlation between standard error and five convergence criteria for the calculations of MeBz at free state with $\Delta\lambda$=0.005, N_{ts}=100.

Table S2: Convergence criteria for $\Delta G^{\mathrm{MM}\rightarrow\mathrm{QM/MM}}_{\mathrm{MeBz,free}}$ with different combinations of $\Delta\lambda$ and N_{ts}. N_{trj} is fixed to 100 and σ has units of RT.

$\Delta\lambda$	N_{ts}	σ	w_{max}	S_w	Q'	Π
0.05	100	8.74±0.61	0.92±0.26	0.08±0.10	0.01±0.01	-3.74±0.29
0.02	100	1.32±0.09	0.10±0.02	0.82±0.02	0.27±0.04	1.04 ±0.08
0.01	50	20.07±6.81	0.11±0.02	0.84±0.02	0.27±0.06	-0.51±0.70
	100	1.05±0.08	0.15±0.04	0.85±0.03	0.25±0.09	1.24± 0.11
	200	0.94±0.06	0.05±0.01	0.91±0.01	0.50±0.04	1.45± 0.05
	300	0.77±0.06	0.06±0.01	0.93±0.01	0.55±0.05	1.58± 0.05
	500	0.74±0.05	0.05±0.01	0.94±0.01	0.59±0.05	1.63± 0.05
0.005	100	0.73±0.06	0.10±0.02	0.92±0.02	0.44±0.11	1.60± 0.09
	150	0.71±0.05	0.05±0.01	0.94±0.01	0.60±0.05	1.66± 0.05
	200	0.68±0.05	0.05±0.01	0.95±0.01	0.66±0.04	1.70± 0.04
	250	0.59±0.04	0.03±0.00	0.96±0.01	0.72±0.02	1.78± 0.03

Table S3: Convergence criteria for $\Delta G^{\mathrm{MM}\rightarrow\mathrm{QM/MM}}_{\mathrm{mClBz,bound}}$ with different combinations of $\Delta\lambda$ and N_{ts}. N_{trj} is fixed to 100 and σ has units of RT.

$\Delta\lambda$	N_{ts}	σ	w_{max}	S_w	Q'	Π
0.005	100	1.07±0.07	0.12±0.03	0.85±0.03	0.28±0.07	1.24±0.09
	200	0.93±0.06	0.08±0.01	0.89±0.02	0.39±0.05	1.39±0.07
	500	1.02±0.08	0.13±0.03	0.84±0.03	0.25±0.06	1.23±0.10
	1000	0.79±0.05	0.05±0.01	0.93±0.01	0.55±0.04	1.57±0.05

Table S4: Convergence criteria for $\Delta G_{L_i,s}^{\mathrm{MM}\to\mathrm{QM/MM}}$ shown in Fig. 4 with $N_{\mathrm{trj}} = 100$. σ has units of RT.

guest molecule	free					bound				
	σ	$w_{\max}$	S_w	Q'	Π	σ	$w_{\max}$	S_w	Q'	Π
Bz	0.97	0.10	0.86	0.29	1.31	0.91	0.04	0.93	0.56	1.48
MeBz	0.73	0.10	0.92	0.44	1.60	0.82	0.05	0.93	0.56	1.57
EtBz	0.93	0.09	0.89	0.38	1.40	0.79	0.07	0.90	0.39	1.50
pClBz	0.81	0.05	0.93	0.52	1.55	0.60	0.05	0.96	0.67	1.76
mClBz	0.99	0.10	0.88	0.37	1.35	1.07	0.12	0.85	0.28	1.24
Hx	0.47	0.03	0.98	0.82	1.91	0.53	0.03	0.97	0.75	1.84
MeHx	0.53	0.03	0.97	0.77	1.84	0.59	0.03	0.96	0.74	1.79
Pen	0.56	0.05	0.97	0.71	1.81	0.58	0.04	0.97	0.77	1.82
Hep	0.47	0.03	0.98	0.81	1.90	0.62	0.04	0.96	0.67	1.74

Table S5: Convergence criteria for $\Delta G^{\mathrm{MM}\to\mathrm{QM/MM}}_{\mathrm{MeBz,free}}$ shown in Fig. 3 with $N_{\mathrm{trj}} = 100$. σ has units of RT.

N_{trj}	0.01–100					0.01–200					0.01–300					0.01–500				
	σ	$w_{\max}$	S_w	Q'	Π	σ	$w_{\max}$	S_w	Q'	Π	σ	$w_{\max}$	S_w	Q'	Π	σ	$w_{\max}$	S_w	Q'	Π
10	0.44	0.22	0.95	0.81	0.93	1.28	0.35	0.79	0.47	0.24	0.50	0.24	0.94	0.76	0.87	0.75	0.43	0.81	0.43	0.53
20	0.86	0.26	0.83	0.39	0.76	1.04	0.18	0.89	0.58	0.80	0.60	0.13	0.95	0.77	1.16	0.75	0.27	0.86	0.44	0.89
30	0.88	0.15	0.86	0.44	0.96	0.99	0.13	0.91	0.59	1.00	0.64	0.13	0.94	0.65	1.26	0.77	0.15	0.91	0.55	1.11
40	0.90	0.12	0.88	0.45	1.09	0.98	0.10	0.90	0.53	1.10	0.66	0.09	0.94	0.64	1.35	0.77	0.11	0.92	0.55	1.23
50	0.90	0.09	0.90	0.50	1.20	0.95	0.08	0.91	0.54	1.21	0.68	0.09	0.93	0.58	1.40	0.79	0.09	0.91	0.52	1.29
60	0.97	0.15	0.87	0.36	1.17	0.97	0.07	0.91	0.52	1.25	0.74	0.07	0.93	0.60	1.45	0.77	0.07	0.92	0.54	1.39
70	0.97	0.12	0.88	0.37	1.24	0.94	0.06	0.91	0.52	1.33	0.73	0.06	0.93	0.59	1.50	0.74	0.07	0.93	0.55	1.48
80	1.00	0.10	0.88	0.39	1.26	0.95	0.06	0.91	0.52	1.37	0.73	0.05	0.94	0.60	1.55	0.73	0.05	0.94	0.59	1.55
90	1.06	0.16	0.84	0.25	1.29	0.95	0.05	0.91	0.51	1.41	0.73	0.05	0.94	0.59	1.59	0.73	0.05	0.94	0.59	1.60
100	1.05	0.15	0.85	0.25	1.24	0.94	0.05	0.91	0.50	1.45	0.77	0.06	0.93	0.55	1.58	0.74	0.05	0.94	0.59	1.63
	0.005–100					0.005–150					0.005–200					0.005–250				
10	0.56	0.19	0.95	0.83	0.87	0.84	0.32	0.84	0.53	0.51	0.49	0.22	0.95	0.79	0.88	0.66	0.22	0.93	0.75	0.77
20	0.56	0.09	0.96	0.83	1.21	0.67	0.17	0.92	0.62	1.03	0.62	0.15	0.93	0.69	1.09	0.67	0.10	0.95	0.77	1.11
30	0.55	0.06	0.97	0.82	1.39	0.66	0.13	0.93	0.62	1.21	0.69	0.15	0.92	0.57	1.18	0.67	0.08	0.94	0.71	1.25
40	0.66	0.11	0.94	0.64	1.36	0.66	0.09	0.94	0.65	1.35	0.65	0.12	0.93	0.60	1.34	0.65	0.06	0.95	0.72	1.38
50	0.69	0.08	0.94	0.64	1.43	0.64	0.08	0.94	0.65	1.45	0.61	0.10	0.94	0.62	1.47	0.63	0.05	0.95	0.71	1.48
60	0.69	0.08	0.94	0.58	1.48	0.66	0.07	0.94	0.65	1.51	0.64	0.08	0.94	0.62	1.52	0.61	0.04	0.95	0.71	1.57
70	0.67	0.07	0.94	0.60	1.55	0.70	0.06	0.94	0.64	1.54	0.63	0.07	0.95	0.64	1.59	0.59	0.04	0.96	0.71	1.64
80	0.69	0.06	0.94	0.60	1.60	0.68	0.06	0.95	0.64	1.61	0.69	0.06	0.95	0.63	1.59	0.59	0.03	0.96	0.72	1.70
90	0.69	0.06	0.94	0.60	1.63	0.68	0.05	0.95	0.65	1.66	0.68	0.05	0.95	0.64	1.65	0.60	0.03	0.96	0.72	1.74
100	0.73	0.10	0.92	0.44	1.60	0.71	0.05	0.94	0.60	1.66	0.68	0.05	0.95	0.66	1.70	0.58	0.03	0.96	0.72	1.78

Table S6: Convergence criteria for $\Delta G_{L_i,s}^{\mathrm{MM}\to\mathrm{QM/MM}}$ shown in Fig. 4 with $N_{\mathrm{trj}} = 100$. σ has units of RT.

guest molecule	N_{trj}	free					bound				
		σ	$w_{\max}$	S_w	Q'	Π	σ	$w_{\max}$	S_w	Q'	Π
Bz	10	1.21	0.57	0.64	0.28	0.07	0.83	0.33	0.85	0.54	0.54
	20	1.09	0.38	0.75	0.27	0.52	1.01	0.20	0.87	0.51	0.77
	30	1.08	0.23	0.78	0.28	0.71	0.95	0.11	0.91	0.61	1.05
	40	1.02	0.19	0.81	0.28	0.89	0.88	0.09	0.92	0.62	1.21
	50	0.95	0.17	0.82	0.27	1.04	0.88	0.07	0.93	0.62	1.30
	60	0.96	0.16	0.83	0.26	1.10	0.88	0.06	0.93	0.60	1.35
	70	0.98	0.14	0.84	0.28	1.16	0.85	0.05	0.93	0.59	1.43
	80	0.96	0.12	0.86	0.30	1.25	0.86	0.05	0.93	0.57	1.49
	90	0.96	0.10	0.87	0.32	1.31	0.86	0.04	0.93	0.57	1.47
	100	0.97	0.10	0.86	0.29	1.31	0.91	0.04	0.93	0.56	1.46
MeBz	10	0.56	0.19	0.95	0.83	0.87	0.73	0.28	0.87	0.59	0.62
	20	0.56	0.09	0.96	0.83	1.21	0.86	0.25	0.85	0.45	0.87
	30	0.55	0.06	0.97	0.82	1.39	0.74	0.18	0.90	0.49	1.11
	40	0.66	0.11	0.94	0.64	1.36	0.73	0.13	0.92	0.55	1.27
	50	0.69	0.08	0.94	0.64	1.43	0.75	0.12	0.92	0.53	1.34
	60	0.69	0.08	0.94	0.58	1.48	0.85	0.10	0.91	0.48	1.32
	70	0.67	0.07	0.94	0.60	1.55	0.82	0.08	0.92	0.51	1.41
	80	0.69	0.06	0.94	0.60	1.60	0.81	0.07	0.93	0.54	1.49
	90	0.69	0.06	0.94	0.60	1.66	0.79	0.06	0.94	0.57	1.56
	100	0.73	0.10	0.92	0.44	1.60	0.82	0.05	0.93	0.56	1.57
EtBz	10	0.61	0.19	0.94	0.80	0.82	0.68	0.22	0.91	0.71	0.72
	20	0.78	0.17	0.90	0.59	0.95	0.75	0.14	0.91	0.62	0.97
	30	1.08	0.26	0.81	0.31	0.77	0.68	0.10	0.93	0.64	1.21
	40	1.04	0.19	0.82	0.30	0.90	0.66	0.07	0.94	0.65	1.35
	50	0.99	0.16	0.85	0.33	1.05	0.79	0.14	0.88	0.38	1.22
	60	0.98	0.15	0.85	0.32	1.14	0.80	0.12	0.88	0.37	1.28
	70	0.98	0.12	0.86	0.34	1.20	0.78	0.10	0.90	0.40	1.38
	80	0.93	0.11	0.88	0.35	1.29	0.80	0.09	0.90	0.39	1.41
	90	0.92	0.10	0.88	0.35	1.39	0.82	0.08	0.89	0.38	1.43
	100	0.93	0.09	0.89	0.38	1.40	0.79	0.07	0.90	0.39	1.50
pClBz	10	0.61	0.20	0.92	0.74	0.78	0.58	0.23	0.93	0.76	0.81
	20	0.88	0.27	0.85	0.43	0.80	0.72	0.19	0.90	0.57	0.97
	30	0.76	0.20	0.90	0.47	1.10	0.71	0.13	0.91	0.57	1.16
	40	0.74	0.15	0.91	0.51	1.25	0.67	0.10	0.93	0.60	1.32
	50	0.74	0.11	0.93	0.58	1.37	0.69	0.09	0.93	0.58	1.30
	60	0.74	0.09	0.93	0.55	1.42	0.66	0.08	0.94	0.60	1.50
	70	0.78	0.08	0.93	0.54	1.45	0.64	0.07	0.95	0.63	1.59
	80	0.78	0.07	0.93	0.54	1.50	0.61	0.06	0.95	0.65	1.66
	90	0.79	0.06	0.93	0.53	1.53	0.62	0.05	0.96	0.66	1.71
	100	0.81	0.05	0.93	0.52	1.55	0.60	0.05	0.96	0.67	1.76
mClBz	10	0.79	0.24	0.89	0.65	0.64	1.10	0.25	0.89	0.67	0.50
	20	0.90	0.23	0.86	0.47	0.81	1.22	0.22	0.81	0.40	0.57
	30	1.13	0.30	0.75	0.24	0.65	1.23	0.25	0.80	0.31	0.70
	40	1.10	0.22	0.80	0.27	0.83	1.13	0.23	0.81	0.28	0.85
	50	1.08	0.18	0.82	0.30	0.95	1.10	0.19	0.82	0.29	0.96
	60	1.02	0.16	0.84	0.31	1.08	1.08	0.17	0.84	0.29	1.06
	70	0.99	0.14	0.85	0.31	1.17	1.07	0.16	0.84	0.28	1.13
	80	0.97	0.12	0.87	0.34	1.26	1.09	0.15	0.84	0.27	1.15
	90	0.96	0.11	0.88	0.36	1.33	1.08	0.14	0.84	0.27	1.18
	100	0.99	0.10	0.88	0.37	1.35	1.07	0.12	0.85	0.28	1.24

guest molecule	N_{trj}	free					bound				
		σ	$w_{\max}$	S	Q'	Π	σ	$w_{\max}$	S_w	Q'	Π
Hx	10	0.47	0.23	0.94	0.77	0.89	0.21	0.14	0.99	0.96	1.18
	20	0.52	0.12	0.96	0.81	1.22	0.36	0.11	0.98	0.87	1.35
	30	0.51	0.09	0.97	0.80	1.40	0.42	0.08	0.97	0.82	1.46
	40	0.53	0.07	0.97	0.79	1.51	0.44	0.06	0.97	0.82	1.58
	50	0.53	0.06	0.97	0.78	1.59	0.48	0.06	0.97	0.78	1.62
	60	0.51	0.05	0.97	0.80	1.68	0.52	0.06	0.96	0.74	1.65
	70	0.49	0.04	0.97	0.82	1.76	0.51	0.05	0.97	0.76	1.72
	80	0.47	0.03	0.98	0.83	1.83	0.51	0.04	0.97	0.77	1.78
	90	0.47	0.03	0.98	0.82	1.87	0.51	0.04	0.97	0.76	1.82
	100	0.47	0.03	0.98	0.82	1.91	0.53	0.03	0.97	0.75	1.84
MeHx	10	0.42	0.17	0.97	0.87	0.98	0.51	0.29	0.92	0.69	0.83
	20	0.55	0.12	0.95	0.73	1.16	0.53	0.13	0.95	0.74	1.17
	30	0.51	0.08	0.96	0.76	1.38	0.56	0.09	0.96	0.76	1.35
	40	0.49	0.06	0.97	0.78	1.52	0.54	0.07	0.96	0.76	1.49
	50	0.54	0.05	0.96	0.75	1.56	0.56	0.06	0.96	0.75	1.55
	60	0.52	0.04	0.97	0.77	1.66	0.57	0.05	0.96	0.74	1.61
	70	0.53	0.04	0.97	0.77	1.71	0.55	0.04	0.96	0.75	1.69
	80	0.51	0.04	0.97	0.77	1.77	0.55	0.04	0.97	0.75	1.74
	90	0.51	0.03	0.97	0.78	1.82	0.58	0.03	0.96	0.74	1.76
	100	0.53	0.03	0.97	0.77	1.84	0.59	0.03	0.96	0.74	1.79
Pen	10	0.70	0.42	0.83	0.45	0.57	0.66	0.20	0.92	0.74	0.76
	20	0.59	0.25	0.91	0.53	1.06	0.61	0.10	0.95	0.79	1.16
	30	0.60	0.18	0.92	0.55	1.25	0.57	0.07	0.96	0.79	1.35
	40	0.56	0.14	0.94	0.58	1.41	0.64	0.06	0.96	0.75	1.41
	50	0.58	0.11	0.94	0.60	1.49	0.59	0.05	0.96	0.77	1.54
	60	0.55	0.09	0.95	0.65	1.60	0.58	0.04	0.97	0.78	1.63
	70	0.57	0.08	0.96	0.68	1.66	0.55	0.03	0.97	0.79	1.71
	80	0.58	0.07	0.96	0.69	1.71	0.59	0.03	0.97	0.79	1.74
	90	0.57	0.06	0.96	0.69	1.76	0.58	0.03	0.97	0.79	1.79
	100	0.56	0.05	0.97	0.71	1.81	0.58	0.04	0.97	0.77	1.82
Hep	10	0.35	0.17	0.98	0.90	1.04	0.52	0.21	0.94	0.76	0.85
	20	0.40	0.09	0.98	0.88	1.33	0.56	0.12	0.94	0.73	1.15
	30	0.48	0.09	0.97	0.82	1.44	0.59	0.09	0.94	0.68	1.29
	40	0.49	0.07	0.97	0.82	1.55	0.66	0.08	0.94	0.65	1.35
	50	0.50	0.06	0.97	0.79	1.62	0.67	0.06	0.94	0.66	1.44
	60	0.49	0.05	0.97	0.80	1.70	0.64	0.05	0.95	0.67	1.54
	70	0.50	0.04	0.97	0.80	1.75	0.61	0.05	0.95	0.69	1.62
	80	0.49	0.04	0.97	0.80	1.81	0.59	0.04	0.96	0.71	1.70
	90	0.48	0.03	0.98	0.80	1.86	0.61	0.03	0.96	0.70	1.72
	100	0.47	0.03	0.98	0.81	1.90	0.62	0.04	0.96	0.67	1.74