Conformational Dynamics of the Human Islet Amyloid Polypeptide in a Membrane Environment – towards the Aggregation Prone Form

Supporting information

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Table S1. Fraction of secondary structure during the simulations determined using STRIDE[1].[a]

Peptide	His18	Membrane (lipids)	Helix (%)[b]	β (%)[c]	Coil (%)[d]
$hIAPP_{1-37}$	HSD/E	HMMM (49)[e]	27	3	71
$hIAPP_{1-37}$	HSP	HMMM (49)	42	0	58
$hIAPP_{1-37}$	HSD/E	-	24	0	75
$hIAPP_{1-37}$	HSP	-	29	0	70
$hIAPP_{1-19}$	HSD/E	HMMM (36)	23	0	77
$hIAPP_{1-19}$	HSP	HMMM (36)	19	0	81
$hIAPP_{20-37}$	-	HMMM (36)	6	1	93

[a] The first 20 ns of each simulation were excluded from the analysis.

[b] The helical fraction comprises α-, 3_{10}- and π-helices.

[c] β-structure comprises isolated β-bridges and larger β-sheet structures.

[d] Coil comprises coil and turn structure.

[e] Lipids in each leaflet.

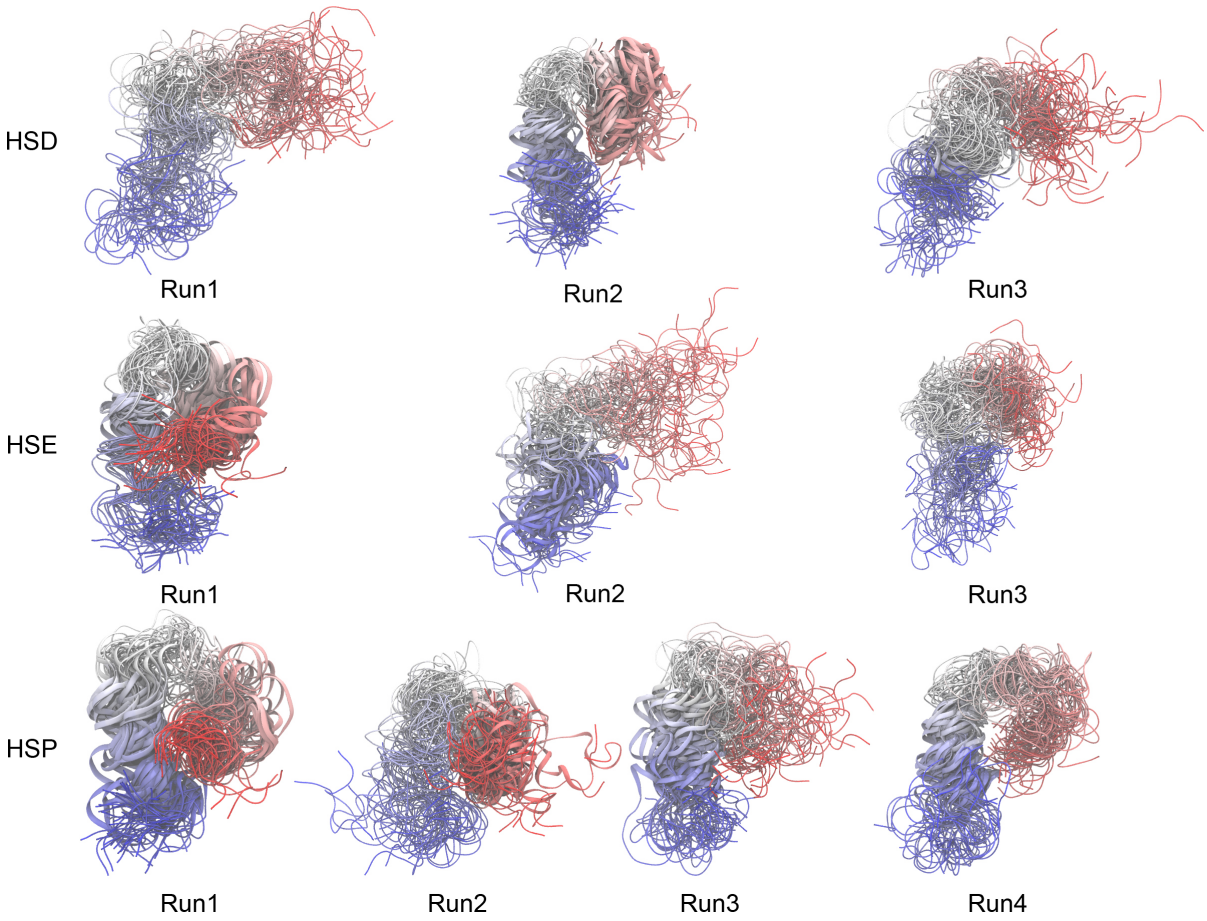

Figure S1. Alignment of hIAPP$_{1\text{-}37}$ structures from simulations of the peptide in water without a membrane. Snapshots were taken every 1 ns, and the structures were aligned by the Cα atoms. The N-terminal is colored blue and the C-terminal is red.

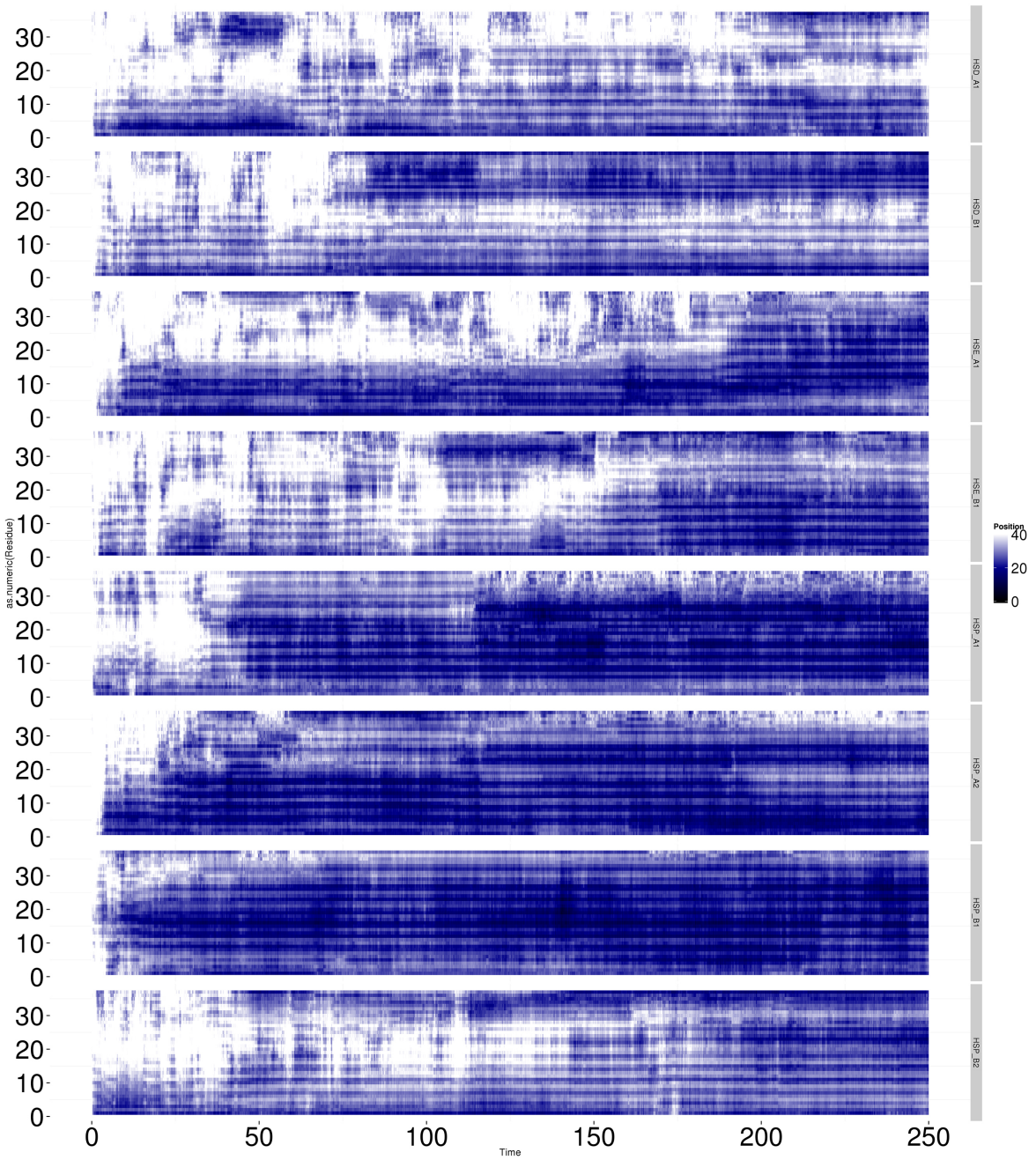

Figure S2. The z-coordinate of the center of mass of each residue side chain for the hIAPP1-37 simulations. The center of the membrane is at z = 0 Å and the average position of the phosphates is at z = 18 Å. Data points with z > 40 Å are white.

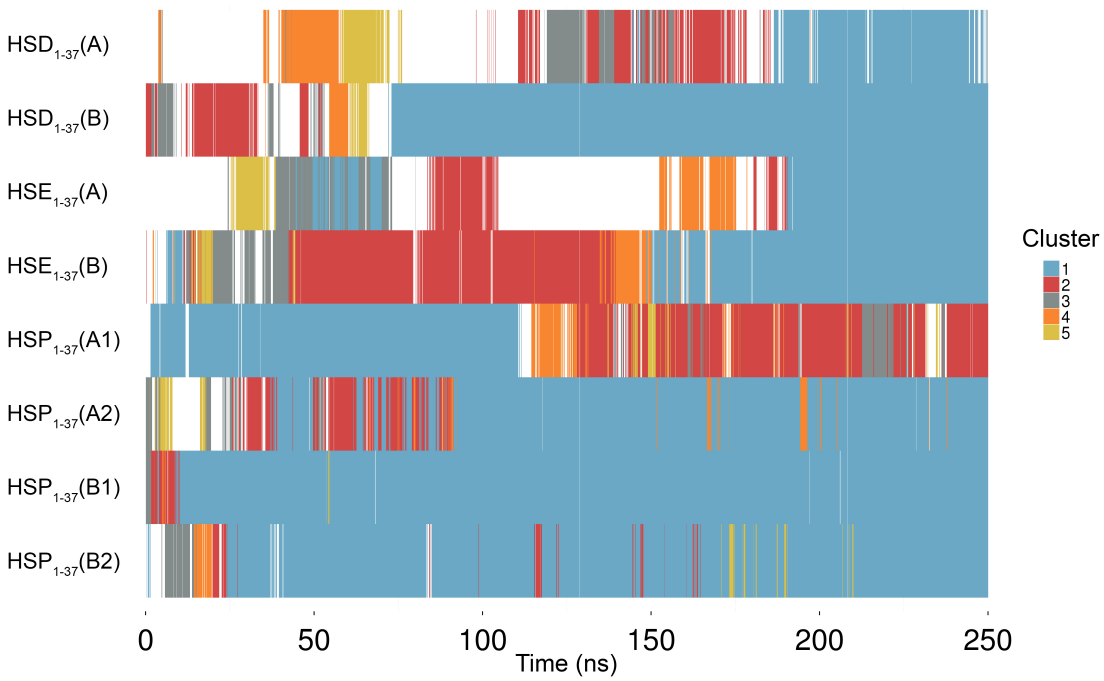

Figure S3. Clustering analysis of the hIAPP$_{1\text{-}37}$(HMMM) simulations. The sizes of the clusters decrease from cluster 1 to 5. Peptide conformations were taken at every 0.1 ns, i.e. 2500 snapshots from each simulation. The clustering was performed using VMD's clustering algorithm with a cutoff of 5 Å on the Cα RMSD, and a maximum number of 5 clusters.

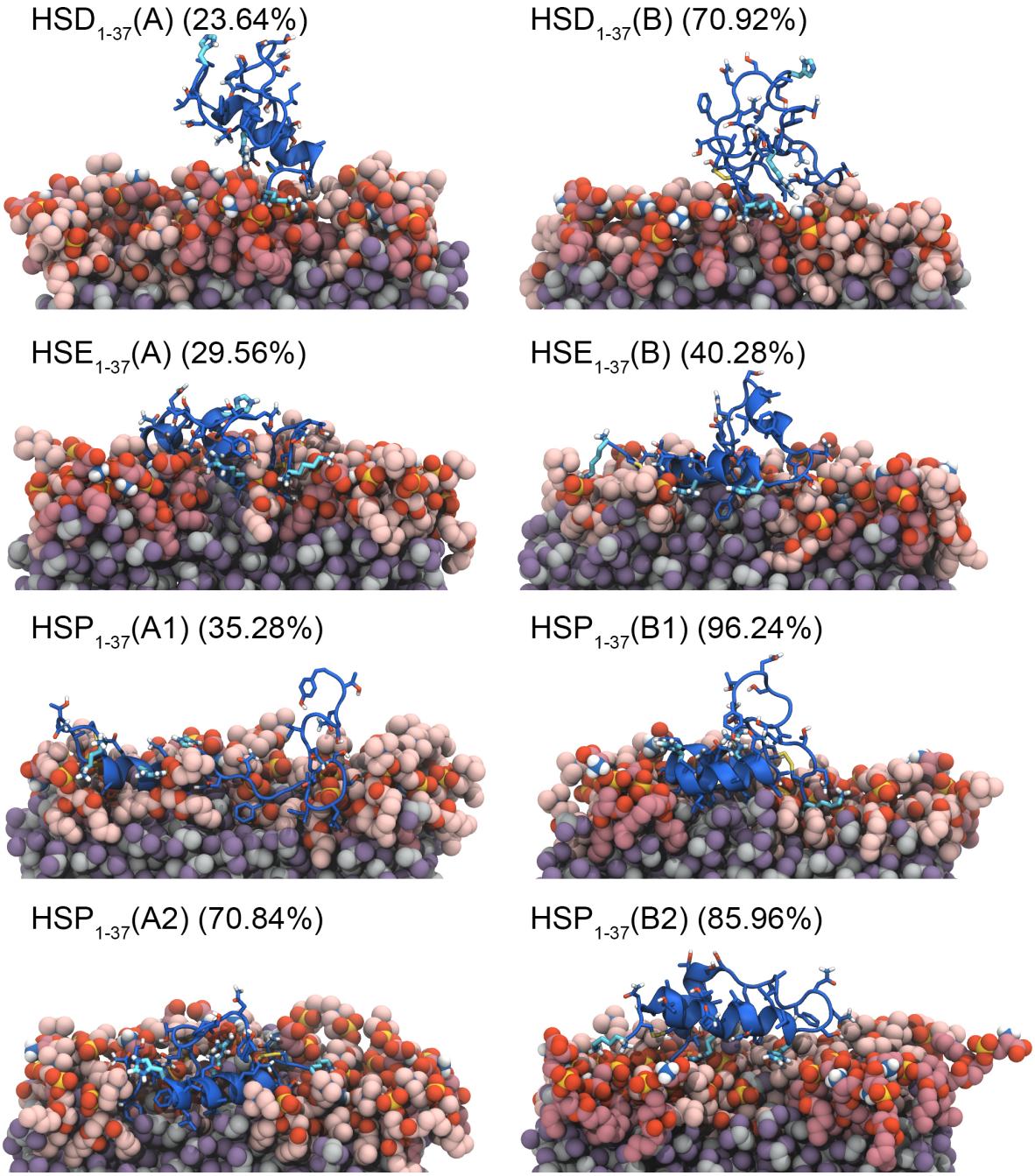

Figure S4. Representative of the largest cluster of all hIAPP$_{1-37}$ peptides ,except HSP$_{1-37}$(A1), bound to the HMMM membrane. The HSP$_{1-37}$(A1) structure is the representative of the second largest cluster. The cluster which is shown, contains the final structure of the simulation. The lipids are shown in red colors, DCLE is shown in grey and purple, and the protein is shown in dark blue. The percentage of structures in the largest cluster is written in parenthesis after the name of the simulation.

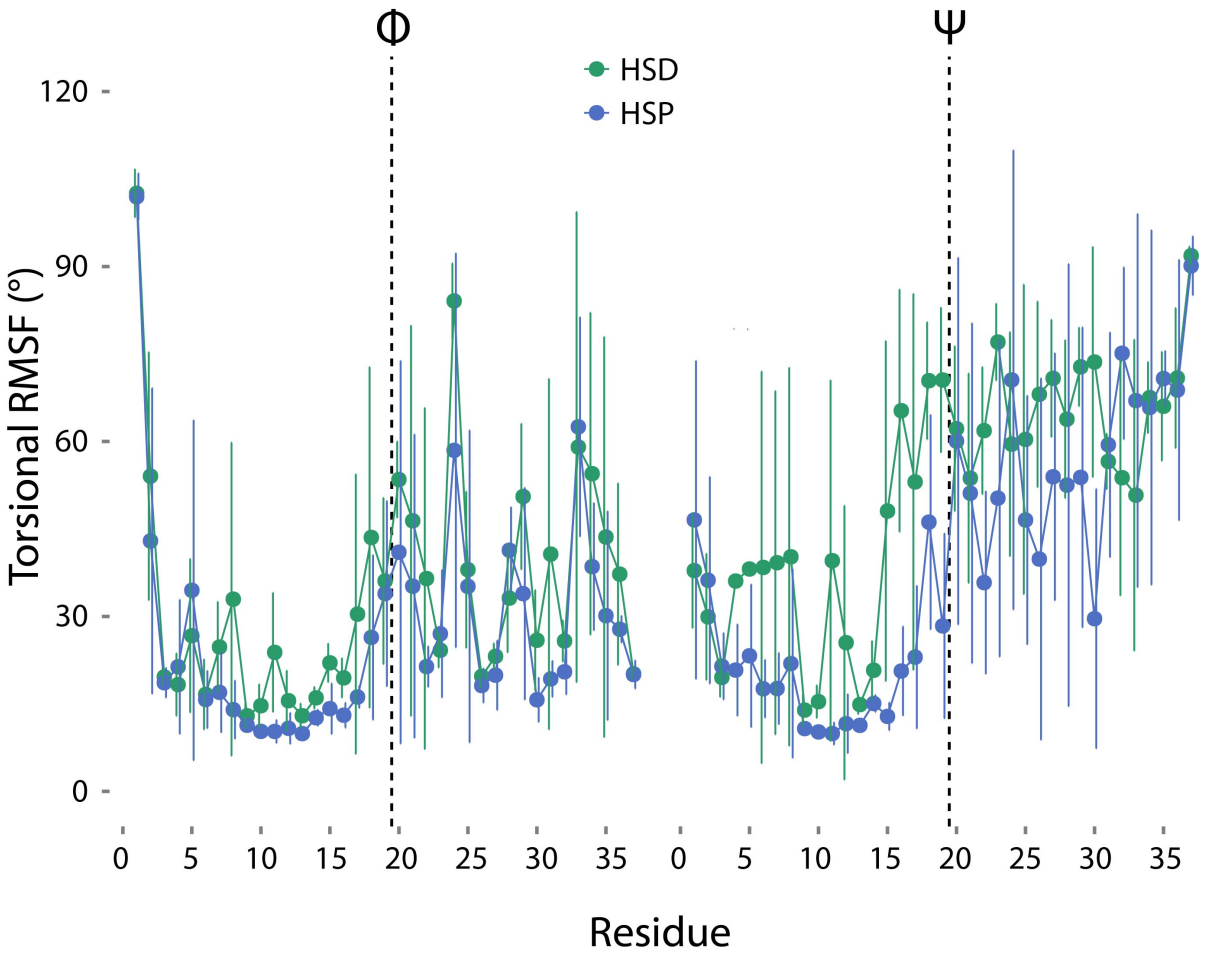

Figure S5. Torsional RMSF of the hIAPP$_{1-37}$ HMMM backbone Φ and Ψ angles with standard deviations included between the individual runs for each system.

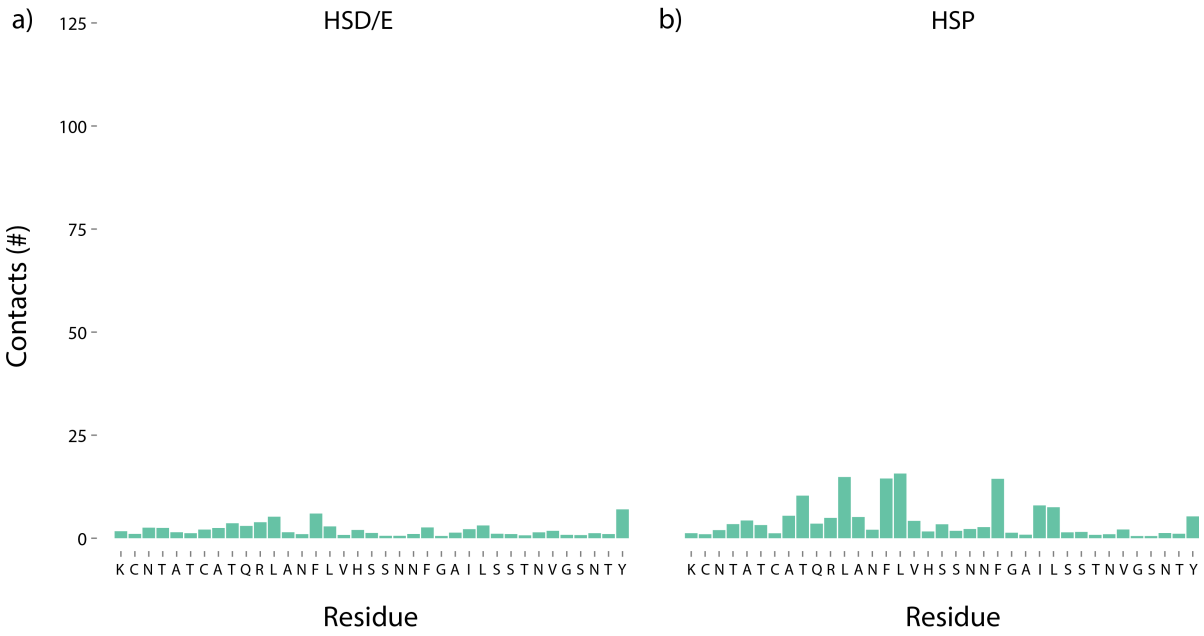

Figure S6. Average heavy atom contacts within 5 Å between DCLE and the peptide for the hIAPP$_{1\text{-}37}$-HMMM simulations excluding the first 20 ns.

References

1. Frishman, D., and Argos, P. (1995) Knowledge-based protein secondary structure assignment. *Proteins: Struct., Funct., Genet. 23*, 566-579.