Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

An Efficient Method to Predict Protein Thermostability in Alanine Mutation

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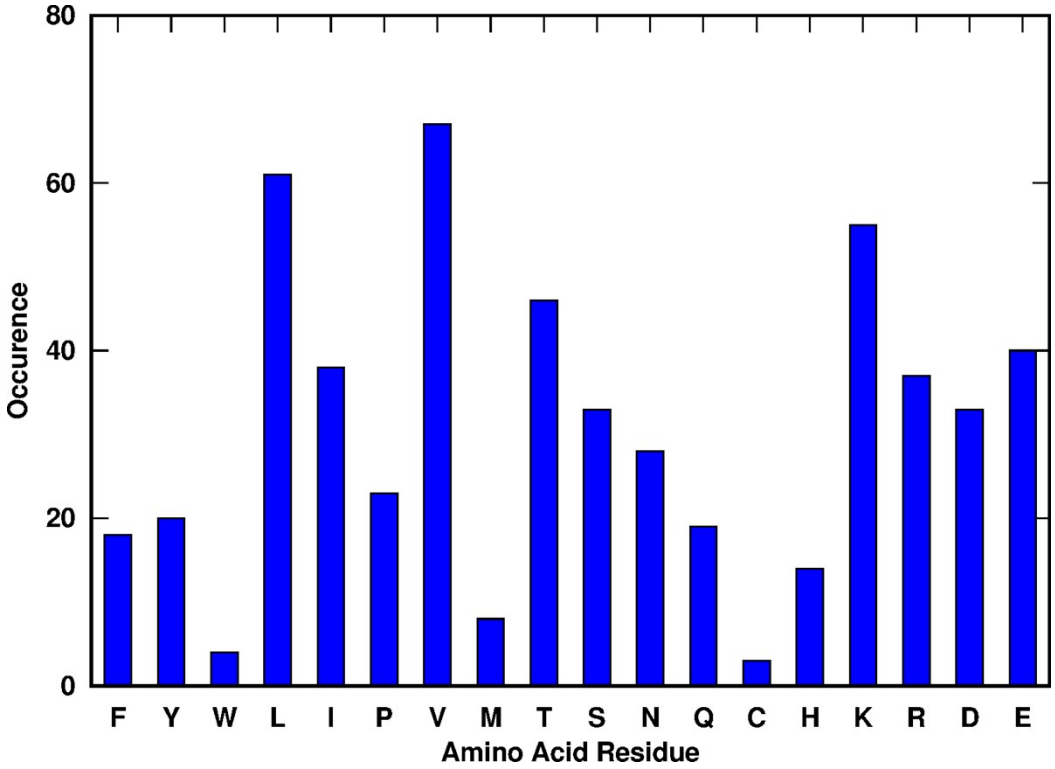

Figure S1. Frequency of occurrences for various amino acids in the data set.

Table S1. Calculated ΔE_{ele}, ΔE_{vdw}, $-T\Delta S$, ΔG_{np}, ΔG_{p}, $\Delta\Delta G$ in kcal/mol for 4GWT.

Residue		ΔE_{ele}	ΔE_{vdw}	$-T\Delta S$	ΔG_{np}	ΔG_{p}	$\Delta\Delta G_{cal}$	$\Delta\Delta G_{exp}$
2	**L**	-0.71 ± 0.08	6.52 ± 0.06	-0.94 ± 0.03	0.50 ± 0.00	-2.93 ± 0.04	2.44 ± 0.11	**1.69**
3	**P**	1.81 ± 0.13	3.51 ± 0.04	-0.88 ± 0.04	0.11 ± 0.00	-2.72 ± 0.03	1.83 ± 0.15	**0.90**
4	**P**	0.26 ± 0.11	0.56 ± 0.03	-0.05 ± 0.03	0.01 ± 0.00	-0.31 ± 0.01	0.47 ± 0.12	**0.19**
7	**E**	23.16 ± 0.08	1.84 ± 0.05	-2.83 ± 0.03	0.27 ± 0.00	-21.30 ± 0.07	1.14 ± 0.12	**0.54**
8	**K**	-12.58 ± 0.08	3.84 ± 0.06	-1.74 ± 0.01	0.37 ± 0.01	11.30 ± 0.07	1.19 ± 0.12	**0.10**
9	**R**	3.66 ± 0.09	5.70 ± 0.06	-2.73 ± 0.03	0.69 ± 0.00	-2.69 ± 0.07	4.63 ± 0.13	**1.46**
10	**M**	-0.14 ± 0.13	3.69 ± 0.07	-1.84 ± 0.04	0.23 ± 0.01	-1.18 ± 0.07	0.76 ± 0.16	**0.54**
11	**S**	1.70 ± 0.08	1.06 ± 0.06	-0.48 ± 0.01	0.05 ± 0.00	-1.40 ± 0.03	0.93 ± 0.11	**0.29**
12	**R**	-8.42 ± 0.05	0.93 ± 0.08	-0.34 ± 0.01	0.05 ± 0.01	8.13 ± 0.05	0.35 ± 0.10	**0.09**
13	**S**	0.29 ± 0.02	0.24 ± 0.02	-0.19 ± 0.01	0.00 ± 0.00	-0.69 ± 0.07	-0.35 ± 0.07	**0.05**
14	**S**	1.58 ± 0.06	0.73 ± 0.04	-1.09 ± 0.01	0.03 ± 0.00	-1.12 ± 0.03	0.13 ± 0.08	**0.16**
16	**R**	-6.73 ± 0.04	4.92 ± 0.09	-2.33 ± 0.06	0.41 ± 0.01	6.17 ± 0.04	2.44 ± 0.12	**0.65**
17	**V**	-0.17 ± 0.08	2.67 ± 0.04	-0.50 ± 0.02	0.22 ± 0.00	-0.69 ± 0.02	1.53 ± 0.09	**0.24**
18	**Y**	1.37 ± 0.11	10.38 ± 0.05	-1.72 ± 0.07	0.57 ± 0.00	-4.34 ± 0.09	6.26 ± 0.17	**1.86**
20	**F**	2.88 ± 0.10	8.64 ± 0.06	-2.00 ± 0.02	0.52 ± 0.00	-5.82 ± 0.04	4.22 ± 0.12	**1.97**
22	**H**	-0.30 ± 0.02	2.62 ± 0.04	-0.75 ± 0.01	0.17 ± 0.00	0.01 ± 0.02	1.75 ± 0.06	**0.17**
23	**I**	0.05 ± 0.07	2.39 ± 0.03	0.35 ± 0.01	0.14 ± 0.00	-0.36 ± 0.001	2.57 ± 0.08	**0.41**
24	**T**	0.37 ± 0.04	1.39 ± 0.03	-0.44 ± 0.01	0.05 ± 0.00	0.19 ± 0.02	1.56 ± 0.06	**1.28**
25	**N**	0.45 ± 0.05	1.70 ± 0.03	-1.51 ± 0.02	0.12 ± 0.00	-0.69 ± 0.07	0.07 ± 0.10	**0.51**
27	**S**	0.41 ± 0.04	0.71 ± 0.03	-0.33 ± 0.01	0.03 ± 0.00	-0.66 ± 0.05	0.16 ± 0.07	**0.35**
28	**Q**	2.55 ± 0.06	4.70 ± 0.05	-1.27 ± 0.05	0.31 ± 0.00	-2.17 ± 0.03	4.12 ± 0.10	**0.79**
29	**W**	7.30 ± 0.13	7.50 ± 0.09	-3.18 ± 0.06	0.77 ± 0.00	-10.19 ± 0.10	2.20 ± 0.20	**0.43**
30	**E**	12.50 ± 0.06	0.88 ± 0.05	-0.83 ± 0.03	0.02 ± 0.00	-11.62 ± 0.12	0.95 ± 0.15	**0.69**
31	**R**	-15.20 ± 0.15	3.78 ± 0.07	-2.67 ± 0.03	0.35 ± 0.01	13.89 ± 0.19	0.15 ± 0.25	**0.45**
33	**S**	0.93 ± 0.28	0.33 ± 0.05	-0.39 ± 0.08	0.03 ± 0.00	-1.85 ± 0.11	-0.95 ± 0.31	**0.26**
RMSE								**1.63**
R								**0.77**

Table S2. Calculated ΔE_{ele}, ΔE_{vdw}, $-T\Delta S$, ΔG_{np}, ΔG_{p}, $\Delta\Delta G$ in kcal/mol for 1RN1.

Residue		ΔE_{ele}	ΔE_{vdw}	$-T\Delta S$	ΔG_{np}	ΔG_{p}	$\Delta\Delta G_{cal}$	$\Delta\Delta G_{exp}$
9	**N**	6.19 ± 0.04	2.10 ± 0.04	-0.48 ± 0.01	0.29 ± 0.00	-5.14 ± 0.04	2.96 ± 0.07	**0.90**
12	**S**	3.97 ± 0.14	-0.08 ± 0.08	-1.96 ± 0.03	0.03 ± 0.00	-2.75 ± 0.10	-0.79 ± 0.19	**1.23**
16	**V**	0.77 ± 0.06	5.32 ± 0.04	-0.44 ± 0.03	0.22 ± 0.00	-1.49 ± 0.01	4.38 ± 0.08	**2.34**
17	**S**	1.48 ± 0.06	0.30 ± 0.04	-0.50 ± 0.01	0.04 ± 0.00	-1.65 ± 0.05	-0.33 ± 0.09	**-0.67**
36	**N**	1.21 ± 0.09	2.15 ± 0.05	-1.31 ± 0.02	0.16 ± 0.00	-1.71 ± 0.09	0.50 ± 0.14	**-0.03**
44	**N**	2.23 ± 0.04	5.27 ± 0.04	-1.11 ± 0.02	0.26 ± 0.00	-1.67 ± 0.03	4.98 ± 0.07	**2.03**
49	**D**	-22.44 ± 0.09	0.36 ± 0.01	-1.69 ± 0.03	0.01 ± 0.00	19.58 ± 0.07	-4.18 ± 0.12	**0.50**
58	**E**	-12.70 ± 0.09	5.09 ± 0.08	-3.26 ± 0.02	0.44 ± 0.00	10.99 ± 0.07	0.56 ± 0.14	**0.74**
64	**S**	1.26 ± 0.09	0.34 ± 0.04	-1.88 ± 0.01	0.02 ± 0.00	-0.81 ± 0.08	-1.07 ± 0.13	**1.44**
78	**V**	0.02 ± 0.07	6.57 ± 0.05	-0.56 ± 0.02	0.19 ± 0.00	-0.92 ± 0.01	5.30 ± 0.08	**4.08**
81	**N**	5.82 ± 0.08	4.69 ± 0.06	-1.94 ± 0.03	0.16 ± 0.00	-3.92 ± 0.04	4.81 ± 0.11	**2.87**
92	**H**	0.55 ± 0.04	6.60 ± 0.07	-1.54 ± 0.03	0.59 ± 0.00	-1.13 ± 0.04	5.07 ± 0.09	**0.62**
RMSE								**2.50**
R								**0.61**

Table S3. Calculated ΔE_{ele}, ΔE_{vdw}, $-T\Delta S$, ΔG_{np}, ΔG_{p}, $\Delta\Delta G$ in kcal/mol for 2CI2.

Residue		ΔE_{ele}	ΔE_{vdw}	$-T\Delta S$	ΔG_{np}	ΔG_{p}	$\Delta\Delta G_{cal}$	$\Delta\Delta G_{exp}$
3	**K**	24.62 ± 0.15	4.27 ± 0.09	-3.29 ± 0.03	0.53 ± 0.00	-22.01 ± 0.12	4.12 ± 0.22	**0.80**
4	**T**	-0.41 ± 0.02	1.36 ± 0.06	-0.42 ± 0.01	0.11 ± 0.00	-0.12 ± 0.09	0.52 ± 0.11	**0.85**
7	**P**	0.49 ± 0.07	2.2 ± 0.03	-0.22 ± 0.01	0.06 ± 0.00	-0.47 ± 0.03	2.06 ± 0.08	**-0.92**
8	**E**	8.31 ± 0.14	2.33 ± 0.06	-3.01 ± 0.03	0.18 ± 0.00	-6.2 ± 0.10	1.61 ± 0.18	**0.75**
9	**L**	0.01 ± 0.08	7.98 ± 0.06	-0.70 ± 0.02	0.43 ± 0.00	-2.11 ± 0.02	5.61 ± 0.10	**2.28**
12	**K**	15.16 ± 0.17	3.55 ± 0.07	-4.25 ± 0.12	0.32 ± 0.01	-13.26 ± 0.15	1.52 ± 0.26	**0.39**
13	**S**	1.87 ± 0.11	0.93 ± 0.06	-0.59 ± 0.09	0.04 ± 0.00	-1.61 ± 0.06	0.64 ± 0.16	**0.96**
18	**K**	22.65 ± 0.21	3.76 ± 0.09	-6.64 ± 0.04	0.53 ± 0.01	-20.82 ± 0.16	-0.52 ± 0.28	**0.81**
19	**K**	20.65 ± 0.24	2.07 ± 0.07	-6.04 ± 0.03	0.31 ± 0.01	-19.09 ± 0.19	-2.10 ± 0.32	**0.39**
20	**V**	0.50 ± 0.15	3.54 ± 0.06	-0.45 ± 0.03	0.24 ± 0.00	-1.77 ± 0.02	2.06 ± 0.16	**0.25**
22	**L**	-0.06 ± 0.07	4.17 ± 0.11	-1.26 ± 0.04	0.35 ± 0.00	-1.31 ± 0.04	1.89 ± 0.14	**1.27**
23	**Q**	0.32 ± 0.08	1.64 ± 0.06	-1.10 ± 0.02	0.14 ± 0.01	-0.72 ± 0.11	0.28 ± 0.15	**0.28**
24	**D**	2.97 ± 0.16	1.24 ± 0.09	-4.10 ± 0.02	0.21 ± 0.00	-2.09 ± 0.10	-1.77 ± 0.21	**1.01**
25	**K**	12.2 ± 0.19	6.26 ± 0.09	-5.33 ± 0.10	0.77 ± 0.00	-11.77 ± 0.14	2.13 ± 0.27	**1.25**
26	**P**	0.05 ± 0.08	2.32 ± 0.05	-0.21 ± 0.05	0.05 ± 0.00	-0.64 ± 0.03	1.57 ± 0.11	**1.49**
27	**E**	10.57 ± 0.20	2.47 ± 0.07	-4.64 ± 0.04	0.19 ± 0.00	-8.75 ± 0.16	-0.16 ± 0.27	**0.55**
30	**I**	0.05 ± 0.05	7.08 ± 0.05	-0.90 ± 0.02	0.38 ± 0.00	-1.13 ± 0.01	5.48 ± 0.07	**3.62**
31	**I**	-0.3 ± 0.06	4.31 ± 0.06	-0.38 ± 0.02	0.25 ± 0.00	-0.96 ± 0.03	2.92 ± 0.09	**2.12**
33	**L**	-0.59 ± 0.05	5.96 ± 0.07	-1.25 ± 0.02	0.35 ± 0.00	-0.72 ± 0.02	3.75 ± 0.09	**2.06**
34	**P**	-0.06 ± 0.10	1.20 ± 0.04	-0.39 ± 0.02	0.03 ± 0.00	-0.07 ± 0.01	0.71 ± 0.11	**0.38**
35	**V**	0.75 ± 0.12	2.85 ± 0.04	-0.77 ± 0.02	0.24 ± 0.00	-1.60 ± 0.01	1.47 ± 0.13	**0.64**
37	**T**	2.73 ± 0.02	1.09 ± 0.04	-0.40 ± 0.01	0.11 ± 0.00	-2.79 ± 0.01	0.74 ± 0.05	**0.60**
38	**I**	0.07 ± 0.06	0.54 ± 0.02	-0.08 ± 0.02	0.01 ± 0.00	-0.14 ± 0.02	0.4 ± 0.07	**0.66**
39	**V**	-0.02 ± 0.06	2.45 ± 0.06	-0.55 ± 0.03	0.19 ± 0.00	-1.25 ± 0.02	0.82 ± 0.09	**1.07**
40	**T**	-0.05 ± 0.05	0.77 ± 0.05	-0.17 ± 0.02	0.06 ± 0.00	-0.17 ± 0.03	0.44 ± 0.08	**0.69**
42	**E**	14.1 ± 0.07	0.33 ± 0.06	-2.69 ± 0.03	0.25 ± 0.00	-12.60 ± 0.05	-0.61 ± 0.11	**0.89**
44	**R**	17.37 ± 0.12	5.22 ± 0.09	-2.98 ± 0.03	0.55 ± 0.01	-15.40 ± 0.1	4.76 ± 0.18	**0.80**

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46	**D**	6.76 ± 0.08	-0.04 ± 0.09	-2.91 ± 0.06	0.11 ± 0.00	-4.82 ± 0.11	-0.9 ± 0.18	**0.91**
48	**V**	-0.31 ± 0.07	5.97 ± 0.04	-0.55 ± 0.04	0.18 ± 0.00	-0.87 ± 0.01	4.42 ± 0.09	**4.93**
49	**R**	15.18 ± 0.1 0	9.82 ± 0.07	-1.97 ± 0.02	1.12 ± 0.00	- 14.27 ± 0.0 7	9.88 ± 0.14	**1.21**
50	**L**	-0.41 ± 0.08	8.47 ± 0.06	-0.70 ± 0.02	0.39 ± 0.00	-1.26 ± 0.01	6.49 ± 0.10	**3.69**
51	**F**	1.22 ± 0.07	9.55 ± 0.06	-0.88 ± 0.03	0.75 ± 0.00	-3.21 ± 0.03	7.43 ± 0.10	**3.53**
52	**V**	0.8 ± 0.10	5.57 ± 0.04	-0.39 ± 0.03	0.20 ± 0.00	-0.79 ± 0.01	5.39 ± 0.11	**1.54**
53	**D**	-1.74 ± 0.07	2.87 ± 0.05	-1.73 ± 0.02	0.11 ± 0.00	2.74 ± 0.09	2.25 ± 0.12	**3.28**
57	**N**	3.52 ± 0.09	3.29 ± 0.09	-0.89 ± 0.03	0.18 ± 0.00	-3.59 ± 0.07	2.51 ± 0.15	**1.03**
58	**I**	-0.26 ± 0.08	10.36 ± 0.0 5	-0.67 ± 0.02	0.32 ± 0.00	-1.41 ± 0.01	8.34 ± 0.10	**4.17**
61	**V**	-0.04 ± 0.10	4.23 ± 0.03	-0.54 ± 0.03	0.21 ± 0.00	-1.22 ± 0.02	2.64 ± 0.11	**1.51**
62	**P**	-0.43 ± 0.07	5.42 ± 0.05	0.71 ± 0.04	0.09 ± 0.00	0.30 ± 0.01	6.09 ± 0.10	**3.42**
64	**V**	0.45 ± 0.09	5.54 ± 0.06	-0.79 ± 0.03	0.28 ± 0.00	-1.94 ± 0.02	3.54 ± 0.11	**1.45**
RMSE								**2.43**
R								**0.64**

Table S4. Calculated ΔE_{ele}, ΔE_{vdw}, $-T\Delta S$, ΔG_{np}, ΔG_{p}, $\Delta\Delta G$ in kcal/mol for 1GUA.

Residue		ΔE_{ele}	ΔE_{vdw}	$-T\Delta S$	ΔG_{np}	ΔG_{p}	$\Delta\Delta G_{cal}$	$\Delta\Delta G_{exp}$
3	**I**	0.24 ± 0.10	8.63 ± 0.07	-0.42 ± 0.07	0.38 ± 0.00	-1.57 ± 0.02	7.26 ± 0.14	**3.27**
4	**R**	-5.95 ± 0.13	4.04 ± 0.07	-3.22 ± 0.11	0.65 ± 0.01	5.38 ± 0.11	0.9 ± 0.21	**-0.18**
5	**V**	-0.20 ± 0.08	5.73 ± 0.05	-0.17 ± 0.02	0.13 ± 0.00	-0.37 ± 0.01	5.12 ± 0.10	**2.25**
7	**L**	-0.88 ± 0.13	8.8 ± 0.06	0.84 ± 0.03	0.43 ± 0.00	-1.41 ± 0.02	7.78 ± 0.15	**3.46**
8	**P**	1.74 ± 0.35	4.49 ± 0.07	-0.81 ± 0.23	0.11 ± 0.00	-2.15 ± 0.01	3.38 ± 0.42	**1.71**
9	**N**	-0.63 ± 0.06	0.82 ± 0.04	-0.67 ± 0.01	0.10 ± 0.01	0.12 ± 0.09	-0.26 ± 0.12	**1.14**
11	**Q**	5.36 ± 0.09	4.64 ± 0.07	2.41 ± 0.05	0.34 ± 0.01	-5.15 ± 0.07	7.60 ± 0.15	**0.50**
13	**T**	-0.12 ± 0.05	3.05 ± 0.06	-0.44 ± 0.01	0.14 ± 0.00	-0.70 ± 0.02	1.93 ± 0.08	**0.11**
14	**V**	0.03 ± 0.08	2.71 ± 0.03	-0.39 ± 0.03	0.21 ± 0.00	-0.91 ± 0.01	1.65 ± 0.09	**1.12**
15	**V**	0.30 ± 0.10	4.71 ± 0.06	-0.57 ± 0.03	0.21 ± 0.00	-1.27 ± 0.01	3.38 ± 0.12	**1.77**
17	**V**	0.57 ± 0.27	5.41 ± 0.08	-1.14 ± 0.12	0.18 ± 0.00	-2.06 ± 0.02	2.96 ± 0.31	**1.05**
21	**M**	5.46 ± 0.19	7.27 ± 0.07	-2.75 ± 0.05	0.57 ± 0.00	-6.87 ± 0.15	3.68 ± 0.26	**0.96**
22	**S**	5.16 ± 0.07	-0.16 ± 0.07	-0.61 ± 0.02	0.03 ± 0.00	-3.68 ± 0.04	0.74 ± 0.10	**1.57**
23	**L**	-0.01 ± 0.12	9.33 ± 0.05	-0.38 ± 0.03	0.47 ± 0.00	-1.35 ± 0.01	8.06 ± 0.13	**3.80**
25	**D**	15.36 ± 0.0 8	0.38 ± 0.07	-2.56 ± 0.02	0.14 ± 0.00	- 13.65 ± 0.0 9	-0.33 ± 0.14	**0.49**
26	**C**	0.73 ± 0.05	2.94 ± 0.07	-0.42 ± 0.02	0.10 ± 0.00	-0.93 ± 0.02	2.42 ± 0.09	**-0.28**
27	**L**	0.79 ± 0.09	7.30 ± 0.05	-0.35 ± 0.04	0.46 ± 0.00	-2.29 ± 0.02	5.91 ± 0.11	**3.53**
31	**L**	1.14 ± 0.12	8.87 ± 0.06	-0.48 ± 0.03	0.52 ± 0.00	-3.24 ± 0.01	6.81 ± 0.14	**3.23**
36	**L**	-0.34 ± 0.17	6.81 ± 0.07	-0.27 ± 0.03	0.49 ± 0.00	-1.50 ± 0.03	5.19 ± 0.19	**1.58**
38	**P**	0.24 ± 0.13	3.58 ± 0.10	-0.89 ± 0.04	0.13 ± 0.00	-1.02 ± 0.03	2.04 ± 0.17	**0.08**
40	**C**	0.46 ± 0.04	0.91 ± 0.04	-0.18 ± 0.01	0.06 ± 0.00	-0.49 ± 0.03	0.76 ± 0.06	**0.08**

41	**C**	1.67 ± 0.04	3.50 ± 0.04	0.28 ± 0.01	0.10 ± 0.00	-1.69 ± 0.01	3.86 ± 0.06	**1.76**
43	**V**	0.24 ± 0.09	6.27 ± 0.04	-0.24 ± 0.05	0.19 ± 0.00	-1.04 ± 0.01	5.42 ± 0.11	**1.98**
45	**R**	7.64 ± 0.08	5.28 ± 0.08	-2.31 ± 0.01	0.65 ± 0.01	-6.63 ± 0.07	4.63 ± 0.13	**0.69**
49	**E**	18.00 ± 0.25	1.01 ± 0.05	-4.93 ± 0.02	0.14 ± 0.01	-16.39 ± 0.21	-2.17 ± 0.33	**-0.02**
54	**K**	2.97 ± 0.11	4.80 ± 0.07	-3.60 ± 0.08	0.52 ± 0.01	-2.15 ± 0.12	2.54 ± 0.19	**0.33**
57	**L**	-0.49 ± 0.06	7.31 ± 0.04	-0.42 ± 0.03	0.42 ± 0.00	-1.17 ± 0.02	5.65 ± 0.08	**2.59**
62	**D**	12.87 ± 0.11	1.68 ± 0.08	-2.49 ± 0.06	0.11 ± 0.00	-11.57 ± 0.09	0.60 ± 0.17	**0.71**
66	**L**	-0.29 ± 0.08	7.57 ± 0.05	0.02 ± 0.03	0.47 ± 0.00	-1.62 ± 0.02	6.15 ± 0.10	**2.53**
69	**E**	24.18 ± 0.12	2.48 ± 0.07	-3.31 ± 0.07	0.33 ± 0.00	-22.27 ± 0.12	1.41 ± 0.20	**0.10**
70	**E**	30.38 ± 0.12	2.70 ± 0.08	-4.02 ± 0.06	0.36 ± 0.00	-28.30 ± 0.15	1.12 ± 0.22	**0.59**
71	**L**	0.75 ± 0.08	8.72 ± 0.05	-0.47 ± 0.03	0.35 ± 0.00	-1.96 ± 0.01	7.39 ± 0.10	**3.41**
73	**V**	0.41 ± 0.07	6.09 ± 0.04	-0.29 ± 0.01	0.20 ± 0.00	-1.25 ± 0.01	5.16 ± 0.08	**3.37**
74	**D**	19.14 ± 0.26	1.37 ± 0.06	-5.32 ± 0.23	0.11 ± 0.00	-17.80 ± 0.19	-2.50 ± 0.40	**0.85**
RMSE								**2.84**
R								**0.75**

Table S5. Calculated ΔE_{ele}, ΔE_{vdw}, $-T\Delta S$, ΔG_{np}, ΔG_{p}, $\Delta\Delta G$ in kcal/mol for 1PGA.

Residue		ΔE_{ele}	ΔE_{vdw}	$-T\Delta S$	ΔG_{np}	ΔG_{p}	$\Delta\Delta G_{cal}$	$\Delta\Delta G_{exp}$
6	**I**	0.21 ± 0.10	5.11 ± 0.04	-0.51 ± 0.04	0.30 ± 0.00	-1.29 ± 0.03	3.82 ± 0.12	**2.09**
7	**L**	-0.29 ± 0.16	7.95 ± 0.05	-0.15 ± 0.06	0.54 ± 0.00	-1.43 ± 0.02	6.62 ± 0.17	**1.85**
11	**T**	-0.95 ± 0.15	0.26 ± 0.03	-0.60 ± 0.02	0.01 ± 0.00	0.78 ± 0.06	-0.50 ± 0.17	**0.60**
15	**E**	-0.13 ± 0.17	1.77 ± 0.05	-3.81 ± 0.06	0.20 ± 0.00	0.00 ± 0.14	-1.97 ± 0.23	**0.47**
16	**T**	-0.27 ± 0.02	2.72 ± 0.04	-0.48 ± 0.01	0.16 ± 0.00	-0.34 ± 0.02	1.79 ± 0.06	**0.38**
18	**T**	0.58 ± 0.03	3.36 ± 0.04	-0.63 ± 0.01	0.12 ± 0.00	-1.11 ± 0.04	2.32 ± 0.07	**0.46**
22	**D**	3.38 ± 0.08	-0.94 ± 0.05	-2.81 ± 0.01	0.03 ± 0.00	-1.90 ± 0.06	-2.24 ± 0.11	**1.75**
25	**T**	5.88 ± 0.05	0.46 ± 0.05	-0.44 ± 0.02	0.18 ± 0.00	-4.63 ± 0.03	1.45 ± 0.08	**-0.22**
29	**V**	0.51 ± 0.08	2.52 ± 0.05	-0.27 ± 0.02	0.21 ± 0.00	-0.85 ± 0.01	2.12 ± 0.09	**0.70**
33	**Y**	1.44 ± 0.14	7.32 ± 0.06	-1.69 ± 0.04	0.73 ± 0.00	-4.36 ± 0.06	3.44 ± 0.17	**0.92**
37	**N**	3.61 ± 0.06	1.82 ± 0.03	-0.99 ± 0.01	0.21 ± 0.00	-3.20 ± 0.04	1.45 ± 0.08	**-0.17**
39	**V**	-0.01 ± 0.27	4.57 ± 0.06	1.39 ± 0.12	0.21 ± 0.00	-0.88 ± 0.02	5.28 ± 0.30	**1.72**
46	**D**	5.11 ± 0.06	0.85 ± 0.04	-1.82 ± 0.02	0.09 ± 0.00	-4.10 ± 0.05	0.13 ± 0.09	**1.74**
47	**D**	10.60 ± 0.22	0.04 ± 0.05	-6.48 ± 0.13	0.14 ± 0.00	-9.31 ± 0.17	-5.01 ± 0.31	**-0.49**
49	**T**	4.56 ± 0.05	-0.40 ± 0.05	-1.10 ± 0.02	0.04 ± 0.00	-3.76 ± 0.03	-0.66 ± 0.08	**0.72**
51	**T**	4.20 ± 0.04	2.84 ± 0.04	-1.08 ± 0.01	0.12 ± 0.00	-3.30 ± 0.03	2.78 ± 0.07	**1.87**
53	**T**	1.13 ± 0.03	3.81 ± 0.04	0.74 ± 0.01	0.12 ± 0.00	-1.45 ± 0.01	4.35 ± 0.05	**2.93**
54	**V**	0.19 ± 0.12	6.61 ± 0.04	-0.59 ± 0.04	0.19 ± 0.00	-0.59 ± 0.01	5.81 ± 0.14	**1.91**
RMSE								**2.62**
R								**0.58**

Table S6. Calculated ΔE_{ele}, ΔE_{vdw}, $-T\Delta S$, ΔG_{np}, ΔG_{p}, $\Delta\Delta G$ in kcal/mol for 2LZM.

Residue		ΔE_{ele}	ΔE_{vdw}	$-T\Delta S$	ΔG_{np}	ΔG_{p}	$\Delta\Delta G_{cal}$	$\Delta\Delta G_{exp}$
7	**L**	0.31 ± 0.08	9.95 ± 0.07	0.66 ± 0.02	0.42 ± 0.00	-2.58 ± 0.02	8.76 ± 0.11	**3.90**
37	**P**	0.66 ± 0.22	0.63 ± 0.03	-0.09 ± 0.09	-0.01 ± 0.00	-0.58 ± 0.01	0.61 ± 0.24	**0.00**
50	**I**	0.24 ± 0.09	6.43 ± 0.04	-0.62 ± 0.03	0.42 ± 0.00	-1.86 ± 0.02	4.61 ± 0.10	**2.90**
87	**V**	0.22 ± 0.13	6.17 ± 0.06	0.09 ± 0.03	0.24 ± 0.00	-2.18 ± 0.01	4.54 ± 0.15	**2.80**
103	**V**	0.3 ± 0.09	6.02 ± 0.05	-0.63 ± 0.03	0.23 ± 0.00	-1.85 ± 0.01	4.07 ± 0.10	**1.91**
121	**L**	0.37 ± 0.09	8.52 ± 0.04	-0.48 ± 0.04	0.58 ± 0.00	-2.14 ± 0.01	6.85 ± 0.10	**4.20**
149	**V**	0.72 ± 0.07	6.53 ± 0.05	-0.45 ± 0.01	0.22 ± 0.00	-1.91 ± 0.01	5.11 ± 0.08	**2.87**
RMSE								**2.58**
R								**0.94**

Table S7. Calculated ΔE_{ele}, ΔE_{vdw}, $-T\Delta S$, ΔG_{np}, ΔG_{p}, $\Delta\Delta G$ in kcal/mol for 1FKJ.

Residue		ΔE_{ele}	ΔE_{vdw}	$-T\Delta S$	ΔG_{np}	ΔG_{p}	$\Delta\Delta G_{cal}$	$\Delta\Delta G_{exp}$
2	**V**	0.05 ± 0.04	5.88 ± 0.06	-0.63 ± 0.06	0.17 ± 0.00	-2.34 ± 0.02	3.13 ± 0.09	**2.43**
4	**V**	0.31 ± 0.04	4.79 ± 0.05	-0.66 ± 0.01	0.23 ± 0.00	-1.52 ± 0.01	3.15 ± 0.07	**2.78**
21	**T**	1.69 ± 0.13	4.44 ± 0.06	0.85 ± 0.02	0.16 ± 0.00	-2.08 ± 0.04	5.06 ± 0.16	**1.60**
23	**V**	-0.20 ± 0.09	5.4 ± 0.05	0.12 ± 0.02	0.25 ± 0.00	-1.38 ± 0.02	4.19 ± 0.11	**2.97**
24	**V**	0.56 ± 0.06	6.14 ± 0.04	-0.48 ± 0.02	0.13 ± 0.00	-0.77 ± 0.01	5.58 ± 0.08	**3.19**
27	**T**	3.24 ± 0.04	2.68 ± 0.04	-0.88 ± 0.01	0.16 ± 0.00	-2.31 ± 0.03	2.89 ± 0.07	**1.97**
36	**F**	0.21 ± 0.05	10.54 ± 0.05	-0.88 ± 0.02	0.62 ± 0.00	-2.27 ± 0.03	8.22 ± 0.08	**3.54**
50	**L**	0.21 ± 0.18	8.54 ± 0.07	-0.40 ± 0.02	0.52 ± 0.00	-2.75 ± 0.02	6.12 ± 0.19	**2.57**
55	**V**	-0.08 ± 0.07	4.53 ± 0.03	-0.44 ± 0.02	0.17 ± 0.00	-0.73 ± 0.01	3.45 ± 0.08	**2.13**
56	**I**	-0.01 ± 0.10	8.21 ± 0.04	-0.70 ± 0.09	0.43 ± 0.00	-1.92 ± 0.01	6.01 ± 0.14	**2.48**
57	**R**	8.49 ± 0.16	5.80 ± 0.06	-3.66 ± 0.15	0.56 ± 0.00	-7.84 ± 0.12	3.35 ± 0.26	**0.81**
60	**E**	21.78 ± 0.10	6.27 ± 0.07	-3.12 ± 0.02	0.44 ± 0.00	-19.15 ± 0.08	6.22 ± 0.15	**2.13**
61	**E**	16.54 ± 0.20	2.80 ± 0.08	-3.23 ± 0.10	0.27 ± 0.00	-15.46 ± 0.16	0.92 ± 0.29	**0.84**
63	**V**	0.22 ± 0.07	6.19 ± 0.06	-0.22 ± 0.01	0.28 ± 0.00	-0.83 ± 0.01	5.64 ± 0.09	**2.97**
75	**T**	0.99 ± 0.05	2.97 ± 0.04	-0.22 ± 0.02	0.16 ± 0.00	-1.39 ± 0.03	2.51 ± 0.07	**2.60**
76	**I**	-0.23 ± 0.08	9.21 ± 0.04	-0.34 ± 0.02	0.24 ± 0.00	-1.00 ± 0.01	7.88 ± 0.10	**3.81**
91	**I**	-0.19 ± 0.08	7.45 ± 0.05	-0.27 ± 0.02	0.32 ± 0.00	-1.08 ± 0.01	6.23 ± 0.10	**1.54**
97	**L**	-0.61 ± 0.08	8.43 ± 0.06	-0.62 ± 0.02	0.34 ± 0.00	-1.09 ± 0.01	6.45 ± 0.10	**3.56**
98	**V**	0.00 ± 0.07	4.23 ± 0.06	-0.51 ± 0.02	0.24 ± 0.00	-0.95 ± 0.02	3.01 ± 0.09	**2.16**
101	**V**	1.13 ± 0.11	5.93 ± 0.04	-0.40 ± 0.03	0.19 ± 0.0	-0.92 ± 0.01	5.93 ± 0.13	**2.75**

					0			
106	**L**	0.36 ± 0.11	7.58 ± 0.05	-0.90 ± 0.02	0.47 ± 0.0	-1.89 ± 0.02	5.62 ± 0.13	**2.32**
					0			
RMSE								**2.83**
R								**0.61**

Table S8. Calculated ΔE_{ele}, ΔE_{vdw}, $-T\Delta S$, ΔG_{np}, ΔG_{p}, $\Delta\Delta G$ in kcal/mol for 2M8I.

Residue		ΔE_{ele}	ΔE_{vdw}	$-T\Delta S$	ΔG_{np}	ΔG_{p}	$\Delta\Delta G_{cal}$	$\Delta\Delta G_{exp}$
6	**K**	1.71 ± 0.19	2.86 ± 0.12	-4.70 ± 0.03	0.32 ± 0.01	-2.09 ± 0.17	-1.90 ± 0.29	**-0.15**
7	**L**	-0.17 ± 0.18	8.36 ± 0.14	-1.84 ± 0.02	0.43 ± 0.00	-2.52 ± 0.04	4.26 ± 0.23	**1.73**
8	**P**	0.39 ± 0.15	3.90 ± 0.05	-0.87 ± 0.05	0.11 ± 0.00	-1.40 ± 0.02	2.13 ± 0.17	**0.97**
9	**P**	0.02 ± 0.11	0.58 ± 0.03	-0.15 ± 0.05	0.00 ± 0.00	-0.09 ± 0.01	0.36 ± 0.13	**0.19**
12	**E**	11.22 ± 0.10	0.92 ± 0.07	-2.30 ± 0.01	0.25 ± 0.00	-10.30 ± 0.10	-0.21 ± 0.16	**0.48**
13	**K**	10.39 ± 0.20	3.77 ± 0.09	-6.13 ± 0.10	0.65 ± 0.01	-9.33 ± 0.17	-0.65 ± 0.30	**0.02**
14	**R**	12.55 ± 0.12	4.09 ± 0.07	-2.87 ± 0.05	0.48 ± 0.00	-11.01 ± 0.10	3.24 ± 0.18	**1.63**
15	**M**	0.78 ± 0.17	3.74 ± 0.06	-1.39 ± 0.05	0.26 ± 0.01	-1.63 ± 0.08	1.76 ± 0.20	**0.59**
16	**S**	1.99 ± 0.08	1.08 ± 0.06	-0.65 ± 0.01	0.05 ± 0.00	-1.60 ± 0.04	0.87 ± 0.11	**0.44**
17	**R**	-2.05 ± 0.03	0.85 ± 0.07	-0.42 ± 0.01	0.06 ± 0.01	2.35 ± 0.04	0.79 ± 0.09	**0.00**
18	**S**	0.13 ± 0.02	0.23 ± 0.02	-0.08 ± 0.01	0.02 ± 0.00	-0.41 ± 0.06	-0.11 ± 0.07	**-0.03**
19	**S**	1.28 ± 0.06	0.56 ± 0.05	-0.83 ± 0.02	0.03 ± 0.00	-0.98 ± 0.04	0.06 ± 0.09	**0.14**
21	**R**	2.14 ± 0.15	5.15 ± 0.10	-5.04 ± 0.04	0.45 ± 0.01	-1.88 ± 0.14	0.82 ± 0.23	**0.65**
22	**V**	0.22 ± 0.12	3.05 ± 0.04	-0.68 ± 0.06	0.21 ± 0.00	-0.90 ± 0.02	1.90 ± 0.14	**0.26**
23	**Y**	1.60 ± 0.18	9.70 ± 0.06	-3.46 ± 0.03	0.53 ± 0.00	-4.50 ± 0.14	3.87 ± 0.24	**2.05**
25	**F**	1.64 ± 0.12	7.33 ± 0.06	-2.24 ± 0.05	0.47 ± 0.00	-4.23 ± 0.05	2.97 ± 0.15	**2.14**
27	**H**	0.61 ± 0.04	2.37 ± 0.05	-0.95 ± 0.02	0.19 ± 0.01	-0.65 ± 0.03	1.57 ± 0.07	**0.12**
28	**I**	0.17 ± 0.09	1.94 ± 0.04	-0.31 ± 0.06	0.10 ± 0.00	-0.50 ± 0.02	1.40 ± 0.12	**0.36**
29	**T**	0.28 ± 0.05	1.33 ± 0.05	-0.55 ± 0.01	0.06 ± 0.00	-0.03 ± 0.06	1.09 ± 0.09	**1.25**
30	**N**	0.17 ± 0.06	1.47 ± 0.0	-0.91 ± 0.02	0.10 ± 0.0	-0.44 ± 0.07	0.39 ± 0.10	**0.47**

			5		0			
32	**S**	0.45 ± 0.04	0.66 ± 0.03	-0.37 ± 0.01	0.03 ± 0.00	-0.75 ± 0.05	0.02 ± 0.07	**0.26**
33	**Q**	3.16 ± 0.05	4.68 ± 0.05	-1.04 ± 0.01	0.31 ± 0.00	-2.84 ± 0.02	4.27 ± 0.08	**0.57**
34	**W**	6.10 ± 0.11	7.44 ± 0.08	-2.43 ± 0.05	0.68 ± 0.01	-8.73 ± 0.13	3.06 ± 0.19	**0.40**
35	**E**	4.72 ± 0.13	0.67 ± 0.06	-2.22 ± 0.02	0.03 ± 0.00	-4.55 ± 0.14	-1.35 ± 0.20	**0.73**
36	**R**	8.13 ± 0.29	5.45 ± 0.13	-12.96 ± 0.03	0.71 ± 0.01	-6.91 ± 0.25	-5.58 ± 0.40	**0.29**
38	**S**	0.19 ± 0.04	0.16 ± 0.04	-0.23 ± 0.01	0.00 ± 0.00	0.25 ± 0.05	0.37 ± 0.08	**-0.05**
RMSE								**1.82**
R								**0.58**

Table S9. Calculated ΔE_{ele}, ΔE_{vdw}, $-T\Delta S$, ΔG_{np}, ΔG_{p}, $\Delta\Delta G$ in kcal/mol for 1N88.

Residue		ΔE_{ele}	ΔE_{vdw}	$-T\Delta S$	ΔG_{np}	ΔG_{p}	$\Delta\Delta G_{cal}$	$\Delta\Delta G_{exp}$
12	**V**	-0.92 ± 0.16	4.47 ± 0.10	-0.21 ± 0.02	0.24 ± 0.00	-1.30 ± 0.03	2.28 ± 0.19	**1.94**
13	**L**	0.82 ± 0.49	3.78 ± 0.08	-2.00 ± 0.13	0.26 ± 0.00	-1.57 ± 0.03	1.29 ± 0.51	**1.52**
18	**Y**	5.40 ± 0.25	11.52 ± 0.13	-8.87 ± 0.16	0.91 ± 0.00	-10.45 ± 0.23	-1.49 ± 0.40	**-0.06**
21	**F**	1.24 ± 0.13	12.41 ± 0.08	-1.3 ± 0.06	0.87 ± 0.00	-4.81 ± 0.03	8.41 ± 0.17	**1.39**
26	**Y**	9.42 ± 0.19	14.5 ± 0.07	-5.72 ± 0.07	0.62 ± 0.00	-10.88 ± 0.19	7.94 ± 0.29	**4.61**
30	**V**	0.32 ± 0.23	5.14 ± 0.06	-0.71 ± 0.04	0.15 ± 0.00	-2.01 ± 0.02	2.89 ± 0.25	**2.84**
39	**I**	0.15 ± 0.10	8.27 ± 0.04	-0.61 ± 0.03	0.45 ± 0.00	-1.91 ± 0.01	6.35 ± 0.11	**1.39**
43	**V**	0.45 ± 0.11	5.01 ± 0.05	-0.67 ± 0.03	0.23 ± 0.00	-1.59 ± 0.01	3.43 ± 0.13	**2.82**
49	**V**	0.09 ± 0.19	5.03 ± 0.11	-0.51 ± 0.02	0.13 ± 0.00	-1.23 ± 0.02	3.51 ± 0.22	**2.83**
51	**V**	-0.15 ± 0.30	6.69 ± 0.06	0.55 ± 0.05	0.14 ± 0.00	-1.14 ± 0.02	6.09 ± 0.31	**3.24**
54	**V**	0.03 ± 0.17	4.81 ± 0.04	-0.65 ± 0.13	0.22 ± 0.00	-1.82 ± 0.02	2.59 ± 0.22	**3.73**
57	**L**	0.23 ± 0.10	2.47 ± 0.07	-0.16 ± 0.02	0.20 ± 0.01	-1.14 ± 0.02	1.60 ± 0.12	**1.11**
80	**I**	-0.44 ± 0.10	5.92 ± 0.06	-0.47 ± 0.04	0.40 ± 0.00	-0.95 ± 0.02	4.46 ± 0.12	**2.79**
81	**V**	0.37 ± 0.11	5.26 ± 0.05	-0.49 ± 0.02	0.18 ± 0.00	-1.48 ± 0.01	3.84 ± 0.12	**2.82**
83	**V**	0.79 ± 0.13	5.60 ± 0.04	-0.49 ± 0.09	0.19 ± 0.00	-2.01 ± 0.01	4.08 ± 0.16	**3.10**
89	**I**	-0.55 ± 0.31	8.72 ± 0.06	-0.68 ± 0.15	0.40 ± 0.00	-0.77 ± 0.02	7.12 ± 0.35	**2.35**
RMSE								**2.80**
R								**0.46**

Table S10. Calculated ΔE_{ele}, ΔE_{vdw}, $-T\Delta S$, ΔG_{np}, ΔG_{p}, $\Delta\Delta G$ in kcal/mol for 4HXJ.

Residue		ΔE_{ele}	ΔE_{vdw}	$-T\Delta S$	ΔG_{np}	ΔG_{p}	$\Delta\Delta G_{cal}$	$\Delta\Delta G_{exp}$
4	**T**	2.33 ± 0.12	3.87 ± 0.09	-0.94 ± 0.03	0.14 ± 0.00	-2.29 ± 0.06	3.11 ± 0.16	**0.64**
5	**F**	1.55 ± 0.09	12.62 ± 0.08	-1.60 ± 0.06	0.64 ± 0.00	-3.52 ± 0.04	9.69 ± 0.13	**0.84**
8	**L**	0.90 ± 0.32	4.39 ± 0.06	-0.89 ± 0.04	0.28 ± 0.00	-1.38 ± 0.01	3.30 ± 0.33	**1.49**
9	**Y**	1.51 ± 0.18	3.30 ± 0.04	-3.52 ± 0.06	0.19 ± 0.00	-3.25 ± 0.14	-1.77 ± 0.24	**0.31**
10	**D**	0.74 ± 0.08	1.30 ± 0.03	-1.78 ± 0.02	0.17 ± 0.00	-0.93 ± 0.07	-0.50 ± 0.11	**0.43**
11	**Y**	17.16 ± 0.39	10.20 ± 0.09	-12.10 ± 0.38	0.68 ± 0.00	-19.17 ± 0.31	-3.23 ± 0.63	**-0.26**
13	**S**	-1.00 ± 0.19	2.47 ± 0.14	2.69 ± 0.06	0.04 ± 0.00	0.45 ± 0.11	4.65 ± 0.27	**-0.52**
14	**R**	22.97 ± 0.11	3.09 ± 0.10	-3.53 ± 0.03	0.34 ± 0.01	-20.10 ± 0.10	2.77 ± 0.18	**0.07**
15	**T**	0.69 ± 0.05	1.68 ± 0.07	-0.11 ± 0.01	0.04 ± 0.00	-0.83 ± 0.03	1.47 ± 0.09	**-0.06**
17	**T**	0.06 ± 0.02	1.00 ± 0.04	-0.04 ± 0.00	0.05 ± 0.00	-0.42 ± 0.03	0.65 ± 0.06	**0.01**
18	**D**	-4.80 ± 0.09	1.38 ± 0.10	-3.74 ± 0.04	0.17 ± 0.00	4.47 ± 0.08	-2.52 ± 0.16	**0.56**
19	**L**	-0.02 ± 0.14	9.37 ± 0.06	-0.12 ± 0.05	0.40 ± 0.00	-1.94 ± 0.02	7.69 ± 0.16	**1.79**
20	**S**	3.58 ± 0.17	-1.05 ± 0.08	-2.13 ± 0.04	0.07 ± 0.00	-2.64 ± 0.09	-2.17 ± 0.21	**0.82**
21	**F**	1.36 ± 0.09	12.26 ± 0.04	-0.74 ± 0.03	0.53 ± 0.00	-3.04 ± 0.02	10.37 ± 0.11	**-0.10**
22	**K**	25.16 ± 0.13	1.54 ± 0.04	-3.12 ± 0.03	0.19 ± 0.01	-22.89 ± 0.11	0.88 ± 0.18	**0.44**
23	**K**	21.37 ± 0.06	2.81 ± 0.05	-1.33 ± 0.01	0.25 ± 0.00	-19.66 ± 0.05	3.44 ± 0.09	**0.09**
25	**E**	-1.75 ± 0.16	4.64 ± 0.06	-4.08 ± 0.02	0.40 ± 0.00	1.09 ± 0.13	0.30 ± 0.22	**1.94**
26	**R**	18.97 ± 0.19	4.73 ± 0.06	-4.97 ± 0.03	0.63 ± 0.00	-16.48 ± 0.15	2.88 ± 0.25	**0.32**

27	**L**	0.06 ± 0.07	9.78 ± 0.06	-0.58 ± 0.02	0.41 ± 0.00	-1.13 ± 0.01	8.54 ± 0.09	**-0.55**
28	**Q**	1.81 ± 0.09	4.26 ± 0.07	-2.12 ± 0.01	0.33 ± 0.01	-2.45 ± 0.07	1.83 ± 0.13	**0.21**
29	**I**	0.23 ± 0.17	9.59 ± 0.06	-0.42 ± 0.05	0.23 ± 0.00	-1.55 ± 0.02	8.08 ± 0.19	**0.32**
30	**V**	0.00 ± 0.13	1.27 ± 0.06	-0.31 ± 0.06	0.10 ± 0.00	-0.58 ± 0.03	0.48 ± 0.16	**0.77**
31	**N**	0.55 ± 0.06	1.07 ± 0.10	-0.87 ± 0.01	0.10 ± 0.00	-1.08 ± 0.07	-0.23 ± 0.13	**0.20**
32	**N**	4.26 ± 0.10	2.53 ± 0.06	-2.80 ± 0.02	0.18 ± 0.00	-3.93 ± 0.07	0.24 ± 0.14	**-0.07**
37	**W**	-0.45 ± 0.08	9.15 ± 0.12	-2.70 ± 0.07	0.76 ± 0.01	-2.96 ± 0.09	3.80 ± 0.19	**1.29**
38	**W**	11.01 ± 0.17	15.41 ± 0.07	-3.61 ± 0.03	1.04 ± 0.00	-16.13 ± 0.17	7.72 ± 0.25	**1.20**
39	**L**	-0.01 ± 0.09	4.12 ± 0.07	-0.71 ± 0.03	0.32 ± 0.00	-0.84 ± 0.02	2.88 ± 0.12	**1.64**
41	**H**	-0.10 ± 0.03	4.89 ± 0.04	-0.38 ± 0.01	0.32 ± 0.00	-0.29 ± 0.02	4.44 ± 0.06	**0.62**
42	**S**	7.91 ± 0.05	-0.67 ± 0.06	-0.66 ± 0.01	0.03 ± 0.00	-5.03 ± 0.02	1.58 ± 0.08	**1.46**
43	**L**	-0.32 ± 0.07	6.28 ± 0.06	-0.82 ± 0.02	0.44 ± 0.00	-1.90 ± 0.02	3.68 ± 0.10	**0.61**
44	**S**	0.79 ± 0.06	0.99 ± 0.05	-0.43 ± 0.01	0.05 ± 0.00	-0.71 ± 0.05	0.69 ± 0.10	**-0.18**
45	**T**	1.20 ± 0.04	2.20 ± 0.04	-0.66 ± 0.01	0.12 ± 0.00	-0.84 ± 0.02	2.02 ± 0.06	**1.79**
47	**Q**	-0.41 ± 0.07	2.40 ± 0.06	-0.66 ± 0.01	0.13 ± 0.00	0.16 ± 0.06	1.62 ± 0.11	**0.35**
48	**T**	1.88 ± 0.04	0.67 ± 0.04	-0.75 ± 0.01	0.09 ± 0.00	-1.97 ± 0.02	-0.08 ± 0.06	**1.11**
50	**Y**	1.61 ± 0.09	6.84 ± 0.06	-1.82 ± 0.03	0.56 ± 0.00	-3.75 ± 0.04	3.44 ± 0.12	**1.52**
51	**I**	0.19 ± 0.08	8.28 ± 0.05	-0.80 ± 0.04	0.19 ± 0.00	-0.09 ± 0.01	7.77 ± 0.10	**1.84**
52	**P**	-0.51 ± 0.14	4.76 ± 0.05	-0.29 ± 0.05	0.10 ± 0.00	0.11 ± 0.01	4.17 ± 0.16	**1.36**
53	**S**	2.23 ± 0.05	0.36 ± 0.05	-0.42 ± 0.02	0.06 ± 0.00	-2.60 ± 0.05	-0.37 ± 0.09	**-0.24**
54	**N**	-0.49 ± 0.09	1.16 ± 0.03	-1.02 ± 0.02	0.03 ± 0.01	0.14 ± 0.11	-0.18 ± 0.14	**0.14**
55	**Y**	2.40 ± 0.10	7.43 ± 0.05	-2.39 ± 0.03	0.55 ± 0.0	-5.84 ± 0.10	2.15 ± 0.15	**-0.23**

					0			
56	**V**	0.23 ± 0.06	5.72 ± 0.04	-0.19 ± 0.01	0.17 ± 0.0	-1.35 ± 0.01	4.58 ± 0.07	**1.18**
					0			
58	**P**	-0.51 ± 0.25	2.00 ± 0.08	2.94 ± 0.24	0.05 ± 0.0	0.20 ± 0.02	4.68 ± 0.35	**0.14**
					0			
59	**S**	1.19 ± 0.24	1.33 ± 0.07	-0.64 ± 0.07	0.04 ± 0.0	-1.41 ± 0.12	0.51 ± 0.29	**-0.44**
					0			
60	**D**	5.92 ± 0.30	0.54 ± 0.14	-2.53 ± 0.17	0.11 ± 0.0	3.38 ± 0.15	7.42 ± 0.40	**-0.13**
					1			
RMSE								**3.96**
R								**0.14**

Table S11. Calculated ΔE_{ele}, ΔE_{vdw}, $-T\Delta S$, ΔG_{np}, ΔG_{p}, $\Delta\Delta G$ in kcal/mol for 1BNI.

Residue		ΔE_{ele}	ΔE_{vdw}	$-T\Delta S$	ΔG_{np}	ΔG_{p}	$\Delta\Delta G_{cal}$	$\Delta\Delta G_{exp}$
3	**N**	0.86 ± 0.06	3.56 ± 0.08	-2.86 ± 0.05	0.21 ± 0.00	-2.31 ± 0.08	-0.54 ± 0.13	**1.89**
4	**T**	0.59 ± 0.06	1.65 ± 0.04	-0.61 ± 0.03	0.05 ± 0.00	-0.96 ± 0.05	0.72 ± 0.09	**2.24**
6	**D**	14.45 ± 0.16	-0.25 ± 0.09	-3.02 ± 0.04	0.12 ± 0.00	-12.65 ± 0.11	-1.35 ± 0.22	**0.95**
8	**V**	0.22 ± 0.10	6.50 ± 0.04	-0.63 ± 0.02	0.25 ± 0.00	-1.54 ± 0.01	4.80 ± 0.11	**3.49**
12	**L**	0.11 ± 0.11	10.05 ± 0.05	-0.70 ± 0.03	0.47 ± 0.00	-2.10 ± 0.01	7.83 ± 0.13	**4.57**
13	**Q**	0.99 ± 0.06	3.81 ± 0.07	-2.42 ± 0.04	0.39 ± 0.01	-1.88 ± 0.06	0.89 ± 0.12	**0.20**
14	**T**	2.91 ± 0.03	-0.48 ± 0.04	-0.70 ± 0.01	0.04 ± 0.00	-2.44 ± 0.01	-0.67 ± 0.05	**0.39**
16	**H**	0.62 ± 0.02	4.68 ± 0.05	-0.91 ± 0.01	0.32 ± 0.00	-0.91 ± 0.01	3.80 ± 0.05	**2.01**
21	**N**	3.60 ± 0.06	4.34 ± 0.05	-1.61 ± 0.02	0.08 ± 0.00	-3.40 ± 0.05	3.01 ± 0.10	**2.32**
23	**I**	-0.09 ± 0.29	7.14 ± 0.06	-0.67 ± 0.22	0.39 ± 0.00	-0.84 ± 0.02	5.93 ± 0.37	**3.59**
24	**T**	1.34 ± 0.23	1.61 ± 0.07	-1.28 ± 0.24	0.13 ± 0.00	-1.58 ± 0.10	0.22 ± 0.35	**1.99**
25	**K**	6.72 ± 0.10	2.14 ± 0.06	-2.52 ± 0.07	0.54 ± 0.01	-5.98 ± 0.07	0.90 ± 0.16	**-0.45**
26	**S**	0.18 ± 0.05	0.34 ± 0.03	-0.16 ± 0.05	0.03 ± 0.00	-0.46 ± 0.14	-0.07 ± 0.16	**-0.51**
27	**E**	9.67 ± 0.08	1.94 ± 0.05	-1.15 ± 0.02	0.16 ± 0.00	-9.02 ± 0.10	1.60 ± 0.14	**1.29**
34	**V**	-0.01 ± 0.11	2.27 ± 0.07	-0.19 ± 0.07	0.12 ± 0.00	-1.14 ± 0.02	1.05 ± 0.15	**1.37**
43	**V**	-0.04 ± 0.08	4.17 ± 0.10	-1.20 ± 0.08	0.18 ± 0.00	-0.96 ± 0.01	2.15 ± 0.15	**1.68**
49	**I**	-0.21 ± 0.22	9.76 ± 0.06	-0.83 ± 0.13	0.45 ± 0.00	-1.38 ± 0.02	7.79 ± 0.26	**4.71**
52	**D**	21.81 ± 0.08	0.42 ± 0.07	-2.51 ± 0.06	0.19 ± 0.00	-19.99 ± 0.08	-0.08 ± 0.15	**3.08**
53	**I**	0.03 ± 0.11	3.72 ± 0.04	-0.50 ± 0.06	0.26 ± 0.00	-0.95 ± 0.02	2.56 ± 0.13	**1.29**
55	**S**	0.38 ± 0.05	0.52 ± 0.05	-0.64 ± 0.02	0.03 ± 0.0	-0.39 ± 0.05	-0.10 ± 0.09	**-0.15**

					0			
57	**R**	-6.22 ± 0.04	0.98 ± 0.04	-0.81 ± 0.01	0.05 ± 0.0 1	5.62 ± 0.24	-0.38 ± 0.24	**-0.64**
64	**K**	-3.75 ± 0.10	1.51 ± 0.08	-1.89 ± 0.08	0.15 ± 0.0 1	3.43 ± 0.11	-0.55 ± 0.19	**-0.59**
71	**E**	15.13 ± 0.1 3	3.59 ± 0.06	-4.21 ± 0.07	0.49 ± 0.0 0	- 14.30 ± 0.1 1	0.70 ± 0.19	**2.40**
75	**N**	2.32 ± 0.10	2.44 ± 0.06	-1.94 ± 0.03	0.24 ± 0.0 1	-2.96 ± 0.09	0.10 ± 0.15	**1.69**
82	**N**	5.78 ± 0.17	2.56 ± 0.14	-2.45 ± 0.04	0.17 ± 0.0 0	-4.77 ± 0.11	1.29 ± 0.25	**2.02**
83	**S**	0.90 ± 0.07	0.42 ± 0.09	-0.83 ± 0.05	0.06 ± 0.0 0	-1.15 ± 0.07	-0.60 ± 0.14	**-0.08**
89	**S**	4.77 ± 0.04	-1.15 ± 0.07	-0.51 ± 0.02	0.02 ± 0.0 0	-2.44 ± 0.02	0.69 ± 0.08	**1.96**
90	**S**	1.45 ± 0.03	1.04 ± 0.04	-0.42 ± 0.01	0.05 ± 0.0 0	-0.82 ± 0.02	1.30 ± 0.06	**2.85**
100	**H**	0.12 ± 0.02	1.69 ± 0.07	-0.74 ± 0.03	0.14 ± 0.0 1	-0.35 ± 0.03	0.86 ± 0.09	**0.24**
102	**Q**	2.16 ± 0.21	2.10 ± 0.06	-2.09 ± 0.03	0.11 ± 0.0 0	-2.23 ± 0.11	0.05 ± 0.24	**0.16**
108	**R**	9.57 ± 0.21	4.84 ± 0.16	-0.27 ± 0.06	0.66 ± 0.0 0	- 14.67 ± 0.0 8	0.13 ± 0.28	**0.36**
RMSE								**1.55**
R								**0.76**

Table S12. Calculated ΔE_{ele}, ΔE_{vdw}, $-T\Delta S$, ΔG_{np}, ΔG_{p}, $\Delta\Delta G$ in kcal/mol for 5EMZ.

Residue		ΔE_{ele}	ΔE_{vdw}	$-T\Delta S$	ΔG_{np}	ΔG_{p}	$\Delta\Delta G_{cal}$	$\Delta\Delta G_{exp}$
3	**I**	-0.04 ± 0.19	8.88 ± 0.05	-0.55 ± 0.03	0.25 ± 0.00	-0.74 ± 0.01	7.80 ± 0.20	**3.18**
5	**V**	-0.17 ± 0.07	6.38 ± 0.05	0.49 ± 0.01	0.16 ± 0.00	-0.68 ± 0.01	6.18 ± 0.08	**2.41**
7	**T**	1.51 ± 0.04	4.19 ± 0.05	-0.37 ± 0.02	0.16 ± 0.00	-1.81 ± 0.02	3.68 ± 0.07	**1.37**
9	**T**	1.24 ± 0.02	1.79 ± 0.03	-0.75 ± 0.01	0.10 ± 0.00	-0.62 ± 0.02	1.76 ± 0.04	**-0.06**
13	**I**	0.45 ± 0.10	7.99 ± 0.05	-0.23 ± 0.05	0.34 ± 0.00	-2.23 ± 0.03	6.32 ± 0.12	**3.40**
15	**L**	0.1 ± 0.12	8.10 ± 0.05	-0.68 ± 0.02	0.37 ± 0.00	-2.50 ± 0.02	5.39 ± 0.13	**3.85**
17	**V**	0.65 ± 0.17	5.52 ± 0.05	-0.32 ± 0.08	0.12 ± 0.00	-2.00 ± 0.02	3.97 ± 0.20	**1.65**
22	**T**	1.23 ± 0.06	2.79 ± 0.04	-0.93 ± 0.01	0.13 ± 0.00	-0.77 ± 0.04	2.45 ± 0.09	**1.74**
26	**V**	0.25 ± 0.07	5.63 ± 0.04	-0.24 ± 0.02	0.24 ± 0.00	-1.29 ± 0.01	4.59 ± 0.09	**3.37**
27	**K**	19.51 ± 0.26	7.49 ± 0.08	-6.99 ± 0.10	0.83 ± 0.00	-18.3 ± 0.21	2.54 ± 0.36	**2.56**
30	**I**	0.14 ± 0.11	9.39 ± 0.05	-0.1 ± 0.01	0.39 ± 0.00	-1.58 ± 0.01	8.24 ± 0.12	**3.22**
41	**Q**	5.05 ± 0.09	10.72 ± 0.05	-0.85 ± 0.02	0.44 ± 0.00	-5.95 ± 0.02	9.41 ± 0.11	**1.46**
43	**L**	0.36 ± 0.11	8.81 ± 0.05	-0.52 ± 0.03	0.42 ± 0.00	-2.61 ± 0.02	6.46 ± 0.12	**4.36**
50	**L**	0.66 ± 0.30	9.09 ± 0.07	-0.28 ± 0.08	0.41 ± 0.00	-2.31 ± 0.02	7.57 ± 0.32	**2.73**
56	**L**	0.66 ± 0.11	9.04 ± 0.04	-0.92 ± 0.06	0.49 ± 0.00	-2.07 ± 0.01	7.20 ± 0.13	**4.05**
61	**I**	0.15 ± 0.06	8.78 ± 0.05	-0.55 ± 0.01	0.28 ± 0.00	-1.18 ± 0.01	7.48 ± 0.08	**3.23**
67	**L**	0.47 ± 0.07	8.77 ± 0.06	-0.71 ± 0.04	0.44 ± 0.00	-1.73 ± 0.01	7.24 ± 0.10	**2.57**
RMSE								**3.67**
R								**0.49**

Table S13. Calculated ΔE_{ele}, ΔE_{vdw}, $-T\Delta S$, ΔG_{np}, ΔG_{p}, $\Delta\Delta G$ in kcal/mol for 2PTL.

Residue		ΔE_{ele}	ΔE_{vdw}	$-T\Delta S$	ΔG_{np}	ΔG_{p}	$\Delta\Delta G_{cal}$	$\Delta\Delta G_{exp}$
18	**V**	-0.30 ± 0.33	1.28 ± 0.11	-1.19 ± 0.19	0.08 ± 0.00	-0.49 ± 0.03	-0.62 ± 0.40	**1.28**
19	**T**	1.52 ± 0.23	2.67 ± 0.09	-3.16 ± 0.03	0.18 ± 0.00	-1.99 ± 0.09	-0.78 ± 0.26	**1.72**
20	**I**	-0.44 ± 0.24	9.24 ± 0.08	-1.46 ± 0.16	0.32 ± 0.00	-1.93 ± 0.02	5.73 ± 0.30	**4.63**
21	**K**	38.11 ± 0.40	3.82 ± 0.08	-12.23 ± 0.04	0.37 ± 0.01	-33.82 ± 0.36	-3.75 ± 0.54	**0.90**
23	**N**	1.80 ± 0.09	3.30 ± 0.09	-1.04 ± 0.02	0.20 ± 0.00	-1.73 ± 0.07	2.53 ± 0.14	**1.79**
24	**L**	0.09 ± 0.08	8.15 ± 0.07	-1.10 ± 0.03	0.50 ± 0.01	-1.80 ± 0.02	5.84 ± 0.12	**2.83**
25	**I**	-0.31 ± 0.09	6.01 ± 0.06	-0.48 ± 0.04	0.31 ± 0.00	-0.99 ± 0.02	4.54 ± 0.11	**1.29**
26	**F**	2.22 ± 0.14	8.92 ± 0.07	-1.24 ± 0.02	0.67 ± 0.00	-4.21 ± 0.06	6.36 ± 0.17	**2.98**
28	**N**	1.23 ± 0.04	1.69 ± 0.03	-0.67 ± 0.01	0.05 ± 0.00	-0.67 ± 0.04	1.63 ± 0.07	**1.74**
30	**S**	0.52 ± 0.05	0.73 ± 0.05	0.29 ± 0.02	0.03 ± 0.00	-0.56 ± 0.03	1.01 ± 0.08	**0.25**
31	**T**	0.57 ± 0.04	2.02 ± 0.04	-0.63 ± 0.02	0.11 ± 0.00	-0.77 ± 0.04	1.30 ± 0.08	**1.17**
33	**T**	1.74 ± 0.15	0.82 ± 0.09	-2.23 ± 0.05	0.10 ± 0.00	-1.63 ± 0.10	-1.20 ± 0.21	**1.04**
35	**E**	-22.62 ± 0.22	2.19 ± 0.10	-4.50 ± 0.13	0.27 ± 0.01	20.23 ± 0.20	-4.43 ± 0.34	**0.63**
36	**F**	-0.47 ± 0.34	8.23 ± 0.09	0.10 ± 0.33	0.49 ± 0.01	-1.06 ± 0.06	7.29 ± 0.48	**4.92**
37	**K**	37.18 ± 0.29	1.74 ± 0.10	-11.02 ± 0.25	0.37 ± 0.01	-33.62 ± 0.26	-5.35 ± 0.47	**0.91**
39	**T**	1.44 ± 0.16	0.69 ± 0.06	-1.17 ± 0.04	0.07 ± 0.00	-1.40 ± 0.09	-0.37 ± 0.19	**1.15**
44	**T**	2.65 ± 0.06	2.20 ± 0.07	-0.13 ± 0.03	0.21 ± 0.00	-2.91 ± 0.01	2.02 ± 0.09	**1.14**
45	**S**	0.96 ± 0.11	0.45 ± 0.05	-1.17 ± 0.02	0.04 ± 0.00	-1.17 ± 0.07	-0.89 ± 0.14	**-0.36**
48	**Y**	-0.69 ± 0.17	7.69 ± 0.08	-1.71 ± 0.04	0.80 ± 0.00	-3.28 ± 0.07	2.81 ± 0.20	**2.81**

50	**Y**	2.29 ± 0.24	6.88 ± 0.16	-4.35 ± 0.04	0.70 ± 0.00	-5.50 ± 0.16	0.02 ± 0.34	**2.48**
52	**D**	-11.60 ± 0.18	0.78 ± 0.06	-4.21 ± 0.04	0.17 ± 0.00	10.64 ± 0.16	-4.22 ± 0.25	**1.10**
54	**L**	-0.61 ± 0.19	4.92 ± 0.07	0.65 ± 0.10	0.39 ± 0.00	-0.68 ± 0.02	4.67 ± 0.22	**2.31**
55	**K**	41.56 ± 0.17	5.23 ± 0.10	-4.56 ± 0.04	0.55 ± 0.01	-38.50 ± 0.13	4.28 ± 0.24	**-0.46**
56	**K**	30.67 ± 0.36	2.68 ± 0.07	-9.75 ± 0.03	0.36 ± 0.01	-27.52 ± 0.25	-3.56 ± 0.44	**-0.21**
58	**N**	0.71 ± 0.17	0.92 ± 0.10	-1.63 ± 0.04	0.06 ± 0.00	-0.78 ± 0.13	-0.72 ± 0.24	**0.35**
60	**E**	-8.60 ± 0.16	3.77 ± 0.15	-7.42 ± 0.03	0.27 ± 0.01	7.80 ± 0.14	-4.18 ± 0.27	**0.18**
62	**T**	0.07 ± 0.03	1.17 ± 0.03	-0.17 ± 0.01	0.10 ± 0.00	-0.40 ± 0.02	0.77 ± 0.05	**1.16**
63	**V**	0.53 ± 0.10	3.88 ± 0.07	-0.54 ± 0.01	0.18 ± 0.00	-1.09 ± 0.02	2.96 ± 0.13	**0.91**
64	**D**	-6.81 ± 0.20	0.54 ± 0.05	-4.15 ± 0.03	0.12 ± 0.00	6.05 ± 0.16	-4.25 ± 0.27	**0.12**
65	**V**	0.33 ± 0.06	2.47 ± 0.03	-0.53 ± 0.01	0.16 ± 0.00	-0.72 ± 0.02	1.71 ± 0.07	**1.03**
68	**K**	14.85 ± 0.06	0.31 ± 0.04	-1.15 ± 0.04	0.01 ± 0.00	-13.70 ± 0.12	0.32 ± 0.15	**0.10**
70	**Y**	6.57 ± 0.30	9.03 ± 0.12	-9.09 ± 0.19	0.82 ± 0.01	-10.04 ± 0.26	-2.71 ± 0.46	**1.56**
71	**T**	2.42 ± 0.11	2.51 ± 0.06	-1.26 ± 0.02	0.17 ± 0.00	-2.86 ± 0.06	0.98 ± 0.14	**1.75**
72	**L**	0.09 ± 0.12	8.13 ± 0.05	-0.28 ± 0.05	0.44 ± 0.00	-1.65 ± 0.03	6.73 ± 0.15	**3.70**
73	**N**	2.04 ± 0.09	3.23 ± 0.06	-0.84 ± 0.02	0.25 ± 0.00	-2.31 ± 0.07	2.37 ± 0.13	**1.62**
74	**I**	-0.02 ± 0.10	9.13 ± 0.06	-0.79 ± 0.02	0.40 ± 0.00	-0.98 ± 0.01	7.74 ± 0.12	**4.74**
75	**K**	27.32 ± 0.22	3.91 ± 0.07	-5.15 ± 0.04	0.39 ± 0.01	-24.56 ± 0.19	1.91 ± 0.30	**0.47**
RMSE								**2.85**
R								**0.69**

Table S14. Calculated ΔE_{ele}, ΔE_{vdw}, $-T\Delta S$, ΔG_{np}, ΔG_{p}, $\Delta\Delta G$ in kcal/mol for 1IGV.

Residue		ΔE_{ele}	ΔE_{vdw}	$-T\Delta S$	ΔG_{np}	ΔG_{p}	$\Delta\Delta G_{cal}$	$\Delta\Delta G_{exp}$
10	**F**	3.09 ± 0.11	14.3 ± 0.06	-0.51 ± 0.02	0.76 ± 0.00	-5.16 ± 0.04	12.48 ± 0.13	**4.83**
23	**L**	-1.92 ± 0.13	9.45 ± 0.07	-0.9 ± 0.11	0.37 ± 0.00	-0.26 ± 0.04	6.74 ± 0.19	**3.73**
28	**L**	0.24 ± 0.11	8.07 ± 0.07	-0.57 ± 0.04	0.47 ± 0.00	-1.70 ± 0.02	6.51 ± 0.13	**2.70**
61	**V**	-0.30 ± 0.20	5.78 ± 0.07	0.01 ± 0.08	0.22 ± 0.00	-0.29 ± 0.02	5.42 ± 0.22	**3.78**
66	**F**	1.16 ± 0.09	11.80 ± 0.06	-0.91 ± 0.02	0.79 ± 0.00	-3.61 ± 0.02	9.23 ± 0.11	**4.98**
RMSE								**4.53**
R								**0.74**

Table S15. Calculated ΔE_{ele}, ΔE_{vdw}, $-T\Delta S$, ΔG_{np}, ΔG_{p}, $\Delta\Delta G$ in kcal/mol for 1AJ3.

Residue		ΔE_{ele}	ΔE_{vdw}	$-T\Delta S$	ΔG_{np}	ΔG_{p}	$\Delta\Delta G_{cal}$	$\Delta\Delta G_{exp}$
1	**H**	1.47 ± 0.36	3.32 ± 0.09	-2.51 ± 0.03	0.35 ± 0.00	-0.90 ± 0.05	1.73 ± 0.38	**-0.50**
3	**F**	1.32 ± 0.21	10.39 ± 0.07	-1.76 ± 0.03	0.65 ± 0.00	-3.59 ± 0.03	7.01 ± 0.23	**3.70**
5	**R**	24.62 ± 0.06	0.86 ± 0.06	-2.31 ± 0.03	0.48 ± 0.00	-20.94 ± 0.05	2.71 ± 0.10	**0.30**
7	**M**	2.18 ± 0.11	9.85 ± 0.10	-2.52 ± 0.02	0.56 ± 0.00	-4.17 ± 0.05	5.90 ± 0.16	**2.20**
8	**D**	6.81 ± 0.07	0.46 ± 0.08	-1.81 ± 0.04	0.21 ± 0.00	-5.97 ± 0.05	-0.30 ± 0.13	**0.20**
12	**S**	3.84 ± 0.10	0.26 ± 0.06	-0.58 ± 0.02	0.05 ± 0.00	-3.67 ± 0.09	-0.10 ± 0.14	**-0.50**
14	**I**	0.61 ± 0.09	8.56 ± 0.05	-0.42 ± 0.02	0.35 ± 0.00	-2.08 ± 0.01	7.02 ± 0.11	**3.65**
16	**E**	-12.45 ± 0.06	1.98 ± 0.04	-1.09 ± 0.01	0.20 ± 0.00	11.00 ± 0.05	-0.36 ± 0.09	**-0.10**
17	**K**	16.82 ± 0.12	5.91 ± 0.07	-2.07 ± 0.05	0.83 ± 0.00	-15.71 ± 0.10	5.78 ± 0.18	**0.00**
21	**V**	0.22 ± 0.37	4.53 ± 0.07	-1.16 ± 0.27	0.29 ± 0.00	-2.49 ± 0.03	1.39 ± 0.47	**0.20**
31	**T**	2.48 ± 0.10	2.08 ± 0.09	-0.73 ± 0.02	0.16 ± 0.00	-2.80 ± 0.04	1.19 ± 0.14	**-0.30**
33	**V**	0.19 ± 0.20	1.40 ± 0.05	-0.42 ± 0.17	0.12 ± 0.00	-0.75 ± 0.02	0.54 ± 0.27	**0.40**
35	**N**	6.61 ± 0.14	3.19 ± 0.08	-3.23 ± 0.03	0.34 ± 0.00	-7.10 ± 0.09	-0.19 ± 0.19	**-0.20**
36	**L**	1.10 ± 0.19	4.17 ± 0.08	-1.51 ± 0.12	0.50 ± 0.01	-3.01 ± 0.04	1.25 ± 0.24	**0.20**
38	**K**	11.44 ± 0.16	2.00 ± 0.05	-4.04 ± 0.04	0.21 ± 0.00	-10.75 ± 0.13	-1.14 ± 0.22	**-0.40**
40	**H**	1.64 ± 0.06	8.39 ± 0.08	-1.08 ± 0.04	0.60 ± 0.00	-1.72 ± 0.04	7.83 ± 0.12	**1.40**
42	**R**	24.51 ± 0.23	1.87 ± 0.14	-4.24 ± 0.03	0.65 ± 0.01	-20.88 ± 0.16	1.91 ± 0.31	**-0.30**
43	**L**	0.89 ± 0.13	7.54 ± 0.07	-1.39 ± 0.03	0.41 ± 0.01	-3.49 ± 0.03	3.96 ± 0.15	**2.80**

47	**L**	0.13 ± 0.16	8.50 ± 0.07	-0.10 ± 0.11	0.47 ± 0.00	-2.49 ± 0.02	6.51 ± 0.21	**3.80**
50	**H**	1.18 ± 0.03	3.80 ± 0.08	-1.47 ± 0.01	0.38 ± 0.00	-1.22 ± 0.03	2.67 ± 0.09	**2.30**
52	**P**	0.46 ± 0.08	2.14 ± 0.03	-0.29 ± 0.02	0.06 ± 0.00	-0.70 ± 0.01	1.67 ± 0.09	**-0.40**
54	**I**	0.43 ± 0.11	8.02 ± 0.06	-0.25 ± 0.03	0.45 ± 0.00	-1.64 ± 0.02	7.01 ± 0.14	**2.80**
55	**Q**	1.43 ± 0.09	3.13 ± 0.05	-1.82 ± 0.01	0.32 ± 0.00	-2.10 ± 0.07	0.96 ± 0.13	**0.70**
57	**V**	0.82 ± 0.12	4.84 ± 0.08	-1.04 ± 0.04	0.30 ± 0.00	-1.62 ± 0.02	3.3 ± 0.15	**2.30**
59	**D**	7.44 ± 0.09	0.18 ± 0.07	-2.60 ± 0.02	0.18 ± 0.00	-6.65 ± 0.08	-1.45 ± 0.14	**0.10**
63	**K**	29.61 ± 0.09	1.51 ± 0.07	-2.37 ± 0.03	0.35 ± 0.00	-26.99 ± 0.08	2.11 ± 0.14	**0.10**
64	**L**	-0.64 ± 0.16	5.52 ± 0.05	-0.15 ± 0.08	0.50 ± 0.00	-1.13 ± 0.02	4.10 ± 0.19	**2.40**
75	**I**	0.98 ± 0.09	7.99 ± 0.10	-1.24 ± 0.02	0.40 ± 0.00	-2.38 ± 0.02	5.75 ± 0.14	**2.00**
77	**Q**	0.12 ± 0.10	2.25 ± 0.04	-2.38 ± 0.04	0.23 ± 0.00	-0.77 ± 0.10	-0.55 ± 0.15	**0.00**
79	**L**	-0.24 ± 0.07	7.92 ± 0.06	-0.83 ± 0.01	0.52 ± 0.00	-1.93 ± 0.02	5.44 ± 0.10	**2.80**
82	**F**	2.74 ± 0.13	12.71 ± 0.05	-0.85 ± 0.03	0.75 ± 0.00	-5.25 ± 0.02	10.10 ± 0.14	**2.80**
84	**D**	3.33 ± 0.14	0.53 ± 0.08	-2.08 ± 0.03	0.15 ± 0.00	-2.82 ± 0.10	-0.89 ± 0.19	**-0.70**
87	**K**	14.77 ± 0.11	2.13 ± 0.07	-2.88 ± 0.02	0.28 ± 0.01	-13.27 ± 0.28	1.03 ± 0.31	**0.40**
89	**L**	0.56 ± 0.10	9.01 ± 0.06	-0.97 ± 0.02	0.49 ± 0.00	-2.68 ± 0.02	6.41 ± 0.12	**3.80**
91	**Q**	2.27 ± 0.10	3.49 ± 0.08	-2.30 ± 0.03	0.27 ± 0.01	-2.97 ± 0.08	0.76 ± 0.15	**-0.40**
96	**R**	10.00 ± 0.15	4.77 ± 0.11	-3.56 ± 0.04	0.86 ± 0.01	-8.75 ± 0.12	3.32 ± 0.23	**0.00**
98	**Q**	0.24 ± 1.05	1.08 ± 0.19	-0.84 ± 0.35	0.08 ± 0.01	-1.20 ± 0.09	-0.64 ± 1.12	**-0.50**
RMSE								**2.69**
R								**0.81**

Table S16. Calculated ΔE_{ele}, ΔE_{vdw}, $-T\Delta S$, ΔG_{np}, ΔG_{p}, $\Delta\Delta G$ in kcal/mol for 1STN.

Residue		ΔE_{ele}	ΔE_{vdw}	$-T\Delta S$	ΔG_{np}	ΔG_{p}	$\Delta\Delta G_{cal}$	$\Delta\Delta G_{exp}$
1	**K**	-13.11 ± 0.13	0.37 ± 0.02	-1.62 ± 0.03	0.01 ± 0.01	19.31 ± 0.06	4.96 ± 0.15	**-0.30**
2	**L**	0.96 ± 0.12	7.72 ± 0.06	-1.19 ± 0.02	0.47 ± 0.00	-5.09 ± 0.04	2.87 ± 0.14	**1.60**
3	**H**	0.29 ± 0.02	1.82 ± 0.04	-0.23 ± 0.01	0.10 ± 0.00	-0.22 ± 0.02	1.76 ± 0.05	**0.40**
4	**K**	-13.30 ± 0.11	5.57 ± 0.06	-3.16 ± 0.02	0.59 ± 0.00	12.31 ± 0.09	2.01 ± 0.15	**1.40**
5	**E**	35.16 ± 0.19	1.39 ± 0.07	-5.06 ± 0.04	0.42 ± 0.00	-32.67 ± 0.14	-0.76 ± 0.25	**1.30**
6	**P**	0.23 ± 0.14	1.05 ± 0.02	-0.26 ± 0.06	0.03 ± 0.00	-0.39 ± 0.01	0.66 ± 0.16	**0.40**
8	**T**	-0.10 ± 0.03	1.09 ± 0.05	0.03 ± 0.01	0.07 ± 0.00	-0.39 ± 0.02	0.70 ± 0.06	**0.70**
9	**L**	0.79 ± 0.04	7.40 ± 0.03	-0.59 ± 0.01	0.36 ± 0.00	-2.62 ± 0.01	5.34 ± 0.05	**2.30**
10	**I**	-0.56 ± 0.04	6.15 ± 0.04	0.11 ± 0.01	0.36 ± 0.00	-0.94 ± 0.02	5.12 ± 0.06	**2.65**
11	**K**	-16.76 ± 0.06	1.74 ± 0.05	-1.41 ± 0.02	0.12 ± 0.01	15.03 ± 0.06	-1.28 ± 0.10	**0.20**
13	**I**	-0.39 ± 0.19	5.86 ± 0.06	1.71 ± 0.06	0.31 ± 0.00	-1.12 ± 0.05	6.37 ± 0.21	**2.50**
14	**D**	32.53 ± 0.20	1.15 ± 0.10	-5.34 ± 0.13	0.23 ± 0.00	-29.48 ± 0.16	-0.91 ± 0.30	**0.10**
16	**D**	29.69 ± 0.11	3.64 ± 0.06	-3.05 ± 0.02	0.18 ± 0.00	-27.38 ± 0.11	3.08 ± 0.17	**-0.70**
17	**T**	2.47 ± 0.08	3.91 ± 0.06	0.09 ± 0.05	0.15 ± 0.00	-2.52 ± 0.03	4.10 ± 0.12	**1.60**
18	**V**	-0.12 ± 0.06	5.68 ± 0.06	-0.34 ± 0.02	0.17 ± 0.00	-1.23 ± 0.01	4.16 ± 0.09	**2.90**
19	**K**	-18.27 ± 0.06	5.42 ± 0.05	-0.82 ± 0.01	0.47 ± 0.00	16.24 ± 0.05	3.04 ± 0.09	**0.20**
20	**L**	-0.19 ± 0.08	9.30 ± 0.05	-0.22 ± 0.01	0.38 ± 0.00	-1.30 ± 0.01	7.97 ± 0.09	**2.70**

21	**M**	1.35 ± 0.09	5.19 ± 0.05	0.03 ± 0.02	0.37 ± 0.00	-2.52 ± 0.05	4.42 ± 0.12	**1.50**
23	**K**	-12.71 ± 0.19	1.08 ± 0.03	-2.76 ± 0.04	0.14 ± 0.01	11.45 ± 0.14	-2.80 ± 0.24	**0.70**
25	**Q**	0.48 ± 0.06	0.90 ± 0.05	-0.82 ± 0.02	0.01 ± 0.00	-0.46 ± 0.06	0.11 ± 0.10	**0.30**
26	**P**	-0.62 ± 0.08	1.32 ± 0.04	0.37 ± 0.02	0.04 ± 0.00	0.47 ± 0.02	1.58 ± 0.09	**0.50**
27	**M**	0.71 ± 0.08	6.12 ± 0.06	-0.79 ± 0.03	0.52 ± 0.00	-2.43 ± 0.05	4.13 ± 0.12	**1.70**
28	**T**	1.41 ± 0.04	3.28 ± 0.04	-0.52 ± 0.01	0.16 ± 0.00	-1.89 ± 0.02	2.44 ± 0.06	**1.40**
29	**F**	2.4 ± 0.07	13.36 ± 0.05	-0.66 ± 0.02	0.56 ± 0.00	-2.91 ± 0.02	12.75 ± 0.09	**3.70**
30	**R**	-7.70 ± 0.16	8.93 ± 0.11	-2.94 ± 0.08	0.67 ± 0.00	6.99 ± 0.12	5.95 ± 0.24	**1.40**
31	**L**	-0.23 ± 0.10	10.80 ± 0.05	0.69 ± 0.02	0.48 ± 0.00	-2.14 ± 0.01	9.60 ± 0.12	**3.55**
32	**L**	1.02 ± 0.09	9.59 ± 0.05	-0.54 ± 0.02	0.42 ± 0.00	-3.50 ± 0.01	6.99 ± 0.10	**1.75**
33	**L**	0.20 ± 0.11	8.53 ± 0.04	0.04 ± 0.08	0.46 ± 0.00	-3.08 ± 0.01	6.15 ± 0.14	**1.65**
34	**V**	0.88 ± 0.22	6.66 ± 0.06	-0.57 ± 0.05	0.15 ± 0.00	-2.49 ± 0.02	4.63 ± 0.24	**2.20**
35	**D**	28.13 ± 0.17	2.06 ± 0.05	-2.84 ± 0.09	0.15 ± 0.00	-26.24 ± 0.13	1.26 ± 0.24	**-0.20**
36	**T**	0.51 ± 0.11	4.17 ± 0.06	-1.06 ± 0.06	0.17 ± 0.00	-1.68 ± 0.06	2.11 ± 0.15	**0.00**
38	**E**	25.15 ± 0.10	4.59 ± 0.05	-1.76 ± 0.03	0.30 ± 0.00	-24.39 ± 0.10	3.89 ± 0.16	**-0.30**
39	**T**	-0.28 ± 0.07	3.05 ± 0.03	-0.77 ± 0.03	0.15 ± 0.00	-0.34 ± 0.08	1.81 ± 0.12	**0.40**
40	**K**	-5.48 ± 0.18	0.63 ± 0.06	-5.33 ± 0.06	0.35 ± 0.01	4.76 ± 0.16	-5.07 ± 0.25	**-0.30**
41	**H**	1.92 ± 0.03	4.58 ± 0.05	-1.03 ± 0.02	0.27 ± 0.00	-1.09 ± 0.02	4.65 ± 0.06	**0.50**
42	**P**	-0.22 ± 0.04	0.68 ± 0.01	-0.02 ± 0.01	0.00 ± 0.00	0.23 ± 0.02	0.67 ± 0.05	**0.60**
43	**K**	-8.34 ± 0.05	0.63 ± 0.03	-0.14 ± 0.02	0.02 ± 0.00	7.68 ± 0.09	-0.15 ± 0.11	**-0.10**
44	**K**	-1.94 ± 0.15	3.66 ± 0.07	-2.85 ± 0.02	0.39 ± 0.0	1.39 ± 0.14	0.65 ± 0.22	**0.30**

					0			
46	**V**	0.15 ± 0.06	2.13 ± 0.03	-0.38 ± 0.02	0.15 ± 0.0 0	-1.19 ± 0.01	0.86 ± 0.07	**0.25**
47	**E**	23.16 ± 0.1 9	3.73 ± 0.06	-5.75 ± 0.13	0.34 ± 0.0 0	- 21.87 ± 0.1 7	-0.39 ± 0.29	**0.10**
48	**K**	- 10.97 ± 0.0 9	0.69 ± 0.02	-2.03 ± 0.06	0.02 ± 0.0 1	9.96 ± 0.08	-2.33 ± 0.13	**0.20**
49	**Y**	1.59 ± 0.26	8.77 ± 0.05	-1.13 ± 0.13	0.59 ± 0.0 1	-5.75 ± 0.18	4.07 ± 0.35	**2.15**
51	**P**	0.94 ± 0.08	3.22 ± 0.04	-0.30 ± 0.01	0.12 ± 0.0 0	-1.03 ± 0.03	2.95 ± 0.09	**0.00**
52	**E**	24.39 ± 0.0 7	2.27 ± 0.04	-1.05 ± 0.02	0.12 ± 0.0 0	- 22.36 ± 0.1 0	3.37 ± 0.13	**0.20**
54	**S**	1.95 ± 0.08	1.59 ± 0.06	-0.24 ± 0.05	0.10 ± 0.0 0	-2.43 ± 0.06	0.97 ± 0.13	**-0.40**
56	**F**	0.87 ± 0.10	8.42 ± 0.05	-0.78 ± 0.04	0.73 ± 0.0 0	-2.92 ± 0.03	6.32 ± 0.12	**2.35**
57	**T**	2.26 ± 0.04	3.75 ± 0.05	-1.10 ± 0.02	0.19 ± 0.0 0	-2.68 ± 0.02	2.42 ± 0.07	**2.40**
58	**K**	-0.45 ± 0.09	1.89 ± 0.05	-2.40 ± 0.02	0.43 ± 0.0 0	0.62 ± 0.09	0.09 ± 0.13	**0.50**
59	**K**	-4.95 ± 0.11	2.31 ± 0.06	-2.94 ± 0.03	0.25 ± 0.0 1	4.10 ± 0.10	-1.23 ± 0.16	**-0.10**
60	**M**	0.98 ± 0.08	7.69 ± 0.04	-0.57 ± 0.03	0.64 ± 0.0 0	-2.85 ± 0.07	5.89 ± 0.11	**2.00**
61	**V**	0.10 ± 0.06	4.64 ± 0.03	-0.39 ± 0.01	0.19 ± 0.0 0	-1.32 ± 0.01	3.22 ± 0.07	**2.20**
62	**E**	34.60 ± 0.1 0	2.01 ± 0.04	-2.88 ± 0.02	0.42 ± 0.0 0	- 31.33 ± 0.0 9	2.82 ± 0.14	**1.00**
63	**N**	0.82 ± 0.07	0.83 ± 0.04	-0.79 ± 0.02	0.14 ± 0.0 0	-1.03 ± 0.06	-0.03 ± 0.10	**0.50**
65	**K**	-4.27 ± 0.11	0.61 ± 0.04	-1.64 ± 0.01	0.03 ± 0.0 1	4.48 ± 0.14	-0.79 ± 0.18	**0.10**
66	**K**	-6.53 ± 0.07	1.03 ± 0.06	-1.46 ± 0.02	0.08 ± 0.0 1	5.80 ± 0.11	-1.08 ± 0.14	**0.40**
67	**I**	-0.06 ± 0.09	8.56 ± 0.04	-0.09 ± 0.02	0.42 ± 0.0 0	-1.39 ± 0.02	7.44 ± 0.10	**5.10**
68	**E**	31.06 ± 0.1 2	4.8 ± 0.06	-2.58 ± 0.02	0.41 ± 0.0 0	- 29.15 ± 0.1 1	4.54 ± 0.17	**1.40**

69	**V**	0.61 ± 0.11	6.03 ± 0.04	-0.09 ± 0.03	0.19 ± 0.00	-0.97 ± 0.01	5.77 ± 0.12	**3.10**
70	**E**	41.81 ± 0.18	4.44 ± 0.07	-4.82 ± 0.07	0.41 ± 0.00	-38.11 ± 0.15	3.73 ± 0.25	**2.20**
71	**F**	4.88 ± 0.11	11.54 ± 0.12	-3.49 ± 0.09	0.81 ± 0.00	-7.52 ± 0.05	6.22 ± 0.19	**4.05**
72	**D**	33.54 ± 0.08	0.94 ± 0.07	-3.32 ± 0.08	0.14 ± 0.00	-29.47 ± 0.09	1.83 ± 0.16	**3.13**
73	**K**	-25.06 ± 0.08	2.36 ± 0.05	-1.58 ± 0.02	0.29 ± 0.01	22.99 ± 0.08	-1.00 ± 0.13	**0.60**
75	**Q**	1.33 ± 0.09	2.89 ± 0.09	-2.67 ± 0.11	0.24 ± 0.01	-1.99 ± 0.10	-0.20 ± 0.19	**0.10**
76	**R**	-13.68 ± 0.18	4.93 ± 0.09	-6.38 ± 0.17	0.65 ± 0.01	12.91 ± 0.14	-1.57 ± 0.30	**1.10**
77	**T**	-0.27 ± 0.09	2.28 ± 0.06	-0.36 ± 0.02	0.12 ± 0.00	-0.03 ± 0.10	1.74 ± 0.14	**0.90**
78	**D**	36.75 ± 0.06	1.48 ± 0.06	-2.68 ± 0.02	0.10 ± 0.00	-30.8 ± 0.07	4.85 ± 0.11	**3.85**
79	**K**	-21.57 ± 0.07	0.34 ± 0.01	-1.18 ± 0.02	0.01 ± 0.01	19.71 ± 0.07	-2.69 ± 0.10	**-0.20**
80	**Y**	0.56 ± 0.09	2.50 ± 0.04	-0.80 ± 0.02	0.14 ± 0.01	-2.23 ± 0.17	0.17 ± 0.20	**0.40**
82	**R**	-9.18 ± 0.10	8.08 ± 0.10	-4.85 ± 0.06	0.84 ± 0.00	8.88 ± 0.09	3.77 ± 0.18	**0.90**
84	**L**	-0.20 ± 0.09	8.47 ± 0.06	-0.29 ± 0.03	0.50 ± 0.00	-2.38 ± 0.02	6.10 ± 0.12	**2.60**
86	**Y**	17.97 ± 0.09	15.07 ± 0.06	-1.65 ± 0.01	0.87 ± 0.00	-15.29 ± 0.04	16.97 ± 0.12	**5.30**
87	**I**	-0.06 ± 0.06	8.57 ± 0.04	-0.55 ± 0.01	0.25 ± 0.00	-0.54 ± 0.01	7.67 ± 0.07	**4.00**
88	**Y**	20.00 ± 0.12	11.11 ± 0.07	-2.69 ± 0.02	0.70 ± 0.00	-18.75 ± 0.09	10.37 ± 0.17	**6.50**
90	**D**	31.54 ± 0.17	1.88 ± 0.05	-3.96 ± 0.07	0.25 ± 0.00	-28.46 ± 0.14	1.25 ± 0.23	**3.40**
92	**K**	-12.91 ± 0.0	2.31 ± 0.06	-1.28 ± 0.04	0.21 ± 0.01	11.86 ± 0.06	0.19 ± 0.12	**0.10**

		7						
93	**M**	4.47 ± 0.15	10.14 ± 0.04	-1.66 ± 0.02	0.53 ± 0.00	-5.61 ± 0.04	7.87 ± 0.16	**4.60**
94	**V**	0.65 ± 0.07	6.15 ± 0.04	-0.32 ± 0.01	0.23 ± 0.00	-1.56 ± 0.01	5.15 ± 0.08	**3.20**
95	**N**	4.54 ± 0.03	7.29 ± 0.04	-0.19 ± 0.01	0.24 ± 0.00	-3.73 ± 0.01	8.15 ± 0.05	**5.20**
96	**E**	32.8 ± 0.10	3.90 ± 0.06	-2.33 ± 0.03	0.42 ± 0.00	-30.49 ± 0.10	4.30 ± 0.16	**1.90**
98	**L**	1.09 ± 0.07	9.99 ± 0.04	-0.88 ± 0.03	0.47 ± 0.00	-3.39 ± 0.01	7.28 ± 0.09	**4.60**
99	**V**	0.46 ± 0.08	6.78 ± 0.04	-0.52 ± 0.02	0.22 ± 0.00	-1.88 ± 0.01	5.06 ± 0.09	**2.90**
100	**R**	-5.26 ± 0.11	5.08 ± 0.07	-2.88 ± 0.06	0.68 ± 0.00	5.49 ± 0.10	3.11 ± 0.18	**1.40**
101	**Q**	0.25 ± 0.07	2.67 ± 0.04	-1.29 ± 0.02	0.25 ± 0.00	-1.20 ± 0.12	0.68 ± 0.14	**-0.10**
103	**L**	-0.02 ± 0.07	9.21 ± 0.04	-0.43 ± 0.04	0.48 ± 0.00	-2.14 ± 0.01	7.10 ± 0.09	**5.80**
105	**K**	-9.30 ± 0.11	4.44 ± 0.06	-2.86 ± 0.03	0.45 ± 0.00	8.06 ± 0.10	0.79 ± 0.16	**1.30**
106	**V**	-0.45 ± 0.20	6.24 ± 0.05	-0.71 ± 0.13	0.23 ± 0.00	-0.80 ± 0.02	4.51 ± 0.25	**4.45**
108	**Y**	0.83 ± 0.09	2.46 ± 0.05	-1.45 ± 0.04	0.13 ± 0.00	-2.32 ± 0.05	-0.35 ± 0.12	**-0.05**
109	**V**	0.29 ± 0.14	4.17 ± 0.05	-1.07 ± 0.04	0.16 ± 0.00	-2.56 ± 0.02	0.99 ± 0.15	**0.00**
110	**Y**	1.38 ± 0.22	3.54 ± 0.06	-1.60 ± 0.18	0.24 ± 0.00	-3.06 ± 0.07	0.50 ± 0.30	**0.30**
111	**K**	-15.04 ± 0.05	2.10 ± 0.05	-1.51 ± 0.03	0.18 ± 0.00	13.89 ± 0.05	-0.38 ± 0.10	**-0.70**
112	**P**	-0.25 ± 0.26	1.64 ± 0.06	0.12 ± 0.23	0.07 ± 0.00	-0.64 ± 0.02	0.94 ± 0.35	**-0.80**
113	**N**	3.27 ± 0.07	5.03 ± 0.06	-1.14 ± 0.07	0.30 ± 0.00	-3.47 ± 0.03	3.99 ± 0.12	**2.05**
114	**N**	2.66 ± 0.13	2.92 ± 0.06	-3.10 ± 0.03	0.17 ± 0.00	-3.11 ± 0.10	-0.46 ± 0.18	**1.25**
115	**T**	6.38 ± 0.09	0.08 ± 0.06	-1.49 ± 0.06	0.14 ± 0.00	-5.10 ± 0.04	0.01 ± 0.13	**1.20**
116	**H**	2.27 ± 0.02	5.53 ± 0.04	-0.95 ± 0.01	0.42 ± 0.00	-2.06 ± 0.02	5.21 ± 0.05	**3.10**
117	**E**	38.79 ± 0.1	2.72 ± 0.06	-2.73 ± 0.01	0.33 ± 0.0	-	4.18 ± 0.16	**0.40**

		0			0	34.93 ± 0.10		
118	**Q**	0.25 ± 0.11	1.56 ± 0.04	-1.95 ± 0.03	0.09 ± 0.01	-0.84 ± 0.16	-0.89 ± 0.20	**0.40**
119	**H**	2.59 ± 0.09	3.57 ± 0.07	-1.07 ± 0.01	0.39 ± 0.00	-2.62 ± 0.04	2.86 ± 0.12	**-0.40**
120	**L**	0.87 ± 0.10	9.22 ± 0.05	-0.75 ± 0..02	0.49 ± 0.00	-2.69 ± 0.02	7.14 ± 0.11	**4.90**
121	**R**	-4.19 ± 0.07	5.19 ± 0.06	-3.24 ± 0.02	0.79 ± 0.00	3.69 ± 0.07	2.24 ± 0.12	**1.70**
122	**K**	-11.74 ± 0.07	1.76 ± 0.04	-1.41 ± 0.03	0.17 ± 0.01	10.43 ± 0.08	-0.79 ± 0.12	**-0.20**
123	**S**	2.36 ± 0.11	1.30 ± 0.06	-0.54 ± 0.02	0.08 ± 0.00	-2.91 ± 0.08	0.29 ± 0.15	**-0.70**
124	**E**	35.96 ± 0.12	6.28 ± 0.07	-2.94 ± 0.07	0.48 ± 0.00	-33.13 ± 0.10	6.65 ± 0.19	**2.40**
126	**Q**	6.73 ± 0.13	3.36 ± 0.05	-4.06 ± 0.02	0.43 ± 0.00	-6.71 ± 0.12	-0.25 ± 0.18	**0.20**
128	**K**	-5.25 ± 0.17	5.10 ± 0.05	-4.73 ± 0.09	0.51 ± 0.01	4.51 ± 0.15	0.14 ± 0.25	**1.40**
129	**K**	-13.68 ± 0.07	1.97 ± 0.04	-1.58 ± 0.03	0.22 ± 0.01	12.12 ± 0.12	-0.95 ± 0.15	**-0.10**
130	**E**	25.21 ± 0.10	0.41 ± 0.06	-3.61 ± 0.01	0.32 ± 0.00	-21.2 ± 0.11	1.13 ± 0.16	**0.70**
131	**K**	-7.43 ± 0.18	2.10 ± 0.04	-3.98 ± 0.03	0.23 ± 0.01	7.15 ± 0.16	-1.93 ± 0.25	**0.80**
132	**L**	0.14 ± 0.07	6.18 ± 0.04	-0.40 ± 0.03	0.30 ± 0.00	-2.33 ± 0.01	3.89 ± 0.08	**2.30**
133	**N**	2.67 ± 0.05	5.98 ± 0.09	7.00 ± 0.06	0.24 ± 0.00	-2.74 ± 0.02	13.15 ± 0.12	**1.05**
134	**I**	0.05 ± 0.09	6.54 ± 0.03	-1.03 ± 0.02	0.38 ± 0.00	-1.76 ± 0.02	4.18 ± 0.10	**3.50**
136	**S**	3.50 ± 0.63	-0.46 ± 0.05	-0.01 ± 0.20	0.04 ± 0.00	-2.99 ± 0.02	0.08 ± 0.66	**0.40**
RMSE								**2.96**
R								**0.74**

Table S17. Calculated ΔE_{ele}, ΔE_{vdw}, $-T\Delta S$, ΔG_{np}, ΔG_{p}, $\Delta\Delta G$ in kcal/mol for 1H7M.

Residue		ΔE_{ele}	ΔE_{vdw}	$-T\Delta S$	ΔG_{np}	ΔG_{p}	$\Delta\Delta G_{cal}$	$\Delta\Delta G_{exp}$
4	**D**	8.54 ± 0.10	2.02 ± 0.04	-2.95 ± 0.05	0.07 ± 0.00	-7.70 ± 0.09	-0.02 ± 0.15	**0.53**
8	**E**	23.16 ± 0.22	3.26 ± 0.12	-5.37 ± 0.02	0.25 ± 0.00	-18.82 ± 0.14	2.48 ± 0.29	**0.77**
10	**R**	13.95 ± 0.11	5.67 ± 0.11	-4.93 ± 0.06	0.59 ± 0.01	-13.09 ± 0.13	2.19 ± 0.21	**0.77**
11	**K**	17.24 ± 0.12	6.53 ± 0.08	-3.34 ± 0.03	0.67 ± 0.01	-15.94 ± 0.09	5.16 ± 0.17	**0.29**
14	**D**	7.68 ± 0.24	1.28 ± 0.04	-4.23 ± 0.03	0.08 ± 0.00	-6.92 ± 0.28	-2.11 ± 0.38	**-0.24**
17	**K**	1.64 ± 0.18	2.38 ± 0.05	-3.01 ± 0.04	0.20 ± 0.01	-1.56 ± 0.17	-0.35 ± 0.25	**0.91**
23	**R**	-1.93 ± 0.08	1.51 ± 0.08	-2.86 ± 0.04	0.21 ± 0.02	1.20 ± 0.15	-1.87 ± 0.20	**-0.07**
24	**K**	-2.48 ± 0.09	3.08 ± 0.07	-2.15 ± 0.02	0.34 ± 0.01	1.79 ± 0.14	0.58 ± 0.18	**-0.43**
30	**K**	0.24 ± 0.09	5.10 ± 0.07	-3.22 ± 0.09	0.49 ± 0.00	-0.82 ± 0.09	1.79 ± 0.17	**1.20**
35	**K**	8.00 ± 0.08	3.64 ± 0.05	-2.15 ± 0.03	0.26 ± 0.01	-6.54 ± 0.08	3.21 ± 0.13	**-0.12**
41	**R**	18.86 ± 0.24	3.25 ± 0.10	-6.29 ± 0.09	0.57 ± 0.01	-16.66 ± 0.18	-0.27 ± 0.33	**0.07**
44	**R**	8.20 ± 0.10	1.46 ± 0.07	-1.37 ± 0.05	0.33 ± 0.00	-6.47 ± 0.09	2.15 ± 0.16	**-0.33**
46	**D**	19.03 ± 0.10	-1.12 ± 0.05	-3.28 ± 0.02	0.07 ± 0.00	-15.94 ± 0.10	-1.24 ± 0.15	**-0.05**
48	**K**	12.56 ± 0.17	4.70 ± 0.11	-5.36 ± 0.11	0.72 ± 0.00	-11.61 ± 0.18	1.01 ± 0.30	**1.10**
49	**E**	8.44 ± 0.19	0.73 ± 0.06	-4.49 ± 0.03	0.23 ± 0.00	-7.27 ± 0.16	-2.36 ± 0.26	**0.05**
50	**D**	14.61 ± 0.14	2.09 ± 0.07	-3.01 ± 0.02	0.14 ± 0.00	-13.80 ± 0.14	0.03 ± 0.21	**-0.36**
52	**E**	6.37 ± 0.21	2.83 ± 0.09	-5.30 ± 0.04	0.37 ± 0.00	-5.95 ± 0.18	-1.68 ± 0.29	**-0.57**

56	**R**	21.05 ± 0.26	4.07 ± 0.07	-9.05 ± 0.04	0.67 ± 0.01	-18.50 ± 0.20	-1.76 ± 0.34	**0.26**
64	**E**	10.73 ± 0.28	2.75 ± 0.07	-8.41 ± 0.08	0.33 ± 0.00	-9.75 ± 0.23	-4.35 ± 0.38	**1.29**
66	**E**	5.61 ± 0.16	0.60 ± 0.13	-2.29 ± 0.06	0.17 ± 0.01	-5.61 ± 0.12	-1.52 ± 0.25	**0.26**
71	**E**	9.58 ± 0.08	1.52 ± 0.06	-1.73 ± 0.02	0.22 ± 0.00	-8.41 ± 0.08	1.18 ± 0.13	**0.74**
78	**R**	-0.28 ± 0.14	6.59 ± 0.07	-3.85 ± 0.02	0.53 ± 0.01	0.29 ± 0.14	3.28 ± 0.21	**-0.19**
80	**H**	0.49 ± 0.05	2.20 ± 0.07	-0.87 ± 0.01	0.11 ± 0.00	-0.46 ± 0.03	1.47 ± 0.09	**0.50**
89	**D**	9.21 ± 0.08	1.71 ± 0.04	-1.67 ± 0.01	0.04 ± 0.00	-7.51 ± 0.08	1.78 ± 0.12	**1.36**
92	**E**	3.15 ± 0.08	1.25 ± 0.05	-1.55 ± 0.03	0.06 ± 0.00	-3.40 ± 0.07	-0.49 ± 0.12	**0.41**
94	**R**	10.64 ± 0.13	3.70 ± 0.08	-2.88 ± 0.06	0.57 ± 0.00	-8.80 ± 0.10	3.23 ± 0.19	**0.31**
RMSE								**2.21**
R								**0.07**

Table S18. Calculated ΔE_{ele}, ΔE_{vdw}, $-T\Delta S$, ΔG_{np}, ΔG_{p}, $\Delta\Delta G$ in kcal/mol for 1TIT.

Residue		ΔE_{ele}	ΔE_{vdw}	$-T\Delta S$	ΔG_{np}	ΔG_{p}	$\Delta\Delta G_{cal}$	$\Delta\Delta G_{exp}$
4	**V**	0.10 ± 0.04	5.27 ± 0.03	-0.41 ± 0.01	0.21 ± 0.00	-1.02 ± 0.01	4.15 ± 0.06	**2.80**
13	**V**	0.85 ± 0.14	4.88 ± 0.06	-0.34 ± 0.04	0.16 ± 0.00	-1.73 ± 0.02	3.82 ± 0.16	**2.15**
23	**I**	0.50 ± 0.08	8.72 ± 0.05	-0.34 ± 0.03	0.33 ± 0.00	-1.19 ± 0.01	8.02 ± 0.10	**2.70**
41	**L**	0.08 ± 0.12	7.27 ± 0.05	-0.60 ± 0.02	0.45 ± 0.00	-1.75 ± 0.02	5.45 ± 0.13	**2.70**
58	**L**	-0.76 ± 0.08	9.34 ± 0.05	-0.20 ± 0.02	0.34 ± 0.00	-0.04 ± 0.01	8.68 ± 0.10	**3.23**
60	**L**	-1.28 ± 0.06	7.73 ± 0.05	-0.30 ± 0.02	0.53 ± 0.00	-0.18 ± 0.01	6.50 ± 0.08	**4.88**
86	**V**	-0.23 ± 0.18	7.56 ± 0.05	-0.21 ± 0.04	0.16 ± 0.00	-1.01 ± 0.01	6.27 ± 0.19	**4.45**
RMSE								**3.30**
R								**0.32**