Supporting material

Table S1 - Interaction energy matrix for cluster representatives for all 20x20 possible pairs between residues within proteins calculated with OPLS-AA/L force-field. Energies are in kcal/mol.

Table S2 - Interaction energy matrix for cluster representatives for all 20x20 possible pairs between residues within proteins calculated with Amber parm03 force-field. Energies are in kcal/mol.

Table S3 – Myiazawa-Jerningan contact energies. Energies are in kcal/mol

Table S4 – Interaction energy matrix fo cluster representatives for all 20x20 possible pairs between residues within proteins calculated with PM6-DH method. Energies are in kcal/mol

Table S1: OPLS Side-chain interaction energy matrix CA

OPLS	G	A	V	I	L	F	Y	W	H	P	T	S	N	Q	C	M	K	R	D	E
G	0.1	-0.5	-0.6	-0.5	-0.6	1.3	-0.7	-1.4	-0.3	-0.2	-0.5	-0.2	-0.6	-0.6	-0.6	-0.7	-0.9	1.1	-0.5	1.1
A	-0.1	-0.4	-0.8	-1.1	-1.0	-1.5	-1.7	-0.5	-0.7	-0.9	-0.7	-0.8	-1.1	-1.3	-1.0	-1.2	-0.8	-1.4	-0.7	1.0
V	-0.6	-1.1	-1.5	-1.5	-1.1	-1.5	-1.3	-1.5	-0.9	-1.5	-0.9	-0.8	-0.8	-1.3	-0.8	-1.0	-0.9	-1.6	-1.5	-1.1
I	-0.8	-1.3	-1.0	-1.2	-1.4	-2.7	0.6	-1.9	-1.3	-0.9	-1.1	-1.0	-0.9	-1.3	-0.9	-0.9	-1.2	-1.7	-1.4	-1.4
L	-0.7	-1.1	-1.1	-1.2	-1.6	-2.1	-1.7	-3.1	-1.6	-1.5	-1.1	-1.1	-1.6	-0.5	-1.1	-1.6	-2.4	-2.5	-0.5	-0.3
F	-1.0	-1.7	-1.9	-2.6	-2.2	-2.0	-1.9	-4.1	-3.4	-2.1	-2.2	-2.0	-4.6	-3.4	-0.4	-2.2	-3.4	-6.0	-2.0	-4.0
Y	-0.4	-1.3	-2.1	-2.6	-1.9	-2.8	-2.9	-4.6	-4.5	-2.9	-1.8	-2.8	-3.5	-3.7	0.2	0.1	-6.2	-8.4	-20.0	-24.3
W	-1.5	-1.8	-3.6	-2.3	-2.0	-4.6	-4.9	-4.6	-4.9	-2.3	-7.7	-6.7	-5.5	-5.4	-2.8	-5.7	-5.7	-9.7	-19.2	-16.7
H	-0.5	-1.2	-1.7	-2.8	-2.1	-2.9	-2.7	-3.3	-2.8	-1.9	-6.3	-7.6	-9.3	-7.6	0.5	-0.2	-2.9	-3.9	-24.7	-20.3
P	-0.8	-0.8	-1.4	0.9	-1.0	-2.1	6.3	-1.6	-1.0	-1.1	-0.9	0.0	-0.5	-1.9	-1.1	-0.4	-0.3	0.3	-2.5	-1.3
T	-0.3	-0.5	-0.4	-0.9	-0.9	-0.8	-3.4	-8.4	-6.0	-0.5	-7.0	-1.1	-0.5	-0.4	-0.8	-1.2	1.4	-17.0	-9.4	-9.9
S	-0.2	-0.4	-0.9	-1.0	-0.9	-1.2	-2.1	-2.4	1.0	-0.9	-6.7	-2.0	-6.6	-0.2	-1.3	-2.3	-7.5	-15.3	-11.0	-9.5
N	-0.5	-0.6	-1.1	-0.7	-1.5	-2.8	-3.2	-4.1	-2.6	-1.4	-0.3	-6.5	-8.5	-6.4	-1.3	-3.0	-21.0	-18.7	-23.5	-22.6
Q	-0.7	-1.0	-1.1	-0.7	-0.5	-1.6	-1.7	-4.8	-3.8	-1.8	-0.6	0.0	-8.8	-9.9	-0.3	-2.5	-3.5	-17.2	-22.5	-21.0
C	-0.6	-0.7	-0.8	-1.0	-1.2	-1.1	-0.9	-2.7	-3.2	-0.8	-0.8	-0.8	-1.7	-1.3	-4.3	-2.2	-5.6	-9.2	-7.0	-6.9
M	-1.1	-0.4	-1.2	-1.3	-1.7	-2.6	-2.5	-2.2	1.6	1.0	-1.7	-1.5	-2.7	-3.6	-1.8	-2.8	-4.9	-5.8	-3.8	-9.1
K	-0.9	-1.3	-1.1	0.1	-1.5	-3.0	-9.2	-6.3	-1.2	7.6	2.7	-6.6	-23.0	-21.8	-5.4	-7.3	67.8	60.4	-109.3	-107.5
R	-0.8	-1.6	-2.1	-2.3	-1.7	-5.2	-5.1	-7.2	-2.4	2.7	-3.0	-15.9	-15.5	-20.0	-3.5	-7.8	53.9	54.0	-107.5	-97.3
D	-0.4	-0.4	-1.5	-2.2	-0.2	-3.5	-26.7	-15.5	-10.8	-4.5	-2.6	-8.2	-22.5	-24.8	-1.6	-3.6	-112.5	-117.7	68.4	52.5
E	-0.7	-1.4	-1.7	-1.6	-1.3	-0.4	-24.4	-16.7	-21.4	-4.4	-9.6	-9.8	-7.4	-21.8	-8.6	-4.4	-108.8	-129.7	54.5	77.3

Table S2: Amber parm03 side-chain interaction energy matrix CA

A03CA	G	A	V	I	L	F	Y	W	H	P	T	S	N	Q	C	M	K	R	D	E
G	0.1	-0.4	-0.5	-0.5	-0.6	0.8	-0.7	-1.5	-0.6	-0.3	-0.5	-0.2	-0.6	-0.6	-0.5	-0.7	-0.9	0.5	-0.5	0.7
A	-0.1	-0.2	-0.8	-1.0	-0.9	-1.7	-1.9	-0.5	-0.7	-0.9	-1.0	-1.3	-1.0	-1.3	-1.0	-1.3	-0.3	-1.7	-0.9	2.1
V	-0.5	-1.1	-1.4	-1.5	-1.1	-1.4	-1.2	-1.1	-1.2	-1.6	-1.0	-1.6	-0.9	-1.4	-0.8	-0.6	-2.0	-2.6	-1.6	-0.6
I	-0.7	-1.2	-1.0	-1.2	-1.4	-2.9	1.0	-2.1	-1.3	-1.0	-0.9	-1.8	-0.8	-1.3	-0.7	-0.8	-1.5	-2.2	0.7	-1.0
L	-0.7	-1.0	-1.1	-1.3	-1.7	-2.4	-1.4	-3.4	-1.7	-1.3	-1.0	-1.0	-1.3	0.2	-1.3	-1.9	-1.5	-2.2	1.0	1.1
F	-1.2	-2.0	-1.8	-2.9	-2.3	-2.3	-1.7	-4.0	-2.9	-1.9	-2.1	-1.9	-4.0	-3.7	-0.8	-2.0	-3.2	-5.8	0.2	-2.7
Y	-0.8	-1.5	-2.1	-2.7	-2.2	-3.0	-3.0	-4.3	-1.5	-2.9	-1.6	-2.4	-3.6	-3.7	-1.3	-1.1	-4.0	-7.8	-15.7	-18.4
W	-1.5	-2.1	-4.0	-2.3	-2.3	-4.7	-4.6	-4.3	-4.4	-2.8	-6.0	-5.2	-4.8	-5.7	-3.2	-5.4	-5.0	-10.8	-14.9	-17.6
H	-0.7	-1.2	-1.6	-2.9	-2.3	-2.8	-2.4	-4.9	-4.9	-2.2	-3.7	-5.6	-7.7	-7.5	-1.2	0.2	-4.1	-4.8	-18.5	-14.9
P	-0.8	-0.9	-1.5	2.4	-0.7	-2.4	7.5	-1.8	-0.7	-1.6	-1.2	0.1	0.4	-1.4	-1.4	-0.6	-0.6	0.7	-0.7	0.2
T	-0.4	-0.7	-0.3	-0.8	-0.9	-0.6	-3.1	-7.2	-7.2	-0.5	-6.7	-1.1	-0.8	-0.9	-0.6	-1.0	1.1	-12.8	-8.4	-9.0
S	-0.4	-0.5	-1.3	-0.9	-0.9	-1.2	-1.8	-2.8	1.0	-1.0	-7.2	-2.0	-8.3	-0.4	-1.3	-1.9	-6.4	-10.5	-10.9	-10.1
N	-0.4	-0.6	-1.3	-0.5	-1.7	-2.7	-3.8	-4.3	-2.6	-1.4	-0.3	-5.0	-7.1	-6.3	-1.0	-2.6	-15.1	-17.6	-18.8	-20.4
Q	-0.7	-1.1	-1.3	-1.3	-0.2	-1.6	-1.7	-4.8	-3.2	-1.7	-0.9	-0.2	-9.0	-11.7	0.8	-2.8	-4.2	-18.9	-21.7	-22.2
C	-0.5	-0.8	-0.8	-0.7	-1.0	-1.2	-1.5	-3.1	-3.5	-1.2	-0.6	-1.3	-1.4	-1.1	0.1	-2.0	-5.5	-8.4	-6.9	-6.3
M	-0.9	-0.5	-0.9	-1.3	-2.0	-2.3	-1.8	-2.1	0.3	1.4	-1.4	-1.2	-2.4	-3.3	-1.2	-2.4	-4.1	-5.3	-3.5	-6.9
K	-0.8	-1.0	-2.4	-1.5	-1.1	-2.6	-5.9	-3.6	-1.7	-0.4	1.2	-4.6	-19.5	-22.3	-5.1	-5.3	62.6	59.6	-92.3	-101.6
R	-0.8	-1.9	-3.0	-2.4	-1.6	-5.7	-6.6	-7.4	-2.8	3.0	-2.4	-11.4	-15.3	-21.7	-3.4	-5.9	53.1	53.9	-91.1	-86.7
D	-0.4	-1.1	-0.4	-3.3	-1.2	-3.0	-18.9	-15.6	-20.2	-4.1	-2.9	-8.8	-18.6	-23.5	-2.6	-3.1	-96.3	-97.2	61.9	53.9
E	-0.7	-2.6	-0.8	-1.4	-2.0	-2.3	-20.4	-17.1	-17.5	-3.5	-8.5	-9.8	-6.4	-23.3	-9.9	-2.0	-102.7	-38.9	51.4	72.9

Table S3: Miyazawa-Jerningan contact energies

	G	A	V	I	L	F	Y	W	H	P	T	S	N	Q	C	M	K	R	D	E
G	-1.3	-1.4	**-2.0**	**-2.2**	**-2.5**	**-2.4**	-1.8	**-2.0**	-1.3	-1.1	-1.2	-1.1	-1.0	-1.0	**-1.9**	**-2.0**	-0.7	-1.0	-0.9	-0.7
A	-1.4	-1.6	**-2.4**	**-2.7**	**-2.9**	**-2.8**	**-2.0**	**-2.3**	-1.4	-1.2	-1.4	-1.2	-1.1	-1.1	**-2.1**	**-2.4**	-0.8	-1.1	-1.0	-0.9
V	**-2.0**	**-2.4**	**-3.3**	**-3.6**	**-3.8**	**-3.7**	**-2.7**	**-3.1**	**-2.1**	**-2.0**	**-2.0**	**-1.8**	-1.7	**-1.8**	**-2.9**	**-3.2**	-1.5	**-1.8**	-1.5	-1.6
I	**-2.2**	**-2.7**	**-3.6**	**-3.9**	**-4.2**	**-4.1**	**-3.1**	**-3.4**	**-2.5**	**-2.2**	**-2.4**	**-2.1**	**-1.9**	**-2.2**	**-3.3**	**-3.6**	-1.8	**-2.1**	**-1.9**	**-1.9**
L	**-2.5**	**-2.9**	**-3.8**	**-4.2**	**-4.4**	**-4.3**	**-3.4**	**-3.6**	**-2.7**	**-2.5**	**-2.6**	**-2.3**	**-2.2**	**-2.4**	**-3.5**	**-3.8**	**-2.0**	**-2.4**	**-2.0**	**-2.1**
F	**-2.4**	**-2.8**	**-3.7**	**-4.1**	**-4.3**	**-4.3**	**-3.4**	**-3.6**	**-2.8**	**-2.5**	**-2.5**	**-2.4**	**-2.2**	**-2.4**	**-3.4**	**-3.9**	**-2.0**	**-2.4**	**-2.1**	**-2.1**
Y	-1.8	**-2.0**	**-2.7**	**-3.1**	**-3.4**	**-3.4**	**-2.5**	**-2.8**	**-2.1**	**-1.9**	-1.8	-1.6	-1.6	-1.8	**-2.5**	**-2.9**	-1.5	**-1.9**	-1.6	-1.7
W	**-2.0**	**-2.3**	**-3.1**	**-3.4**	**-3.6**	**-3.6**	**-2.8**	**-3.0**	**-2.4**	**-2.2**	**-1.9**	-1.8	**-1.8**	**-1.8**	**-2.9**	**-3.3**	-1.6	**-2.0**	-1.7	-1.8
H	-1.3	-1.4	**-2.1**	**-2.5**	**-2.7**	**-2.8**	**-2.1**	**-2.4**	**-1.8**	-1.3	-1.4	-1.2	-1.2	-1.2	**-2.1**	**-2.4**	-0.8	-1.3	-1.4	-1.3
P	-1.1	-1.2	**-2.0**	**-2.2**	**-2.5**	**-2.5**	**-1.9**	**-2.2**	-1.3	-1.0	-1.1	-0.9	-0.9	-1.0	**-1.8**	**-2.0**	-0.6	-1.0	-0.8	-0.7
T	-1.2	-1.4	**-2.0**	**-2.4**	**-2.6**	**-2.5**	-1.8	**-1.9**	-1.4	-1.1	-1.3	-1.2	-1.1	-1.1	**-1.8**	**-2.1**	-0.8	-1.1	-1.1	-1.0
S	-1.1	-1.2	**-1.8**	**-2.1**	**-2.3**	**-2.4**	-1.6	-1.8	-1.2	-0.9	-1.2	-1.0	-0.9	-0.9	-1.7	**-1.8**	-0.6	-1.0	-1.0	-0.9
N	-1.0	-1.1	-1.7	**-1.9**	**-2.2**	**-2.2**	-1.6	**-1.8**	-1.2	-0.9	-1.1	-0.9	-1.0	-1.0	-1.5	-1.7	-0.7	-1.0	-1.0	-0.9
Q	-1.0	-1.1	**-1.8**	**-2.2**	**-2.4**	**-2.4**	-1.8	**-1.8**	-1.2	-1.0	-1.1	-0.9	-1.0	-0.9	-1.7	**-2.0**	-0.8	-1.1	-0.9	-0.8
C	**-1.9**	**-2.1**	**-2.9**	**-3.3**	**-3.5**	**-3.4**	**-2.5**	**-2.9**	**-2.1**	**-1.8**	**-1.8**	-1.7	-1.5	-1.7	**-3.2**	**-3.0**	-1.2	-1.5	-1.4	-1.3
M	**-2.0**	**-2.4**	**-3.2**	**-3.6**	**-3.8**	**-3.9**	**-2.9**	**-3.3**	**-2.4**	**-2.0**	**-2.1**	**-1.8**	-1.7	**-2.0**	**-3.0**	**-3.2**	-1.5	**-1.8**	-1.5	-1.7
K	-0.7	-0.8	-1.5	-1.8	**-2.0**	**-2.0**	-1.5	-1.6	-0.8	-0.6	-0.8	-0.6	-0.7	-0.8	-1.2	-1.5	-0.1	-0.3	-1.0	-1.1
R	-1.0	-1.1	**-1.8**	**-2.1**	**-2.4**	**-2.4**	**-1.9**	**-2.0**	-1.3	-1.0	-1.1	-1.0	-1.0	-1.1	-1.5	**-1.8**	-0.3	-0.9	-1.4	-1.3
D	-0.9	-1.0	-1.5	**-1.9**	**-2.0**	**-2.1**	-1.6	-1.7	-1.4	-0.8	-1.1	-1.0	-1.0	-0.9	-1.4	-1.5	-1.0	-1.4	-0.7	-0.6
E	-0.7	-0.9	-1.6	**-1.9**	**-2.1**	**-2.1**	-1.7	-1.8	-1.3	-0.7	-1.0	-0.9	-0.9	-0.8	-1.3	-1.7	-1.1	-1.3	-0.6	-0.5

Table S4: Side-chain interaction energy matrix CA evaluated by PM6-DH method

PM6DH	G	A	V	I	L	F	Y	W	H	P	T	S	N	Q	C	M	K	R	D	E
G	-0.7	-0.7	-0.8	-0.8	-1.0	-1.2	-1.6	-2.3	-1.5	-0.9	-0.8	-1.1	-0.6	-1.1	-0.8	-1.0	-1.5	-1.4	-0.8	-3.0
A	-0.6	-1.1	-1.0	-1.5	-1.6	-2.3	-2.1	-1.9	-1.4	-1.3	-1.0	-1.2	-1.1	-1.8	-0.9	-1.4	-1.8	-3.5	-1.8	-2.9
V	-0.9	-1.6	-2.2	-2.3	-1.4	-1.9	-1.4	-3.5	-1.8	-2.3	-1.2	-1.4	-1.1	-1.6	-0.7	-1.2	-2.2	-3.0	-2.8	-1.8
I	-1.3	-2.0	-1.6	-1.7	-1.8	-3.5	-2.9	-4.6	-1.8	-1.2	-1.6	-1.1	-1.3	-1.4	-0.7	-0.9	-2.4	-2.8	-3.5	-2.2
L	-1.1	-1.8	-1.6	-1.6	-2.0	-2.6	-2.9	-4.8	-1.9	-2.7	-1.5	-1.8	-2.2	-3.0	-0.9	-1.7	-4.5	-4.7	-4.5	-5.2
F	-1.9	-2.7	-3.0	-3.6	-2.8	-2.8	-2.5	-5.9	-3.6	-3.3	-2.6	-2.3	-5.3	-4.1	-1.4	-2.1	-5.3	-9.7	-6.8	-6.8
Y	-1.9	-2.3	-2.4	-3.3	-2.7	-3.5	-5.2	-7.0	-5.2	-4.9	-2.8	-3.9	-5.0	-3.9	-1.6	-4.4	-7.8	-9.9	-24.1	-28.5
W	-1.8	-2.4	-4.6	-3.5	-4.4	-5.3	-6.4	-6.2	-5.9	-5.6	-7.6	-6.5	-6.6	-6.1	-3.6	-6.5	-9.2	-13.3	-20.5	-21.2
H	-1.8	-1.9	-1.9	-3.6	-3.5	-3.0	-3.2	-6.8	-5.6	-3.2	-6.2	-5.6	-7.7	-8.0	-2.6	-2.1	-5.9	-8.8	-24.0	-22.2
P	-1.2	-1.2	-1.9	-3.3	-2.5	-3.9	-4.7	-5.0	-4.8	-2.8	-3.5	-3.4	-1.9	-3.1	-1.4	-0.9	-0.8	-2.3	-6.2	-3.6
T	-0.8	-1.2	-1.1	-1.3	-1.2	-1.4	-3.7	-7.6	-8.5	-1.0	-7.7	-1.6	-2.4	-2.5	-0.8	-1.4	0.3	-16.3	-10.6	-11.9
S	-0.6	-0.7	-1.6	-1.3	-1.6	-1.6	-2.5	-4.2	-0.1	-2.7	-7.6	-2.9	-6.2	-1.7	-1.2	-2.4	-8.2	-15.2	-11.3	-9.8
N	-0.6	-1.6	-1.6	-1.5	-3.2	-3.5	-4.7	-5.2	-3.6	-2.1	-0.9	-5.9	-9.1	-7.1	-1.2	-2.7	-25.6	-21.9	-22.6	-23.1
Q	-1.2	-1.4	-2.2	-2.2	-3.5	-3.8	-2.0	-5.7	-3.4	-2.7	-2.3	-1.6	-7.7	-11.0	-3.3	-2.1	-5.7	-21.8	-21.5	-22.3
C	-0.5	-0.6	-0.7	-0.8	-1.0	-1.5	-2.0	-3.5	-4.8	-1.1	-0.8	-2.0	-1.7	-2.9	-60.9	-2.4	-5.7	-9.0	-9.1	-8.4
M	-1.2	-0.7	-1.2	-1.4	-1.9	-3.0	-2.3	-3.0	-0.8	-2.7	-1.5	-1.8	-3.5	-3.4	-1.5	-2.7	-5.5	-8.0	-4.7	-9.6
K	-1.7	-2.5	-2.5	-2.6	-2.4	-5.4	-9.5	-9.5	-3.5	-2.9	-0.6	-6.5	-25.0	-24.8	-6.2	-6.7	60.7	52.0	-105.1	-103.3
R	-1.4	-3.2	-3.7	-4.0	-3.1	-9.5	-9.4	-12.6	-6.6	-4.3	-3.2	-14.0	-21.2	-22.1	-6.2	-9.0	49.4	51.1	-105.0	-98.1
D	-0.5	-2.0	-2.6	-3.6	-4.2	-5.0	-31.5	-18.9	-27.7	-7.0	-3.7	-9.4	-24.7	-24.6	-5.2	-4.4	-109.0	-115.2	62.4	49.7
E	-1.4	-2.5	-2.7	-3.1	-3.9	-3.6	-30.1	-20.9	-22.6	-7.6	-11.7	-11.7	-8.5	-24.1	-10.1	-7.0	-103.2	-127.5	51.3	66.8