Supporting Information

Investigation of the structural preference and flexibility of the loop residues in amyloid fibrils of the HET-s prion

Jozica Dolenc[§], Beat H. Meier, Victor H. Rusu, Wilfred F. van Gunsteren*

Laboratory of Physical Chemistry, Swiss Federal Institute of Technology, ETH, Zurich, Switzerland

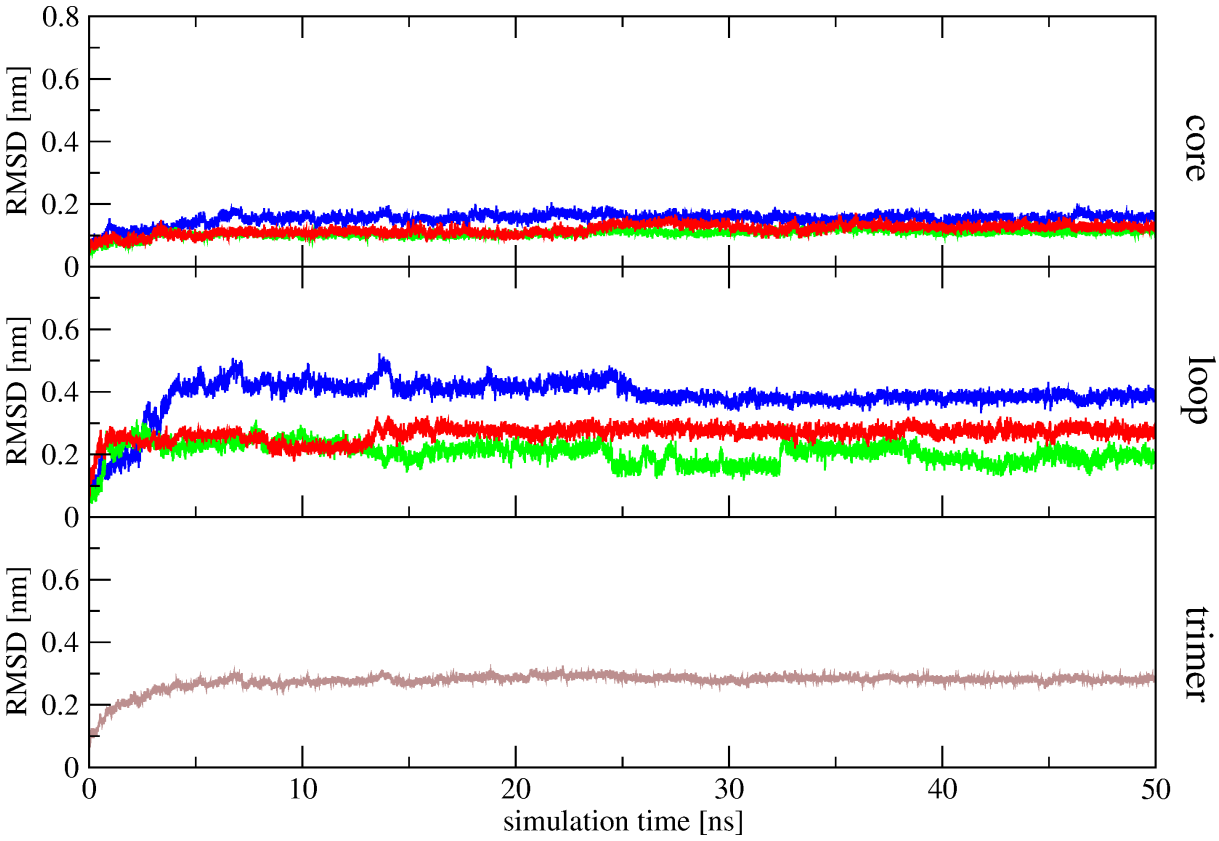
Corresponding author:

Wilfred F. van Gunsteren
Laboratory of Physical Chemistry
Swiss Federal Institute of Technology, ETH
Vladimir-Prelog-Weg 2
8093 Zurich, Switzerland

wfvgn@igc.phys.chem.ethz.ch

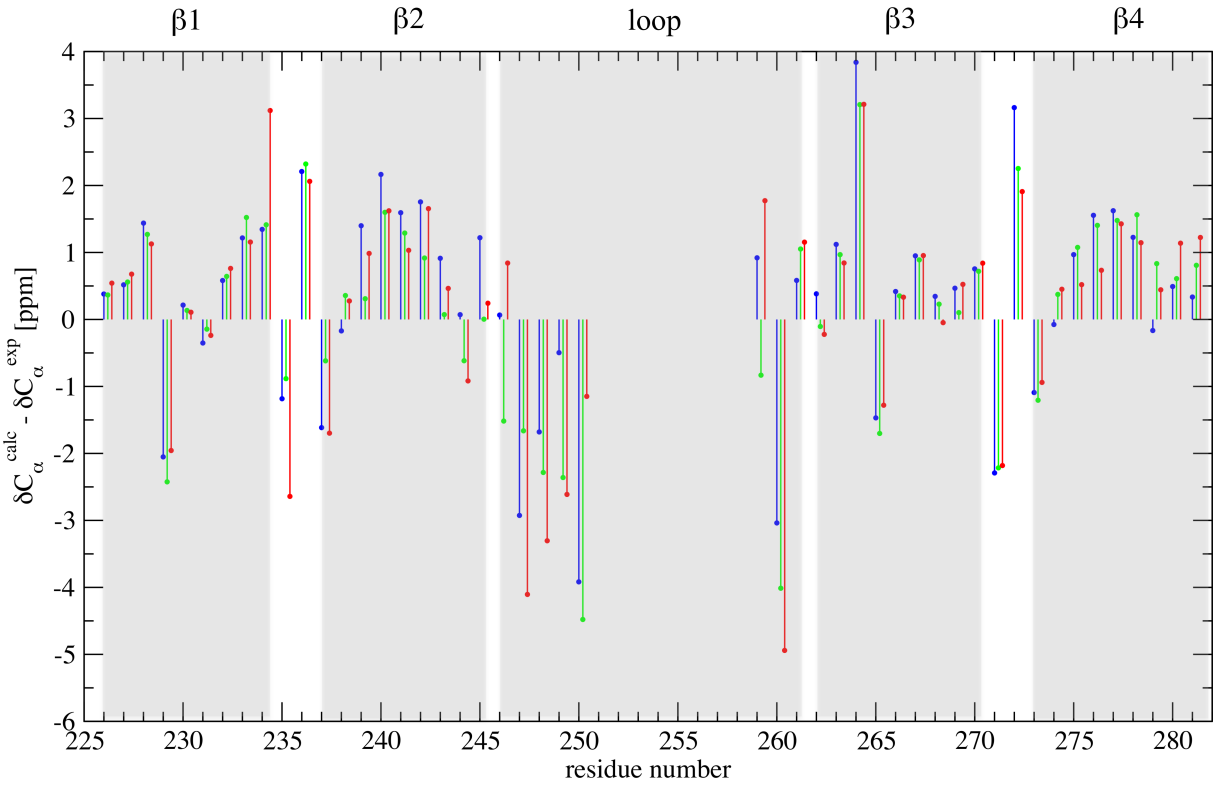
§ Current address: Chemistry | Biology | Pharmacy Information Center, ETH Zurich, Zurich CH-8093, Switzerland

Figure S1



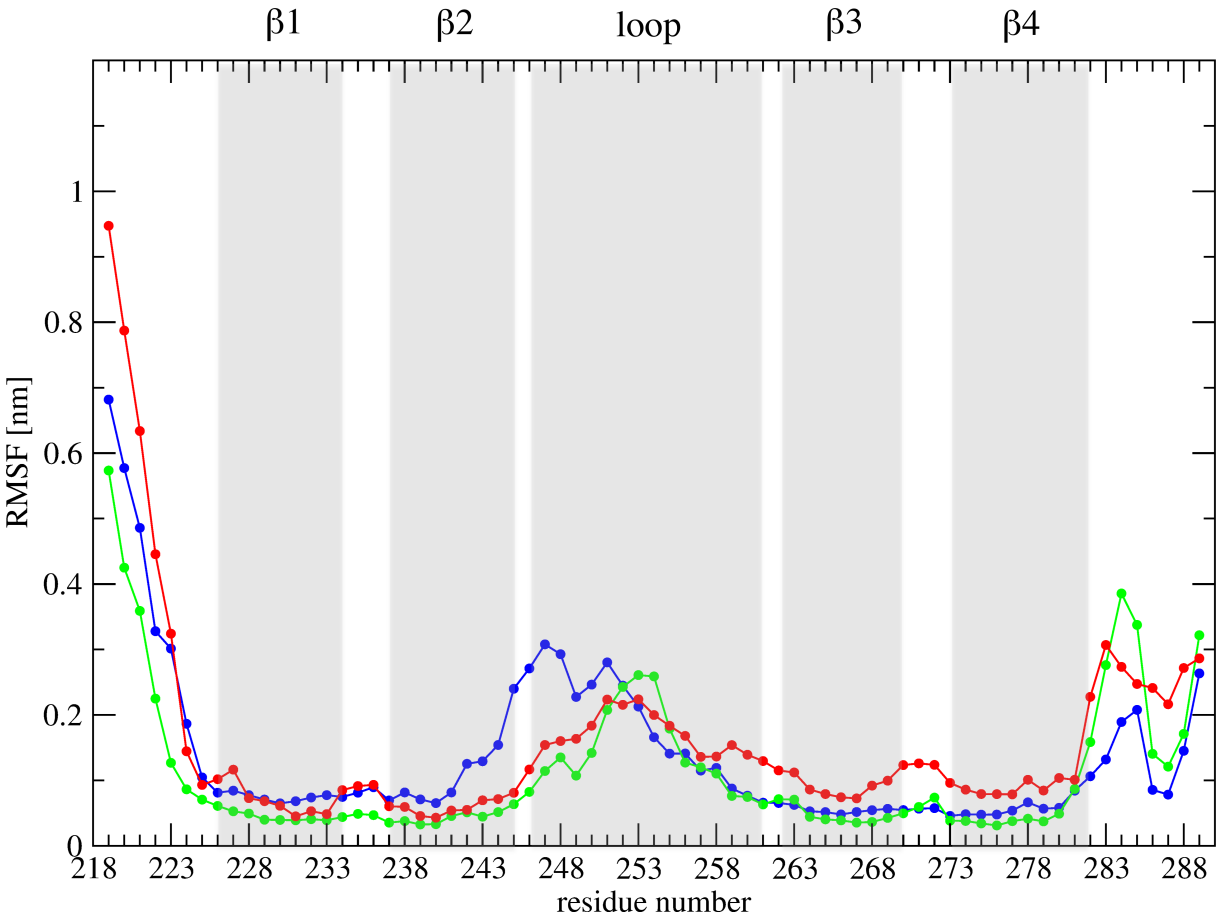
Time series of atom-positional root-mean-square deviations (RMSD) of the Cα atoms of the HET-s backbone from the energy-minimized HET-s trimer starting conformation for the HET-s core, its loops, the trimer and for the "free loop" in water. The structures were taken at regular intervals of 1 ps from the MD trajectories generated at 298 K. Blue line corresponds to the bottom molecule 1, green to the middle molecule 2, red to the top molecule 3, brown to the trimer, and black line to the MD simulations of the "free loop" in water.

Figure S2



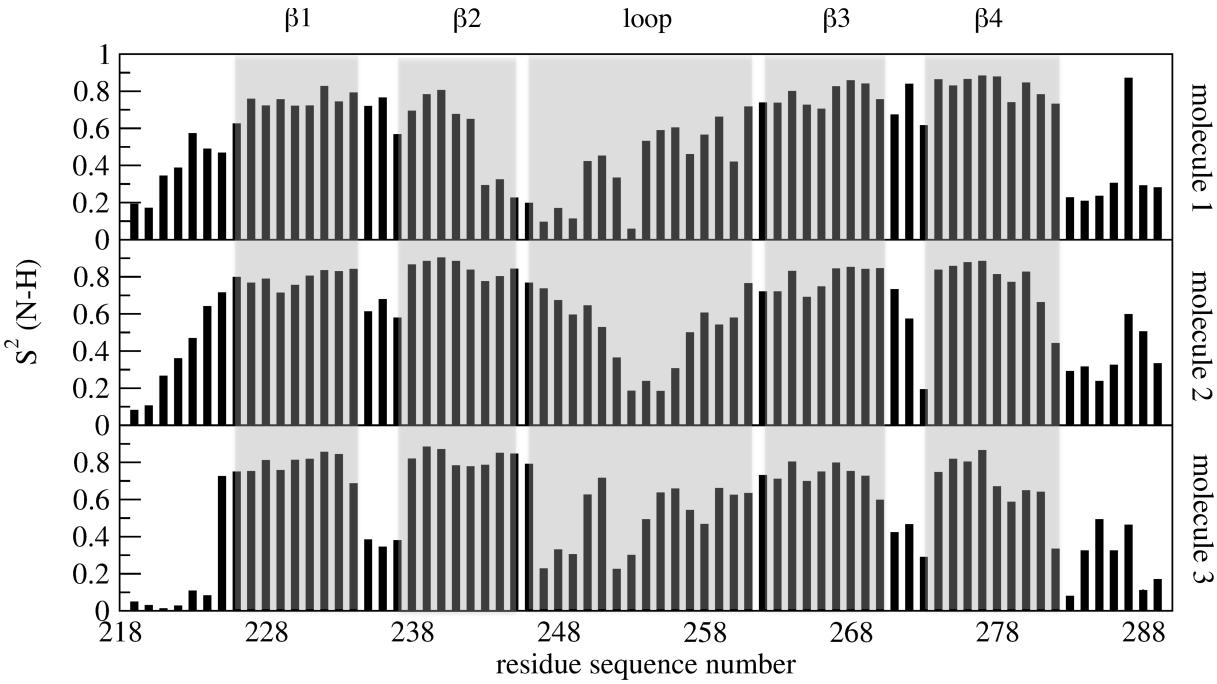
Difference between the predicted and experimental Cα chemical shifts for the core (226-245, 262-281) and the loop (246-261) residues of the bottom molecule 1 (blue), middle molecule 2 (green) and the top molecule 3 (red) of the HET-s trimer at 298 K. β-strands and the loop between β2 and β3 are shaded in gray. Experimental values for the loop are only available for the residues 246-250 and 259-261. The values of the calculated and experimental Cα chemical shifts are reported in Table S2 of the Supporting Information.

Figure S3



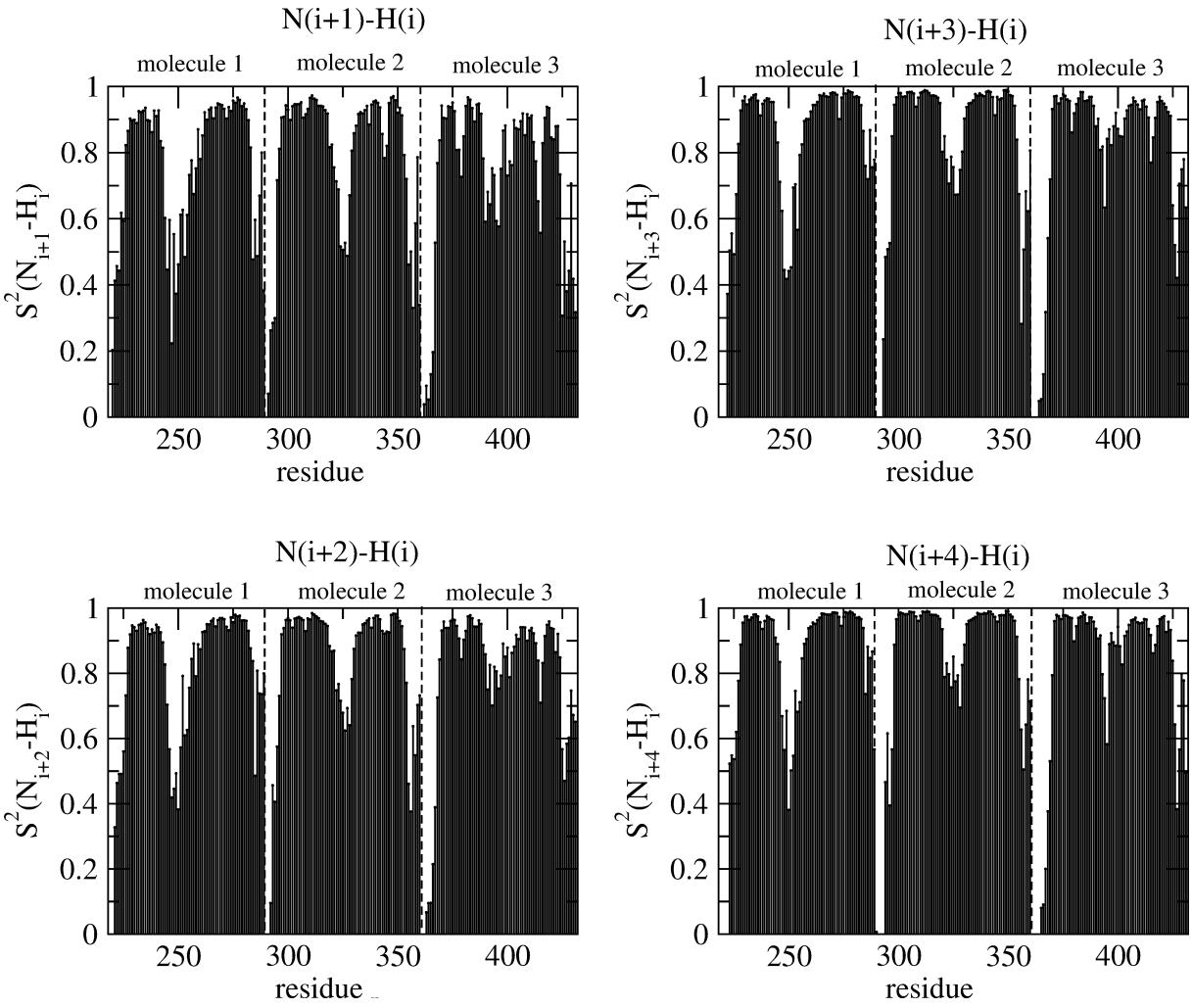
Atom-positional root-mean-square fluctuations (RMSF) of the Cα atoms for the bottom molecule 1 (blue), middle molecule 2 (green) and top molecule 3 (red) of the HET-s trimer as derived from the MD simulations of HET-s trimer at 298 K. β-strands and the loop between β2 and β3 are shaded in gray.

Figure S4



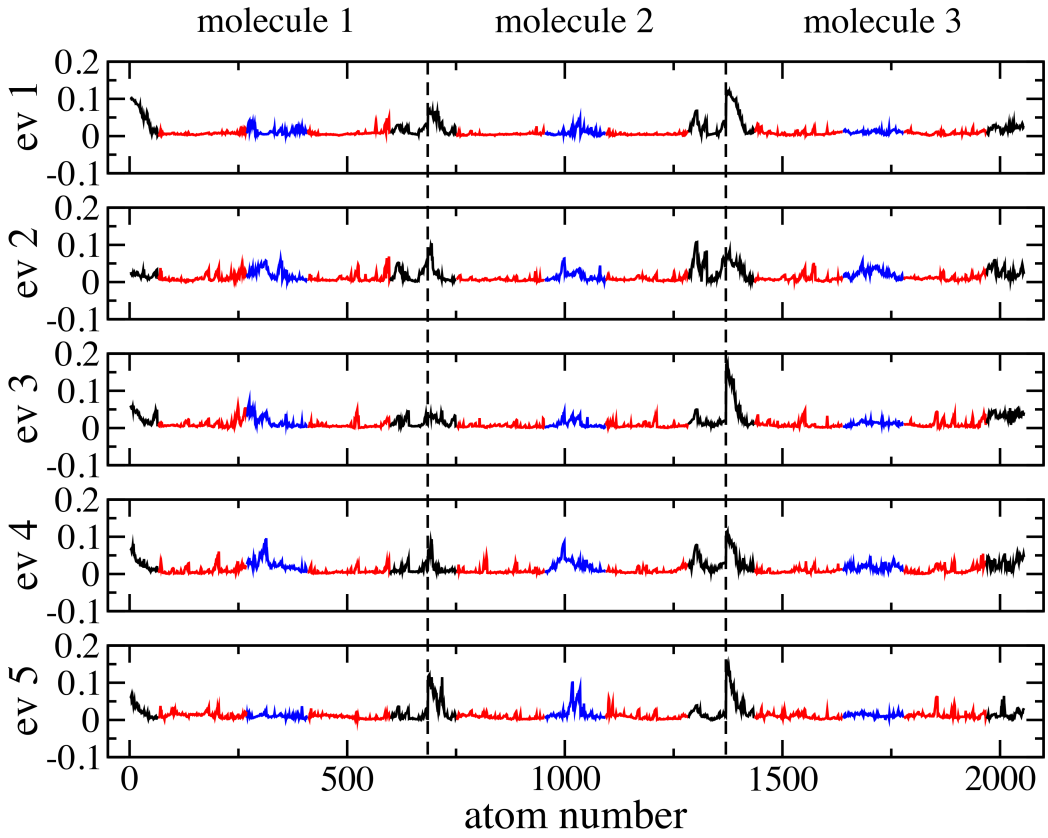
Backbone N-H order parameters for the bottom molecule 1, middle molecule 2 and top molecule 3 of the HET-s trimer calculated from the MD simulations at 298 K. β strands and the loop between them are shaded in gray. β-strands and the loop between β2 and β3 are shaded in gray.

Figure S5



Backbone N_{i+n}-H_i (n = 1,2,3,4) order parameters for the bottom molecule 1, middle molecule 2 and the top molecule 3 of the HET-s trimer determined from the simulations of the HET-s trimer at 298 K.

Figure S6



Atomic contributions to the first five eigenvectors from the terminal (black), core (red) and loop (blue) atoms of HET-s trimer at 298 K. Atom numbers 1-65 correspond to the terminal residues 218-224, atom numbers 66-268 to the core residues 225-244, atom numbers 269-408 to the loop residues 245-260, atom numbers 409-598 to the core residues 261-280, and atom numbers 590-685 to the terminal residues 281-288.

Table S1

Percentages of hydrogen bonds in the loops of molecule 1, 2 and 3 of the HET-s trimer at 298 K. Only hydrogen bonds with populations greater than 5% are shown.

Hydrogen Bond	Loop 1	Loop 2	Loop 3
248ALA:NH – 246THR:O			5.2
249ALA:NH – 246THR:OG1	11.9	15.9	
249ALA:NH – 246THR:O	10.2	62.4	
249ALA:NH – 252GLY:O			9.7
250LEU:NH – 246THR:O	25.9		
250LEU:NH – 247ALA:O	14.6		
250LEU:NH – 248ALA:O	9.1		
252GLY:NH – 249ALA:O			10.1
252GLY:NH – 250LEU:O	23.7		
252GLY:NH – 251HIS:O	6.6		
253ILE:NH – 252GLY:O			21.7
255ARG:NH – 253GLY:O	18.0		
257SER:NH – 251HIS:NE2		13.5	
257SER:OGHG – 251HIS:NE2		27.3	
257SER:NH – 255ARG:O		6.2	
257SER:OGHG – 256ILE:O	9.2		
258ASP:NH – 258ASP:OD1		5.2	
258ASP:NH – 258ASP:OD2		6.75	30.4
260GLN:NE2HE22 – 257SER:O			8.7
260THR:NH – 258ASP:OD1	15.4		
260THR:NH – 258ASP:OD2	5.2		
260THR:OG1HG1 – 258ASP:OD1	19.7		
260THR:NH – 259GLN:NE2		6.5	

Table S2

Average Cα chemical shifts of the HET-s trimer calculated using the program SHIFTX2[1] from the simulations of the HET-s trimer at 298 K and 323 K and of the "free loop" at 323 K, and Cα chemical shift values from the initial structure, and measured and random coil values.

Residue	Molecule 1			Molecule 2			Molecule 3			"Free Loop"	Exp.[2]	Random coil[3]
	298 K	323 K	Initial struct.	298 K	323 K	Initial struct.	298 K	323 K	Initial struct.	323 K		
219ILE	60.8	60.8	60.8	60.8	60.7	60.8	60.9	60.8	60.9			60.6
220ASP	53.7	54.8	53.8	54.4	54.5	54.5	54.3	54.3	53.9			54.1
221ALA	51.8	52.6	53.3	52.1	52.1	53.2	52.2	52.6	51.4			52.7
222ILE	60.8	60.6	59.7	61.1	61.1	60.2	60.7	60.8	60.9		62.0	
223VAL	61.6	61.2	60.6	61.8	62.8	61.4	62.7	62.6	64.8		59.1	
224GLY	46.0	45.2	46.0	45.9	45.4	46.2	45.2	45.4	43.9		43.8	
225ARG	54.7	54.9	56.0	56.4	55.2	55.9	58.2	57.9	57.9		54.7	
226ASN	52.5	52.7	52.3	52.5	52.6	52.5	52.6	52.5	52.2		52.1	
227SER	57.3	57.3	56.7	57.4	57.5	56.8	57.5	57.6	57.2		56.8	
228ALA	50.9	51.1	50.2	50.8	50.8	50.2	50.6	50.8	50.9		49.5	
229LYS	57.8	57.7	57.3	57.5	57.5	57.5	57.9	57.6	58.9		59.9	
230ASP	53.4	53.5	54.3	53.3	53.3	54.3	53.3	53.4	54.2		53.2	
231ILE	60.5	60.8	60.0	60.8	60.8	60.0	60.7	60.7	60.0		60.9	
232ARG	54.9	54.9	55.4	54.9	55.1	55.2	55.1	55.1	55.0		54.3	
233THR	60.8	60.2	60.1	61.1	61.0	61.0	60.7	61.5	61.1		59.6	
234GLU	55.1	56.0	55.3	55.2	55.4	54.3	56.9	55.4	54.8		53.8	
235GLU	57.5	58.6	57.3	57.8	57.7	57.6	56.1	58.3	57.3		58.7	
236ARG	57.0	57.1	56.6	57.1	56.2	56.6	56.9	56.8	57.1		54.8	
237ALA	51.6	52.3	50.7	52.6	52.4	51.7	51.5	51.9	52.0		53.2	
238ARG	54.5	54.2	54.4	55.1	54.9	54.7	55.0	55.9	54.6		54.7	
239VAL	61.4	61.6	61.0	60.3	61.1	60.9	61.0	62.1	60.9		60.0	
240GLN	55.0	55.1	55.0	54.4	54.4	54.6	54.4	54.6	54.6		52.8	

241LEU	54.4	54.4	53.3	54.1	54.1	53.3	53.8	54.2	53.0		52.8	
242GLY	45.5	45.3	45.1	44.7	45.1	45.2	45.4	45.2	45.1		43.8	
243ASN	52.2	53.3	53.1	51.4	52.1	53.2	51.8	52.0	52.8		51.3	
244VAL	62.2	61.9	61.2	61.5	62.1	62.0	61.2	61.0	61.2		62.1	
245VAL	62.3	61.6	61.2	61.1	61.6	61.1	61.3	60.7	61.1		61.1	
246THR	62.5	61.7	61.2	60.9	60.5	61.2	63.2	62.0	61.3	62.3	62.4	62.0
247ALA	53.3	51.7	55.0	54.5	54.3	54.6	52.1	53.8	54.7	53.0	56.2	52.7
248ALA	53.4	52.8	54.1	52.8	53.5	53.9	51.8	53.1	53.8	52.3	55.1	52.7
249ALA	53.4	53.7	53.8	51.5	52.3	53.1	51.3	51.8	53.4	52.3	53.9	52.7
250LEU	54.5	55.1	56.1	53.9	55.4	56.6	57.2	54.6	54.0	55.1	58.4	54.8
251HIS	56.4	56.0	56.5	55.0	55.4	56.4	55.7	55.5	56.4	55.5		55.8
252GLY	45.6	45.3	45.4	45.3	45.1	45.4	45.4	45.4	45.4	45.7		45.3
253GLY	45.0	45.5	44.8	45.2	45.0	44.6	45.4	45.3	45.4	45.7		45.3
254ILE	61.1	61.5	62.6	61.5	60.8	60.1	60.9	61.5	62.9	61.0		60.6
255ARG	55.4	57.5	56.9	55.5	56.9	55.1	54.8	55.5	56.1	55.8		56.0
256ILE	60.4	60.0	60.1	60.8	60.3	60.3	59.8	60.5	62.5	61.2		60.6
257SER	58.1	58.1	59.4	58.2	57.8	58.6	58.0	58.6	57.5	58.5		58.4
258ASP	53.4	55.9	52.6	54.8	54.4	54.8	55.0	55.5	54.1	54.3		54.1
259GLN	55.9	56.6	55.8	54.2	54.6	55.2	56.8	56.1	56.5	55.5	55.0	56.0
260THR	63.1	61.0	60.9	62.2	62.4	64.1	61.3	61.9	60.9	62.1	66.2	61.6
261THR	61.8	62.0	61.8	62.2	62.6	61.4	62.3	61.8	62.1	62.7	61.2	61.6
262ASN	52.8	52.3	52.2	52.3	52.8	52.2	52.2	52.3	52.2		52.4	
263SER	57.6	57.4	57.3	57.5	57.5	57.5	57.3	57.4	57.5		56.5	
264VAL	60.9	60.8	59.4	60.3	60.5	59.5	60.3	60.4	59.2		57.1	
265GLU	58.0	58.2	57.8	57.8	57.9	58.2	58.2	58.3	57.4		59.5	
266THR	61.3	61.3	62.1	61.2	61.4	61.8	61.2	61.2	60.7		60.9	
267VAL	61.6	61.5	61.1	61.6	61.8	61.1	61.6	61.7	60.3		60.7	
268VAL	61.5	61.5	61.1	61.4	61.6	61.2	61.1	61.0	60.9		61.2	
269GLY	45.1	45.0	45.0	44.7	45.1	45.0	45.1	45.4	44.7		44.6	
270LYS	55.0	55.1	54.6	55.0	55.1	54.7	55.1	55.5	54.8		54.3	
271GLY	46.2	46.1	46.2	46.3	45.6	46.1	46.3	46.0	46.3		48.5	
272GLU	57.4	55.8	56.8	56.4	56.4	56.8	56.1	57.1	57.0		54.2	
273SER	58.2	58.4	57.6	58.1	58.1	58.2	58.4	58.5	58.2		59.3	
274ARG	54.8	55.0	55.2	55.3	55.7	55.2	55.3	55.4	55.3		54.9	
275VAL	61.3	61.3	61.1	61.4	61.7	61.0	60.8	61.0	60.9		60.3	

276LEU	54.2	54.2	53.5	54.1	54.1	53.4	53.4	53.6	53.6	52.7	
277ILE	60.3	60.3	60.1	60.2	60.3	60.1	60.1	60.3	59.9	58.7	
278GLY	45.2	44.7	44.7	45.6	45.4	44.3	45.1	45.4	44.5	44.0	
279ASN	51.7	52.8	52.9	52.7	51.9	52.3	52.3	52.3	51.7	51.9	
280GLU	55.1	55.2	54.4	55.2	55.4	54.5	55.7	58.0	54.8	54.6	
281TYR	56.4	57.5	56.3	56.9	57.3	55.7	57.3	57.8	56.7	56.1	
282GLY	45.5	45.1	45.2	44.4	44.6	45.2	45.9	45.3	44.6	46.1	
283GLY	45.8	46.1	45.4	46.0	46.2	46.1	45.4	46.3	44.9	43.9	
284LYS	56.5	56.1	56.1	55.8	57.0	57.5	55.8	56.7	56.0	57.3	
285GLY	44.9	45.5	45.7	45.8	45.4	45.2	45.2	45.6	46.0	44.3	
286PHE	57.5	57.4	57.7	58.0	57.1	58.7	58.1	57.2	57.0	59.7	
287TRP	58.1	57.8	59.8	57.6	60.0	58.1	57.1	58.2	59.8	57.4	
288ASP	54.5	54.0	53.9	53.5	54.9	53.6	54.5	54.5	54.1		54.1
289ASN	54.6	54.6	54.4	54.5	54.8	54.6	54.7	54.5	54.3		53.0

References:

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