

Supplementary Information

Thermodynamic Quantification of Multi-Sequence DNA Recognition by Prokaryotic Transcription Factor: A Molecular Dynamics Simulation Study

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Supplementary Figure

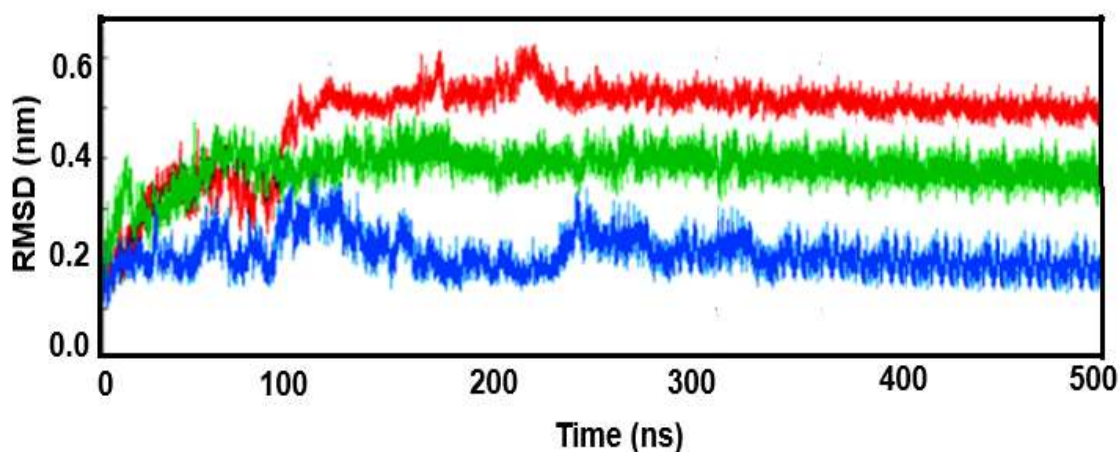


Figure S1: RMSD of Ca atoms of Lac repressor protein with respect to the energy minimized structure using Amber ff99SB-ILDN force field for lac operator SymL bound (blue), lac operator O2-bound (green), and operator unbound (red) states.

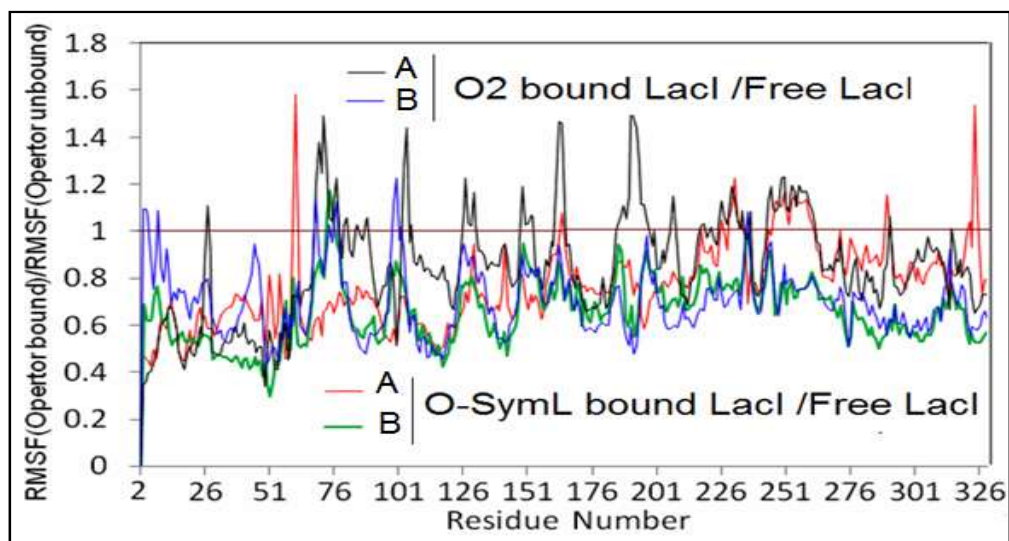


Figure S2: Ratio of Ca atom root-mean-square fluctuation (RMSF) for each subunit of the Lac repressor dimer, comparing both chains in the free state and in the operator DNA-bound state, computed using the Amber ff99SB-ILDN force field. This figure is reproduced from the author's Ph.D. thesis [Das, S. (2023). "Computational Study Of Structure And Dynamics of Protein-DNA Complexes" (Doctoral thesis). University of Calcutta. <http://hdl.handle.net/10603/508120>] and a preprint [Das, S., Roy, S. and Bhattacharyya, D. (2024), "In-silico studies on structural and thermodynamics basis of interaction of lac repressor protein binding to different DNA operators." <https://doi.org/10.1101/2024.07.07.602393>] available on bioRxiv.

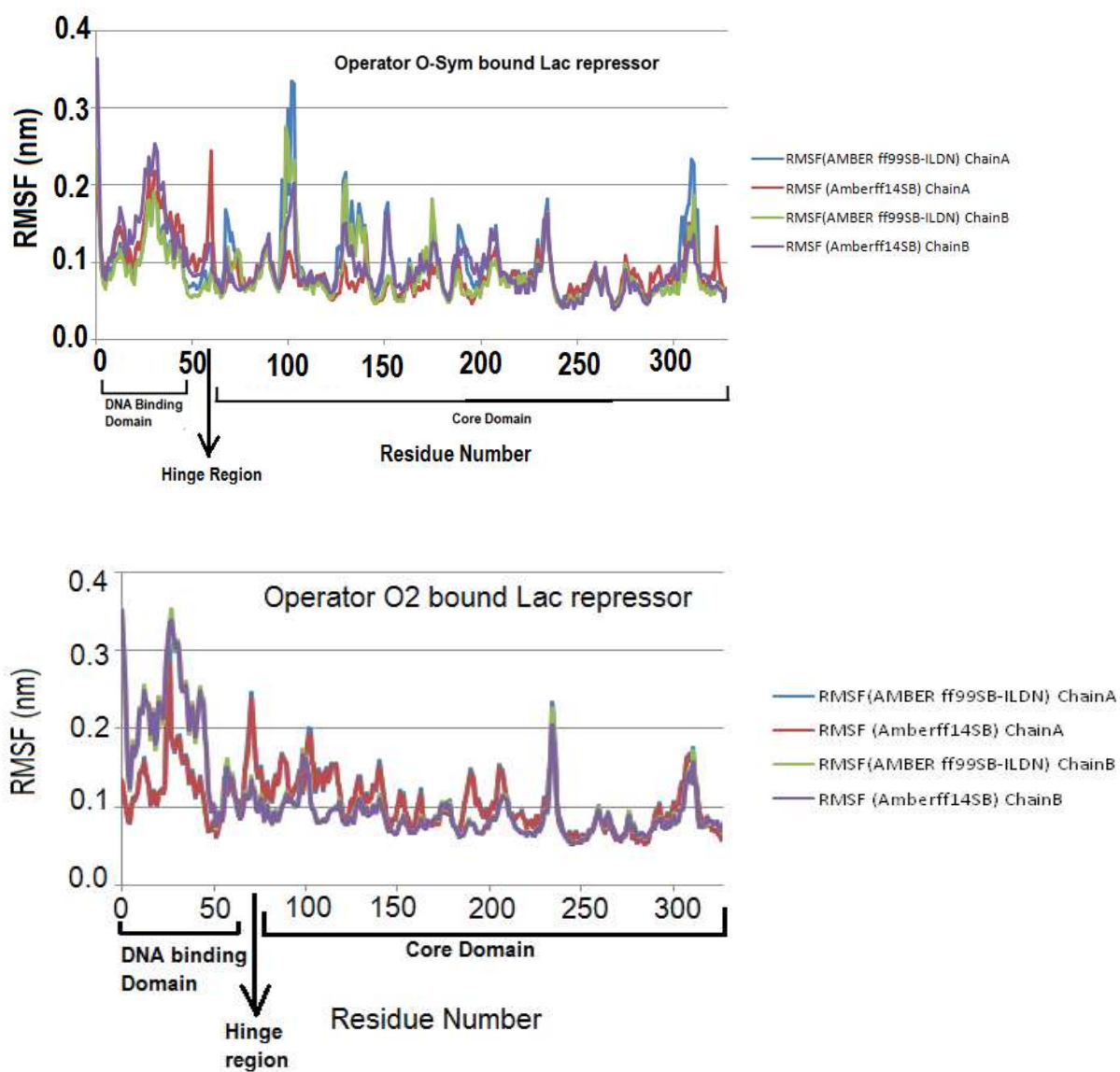


Figure S3: Comparison of RMSF of Ca atoms of individual subunits of Lac repressor chain A and chain B with two different force fields (*Amber-ff99SB-ILDN* and *Amber ff14SB*). In both cases, DNA was parameterized using the *AMBER ParmBSC1* force field. The asymmetric protein dynamics observed in the Lac-SymL and Lac-O2 complexes are consistently reproduced across both protein force fields. The Ca RMSF trends across the protein subunits remain consistent between *AMBER ff99SB-ILDN* and *AMBER ff14SB*. These results confirm that the reported differential motions and interface asymmetry reflect intrinsic molecular behaviour rather than artifacts of force-field selection.

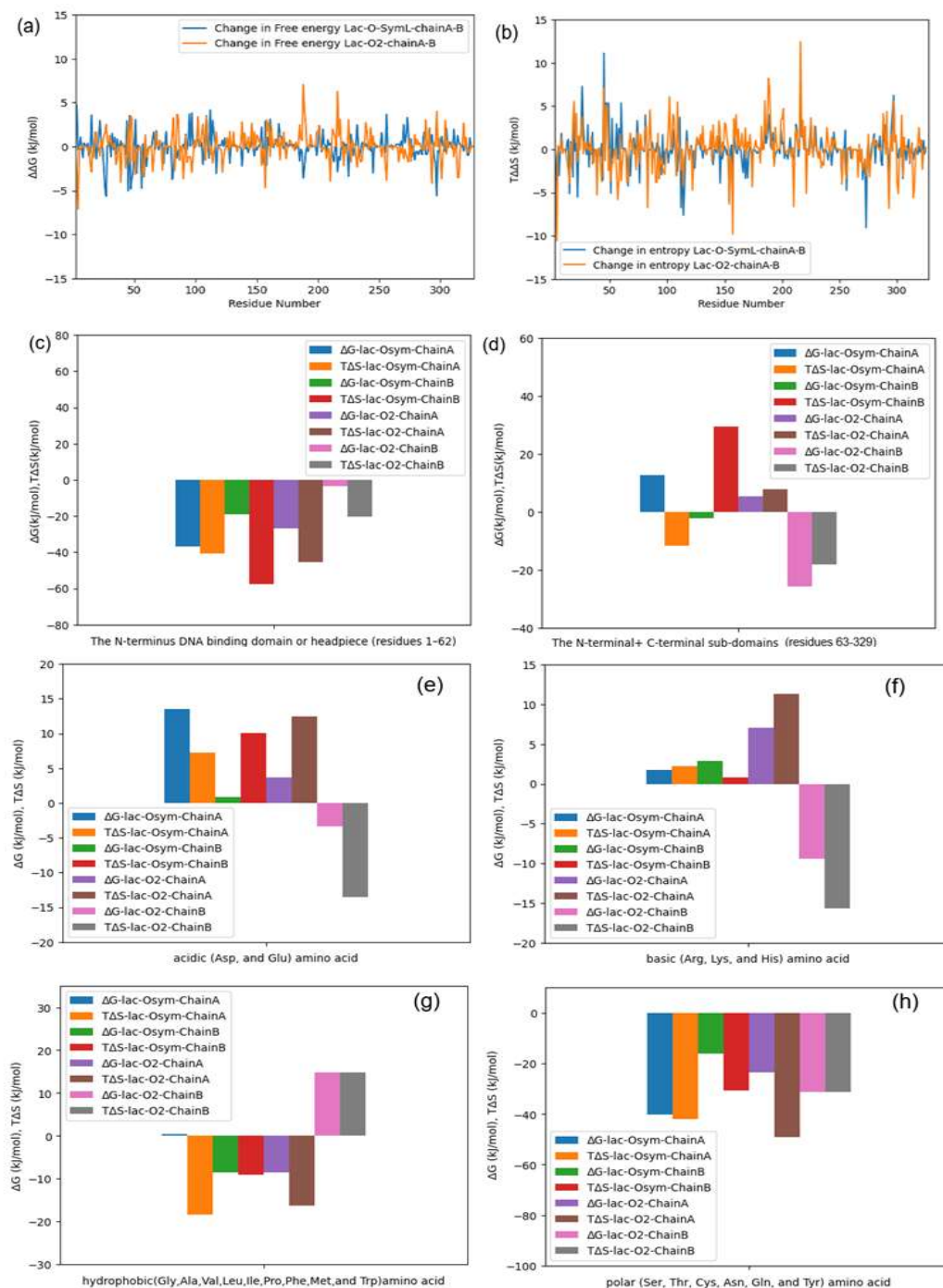


Figure S4: Residue-wise (a) Free energy change ($\Delta\Delta G$) and (b) Conformational entropy change ($T\Delta\Delta S$) of Lac-O-SymL and Lac-O2 systems (Difference between chain A and chain B); Figure 4: Bar diagram showing total changes in conformational free energy (ΔG) and entropy ($T\Delta S$) of chain A & chain B Lac repressor protein (operator O-Sym and O2 bound) with respect to chain A & chain B Lac repressor protein (free) for (c) DNA binding domain and (d) core domain; Figure 4: Bar diagram showing total changes in conformational free energy (ΔG) and entropy ($T\Delta S$) of chain A & chain B Lac repressor protein (operator O-Sym and O2 bound) with respect to chain A & chain B Lac repressor protein (free) for (e) acidic amino acid, (f) basic amino acid, (g) hydrophobic amino acid, and (h) polar amino acid using Amber-ff99SB-ILDN force field.

Supplementary Table

Table S1 (a): Mean and standard error of the mean for Residue-wise changes in free energy (in kJ/mol) of lac repressor (operator bound) with respect to lac repressor (free) based on conformational variable namely side chain dihedral χ_1 using Amber-ff99SB-ILDN force field for protein

Residue	Secondary Structural Element	ΔG (kJ/mol)	ΔG (kJ/mol)	ΔG (kJ/mol)	ΔG (kJ/mol)
2LYS	LOOP1	ChainA (O-Sym) bound	ChainB (O-Sym) bound	ChainA (O2) bound	ChainB (O2) bound
3PRO		0.91±0.007	0.96±0.006	0.15±0.001	0.36±0.003
4VAL		-1.11±0.010	-1.61±0.020	-3.47±0.02	-1.09±0.002
5THR	HELIX-1	-0.73±0.10	-0.35±0.02	-0.60 ±0.04	-0.66±0.04
6LEU		1.98±0.04	-2.78±0.04	-2.26±0.04	0.64±0.03
7TYR		-1.56±0.02	-1.21±0.01	-1.83±0.02	5.3±0.02
8ASP		0.1±0.01	0.08±0.02	-0.17±0.02	-0.09±0.003
9VAL		0.6±0.02	-0.48±0.03	-0.24±0.01	0.14±0.002
10ALA		0	0	0	0
11GLU		-1.44±0.01	-0.19±0.002	-0.33±0.01	-0.48±0.01
12TYR		0.4±0.03	-0.01±0.04	0.21±0.001	0.29±0.01
13ALA	LOOP2	0	0	0	0
14GLY		0	0	0	0
15VAL		-0.03±0.008	-0.4±0.03	-0.48±0.03	-0.02±0.003
16SER	HELIX2	-3.17±0.01	-2.13±0.01	-2.09±0.01	-1.93±0.001
17TYR		-1.82±0.01	-1.09±0.01	-0.84±0.003	1.09±0.01
18GLN		0.66±0.002	-2.92±0.01	-1.91±0.01	0.98±0.003
19THR		-1.39±0.01	-0.82±0.01	-0.86±0.001	-0.92±0.02
20VAL		-2.47±0.02	-2.03±0.01	-1.91±0.01	-0.64±0.005
21SER		0.91±0.002	-0.10 ±0.001	3.19±0.02	1.54±0.01
22ARG		-0.98±0.01	0.42±0.002	0.62±0.01	-0.99±0.001
23VAL		-0.24±0.002	-0.12±0.002	0.39±0.006	0.14±0.001
24VAL		2.22±0.01	1.03±0.02	2.52±0.01	2.65±0.01
25ASN		-0.13±0.001	-3.08±0.01	-1.97±0.02	-0.91±0.002
26GLN	LOOP3	0.12±0.001	-0.28±0.002	0.86±0.01	0.14±0.001
27ALA		0	0	0	0
28SER		-2.26±0.01	-0.06±0.001	0.27±0.01	-0.88±0.001
29HIS		-3.26±0.02	1.40 ±0.01	0.81±0.01	-0.71±0.01
30VAL		-6.36±0.10	-0.72±0.02	-1.14±0.01	-3.67±0.02
31SER		0.76±0.01	0.65±0.001	-1.74±0.01	-2.35±0.01
32ALA	HELIX3	0	0	0	0
33LYS		1.4±0.01	0.85±0.01	2.67±0.01	1.41±0.01
34THR		-1.08±0.01	0.09±0.001	-0.76±0.01	-1.47±0.01
35ARG		1.71±0.01	0.23±0.002	0.72±0.01	0.60 ±0.01
36GLU		-0.49±0.01	-0.13±0.001	0.04±0.001	0.14±0.002
37LYS		1.3±0.01	0.23±0.002	0.60 ±0.01	0.20 ±0.002
38VAL		-0.98±0.01	-0.14±0.002	0.01±0.001	2.05±0.02
39GLU		0.89±0.01	0.03±0.002	0.81±0.01	2.18±0.02

40ALA		0	0	0	0
41ALA		0	0	0	0
42MET		0.61±0.001	-0.03±0.002	-0.2±0.01	3.85±0.02
43ALA		0	0	0	0
44GLU		-0.63±0.01	-0.78±0.01	-0.16±0.002	-0.51±0.01
45LEU		-0.06±0.001	-0.17±0.002	-0.11±0.002	0.20±0.01
46ASN		-0.77±0.01	0.13±0.002	-1.69±0.02	0.75±0.01
47TYR	LOOP4	1.65±0.01	-1.28±0.01	-1.35±0.01	-0.26±0.01
48ILE		-2.36±0.01	2.67±0.01	1.75±0.01	-0.71±0.005
49PRO		1.91±0.01	-1.61±0.01	-1.22±0.01	0.69±0.006
50ASN	HELIX4	-5.96±0.01	-1.14±0.03	-1.38±0.01	-4.88±0.14
51ARG		-2.66±0.01	0.97±0.002	-0.35±0.004	-3.55±0.15
52VAL		-2.98±0.01	0.01±0.003	-2.12±0.01	-0.51±0.03
53ALA		0	0	0	0
54GLN		1.49±0.01	-1.58±0.01	-1.13±0.01	2.03±0.01
55GLN		-3.67±0.01	-0.65±0.02	-2.91±0.01	-2.65±0.01
56LEU		-0.81±0.08	-0.99±0.03	-0.98±0.001	-0.45±0.004
57ALA		0	0	0	0
58GLY	LOOP5	0	0	0	0
59LYS		-5.1±0.08	-0.36±0.002	-2.61±0.01	-1.82±0.01
60GLN		-1.17±0.01	-1.49±0.01	-4.22±0.02	-0.86±0.01
61SER		-1.35±0.01	2.08±0.01	-1.02±0.01	1.74±0.01
62LEU		0.41±0.006	-0.11±0.002	1.71±0.01	0.39±0.005
63LEU	β-SHEET 1	-1.6±	0.65±0.07	-1.00±0.01	0.23±0.001
64ILE		-0.3±0.001	0.07±0.004	-0.07±0.005	0.87±0.01
65GLY		0	0	0	0
66VAL		-0.19±0.001	-0.12±0.001	-0.06±0.04	0.09±0.003
67ALA		0	0	0	0
68THR		0.13±0.001	-0.8±0.02	0	2.84±0.01
69SER	LOOP6	0.24±0.001	-1.41±0.01	0.41±0.001	1.55±0.01
70SER		-0.88±0.01	-0.56±0.001	-0.06±0.001	-1.01±0.001
71LEU		0.47±0.001	-1.33±0.01	1.81±0.01	0.14±0.01
72ALA		0	0	0	0
73LEU	HELIX5	0.60±0.001	0.99±0.01	0.58±0.002	0.13±0.01
74HIS		-0.05±0.003	-0.33±0.006	-0.18±0.001	-0.89±0.01
75ALA		0	0	0	0
76PRO		-0.49±0.001	-0.95±0.01	-1.17±0.01	1.49±0.01
77SER		-1.95±0.01	-0.04±0.001	-2.21±0.01	-1.82±0.01
78GLN		0.62±0.001	0.59±0.003	0.03±0.001	-0.09±0.001
79ILE		0.67±0.002	-1.01±0.01	-0.43±0.001	-0.25±0.004
80VAL		0.42±0.001	1.24±0.01	-1.11±0.01	-1.18±0.01
81ALA		0	0	0	0
82ALA		0	0	0	0
83ILE		-0.04±0.001	-0.10±0.001	-0.10±0.001	-0.15±0.001

84LYS		-4.03±0.02	-0.29±0.001	0.66±0.001	-0.77±0.002
85SER		-2.83±0.01	-0.19±0.001	-0.03±0.002	-3.3±0.01
86ARG		-0.64±0.01	-0.74±0.01	-0.98±0.01	1.77±0.01
87ALA		0	0	0	0
88ASP		-2.11±0.01	-0.79±0.002	1.06±0.01	-2.60±0.01
89GLN		-0.39±0.001	0.05±0.001	1.35±0.01	-1.8±0.01
90LEU		-0.23±0.001	0	-0.44±0.001	1.13±0.01
91GLY	LOOP7	0	0	0	0
92ALA		0	0	0	0
93SER	β-SHEET 2	-0.60±0.003	-0.85±0.001	-1.78±0.01	1.88±0.01
94VAL		-0.10±0.001	0.17±0.001	-0.88±0.01	0.25±0.001
95VAL		0.27±0.001	-1.10±0.01	-0.10±0.001	-1.33±0.01
96VAL		-0.16±0.001	0.24±0.001	-1.35±0.01	0.47±0.002
97SER		0.75±0.001	0.47±0.001	-0.85±0.001	0.38±0.001
98MET		1.49±0.01	-2.22±0.01	-1.57±0.01	-0.44±0.001
99VAL	LOOP8	-0.26±0.001	-0.29±0.001	0.17±0.001	1.44±0.01
100GLU		2.54±0.01	-1.29±0.01	-2.79±0.01	0.14±0.001
101ARG		0.66±0.001	0.45±0.001	-0.60±0.001	0.59±0.001
102SER		-0.32±0.002	-0.17±0.001	-0.04±0.001	-0.75±0.001
103GLY	HELIX6	0	0	0	0
104VAL		0.17±0.001	-0.66±0.002	0.56±0.001	-0.12±0.001
105GLU		1.67±0.01	0.88±0.004	0.54±0.001	-2.87±0.01
106ALA		0	0	0	0
107CYS		-0.01±0.001	-0.07±0.003	-0.19±0.008	-0.52±0.02
108LYS		1.47±0.01	1.01±0.01	1.13±0.01	-0.4±0.004
109THR		-0.51±0.001	1.53±0.01	0.32±0.001	-2.24±0.01
110ALA		0	0	0	0
111VAL		1.19±0.01	0.06±0.001	0.05±0.001	1.59±0.01
112HIS		3.06±0.01	-0.45±0.001	1.23±0.01	-2.17±0.01
113ASN		-0.59±0.001	-0.89±0.002	-1.79±0.01	-3.18±0.01
114LEU		0.35±0.001	1.68±0.01	0.16±0.001	0.08±0.001
115LEU		3.51±0.01	-0.65±0.002	-0.33±0.001	0.60±0.001
116ALA		0	0	0	0
117GLN		2.00±0.01	-0.98±0.003	-1.33±0.01	0.53±0.001
118ARG	LOOP9	-0.45±0.001	-2.01±0.01	0.39±0.001	0.94±0.01
119VAL		0.38±0.001	-0.07±0.001	0.05±0.001	0.10±0.001
120SER		-3.71±0.01	-0.65±0.001	0.93±0.003	-0.70±0.001
121GLY	β-SHEET 3	0	0	0	0
122LEU		0.36±0.001	0.17±0.001	-0.21±0.001	-0.20±0.001
123ILE		0.01±0.001	-0.09±0.001	-0.16±0.001	0.10±0.001
124ILE		0.81±0.004	0.67±0.006	0.15±0.001	0.50±0.001
125ASN		0.06±0.001	-0.68±0.005	1.33±0.01	4.25±0.01
126TYR	LOOP10	-0.38±0.008	-0.38±0.006	-0.10±0.002	1.12±0.01
127PRO		0.24±0.001	-0.71±0.008	0.38±0.008	0.83±0.005

128LEU		-0.02±0.001	0.02±0.001	0.13±0.001	0.02±0.001
129ASP	HELIX7	1.34±0.01	1.34±0.01	2.5±0.01	1.49±0.01
130ASP		1.35±0.01	0.97±0.006	-0.41±0.001	0.19±0.002
131GLN		-1.75±0.01	0.15±0.001	0.69±0.005	-1.03±0.01
132ASP		0.42±0.006	0.23±0.001	0.09±0.001	0.05±0.001
133ALA		0	0	0	0
134ILE		0	-0.36±0.001	1.16±0.01	-0.48±0.02
135ALA		0	0	0	0
136VAL		0.08±0.001	0.12±0.001	0.2±0.001	0.060±0.005
137GLU		-0.10±0.001	-0.15±0.001	-0.79±0.001	-0.21±0.001
138ALA		0	0	0	0
139ALA		0	0	0	0
140CYS		-0.01±0.001	0.18±0.003	0.06±0.001	-0.27±0.002
141THR	LOOP11	-1.85±0.01	0.34±0.007	0.42±0.006	-2.36±0.01
142ASN		1.40±0.01	1.26±0.01	0.40±0.008	0.80±
143VAL		1.20±0.01	-0.29±0.001	0.12±±0.001	-1.35±0.01
144PRO		-0.39±0.002	-0.12±0.001	-0.36±0.003	-0.77±0.001
145ALA	β-SHEET 4	0	0	0	0
146LEU		-2.31±0.01	-1.62±0.01	0.85±0.003	-0.24±0.001
147PHE		0.17±0.001	0.34±0.006	0.10±0.001	0.26±0.001
148LEU	LOOP12	-0.25±0.001	-0.21±0.001	-0.36±0.001	-1.05±0.01
149ASP		1.50±0.01	0.33±0.001	2.27±0.01	-0.37±0.002
150VAL		-0.51±0.005	-0.37±0.006	-0.20±0.001	0.25±0.001
151SER		-1.55±0.01	-0.47±0.001	-0.70±0.001	-2.37±0.01
152ASP		0.02±0.001	-0.12±0.001	-0.09±0.001	0.11±0.001
153GLN		-0.41±0.001	0.080±0.001	0.40±0.001	-0.9±0.001
154THR		0.40±0.001	0.53±0.004	1.56±0.01	0.44±0.001
155PRO		0	-0.16±0.001	0.58±0.006	0.08±0.001
156ILE		2.04±0.01	1.70±0.01	1.41±0.01	0.70±0.001
157ASN		1.01±0.01	-1.20±0.01	-1.19±0.01	0.96±0.002
158SER	β-SHEET 5	-0.54±0.008	-0.08±0.001	-0.35±0.001	-0.13±0.001
159ILE		-3.22±0.01	-1.25±0.01	-0.19±0.001	0.08±0.001
160ILE		0.38±0.001	-2.50±0.01	-3.08±0.01	1.61±0.01
161PHE		-1.69±0.01	0.45±0.001	1.64±0.01	-1.39±0.01
162SER	HELIX8	1.94±0.01	0.88±0.001	2.26±0.01	0.47±0.001
163HIS		-0.10±0.001	-0.21±0.001	2.32±0.01	-0.47±0.003
164GLU		2.88±0.01	-0.24±0.001	1.01±0.01	2.14±0.01
165ASP		1.74±0.01	1.09±0.01	2.54±0.01	0.41±0.001
166GLY		0	0	0	0
167THR		0.05±0.001	0.18±0.001	0.08±0.001	-0.13±0.001
168ARG		0.42±0.001	-0.21±0.001	0.21±0.003	-0.65±0.001
169LEU		0.76±0.001	-0.03±0.001	0.01±0.001	-0.26±0.001
170GLY		0	0	0	0
171VAL		2.86±0.01	0.28±0.006	1.82±0.01	0.30±0.001

172GLU		1.48±0.01	0.27±0.001	-0.40±	1.10±0.01
173HIS		1.32±0.01	0.23±0.008	0.23±0.001	-0.48±0.001
174LEU		0.56±0.001	0.18±0.001	0.36±0.001	0.22±0.001
175VAL		1.41±0.01	1.66±0.01	2.17±0.01	0.57±0.001
176ALA		0	0	0	0
177LEU		0.38±0.001	-0.09±0.001	-0.56±0.001	0.80±0.001
178GLY	LOOP13	0	0	0	0
179HIS		0.18±0.001	0.18±0.002	0.32±0.006	0.15±0.001
180GLN		0.30±0.001	-0.01±0.001	0.03±0.001	-0.72±0.002
181GLN		-0.13±0.001	-0.23±0.001	0.04±0.001	-0.45±0.001
182ILE	β-SHEET 6	-0.04±0.001	-0.30±0.001	-0.07±0.001	0.02±0.001
183ALA		0	0	0	0
184LEU		0.08±0.001	-0.17±0.001	-0.34±0.001	0.15±0.001
185LEU		-0.44±0.001	-0.19±0.001	0.23±0.001	-0.30±0.006
186ALA		0	0	0	0
187GLY	LOOP14	0	0	0	0
188PRO		-0.76±0.001	0.86±0.006	0.35±0.008	-2.09±0.01
189LEU		-0.03±0.001	0.27±0.001	-0.08±0.001	-0.97±0.001
190SER		-0.45±0.005	0.18±0.001	0.43±0.006	-0.28±0.003
191SER	HELIX9	-2.95±0.01	0.65±0.001	1.76±0.01	-5.28±0.04
192VAL		-1.67±0.01	0.62±0.001	1.63±0.01	-2.39±0.01
193SER		-0.86±0.007	-0.17±0.001	0.64±0.001	-1.83±0.01
194ALA		0	0	0	0
195ARG		0.45±0.001	1.03±0.01	-0.55±0.001	-0.51±0.001
196LEU		-0.40±0.001	-0.55±0.001	-0.47±0.001	-0.25±0.001
197ARG		-0.33±0.005	-0.58±0.001	1.59±0.01	0.25±0.001
198LEU		-0.14±0.001	-0.09±0.001	-0.09±0.001	-0.51±0.006
199ALA		0	0	0	0
200GLY		0	0	0	0
201TRP		-0.04±0.001	-0.20±0.001	-0.23±0.001	-0.31±0.001
202HIS		-0.49±0.001	0.53±0.006	0.13±0.001	-1.56±0.01
203LYS		0.72±0.001	0.44±0.001	1.18±0.01	-0.52±0.001
204TYR		3.43±0.01	1.06±0.01	2.20±0.01	-0.08±0.001
205LEU		0.52±0.006	0.21±0.001	0.17±0.001	-0.20±0.002
206THR		0.51±0.008	1.10±0.01	-0.66±0.006	-0.15±0.001
207ARG		1.98±0.01	0.03±0.001	0.28±0.002	0.65±0.005
208ASN	LOOP15	0.41±0.006	0.17±0.001	0.09±0.001	0.18±0.001
209GLN		-0.07±0.001	-0.15±0.001	-0.33±0.004	-0.11±0.001
210ILE		-1.06±0.01	-0.34±0.001	-1.59±0.01	-0.22±0.001
211GLN		1.05±0.01	0.27±0.001	0.19±0.001	0.61±0.004
212PRO		0.13±0.001	0.01±0.001	-0.13±0.001	0.11±0.001
213ILE		-0.21±0.001	-0.59±0.002	-0.85±0.008	3.07±0.001
214ALA	β-SHEET 7	0	0	0	0
215GLU		0.18±0.001	1.31±0.01	0.84±0.001	-1.13±0.01

216ARG		-1.14±0.01	0.59±0.001	0.59±0.001	-0.88±0.001
217GLU		-0.47±0.002	-0.44±0.001	0.07±0.001	-1.04±0.01
218GLY	LOOP16	0	0	0	0
219ASP		-1.27±0.01	1.59±0.01	2.84±0.01	-3.44±0.01
220TRP		-0.25±0.001	0.90±0.002	0.47±0.001	-0.70±0.001
221SER	HELIX10	0.04±0.001	1.54±0.01	1.44±0.01	-1.67±0.01
222ALA		0	0	0	0
223MET		-0.40±0.001	-0.05±0.001	0.25±0.001	-0.29±0.001
224SER		-0.27±0.001	-0.74±0.001	-1.10±0.01	1.06±0.01
225GLY		0	0	0	0
226PHE		-0.33±0.001	-0.59±0.001	-0.63±0.001	0.08±0.001
227GLN		-0.81±0.002	-0.41±0.001	-0.52±0.001	-0.03±0.001
228GLN		-3.51±0.01	-0.11±0.001	0.04±0.001	-3.00±0.01
229THR		-0.27±0.001	-0.22±0.001	0.22±0.001	-0.10±0.001
230MET		1.71±0.01	0.34±0.001	-0.77±0.001	0.94±0.001
231GLN		0.40±0.001	0.21±0.001	0.32±0.001	-0.42±0.001
232MET		0.18±0.001	1.22±0.01	1.51±0.01	1.34±0.01
233LEU		-0.03±0.001	0.15±0.001	0.20±0.001	-0.05±0.001
234ASN		-0.03±0.001	-0.36±0.001	-0.85±0.001	0.34±0.001
235GLU		2.75±0.01	0.27±0.001	-0.50±0.001	1.84±0.01
236GLY	LOOP17	0	0	0	0
237ILE		0.63±0.001	1.88±0.01	-0.25±0.001	1.00±0.01
238VAL		1.65±0.01	1.99±0.01	-0.08±0.001	1.67±0.01
239PRO		0.67±0.008	0.19±0.001	-0.22±0.002	1.31±0.01
240THR		0.20±0.002	-0.05±0.001	0.17±0.001	-0.04±0.001
241ALA	β-SHEET 8	0	0	0	0
242MET		-0.16±0.001	-0.51±0.006	1.15±0.01	-1.58±0.01
243LEU		-0.22±0.004	-0.17±0.001	0.65±0.001	-1.04±0.01
244VAL		0.14±0.001	0.12±0.001	0.06±0.001	0.42±0.005
245ALA	LOOP	0	0	0	0
246ASN	HELIX11	-1.99±0.01	-1.49±0.01	-0.90±0.008	-3.04±0.01
247ASP		-0.02±0.001	-0.37±0.005	-0.08±0.001	0.08±0.001
248GLN		-2.65±0.01	0.36±0.006	-0.32±0.008	-1.56±0.01
249MET		-0.04±0.001	-0.45±0.006	0.27±0.002	0.29±0.004
250ALA		0	0	0	0
251LEU		-0.52±0.001	-0.40±0.008	-0.34±0.005	-0.49±0.001
252GLY		0	0	0	0
253ALA		0	0	0	0
254MET		-0.08±0.001	-0.13±0.001	0	-0.02±0.001
255ARG		0.60±0.001	-0.96±0.007	-0.22±0.002	0.94±0.005
256ALA		0	0	0	0
257ILE		-0.21±0.002	-0.11±0.002	-0.20±0.003	-0.04±0.001
258THR		-0.64±0.001	0.03±0.001	-0.15±0.001	1.85±0.01
259GLU		0.41±0.001	-3.26±0.01	-3.22±0.01	0.62±0.002

260SER	LOOP18	-0.01±0.001	0.05±0.001	0.21±0.001	0.05±0.001
261GLY		0	0	0	0
262LEU		-0.06±0.001	-0.01±0.001	0.01±0.001	-0.13±0.001
263ARG		0.17±0.001	-0.02±0.001	0.06±0.001	0.01±0.001
264VAL		0.21±0.001	0.20±0.001	0.10±0.001	0.44±0.002
265GLY		0	0	0	0
266ALA		0	0	0	0
267ASP		0.15±0.001	-0.12±0.001	-0.11±0.001	-0.05±0.001
268ILE		0.34±0.001	0.08±0.001	-0.01±0.001	0.04±0.001
269SER	β-SHEET 9	0.35±0.001	0.08±0.001	-0.57±0.006	1.18±0.01
270VAL		-0.20±0.001	-0.23±0.002	-0.05±0.001	-0.02±0.001
271VAL		0.52±0.001	-0.10±0.001	-0.40±0.006	0.36±0.001
272GLY		0	0	0	0
273TYR		0.40±0.001	-2.09±0.01	-1.27±0.01	0.12±0.001
274ASP		-0.20±0.001	-0.62±0.001	-0.87±0.001	-0.57±0.001
275ASP	LOOP	0.18±0.002	-0.96±0.01	-1.22±0.01	-0.20±0.003
276THR	HELIX12	-1.32±0.01	-4.62±0.01	-3.64±0.01	-2.30±0.01
277GLU		2.02±0.01	0.93±0.001	-0.05±0.001	1.70±0.01
278ASP		-0.53±0.006	0.26±0.003	0.21±0.003	-0.69±0.001
279SER		1.70±0.01	0.84±0.005	-0.46±0.008	1.18±0.01
280SER		0.17±0.001	1.30±0.01	0.15±0.001	0.36±0.006
281CYS		0	-0.05±0.001	-0.42±0.008	0.21±0.002
282TYR		-1.71±0.01	-0.18±0.001	-0.01±0.001	-1.36±0.01
283ILE	LOOP19	-0.48±0.008	0.12±0.001	-0.18±0.001	-0.39±0.005
284PRO		-0.40±0.006	0.17±0.001	0.50±0.006	-0.30±0.001
285PRO		-1.86±0.01	-0.95±0.001	-1.36±0.01	-1.55±0.01
286LEU		-0.19±0.001	0.30±0.006	0.25±0.002	-0.18±0.001
287THR		-0.36±0.005	-0.01±0.001	-0.13±0.001	-0.10±0.001
288THR	β-SHEET 10	0.27±0.001	1.19±0.01	-0.13±0.001	0.22±0.002
289ILE		0.48±0.001	-0.60±0.001	0.13±0.001	0.03±0.001
290LYS		1.16±0.01	-0.48±0.001	-0.58±0.002	-0.16±0.001
291GLN	LOOP	-1.69±0.01	-0.83±0.005	0.06±0.001	-2.98±0.01
292ASP	HELIX13	-0.62±0.001	0.30±0.003	-0.26±0.004	-0.64±0.007
293PHE		-0.15±0.001	0.24±0.005	-0.04±0.001	0.27±0.003
294ARG		2.52±0.01	0.44±0.008	0.18±0.001	-1.77±0.01
295LEU		0.37±0.005	0.08±0.001	-0.09±0.001	0.75±0.001
296LEU		0.51±0.005	-0.84±0.006	-1.60±0.01	2.60±0.01
297GLY		0	0	0	0
298GLN		0.23±0.002	1.44±0.01	2.76±0.01	2.33±0.01
299THR		0.07±0.001	1.97±0.01	-0.08±0.001	-0.09±0.001
300SER		-3.16±0.01	2.42±0.01	0.32±0.002	-3.68±0.01
301VAL		0.09±0.001	0.56±0.006	0.03±0.001	0.07±0.001
302ASP		-0.23±0.003	0.41±0.001	0.32±0.008	-0.64±0.001
303ARG		0.06±0.001	-0.34±0.001	-1.18±0.01	0.04±0.001

304LEU		0.45±0.008	-0.67±0.001	-0.59±0.001	3.08±0.01
305LEU		0.54±0.006	0.49±0.008	-0.06±0.001	0.65±0.006
306GLN		0.13±0.002	0.18±0.002	-0.21±0.003	-0.20±0.002
307LEU		-0.39±0.006	0.17±0.003	1.44±0.01	-1.52±0.01
308SER		2.03±0.01	-0.02±0.001	-0.26±0.002	0.58±0.001
309GLN		-0.51±0.008	-0.36±0.001	-0.26±0.004	-0.92±0.01
310GLY	LOOP20	0	0	0	0
311GLN		0.70±0.005	0.17±0.001	0.04±0.001	-0.11±0.001
312ALA		0	0	0	0
313VAL		-0.17±0.001	0.11±0.001	-0.08±0.001	-0.43±0.006
314LYS		0.61±0.008	-1.33±0.01	-1.44±0.01	-0.29±0.002
315GLY		0	0	0	0
316ASN	β-SHEET 11	-0.28±0.001	-0.03±0.001	0.07±0.001	0.03±0.001
317GLN		0.16±0.001	-1.09±0.01	-2.51±0.01	1.01±0.01
318LEU		-0.74±0.006	-1.24±0.01	-1.27±0.01	2.28±0.01
319LEU		-0.44±0.001	-0.64±0.001	-0.26±0.003	0.23±0.001
320PRO	LOOP	-0.12±0.001	-0.05±0.001	0.10±0.001	-0.11±0.001
321VAL		1.15±0.01	0.95±0.01	0.77±0.001	0.52±0.002
322SER	β-SHEET 12	-0.20±0.002	0.30±0.001	1.94±0.01	-0.73±0.001
323LEU		0.29±0.002	-0.02±0.001	-0.03±0.001	0.06±0.001
324VAL		1.77±0.01	1.41±0.01	0.43±0.001	-0.61±0.008
325LYS	LOOP21	0.95±0.001	1.93±0.01	-0.23±0.002	0.47±0.001
326ARG		-0.53±0.01	0.45±0.01	-0.01±0.001	0.35±0.001
327LYS		0.81±0.01	-0.16±0.001	0.12±0.001	0.79±0.01
328THR		-0.03±0.001	0.07±0.001	0.15±0.001	-0.09±0.001

Table S1 (b): Mean and standard error of the mean for Residue-wise changes in entropy (in kJ/mol) of lac repressor (operator bound) with respect to lac repressor (free) based on conformational variable namely side chain dihedral χ_1 using Amber-ff99SB-ILDN force field for protein

Residue	Secondary Structural Element	T ΔS (kJ/mol)	T ΔS (kJ/mol)	T ΔS (kJ/mol)	T ΔS (kJ/mol)
2LYS	LOOP1	chainA(O-Sym) bound	ChainB(O-Sym) bound	ChainA (O2) bound	ChainB(O2) bound
3PRO		0.40±0.001	0.19±0.001	-0.17±0.001	0.12±0.001
4VAL		-1.94±0.01	-1.97±0.01	-5.8±0.01	-1.83±0.01
5THR	HELIX-1	-0.62±	-0.86±0.001	-1.00±0.01	-0.80±0.001
6LEU		-4.36±0.12	1.89±0.01	-3.82±0.01	1.17±0.01
7TYR		-3.32±0.01	-2.34±0.01	-4.23±0.1	6.35±0.01
8ASP		0.11±0.001	-0.08±0.001	-0.10±0.001	-0.52±0.001
9VAL		-0.84±0.001	2.20±0.01	-0.38±0.001	-0.02±0.001
10ALA		0	0	0	0
11GLU		-0.15±0.001	-2.00±0.01	-0.23±0.001	-1.59±0.01
12TYR		-0.21±0.001	-0.21±0.001	-0.21±0.001	0.24±0.001
13ALA	LOOP2	0	0	0	0
14GLY		0	0	0	0

15VAL		-0.64±0.001	-0.21±0.001	-0.66±	-0.21±0.001
16SER	HELIX2	-4.87±0.1	-5.73±0.1	-4.83±0.10	-3.37±0.01
17TYR		-1.79±0.001	-2.94±0.001	-1.60±	0.84±0.001
18GLN		-5.91±0.1	-0.77±0.001	-4.33±0.05	-0.38±0.001
19THR		-1.18±0.01	-2.06±0.01	-1.15±0.01	-1.79±0.01
20VAL		-5.05±0.11	-5.35±0.10	-4.74±0.01	-2.62±0.01
21SER		-0.65±0.001	2.56±0.01	6.69±0.01	3.38±0.01
22ARG		0.45±0.001	-2.78±0.01	2.48±0.01	-3.08±0.01
23VAL		-0.34±0.001	-0.14±0.001	1.66±0.01	0.39±0.001
24VAL		2.99±0.01	2.31±0.01	5.84±0.01	1.67±0.01
25ASN		-5.70±0.01	-0.18±0.001	-3.18±0.01	-1.74±0.01
26GLN	LOOP3	0.17±0.001	0.10±0.001	2.08±0.01	0.52±0.001
27ALA		0	0	0	0
28SER		0.60±0.001	-1.25±0.01	1.06±0.01	-1.05±0.01
29HIS		1.76±0.01	-5.50±0.10	-0.18±0.01	-3.91±
30VAL		-1.45±0.01	-4.26±0.01	-2.15±0.01	-1.64±0.01
31SER		0.92±0.001	0.17±0.001	-1.97±0.01	-2.85±0.01
32ALA	HELIX3	0	0	0	0
33LYS		0.66±0.001	1.27±0.01	2.31±0.01	1.47±0.01
34THR		0.14±0.001	-2.7±0.01	-2.05±0.01	-2.00±0.01
35ARG		0.18±0.001	2.23±0.01	1.83±0.01	1.56±0.01
36GLU		0	-0.59±0.001	0.23±0.001	0.53±0.001
37LYS		0.96±0.001	1.50±0.01	1.52±0.01	0.04±0.001
38VAL		0.13±0.001	-1.82±0.01	0.20±0.001	1.91±0.01
39GLU		0.24±0.001	1.76±0.01	1.91±0.01	3.15±0.01
40ALA		0	0	0	0
41ALA		0	0	0	0
42MET		-0.56±0.005	1.67±0.01	-1.01±	4.28±0.01
43ALA		0	0	0	0
44GLU		-0.10±0.001	0.07±0.001	0.14±0.001	-0.04±0.001
45LEU		-0.68±0.001	0.11±0.001	-0.91±0.001	0.85±0.002
46ASN		0	-0.66±0.001	-2.68±0.01	1.07±0.01
47TYR	LOOP4	-1.95±0.01	1.61±0.01	-2.20±0.01	-0.27±0.001
48ILE		6.78±0.10	-4.35±0.11	6.21±0.10	-0.88±0.001
49PRO		-0.65±0.001	0.63±0.001	-0.70±0.001	0.51±0.001
50ASN	HELIX4	-2.54±0.01	-7.94±0.01	-2.86±0.01	-7.95±0.001
51ARG		0.24±0.001	-3.12±0.01	0.07±0.001	-4.78±0.01
52VAL		-0.78±0.001	-6.16±0.01	-5.07±0.01	-2.62±0.01
53ALA		0	0	0	0
54GLN		-4.19±0.01	0.88±0.006	-2.11±0.01	1.58±0.01
55GLN		-1.59±0.01	-5.16±0.01	-6.02±0.01	-4.34±0.01
56LEU		-3.04±0.01	-2.05±0.01	-3.19±0.01	-1.62±0.01
57ALA		0	0	0	0
58GLY	LOOP5	0	0	0	0

59LYS		-1.85±0.01	-4.81±0.01	-4.19±0.01	-1.50±0.01
60GLN		-0.65±0.001	0.46±0.001	-5.54±0.01	0.28±0.001
61SER		0.96±0.001	-1.45±0.01	-2.17±0.01	1.26±0.01
62LEU		-0.75±0.01	0.39±0.01	1.57±0.01	-0.22±0.001
63LEU	β-SHEET 1	1.90±0.01	-3.46±0.01	-3.08±0.01	0.55±0.001
64ILE		-0.04±0.001	-0.16±0.001	-0.20±0.001	1.48±0.001
65GLY		0	0	0	0
66VAL		-0.03±0.001	-0.16±0.001	0.07±0.001	0.22±0.001
67ALA		0	0	0	0
68THR		-0.94±0.001	0.10±0.001	1.27±0.01	5.11±0.01
69SER	LOOP6	-3.43±0.01	0.82±0.001	0.19±0.001	3.87±0.01
70SER		-2.35±0.01	-1.71±0.01	-1.10±0.001	-1.90±0.001
71LEU		-2.56±0.01	0.53±0.001	3.14±0.01	1.27±0.001
72ALA		0	0	0	0
73LEU	HELIX5	1.79±0.01	0.85±0.001	1.41±0.01	0.47±0.005
74HIS		0.88±0.001	-0.43±0.001	0.19±0.001	0.74±0.001
75ALA		0	0	0	0
76PRO		-0.40±0.001	-0.52±0.001	-1.09±0.01	1.27±0.01
77SER		-0.08±0.001	-3.40±0.01	-1.21±0.01	-3.08±0.01
78GLN		1.86±0.01	1.18±0.01	1.12±0.01	-0.83±0.001
79ILE		-2.34±0.01	1.57±0.01	-1.44±0.01	0.21±0.001
80VAL		1.29±0.01	0.16±0.001	-1.64±0.01	-3.34±0.01
81ALA		0	0	0	0
82ALA		0	0	0	0
83ILE		-0.33±0.001	-0.08±0.001	-0.11±0.001	-0.05±0.001
84LYS		0.38±0.001	-3.60±0.01	2.18±0.01	-0.49±0.001
85SER		-0.48±0.001	-0.98±0.01	-0.56±0.001	-3.30±0.01
86ARG		-3.08±0.01	-0.42±0.001	-3.32±0.01	3.44±0.001
87ALA		0	0	0	0
88ASP		-1.24±0.01	-1.15±0.01	0.19±0.001	-4.39±0.01
89GLN		-0.08±0.001	-0.06±0.001	0.16±0.001	-0.98±0.008
90LEU		-0.42±0.001	-1.23±0.01	-1.07±0.01	1.77±0.01
91GLY	LOOP7	0	0	0	0
92ALA		0	0	0	0
93SER	β-SHEET 2	-0.77±0.005	-0.46±0.001	-2.58±0.01	1.23±0.01
94VAL		0.08±0.001	-0.64±0.001	-2.78±0.01	1.03±0.01
95VAL		-1.01±0.01	-0.74±0.001	0.25±0.001	-1.60±0.01
96VAL		0.15±0.001	-0.18±0.001	-2.82±0.01	0.59±0.001
97SER		-0.82±0.001	0.16±0.001	-0.8±0.001	0.88±0.006
98MET		-0.9±0.001	2.05±0.01	-1.09±0.01	-0.12±0.001
99VAL	LOOP8	0.58±0.001	-1.10±0.01	0.97±0.001	3.04±0.01
100GLU		-0.90±0.001	0.86±0.001	-3.04±0.01	-0.30±0.001
101ARG		0.69±0.001	1.05±0.01	-1.87±0.01	1.01±0.01
102SER		-0.14±0.001	-0.18±0.001	-0.24±0.001	-0.31±0.001

103GLY	HELIX6	0	0	0	0
104VAL		-1.74±0.01	-0.16±0.001	1.34±0.01	-0.97±0.001
105GLU		0.73±0.001	1.06±0.01	1.89±0.01	-4.21±0.12
106ALA		0	0	0	0
107CYS		-0.35±0.001	0.19±0.001	-0.13±0.001	-0.55±0.001
108LYS		2.45±0.01	2.46±0.01	2.99±0.01	-1.06±0.01
109THR		2.05±0.01	-0.27±0.001	0.83±0.001	-2.89±0.01
110ALA		0	0	0	0
111VAL		0.07±0.001	2.54±0.01	0.08±0.001	3.13±0.01
112HIS		-0.57±0.001	1.99±0.01	1.36±0.01	-4.12±0.01
113ASN		-0.75±0.001	-0.51±0.001	-3.24±0.01	-4.08±0.01
114LEU		4.08±0.01	0.39±0.001	0.05±0.001	0.07±0.001
115LEU		-1.76±0.01	4.98±0.01	-1.18±0.01	1.24±0.01
116ALA		0	0	0	0
117GLN		-3.15±0.01	4.48±0.01	-3.64±0.01	0.58±0.001
118ARG	LOOP9	-4.64±0.01	0.05±0.001	0.21±0.001	1.22±0.01
119VAL		-0.22±0.001	0.24±0.001	-0.05±0.001	0.10±0.001
120SER		-0.60±0.001	-2.77±0.01	0.03±0.001	-0.92±0.001
121GLY	β-SHEET 3	0	0	0	0
122LEU		0.85±0.001	1.03±0.001	-0.29±0.001	0.95±0.001
123ILE		0.09±0.001	0.13±0.001	-0.13±0.001	-0.05±0.001
124ILE		0.77±0.008	0.33±0.001	0.27±0.001	0.05±0.001
125ASN		-2.08±0.01	0.32±0.001	1.78±0.01	6.51±0.05
126TYR	LOOP10	-0.44±0.001	-0.27±0.001	0.01±0.001	1.5±0.01
127PRO		-1.80±0.01	0.37±0.001	0.88±0.001	1.18±0.01
128LEU		0.15±0.001	0.05±0.001	0.54±0.001	0.04±0.001
129ASP	HELIX7	2.94±0.01	1.73±0.01	3.36±0.01	1.93±0.01
130ASP		1.71±0.01	0.70±0.001	0.42±0.001	-0.13±0.001
131GLN		0.03±0.001	-0.77±0.001	0.63±0.001	-0.27±0.001
132ASP		0.34±0.001	0.34±0.001	1.63±0.01	-0.10±0.001
133ALA		0	0	0	0
134ILE		-0.94±0.001	0.09±0.001	1.90±0.01	-0.82±0.005
135ALA		0	0	0	0
136VAL		0.09±0.001	0	0.66±0.001	0.23±0.001
137GLU		-0.76±0.001	-0.15±0.001	-0.71±0.001	-0.10±0.001
138ALA		0	0	0	0
139ALA		0	0	0	0
140CYS		0.11±0.001	0.07±0.001	0.08±0.001	-0.26±0.001
141THR	LOOP11	0.55±0.001	-1.06±0.01	0.07±0.001	-2.06±0.01
142ASN		1.61±0.01	2.47±0.01	0.54±0.001	1.99±0.01
143VAL		-0.57±0.007	1.22±0.01	0.65±0.001	-2.18±0.01
144PRO		-0.31±0.01	-0.26±0.001	-0.66±0.01	-0.88±0.01
145ALA	β-SHEET 4	0	0	0	0
146LEU		-4.04±0.01	-3.59±0.01	0.77±0.005	-0.76±0.01

147PHE		0.45±0.001	0.19±0.001	0.09±0.001	0.29±0.001
148LEU	LOOP12	0.52±0.006	-0.99±0.01	0.48±0.008	-2.81±0.01
149ASP		-1.16±0.01	2.76±0.01	2.59±0.01	0.49±0.001
150VAL		-0.66±0.001	-0.56±0.001	-0.37±0.001	0.33±0.001
151SER		-0.94±0.006	0.16±0.001	-1.21±0.01	-2.04±0.01
152ASP		-0.36±0.001	-0.06±0.001	-0.23±0.001	-0.15±0.001
153GLN		-0.33±0.001	-0.71±0.001	1.32±0.01	-1.72±0.01
154THR		1.16±0.01	1.23±0.01	3.79±0.01	0.96±0.01
155PRO		-0.36±0.001	0.30±0.005	1.57±0.01	0.37±0.001
156ILE		1.77±0.01	1.64±0.01	1.34±0.01	0.95±0.01
157ASN		-3.31±0.01	2.68±0.01	-3.36±0.01	2.97±0.01
158SER	β-SHEET 5	-0.42±0.001	-0.32±0.001	-0.71±0.001	0.12±0.001
159ILE		-2.74±0.01	-3.25±0.01	-0.85±0.006	0.98±0.008
160ILE		-3.73±0.01	1.68±0.01	-5.91±0.01	3.91±0.10
161PHE		0.72±0.001	-1.61±0.01	1.94±0.01	-1.59±0.01
162SER	HELIX8	1.82±0.01	1.26±0.01	2.09±0.01	0.62±0.001
163HIS		-0.59±0.001	-0.25±0.001	3.34±0.01	-0.66±0.001
164GLU		1.53±0.01	2.05±0.01	1.64±0.01	1.46±0.01
165ASP		2.55±0.01	2.10±0.01	3.32±0.01	0.97±0.001
166GLY		0	0	0	0
167THR		0.22±0.001	0.25±0.001	0.33±0.001	0
168ARG		0.22±0.001	1.68±0.01	1.15±0.001	-0.72±0.001
169LEU		-0.42±0.001	2.26±0.01	0.15±0.001	-0.07±0.001
170GLY		0	0	0	0
171VAL		0.58±0.001	3.93±0.01	3.03±0.01	0.57±0.001
172GLU		-0.42±0.001	0.56±0.001	-1.50±0.01	-0.56±0.001
173HIS		0.37±0.001	3.69±0.01	0.43±0.001	-0.43±0.001
174LEU		0.12±0.001	0.58±0.001	0.33±0.001	0.13±0.001
175VAL		1.70±0.01	1.43±0.01	2.11±0.01	0.39±0.001
176ALA		0	0	0	0
177LEU		-0.41±0.001	0.87±0.001	-1.91±0.01	2.43±0.01
178GLY	LOOP13	0	0	0	0
179HIS		0.06±0.001	0.17±0.001	0.32±0.001	0.09±0.001
180GLN		-0.04±0.001	0.13±0.001	0.08±0.001	-0.96±0.01
181GLN		-0.17±0.001	0.29±0.001	0.10±0.001	-0.08±0.001
182ILE	β-SHEET 6	-0.16±0.001	0.24±0.001	0.28±0.001	0.05±0.001
183ALA		0	0	0	0
184LEU		-0.54±0.001	0.25±0.001	-1.40±0.01	0.20±0.001
185LEU		-0.16±0.001	-1.10±0.01	1.03±0.01	-1.65±0.01
186ALA		0	0	0	0
187GLY	LOOP14	0	0	0	0
188PRO		2.25±0.01	-0.96±0.001	1.24±0.01	-4.38±0.01
189LEU		0.43±0.001	-0.27±0.001	-0.22±0.001	-2.16±0.01
190SER		0.44±0.001	-0.87±0.001	0.93±0.001	-0.58±0.001

191SER	HELIX9	1.09±0.01	-1.26±0.01	2.56±0.01	-5.65±0.01
192VAL		2.20±0.01	-1.83±0.01	3.06±0.01	-3.94±0.01
193SER		0.01±0.001	-0.40±0.001	0.30±0.001	-2.28±0.01
194ALA		0	0	0	0
195ARG		2.44±0.01	0.49±0.001	-0.41±0.01	-1.30±0.01
196LEU		-2.12±0.01	-0.36±0.001	-2.58±0.01	-0.59±0.01
197ARG		-1.53±0.01	-0.94±0.01	3.25±0.01	0.71±0.01
198LEU		0.16±0.001	0.55±0.001	-0.22±0.001	-1.13±0.01
199ALA		0	0	0	0
200GLY		0	0	0	0
201TRP		-0.41±0.03	0.08±0.001	-0.32±0.001	-0.34±0.001
202HIS		1.95±0.01	-0.31±0.001	0.28±0.001	-3.18±0.01
203LYS		1.46±0.01	0.83±0.005	2.78±0.01	-0.76±0.006
204TYR		3.41±0.01	2.59±0.01	4.81±0.01	0.10±0.001
205LEU		0.27±0.001	1.33±0.01	0.27±0.001	-0.03±0.001
206THR		0.45±0.02	0.80±0.02	-0.53±0.01	0.04±0.001
207ARG		-0.12±0.001	0.61±0.008	-0.13±0.001	0.14±0.001
208ASN	LOOP15	0.68±0.01	1.83±0.01	0.94±0.01	0.96±0.01
209GLN		-0.52±0.01	-0.52±0.001	-0.91±0.01	-0.81±0.01
210ILE		-0.22±0.001	-1.55±0.01	-1.57±0.01	-1.50±0.01
211GLN		0.18±0.001	0.41±0.01	-0.21±0.001	0.69±0.002
212PRO		-0.08±0.001	0.57±0.001	0.52±0.001	0.36±0.001
213ILE		-2.78±0.01	-1.66±0.01	-2.70±0.01	3.91±0.01
214ALA	β-SHEET 7	0	0	0	0
215GLU		1.91±0.01	-0.98±0.001	1.02±0.01	-1.48±0.01
216ARG		1.35±0.01	-0.95±0.01	0.97±0.001	-0.69±0.01
217GLU		-0.67±0.001	0.17±0.001	-0.09±0.001	-0.19±0.001
218GLY	LOOP16	0	0	0	0
219ASP		4.76±0.01	0.01±0.001	6.46±0.10	-5.97±0.12
220TRP		1.30±0.01	-0.17±0.001	0.60±0.001	-0.97±0.001
221SER	HELIX10	1.91±0.01	0.14±0.001	1.83±0.01	-1.55±0.01
222ALA		0	0	0	0
223MET		0.12±0.001	-0.78±0.02	1.37±0.01	-1.25±0.01
224SER		-0.50±0.001	-0.25±0.001	-2.43±0.01	2.66±0.01
225GLY		0	0	0	0
226PHE		-0.65±0.01	-0.19±0.001	-0.64±0.001	0.03±0.001
227GLN		0.04±0.001	-1.11±0.01	-0.62±0.001	-0.20±0.001
228GLN		-1.16±0.01	-4.18±0.01	-0.66±0.001	-4.30±0.01
229THR		-0.03±0.001	-0.16±0.001	0.27±0.001	-0.18±0.001
230MET		0.24±0.001	0.58±0.001	-0.36±0.001	0.55±0.001
231GLN		0.57±0.006	-0.04±0.001	1.71±0.01	-1.02±0.01
232MET		3.20±0.01	0.57±0.001	3.62±0.01	3.24±0.01
233LEU		-0.32±0.001	-0.16±0.001	0.30±0.001	-0.14±0.001
234ASN		-0.14±0.001	0.25±0.004	-0.55±0.001	0.24±0.001

235GLU		0.33±0.001	1.08±0.01	-0.43±0.001	0.61±0.001
236GLY	LOOP17	0	0	0	0
237ILE		2.05±0.001	0.70±0.001	-0.59±0.001	1.54±0.01
238VAL		1.51±0.01	1.32±0.01	-0.34±0.001	1.09±0.01
239PRO		0.13±0.001	0.54±0.001	-0.16±0.001	1.70±0.01
240THR		0.01±0.001	0.27±0.001	0.22±0.001	0.23±0.001
241ALA	β-SHEET 8	0	0	0	0
242MET		-0.42±0.001	0	0.73±0.001	-1.76±0.01
243LEU		-1.35±0.01	-0.10±0.001	0.26±0.002	-0.61±0.001
244VAL		0.18±0.001	0.25±0.001	0.01±0.001	0.60±0.001
245ALA	LOOP	0	0	0	0
246ASN	HELIX11	-2.34±0.01	-0.48±0.001	-1.50±0.01	-2.90±0.01
247ASP		-0.32±0.001	0.04±0.001	0.34±0.001	0.27±0.001
248GLN		-0.19±0.001	-2.18±0.01	-0.66±0.001	-1.68±0.01
249MET		-0.07±0.001	-0.08±0.001	1.09±0.01	-0.15±0.001
250ALA		0	0	0	0
251LEU		-0.47±0.001	-0.07±0.001	-0.39±0.001	-0.49±0.001
252GLY		0	0	0	0
253ALA		0	0	0	0
254MET		-0.28±0.001	-0.20±0.001	-0.28±0.001	-0.16±0.001
255ARG		-2.43±0.01	0.57±0.001	-1.53±0.01	2.53±0.01
256ALA		0	0	0	0
257ILE		0.11±0.001	-0.10±0.001	0.01±0.001	0.15±0.001
258THR		0.06±0.001	-2.14±0.01	-0.43±0.001	2.24±0.01
259GLU		-5.05±0.01	-0.30±0.001	-3.85±0.01	-0.52±0.001
260SER	LOOP18	-0.06±0.001	-0.10±0.001	0.21±0.001	0.02±0.001
261GLY		0	0	0	0
262LEU		0.07±0.001	-0.08±0.001	0.12±0.001	-0.19±0.001
263ARG		-0.26±0.001	0.77±0.01	0.62±0.001	0.46±0.001
264VAL		-0.06±0.001	0.47±0.001	-0.15±0.001	0.96±0.001
265GLY		0	0	0	0
266ALA		0	0	0	0
267ASP		-0.03±0.001	0.04±0.001	-0.08±0.001	0.03±0.001
268ILE		0.08±0.001	0.21±0.001	0.07±0.001	0.11±0.001
269SER	β-SHEET 9	-0.08±0.001	0.11±0.001	-1.35±0.01	1.86±0.01
270VAL		-0.28±0.001	-0.25±0.001	0.19±0.001	-0.41±0.001
271VAL		-0.9±0.01	0.22±0.001	-1.22±0.01	0.25±0.001
272GLY		0	0	0	0
273TYR		-3.40±0.01	0.10±0.001	-2.50±0.01	-0.10±0.001
274ASP		-2.38±0.01	-0.22±0.001	-2.41±0.01	-0.74±0.01
275ASP	LOOP	-1.06±0.01	0.13±0.001	-1.35±0.01	-0.24±0.001
276THR	HELIX12	-9.2±0.01	-0.13±0.001	-5.82±0.01	-2.77±0.01
277GLU		1.21±0.01	1.76±0.01	0.11±0.001	2.02±0.01
278ASP		0.66±0.005	-0.21±0.001	0.81±0.005	-0.92±0.001

279SER		-0.78±0.001	1.91±0.01	-1.62±0.01	1.58±0.01
280SER		-0.29±0.001	0.23±0.001	-0.56±0.001	0.78±0.001
281CYS		-0.39±0.006	-0.92±0.001	-0.97±0.001	-0.64±0.001
282TYR		-0.22±0.002	-1.19±0.01	-0.09±0.001	-1.28±0.01
283ILE	LOOP19	1.15±0.01	-0.63±0.001	0.50±0.001	-0.78±0.001
284PRO		-1.78±0.01	-0.16±0.001	0.26±0.001	-0.20±0.001
285PRO		-0.72±0.008	-1.74±0.01	-1.10±0.01	-1.89±0.01
286LEU		0.20±0.001	-0.23±0.001	0.12±0.001	-0.28±0.001
287THR		-0.01±0.001	-0.24±0.001	0.01±0.001	-0.10±0.001
288THR	β-SHEET 10	1.72±0.01	0.18±0.001	-0.04±0.001	0.09±0.001
289ILE		-0.80±0.01	0.51±0.006	0.14±0.002	0.06±0.001
290LYS		-0.89±0.01	0.97±0.001	-0.21±0.002	-0.90±0.001
291GLN	LOOP	0.45±0.001	-1.00±0.01	0.61±0.005	-3.53±0.01
292ASP	HELIX13	1.81±0.01	-1.07±0.01	-0.26±0.001	-1.92±0.01
293PHE		0.44±0.006	-0.08±0.001	-0.08±0.001	0.50±0.001
294ARG		1.14±0.01	1.10±0.01	0.92±0.01	-3.45±0.01
295LEU		0.30±0.001	0.15±0.001	-0.22±0.001	1.85±0.01
296LEU		-2.09±0.01	0.50±0.001	-3.03±0.01	3.80±0.01
297GLY		0	0	0	0
298GLN		2.64±0.01	0.14±0.001	3.57±0.01	1.84±0.01
299THR		4.46±0.01	0.22±0.001	-0.13±0.001	0.08±0.001
300SER		4.97±0.01	-1.27±0.01	0.86±0.001	-4.74±0.01
301VAL		1.15±0.01	0.22±0.001	0.51±0.001	-0.34±0.001
302ASP		1.05±0.01	-0.35±0.001	0.65±0.01	-0.96±0.01
303ARG		-0.56±0.006	-0.04±0.001	-3.19±0.01	0.74±0.01
304LEU		-0.89±0.01	0.14±0.001	-0.22±0.001	4.89±0.01
305LEU		0.52±0.001	0.45±0.006	-0.15±0.001	0.65±0.008
306GLN		0.42±0.01	0.41±0.001	-0.80±0.01	0.06±0.001
307LEU		0.36±0.001	-0.54±0.01	1.10±0.01	-2.85±0.01
308SER		-0.20±0.001	3.18±0.01	-1.13±0.01	1.99±0.01
309GLN		-1.16±0.01	-0.57±0.01	-0.61±0.001	-2.03±0.01
310GLY	LOOP20	0	0	0	0
311GLN		0.49±0.01	1.76±0.01	0.03±0.001	-0.42±0.005
312ALA		0	0	0	0
313VAL		0.89±0.005	-0.28±0.001	-0.28±0.001	-0.29±0.001
314LYS		-1.04±0.01	0.58±0.001	-1.71±0.01	-0.25±0.001
315GLY		0	0	0	0
316ASN	β-SHEET 11	-0.1±0.001	-0.21±0.001	0.69±0.001	-0.07±0.001
317GLN		-1.14±0.01	0.01±0.001	-3.76±0.01	1.85±0.01
318LEU		-2.26±0.01	-1.92±0.01	-2.11±0.01	2.52±0.01
319LEU		-0.25±0.001	-0.35±0.001	-0.27±0.001	0.32±0.001
320PRO	LOOP	-0.17±0.001	-0.05±0.001	0.12±0.001	0.01±0.001
321VAL		1.96±0.01	2.54±0.01	2.08±0.01	1.49±0.01
322SER	β-SHEET 12	0.27±0.001	-0.05±0.001	1.75±0.01	-0.77±0.001

323LEU		-0.30±0.001	0.02±0.001	-0.01±0.001	-0.20±0.002
324VAL		1.67±0.01	0.61±0.005	0.50±0.001	-0.58±0.001
325LYS	LOOP21	1.96±0.01	2.24±0.01	-1.10±0.01	1.21±0.01
326ARG		0.63±0.001	-0.40±0.005	0.02±0.001	0.30±0.001
327LYS		-0.47±0.02	0.07±0.001	-0.09±0.001	-0.07±0.001
328THR		0.19±0.001	0.05±0.001	0.17±0.001	-0.05±0.001