Table S3. List of the outliers.

Name	ΔE_{QM}	AL		AE		AT		F94		F03	
		ΔE_{MM}	RES	ΔE_{MM}	RES	ΔE_{MM}	RES	ΔE_{MM}	RES	ΔE_{MM}	RES
π-π Interaction (13 pairs)											
trp_trp_4	-13.48	-9.24	4.24	-9.24	4.24	-9.25	4.23	-7.79	5.69	-8.56	4.92
tyr_tyr_3	-7.66	-4.26	3.41	-4.21	3.45	-4.25	3.41	-3.59	4.07	-3.60	4.06
tyr_trp_2	-8.57	-5.23	3.34	-5.19	3.38	-5.23	3.34	-4.67	3.90	-4.71	3.86
tyr_tyr_5	-10.01	-6.68	3.33	-6.60	3.41	-6.68	3.33	-6.24	3.77	-6.39	3.62
phe_tyr_7	-8.13	-4.92	3.20	-4.90	3.23	-4.93	3.20	-4.43	3.70	-4.54	3.59
phe_trp_5	-10.58	-7.48	3.11	-7.50	3.08	-7.49	3.09	-6.46	4.12	-6.95	3.63
phe_trp_6	-10.48	-7.38	3.10	-7.40	3.08	-7.39	3.09	-6.35	4.13	-6.84	3.63
phe_trp_1	-7.60	-4.56	3.05	-4.56	3.05	-4.56	3.04	-4.16	3.45	-4.29	3.32
tyr_tyr_6	-9.65	-6.81	2.85	-6.79	2.86	-6.81	2.84	-6.61	3.04	-6.70	2.95
phe_phe_4	-6.96	-4.13	2.83	-4.09	2.87	-4.13	2.83	-3.56	3.40	-3.73	3.23
tyr_trp_4	-8.19	-5.61	2.59	-5.57	2.62	-5.60	2.59	-5.00	3.20	-4.93	3.26
phe_trp_2	-9.63	-7.05	2.58	-7.09	2.54	-7.06	2.57	-6.30	3.33	-6.74	2.89
phe_trp_4	-6.27	-3.72	2.55	-3.72	2.55	-3.73	2.54	-3.67	2.60	-3.59	2.68
H-Bonding (4 pairs)											
thr_asp_2	-19.55	-22.93	3.38	-22.66	3.11	-23.58	4.03	-17.37	2.19	-17.59	1.96
thr_asp_1	-19.55	-22.93	3.38	-22.65	3.10	-23.57	4.02	-17.36	2.18	-17.59	1.96
ser_glu_1	-19.36	-21.62	2.26	-21.93	2.56	-22.82	3.46	-17.08	2.28	-17.75	1.61
ser_glu_2	-19.37	-21.62	2.26	-21.93	2.56	-22.82	3.46	-17.08	2.28	-17.76	1.61
n-σ* Interaction (9 pairs)											
glu_phe_1	-7.21	-2.22	4.99	-1.45	5.76	-2.11	5.10	2.08	9.29	2.47	9.68
glu_phe_5	-7.46	-2.95	4.52	-2.23	5.23	-2.85	4.62	1.08	8.54	1.47	8.94
asp_tyr_4	-10.15	-6.57	3.59	-6.11	4.04	-6.51	3.65	0.09	10.24	1.02	11.17
asp_tyr_1	-11.25	-7.87	3.38	-7.59	3.66	-7.84	3.41	-0.83	10.42	0.13	11.38
asp_tyr_6	-11.25	-7.91	3.34	-7.63	3.63	-7.87	3.38	-0.87	10.39	0.09	11.34
glu_tyr_6	-11.11	-7.93	3.18	-7.62	3.49	-7.90	3.21	-0.91	10.20	0.01	11.12
glu_tyr_3	-11.11	-7.94	3.17	-7.62	3.49	-7.90	3.21	-0.92	10.20	0.00	11.12
asp_trp_3	-9.92	-7.17	2.76	-6.86	3.06	-7.15	2.77	0.95	10.87	2.47	12.40
asp_phe_1	-11.31	-8.61	2.70	-8.41	2.90	-8.60	2.71	-1.37	9.94	-1.40	9.91
Cation-π Interaction (13 pairs)											
lys_phe_2	-19.33	-23.25	3.92	-22.74	3.40	-23.20	3.87	-13.32	6.02	-13.03	6.31
lys_phe_1	-20.12	-23.75	3.63	-23.12	3.00	-23.70	3.58	-13.51	6.61	-13.18	6.94
lys_phe_3	-20.16	-23.79	3.62	-23.15	2.98	-23.71	3.55	-13.66	6.50	-13.37	6.80
lys_phe_4	-19.65	-23.15	3.50	-22.51	2.86	-23.11	3.46	-12.69	6.96	-12.34	7.31
lys_phe_6	-19.65	-23.15	3.50	-22.52	2.86	-23.11	3.46	-12.71	6.94	-12.35	7.30
lys_phe_5	-19.78	-23.04	3.26	-22.41	2.64	-22.99	3.21	-12.85	6.93	-12.50	7.28
lys_trp_4	-25.81	-28.81	3.01	-28.33	2.52	-28.76	2.96	-17.54	8.27	-18.20	7.60
lys_trp_6	-27.10	-30.10	3.00	-29.45	2.35	-30.03	2.93	-18.97	8.14	-19.34	7.76
lys_trp_3	-27.09	-30.07	2.97	-29.41	2.32	-29.99	2.89	-18.97	8.12	-19.35	7.74
lys_trp_5	-26.48	-29.30	2.82	-28.72	2.24	-29.23	2.75	-18.59	7.89	-18.88	7.60
lys_trp_1	-23.29	-25.95	2.66	-25.21	1.92	-25.93	2.64	-16.87	6.42	-14.96	8.33
lys_trp_2	-23.22	-25.84	2.62	-25.11	1.89	-25.83	2.61	-16.70	6.51	-14.79	8.43
arg_phe_3	-16.30	-18.84	2.53	-18.56	2.25	-18.83	2.53	-12.64	3.67	-12.19	4.11
Sulfur-containing analog-analog pairs (5 pairs)											

cys_trp_2	-6.37	-3.44	2.92	-3.45	2.91	-3.45	2.92	-3.54	2.83	-3.74	2.62
met_tyr_2	-8.55	-5.69	2.86	-5.60	2.95	-5.71	2.84	-5.26	3.29	-5.76	2.79
met_tyr_3	-8.14	-5.46	2.69	-5.39	2.75	-5.48	2.67	-5.16	2.98	-5.63	2.51
met_tyr_5	-8.06	-5.44	2.62	-5.34	2.72	-5.44	2.62	-4.96	3.10	-5.48	2.58
cys_trp_1	-5.61	-3.07	2.54	-3.04	2.57	-3.07	2.54	-2.75	2.86	-2.53	3.08

The outliers were identified when the energy differences between QM and MM are greater than 2.5 kcal/mol using the MM energies of AT. ΔE_{MM}: interaction energies by MM model. All energies are in kcal/mol.

Table S6. The predicted (PRED) interaction energies and the residuals (RES) of the amino acids dimer outliers[a] for three Set A models (AL, AE and AT) and two non-polarizable models (F1 and F2) using the new van der Waals parameters[b]. All energies are in kcal/mol.

Name	QM	AL		AE		AT		FF94		FF03	
		PRED.	RES	PRED	RES	PRED	RES	PRED	RES	PRED	RES
π-π Interaction											
trp_trp_4	-13.48	-10.75	2.73	-10.75	2.73	-10.76	2.72	-9.30	4.18	-10.07	3.41
tyr_tyr_3	-7.66	-7.59	0.07	-7.55	0.11	-7.59	0.07	-6.93	0.73	-6.94	0.72
tyr_trp_2	-8.57	-7.24	1.33	-7.20	1.37	-7.23	1.33	-6.68	1.89	-6.72	1.85
tyr_tyr_5	-10.01	-9.49	0.52	-9.41	0.60	-9.49	0.52	-9.05	0.96	-9.20	0.81
phe_tyr_7	-8.13	-8.08	0.05	-8.06	0.07	-8.08	0.04	-7.58	0.54	-7.70	0.43
phe_trp_5	-10.58	-9.45	1.14	-9.47	1.11	-9.46	1.12	-8.43	2.15	-8.92	1.66
phe_trp_6	-10.48	-9.36	1.12	-9.38	1.09	-9.37	1.10	-8.33	2.14	-8.83	1.65
phe_trp_1	-7.60	-6.41	1.20	-6.41	1.19	-6.41	1.19	-6.01	1.59	-6.14	1.46
tyr_tyr_6	-9.65	-9.88	0.22	-9.86	0.21	-9.88	0.23	-9.68	0.03	-9.77	0.12
phe_phe_4	-6.96	-7.32	0.37	-7.28	0.33	-7.32	0.37	-6.75	0.21	-6.92	0.03
tyr_trp_4	-8.19	-7.95	0.24	-7.92	0.28	-7.95	0.25	-7.34	0.85	-7.28	0.92
phe_trp_2	-9.63	-8.87	0.76	-8.92	0.71	-8.88	0.75	-8.13	1.50	-8.57	1.06
phe_trp_4	-6.27	-5.28	0.99	-5.28	0.98	-5.29	0.98	-5.23	1.03	-5.15	1.12
H-Bonding											
thr_asp_2	-19.55	-22.99	3.44	-22.72	3.17	-23.64	4.09	-17.43	2.12	-17.65	1.90
thr_asp_1	-19.55	-22.99	3.44	-22.71	3.16	-23.63	4.08	-17.43	2.12	-17.65	1.90
ser_glu_1	-19.36	-21.55	2.19	-21.86	2.49	-22.75	3.39	-17.01	2.35	-17.68	1.68
ser_glu_2	-19.37	-21.55	2.19	-21.86	2.49	-22.75	3.39	-17.01	2.35	-17.68	1.68
n-σ* Interaction											
glu_phe_1	-7.21	-2.51	4.70	-1.74	5.47	-2.40	4.81	1.79	9.00	2.18	9.39
glu_phe_5	-7.46	-3.35	4.11	-2.63	4.83	-3.25	4.21	0.67	8.13	1.07	8.53
asp_tyr_4	-10.15	-6.80	3.35	-6.35	3.81	-6.74	3.41	-0.14	10.01	0.79	10.94
asp_tyr_1	-11.25	-8.24	3.01	-7.96	3.29	-8.21	3.04	-1.20	10.05	-0.25	11.01
asp_tyr_6	-11.25	-8.28	2.97	-8.00	3.25	-8.24	3.01	-1.24	10.01	-0.29	10.97
glu_tyr_6	-11.11	-8.31	2.80	-8.00	3.11	-8.29	2.82	-1.29	9.82	-0.37	10.74
glu_tyr_3	-11.11	-8.33	2.79	-8.01	3.11	-8.29	2.82	-1.30	9.81	-0.38	10.73
asp_trp_3	-9.92	-7.38	2.54	-7.08	2.84	-7.37	2.56	0.73	10.65	2.26	12.18
asp_phe_1	-11.31	-8.97	2.33	-8.77	2.54	-8.96	2.34	-1.73	9.57	-1.76	9.55
Cation-π Interaction											
lys_phe_2	-19.33	-23.72	4.39	-23.21	3.87	-23.67	4.34	-13.79	5.54	-13.50	5.83
lys_phe_1	-20.12	-24.26	4.15	-23.63	3.51	-24.21	4.09	-14.02	6.10	-13.69	6.43
lys_phe_3	-20.16	-24.29	4.13	-23.65	3.49	-24.22	4.05	-14.17	6.00	-13.87	6.29
lys_phe_4	-19.65	-23.59	3.94	-22.95	3.30	-23.55	3.90	-13.14	6.51	-12.79	6.86
lys_phe_6	-19.65	-23.59	3.94	-22.96	3.31	-23.55	3.90	-13.15	6.50	-12.80	6.85
lys_phe_5	-19.78	-23.54	3.76	-22.92	3.14	-23.50	3.72	-13.35	6.42	-13.01	6.77
lys_trp_4	-25.81	-28.92	3.11	-28.43	2.62	-28.87	3.06	-17.64	8.16	-18.31	7.50
lys_trp_6	-27.10	-30.29	3.19	-29.63	2.53	-30.21	3.11	-19.15	7.95	-19.53	7.57
lys_trp_3	-27.09	-30.26	3.17	-29.60	2.51	-30.18	3.09	-19.16	7.93	-19.54	7.55
lys_trp_5	-26.48	-29.45	2.97	-28.87	2.39	-29.38	2.90	-18.74	7.74	-19.03	7.45
lys_trp_1	-23.29	-26.57	3.28	-25.83	2.54	-26.55	3.26	-17.49	5.80	-15.58	7.71
lys_trp_2	-23.22	-26.42	3.20	-25.69	2.47	-26.41	3.20	-17.28	5.93	-15.37	7.85

arg_phe_3	-16.30	-20.20	3.90	-19.92	3.62	-20.20	3.89	-14.00	2.30	-13.56	2.75
Sulfur-contained analog-analog pairs											
cys_trp_2	-6.37	-3.76	2.61	-3.76	2.60	-3.76	2.61	-3.85	2.52	-4.06	2.31
met_tyr_2	-8.55	-6.46	2.09	-6.37	2.18	-6.48	2.07	-6.03	2.52	-6.53	2.02
met_tyr_3	-8.14	-6.17	1.98	-6.11	2.04	-6.19	1.95	-5.87	2.27	-6.34	1.80
met_tyr_5	-8.06	-6.23	1.82	-6.14	1.92	-6.24	1.82	-5.76	2.30	-6.27	1.79
cys_trp_1	-5.61	-3.43	2.18	-3.40	2.21	-3.43	2.18	-3.11	2.50	-2.89	2.72

[a] The outliers were identified when the energy differences between QM and MM (predicted by Model AT) are large than 2.5 kcal/mol.

[b] The following new van der Waals parameter were applied in MM calculations: HO (the hydroxyl hydrogen) changed from (r_0 = 0 and ε = 0) to (r_0 = 0.25 and ε = 0.028), H (amine or amide hydrogen) changed from (r_0 =0.6 and ε = 0.0157) to (r_0 = 0.65 and ε = 0.0055), and CA (aromatic carbon) changed from (r_0 = 1.908 and ε = 0.086) to (r_0 = 1.908 and ε = 0.180).