Supporting Information for

Unraveling the degradation of artificial amide bonds in Nylon oligomer hydrolase: From induced-fit to acylation processes

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SI-1 details of the QM region

Details concerning the QM region of the enzyme and its boundaries are reported in Table S1. A total number of 17 monovalent hydrogen-like link atoms were used to compensate the dangling bonds at the frontier between the QM and the MM subsystems. These boundaries, cutting across chemical bond, are listed in Table S1. C and N are in all cases carbonyl carbon atoms and amide nitrogen atoms, respectively. The QM region of Ald contains atoms within two carbon and hydrogen pairs from carbonyl carbon or nitrogen atom of the amide bond.

Table S1 details of the QM region

Amino acid residue	True bond Atom1(QM)-Atom2(MM)	QM/MM border Atom1-H(cap)-Atom2
MET111	$C_\alpha - C_\beta$	$C_\alpha - H - C_\beta$
	$C_\alpha - N$	$C_\alpha - H - N$
SER112	$C_\alpha - C$	$C_\alpha - H - C$
LYS115	$C_\delta - C_\gamma$	$C_\delta - H - C_\gamma$
GLU168	$C_\beta - C_\alpha$	$C_\beta - H - C_\alpha$
TYR170	$C_\beta - C_\alpha$	$C_\beta - H - C_\alpha$
TYR215	$C_\beta - C_\alpha$	$C_\beta - H - C_\alpha$
SER217	$C_\alpha - N$	$C_\alpha - H - N$
	$C_\alpha - C$	$C_\alpha - H - C$
GLN266	$C_\alpha - N$	$C_\alpha - H - N$
	$C_\alpha - C_\beta$	$C_\alpha - H - C_\beta$
GLY267	$C_\alpha - C$	$C_\alpha - H - C$
GLY344	$C_\alpha - N$	$C_\alpha - H - N$
ILE345	$C_\alpha - C_\beta$	$C_\alpha - H - C_\beta$
	$C_\alpha - C$	$C_\alpha - H - C$

SI-2 Details about the parameters used in QM/MM metadynamics simulations

In the practical use the extended Lagrangean for our specific simulations

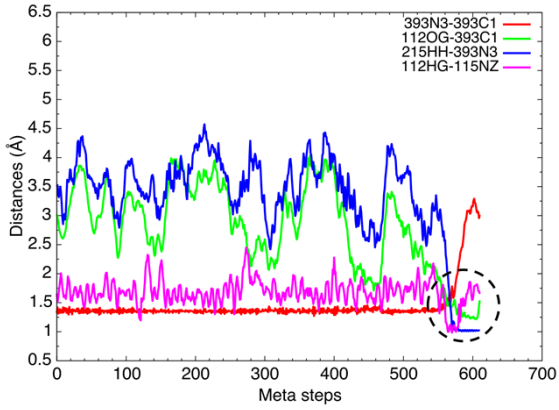
$$L = L^{\mathrm{CP}} + \frac{1}{2}\sum_{\alpha} M_{\alpha}\dot{s}_{\alpha}^{2} - \frac{1}{2}\sum_{\alpha} k_{\alpha}\left[S_{\alpha}\left(\{\mathbf{R}_{I}\}\right) - s_{\alpha}\right]^{2} + V\left(t, s_{\alpha}\right), \qquad (2)$$

the single collective variable (CV) s_1 (α = 1) evolves according to a fictitious dynamics in which the mass M_{α} and spring constant k_{α} are set to 20 a.u. and 0.24 a.u., respectively. These parameters to ensure a good control of the conserved quantities along at least for the simulation times investigated in the present work[1,2]. The history dependent potential $V\left(t, s_{\alpha}\right)$ was constructed by accumulation of small Gaussian with a height of 0.5 kcal/mol and a width of 0.3 au and a new Gaussian function was added every 140 steps (13.44 fs). After the reaction occurred, and to speed up the simulations, after 226 meta-steps, we increased the height $W_i = 1.0$ kcal/mol. This does not penalize too much our simulations since, in any case, our accuracy is bound by the typical DFT error[3] bar which is at very best of the order of this order of magnitude. These simulations lasted in any case long enough to reproduce the cleavage of the amide bond.

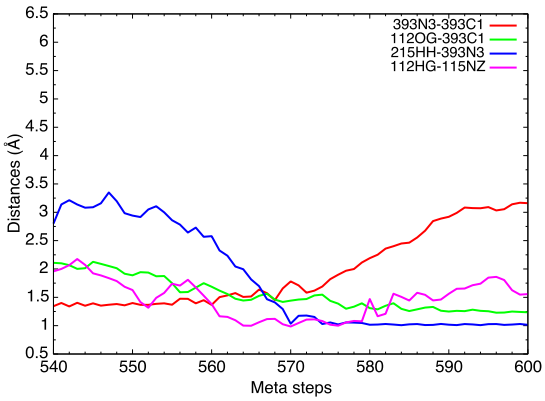
SI-3 Results for the WT system

Evolution of the reaction coordinate adopted for the metadynamics and the more relevant distances in case of the WT; r_1 = N3(Ald393)-C1(Ald393) in red, r_2 = OG(Ser112)-C1(Ald393) in green, r_3 = HH(Tyr215)- N3(Ald393) in blue, and r_4 = HG(Ser112)-NZ(Lys115) in magenta. Panel (i) refers to the whole simulation, panel (ii) to the specific region encircled in (i), and (iii) shows the reaction mechanism of WT going from (a) to (f). (iv) is described Free-energy surface as a function of the Ser112-O_γ–Ald-C and the Ald-N–Ald-C distances based on Ref 4. The free energy value of between (a) and (c), between (b) and (c) are ~35 kcal/mol and ~21 kcal/mol, respectively.

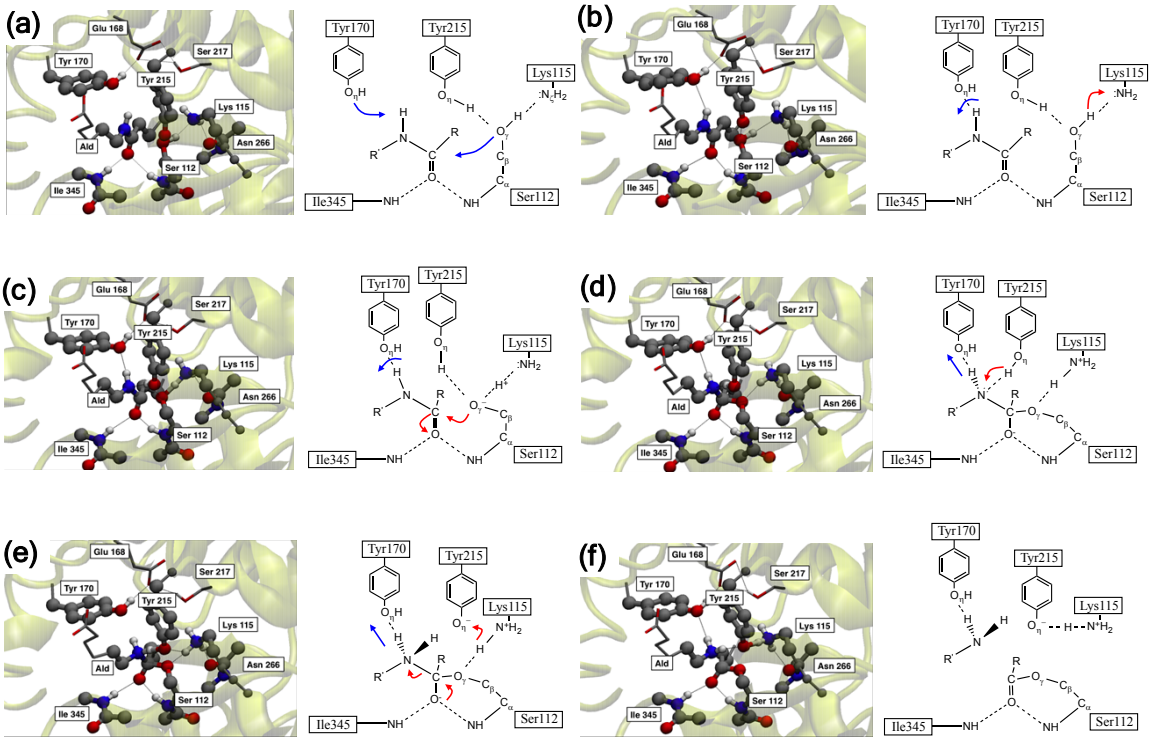
(i)



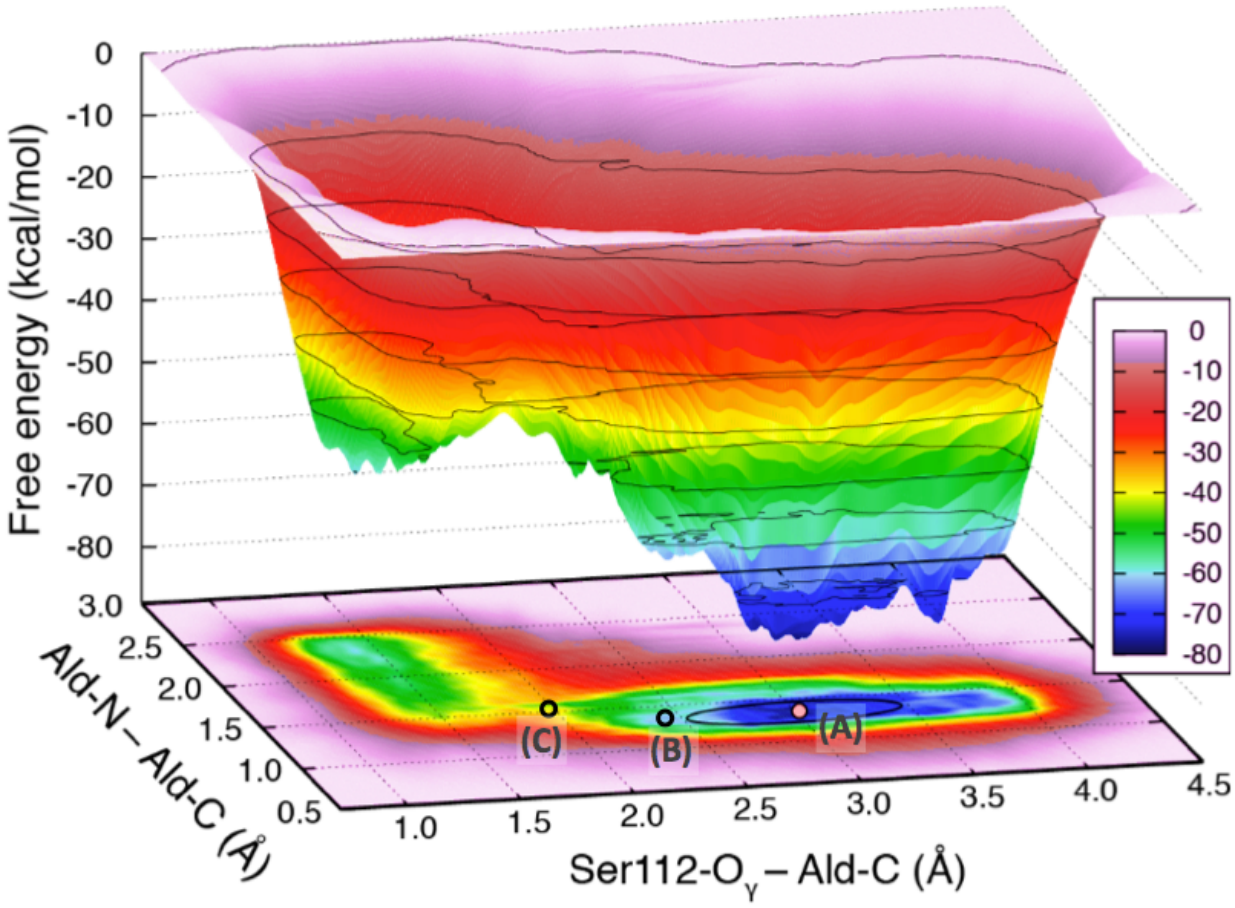
(ii)



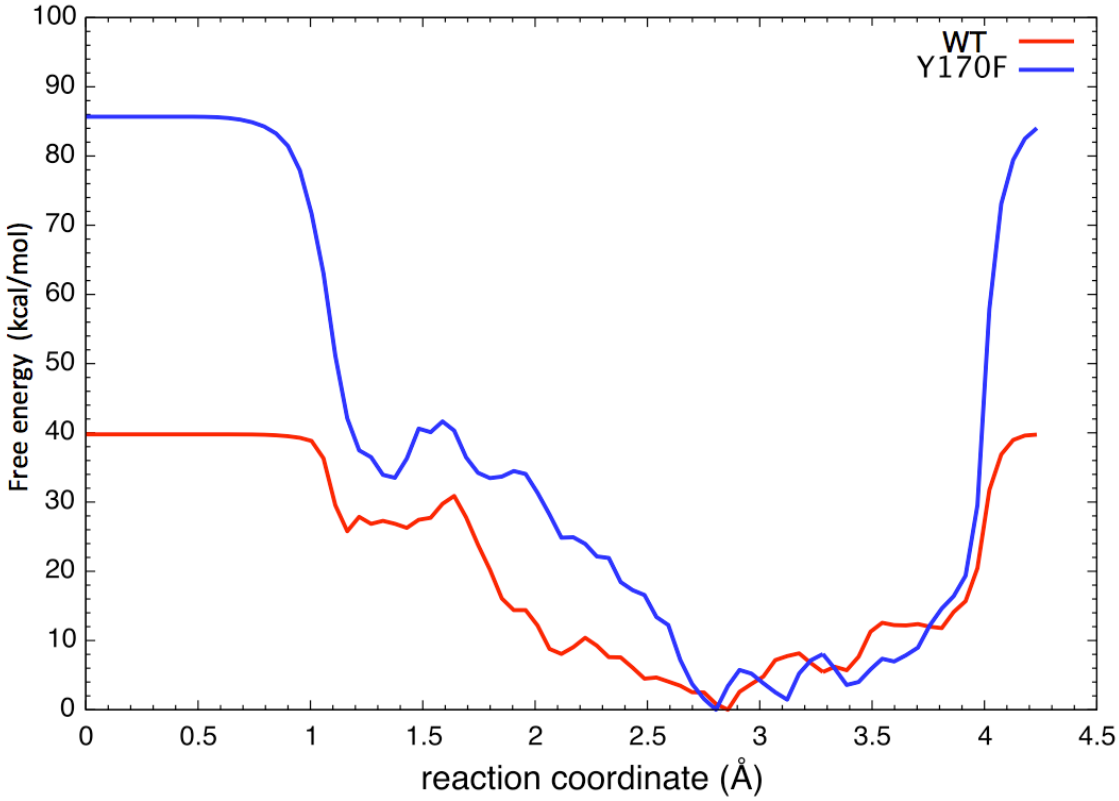
(iii)



(iv)


Free energy (kcal/mol)
0
-10
-20
-30
-40
-50
-60
-70
-80
Ald-N – Ald-C (Å)
3.0
2.5
2.0
1.5
1.0
0.5
Ser112-Oγ – Ald-C (Å)
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
(A)
(B)
(C)

SI-4 Free energy profile based on QM/MM CPMD complemented with metadynamics



In the present study, free energy differences have to be intended as approximate estimates based on the comparison of the maxima for the acylation of the two systems WT and Y170F. As explained in the main text, we followed the simulation until the first reaction occurs. Because of the specific choice of collective variable, the system is unable to realize the reverse reaction thus our estimations are more to be intended as an upper bound reflecting the behavior of WT and Y170F, which in any case are clearly different.

SI-5 Metastable state from Open form to Close form of Y170F

Monitored distances and related free energy differences for the four minima of the free energy surface of Y170F reported and discussed in the main text.

Table S2. Information of meta-stable states

State	d_1 [a]	d_2 [a]	Difference of Free energy [b]
A	10.95	15.05	0.651
B	9.05	7.45	0.761
C	7.15	5.55	0.238
D	4.85	5.25	0.000

[a] in *Å*. [b] in *kcal/mol*.

SI-6 IFIE DATA

IFIE values between all the amino acid residues and the substrate

WT

	ALD(1) [a]	ALD(2) [a]	ALD(3) [a]
MET1	-9.559105	0.120429	15.541572
ASN2	-0.099988	-0.002394	0.294895
ALA3	-0.208065	0.00067	0.530807
ARG4	-7.628464	0.092898	10.55693
SER5	-0.103114	0.007902	0.161818
THR6	0.046946	0.007066	-0.088301
GLY7	0.095201	-0.003008	0.017426
GLN8	0.155201	-0.012151	-0.536121
HIS9	0.118038	-0.026095	-0.070555
PRO10	-0.347083	0.000019	0.777611
ALA11	-0.020774	-0.011264	-0.173986
ARG12	-9.674934	-0.159452	16.133624
TYR13	-0.079836	0.016542	0.19251
PRO14	-0.042097	-0.013561	0.023097
GLY15	-0.1559	-0.012206	0.276628
ALA16	0.009494	-0.000173	-0.099475
ALA17	-0.090343	0.001898	0.282617
ALA18	0.198787	0.007237	-0.478046
GLY19	-0.017626	-0.017821	-0.021486
GLU20	7.983794	0.021745	-12.213142
PRO21	0.05459	0.017722	-0.016057
THR22	0.21052	0.013243	-0.506131
LEU23	-0.211674	0.012757	0.611199
ASP24	8.586803	0.001138	-13.780593
SER25	-0.159206	0.009076	0.451719
TRP26	-0.327861	0.00861	0.846426
GLN27	-0.041524	0.010702	0.179758
GLU28	7.139964	0.046398	-10.36759
PRO29	0.082767	0.00334	-0.169108
PRO30	0.014867	-0.007936	-0.060348

HIS31	-7.74626	-0.056736	11.716641
ASN32	0.138282	0.013128	-0.249269
ARG33	-6.887792	-0.112268	9.468759
TRP34	-0.114681	-0.001626	0.311337
ALA35	0.10693	0.01984	-0.144002
PHE36	0.024368	0.016002	0.026182
ALA37	-0.034788	0.007417	0.144205
HIS38	0.129999	0.023215	-0.067562
LEU39	0.253444	0.011694	-0.613456
GLY40	0.245745	0.011414	-0.673626
GLU41	10.613675	0.368447	-17.32395
MET42	0.256839	-0.028055	-1.136363
VAL43	0.316043	0.020554	-0.930516
PRO44	-0.37699	-0.027408	1.061092
SER45	0.101507	0.007718	-0.224966
ALA46	-0.284134	-0.034707	0.735137
ALA47	0.294807	0.056224	-0.684642
VAL48	0.318419	0.080449	-0.211522
SER49	-0.058196	0.002172	-0.197856
ARG50	-10.670808	-0.676027	11.822075
ARG51	-10.247762	-0.631839	11.430985
PRO52	0.213996	0.030078	-0.322982
VAL53	0.06956	0.007051	0.030605
ASN54	0.015723	-0.011807	0.242884
ALA55	0.233824	0.031839	-0.192446
PRO56	0.211556	0.019658	-0.171052
GLY57	0.175369	0.039012	-0.271799
HIS58	-0.26031	-0.049652	0.380538
ALA59	0.06453	0.024468	-0.155699
LEU60	-0.51379	-0.048167	0.409192
ALA61	0.589845	0.051733	-0.41024
ARG62	-11.811668	-0.456322	10.154445
LEU63	0.131033	-0.004298	-0.034677
GLY64	0.108675	-0.024926	0.067195
ALA65	-0.066669	-0.020831	0.137667

ILE66	0.077457	-0.013879	0.025271
ALA67	0.211631	-0.017283	-0.003948
ALA68	-0.167816	-0.020169	0.168231
GLN69	-0.710903	-0.017373	0.39254
LEU70	0.472863	-0.014462	-0.138425
PRO71	0.183086	0.035569	-0.218609
ASP72	14.672041	0.209267	-10.048642
LEU73	0.630594	0.029418	-0.374646
GLU74	12.836173	0.446491	-10.328868
GLN75	0.166811	0.033102	-0.258711
ARG76	-18.671189	-0.166199	11.282428
LEU77	1.328207	0.091747	-0.767316
GLU78	14.187329	0.693786	-12.230563
GLN79	1.138773	0.059664	-0.717556
THR80	1.470589	0.030982	-0.614918
TYR81	0.925971	0.249981	-0.958437
THR82	0.463422	0.285393	-0.999761
ASP83	15.847434	1.727509	-17.118824
ALA84	-1.065962	-0.195416	0.856767
PHE85	1.304081	0.167498	-0.744626
LEU86	-1.167311	-0.103346	0.644698
VAL87	0.96966	0.035967	-0.474355
LEU88	-0.869016	-0.011066	0.36206
ARG89	-10.734146	-0.243158	8.894021
GLY90	-0.640346	-0.008532	0.379059
THR91	0.124908	0.016317	-0.201727
GLU92	10.424515	0.293551	-8.927034
VAL93	0.451387	0.005578	-0.23686
VAL94	-0.183321	0.018156	0.056001
ALA95	-0.149818	-0.021426	0.200229
GLU96	12.229774	0.603423	-11.046477
TYR97	-0.602938	-0.096169	0.600861
TYR98	0.598861	0.096551	-0.52889
ARG99	-15.657095	-1.344363	16.002247
ALA100	-0.240308	0.006773	-0.006454

GLY101	-0.41925	-0.05882	0.305524
PHE102	0.491904	0.122051	-0.768683
ALA103	-0.503871	-0.108289	0.677862
PRO104	0.344685	0.076324	-0.441209
ASP105	10.7691	0.697856	-11.862228
ASP106	12.245579	1.08349	-15.04756
ARG107	-11.723863	-0.996816	15.945859
HIS108	-19.371455	-3.768979	22.865095
LEU109	0.104976	0.037413	-0.192457
LEU110	1.16147	0.778233	-0.231846
MET111	2.020261	0.851165	-0.517182
SER112	-0.963782	-9.458539	-0.775507
VAL113	0.350456	-5.669906	4.178238
SER114	-1.764626	-2.067289	3.325766
LYN115	-0.613732	-0.775869	0.87164
SER116	-0.275939	-0.321632	1.453443
LEU117	-1.364802	-0.255339	1.722693
CYS118	-0.895955	-0.300718	1.284316
GLY119	-0.777877	-0.156759	1.196633
THR120	-0.847222	-0.091779	1.517197
VAL121	-0.815512	-0.054301	0.987524
VAL122	-0.637157	-0.053994	0.67911
GLY123	-0.40779	-0.038101	0.689443
ALA124	-0.575881	-0.031851	0.738451
LEU125	-0.510292	-0.021245	0.583563
VAL126	-0.371798	-0.032953	0.444758
ASP127	10.419469	0.077291	-10.473937
GLU128	9.217565	0.108916	-10.625486
GLY129	-0.351852	-0.009637	0.405891
ARG130	-9.480139	-0.078931	10.996887
ILE131	-0.131013	-0.010414	-0.008534
ASP132	10.045765	-0.140248	-10.534792
PRO133	0.070093	-0.023549	-0.108275
ALA134	0.499295	-0.042641	-0.467954
GLN135	-0.256718	-0.009053	0.2331

PRO136	0.560682	-0.027698	-0.640066
VAL137	-0.2006	0.029251	0.050746
THR138	-0.237498	0.033816	0.095051
GLU139	8.994867	-0.151898	-10.788767
TYR140	-0.264696	0.03576	0.313757
VAL141	-0.047779	0.023241	-0.238862
PRO142	0.19014	-0.0325	-0.362651
GLU143	9.805342	-0.172272	-13.820354
LEU144	0.033344	-0.019177	-0.216843
ALA145	0.267967	-0.033414	-0.221132
GLY146	-0.296895	0.015934	0.611486
SER147	0.197355	-0.030952	-0.171749
VAL148	-0.280009	0.030599	0.820119
TYR149	0.079723	-0.009376	-0.241851
ASP150	10.178443	-0.280972	-12.382175
GLY151	-0.140575	0.002425	0.424641
PRO152	0.012827	0.011622	0.265089
SER153	-0.046178	0.014313	-0.274516
VAL154	0.648353	-0.050477	-0.88461
LEU155	0.813225	-0.03152	-0.775168
GLN156	0.291587	-0.008155	0.059348
VAL157	0.951961	-0.106743	-0.860962
LEU158	1.296182	-0.098122	-1.420103
ASP159	19.542372	-0.646275	-16.342737
MET160	2.142156	-0.380107	-0.757636
GLN161	0.082866	-0.061295	0.253753
ILE162	-1.361671	0.124829	0.93811
SER163	1.390496	-0.163177	-1.364028
ILE164	-1.103558	0.095155	0.422396
ASP165	15.400628	-0.834072	-19.521998
TYR166	-0.786062	0.141132	-1.881532
ASN167	2.561385	-0.149309	1.451233
GLU168	24.24511	-7.063472	-73.481856
ASP169	35.936394	-2.698432	-30.937992
TYR170	-2.067283	-6.006361	0.730654

VAL171	-1.748349	0.55526	1.012574
ASP172	17.419074	-0.75964	-21.79362
PRO173	-0.197922	-0.131417	-2.948337
ALA174	-0.659754	0.018601	-0.950819
SER175	-0.641129	-0.038634	-0.790383
GLU176	15.146321	-0.948664	-30.507103
VAL177	-0.782818	0.004148	-5.224215
GLN178	-1.129122	0.225854	-9.718468
THR179	-0.801534	0.191929	2.371857
HIS180	-18.415167	1.941628	65.527575
ASP181	18.309799	-2.629315	-115.268702
ARG182	-14.646513	0.866617	34.52045
SER183	-0.833071	0.16465	4.573826
ALA184	-0.49807	0.107177	2.616624
GLY185	-0.425965	0.133804	2.345636
TRP186	0.119336	-0.052028	-1.853828
ARG187	-17.108564	0.820202	42.746472
THR188	-0.319277	-0.011431	1.136007
ARG189	-11.222017	0.243305	22.124365
ARG190	-11.345035	0.208901	19.052732
HIS191	-0.483167	0.044325	2.264109
GLY192	-0.060722	0.008879	-0.339831
ASP193	13.108294	-0.59058	-26.06609
PRO194	-0.407842	0.057727	0.994202
ALA195	0.257771	-0.010827	-1.452841
ASP196	10.713239	-0.166453	-19.247558
THR197	0.430341	-0.084926	-1.605809
TYR198	0.314016	-0.065973	-0.522515
GLU199	10.474911	-0.31919	-17.394122
PHE200	0.198799	-0.067516	-0.521303
LEU201	0.083677	-0.034032	0.749833
THR202	-0.118996	0.004537	1.353393
THR203	-0.197119	0.004578	0.848128
LEU204	0.166999	-0.03067	-0.287569
ARG205	-12.149705	0.54587	17.736528

GLY206	0.714023	-0.079176	-0.981955
ASP207	15.793575	-0.778906	-16.669753
GLY208	-0.264136	0.030998	0.535535
SER209	-0.363367	0.042015	0.757417
THR210	0.23001	-0.031552	-0.624296
GLY211	-0.425448	0.042153	0.351421
GLU212	19.743205	-0.900134	-14.687383
PHE213	0.327373	-0.078711	-0.944588
GLN214	0.046765	0.120239	1.889925
TYR215	-1.306776	-4.22365	0.835303
CYS216	-0.100588	-0.19701	-2.717152
SER217	-0.986113	0.26505	-1.62388
ALA218	-0.931214	0.563496	2.077056
ASN219	-2.185962	0.436372	4.168364
THR220	-0.45709	0.144577	1.109075
ASP221	15.977749	-0.459309	-39.276132
VAL222	-0.892037	0.109628	2.11968
LEU223	-0.720923	0.086693	1.702197
ALA224	-0.664962	0.057888	1.309423
TRP225	-0.538021	0.032757	1.045097
ILE226	-0.549943	0.013252	1.127015
VAL227	-0.466916	0.018349	0.925932
GLU228	10.698042	0.072031	-17.141222
ARG229	-10.338744	0.113835	14.806172
VAL230	-0.32786	-0.004804	0.650121
THR231	-0.420077	0.007757	0.68344
GLY232	-0.390519	-0.000218	0.637843
LEU233	-0.119893	0.005441	-0.011326
ARG234	-9.959583	-0.281332	15.639432
TYR235	-0.07449	-0.014224	0.530295
VAL236	0.231893	0.067963	-0.111344
GLU237	9.787511	0.425068	-13.301202
ALA238	-0.040914	0.006298	0.486252
LEU239	0.095224	0.012733	0.376178
SER240	0.224074	0.043559	0.285256

THR241	-0.205581	-0.019855	0.689263
TYR242	-0.209982	-0.02124	0.454198
LEU243	0.251006	-0.013491	-0.030625
TRP244	0.04969	0.032008	0.137874
ALA245	-0.17211	-0.009826	0.463173
LYS246	-10.77263	-0.292437	12.133086
LEU247	-0.01758	-0.020814	0.305136
ASP248	9.826716	0.402301	-10.214114
ALA249	0.185697	0.022083	-0.023869
ASP250	10.280141	0.57922	-11.122026
ARG251	-11.925782	-0.931392	14.110488
ASP252	11.221428	0.758333	-14.313644
ALA253	0.3287	0.104879	-0.462719
THR254	-0.45993	-0.114174	0.684177
ILE255	0.713931	0.248212	-1.172248
THR256	-0.436526	-0.216701	0.128852
VAL257	0.238766	-0.037382	-0.771872
ASP258	11.771218	-0.158765	-24.219036
THR259	-0.533908	0.059779	2.295547
THR260	-0.497567	0.019315	1.754337
GLY261	-0.339505	0.006201	1.159116
PHE262	0.162819	0.073656	-0.060654
GLY263	0.145004	0.016056	-0.986771
PHE264	0.23648	-0.036665	0.180993
ALA265	0.892707	0.309494	-2.860072
ASN266	1.363033	0.015909	-9.424401
GLY267	1.772201	0.561793	-2.834516
GLY268	0.255502	1.286823	0.764669
VAL269	-1.067895	-0.413345	3.389109
SER270	0.83157	0.706344	-0.892748
CYS271	-0.366531	-0.241333	0.780855
THR272	0.317796	0.12287	-0.198238
ALA273	0.39232	0.069964	-0.330877
ARG274	-12.181812	-0.679847	11.773962
ASP275	12.367408	0.802364	-13.283889

LEU276	-0.123725	-0.076376	0.081216
ALA277	0.384468	-0.083297	0.005018
ARG278	-12.002905	-0.754004	12.512926
VAL279	-0.342389	-0.079628	0.33539
GLY280	0.223367	-0.077167	0.027259
ARG281	-12.55688	-0.361173	11.017474
MET282	-0.362561	-0.069701	0.401352
MET283	-0.646265	-0.080465	0.583227
LEU284	-0.16971	-0.060882	0.247161
ASP285	11.295597	0.21848	-10.006217
GLY286	-0.413879	-0.012206	0.211
GLY287	-0.195553	-0.023593	0.049183
VAL288	-0.362026	0.00512	-0.014828
ALA289	0.318348	0.024094	-0.162028
PRO290	-0.324341	-0.031497	0.312714
GLY291	-0.285443	-0.02466	0.314397
GLY292	-0.297711	-0.019194	0.181198
ARG293	-10.569248	-0.080121	10.253831
VAL294	-0.165115	0.010418	-0.080672
VAL295	0.191668	-0.007662	-0.400615
SER296	-0.293577	-0.009889	0.428635
GLU297	11.541082	0.012829	-10.028036
ASP298	12.672044	-0.144866	-10.987144
TRP299	0.415752	-0.069899	-0.031162
VAL300	0.819616	-0.01791	-0.593706
ARG301	-11.214836	-0.020876	9.665966
ARG302	-16.098126	0.423248	13.473441
VAL303	0.539346	-0.063492	-0.062418
LEU304	0.806216	-0.047943	-0.001335
ALA305	0.091966	-0.009221	0.22342
GLY306	0.519778	-0.037961	0.062869
GLY307	-0.919896	0.047676	0.052551
SER308	-0.143411	0.029981	0.396158
HIS309	-19.542306	0.595381	12.08081
GLU310	15.474091	-0.534295	-11.768014

ALA311	-0.392586	0.015456	0.080629
MET312	0.892691	-0.127809	-1.133597
THR313	1.068631	-0.024193	0.106939
ASP314	47.985953	-2.035407	-17.539676
LYS315	-57.317851	3.518075	28.361858
GLY316	-1.558514	0.157355	0.124457
PHE317	3.202851	0.017556	0.19949
THR318	-6.524152	0.328169	0.94828
ASN319	-8.945864	0.320406	1.495534
THR320	-3.74981	0.26077	0.476802
PHE321	-5.192517	0.219183	0.731543
PRO322	1.087453	-0.126318	-0.417379
ASP323	18.379509	-0.542201	-11.363003
GLY324	-0.862693	0.031347	0.019027
SER325	-1.653176	0.057415	0.179851
TYR326	0.401471	0.073698	-0.111929
THR327	-2.308376	0.172053	0.696054
ARG328	-15.382928	0.405859	14.125394
GLN329	-0.55131	0.269274	-1.87294
TRP330	1.190906	0.364609	-1.21948
TRP331	1.478462	-0.673261	0.875457
CYS332	-2.045188	0.364968	0.4819
THR333	2.025287	-0.188595	-0.153037
GLY334	0.13855	-0.001804	0.183817
ASN335	-1.02996	0.02489	0.358838
GLU336	14.950416	-0.099308	-9.568799
ARG337	-16.29133	0.01857	10.531807
GLY338	-0.273781	0.023148	-0.04645
ASN339	-0.353138	0.01556	0.133794
VAL340	1.04918	-0.143995	-0.249715
SER341	-0.963013	0.287916	-0.130849
GLY342	-0.649423	-0.368959	-0.252498
ILE343	-1.808559	0.195445	0.847046
GLY344	-1.859092	-0.427326	-3.181544
ILE345	1.901621	-14.118838	7.42136

HIS346	-3.737777	-1.522903	-1.494674
GLY347	-1.7869	-1.29356	2.27303
GLN348	-3.307946	-2.680984	3.913188
ASN349	5.445004	0.586034	-1.627315
LEU350	-2.634866	-0.021757	0.937467
TRP351	3.381356	-0.261097	-1.012196
LEU352	-1.614197	0.111605	0.450295
ASP353	17.152405	-0.075388	-10.955283
PRO354	-0.832861	0.031893	0.343056
LEU355	-0.632947	0.00492	0.305377
THR356	-0.539576	0.020075	0.249809
ASP357	11.91273	0.203614	-10.005015
SER358	-0.419049	0.05485	-0.006211
VAL359	0.794235	-0.006312	-0.466786
ILE360	-0.758171	0.00146	0.448713
VAL361	1.13492	0.074812	-0.76594
LYS362	-25.223541	-1.525117	17.409468
LEU363	1.398439	0.463482	-1.261618
SER364	-1.703517	-0.736272	1.942157
SER365	0.327354	0.863788	-2.111375
TRP366	-0.428201	-0.167101	0.432976
PRO367	-0.754584	0.148917	-0.986379
ASP368	23.362522	0.214316	-20.000239
PRO369	0.35101	0.690696	-0.189405
TYR370	5.895507	-0.046085	0.438179
THR371	-3.275785	-0.216496	0.387912
GLU372	42.901125	-0.965073	-16.952082
HIS373	-1.78095	-0.066707	1.13267
TRP374	-1.217268	0.059575	0.732631
HIS375	-25.833371	0.427367	1.282801
ARG376	-29.988461	0.353907	13.923294
LEU377	-0.972467	0.040917	0.146012
GLN378	-5.786581	-0.021959	1.426891
ASN379	-6.642828	0.125127	0.137429
GLY380	-2.763892	0.028966	0.565693

ILE381	-2.109224	0.023356	0.532274
LEU382	-1.712215	0.038703	0.38311
LEU383	-1.669506	-0.020618	0.484293
ASP384	17.406536	0.092144	-10.721909
VAL385	-1.322745	0.008089	0.463177
SER386	-0.880121	-0.00644	0.264542
ARG387	-19.26445	0.03515	11.114353
ALA388	-0.774089	-0.003735	0.353422
LEU389	-0.461068	0.021133	0.117418
ASP390	12.457953	0.031771	-8.871304
ALA391	-0.46415	-0.014131	0.272119
VAL392	10.719651	0.187994	-8.522309

[a] unit of *kcal* / *mol*

Y170F

	ALD(1) [a]	ALD(2) [a]	ALD(3) [a]
MET1	-7.534322	0.111138	10.134143
ASN2	-0.072172	-0.003531	0.235231
ALA3	0.143249	-0.012339	-0.235281
ARG4	-10.559304	0.314298	16.024438
SER5	-0.065074	0.018747	-0.070259
THR6	0.182304	-0.030598	-0.221823
GLY7	0.176864	0.003007	-0.265255
GLN8	-0.16479	0.001148	0.155359
HIS9	0.130014	-0.021129	-0.095134
PRO10	-0.403862	0.010806	0.799856
ALA11	0.022713	-0.012437	-0.216371
ARG12	-10.181877	-0.085395	16.88911
TYR13	0.038994	0.03188	-0.005824
PRO14	-0.096005	-0.01887	0.154844
GLY15	-0.147915	-0.011583	0.27196
ALA16	-0.154846	-0.006883	0.243715
ALA17	0.027342	-0.000106	0.012252
ALA18	0.125205	0.010553	-0.307402
GLY19	0.069884	-0.022187	-0.101462

GLU20	7.622941	0.010399	-10.862239
PRO21	-0.030923	0.013527	0.123303
THR22	0.178529	0.000294	-0.397515
LEU23	-0.115876	0.018676	0.277236
ASP24	8.236298	0.032579	-12.262215
SER25	-0.076219	0.019553	0.189797
TRP26	-0.28617	0.024374	0.689694
GLN27	-0.134699	0.027742	0.37117
GLU28	6.93329	0.062678	-9.546005
PRO29	0.12284	0.009036	-0.225302
PRO30	-0.006449	-0.010046	-0.007059
HIS31	-7.58338	-0.053251	10.851961
ASN32	0.101931	0.011645	-0.174602
ARG33	-6.693574	-0.102464	8.977017
TRP34	-0.03505	0.000918	0.091931
ALA35	0.16218	0.024551	-0.281239
PHE36	0.183336	0.030179	-0.353544
ALA37	-0.007024	0.018373	0.092667
HIS38	0.289264	0.055425	-0.384601
LEU39	0.207014	-0.009605	-0.609637
GLY40	0.163481	-0.016038	-0.498379
GLU41	10.990937	0.275474	-18.523748
MET42	0.155889	-0.067091	-0.668002
VAL43	-0.019977	-0.045352	-0.054977
PRO44	-0.057024	0.074614	0.483503
SER45	-0.31293	-0.067168	0.944991
ALA46	0.145476	0.083593	-0.306294
ALA47	-0.44773	-0.101459	0.868944
VAL48	-0.111186	-0.018562	0.472272
SER49	0.155784	0.048535	-0.126058
ARG50	-9.882372	-0.741259	12.259007
ARG51	-9.418622	-0.651828	11.407721
PRO52	0.119862	0.01306	-0.222281
VAL53	0.08424	0.01489	-0.043418
ASN54	0.170037	0.02835	-0.165941

ALA55	0.047106	0.009361	0.027093
PRO56	0.229717	0.031385	-0.172194
GLY57	0.032494	0.016759	-0.082485
HIS58	-0.264696	-0.042326	0.291814
ALA59	0.159563	0.037615	-0.253472
LEU60	-0.461666	-0.059921	0.426145
ALA61	0.495076	0.067745	-0.431084
ARG62	-10.369432	-0.626167	10.363757
LEU63	0.291676	0.032546	-0.250317
GLY64	0.140608	-0.01963	0.016932
ALA65	-0.057151	-0.02298	0.132565
ILE66	0.167983	-0.000199	-0.086287
ALA67	0.150054	-0.022531	0.02106
ALA68	-0.19789	-0.02154	0.188829
GLN69	-0.11558	-0.023711	0.169097
LEU70	0.410634	-0.00704	-0.16488
PRO71	0.042385	0.035386	-0.150462
ASP72	12.238584	0.343335	-9.906999
LEU73	0.429747	0.027346	-0.309506
GLU74	11.480913	0.582463	-10.45678
GLN75	0.025222	0.06986	-0.287471
ARG76	-15.282349	-0.318182	11.107337
LEU77	1.076986	0.090503	-0.699007
GLU78	13.587924	0.745635	-12.19959
GLN79	0.722372	0.015549	-0.395103
THR80	1.066175	0.044203	-0.589354
TYR81	1.300623	0.248663	-0.989353
THR82	0.427228	0.318343	-0.955738
ASP83	16.12608	2.224665	-18.150963
ALA84	-1.080967	-0.223574	0.819336
PHE85	0.917009	0.222577	-0.735087
LEU86	-0.852249	-0.135643	0.64248
VAL87	0.657688	0.061801	-0.469258
LEU88	-0.617567	-0.036169	0.392331
ARG89	-10.262285	-0.325061	9.262188

GLY90	-0.499982	-0.019157	0.340094
THR91	0.20729	0.038123	-0.285965
GLU92	9.060323	0.337253	-8.641994
VAL93	0.356628	0.023747	-0.260884
VAL94	-0.237598	-0.011332	0.182821
ALA95	-0.24546	-0.029804	0.261789
GLU96	11.020934	0.757151	-11.221431
TYR97	-0.148207	-0.0572	0.270049
TYR98	0.413526	0.106617	-0.468276
ARG99	-15.027823	-1.5701	16.227549
ALA100	-0.196359	-0.000391	-0.01245
GLY101	-0.352743	-0.06711	0.282368
PHE102	0.489767	0.139806	-0.807616
ALA103	-0.295924	-0.092488	0.583499
PRO104	0.290508	0.092414	-0.481828
ASP105	10.202577	0.811166	-12.281846
ASP106	11.88291	1.230706	-15.710712
ARG107	-11.318701	-1.011005	16.107206
HIS108	-17.700226	-3.948512	22.224646
LEU109	0.027119	-0.052096	0.173958
LEU110	0.565418	0.404378	0.824605
MET111	1.814562	-0.083785	-1.363302
SER112	-1.515613	-16.214838	-2.01586
VAL113	0.278453	-5.325664	3.038484
SER114	-1.861959	-2.251183	3.305269
LYN115	-1.048929	-0.368465	0.775115
SER116	-0.627284	-0.246486	1.315728
LEU117	-1.317444	-0.2339	1.749145
CYS118	-1.181444	-0.317265	1.813956
GLY119	-0.751824	-0.171685	1.101239
THR120	-0.790031	-0.141531	1.382353
VAL121	-0.737183	-0.067626	0.909551
VAL122	-0.551741	-0.065411	0.743329
GLY123	-0.530687	-0.035243	0.807636
ALA124	-0.502571	-0.024912	0.697947

LEU125	-0.478941	-0.018429	0.527957
VAL126	-0.32731	-0.021011	0.467108
ASP127	9.619505	0.132987	-10.232213
GLU128	9.121045	0.136869	-11.006571
GLY129	-0.273744	-0.011085	0.279329
ARG130	-9.583391	-0.085641	11.734425
ILE131	0.071318	-0.015187	-0.237331
ASP132	10.735958	-0.109109	-10.8884
PRO133	0.119085	-0.022366	-0.165881
ALA134	0.472346	-0.04648	-0.411028
GLN135	-0.26671	-0.0171	0.310748
PRO136	0.557284	-0.029894	-0.575766
VAL137	-0.100579	0.027165	-0.11362
THR138	-0.215342	0.031368	-0.077144
GLU139	9.149546	-0.135108	-10.578643
TYR140	-0.163343	0.028033	0.162629
VAL141	-0.153551	0.0279	-0.133668
PRO142	0.287861	-0.039865	-0.348922
GLU143	9.966312	-0.218068	-13.0255
LEU144	0.108423	-0.02392	-0.232673
ALA145	0.288637	-0.033967	-0.156649
GLY146	-0.155925	0.003637	0.396357
SER147	0.101068	-0.015291	-0.082478
VAL148	-0.364738	0.038288	0.631003
TYR149	0.163995	-0.018351	-0.299436
ASP150	10.807732	-0.324753	-12.086223
GLY151	-0.367146	0.032532	0.499934
PRO152	-0.219291	0.026964	0.409825
SER153	-0.188299	0.021644	-0.080199
VAL154	0.745736	-0.051379	-0.768896
LEU155	0.687702	-0.023164	-0.786709
GLN156	0.388214	-0.011586	-0.30931
VAL157	1.155423	-0.131078	-0.994876
LEU158	1.314129	-0.079332	-1.377182
ASP159	18.634016	-0.479643	-16.313315

MET160	2.43642	-0.38639	-0.145204
GLN161	0.728674	-0.117921	0.193015
ILE162	-1.658399	0.147804	0.932464
SER163	2.325329	-0.231435	-1.584448
ILE164	-1.468524	0.118025	0.514842
ASP165	19.659889	-1.120243	-19.3753
TYR166	-0.500799	-0.127927	-2.875386
ASN167	6.139156	-0.44786	-0.524494
GLU168	30.519112	-8.575525	-63.770746
ASP169	33.433568	-2.614493	-36.089774
PHE170	-4.690883	0.32942	-1.440913
VAL171	-2.736221	0.36875	-0.517286
ASP172	20.564406	-0.899723	-20.197353
PRO173	-0.877961	-0.012626	-1.592525
ALA174	-1.337316	0.100267	0.736968
SER175	-1.17481	0.112774	0.591974
GLU176	20.253932	-1.459674	-28.77847
VAL177	-1.422943	0.160666	-2.049404
GLN178	-2.350502	0.213485	-9.032806
THR179	-0.819824	0.148988	0.723245
HIS180	-20.999473	2.451996	67.126788
ASP181	20.185717	-3.045796	-118.207885
ARG182	-16.403788	1.122447	33.886221
SER183	-1.003065	0.187057	4.11094
ALA184	-0.692108	0.132264	2.835548
GLY185	-0.499852	0.150344	1.886447
TRP186	0.111519	-0.302895	-5.545921
ARG187	-19.987662	1.807865	58.168916
THR188	-0.386231	-0.002038	1.759643
ARG189	-12.08451	0.370309	22.399033
ARG190	-14.631981	0.59658	23.912945
HIS191	-0.113426	-0.010975	0.159645
GLY192	-0.253617	0.017083	0.551092
ASP193	13.927328	-0.65608	-24.247253
PRO194	-0.524388	0.064265	1.086912

ALA195	0.215646	-0.015412	-1.287483
ASP196	11.388488	-0.276448	-19.171574
THR197	0.602885	-0.121706	-1.883815
TYR198	0.43197	-0.076413	-0.31818
GLU199	11.30353	-0.405996	-17.008949
PHE200	0.183172	-0.058239	-0.521398
LEU201	0.219364	-0.03475	0.746627
THR202	-0.166827	0.020221	1.271615
THR203	-0.346071	0.02328	0.846765
LEU204	0.231173	-0.035662	-0.282812
ARG205	-13.763735	0.67955	17.557844
GLY206	1.038813	-0.103644	-1.047953
ASP207	16.122775	-0.738152	-13.996814
GLY208	-0.778763	0.062824	0.748664
SER209	-0.373579	0.038041	0.319385
THR210	0.327695	-0.032551	-0.458969
GLY211	0.044034	0.009102	0.023749
GLU212	19.337078	-0.829937	-13.286546
PHE213	0.368574	-0.07617	-0.744625
GLN214	-1.632768	0.247696	1.98424
TYR215	-2.100669	-0.822399	0.091161
CYS216	3.116662	-0.444298	-1.879472
SER217	-1.983592	0.147119	0.300185
ALA218	-1.723839	0.496484	0.211572
ASN219	-2.667711	0.403269	2.539117
THR220	-0.790344	0.109929	1.05963
ASP221	17.54445	-0.94682	-40.408625
VAL222	-1.128936	0.120861	1.895074
LEU223	-0.893596	0.116357	1.632727
ALA224	-0.848655	0.078742	1.566086
TRP225	-0.562826	0.027961	0.777137
ILE226	-0.690909	0.047088	1.317877
VAL227	-0.543909	0.036302	0.943255
GLU228	11.360536	0.049086	-18.128073
ARG229	-10.799206	0.166061	14.790182

VAL230	-0.423431	0.013543	0.698678
THR231	-0.449925	0.012532	0.704568
GLY232	-0.346289	0.005789	0.58976
LEU233	-0.212109	0.012257	0.256622
ARG234	-10.279664	-0.233643	16.271265
TYR235	0.156165	0.126312	-0.212638
VAL236	0.206762	0.083354	-0.076707
GLU237	9.192397	0.302292	-12.414976
ALA238	0.005181	0.029674	0.253334
LEU239	0.066506	0.0291	0.291657
SER240	0.109978	0.074699	0.311106
THR241	-0.043608	0.00352	0.287221
TYR242	-0.196097	-0.035626	0.360005
LEU243	0.234504	0.014462	-0.008255
TRP244	0.021835	0.050001	0.138044
ALA245	-0.165767	-0.003108	0.418717
LYS246	-10.347682	-0.367416	12.268647
LEU247	-0.083814	-0.021019	0.359339
ASP248	9.270362	0.497535	-10.43335
ALA249	0.033614	0.017264	0.076214
ASP250	9.39925	0.620181	-11.038141
ARG251	-11.098583	-0.974002	14.181113
ASP252	10.839594	0.744231	-14.119291
ALA253	0.167677	0.088024	-0.369037
THR254	-0.567473	-0.203719	0.814424
ILE255	0.738262	0.280114	-1.344438
THR256	-0.530263	-0.196985	1.004004
VAL257	0.297719	-0.026117	-0.801936
ASP258	13.032169	-0.411172	-26.472157
THR259	-0.609978	0.099964	2.444128
THR260	-0.488181	0.063287	1.590106
GLY261	-0.411376	0.024847	1.301665
PHE262	-0.09831	0.100421	0.612079
GLY263	0.188888	-0.005477	-1.284029
PHE264	0.506962	-0.10044	-1.521264

ALA265	0.918789	0.205615	-4.086181
ASN266	1.737119	-0.486714	-14.31205
GLY267	2.090277	0.075549	-2.873369
GLY268	0.047077	1.63476	0.136894
VAL269	-1.145138	-0.409637	3.502403
SER270	0.857387	0.911176	-0.896411
CYS271	-0.503372	-0.327489	0.851667
THR272	0.495664	0.215111	-0.448692
ALA273	0.257991	0.060423	-0.215943
ARG274	-10.884943	-0.77914	11.6904
ASP275	11.193973	0.883274	-13.132407
LEU276	-0.03779	-0.043201	-0.078539
ALA277	0.182444	-0.10391	0.180125
ARG278	-10.908344	-0.843939	12.390075
VAL279	-0.247932	-0.09246	0.400355
GLY280	0.05763	-0.083338	0.169485
ARG281	-11.424836	-0.503861	11.102015
MET282	-0.138116	-0.05059	0.150282
MET283	-0.253831	-0.072847	0.207932
LEU284	0.012068	-0.080152	0.252513
ASP285	10.454177	0.352976	-10.170386
GLY286	-0.33149	-0.022401	0.223795
GLY287	-0.135554	-0.033751	0.086185
VAL288	-0.189945	0.002799	-0.068674
ALA289	0.23913	0.031992	-0.165246
PRO290	-0.30033	-0.037481	0.324017
GLY291	-0.306953	-0.024466	0.349242
GLY292	-0.124464	-0.016262	0.035614
ARG293	-9.815899	-0.151648	10.012967
VAL294	-0.159898	-0.003395	0.0252
VAL295	0.116057	-0.024289	-0.207015
SER296	-0.207302	-0.000836	0.383914
GLU297	10.014889	0.129905	-9.610924
ASP298	11.879152	-0.069095	-10.892739
TRP299	0.193493	-0.064386	0.086765

VAL300	0.683479	-0.021262	-0.462615
ARG301	-11.103234	0.051456	10.142303
ARG302	-12.032159	0.097829	11.229978
VAL303	0.473252	-0.053064	-0.116537
LEU304	0.782973	-0.028131	-0.229251
ALA305	-0.414441	-0.004752	0.459918
GLY306	0.156168	-0.03668	0.179764
GLY307	-0.474095	0.03633	-0.081078
SER308	-0.218076	0.023046	0.335617
HIS309	-15.844719	0.365735	11.354373
GLU310	16.497668	-0.549245	-11.81465
ALA311	0.07686	-0.014542	-0.001263
MET312	2.272388	-0.195108	-0.988682
THR313	0.2351	0.010277	0.233822
ASP314	49.101437	-2.446904	-18.873331
LYS315	-23.203997	1.012194	14.270423
GLY316	-1.993158	0.152499	0.62177
PHE317	-1.175806	0.08029	0.327456
THR318	-3.423626	0.231609	0.697291
ASN319	-3.218816	0.165364	0.89325
THR320	-0.494264	0.064544	0.257323
PHE321	-2.067007	0.173835	0.368706
PRO322	-0.222862	-0.030699	-0.092238
ASP323	15.152994	-0.338151	-10.599826
GLY324	-0.584887	0.055827	-0.006366
SER325	-0.532321	0.002866	0.140951
TYR326	0.457135	0.05616	-0.393243
THR327	-1.545522	0.065141	0.721825
ARG328	-14.297201	0.245872	13.373313
GLN329	-0.46037	0.28484	-1.749275
TRP330	0.616614	0.487525	-0.969713
TRP331	0.206698	-0.415441	1.234809
CYS332	-1.941227	0.351025	0.58356
THR333	-0.058868	-0.090614	0.478487
GLY334	0.246696	-0.048415	0.149501

ASN335	-1.644119	0.033669	0.826213
GLU336	14.648194	-0.039754	-10.112079
ARG337	-14.434468	-0.136875	10.811836
GLY338	-0.427929	0.025782	0.0954
ASN339	0.029272	-0.014752	-0.01097
VAL340	0.917062	-0.127072	-0.223263
SER341	-0.922658	0.398174	-0.186185
GLY342	0.723403	-0.42882	-0.479333
ILE343	-1.132753	0.172671	0.578969
GLY344	1.036291	-0.476564	-3.115081
ILE345	0.00383	-18.194279	5.213361
HIS346	-2.948252	-1.307992	-0.86731
GLY347	-1.866386	-1.063742	1.830169
GLN348	-3.79937	-2.698043	3.768347
ASN349	3.341797	1.037431	-1.98343
LEU350	-1.941375	-0.12607	0.833143
TRP351	2.107964	-0.166317	-0.810323
LEU352	-1.114209	0.041273	0.435675
ASP353	14.733367	0.123149	-11.032878
PRO354	-0.697772	0.010864	0.396631
LEU355	-0.509695	-0.006301	0.331505
THR356	-0.369998	0.009302	0.230643
ASP357	10.906529	0.343263	-10.111143
SER358	-0.458694	0.041286	0.109828
VAL359	0.662984	-0.006918	-0.403765
ILE360	-0.521334	0.011026	0.297121
VAL361	0.838683	0.11946	-0.748018
LYS362	-21.518938	-1.923421	17.550132
LEU363	1.107249	0.561567	-1.262767
SER364	-1.224259	-0.902084	2.043552
SER365	0.343232	0.634118	-1.468846
TRP366	-0.04463	-0.0776	0.160672
PRO367	-0.272573	0.178168	-1.16489
ASP368	30.695836	0.148431	-23.61403
PRO369	0.772981	0.160511	0.853721

TYR370	1.467376	-1.04368	0.031054
THR371	-0.001121	-0.444865	0.727515
GLU372	40.422614	-0.975621	-15.923444
HIS373	-4.031233	0.156652	0.994623
TRP374	-2.558644	0.010348	1.077344
HIS375	-1.125493	-0.117342	-0.116852
ARG376	-24.523442	0.169239	13.402926
LEU377	-2.101336	0.042422	0.640081
GLN378	-3.068874	-0.135376	1.326564
ASN379	-1.150791	0.184362	-0.306284
GLY380	-1.476795	-0.002279	0.583234
ILE381	-1.107545	0.031032	0.347853
LEU382	-1.046383	0.023683	0.379658
LEU383	-0.925004	-0.020088	0.37315
ASP384	15.049143	0.198402	-10.728878
VAL385	-0.879051	0.002679	0.404659
SER386	-0.736627	-0.003469	0.301849
ARG387	-15.392954	-0.073625	10.67609
ALA388	-0.531658	-0.014958	0.321951
LEU389	-0.449666	0.003453	0.225477
ASP390	10.031192	0.179643	-8.451309
ALA391	-0.18284	-0.02397	0.190407
VAL392	9.323891	0.157335	-7.688783

[a] unit of *kcal* / *mol*

Hyb-24

	ALD(1) [a]	ALD(2) [a]	ALD(3) [a]
MET1	-7.740148	0.078814	9.554687
ASN2	-0.066077	0.013111	-0.133978
ALA3	0.019475	-0.0099	0.075913
ARG4	-10.00453	0.151227	13.824097
SER5	-0.165184	0.020141	0.199928
THR6	-0.127622	0.002141	0.408511
GLY7	0.19818	-0.000952	-0.190424
GLN8	-0.020036	0.005414	-0.264574

HIS9	0.191921	-0.022743	-0.240023
PRO10	-0.413211	0.014763	0.619481
ALA11	0.014445	-0.003976	-0.244829
ARG12	-10.347663	-0.186092	15.979664
TYR13	0.068877	0.039625	-0.244689
PRO14	-0.078763	-0.031841	0.201594
GLY15	-0.132251	0.005698	0.122959
ALA16	-0.203571	-0.003744	0.258215
ALA17	0.020101	-0.010539	0.097769
ALA18	0.102405	0.015251	-0.277212
GLY19	-0.164202	-0.010188	0.267499
GLU20	7.873092	0.065497	-10.720534
PRO21	0.118578	0.014303	-0.159215
THR22	0.240205	-0.009911	-0.455871
LEU23	-0.178129	0.027799	0.307266
ASP24	8.349365	0.039967	-12.19847
SER25	-0.169338	0.009554	0.352461
TRP26	-0.252461	0.02809	0.504482
GLN27	-0.209726	0.006953	0.465932
GLU28	7.32327	0.070854	-10.055382
PRO29	0.102145	0.009432	-0.163406
PRO30	-0.051607	-0.01231	0.119318
HIS31	-7.882643	-0.096532	10.983053
ASN32	0.200664	0.022608	-0.372313
ARG33	-7.252347	-0.212655	9.996536
TRP34	-0.097913	-0.00309	0.195895
ALA35	0.134757	0.031258	-0.269104
PHE36	0.122255	0.03462	-0.330933
ALA37	-0.058859	0.015105	0.124349
HIS38	0.098172	0.020552	0.060082
LEU39	0.269015	0.009926	-0.714437
GLY40	0.13023	-0.014962	-0.492358
GLU41	11.328916	0.45147	-18.316982
MET42	0.253108	-0.070353	-0.764979
VAL43	-0.086409	-0.032301	0.020753

PRO44	-0.021123	0.088727	0.289523
SER45	0.262478	0.11777	-0.62112
ALA46	-0.090533	0.049513	0.586352
ALA47	-0.101149	-0.02433	0.350715
VAL48	-0.120545	-0.022247	0.363642
SER49	-0.197186	-0.022069	0.546521
ARG50	-8.520914	-0.569045	11.906775
ARG51	-10.314865	-1.022824	14.283636
PRO52	-0.096692	-0.024775	0.089287
VAL53	0.172837	0.039434	-0.362897
ASN54	0.137993	0.022625	-0.228604
ALA55	0.291868	0.054913	-0.656418
PRO56	-0.123144	-0.004418	0.243157
GLY57	-0.223759	-0.043221	0.220179
HIS58	0.000178	-0.013774	0.107308
ALA59	0.10516	0.038505	-0.231678
LEU60	-0.382712	-0.076205	0.530566
ALA61	0.466837	0.086427	-0.516097
ARG62	-10.065313	-0.744893	10.90844
LEU63	0.143199	0.014703	-0.105439
GLY64	0.058929	-0.024375	0.087988
ALA65	-0.1768	-0.032424	0.23283
ILE66	0.051702	-0.019466	0.063543
ALA67	0.152407	-0.008343	-0.034927
ALA68	-0.072324	-0.013988	0.081569
GLN69	-0.329169	-0.023937	0.259205
LEU70	0.306712	0.003926	-0.167479
PRO71	-0.023063	0.038708	-0.151567
ASP72	11.065874	0.517174	-10.472024
LEU73	0.455425	0.050493	-0.437326
GLU74	10.868467	0.730657	-11.077919
GLN75	0.231338	0.103555	-0.590709
ARG76	-13.62544	-0.545179	11.388533
LEU77	0.957992	0.123289	-0.7887
GLU78	12.008342	1.02574	-13.409891

GLN79	-0.151697	0.040377	-0.330491
THR80	0.667638	0.072605	-0.631323
TYR81	0.953434	0.336005	-1.251592
THR82	0.574423	0.3723	-1.237912
ASP83	14.298506	2.324701	-19.997542
ALA84	-0.833739	-0.284062	1.106901
PHE85	0.764356	0.231758	-0.710006
LEU86	-0.725703	-0.150965	0.638089
VAL87	0.641541	0.055225	-0.370091
LEU88	-0.61148	-0.051013	0.405709
ARG89	-10.184984	-0.340436	9.135492
GLY90	-0.436036	-0.015883	0.29139
THR91	0.16654	0.018302	-0.204447
GLU92	8.96614	0.452123	-9.13674
VAL93	0.269493	0.013113	-0.14855
VAL94	-0.314783	-0.031854	0.279911
ALA95	-0.199809	-0.035217	0.253755
GLU96	10.517062	0.828504	-11.405481
TYR97	-0.204013	-0.05424	0.273282
TYR98	0.431001	0.128316	-0.593247
ARG99	-13.138094	-1.652378	17.381202
ALA100	-0.344646	-0.047099	0.261911
GLY101	0.291995	0.053976	-0.457627
PHE102	0.313927	0.112124	-0.787144
ALA103	-0.291533	-0.092902	0.661947
PRO104	0.263686	0.088116	-0.484155
ASP105	10.330366	1.024094	-13.45548
ASP106	11.530973	1.416892	-17.396818
ARG107	-11.456712	-1.240264	17.314097
HIS108	-16.911935	-4.253013	24.990009
LEU109	0.189932	-0.009141	0.421924
LEU110	0.477008	0.647119	-0.167436
MET111	1.550659	0.940665	-3.842521
SER112	-1.682727	-14.829049	-0.524252
VAL113	0.877097	-5.659437	4.436396

SER114	-2.014071	-2.205422	3.516246
LYN115	-0.088509	-1.521926	0.745257
SER116	-0.605552	-0.25202	1.438607
LEU117	-1.567917	-0.228628	1.700959
CYS118	-1.413404	-0.297277	1.817542
GLY119	-0.827272	-0.172345	1.027776
THR120	-0.993033	-0.094164	1.288735
VAL121	-0.838909	-0.036334	0.782438
VAL122	-0.677762	-0.06425	0.702444
GLY123	-0.553037	-0.027149	0.679709
ALA124	-0.593722	-0.000502	0.654215
LEU125	-0.567502	-0.017626	0.54948
VAL126	-0.327319	-0.025784	0.437485
ASP127	10.242594	0.120521	-10.07063
GLU128	9.490255	0.09747	-10.305856
GLY129	-0.301315	-0.010313	0.275263
ARG130	-9.99488	-0.056796	10.959783
ILE131	0.256649	-0.016801	-0.374216
ASP132	11.617228	-0.271733	-10.210427
PRO133	0.196335	-0.036057	-0.140385
ALA134	0.588645	-0.072815	-0.309551
GLN135	-0.262852	-0.016918	0.248224
PRO136	0.815778	-0.059337	-0.605217
VAL137	-0.2418	0.045835	-0.049613
THR138	-0.486376	0.065891	0.123722
GLU139	9.933961	-0.263319	-9.766275
TYR140	-0.29489	0.041551	0.144329
VAL141	-0.29407	0.043889	-0.051918
PRO142	0.378419	-0.056607	-0.280081
GLU143	10.88472	-0.330195	-12.203111
LEU144	0.222945	-0.036491	-0.349322
ALA145	0.400753	-0.054315	-0.032966
GLY146	-0.172822	0.011827	-0.047462
SER147	0.443144	-0.057781	-0.380473
VAL148	-0.142332	0.021584	0.419438

TYR149	0.058513	-0.000847	-0.098941
ASP150	11.904288	-0.514492	-11.090147
GLY151	-0.380132	0.046045	0.368257
PRO152	-0.246354	0.040487	0.219824
SER153	-0.163002	0.028026	-0.144353
VAL154	1.047419	-0.106759	-0.760193
LEU155	0.867056	-0.047134	-0.688718
GLN156	0.773334	-0.073384	-0.372822
VAL157	1.633342	-0.208011	-0.616631
LEU158	1.688134	-0.20652	-1.201572
ASP159	22.258334	-1.021629	-15.314556
MET160	3.618143	-0.555135	-0.209498
GLN161	0.730628	-0.113951	0.30404
ILE162	-1.829404	0.219724	0.906099
SER163	2.681662	-0.303724	-0.901293
ILE164	-1.460553	0.114849	0.006151
ASP165	21.198653	-1.505407	-16.698601
TYR166	-1.0683	0.040036	-1.946542
ASN167	5.300198	-0.697384	-1.241414
GLU168	35.096006	-7.922892	-40.140033
ASP169	37.174346	-3.544465	-29.553
TYR170	-4.871406	-4.789493	-4.343873
VAL171	-2.750931	1.335447	-4.3729
ASP172	17.656875	-0.640897	-23.423044
PRO173	0.122903	-0.061279	-4.268483
ALA174	-0.71394	0.041653	-1.142263
SER175	-1.292348	0.136733	1.596754
GLU176	18.55872	-1.379263	-23.782244
VAL177	-1.291936	0.311865	-0.014394
GLN178	-0.991192	0.15573	-25.258656
THR179	-1.685319	0.402911	3.637739
HIS180	-18.31107	1.223399	37.87097
GLY181	-0.522718	0.128568	1.217023
ARG182	-14.224286	0.558408	24.956725
SER183	-0.487982	0.070001	1.026975

ALA184	-0.420068	0.052659	1.49057
GLY185	-0.341089	0.120922	0.707877
TRP186	-0.274959	0.081802	0.255933
ARG187	-13.687644	-0.234827	29.940678
THR188	-0.07072	-0.049499	0.64046
ARG189	-10.978372	0.261943	16.332075
ARG190	-12.108034	0.281795	18.534827
HIS191	-0.000306	-0.019228	0.075726
GLY192	0.162071	-0.01806	-0.106854
ASP193	13.62496	-0.541796	-21.305856
PRO194	-0.583427	0.070643	0.955257
ALA195	0.002119	0.034856	-0.787689
ASP196	11.861091	-0.251559	-17.622826
THR197	0.563908	-0.07869	-1.420116
TYR198	0.513744	-0.113404	-0.365809
GLU199	11.627523	-0.435352	-15.334541
PHE200	0.073722	-0.021537	0.323561
LEU201	0.593859	-0.122616	-0.014987
THR202	0.120279	-0.033688	0.696166
THR203	-0.246675	0.012611	0.480506
LEU204	0.349917	-0.06495	-0.689601
ARG205	-17.023445	1.18698	18.236662
GLY206	1.757948	-0.242775	-1.082043
ASP207	15.196374	-0.848913	-11.99838
GLY208	-0.651356	0.072835	0.390778
SER209	-0.584613	0.071302	0.410829
THR210	1.04726	-0.10686	-0.459065
GLY211	-0.937199	0.091544	0.516925
GLU212	25.85167	-1.481533	-13.231565
PHE213	-0.635953	-0.028529	-0.38554
GLN214	-0.363001	0.249387	0.981913
TYR215	-6.34866	-1.095513	0.98715
CYS216	-0.415294	0.074872	-0.476236
SER217	-1.899182	-0.162137	0.059206
ALA218	-2.102911	0.984445	0.860043

ASN219	-3.867554	0.817019	2.035642
THR220	-0.822334	0.146761	0.880011
ASP221	18.432564	-0.46534	-32.257148
VAL222	-1.316076	0.184387	1.438564
LEU223	-1.024794	0.168283	1.138114
ALA224	-1.000924	0.123121	1.034452
TRP225	-0.794899	0.082111	0.770789
ILE226	-0.744737	0.063314	0.923799
VAL227	-0.583484	0.054639	0.693405
GLU228	11.887228	0.043755	-16.431149
ARG229	-11.810171	0.291847	13.620259
VAL230	-0.444892	0.004152	0.630356
THR231	-0.51021	0.029949	0.579461
GLY232	-0.386127	0.016555	0.451081
LEU233	-0.359246	0.007696	0.312714
ARG234	-10.550108	-0.345067	15.796242
TYR235	0.100034	0.138502	-0.348459
VAL236	0.215563	0.10291	-0.335338
GLU237	9.718824	0.385115	-13.011
ALA238	-0.163008	0.011055	0.55444
LEU239	0.139205	0.023191	0.181372
SER240	0.017441	0.021141	0.307338
THR241	-0.354226	-0.036304	0.727519
TYR242	-0.258141	-0.021374	0.430464
LEU243	0.234086	-0.006059	0.052357
TRP244	0.027759	0.055827	0.115858
ALA245	-0.199134	0.013109	0.255561
LYS246	-10.428361	-0.300734	11.543511
LEU247	-0.028862	-0.019321	0.267288
ASP248	9.476672	0.539769	-10.523092
ALA249	0.003993	0.021021	0.071796
ASP250	9.607064	0.763391	-11.906656
ARG251	-10.912304	-1.088507	14.755631
ASP252	11.581468	0.926059	-15.488092
ALA253	0.103112	0.097404	-0.579033

THR254	-0.300194	-0.171927	0.119084
ILE255	0.5638	0.299894	-1.32392
THR256	-0.493221	0.006033	1.023516
VAL257	0.582809	-0.081957	-1.31116
ASP258	12.928873	-0.205748	-23.006039
THR259	-0.634756	0.058979	2.149645
THR260	-0.392088	0.031096	1.159591
GLY261	-0.303021	0.004379	0.972283
PHE262	0.104127	0.069985	0.067879
GLY263	0.100021	0.054013	-1.33994
PHE264	0.589164	-0.262614	-0.711638
ALA265	0.724638	0.597787	-2.3017
HIS266	1.000811	-0.30047	-9.87552
GLY267	2.25378	0.23484	-2.200517
GLY268	-0.283406	1.764609	-3.702466
VAL269	-1.216872	-0.502688	2.752024
SER270	0.687878	0.909144	-1.489459
CYS271	-0.519667	-0.386976	1.387258
THR272	0.380177	0.231364	-0.621185
ALA273	0.298141	0.052364	-0.161583
ARG274	-9.957407	-0.791255	11.388297
ASP275	11.183376	0.952915	-13.315489
LEU276	0.136189	-0.023974	-0.100836
ALA277	0.442576	-0.068194	0.029185
ARG278	-10.974205	-0.952296	12.836946
VAL279	-0.239307	-0.118792	0.411012
GLY280	0.238125	-0.111561	0.162815
ARG281	-11.664584	-0.555775	11.115033
MET282	-0.25423	-0.107106	0.48194
MET283	-0.459157	-0.089216	0.447499
LEU284	-0.122471	-0.083172	0.347962
ASP285	10.782631	0.357416	-10.125701
GLY286	-0.308335	-0.020536	0.186626
GLY287	-0.185496	-0.042148	0.156031
VAL288	-0.171809	0.010882	-0.100176

ALA289	0.170065	0.038495	-0.147225
PRO290	-0.321516	-0.045156	0.360095
GLY291	-0.327424	-0.021632	0.277682
GLY292	-0.175304	-0.030149	0.141083
ARG293	-10.506372	-0.116006	9.83711
VAL294	-0.097599	0.000881	-0.07213
VAL295	0.183465	-0.03107	-0.209295
SER296	-0.309924	-0.00973	0.437941
GLU297	10.984307	0.088849	-9.684946
ASP298	12.259061	-0.176316	-9.950337
TRP299	0.209332	-0.10251	0.222148
VAL300	0.830985	-0.039418	-0.446395
ARG301	-10.784199	0.035032	9.272275
ARG302	-12.493612	0.210439	10.175833
VAL303	0.629873	-0.072344	-0.186211
LEU304	0.671482	-0.022696	-0.146226
ALA305	-0.560055	0.014399	0.405081
GLY306	-0.068315	-0.02703	0.197657
GLY307	-0.467086	0.005094	0.044496
SER308	-0.9157	0.09041	0.568641
HIS309	-18.437659	0.573198	11.257926
GLU310	16.807297	-0.734311	-10.536095
ALA311	-0.22687	-0.00854	-0.004318
MET312	2.793691	-0.239011	-0.649295
THR313	-0.698051	0.097836	0.334628
ASP314	77.968992	-4.03046	-18.784849
LYS315	-30.478616	1.700995	14.503195
GLY316	-6.899479	0.432163	0.775852
PHE317	-8.832499	0.483252	0.684051
THR318	-7.326068	0.479813	0.814129
ASN319	-3.945826	0.320087	0.513798
THR320	-3.996918	0.299003	0.658486
PHE321	-3.583787	0.282979	0.571137
PRO322	1.430379	-0.155816	-0.230597
ASP323	18.21261	-0.602948	-10.756911

GLY324	-0.828702	0.067425	0.053995
SER325	-0.340639	-0.043259	0.204373
TYR326	1.041705	-0.067592	-0.258626
THR327	-1.884866	0.092426	0.602117
ARG328	-15.450798	0.419174	12.24518
GLN329	-0.526482	0.35326	-1.646295
TRP330	0.597368	0.484158	-1.389286
TRP331	-1.779008	-0.258113	1.170138
CYS332	-3.629397	0.504607	0.814521
THR333	1.458067	-0.183371	0.022541
GLY334	0.106815	-0.055725	0.235171
ASN335	-0.887703	-0.017717	0.48061
GLU336	14.019454	0.020316	-9.970756
ARG337	-14.464822	-0.207045	10.829371
GLY338	-0.333133	0.022031	0.053021
ASN339	-0.337988	-0.005563	0.155343
VAL340	1.047366	-0.155259	-0.169056
SER341	-0.931709	0.381998	-0.266887
GLY342	1.570249	-0.60128	-0.237021
ILE343	-1.766331	-0.255118	0.708147
GLY344	1.167788	-0.185519	-2.515421
ILE345	-0.544895	-12.576963	4.912621
HIS346	-1.824776	-1.474975	-4.972762
GLY347	-1.698456	-0.845834	1.975616
GLN348	-2.968204	-2.845949	4.314277
ASN349	1.72324	0.435088	-0.332758
LEU350	-1.632417	-0.190638	0.56915
TRP351	1.832133	-0.156085	-0.55189
LEU352	-1.163357	0.04635	0.358631
ASP353	14.82453	0.220487	-11.11846
PRO354	-0.755195	0.005064	0.37035
LEU355	-0.503973	-0.011912	0.301363
THR356	-0.499879	0.021336	0.221688
ASP357	11.067294	0.362655	-10.045605
SER358	-0.434825	0.038976	0.053485

VAL359	0.7659	0.000238	-0.390507
ILE360	-0.701669	-0.005203	0.346331
VAL361	0.93283	0.151348	-0.772422
LYS362	-19.081678	-2.530896	18.982714
LEU363	0.979383	0.465803	-1.010682
SER364	-1.377701	-0.979642	2.387886
SER365	0.576008	0.884881	-2.892911
TRP366	-0.687132	-0.332532	0.651448
PRO367	0.414805	0.254756	-2.285402
ASP368	24.470675	0.487452	-25.109615
PRO369	0.243292	0.501665	0.328329
ASP370	51.73205	-0.425744	-29.898572
THR371	-0.613534	-0.958152	1.74606
GLU372	50.899253	-1.646276	-21.300461
HIS373	-2.174169	0.181056	0.997022
TRP374	-1.784204	-0.024098	1.275881
HIS375	-3.646972	0.101702	1.654904
ARG376	-35.231392	0.893217	16.620622
LEU377	-1.899567	0.005693	0.834956
GLN378	-2.060173	-0.102468	0.675981
ASN379	-0.293511	0.070096	-0.021441
GLY380	-0.891802	-0.10482	0.605571
ILE381	-1.097803	-0.041644	0.580605
LEU382	-0.952389	-0.019239	0.453486
LEU383	-0.901935	-0.075398	0.556628
ASP384	12.688018	0.413463	-10.535275
VAL385	-0.797686	-0.015424	0.412843
SER386	-0.548117	-0.023656	0.30049
ARG387	-15.215572	-0.150116	10.860821
ALA388	-0.589758	-0.027975	0.39519
LEU389	-0.538856	-0.006207	0.289399
ASP390	10.166484	0.170911	-8.439129
ALA391	0.567528	0.007829	-0.320643
VAL392	10.863196	0.05188	-8.335778

[a] units of *kcal* / *mol*

References:

[1] A. Laio, A. Rodriguez-Fortea, F. L. Gervasio, M. Ceccarelli, and M. Parrinello, *J. Phys. Chem. B* **2005**, *109*, 6714-6721.

[2] A. Laio and F. L. Gervasio, *Rep. Prog. Phys.* **2008**, *71*, 126601.

[3] B. G. Johnson, P. M. W. Gill, and J. A. Pople, *J. Chem. Phys.* **1993**, *98*, 5612-5626).

[4] K. Kamiya, T. Baba, M. Boero, T. Matsui, S. Negoro, and Y. Shigeta, *J. Phys. Chem. Lett.,* **2014**, 5, 1210.