Supplementary Information for

"Salt Bridges in the Prion Protein: Implications for Stability and Misfolding"

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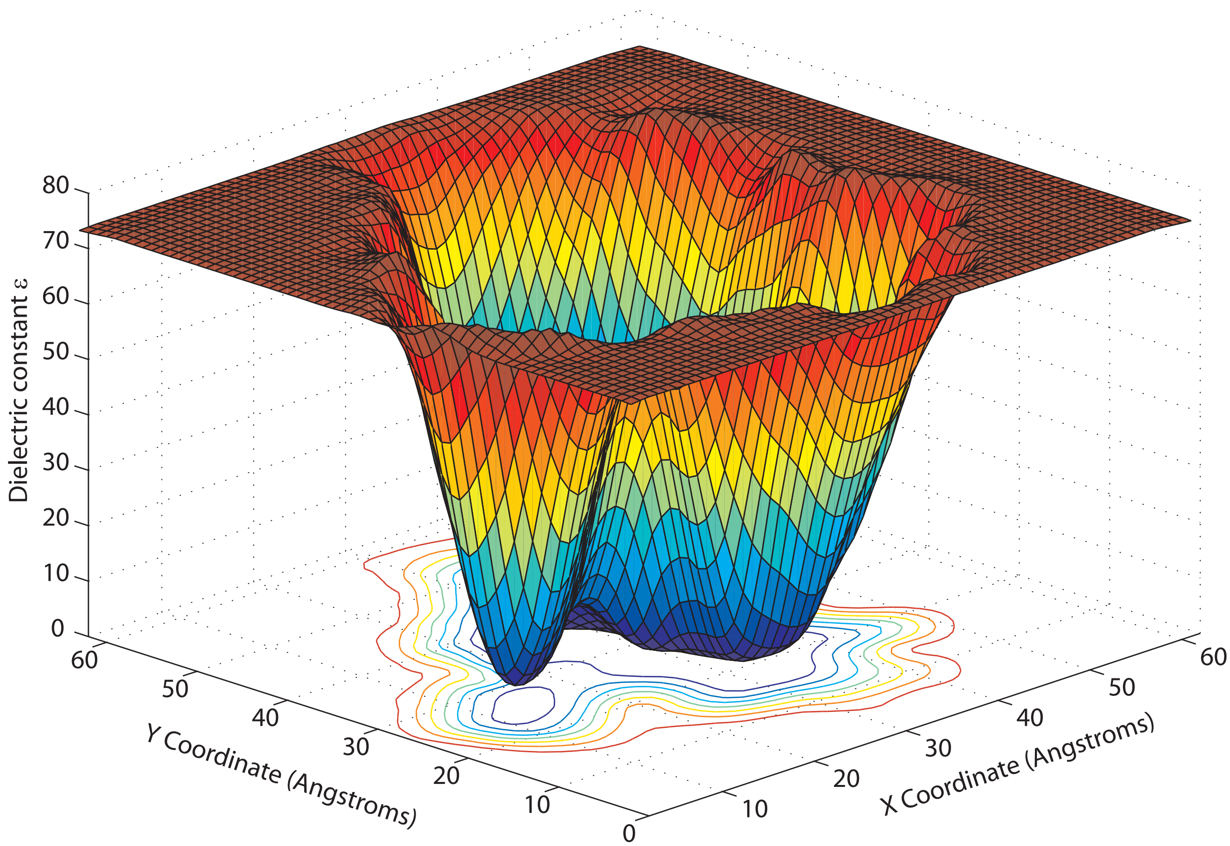

Figure 1: Local heterogeneous dielectric map of human PrP as calculated by mesoscopic dielectric theory (Guest et al., 2009). This is a slice taken through the geometric centre of the molecule in the X-Y plane.

Table 1: Salt bridges in 13 structures of the prion protein with a repulsive or attractive energy greater than 3 kJ/mol. The number of NMR conformers in which the participating charged groups are within a distance of 12Å is n. $E_{sb}(1)$ is the salt bridge energy calculated according to Equation 2 with the heterogeneous dielectric theory, and $E_{sb}(2)$ is the same energy calculated with a constant protein dielectric of 4. The standard deviation of salt bridge energy over the structures in the NMR ensemble containing the salt bridge is given by δE_{sb} and as a fraction of the total salt bridge energy by $\frac{\delta E_{sb}}{E_{sb}}$.

PDB	Species	Residues Involved		n (/20)	$E_{sb}(1)$ (kJ/mol)	$\delta E_{sb}(1)$ (kJ/mol)	$\frac{\delta E_{sb}(1)}{E_{sb}(1)}$	$E_{sb}(2)$ (kJ/mol)	$\delta E_{sb}(2)$ (kJ/mol)	$\frac{\delta E_{sb}(2)}{E_{sb}(2)}$
1DX0	Bovine	147	151	20	-6.4	3.5	0.54	-15.2	12.6	0.83
1DX0	Bovine	164	178	20	-3.1	1.9	0.60	-6.2	6.3	1.02
1DX0	Bovine	156	196	20	-6.0	2.8	0.47	-12.1	8.7	0.72
1DX0	Bovine	156	202	20	-7.8	5.5	0.71	-13.0	10.7	0.82
1DX0	Bovine	200	204	20	-3.1	1.4	0.46	-4.1	5.9	1.44
1DX0	Bovine	208	211	20	-5.1	1.9	0.38	-10.4	10.2	0.98
1FKC	Human E200K	164	167	19	-3.0	1.1	0.38	-3.2	2.0	0.64
1FKC	Human E200K	164	178	20	-4.6	1.0	0.23	-7.0	3.8	0.55
1FKC	Human E200K	156	196	20	-3.1	0.7	0.22	-3.2	1.5	0.46
1FKC	Human E200K	156	202	20	-3.2	0.7	0.21	-4.6	1.5	0.34
1FKC	Human E200K	146	204	20	-5.2	1.6	0.31	-8.6	5.1	0.59
1FKC	Human E200K	204	208	20	3.4	0.5	0.15	3.7	0.9	0.25
1FKC	Human E200K	208	211	20	-4.2	0.6	0.14	-5.2	1.8	0.33
1QLZ	Human WT	144	147	19	4.4	0.8	0.19	5.4	1.7	0.32
1QLZ	Human WT	144	151	16	-3.5	1.0	0.29	-4.1	2.5	0.60
1QLZ	Human WT	147	151	20	-9.9	3.8	0.39	-30.4	16.2	0.53
1QLZ	Human WT	148	152	19	-5.0	1.2	0.25	-14.6	7.5	0.51
1QLZ	Human WT	164	168	12	-3.3	1.7	0.53	-4.9	6.5	1.32
1QLZ	Human WT	164	178	15	-4.8	5.9	1.23	-8.2	11.8	1.44
1QLZ	Human WT	156	196	20	-5.1	1.6	0.32	-11.8	11.4	0.96
1QLZ	Human WT	146	204	18	-3.0	0.9	0.29	-3.4	1.4	0.43
1QLZ	Human WT	200	204	20	-3.7	1.5	0.39	-6.5	5.5	0.85
1QLZ	Human WT	204	207	15	-3.1	1.4	0.45	-3.7	5.9	1.58
1QLZ	Human WT	208	211	20	-5.8	1.8	0.30	-14.9	9.9	0.66
1QLZ	Human WT	167	228	11	-13.1	0.9	0.07	-75.5	5.7	0.07
1QLZ	Human WT	221	228	12	-13.7	1.0	0.07	-76.6	5.7	0.07
1U3M	Chicken	150	153	20	-5.0	1.3	0.25	-10.1	7.3	0.72
1U3M	Chicken	155	159	20	-3.8	0.7	0.19	-5.2	2.3	0.43
1U3M	Chicken	171	185	20	-5.4	1.6	0.29	-12.4	6.7	0.54
1U3M	Chicken	159	215	20	5.2	0.8	0.15	6.2	2.7	0.44
1U3M	Chicken	163	219	20	-8.4	4.3	0.51	-20.6	15.9	0.77
1U3M	Chicken	217	221	20	-5.7	1.1	0.20	-15.3	7.6	0.50
1U3M	Chicken	225	229	20	-4.1	1.8	0.44	-5.9	7.7	1.30
1U3M	Chicken	139	237	20	-4.1	2.0	0.48	-6.0	6.0	0.99
1U5L	Turtle	143	146	20	-3.3	0.7	0.21	-5.8	2.3	0.40
1U5L	Turtle	165	169	18	-3.0	2.2	0.74	-5.0	7.1	1.42
1U5L	Turtle	164	179	20	-5.1	2.8	0.55	-7.9	7.9	1.00
1U5L	Turtle	175	179	20	-4.2	2.8	0.68	-6.9	7.3	1.06

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PDB	Species	Residues Involved		n (/20)	$E_{sb}(1)$ (kJ/mol)	$\delta E_{sb}(1)$ (kJ/mol)	$\frac{\delta E_{sb}(1)}{E_{sb}(1)}$	$E_{sb}(2)$ (kJ/mol)	$\delta E_{sb}(2)$ (kJ/mol)	$\frac{\delta E_{sb}(2)}{E_{sb}(2)}$
1U5L	Turtle	156	202	16	-3.1	2.5	0.79	-4.2	6.8	1.63
1U5L	Turtle	146	204	20	-5.7	1.8	0.32	-15.1	10.8	0.71
1U5L	Turtle	191	207	20	-4.6	2.6	0.56	-7.5	8.7	1.15
1XU0	Frog	148	152	20	-3.3	1.3	0.39	-4.7	6.2	1.31
1XU0	Frog	169	176	19	-3.1	1.6	0.52	-5.6	6.6	1.17
1XU0	Frog	175	179	20	-3.1	1.3	0.43	-4.8	7.0	1.45
1XU0	Frog	169	180	19	3.0	1.4	0.46	4.1	2.8	0.69
1XU0	Frog	188	192	20	-9.4	1.8	0.19	-19.3	6.3	0.33
1XU0	Frog	197	206	20	-5.3	3.4	0.63	-10.2	11.9	1.16
1XU0	Frog	197	210	19	4.7	2.3	0.50	7.7	6.5	0.85
1XU0	Frog	206	210	20	-21.4	6.7	0.32	-42.2	15.9	0.38
1XU0	Frog	163	221	20	-9.4	6.1	0.64	-16.9	13.6	0.80
1XU0	Frog	221	224	20	-5.0	3.6	0.72	-11.5	12.1	1.05
1XYJ	Cat	147	151	20	-11.6	3.1	0.27	-40.9	13.4	0.33
1XYJ	Cat	164	178	20	-4.7	2.5	0.54	-11.7	11.9	1.01
1XYJ	Cat	156	202	20	-11.8	5.3	0.44	-21.5	15.0	0.70
1XYJ	Cat	146	204	20	-3.9	2.0	0.51	-5.7	8.7	1.51
1XYJ	Cat	200	204	20	-3.5	0.9	0.26	-4.0	3.4	0.85
1XYJ	Cat	208	211	20	-5.8	3.0	0.52	-11.8	11.3	0.96
1XYK	Dog	144	147	20	3.1	1.0	0.32	3.9	2.0	0.52
1XYK	Dog	144	148	20	-4.1	2.1	0.51	-9.3	9.1	0.97
1XYK	Dog	147	151	20	-8.4	4.5	0.54	-22.5	16.5	0.73
1XYK	Dog	148	152	20	-3.1	1.2	0.39	-5.3	5.8	1.09
1XYK	Dog	164	178	20	-3.6	2.2	0.60	-7.4	9.3	1.25
1XYK	Dog	136	202	2	-4.0	0.8	0.19	-6.1	0.8	0.12
1XYK	Dog	200	204	20	-3.1	1.2	0.40	-3.8	4.7	1.22
1XYK	Dog	204	207	20	-3.8	1.4	0.38	-5.6	6.2	1.11
1XYK	Dog	207	211	20	4.0	0.7	0.16	4.8	1.2	0.26
1XYK	Dog	208	211	20	-5.3	2.5	0.48	-11.5	11.3	0.98
1XYQ	Pig	147	151	20	-4.3	1.3	0.29	-6.0	4.1	0.69
1XYQ	Pig	148	151	20	3.5	0.3	0.09	4.1	1.0	0.24
1XYQ	Pig	164	178	20	-5.9	1.5	0.25	-11.9	7.0	0.59
1XYQ	Pig	200	204	20	-4.0	1.3	0.33	-7.0	6.4	0.91
1XYQ	Pig	204	207	20	-3.3	1.2	0.37	-3.0	2.1	0.71
1XYQ	Pig	207	211	20	3.4	0.8	0.23	4.0	1.2	0.30
1XYQ	Pig	208	211	20	-5.9	2.5	0.42	-9.8	12.1	1.24
1XYQ	Pig	220	223	19	-3.8	1.2	0.33	-3.6	2.4	0.67
1XYX	Mouse	144	147	12	3.2	0.8	0.25	3.2	1.3	0.41
1XYX	Mouse	147	151	16	-5.1	2.0	0.38	-9.2	7.9	0.85
1XYX	Mouse	148	152	12	-3.8	1.7	0.44	-7.8	9.3	1.18
1XYX	Mouse	164	178	18	-5.4	2.4	0.45	-10.8	11.0	1.02
1XYX	Mouse	156	196	13	-3.7	1.0	0.28	-4.2	2.5	0.61
1XYX	Mouse	194	196	16	-3.5	0.7	0.21	-3.0	0.7	0.23
1XYX	Mouse	156	202	20	-10.4	3.9	0.37	-18.9	8.8	0.46
1XYX	Mouse	146	204	20	-9.7	2.5	0.26	-27.2	11.9	0.44
1XYX	Mouse	146	208	10	-3.2	0.3	0.10	-3.8	0.9	0.23
1XYX	Mouse	204	208	18	3.2	0.4	0.13	3.6	0.9	0.24
1XYX	Mouse	207	211	10	3.5	0.5	0.15	4.0	0.8	0.20

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PDB	Species	Residues Involved		n (/20)	$E_{sb}(1)$ (kJ/mol)	$\delta E_{sb}(1)$ (kJ/mol)	$\frac{\delta E_{sb}(1)}{E_{sb}(1)}$	$E_{sb}(2)$ (kJ/mol)	$\delta E_{sb}(2)$ (kJ/mol)	$\frac{\delta E_{sb}(2)}{E_{sb}(2)}$
1XYX	Mouse	208	211	10	-4.4	1.1	0.24	-6.2	5.8	0.94
1XYX	Mouse	167	221	2	4.5	0.1	0.03	5.7	0.8	0.14
1XYX	Mouse	227	230	10	-3.7	1.9	0.51	-6.9	7.9	1.15
2K1D	Human D178N	144	147	20	3.3	0.4	0.13	3.6	0.9	0.23
2K1D	Human D178N	147	151	20	-3.7	1.1	0.30	-5.1	3.2	0.63
2K1D	Human D178N	164	185	19	3.3	1.5	0.45	3.7	2.8	0.78
2K1D	Human D178N	156	194	20	3.4	1.4	0.40	4.9	4.1	0.85
2K1D	Human D178N	156	202	16	-3.5	1.9	0.53	-5.5	5.1	0.93
2K1D	Human D178N	208	211	19	-3.6	1.2	0.32	-3.0	1.4	0.46
2KFL	Wallaby	147	151	20	-5.4	2.7	0.51	-14.6	11.3	0.77
2KFL	Wallaby	148	152	20	-3.6	1.4	0.40	-7.9	7.6	0.96
2KFL	Wallaby	164	178	20	-4.8	1.9	0.39	-8.3	7.8	0.93
2KFL	Wallaby	178	185	19	-3.3	0.9	0.27	-3.7	1.6	0.42
2KFL	Wallaby	156	196	20	-10.9	3.5	0.32	-29.6	15.1	0.51
2KFL	Wallaby	156	202	20	-13.3	11.7	0.88	-18.0	16.2	0.90
2KFL	Wallaby	196	202	20	4.9	0.7	0.13	7.4	1.6	0.22
2KFL	Wallaby	200	204	20	-4.6	1.1	0.24	-7.4	5.5	0.74
2KFL	Wallaby	204	207	20	-4.2	0.7	0.17	-4.4	1.2	0.28
2KFL	Wallaby	146	208	20	-3.7	0.3	0.09	-4.6	0.9	0.20
2KFL	Wallaby	208	211	20	-3.8	0.9	0.25	-4.8	5.0	1.04

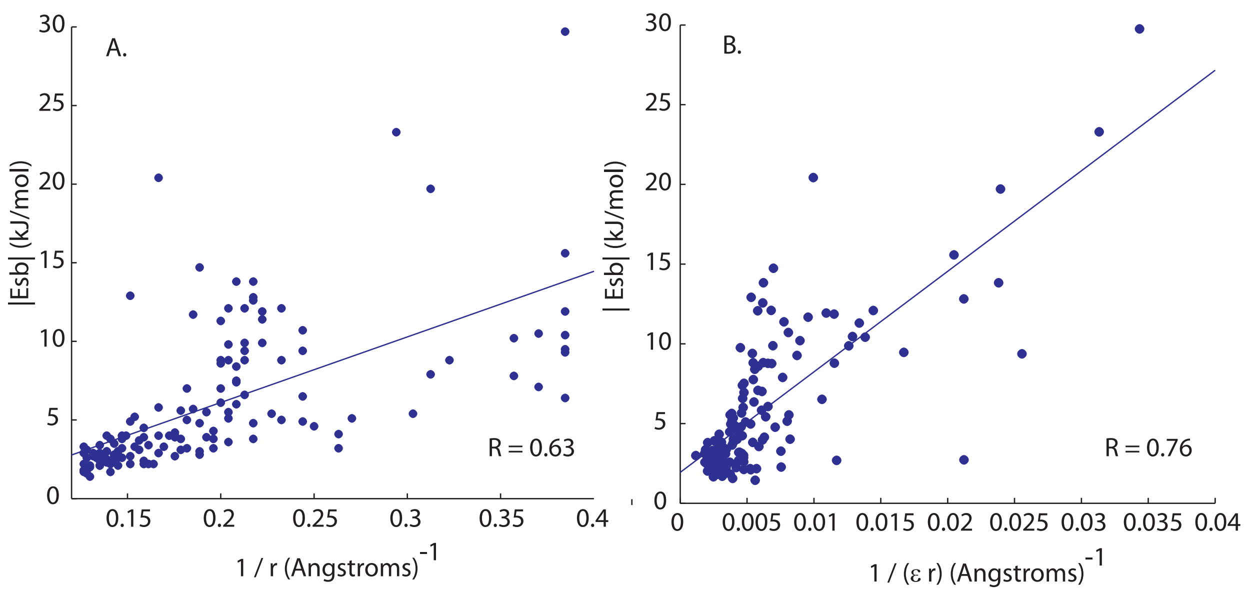

Figure 2: A. Absolute salt bridge energies as a function of the reciprocal of the separation distance between the participating charged groups. B. Absolute salt bridge energies as a function of the reciprocal of the separation distance multiplied by the dielectric constant ϵ at the midpoint of the line joining the charged groups. In a homogeneous dielectric environment, the energy of a salt bridge connecting charges q_A and q_B would be given by $E_{sb} = \frac{1}{4\pi\epsilon_0}\frac{q_A q_B}{\epsilon\, r}$. Including $1/\epsilon$ in the fit in addition to $1/r$ improves the correlation from 0.63 to 0.76, but even taken together the quantities ϵ and r do not reliably predict salt bridge energies. Thus a direct calculation of energies from the full heterogeneous dielectric map is necessary to obtain accurate results.

Table 2: Total electrostatic energies in kJ/mol for every residue in a selection of 13 prion protein structures at pH 7. The energies are calculated according to Equation 3.

Res	2KFL Wallaby	1QLX Human WT	1FKC Human E200K	2K1D Human D178N	1DX0 Bovine	1U3M Chicken	1U5L Turtle	1XU0 Frog	1XYJ Cat	1XYK Dog	1XYQ Pig	1XYX Mouse	1AG2 Mouse
120	S -11						S -7						
121	V -9						V -2						
122	V -2						V -4		V -4	V -2	V -4	V -3	
123	G -1						G 0		G -1	G -1	G -1	G -1	
124	G -1						G 0		G -1	G -1	G -1	G -1	
125	L -19				L -7		L -7		L -15	L -5	L -8	L -23	L -6
126	G -1	G -1	G -1	G -1	G -1		G 0	G -2	G -1	G -1	G -1	G -1	G -1
127	G -1	G -1	G -1	G -2	G 0	S -7	G 0	G -2	G 0	G -1	G 0	G -1	G -1
128	Y -42	Y -32	Y -28	Y -18	Y -52	V -2	Y -23	Y -18	Y -21	Y -18	Y -27	Y -28	Y -27
129	M -11	M -9	M -8	V -6	M -7	V -2	A -2	M -8	M -7	M -5	M -4	M -9	M -8
130	L -15	L -10	L -10	L -4	L -12	G -1	L -9	L -11	L -14	L -7	L -7	L -5	L -14
131	G -2	G -5	G -5	G -1	G -2	G 0	G -2	G -3	G -2	G -1	G 0	G -3	G -4
132	S -21	S -18	S -16	S -7	S -11	L -3	S -11	N -34	S -9	S -14	S -8	S -12	S -13
133	A -1	A -3	A -1	A -1	A -1	G 0	A -2	A -2	A -1	A -1	A -1	A -3	A -3
134	M -8	M -6	M -24	M -9	M -30	G 0	M -10	V -19	M -11	M -6	M -8	M -8	M -22
135	S -8	S -8	S -14	S -9	S -15	Y -10	S -16	G -1	S -38	S -19	S -10	S -9	S -11
136	R -382	R -151	R -140	R -55	R -63	A -3	G -1	R -55	R -44	R -46	R -56	R -22	R -119
137	P -8	P -10	P -15	P -4	P -7	M -7	M -16	M -22	P -15	P -6	P -12	P -15	P -8
138	V -6	I -11	I -10	I -5	L -7	G -3	R -35	S -15	L -4	L -22	L -5	M -3	M -4
139	M -15	I -20	I -18	I -37	I -43	R -59	M -7	Y -16	I -18	I -9	I -20	I -16	I -26
140	H -23	H -25	H -27	H -20	H -20	V -13	N -14	Q -13	H -12	H -15	H -25	H -16	H -15
141	F -29	F -18	F -47	F -24	F -32	M -13	F -23	F -24	F -23	F -20	F -27	F -27	F -19
142	G 1	G 1	G -1	G 0	G 0	S -16	D -26	N -15	G 0	G 0	G 0	G 0	G 0
143	N -17	S -9	S -19	S -10	S -26	G -1	R -32	N -27	N -33	N -14	S -10	N -12	N -15
144	E -46	D -36	D -39	D -40	D -36	M -10	P -4	P -3	D -37	D -40	D -37	D -37	D -45
145	Y -13	Y -11	Y -12	Y -10	Y -11	N -11	E -29	M -6	Y -12	Y -19	Y -10	W -19	W -18
146	E -40	E -39	E -80	E -43	E -78	Y -40	E -90	E -127	E -54	E -70	E -43	E -51	E -45
147	D -75	D -196	D -70	D -61	D -91	H -14	R -76	S -31	D -57	D -53	D -92	D -54	D -86
148	R -54	R -34	R -48	R -59	R -34	F -12	Q -26	R -50	R -36	R -25	R -48	R -40	R -70
149	Y -52	Y -20	Y -42	Y -23	Y -27	D -32	W -57	Y -77	Y -25	Y -31	Y -19	Y -52	Y -106
150	Y -86	Y -171	Y -132	Y -68	Y -143	R -42	W -81	Y -58	Y -49	Y -58	Y -79	Y -52	Y -114
151	R -97	R -43	R -55	R -43	R -69	P -2	N -47	N -57	R -51	R -37	R -61	R -36	R -46
152	E -39	E -31	E -39	E -57	E -31	D -33	E -45	D -73	E -37	E -42	E -67	E -50	E -78
153	N -53	N -25	N -49	N -31	N -30	E -33	N -36	Y -23	N -28	N -85	N -41	N -74	N -158
154	Q -25	M -24	M -16	M -4	M -8	Y -17	S -10	Y -16	M -8	M -5	M -13	M -10	M -13
155	Y -17	H -19	H -27	H -19	H -18	R -41	N -15	N -13	Y -13	Y -9	Y -13	Y -13	Y -21
156	R -128	R -29	R -41	R -60	R -97	W -36	R -77	Q -14	R -53	R -68	R -57	R -133	R -242
157	Y -145	Y -75	Y -148	Y -18	Y -140	W -52	Y -9	M -41	Y -109	Y -66	Y -52	Y -128	Y -228
158	P -16	P -12	P -9	P -6	P -37	S -13	P -3	P -32	P -9	P -4	P -5	P -10	P -12
159	N -21	N -32	N -52	N -14	N -38	E -54	N -59	N -17	N -17	D -54	N -16	N -17	N -22
160	Q -23	Q -34	Q -18	Q -24	Q -16	N -56	Q -27	R -80	Q -26	Q -23	Q -34	Q -26	Q -24
161	V -63	V -53	V -64	V -26	V -54	S -20	V -34	V -61	V -50	V -27	V -43	V -51	V -49
162	M -19	Y -25	Y -25	Y -34	Y -32	A -1	Y -29	Y -38	Y -32	Y -34	Y -21	Y -40	Y -50
163	Y -59	Y -51	Y -40	Y -31	Y -39	R -30	Y -42	R -83	Y -45	Y -26	Y -23	Y -36	Y -30
164	R -59	R -99	R -63	R -62	R -74	Y -15	K -30	P -28	R -52	R -82	R -84	R -56	R -182
165	P -16	P -5	P -5	P -8	P -5	P -5	E -47	M -7	P -3	P -3	P -3	P -5	P -4
166	I -25	M -19	M -21	M -2	V -13	N -48	Y -152	Y -33	V -15	V -7	V -24	V -16	V -34
167	D -34	D -41	D -58	D -48	D -31	R -67	N -12	R -35	D -35	D -38	D -54	D -32	D -39
168	Q -20	E -31	E -39	E -70	Q -11	V -47	D -34	G -1	Q -18	Q -16	Q -17	Q -15	Q -20
169	Y -137	Y -16	Y -8	Y -7	Y -8	Y -31	R -48	E -93	Y -7	Y -6	Y -15	Y -40	Y -10
170	G -1	S -25	S -27	S -9	S -18	Y -52	S -10	E -41	S -28	S -25	S -8	S -13	S -10
171	S -12	N -20	N -17	N -13	N -19	R -36	V -22	Y -10	N -15	N -28	N -18	N -13	N -13
172	Q -22	Q -11	Q -21	Q -15	Q -30	D -29	P -3	V -17	Q -15	Q -15	Q -24	Q -12	Q -70
173	N -15	N -11	N -16	N -13	N -18	Y -131	E -36	S -14	N -10	N -13	N -17	N -13	N -17
174	S -14	N -12	N -14	N -17	N -15	S -7	G -1	E -49	N -11	N -11	S -11	N -13	N -34

Continued...

Res	2KFL Wallaby		1QLX Human WT		1FKC Human E200K		2K1D Human D178N		1DX0 Bovine		1U3M Chicken		1U5L Turtle		1XU0 Frog		1XYJ Cat		1XYK Dog		1XYQ Pig		1XYX Mouse		1AG2 Mouse	
175	F	-79	F	-53	F	-54	F	-28	F	-45	S	-12	R	-134	D	-36	F	-30	F	-18	F	-73	F	-24	F	-79
176	V	-18	V	-9	V	-19	V	-19	V	-14	P	-3	F	-68	R	-47	V	-6	V	-14	V	-46	V	-10	V	-10
177	H	-17	H	-17	H	-16	H	-16	H	-18	V	-4	V	-9	F	-56	H	-14	R	-29	H	-15	H	-11	H	-17
178	D	-69	D	-96	D	-63	N	-32	D	-56	P	-3	R	-39	V	-10	D	-42	D	-52	D	-39	D	-41	D	-78
179	C	-14	C	-15	C	-12	C	-11	C	-13	Q	-24	D	-127	R	-46	C	-6	C	-8	C	-11	C	-9	C	-16
180	V	-22	V	-11	V	-12	V	-18	V	-9	D	-31	C	-13	D	-60	V	-16	V	-15	V	-38	V	-9	V	-6
181	N	-19	N	-14	N	-18	N	-17	N	-14	V	-3	V	-21	C	-11	N	-13	N	-20	N	-24	N	-9	N	-19
182	I	-30	I	-29	I	-14	I	-31	I	-18	F	-60	N	-19	Y	-13	I	-26	I	-9	I	-26	I	-10	I	-31
183	T	-212	T	-197	T	-172	T	-158	T	-193	V	-20	I	-36	N	-18	T	-166	T	-157	T	-165	T	-174	T	-219
184	V	-14	I	-34	I	-37	I	-22	V	-14	A	-1	T	-178	M	-15	V	-41	V	-8	V	-48	I	-12	I	-10
185	K	-21	K	-19	K	-23	K	-29	K	-23	D	-37	V	-31	S	-133	R	-50	K	-16	K	-21	K	-18	K	-18
186	Q	-51	Q	-23	Q	-26	Q	-20	E	-88	C	-13	T	-19	V	-9	Q	-20	Q	-58	Q	-24	Q	-28	Q	-33
187	H	-29	H	-37	H	-43	H	-34	H	-41	F	-22	E	-59	T	-26	H	-26	H	-76	H	-19	H	-50	H	-39
188	T	-29	T	-22	T	-34	T	-56	T	-34	N	-15	Y	-20	E	-84	T	-66	T	-11	T	-56	T	-18	T	-24
189	T	-21	V	-4	V	-6	V	-4	V	-4	I	-14	K	-13	Y	-107	V	-7	V	-3	V	-8	V	-3	V	-4
190	T	-16	T	-18	T	-11	T	-12	T	-26	T	-133	I	-29	I	-13	T	-18	T	-17	T	-26	T	-15	T	-28
191	T	-19	T	-23	T	-19	T	-73	T	-99	V	-20	D	-149	I	-8	T	-22	T	-31	T	-51	T	-54	T	-26
192	T	-49	T	-51	T	-50	T	-33	T	-16	T	-18	P	-4	K	-21	T	-27	T	-8	T	-20	T	-19	T	-26
193	T	-11	T	-17	T	-21	T	-8	T	-16	E	-43	N	-15	P	-4	T	-13	T	-8	T	-13	T	-10	T	-15
194	K	-16	K	-19	K	-15	K	-16	K	-20	Y	-43	E	-50	A	-2	K	-14	K	-25	K	-19	K	-18	K	-16
195	G	0	G	0	G	0	G	0	G	0	S	-8	N	-36	E	-29	G	0	G	0	G	0	G	0	G	-1
196	E	-53	E	-30	E	-41	E	-37	E	-48	I	-14	Q	-13	G	0	E	-83	E	-67	E	-46	E	-40	E	-78
197	N	-22	N	-12	N	-18	N	-18	N	-13	G	-1	N	-13	K	-19	N	-11	N	-13	N	-11	N	-19	N	-18
198	F	-34	F	-10	F	-34	F	-11	F	-42	P	-2	V	-19	N	-17	F	-24	F	-21	F	-16	F	-35	F	-23
199	T	-37	T	-29	T	-55	T	-32	T	-16	A	-2	T	-14	N	-22	T	-17	T	-34	T	-16	T	-30	T	-63
200	E	-35	E	-37	K	-17	E	-33	E	-30	A	-1	Q	-17	S	-8	E	-31	E	-31	E	-33	E	-36	E	-33
201	T	-34	T	-20	T	-25	T	-20	T	-14	K	-9	V	-6	E	-27	T	-14	T	-25	T	-13	T	-23	T	-25
202	D	-304	D	-137	D	-290	D	-122	D	-235	K	-14	E	-104	L	-14	D	-123	D	-340	D	-86	D	-161	D	-372
203	I	-9	V	-5	V	-5	V	-8	I	-7	N	-14	V	-18	N	-16	M	-8	M	-5	V	-7	V	-6	V	-7
204	K	-12	K	-9	K	-12	K	-8	K	-7	T	-12	R	-46	Q	-15	K	-15	K	-11	K	-13	K	-12	K	-11
205	I	-58	M	-20	M	-40	M	-13	M	-42	S	-10	V	-74	L	-14	I	-39	I	-70	M	-15	M	-40	M	-18
206	M	-49	M	-37	M	-46	M	-17	M	-39	E	-27	M	-28	D	-119	M	-24	M	-34	I	-42	M	-47	M	-32
207	E	-61	E	-44	E	-36	E	-60	E	-42	A	-2	K	-23	T	-14	E	-51	E	-36	E	-69	E	-39	E	-45
208	R	-35	R	-35	R	-32	R	-73	R	-41	V	-4	Q	-16	T	-13	R	-58	R	-30	R	-45	R	-32	R	-27
209	V	-86	V	-66	V	-58	V	-30	V	-56	A	-1	V	-60	V	-51	V	-50	V	-41	V	-84	V	-47	V	-63
210	V	-80	V	-73	V	-73	V	-55	V	-75	A	-3	I	-81	K	-95	V	-67	V	-61	V	-82	V	-66	V	-86
211	E	-52	E	-41	E	-42	E	-59	E	-44	A	-2	Q	-16	S	-11	E	-53	E	-47	E	-94	E	-37	E	-56
212	Q	-24	Q	-17	Q	-21	Q	-104	Q	-20	N	-18	E	-46	Q	-19	Q	-33	Q	-23	Q	-25	Q	-14	Q	-23
213	M	-31	M	-27	M	-38	M	-30	M	-41	Q	-13	M	-31	I	-82	M	-36	M	-26	M	-35	M	-36	M	-38
214	C	-14	C	-12	C	-16	C	-13	C	-14	T	-12	C	-12	I	-54	C	-8	C	-12	C	-11	C	-7	C	-19
215	I	-7	I	-7	I	-17	I	-28	I	-10	E	-44	M	-5	R	-40	V	-10	V	-7	I	-24	V	-5	V	-33
216	T	-17	T	-24	T	-57	T	-51	T	-20	V	-9	Q	-29	E	-50	T	-23	T	-24	T	-30	T	-28	T	-50
217	Q	-66	Q	-53	Q	-82	Q	-21	Q	-54	E	-25	Q	-36	M	-52	Q	-43	Q	-53	Q	-60	Q	-45	Q	-46
218	Y	-34	Y	-23	Y	-51	Y	-91	Y	-22	M	-3	Y	-22	C	-14	Y	-40	Y	-37	Y	-48	Y	-22	Y	-122
219	Q	-17	E	-37	E	-44	E	-26	Q	-15	E	-55	Q	-28	I	-10	Q	-19	Q	-17	Q	-27	Q	-15	Q	-32
220	N	-25	R	-53	R	-77	R	-33	R	-56	N	-13	Q	-18	T	-23	K	-16	K	-15	K	-16	K	-20	K	-16
221	E	-220	E	-92	E	-77	E	-88	E	-91	K	-9	Y	-33	E	-196	E	-42	E	-43	E	-58	E	-53	E	-43
222	Y	-18	S	-19	S	-40	S	-14	S	-11	V	-29	Q	-56	Y	-64	S	-52	S	-25	Y	-16	S	-29	S	-43
223	Q	-22	Q	-15	Q	-17	Q	-13	Q	-17	V	-19	L	-8	R	-41	E	-39	E	-43	E	-79	Q	-13	Q	-16
224	A	-2	A	-2	A	-2	A	-2	A	-3	T	-24	A	-2	R	-63	A	-2	A	-1	A	-2	A	-2	A	-2
225	A	-2	Y	-16	Y	-26	Y	-17	Y	-21	K	-15			G	0	Y	-11	Y	-11	Y	-11	Y	-11	Y	-15
226	Q	-21	Y	-9	Y	-22	Y	-9	Y	-13	V	-16					Y	-35	Y	-11	A	-1	Y	-11		
227	R	-46	Q	-14	Q	-24	Q	-14			I	-56					Q	-18	Q	-22	Q	-13	D	-29		
228	Y	-9			R	-41	R	-30			R	-47					R	-28	R	-33	R	-37	G	0		
229	Y	-11			G	0	G	0			E	-47					R	-29	G	1	G	-1	R	-39		
230					S	-8	S	-9			M	-41					A	-1	A	-1	A	-1	R	-26		
231											C	-9											S	-8		
232											V	-12														
233											Q	-22														
234											Q	-67														
235											Y	-41														

Continued. . .

Res	2KFL Wallaby	1QLX Human WT	1FKC Human E200K	2K1D Human D178N	1DX0 Bovine	1U3M Chicken	1U5L Turtle	1XU0 Frog	1XYJ Cat	1XYK Dog	1XYQ Pig	1XYX Mouse	1AG2 Mouse
236						R -35							
237						E -55							
238						Y -22							
239						R -36							
240						L -3							
241						A -1							

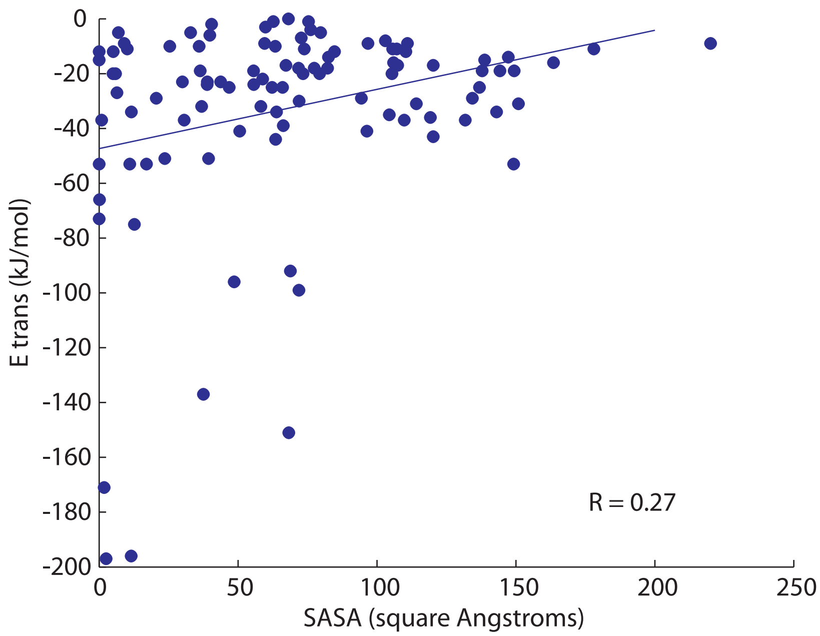

Figure 3: Total electrostatic energies of side chains in human PrP calculated from Equation 3 plotted as a function of solvent-accessible surface area (SASA), a statistic related to burial in the core of the protein. There is a weak but significant ($p = 0.01$) correlation between the energy and SASA, but SASA alone is a poor proxy for the electrostatic energy.

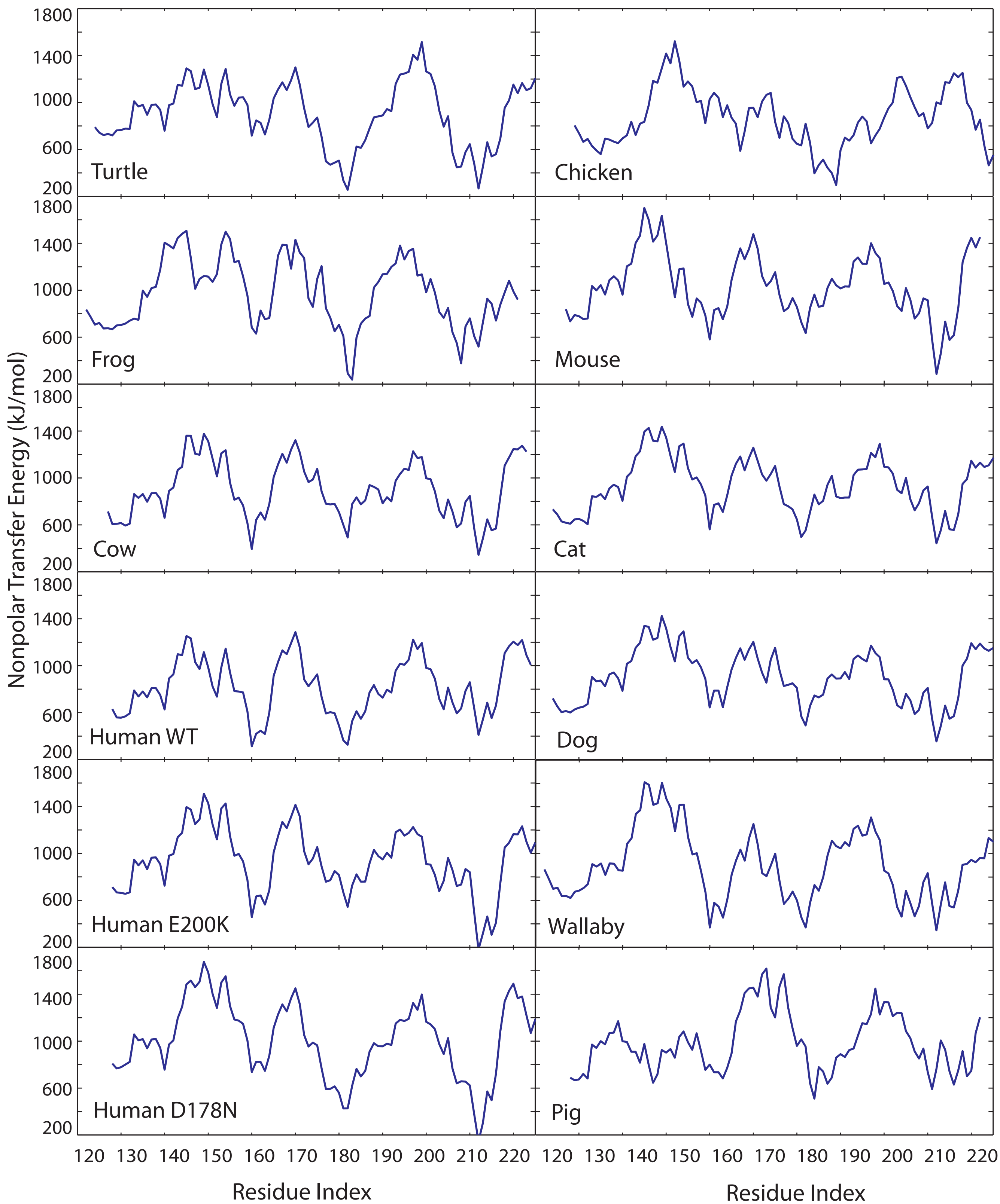

Figure 4: Hydrophobic transfer energies from Equation 4 for seven residue contiguous segments of 12 prion protein structures. The residue index gives the position of the middle residue in each segment.