The Role of the Protonation State on the Structure and Dynamics of Albumin

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Supporting Information

Table S1. *pKa* values computed for all the ionizable amino acids in the free form of HSA considering different crystal structures (PDB codes: 1AO6, 3JRY, 4G03, and 4EMX) and four dielectric constants for the interior of the protein (ε_{int}). In bold, we highlight those pK_a values that point to a non-standard protonation state at *pH* 7 and also those results that suggest deprotonation of the corresponding residue when the *pH* rises to 9.

Residue	**1AO6** (mol. A, 2.50 Å)				**3JRY** (mol. A, 2.30 Å)				**4G03** (mol. A, 2.22 Å)				**4EMX** (mol. A, 2.30 Å)			
	ε_{int}=4	ε_{int}=6	ε_{int}=10	ε_{int}=20	ε_{int}=4	ε_{int}=6	ε_{int}=10	ε_{int}=20	ε_{int}=4	ε_{int}=6	ε_{int}=10	ε_{int}=20	ε_{int}=4	ε_{int}=6	ε_{int}=10	ε_{int}=20
His3	--	--	--	--	--	--	--	--	--	--	--	--	4.7	4.8	5.3	5.9
Lys4	--	--	--	--	--	--	--	--	--	--	--	--	>12.0	>12.0	>12.0	>12.0
Glu6	<0.0	<0.0	0.1	1.0	<0.0	0.7	0.4	1.2	<0.0	<0.0	0.4	1.1	<0.0	<0.0	<0.0	<0.0
His9	4.3	6.3	**8.0**	**8.4**	**9.6**	**9.6**	**9.5**	**9.2**	3.7	5.8	**7.3**	**7.7**	**10.3**	**9.6**	**9.0**	**8.4**
Arg10	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Lys12	>12.0	>12.0	>12.0	>12.0	10.9	11.1	11.3	11.5	11.5	11.7	>12.0	>12.0	11.4	11.7	>12.0	>12.0
Asp13	9.1	6.9	5.1	4.3	7.0	5.9	4.9	4.0	7.8	6.1	4.5	3.8	6.0	4.7	3.3	2.6
Glu16	2.7	2.4	2.3	2.2	2.7	2.5	2.3	2.2	0.9	1.3	1.6	1.8	1.4	1.6	1.7	1.8
Glu17	2.8	3.0	3.1	3.2	1.7	1.9	2.1	2.3	2.1	2.3	2.5	2.6	1.7	1.7	1.8	2.1
Lys20	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	9.5	9.9	10.3	10.6	11.6	11.7	>12.0	>12.0
Tyr30	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Cys34	>12.0	>12.0	>12.0	10.8	>12.0	>12.0	10.9	9.7	>12.0	>12.0	>12.0	10.5	>12.0	>12.0	>12.0	11.4
Glu37	3.4	3.4	3.4	3.2	3.2	3.4	3.4	3.3	3.6	3.6	3.4	3.3	3.1	3.2	3.2	3.0
Asp38	4.7	4.2	3.8	2.6	4.3	3.9	3.4	2.4	3.8	3.6	2.8	2.3	3.5	3.3	2.8	1.9
His39	<0.0	<0.0	<0.0	5.0	<0.0	<0.0	<0.0	4.9	<0.0	<0.0	1.7	5.5	<0.0	<0.0	<0.0	5.2
Lys41	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	11.5	11.6	11.7	>12.0

Glu45	0.5	1.1	1.5	1.8	1.8	2.1	2.3	2.3	4.3	3.8	3.3	2.9	2.8	3.0	2.9	2.7
Glu48	3.8	3.8	3.8	3.8	4.1	4.0	3.9	3.8	3.5	3.6	3.7	3.8	3.7	3.7	3.8	3.8
Lys51	10.8	11.0	11.2	11.4	10.9	11.1	11.3	11.5	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Asp56	3.4	3.5	3.6	3.6	5.1	4.7	4.4	4.1	4.6	4.4	4.2	3.9	3.8	3.9	3.8	3.7
Glu57	5.9	4.9	4.2	3.7	5.4	5.2	4.3	3.6	3.5	3.3	3.2	3.2	3.6	3.0	2.8	2.7
Glu60	3.5	3.7	3.9	4.0	5.5	5.2	4.9	4.5	4.1	4.2	4.3	4.3	7.3	6.3	5.4	4.3
Asp63	3.6	3.6	3.6	3.5	4.3	4.2	3.8	3.5	3.3	3.3	3.4	3.4	1.8	1.9	1.9	1.8
Lys64	>12.0	>12.0	>12.0	>12.0	10.8	11.0	11.3	11.5	10.8	11.1	11.4	11.6	>12.0	>12.0	>12.0	>12.0
His67	**11.1**	**9.5**	**9.0**	**8.3**	**8.1**	**8.1**	**8.0**	**7.8**	**10.8**	**9.4**	**9.0**	**8.5**	**>12.0**	**11.0**	**10.1**	**9.2**
Asp72	0.9	1.2	1.5	1.7	1.3	1.7	1.9	1.9	1.0	1.4	1.6	1.7	<0.0	<0.0	<0.0	<0.0
Lys73	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	11.2	11.5	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Arg81	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu82	3.6	3.7	3.9	3.9	3.6	3.7	3.8	3.9	3.6	3.8	3.8	3.9	4.1	4.1	4.2	4.2
Tyr84	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu86	3.7	3.7	3.6	3.5	4.2	4.1	4.1	4.1	3.5	3.6	3.6	3.6	3.6	3.6	3.6	3.5
Asp89	2.6	2.8	2.9	3.0	1.8	1.9	2.1	2.2	2.6	2.8	2.9	3.0	0.8	0.9	1.0	1.1
Lys93	9.7	10.3	10.8	11.3	9.3	9.9	10.5	11.0	11.1	11.2	11.4	11.6	>12.0	>12.0	>12.0	>12.0
Glu95	<0.0	<0.0	<0.0	0.1	<0.0	<0.0	<0.0	0.5	<0.0	<0.0	<0.0	0.5	<0.0	<0.0	<0.0	<0.0
Glu97	4.9	4.7	4.5	4.3	5.3	5.0	4.7	4.4	3.5	3.7	3.8	3.9	7.0	5.8	4.7	3.5
Arg98	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu100	3.1	3.1	3.1	3.1	3.8	3.6	3.5	3.5	5.1	4.2	3.6	3.3	1.6	1.7	1.7	1.9
His105	**7.6**	**7.5**	**7.4**	**7.3**	3.6	5.2	6.1	6.7	**7.4**	**7.4**	**7.4**	**7.4**	**8.6**	**8.5**	**8.4**	**8.3**
Lys106	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Asp107	0.2	0.4	0.5	0.6	1.0	0.9	0.8	0.7	<0.0	0.2	0.3	0.5	0.1	0.3	0.3	0.3
Asp108	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0
Arg114	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Arg117	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu119	4.6	4.5	4.3	4.0	3.5	3.6	3.7	3.8	5.0	4.8	4.5	4.3	3.7	3.7	3.8	3.8
Asp121	1.3	1.6	1.9	2.0	1.1	1.6	2.0	2.3	1.8	2.0	2.1	2.3	3.1	3.0	2.9	2.8
His128	**7.6**	**7.7**	**7.8**	**7.7**	6.1	6.7	**7.0**	**7.3**	6.6	6.8	**7.0**	**7.0**	6.5	6.7	6.9	**7.0**
Asp129	3.1	3.2	3.3	3.4	3.4	3.5	3.5	3.5	3.2	3.3	3.3	3.4	3.2	3.3	3.4	3.4
Glu131	5.9	5.3	4.7	4.1	3.9	3.6	3.5	3.3	5.4	4.8	4.2	3.7	4.8	4.3	3.9	3.5

Glu132	1.9	2.0	2.1	2.3	3.9	3.8	3.7	3.6	2.8	1.8	1.2	1.1	2.2	2.2	2.3	2.3
Lys136	**9.0**	9.7	10.3	11.1	**7.8**	**8.6**	9.4	10.4	**5.5**	**7.5**	**8.8**	10.3	**7.9**	**8.8**	9.7	10.9
Lys137	10.6	10.7	10.9	11.4	10.0	10.3	10.7	11.3	10.8	11.0	11.2	11.7	10.5	10.7	10.9	11.5
Tyr138	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Tyr140	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu141	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0
Arg144	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Arg145	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
His146	<0.0	<0.0	<0.0	2.7	<0.0	<0.0	0.6	2.9	<0.0	<0.0	<0.0	2.1	<0.0	<0.0	1.2	3.2
Tyr148	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Tyr150	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu153	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0
Lys159	>12.0	>12.0	>12.0	>12.0	9.5	9.9	10.3	10.7	10.3	10.8	11.3	>12.0	11.5	11.4	11.4	11.5
Arg160	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Tyr161	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	11.6	10.3	>12.0	>12.0	>12.0	11.5	>12.0	>12.0	>12.0	10.9
Lys162	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	11.4	11.7	>12.0	>12.0
Glu167	<0.0	<0.0	<0.0	0.2	3.1	3.2	3.3	3.4	<0.0	<0.0	<0.0	<0.0	2.1	2.5	2.8	3.0
Asp173	0.5	0.2	0.1	0.1	3.0	3.1	3.2	3.2	<0.0	<0.0	<0.0	<0.0	3.2	3.2	3.2	3.2
Lys174	>12.0	>12.0	>12.0	>12.0	11.1	11.3	11.4	11.6	10.6	11.1	11.6	>12.0	11.3	11.3	11.4	11.5
Lys181	9.8	11.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Asp183	<0.0	<0.0	<0.0	<0.0	<0.0	0.3	0.8	1.1	0.3	<0.0	<0.0	<0.0	0.3	0.4	0.6	0.8
Glu184	2.2	2.2	2.1	2.0	4.2	3.9	3.7	3.5	3.5	3.1	2.8	2.6	4.3	3.9	3.6	3.3
Arg186	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Asp187	<0.0	<0.0	<0.0	<0.0	1.1	0.3	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0
Glu188	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0
Lys190	**5.5**	**6.5**	**7.6**	**8.8**	**5.8**	**6.7**	**7.6**	**8.7**	**4.7**	**6.0**	**7.3**	**8.9**	**8.1**	**8.5**	**8.8**	10.0
Lys195	**8.4**	10.6	>12.0	>12.0	11.1	11.3	11.8	>12.0	9.9	11.5	>12.0	>12.0	**5.8**	**7.1**	**8.6**	9.5
Arg197	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Lys199	**<0.0**	**1.6**	**6.1**	**9.0**	**<0.0**	**4.0**	**6.9**	9.3	**<0.0**	**1.8**	**6.1**	9.1	**<0.0**	**<0.0**	**5.9**	9.7
Lys205	11.5	11.5	11.6	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu208	2.6	2.6	2.5	2.5	2.6	2.6	2.6	2.7	2.8	2.7	2.7	2.7	1.5	1.6	1.6	1.7
Arg209	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0

Lys212	10.7	10.9	11.2	11.4	10.6	10.8	11.1	11.3	10.1	10.5	10.9	11.3	10.7	10.9	11.3	11.7
Arg218	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Arg222	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Lys225	>12.0	>12.0	>12.0	>12.0	11.4	11.5	11.7	11.8	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu227	4.1	4.2	4.2	4.1	3.6	3.7	3.9	4.1	3.9	4.1	4.2	4.2	3.8	4.0	4.1	4.2
Glu230	2.9	2.9	2.9	3.1	6.8	5.8	4.9	4.1	3.9	3.6	3.4	3.4	4.2	3.8	3.5	3.4
Lys233	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Asp237	2.0	1.5	1.2	1.4	0.8	0.7	1.0	1.3	0.0	0.1	0.4	0.9	<0.0	0.0	0.2	0.6
Lys240	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
His242	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0
Glu244	**>12.0**	**>12.0**	**8.4**	5.5	**>12.0**	**>12.0**	**8.6**	5.5	**>12.0**	**>12.0**	**9.6**	6.2	**>12.0**	**>12.0**	**9.7**	5.6
His247	5.8	6.1	6.5	7.0	6.7	6.9	6.9	7.2	3.2	4.8	5.6	6.3	6.7	6.9	7.0	7.4
Asp249	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0
Glu252	1.5	1.6	1.7	1.9	2.3	2.0	1.8	2.0	1.9	1.9	2.0	2.3	<0.0	<0.0	<0.0	<0.0
Asp255	<0.0	<0.0	<0.0	0.5	<0.0	<0.0	0.1	1.0	<0.0	<0.0	<0.0	0.1	<0.0	<0.0	<0.0	<0.0
Asp256	7.3	5.9	4.4	3.2	8.2	6.3	4.6	2.9	8.0	6.1	3.6	1.8	8.3	6.0	3.1	1.4
Arg257	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Asp259	2.9	3.0	3.0	3.1	4.0	3.7	3.7	3.6	4.3	3.8	3.8	3.6	3.5	3.2	3.1	3.1
Lys262	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Tyr263	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu266	5.3	4.9	4.5	4.2	4.8	4.4	4.0	3.8	4.7	4.4	4.2	4.0	5.7	5.1	4.7	4.3
Asp269	3.8	3.9	3.9	3.9	3.1	3.1	3.1	3.2	3.5	3.6	3.7	3.7	3.5	3.6	3.7	3.7
Lys274	11.6	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Lys276	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	11.7	11.6	>12.0	>12.0	>12.0	>12.0	11.2	11.2	11.2	11.2
Glu277	1.8	2.1	2.3	2.6	5.8	5.1	4.4	3.9	2.4	2.4	2.4	2.4	2.7	2.9	3.1	3.3
Glu280	4.5	4.3	4.1	3.9	4.5	4.3	4.1	4.0	4.6	4.4	4.2	4.1	5.1	4.7	4.4	4.1
Lys281	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	11.0	11.5	11.7	>12.0
Glu285	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	0.4	0.9	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	0.4	0.9
Lys286	11.2	11.5	11.7	>12.0	9.5	10.0	10.5	11.1	10.1	10.6	11.1	11.6	9.9	10.6	11.0	11.5
His288	**>12.0**	**8.6**	**7.9**	**7.3**	**7.8**	**7.4**	**7.0**	6.9	**9.7**	**7.9**	**7.3**	6.9	**>12.0**	**9.4**	**7.9**	**7.3**
Glu292	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0
Glu294	2.1	1.9	1.7	1.9	3.6	3.4	3.2	3.1	3.0	2.6	2.3	2.3	3.9	3.6	3.0	2.8

Asp296	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	0.5	1.1	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	0.3
Glu297	2.6	2.8	3.0	3.1	4.8	4.5	4.3	4.1	2.8	3.0	3.1	3.1	3.1	3.2	3.3	3.3
Asp301	3.7	3.8	3.8	3.8	3.8	3.8	3.8	3.8	3.7	3.7	3.7	3.7	3.8	3.8	3.8	3.8
Asp308	4.8	4.4	4.1	3.8	3.4	3.4	3.4	3.4	4.6	4.3	4.1	3.7	3.7	3.7	3.6	3.5
Glu311	4.1	4.2	4.2	4.2	4.2	4.1	4.1	4.0	4.0	4.1	4.1	4.1	4.6	4.4	4.2	4.1
Lys313	11.0	11.0	11.0	11.0	11.1	11.1	11.0	11.0	11.0	11.0	11.0	11.0	11.2	11.1	11.1	11.1
Asp314	2.3	2.5	2.7	2.8	2.3	2.5	2.7	2.9	3.2	3.1	3.1	3.1	2.3	2.6	2.8	2.9
Lys317	>12.0	11.7	11.6	11.5	11.3	11.3	11.4	11.4	11.8	11.7	11.7	11.7	11.5	11.6	11.7	11.7
Tyr319	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu321	5.0	4.7	4.5	4.3	5.2	5.0	4.7	4.5	5.6	5.2	4.9	4.6	5.1	4.8	4.5	4.2
Lys323	11.7	11.6	11.6	11.6	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	11.8	11.7	>12.0	>12.0	>12.0	>12.0
Asp324	1.0	1.1	1.3	1.4	0.7	0.9	1.1	1.4	0.5	0.9	1.2	1.6	3.1	2.4	1.8	1.5
Tyr332	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu333	<0.0	0.6	1.1	1.7	0.8	1.2	1.6	2.0	<0.0	0.6	1.2	1.9	<0.0	0.6	1.2	1.8
Tyr334	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	11.1	>12.0	>12.0	>12.0	11.3	>12.0	>12.0	>12.0	11.7
Arg336	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Arg337	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
His338	**7.8**	**7.6**	**7.5**	**7.4**	**7.5**	**7.4**	**7.3**	**7.3**	**7.3**	**7.3**	**7.2**	**7.1**	**7.1**	**7.1**	**7.0**	6.9
Asp340	<0.0	0.3	0.6	1.0	0.9	1.0	1.1	1.3	1.2	1.3	1.4	1.4	1.0	1.1	1.1	1.3
Tyr341	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Arg348	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Lys351	10.7	10.8	10.9	11.1	8.4	9.0	9.5	10.2	10.6	10.6	10.8	10.9	11.2	11.3	11.5	11.7
Tyr353	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu354	1.0	0.9	1.1	1.4	3.5	3.1	2.7	2.5	3.1	2.4	2.1	2.0	2.6	2.8	2.6	2.5
Glu358	3.2	3.4	3.5	3.6	1.9	2.4	2.9	3.1	2.8	3.2	3.4	3.5	<0.0	0.2	1.2	2.1
Lys359	10.7	10.8	10.8	10.9	11.1	11.1	11.1	11.2	10.9	11.0	11.2	11.3	11.3	11.4	11.4	11.5
Asp365	2.9	3.0	3.2	3.2	2.9	3.0	3.0	3.0	3.0	3.0	3.1	3.2	3.2	3.1	3.0	3.0
His367	5.3	5.9	6.4	6.7	**8.7**	**8.3**	**7.9**	**7.6**	**8.1**	**8.0**	**7.9**	**7.9**	**7.5**	**7.4**	**7.4**	**7.3**
Glu368	3.7	3.8	3.9	4.0	4.0	3.9	3.9	3.9	3.8	4.0	4.1	4.2	3.5	3.7	3.8	3.9
Tyr370	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Lys372	11.1	11.1	11.2	11.3	11.7	11.8	>12.0	>12.0	11.1	11.2	11.2	11.3	11.1	11.1	11.2	11.3
Asp375	3.1	3.1	3.1	3.1	2.5	2.6	2.7	2.8	3.6	3.4	3.3	3.2	3.2	3.1	3.1	3.0

Glu376	4.8	4.5	4.3	4.1	6.5	5.8	5.1	4.6	5.9	5.2	4.6	4.0	5.5	5.1	4.7	4.3
Lys378	11.0	11.1	11.2	11.4	11.2	11.3	11.6	>12.0	10.7	10.9	11.0	11.2	10.8	10.9	11.0	11.1
Glu382	4.6	4.4	4.1	3.9	3.9	3.7	3.5	3.4	4.4	4.2	4.0	3.8	4.6	4.4	4.2	4.0
Glu383	<0.0	<0.0	0.5	0.9	<0.0	<0.0	<0.0	<0.0	<0.0	0.2	0.7	1.1	<0.0	<0.0	0.3	0.9
Lys389	10.5	10.6	10.8	11.0	11.7	11.8	>12.0	>12.0	10.4	10.7	11.0	11.3	10.5	10.9	11.1	11.4
Glu393	3.0	3.0	3.0	3.0	3.1	2.9	2.7	2.6	3.6	3.4	3.4	3.3	3.6	3.5	3.3	3.2
Glu396	2.9	2.7	2.3	2.2	4.7	4.4	4.0	3.7	3.7	3.1	2.4	1.9	5.6	4.9	4.3	3.7
Glu400	<0.0	<0.0	<0.0	<0.0	1.4	1.3	1.2	1.1	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	0.2
Tyr401	>12.0	>12.0	>12.0	10.2	>12.0	>12.0	>12.0	8.6	>12.0	>12.0	>12.0	8.4	>12.0	>12.0	>12.0	9.1
Lys402	>12.0	>12.0	>12.0	>12.0	10.7	10.8	10.9	11.1	>12.0	>12.0	>12.0	>12.0	10.7	10.9	11.0	11.2
Arg410	9.7	11.2	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	9.0	10.4	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Tyr411	>12.0	>12.0	>12.0	**8.6**	>12.0	>12.0	**8.9**	**8.4**	>12.0	>12.0	11.6	**8.2**	>12.0	>12.0	9.8	**8.8**
Lys413	11.0	10.7	10.5	10.8	>12.0	>12.0	>12.0	>12.0	8.8	9.3	9.9	10.6	9.2	9.8	10.2	10.8
Lys414	**6.8**	**7.9**	9.9	11.7	**7.0**	**8.6**	>12.0	>12.0	**1.9**	**5.4**	**7.3**	10.1	9.1	9.5	11.7	>12.0
Glu425	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0
Arg428	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Lys432	**8.1**	**8.7**	9.4	10.8	9.3	9.5	9.8	10.8	**7.5**	**8.1**	**9.0**	10.8	**6.7**	**7.9**	9.2	11.1
Lys436	11.2	11.4	11.5	>12.0	8.1	9.0	9.9	>12.0	11.6	11.8	>12.0	>12.0	9.7	10.5	11.0	>12.0
Lys439	11.4	11.5	11.5	11.6	11.1	11.1	11.2	11.2	9.5	10.1	10.6	11.1	11.0	11.1	11.1	11.1
His440	<0.0	1.0	2.8	4.3	0.9	2.1	3.4	4.6	<0.0	0.6	2.7	4.4	0.4	1.8	3.1	4.5
Glu442	3.1	3.1	3.1	3.1	2.9	3.0	3.0	3.1	2.5	2.6	2.5	2.6	2.9	2.9	2.9	3.0
Lys444	9.4	9.9	10.2	10.6	9.4	9.8	10.2	10.6	9.6	10.0	10.3	10.7	9.2	9.6	10.1	10.4
Arg445	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu450	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0
Asp451	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0
Tyr452	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	10.7
His464	<0.0	2.3	4.7	5.8	<0.0	<0.0	2.0	4.8	<0.0	<0.0	0.8	4.4	<0.0	<0.0	0.4	4.4
Glu465	3.7	2.7	1.9	1.9	1.8	1.8	1.3	1.3	1.8	1.7	1.4	1.2	2.3	2.0	1.3	0.7
Lys466	>12.0	>12.0	>12.0	>12.0	11.1	11.4	11.7	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Asp471	2.2	2.3	2.4	2.5	2.3	2.5	2.5	2.3	2.3	2.5	2.6	2.4	2.2	2.5	2.6	2.5
Arg472	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Lys475	10.0	10.2	10.4	10.7	>12.0	>12.0	>12.0	>12.0	10.4	10.5	10.7	10.9	11.5	11.5	11.5	11.6

Glu479	3.6	3.5	3.4	3.3	1.8	2.0	2.1	2.2	3.9	3.7	3.5	3.3	2.5	2.5	2.5	2.5
Arg484	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Arg485	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu492	2.2	2.3	2.4	2.5	<0.0	<0.0	<0.0	<0.0	3.7	3.3	3.3	3.4	3.1	3.1	3.2	3.3
Asp494	<0.0	<0.0	0.6	1.1	0.0	0.2	0.0	0.2	0.4	0.7	0.9	1.2	0.2	0.7	1.1	1.3
Glu495	4.2	4.1	4.0	3.9	2.6	2.0	1.8	1.7	5.2	4.6	4.2	3.9	4.7	4.5	4.3	4.1
Tyr497	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	11.5	>12.0	>12.0	>12.0	11.3
Lys500	11.1	11.0	10.9	10.9	>12.0	>12.0	>12.0	>12.0	10.7	10.7	10.8	10.9	>12.0	>12.0	>12.0	>12.0
Glu501	3.9	3.9	3.9	3.9	3.2	3.3	3.4	3.4	4.3	3.9	3.8	3.8	3.7	3.7	3.8	3.8
Glu505	3.5	3.5	3.6	3.6	2.6	2.9	3.2	3.3	3.1	3.2	3.3	3.4	3.6	3.7	3.7	3.8
His510	7.3	7.4	7.5	7.5	<0.0	1.3	4.7	5.7	6.8	6.9	6.9	7.0	7.9	7.5	7.3	7.1
Asp512	1.9	1.9	2.0	2.0	5.1	4.5	2.6	2.5	2.5	2.3	2.1	2.0	1.4	1.4	1.5	1.6
Glu518	0.9	0.2	<0.0	<0.0	2.5	2.4	2.2	2.1	<0.0	<0.0	<0.0	<0.0	2.8	1.8	1.5	1.4
Lys519	>12.0	>12.0	>12.0	>12.0	11.0	10.8	10.8	10.9	**8.1**	**8.4**	**8.8**	9.4	**0.7**	**4.6**	**6.6**	**8.5**
Glu520	<0.0	<0.0	<0.0	<0.0	0.3	0.8	1.2	1.5	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	0.0	0.5
Arg521	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Lys524	10.1	10.3	10.6	10.9	8.3	9.0	9.7	10.4	10.5	10.7	10.9	11.1	9.4	9.9	10.3	10.7
Lys525	**7.9**	9.3	11.1	>12.0	**7.2**	**8.1**	9.6	11.7	**6.1**	**8.0**	10.8	>12.0	**7.0**	**8.1**	9.4	>12.0
Glu531	0.7	0.8	1.1	1.4	<0.0	<0.0	0.2	0.6	<0.0	<0.0	<0.0	0.2	<0.0	<0.0	<0.0	0.6
Lys534	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
His535	7.5	7.2	7.2	7.2	4.7	5.4	5.8	6.1	3.1	4.6	5.5	6.1	4.3	5.2	5.9	6.3
Lys536	8.7	10.2	11.3	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	11.1	11.2	11.2	11.2
Lys538	10.9	10.9	10.9	10.9	8.4	9.1	9.8	10.7	10.5	10.8	10.9	11.2	10.7	10.7	10.6	10.7
Lys541	10.2	10.3	10.3	10.4	7.8	8.1	8.7	9.4	10.5	10.5	10.5	10.5	7.6	8.2	8.8	9.4
Glu542	2.5	2.8	3.0	3.1	1.4	1.6	1.7	1.9	2.2	2.4	2.7	2.9	2.8	2.7	2.7	2.7
Lys545	9.2	9.5	9.9	10.6	11.5	11.5	11.6	11.7	7.7	8.6	9.5	10.3	9.7	10.3	10.7	11.1
Asp549	2.9	2.2	1.9	1.8	2.6	2.3	2.1	2.0	2.9	2.1	1.5	1.2	1.5	1.6	1.8	2.0
Asp550	5.9	5.0	4.3	3.5	5.4	4.9	4.5	4.1	7.0	5.5	4.4	3.5	>12.0	9.2	6.8	5.1
Glu556	3.0	2.7	2.4	2.3	2.8	2.8	2.8	2.9	2.5	2.3	2.0	1.8	3.1	3.1	3.1	3.1
Lys557	11.8	>12.0	>12.0	>12.0	11.3	11.3	11.3	11.4	11.3	11.6	11.8	>12.0	>12.0	>12.0	>12.0	>12.0
Lys560	>12.0	>12.0	>12.0	>12.0	10.5	10.6	10.7	10.8	>12.0	>12.0	>12.0	>12.0	11.6	11.5	11.3	11.2
Asp562	3.7	3.6	3.6	3.5	4.0	3.9	3.9	3.8	4.3	4.1	3.8	3.6	4.0	4.0	4.0	3.9

Asp563	1.9	2.1	2.3	2.4	2.3	2.6	2.9	3.0	0.8	1.3	1.7	2.0	0.1	1.1	1.8	2.4
Lys564	11.4	11.4	11.4	11.4	11.5	11.5	11.5	11.6	11.1	11.2	11.2	11.3	11.0	11.1	11.1	11.2
Glu565	3.6	3.8	3.8	3.9	4.2	4.3	4.2	4.1	3.4	3.6	3.7	3.9	3.8	3.9	4.0	4.0
Glu570	3.7	3.8	3.8	3.8	3.2	3.4	3.5	3.6	3.7	3.8	3.8	3.8	4.1	4.1	4.2	4.3
Glu571	4.5	4.3	4.1	4.0	3.5	3.4	3.3	3.2	5.0	4.6	4.4	4.2	7.0	6.0	5.1	4.3
Lys573	10.8	10.9	10.9	10.9	8.0	9.0	9.8	10.4	10.9	10.9	11.0	11.0	10.5	10.6	10.7	10.7
Lys574	10.6	10.7	10.7	10.8	10.4	10.7	10.9	11.1	10.4	10.6	10.7	10.9	10.8	11.2	11.2	11.2
Residue	**1AO6** (mol. B, 2.50 Å)				**3JRY** (mol. B, 2.30 Å)				**4G03** (mol. B, 2.22 Å)				**4EMX** (mol. B, 2.30 Å)			
	ε_{int}=4	**ε_{int}=6**	**ε_{int}=10**	**ε_{int}=20**	**ε_{int}=4**	**ε_{int}=6**	**ε_{int}=10**	**ε_{int}=20**	**ε_{int}=4**	**ε_{int}=6**	**ε_{int}=10**	**ε_{int}=20**	**ε_{int}=4**	**ε_{int}=6**	**ε_{int}=10**	**ε_{int}=20**
Lys4	--	--	--	--	--	--	--	--	--	--	--	--	>12.0	>12.0	>12.0	>12.0
Glu6	<0.0	<0.0	<0.0	0.5	<0.0	0.5	0.4	1.2	<0.0	<0.0	0.1	1.0	<0.0	<0.0	<0.0	<0.0
His9	**9.8**	**9.8**	**9.5**	**9.1**	**8.7**	**9.3**	**9.3**	**9.1**	3.4	5.2	**7.2**	**7.7**	4.1	5.3	**7.1**	**7.7**
Arg10	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Lys12	11.6	11.8	>12.0	>12.0	10.9	11.1	11.3	11.4	>12.0	>12.0	>12.0	>12.0	11.2	11.6	>12.0	>12.0
Asp13	7.6	6.2	5.2	4.3	6.5	5.2	4.4	3.8	8.5	7.0	5.0	4.2	9.3	7.4	5.0	4.1
Glu16	2.3	2.3	2.3	2.3	2.5	2.4	2.3	2.2	1.4	1.7	1.9	2.0	1.7	1.9	2.0	2.1
Glu17	3.2	3.3	3.3	3.3	1.7	1.9	2.1	2.3	1.5	1.5	1.6	1.8	0.9	1.1	1.4	1.7
Lys20	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	11.4	11.6	11.8	>12.0	10.4	10.7	11.0	11.2
Tyr30	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Cys34	>12.0	>12.0	>12.0	11.1	>12.0	>12.0	10.7	9.6	>12.0	>12.0	>12.0	11.0	>12.0	>12.0	>12.0	>12.0
Glu37	4.0	3.9	3.7	3.4	3.4	3.5	3.5	3.3	3.8	3.7	3.5	3.2	4.2	4.1	3.8	3.5
Asp38	3.7	3.6	3.3	2.5	4.0	3.7	3.4	2.4	3.5	3.4	3.2	2.4	3.8	3.4	2.9	2.1
His39	<0.0	<0.0	<0.0	5.1	<0.0	<0.0	<0.0	4.7	<0.0	<0.0	<0.0	4.8	<0.0	<0.0	0.6	5.4
Lys41	11.5	11.5	11.5	11.6	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	11.6	11.6	11.6	11.8
Glu45	2.1	2.3	2.4	2.4	2.1	2.3	2.4	2.3	3.6	3.3	3.0	2.7	3.3	3.3	3.3	3.1
Glu48	4.2	4.1	4.0	3.9	4.1	4.0	3.9	3.8	3.6	3.7	3.8	3.8	3.9	3.9	3.9	3.8
Lys51	10.9	11.0	11.2	11.4	11.1	11.3	11.4	11.6	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	11.7	11.7
Asp56	4.6	4.3	4.0	3.8	5.2	4.8	4.4	4.1	4.7	4.4	4.1	3.8	4.5	4.2	3.9	3.7
Glu57	3.1	3.2	3.4	3.5	5.4	5.1	4.3	3.6	3.4	3.2	3.2	3.2	3.1	2.9	2.9	2.9
Glu60	3.5	3.7	3.8	3.9	5.4	5.1	4.8	4.5	4.4	4.4	4.3	4.3	4.4	4.4	4.3	4.3
Asp63	3.7	3.7	3.6	3.5	4.4	4.3	3.9	3.5	3.9	3.8	3.7	3.6	2.8	2.9	2.9	2.8
Lys64	11.3	11.4	11.6	11.7	10.8	11.0	11.3	11.5	11.2	11.4	11.5	11.7	>12.0	>12.0	>12.0	>12.0

His67	**>12.0**	**10.5**	**9.6**	**8.6**	**7.7**	**7.7**	**7.7**	**7.6**	**9.7**	**9.0**	**8.7**	**8.3**	**9.4**	**9.2**	**9.0**	**8.8**
Asp72	1.7	1.8	1.9	1.9	1.1	1.5	1.7	1.9	0.7	1.1	1.4	1.6	1.9	2.0	2.0	1.9
Lys73	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	11.3	11.5	11.7	>12.0	>12.0	>12.0	>12.0	>12.0
Arg81	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu82	3.8	3.9	4.0	4.0	3.6	3.7	3.8	3.9	3.4	3.6	3.8	3.9	4.0	4.1	4.1	4.1
Tyr84	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu86	4.0	4.0	3.8	3.7	4.2	4.1	4.1	4.0	3.2	3.4	3.5	3.5	4.9	4.7	4.6	4.4
Asp89	2.3	2.5	2.8	2.9	1.6	1.8	2.0	2.2	1.7	2.1	2.4	2.6	1.6	1.6	1.7	1.8
Lys93	10.4	10.9	11.2	11.5	9.5	10.0	10.5	11.0	11.0	11.2	11.4	11.6	>12.0	>12.0	>12.0	>12.0
Glu95	<0.0	<0.0	<0.0	0.8	<0.0	<0.0	<0.0	0.3	<0.0	<0.0	<0.0	0.2	<0.0	<0.0	<0.0	<0.0
Glu97	3.1	3.3	3.5	3.6	5.2	4.9	4.6	4.4	5.4	5.1	4.8	4.5	0.0	0.0	<0.0	0.0
Arg98	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu100	1.9	2.0	2.1	2.2	3.7	3.6	3.5	3.4	4.7	4.1	3.8	3.6	1.2	0.1	<0.0	<0.0
His105	**7.4**	**7.4**	**7.5**	**7.4**	4.3	5.4	6.2	6.7	**7.6**	**7.5**	**7.5**	**7.4**	**10.7**	**10.1**	**9.7**	**9.3**
Lys106	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Asp107	<0.0	0.2	0.2	0.3	<0.0	<0.0	<0.0	0.2	<0.0	<0.0	<0.0	0.1	<0.0	<0.0	<0.0	<0.0
Asp108	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0
Arg114	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Arg117	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu119	6.2	5.7	5.2	4.7	3.5	3.6	3.7	3.8	4.1	4.0	4.0	3.9	3.6	3.7	3.7	3.8
Asp121	1.9	2.0	2.1	2.2	0.9	1.5	1.9	2.3	2.0	2.0	2.1	2.2	3.0	2.9	2.8	2.7
His128	**7.6**	**7.7**	**7.7**	**7.7**	6.2	6.6	**7.0**	**7.3**	4.8	5.8	6.3	6.6	6.1	6.5	6.8	**7.0**
Asp129	3.2	3.3	3.3	3.4	3.3	3.4	3.5	3.5	3.2	3.3	3.3	3.4	3.4	3.4	3.4	3.4
Glu131	4.3	4.0	3.7	3.4	4.5	3.9	3.6	3.4	5.2	4.3	3.7	3.2	5.5	4.8	4.4	4.0
Glu132	0.6	0.8	1.1	1.3	3.7	3.8	3.8	3.6	1.1	1.3	1.6	1.9	3.2	3.1	3.1	3.0
Lys136	9.4	10.0	10.6	11.3	**7.8**	**8.6**	9.4	10.3	**8.1**	**9.0**	9.9	11.0	**6.4**	**7.7**	**8.9**	10.1
Lys137	10.0	10.2	10.5	11.1	9.9	10.2	10.7	11.2	10.7	10.9	11.2	11.7	10.6	10.7	10.8	11.4
Tyr138	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Tyr140	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu141	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0
Arg144	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Arg145	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0

His146	<0.0	<0.0	<0.0	1.9	<0.0	<0.0	0.8	3.0	<0.0	<0.0	<0.0	2.3	<0.0	<0.0	1.3	3.3
Tyr148	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Tyr150	>12.0	>12.0	>12.0	11.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu153	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0
Lys159	>12.0	>12.0	>12.0	>12.0	9.2	9.7	10.1	10.6	10.5	10.9	11.4	>12.0	7.6	8.5	9.3	10.0
Arg160	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Tyr161	>12.0	>12.0	>12.0	11.6	>12.0	>12.0	11.7	10.4	>12.0	>12.0	>12.0	11.6	>12.0	>12.0	>12.0	10.9
Lys162	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu167	<0.0	<0.0	<0.0	0.3	3.2	3.3	3.4	3.4	<0.0	<0.0	<0.0	0.2	1.7	2.2	2.6	2.9
Asp173	<0.0	<0.0	<0.0	<0.0	3.4	3.3	3.3	3.3	<0.0	<0.0	<0.0	<0.0	2.9	3.1	3.2	3.2
Lys174	10.7	11.2	11.6	>12.0	11.2	11.3	11.5	11.6	10.8	11.3	11.8	>12.0	11.2	11.3	11.4	11.5
Lys181	>12.0	>12.0	>12.0	>12.0	11.8	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	11.2	11.5	11.7	>12.0
Asp183	<0.0	<0.0	<0.0	<0.0	0.1	0.6	1.0	1.3	<0.0	<0.0	<0.0	<0.0	0.7	0.8	0.8	0.9
Glu184	3.5	2.8	2.4	2.1	4.2	3.9	3.7	3.5	2.6	2.4	2.3	2.1	5.0	4.5	4.0	3.7
Arg186	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Asp187	<0.0	<0.0	<0.0	<0.0	1.1	0.4	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0
Glu188	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0
Lys190	**2.7**	**4.8**	**6.3**	**8.0**	**6.0**	**6.9**	**7.8**	**8.8**	**6.9**	**7.6**	**8.5**	9.8	**8.6**	**8.7**	9.1	10.0
Lys195	>12.0	>12.0	>12.0	>12.0	11.4	11.6	>12.0	>12.0	8.1	9.5	11.3	>12.0	8.6	11.2	>12.0	>12.0
Arg197	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Lys199	**<0.0**	**2.3**	**6.4**	**8.9**	**0.5**	**4.2**	**7.1**	9.4	**<0.0**	**3.0**	**6.4**	9.5	**<0.0**	**0.5**	**6.2**	9.7
Lys205	10.7	11.2	11.7	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu208	3.1	3.1	2.9	2.9	2.5	2.5	2.6	2.7	1.9	2.0	2.1	2.3	<0.0	<0.0	<0.0	0.5
Arg209	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Lys212	9.8	10.3	10.8	11.3	10.6	10.8	11.1	11.3	11.6	11.6	11.6	11.7	>12.0	>12.0	>12.0	>12.0
Arg218	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Arg222	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Lys225	11.6	11.6	11.6	11.7	11.4	11.5	11.6	11.8	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu227	3.5	3.6	3.9	4.1	3.5	3.7	3.9	4.0	3.7	3.9	4.1	4.2	3.6	3.8	3.9	4.0
Glu230	6.0	5.3	4.5	3.8	6.9	5.9	4.9	4.1	5.0	4.5	4.0	3.7	5.6	5.1	4.5	4.0
Lys233	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Asp237	0.8	0.6	0.7	1.0	0.5	0.6	0.9	1.2	<0.0	<0.0	0.3	0.9	<0.0	<0.0	0.1	0.5

Lys240	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
His242	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0
Glu244	**>12.0**	**>12.0**	**8.6**	5.8	**>12.0**	**>12.0**	**8.5**	5.4	**>12.0**	**>12.0**	**8.5**	5.3	**>12.0**	**>12.0**	**10.5**	6.1
His247	7.5	7.5	7.5	7.7	5.6	5.9	6.2	6.6	4.2	5.1	5.8	6.4	>12.0	>12.0	>12.0	10.2
Asp249	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0
Glu252	1.8	1.9	2.2	2.5	1.9	1.7	1.6	1.9	1.5	1.5	1.8	2.0	<0.0	<0.0	<0.0	<0.0
Asp255	<0.0	<0.0	<0.0	0.7	0.6	0.8	1.2	1.8	<0.0	<0.0	<0.0	0.5	<0.0	<0.0	<0.0	0.6
Asp256	7.6	5.8	4.0	2.2	7.3	5.6	4.2	2.7	8.0	6.4	4.6	2.8	8.3	6.3	4.0	2.1
Arg257	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Asp259	3.7	3.5	3.5	3.4	4.0	3.7	3.7	3.5	4.1	3.7	3.7	3.6	3.1	2.9	2.9	3.0
Lys262	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Tyr263	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu266	4.0	3.9	3.9	3.8	4.8	4.4	4.1	3.8	2.9	3.1	3.2	3.3	5.2	4.7	4.3	3.9
Asp269	3.6	3.7	3.7	3.7	3.0	3.1	3.1	3.2	3.8	3.8	3.8	3.8	3.8	3.8	3.8	3.7
Lys274	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Lys276	11.5	11.5	11.7	11.8	>12.0	11.8	11.6	11.6	11.6	11.7	>12.0	>12.0	10.7	10.8	11.0	11.1
Glu277	1.2	1.5	1.8	2.2	6.0	5.2	4.5	3.9	0.5	0.9	1.4	2.0	2.8	3.0	3.1	3.3
Glu280	4.2	4.1	4.0	3.9	4.3	4.2	4.1	4.0	4.5	4.3	4.1	3.8	4.3	4.2	4.1	4.0
Lys281	11.7	11.7	11.8	>12.0	>12.0	>12.0	>12.0	>12.0	10.3	11.2	11.8	>12.0	>12.0	>12.0	>12.0	>12.0
Glu285	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	0.3	1.0	<0.0	<0.0	<0.0	<0.0	1.1	1.0	1.0	1.1
Lys286	10.3	10.7	11.1	11.5	9.8	10.3	10.8	11.3	10.9	11.2	11.6	>12.0	9.2	10.1	10.7	11.3
His288	6.7	6.6	6.3	6.4	**8.0**	**7.5**	**7.1**	**7.0**	**>12.0**	**10.9**	**8.4**	**7.6**	**8.8**	**7.5**	**7.1**	**7.0**
Glu292	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	0.0
Glu294	2.8	2.3	1.8	1.8	3.6	3.3	3.2	3.1	4.8	4.2	3.5	2.8	4.2	3.7	2.9	2.7
Asp296	<0.0	<0.0	<0.0	0.6	<0.0	<0.0	0.5	1.2	<0.0	<0.0	<0.0	0.1	0.3	0.5	0.7	1.0
Glu297	2.5	2.7	2.9	3.0	4.8	4.5	4.3	4.1	2.6	2.8	2.9	3.0	3.2	3.3	3.4	3.3
Asp301	3.6	3.6	3.6	3.7	3.8	3.8	3.8	3.8	3.7	3.7	3.7	3.7	3.7	3.8	3.8	3.8
Asp308	5.1	4.7	4.2	3.8	3.5	3.5	3.4	3.4	4.1	3.9	3.7	3.5	3.8	3.7	3.7	3.6
Glu311	4.1	4.1	4.1	4.1	4.1	4.1	4.1	4.0	4.9	4.6	4.4	4.2	4.5	4.3	4.2	4.0
Lys313	11.0	11.0	11.0	11.1	11.1	11.1	11.0	11.0	11.3	11.2	11.2	11.2	11.3	11.2	11.2	11.2
Asp314	2.2	2.4	2.6	2.7	2.3	2.5	2.7	2.9	2.3	2.4	2.6	2.7	6.6	5.4	4.2	3.1
Lys317	11.4	11.4	11.4	11.4	11.4	11.4	11.4	11.4	11.4	11.4	11.5	11.5	>12.0	>12.0	>12.0	>12.0

Tyr319	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu321	4.5	4.3	4.2	4.1	5.2	5.0	4.7	4.5	4.9	4.7	4.5	4.4	4.8	4.6	4.3	4.1
Lys323	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Asp324	1.5	1.6	1.7	2.0	0.6	0.8	1.1	1.4	0.5	0.7	1.0	1.3	<0.0	<0.0	<0.0	<0.0
Tyr332	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu333	2.1	2.2	2.2	2.4	0.5	1.0	1.5	2.0	2.0	2.1	2.3	2.5	<0.0	<0.0	0.8	1.5
Tyr334	>12.0	>12.0	>12.0	11.7	>12.0	>12.0	>12.0	11.4	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	11.4
Arg336	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Arg337	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
His338	**8.2**	**7.9**	**7.7**	**7.5**	**7.6**	**7.4**	**7.4**	**7.3**	6.8	6.9	6.9	6.9	6.8	6.9	6.9	**7.0**
Asp340	0.1	0.4	0.7	1.0	1.1	1.1	1.2	1.3	1.3	1.2	1.2	1.3	0.8	0.9	1.1	1.3
Tyr341	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Arg348	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Lys351	11.1	11.1	11.2	11.3	8.7	9.2	9.7	10.2	10.2	10.4	10.6	10.8	10.6	10.8	11.2	11.6
Tyr353	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu354	0.5	0.8	1.2	1.7	3.7	3.3	2.9	2.7	2.9	2.2	1.9	1.8	1.8	1.5	1.1	1.0
Glu358	3.9	4.0	4.0	3.9	1.8	2.4	2.8	3.1	3.2	3.5	3.6	3.6	<0.0	<0.0	0.1	1.1
Lys359	10.8	10.8	10.9	10.9	11.0	11.1	11.1	11.1	10.7	10.8	10.9	11.0	11.6	11.6	11.7	11.7
Asp365	2.9	3.1	3.2	3.3	3.1	3.1	3.1	3.1	3.1	3.3	3.4	3.5	2.1	2.2	2.3	2.3
His367	6.2	6.5	6.8	6.9	**8.5**	**8.2**	**7.9**	**7.7**	6.5	6.9	**7.1**	**7.3**	**7.9**	**7.8**	**7.6**	**7.5**
Glu368	3.8	3.9	4.0	4.1	4.0	4.0	3.9	3.9	4.7	4.5	4.4	4.4	3.6	3.7	3.8	3.9
Tyr370	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Lys372	10.9	11.0	11.1	11.2	11.8	>12.0	>12.0	>12.0	10.8	10.9	11.0	11.1	11.3	11.3	11.4	11.5
Asp375	3.0	3.1	3.1	3.1	2.7	2.7	2.7	2.8	3.4	3.3	3.2	3.1	2.8	2.8	2.9	2.9
Glu376	4.8	4.5	4.2	3.9	6.6	5.8	5.1	4.5	6.0	5.4	4.8	4.4	5.3	4.9	4.5	4.2
Lys378	11.2	11.3	11.4	11.5	11.1	11.2	11.5	>12.0	11.1	11.1	11.2	11.4	10.8	10.9	11.0	11.1
Glu382	4.6	4.4	4.1	3.9	4.0	3.7	3.5	3.4	4.9	4.5	4.2	3.9	4.8	4.5	4.3	4.1
Glu383	<0.0	<0.0	0.5	1.0	<0.0	<0.0	<0.0	<0.0	0.5	0.8	1.0	1.3	<0.0	<0.0	0.3	0.9
Lys389	10.9	11.0	11.0	11.2	11.7	11.8	>12.0	>12.0	11.1	11.2	11.3	11.5	11.4	11.5	11.6	11.7
Glu393	3.7	3.5	3.2	3.0	2.9	2.7	2.6	2.6	3.4	3.4	3.4	3.3	2.9	3.0	3.0	3.0
Glu396	3.6	3.2	2.6	2.2	4.9	4.5	4.1	3.7	3.6	3.0	2.3	1.9	4.9	4.4	4.0	3.6
Glu400	<0.0	<0.0	<0.0	<0.0	1.2	1.1	1.0	1.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	0.2

Tyr401	>12.0	>12.0	>12.0	10.8	>12.0	>12.0	10.5	**8.4**	>12.0	>12.0	>12.0	9.4	>12.0	>12.0	>12.0	9.6
Lys402	11.7	11.7	11.7	>12.0	10.6	10.7	10.9	11.1	11.7	11.7	11.7	>12.0	10.5	10.8	10.9	11.2
Arg410	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Tyr411	>12.0	>12.0	9.5	**8.8**	>12.0	>12.0	**9.0**	**8.3**	>12.0	**7.9**	**7.7**	**8.0**	>12.0	>12.0	9.8	**8.8**
Lys413	10.5	10.3	10.2	10.6	>12.0	>12.0	>12.0	>12.0	9.8	10.1	10.5	10.9	9.8	10.3	10.5	10.9
Lys414	**7.6**	**8.6**	11.0	>12.0	**6.7**	**8.2**	>12.0	>12.0	9.8	10.1	10.5	10.9	9.8	10.3	10.5	10.9
Glu425	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0
Arg428	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Lys432	**8.8**	9.6	10.4	>12.0	**8.8**	**9.0**	9.5	10.4	**4.9**	**6.2**	**7.7**	10.3	**7.5**	**8.3**	9.5	11.3
Lys436	10.8	11.0	11.3	>12.0	7.9	8.8	9.7	11.5	10.6	11.1	11.8	>12.0	10.2	10.5	11.1	>12.0
Lys439	>12.0	>12.0	>12.0	>12.0	11.1	11.2	11.2	11.2	11.3	11.4	11.3	11.3	11.1	11.1	11.1	11.1
His440	<0.0	1.0	2.9	4.4	0.9	2.2	3.5	4.6	<0.0	<0.0	1.9	3.9	0.6	2.0	3.4	4.7
Glus442	3.2	3.3	3.3	3.2	2.9	3.0	3.1	3.1	2.7	2.7	2.6	2.4	2.9	2.9	2.9	3.0
Lys444	9.5	9.9	10.4	10.8	9.5	9.9	10.2	10.6	9.3	9.6	10.0	10.5	9.4	9.9	10.3	10.7
Arg445	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu450	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0
Asp451	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0	<0.0
Tyr452	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	9.3	>12.0	>12.0	>12.0	10.6
His464	<0.0	<0.0	3.2	5.2	<0.0	<0.0	1.8	4.7	<0.0	<0.0	2.4	5.0	<0.0	<0.0	0.4	4.6
Glu465	2.2	2.0	1.0	1.2	1.7	1.7	1.3	1.2	2.7	2.4	1.7	1.5	2.6	2.0	0.7	0.1
Lys466	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Asp471	2.4	2.6	2.5	2.6	2.2	2.5	2.5	2.3	2.2	2.4	2.4	2.4	2.0	2.2	2.4	2.2
Arg472	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Lys475	11.0	11.0	11.0	11.1	>12.0	>12.0	>12.0	>12.0	8.6	9.5	10.1	10.7	11.7	11.5	11.6	11.6
Glu479	3.9	3.6	3.4	3.2	1.7	1.9	2.1	2.3	3.9	3.7	3.5	3.3	2.2	2.3	2.3	2.2
Arg484	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Arg485	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Glu492	2.9	3.0	3.1	3.2	<0.0	<0.0	<0.0	<0.0	2.7	2.8	2.9	3.0	3.2	3.2	3.3	3.4
Asp494	1.1	1.3	1.4	1.6	<0.0	<0.0	<0.0	<0.0	0.9	1.2	1.3	1.5	0.6	1.0	1.3	1.5
Glu495	4.5	4.4	4.3	4.2	1.6	1.6	1.5	1.5	4.7	4.5	4.2	4.0	4.7	4.5	4.3	4.1
Tyr497	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	11.5	>12.0	>12.0	>12.0	11.8	>12.0	>12.0	>12.0	11.3
Lys500	11.0	11.0	11.0	11.0	>12.0	>12.0	>12.0	>12.0	11.0	11.0	11.0	11.2	>12.0	>12.0	>12.0	>12.0

Glu501	3.6	3.7	3.7	3.8	3.2	3.3	3.4	3.4	4.3	4.2	3.9	3.8	3.6	3.7	3.8	3.8
Glu505	3.7	3.7	3.7	3.7	2.7	3.0	3.2	3.4	3.7	3.6	3.6	3.7	3.7	3.7	3.8	3.8
His510	7.6	7.6	7.7	7.7	<0.0	1.4	4.8	5.7	6.1	6.6	6.9	7.1	5.9	6.2	6.4	6.6
Asp512	0.5	0.9	1.3	1.5	5.1	4.5	2.6	2.4	1.4	1.5	1.7	1.8	1.1	1.3	1.4	1.6
Glu518	1.7	0.8	0.2	<0.0	2.6	2.4	2.2	2.1	<0.0	<0.0	<0.0	<0.0	2.5	2.1	1.8	1.6
Lys519	**8.9**	**9.0**	9.3	9.7	11.0	10.8	10.8	10.8	11.3	11.4	11.5	>12.0	**5.7**	**7.2**	**8.4**	9.5
Glu520	<0.0	<0.0	<0.0	<0.0	0.5	0.8	1.2	1.5	<0.0	<0.0	<0.0	<0.0	0.6	0.8	0.9	1.1
Arg521	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
Lys524	9.3	9.8	10.3	10.9	8.2	8.9	9.6	10.4	9.9	10.4	10.8	11.2	9.3	9.8	10.2	10.6
Lys525	**8.5**	10.1	11.7	>12.0	**7.0**	**8.0**	9.7	11.6	**7.0**	**8.4**	9.7	>12.0	**7.5**	**8.6**	9.7	>12.0
Glu531	0.7	0.9	1.1	1.4	<0.0	<0.0	0.0	0.6	0.3	<0.0	<0.0	0.5	<0.0	<0.0	<0.0	0.2
Lys534	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0	>12.0
His535	9.7	8.3	7.9	7.7	4.3	5.1	5.7	6.0	2.1	3.2	5.0	5.9	5.0	5.4	5.7	6.4
Lys536	**7.8**	10.2	11.3	>12.0	>12.0	>12.0	>12.0	>12.0	**1.3**	**7.3**	**8.9**	10.6	10.4	11.2	11.3	11.3
Lys538	10.7	10.8	10.8	10.8	8.4	9.1	9.9	10.8	11.1	11.0	11.0	10.9	10.5	10.6	10.6	10.6
Lys541	10.1	10.1	10.2	10.3	7.7	8.2	8.8	9.5	10.6	10.6	10.7	10.7	11.6	11.2	10.8	10.6
Glu542	2.5	2.7	3.0	3.1	1.2	1.4	1.6	1.8	3.1	3.0	3.1	3.2	2.3	2.3	2.3	2.3
Lys545	9.2	9.5	9.9	10.4	11.5	11.5	11.6	11.7	10.1	10.2	10.4	10.6	9.1	9.7	10.4	10.9
Asp549	1.7	1.6	1.6	1.7	2.6	2.3	2.1	2.0	0.2	0.4	0.7	1.1	2.0	2.0	2.1	2.1
Asp550	6.1	5.2	4.3	3.5	5.4	4.9	4.4	4.0	6.5	5.0	3.9	3.0	>12.0	8.8	6.7	5.0
Glu556	3.1	2.8	2.5	2.3	2.9	2.8	2.8	2.9	0.8	1.0	1.3	1.5	3.1	3.2	3.2	3.2
Lys557	11.8	11.8	>12.0	>12.0	11.3	11.4	11.4	11.4	9.8	10.7	11.3	11.8	>12.0	>12.0	>12.0	>12.0
Lys560	>12.0	>12.0	>12.0	>12.0	10.5	10.6	10.7	10.8	>12.0	>12.0	>12.0	>12.0	10.9	10.9	10.9	10.9
Asp562	3.3	3.3	3.4	3.4	4.1	4.0	3.9	3.9	3.9	3.8	3.7	3.5	3.5	3.6	3.6	3.7
Asp563	4.2	3.0	2.7	2.5	2.3	2.6	2.8	3.0	<0.0	<0.0	0.8	1.4	10.4	8.3	6.6	5.1
Lys564	11.5	11.5	11.4	11.4	11.4	11.5	11.5	11.5	11.1	11.2	11.2	11.2	>12.0	>12.0	>12.0	>12.0
Glu565	3.5	3.7	3.8	3.9	4.3	4.3	4.2	4.1	3.4	3.5	3.6	3.6	3.1	3.3	3.5	3.6
Glu570	3.8	3.9	3.9	3.9	3.4	3.5	3.5	3.6	4.8	4.6	4.5	4.3	4.4	4.3	4.3	4.3
Glu571	4.7	4.4	4.2	4.0	3.2	3.3	3.2	3.2	3.0	3.2	3.4	3.6	6.3	5.4	4.5	3.9
Lys573	10.9	10.9	10.9	11.0	8.0	9.0	9.8	10.5	9.8	10.1	10.4	10.6	10.7	10.7	10.8	10.8
Lys574	10.7	10.7	10.8	10.8	10.5	10.7	10.9	11.1	10.6	10.6	10.7	10.8	10.7	11.2	11.2	11.2

Figure S1. Time evolution along the **STD-a** trajectory of the root mean squared deviation (RMSD, in Å) computed for the heavy backbone atoms in the three domains, six subdomains, and three subdomain connecting loops with respect to the 3JRY crystal structure (molecule A). Average values and standard deviations for the last 200 ns are included.

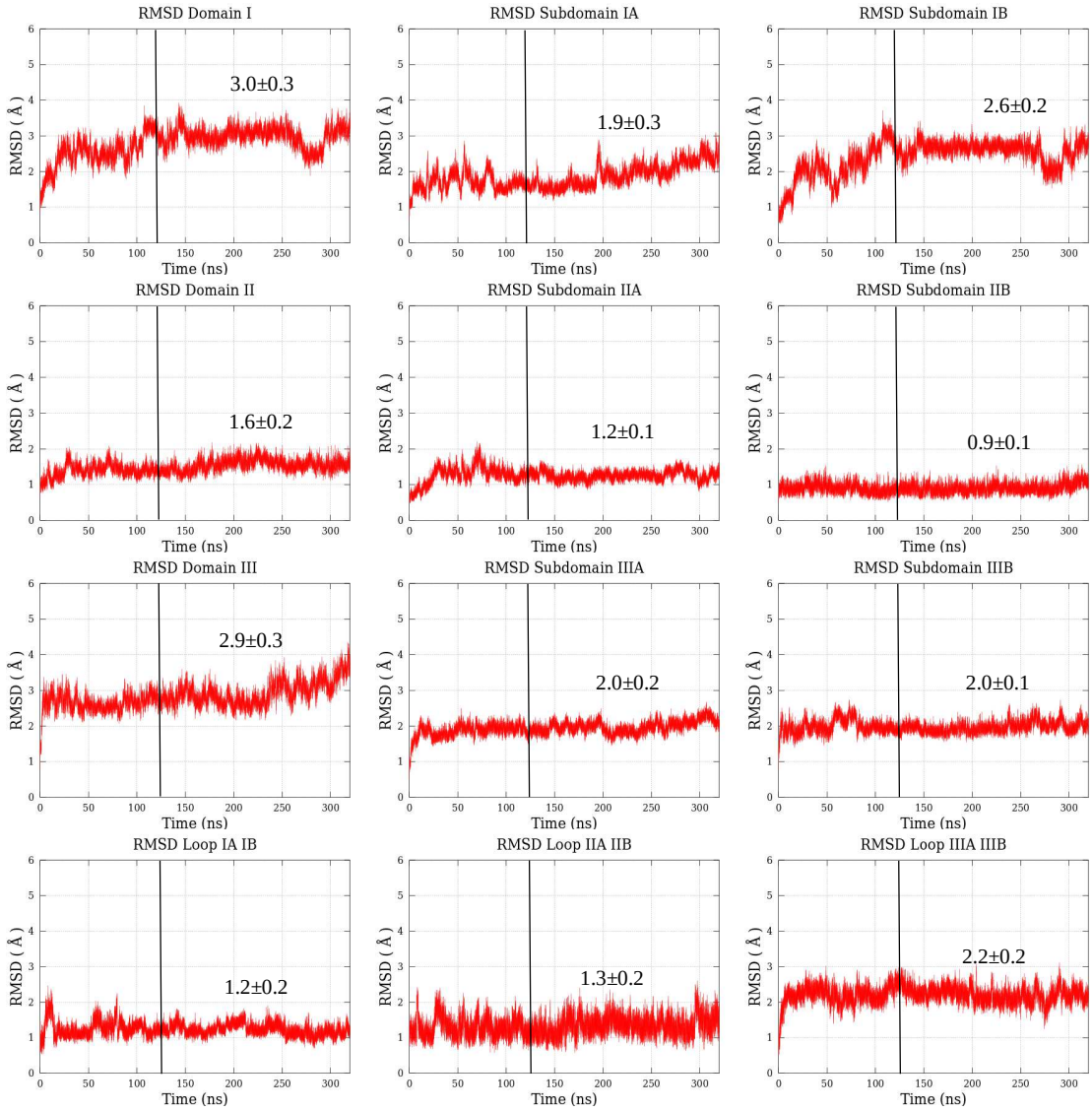

Figure S1 (cont). Time evolution along the **STD-b** trajectory of the root mean squared deviation (RMSD, in Å) computed for the heavy backbone atoms in the three domains, six subdomains, and three subdomain connecting loops with respect to the 3JRY crystal structure (molecule A). Average values and standard deviations for the last 200 ns are included.

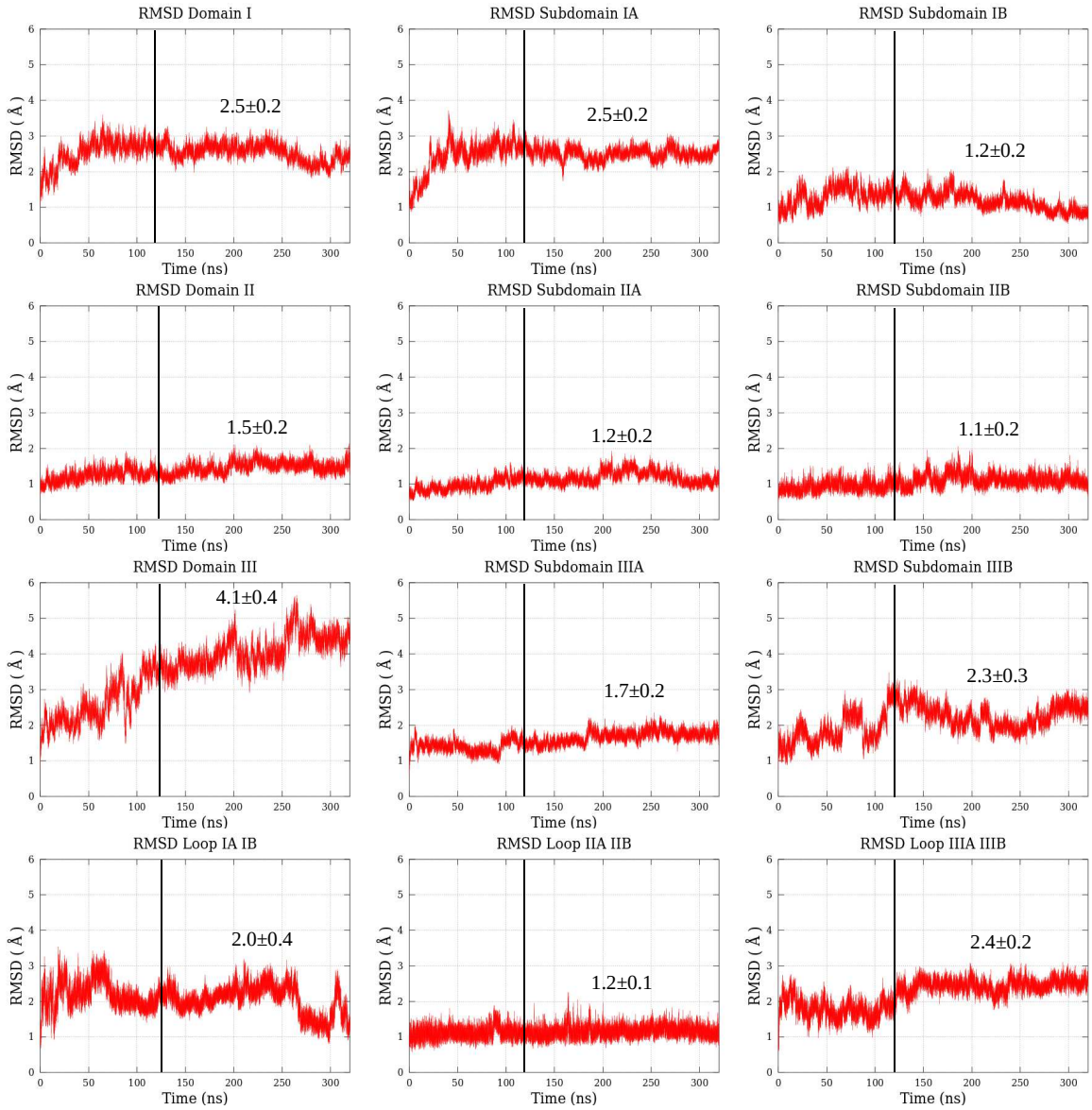

Figure S2. Time evolution along the **PK-PH7-a** trajectory of the root mean squared deviation (RMSD, in Å) computed for the heavy backbone atoms in the three domains, six subdomains, and three subdomain connecting loops with respect to the 3JRY crystal structure (molecule A). Average values and standard deviations for the last 200 ns are included.

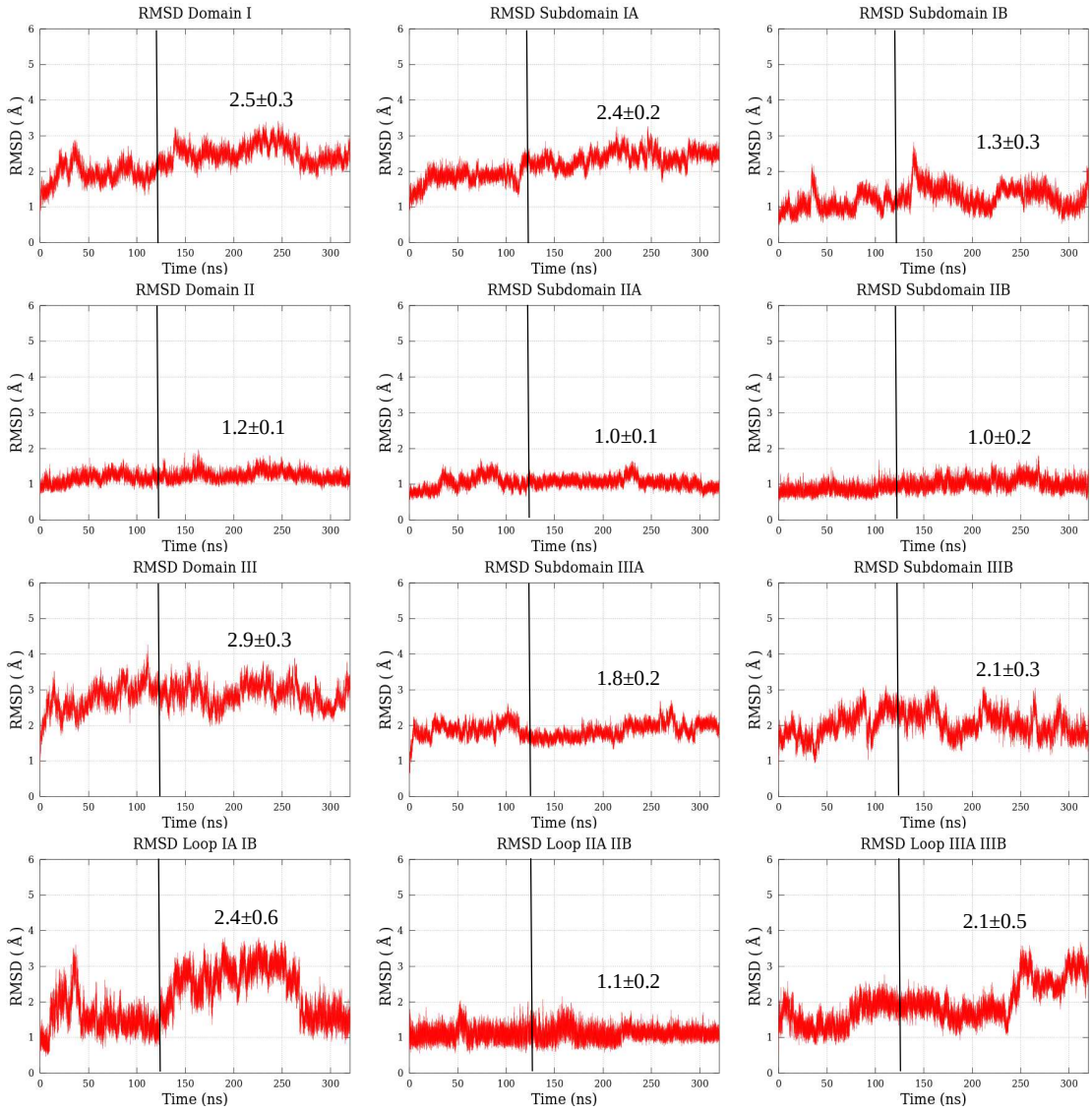

Figure S2 (cont.). Time evolution along the **PK-PH7-b** trajectory of the root mean squared deviation (RMSD, in Å) computed for the heavy backbone atoms in the three domains, six subdomains, and three subdomain connecting loops with respect to the 3JRY crystal structure (molecule A). Average values and standard deviations for the last 200 ns are included.

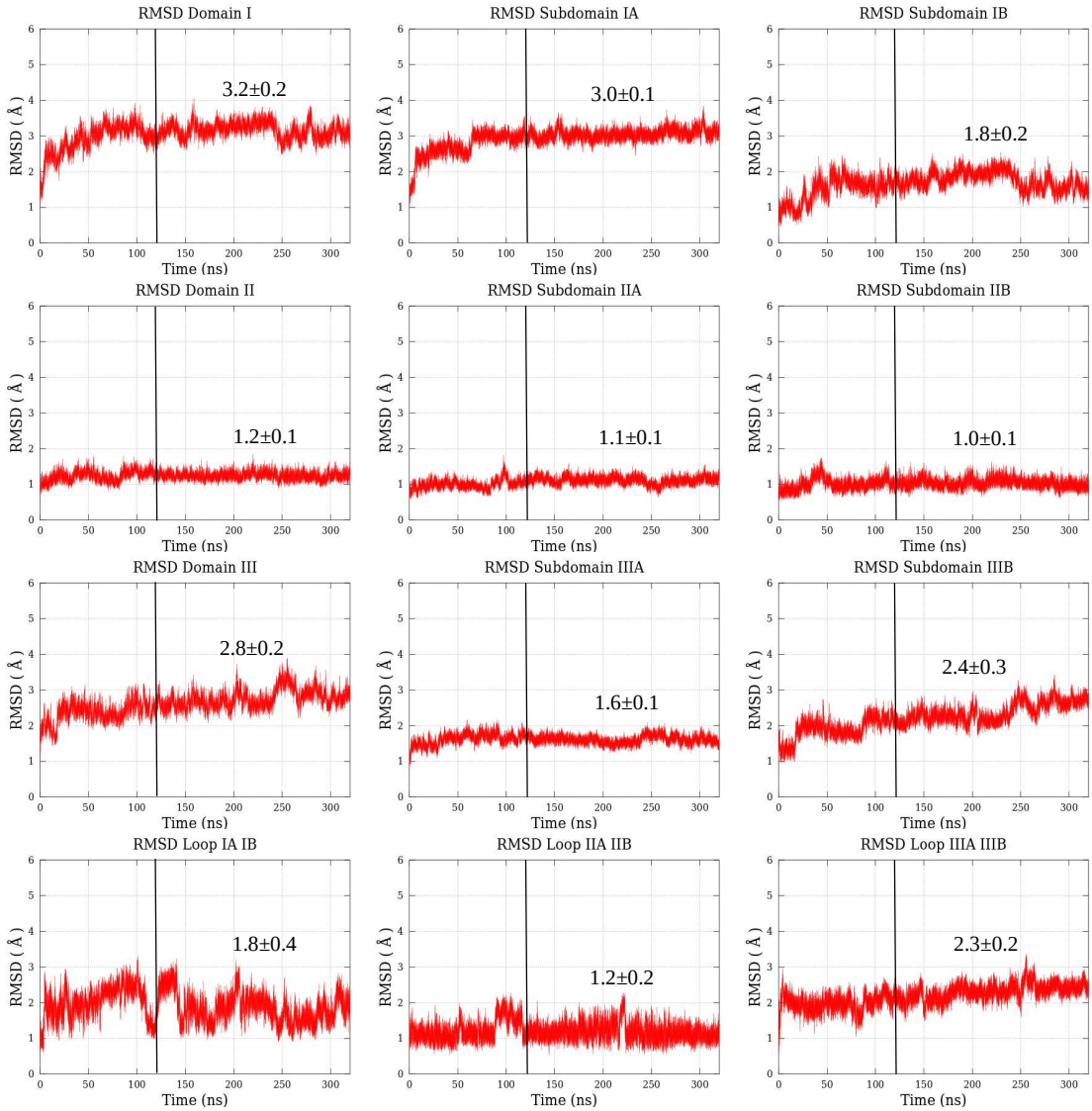

Figure S3. Time evolution along the constant *pH* trajectory of the root mean squared deviation (RMSD, in Å) computed for the heavy backbone atoms in the full protein, three domains, six subdomains, and three subdomain connecting loops with respect to the 3JRY crystal structure (molecule A).

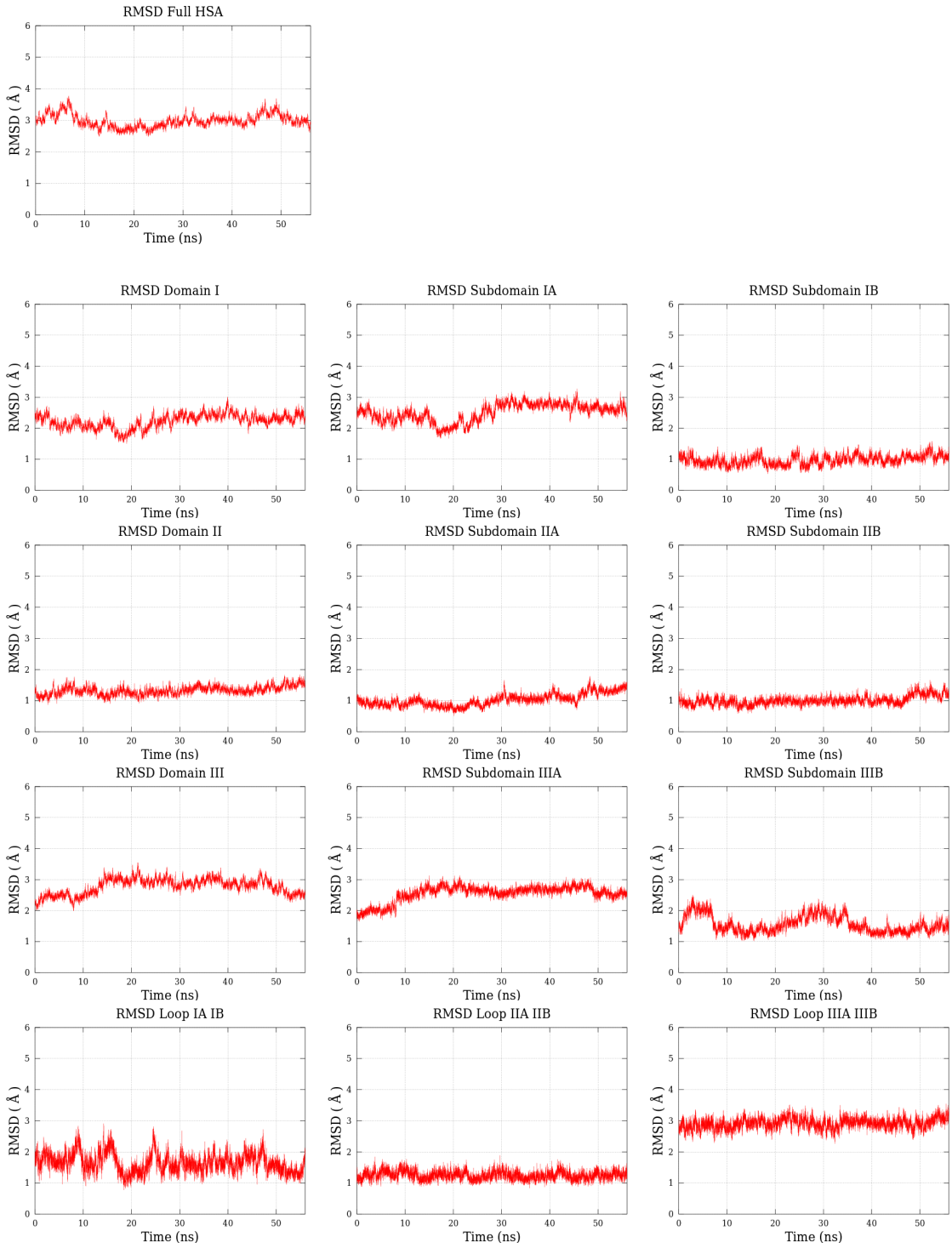

Figure S4. Time evolution along the **PK-PH9-a** trajectory of the root mean squared deviation (RMSD, in Å) computed for the heavy backbone atoms in the three domains, six subdomains, and three subdomain connecting loops with respect to the 3JRY crystal structure (molecule A). Average values and standard deviations for the last 200 ns are included.

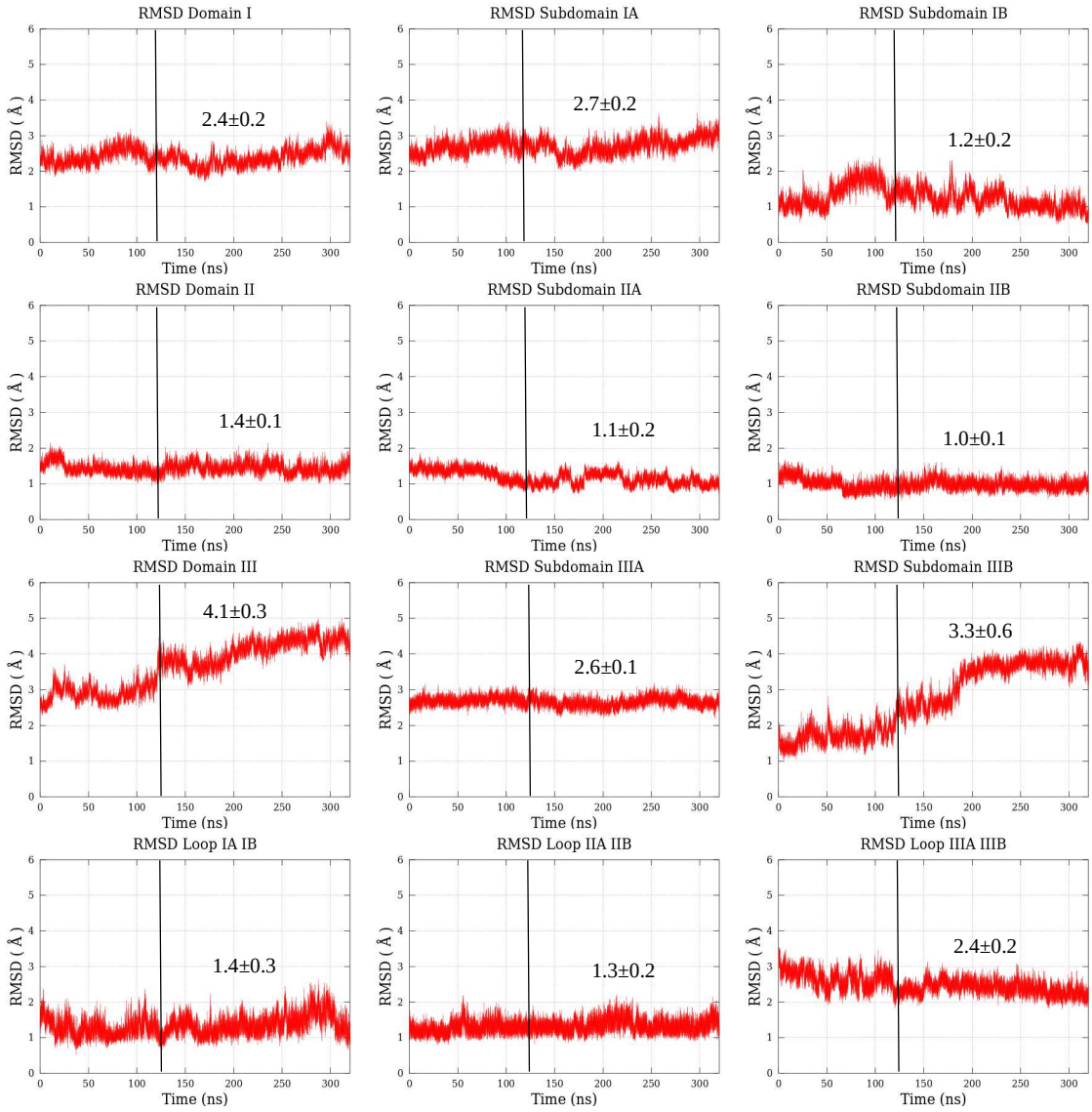

Figure S4 (cont.). Time evolution along the **PK-PH9-b** trajectory of the root mean squared deviation (RMSD, in Å) computed for the heavy backbone atoms in the three domains, six subdomains, and three subdomain connecting loops with respect to the 3JRY crystal structure (molecule A). Average values and standard deviations for the last 200 ns are included.

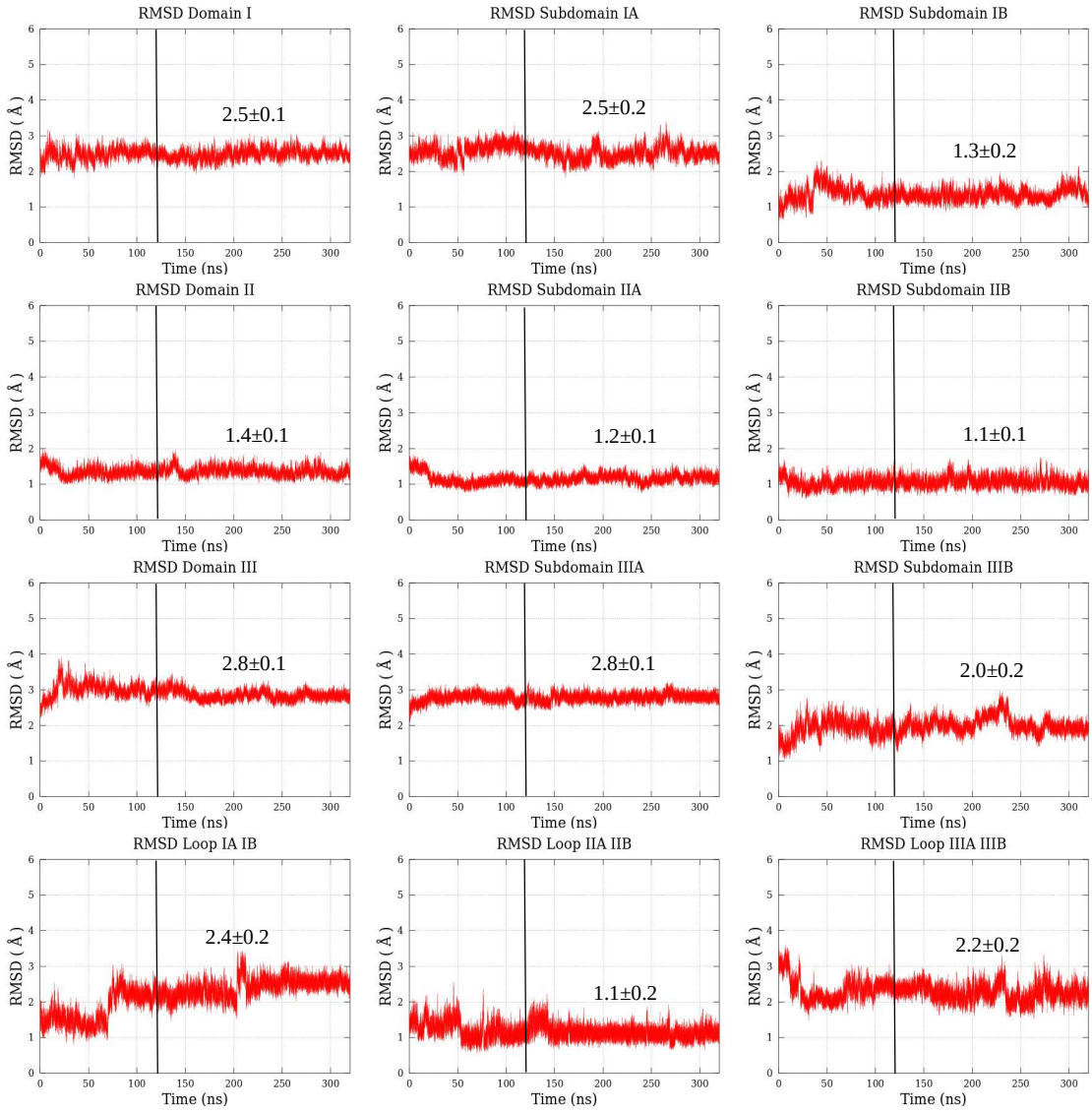
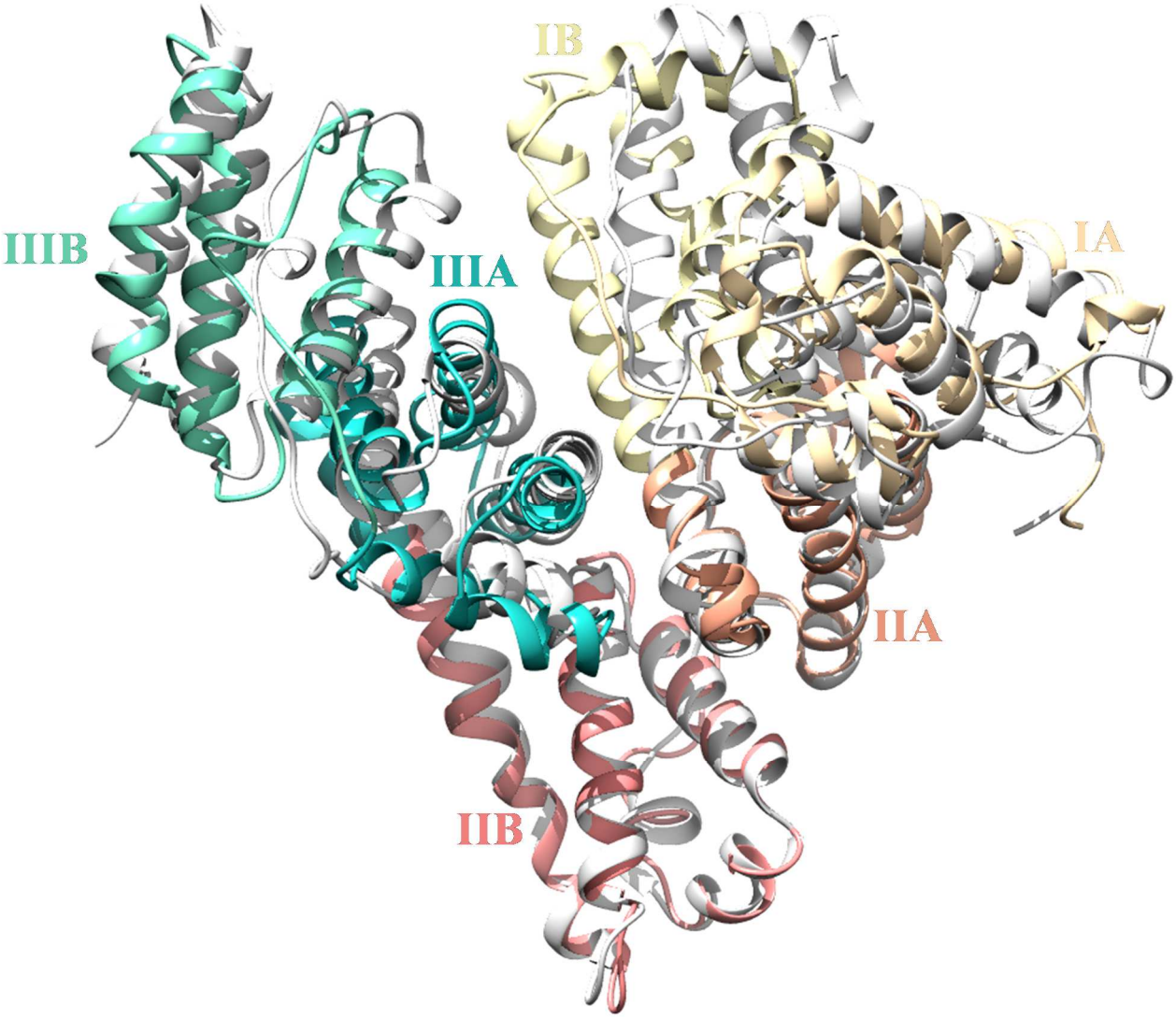
Figure S5. Ribbon model of the last snapshot obtained from the constant-p*H* simulation (colored defining the six different subdomains) superposed on the ribbon model of the 3JRY crystal structure (in light grey).