Could Microwave Irradiation Cause Misfolding of Peptides? - Supporting Material

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Figures

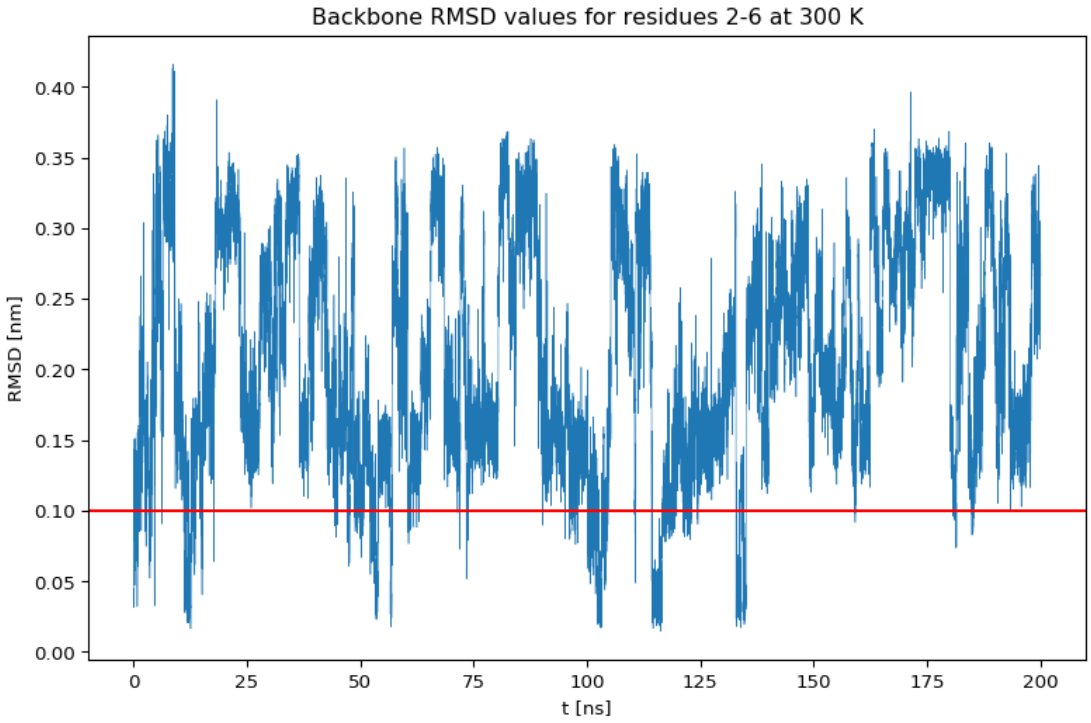

Figure S1: Backbone atom-positional RMSD values plot as a function of time for the simulation at 300 K. The 0.1 nm cutoff RMSD value between the folded and unfolded structures is depicted with a red line.

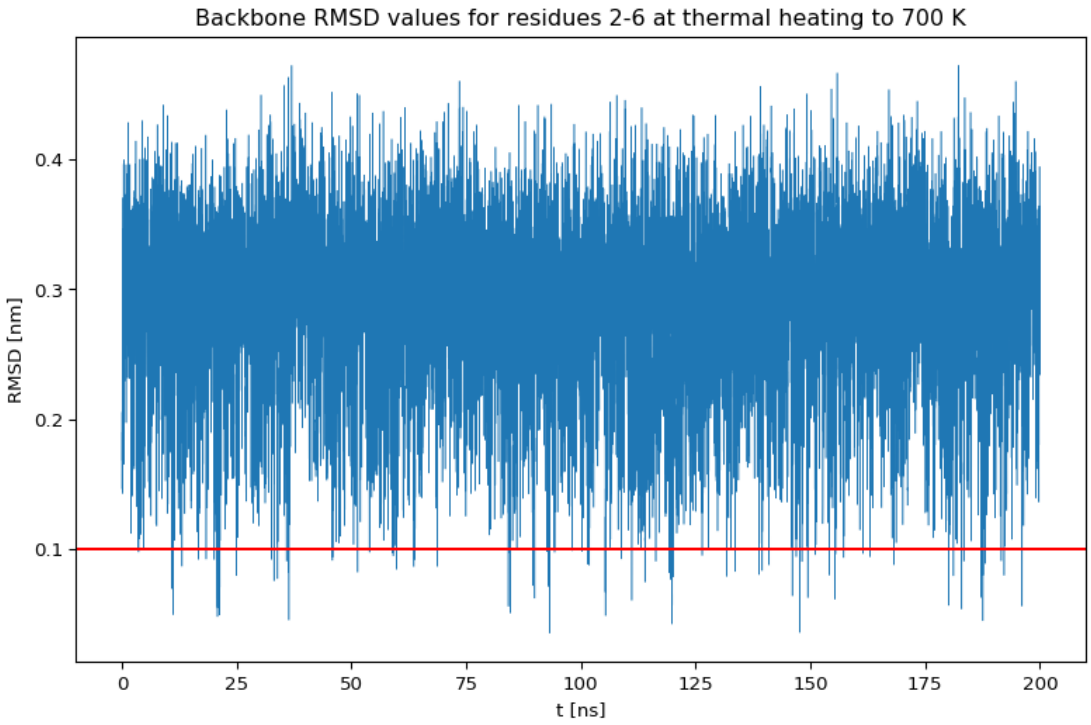

Figure S2: Backbone atom-positional RMSD values plot as a function of time for the simulation of thermal heating to 700 K. The 0.1 nm cutoff RMSD value between the folded and unfolded structures is depicted with a red line.

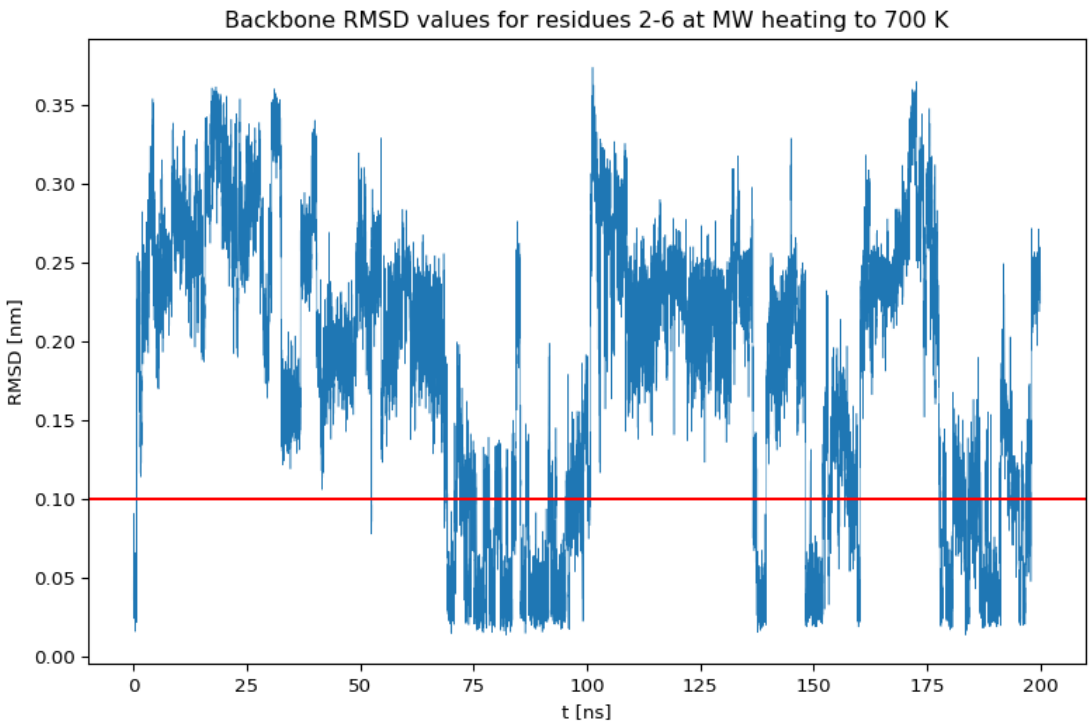

Figure S3: Backbone atom-positional RMSD values plot as a function of time for the simulation of MW heating to 700 K. The 0.1 nm cutoff RMSD value between the folded and unfolded structures is depicted with a red line.

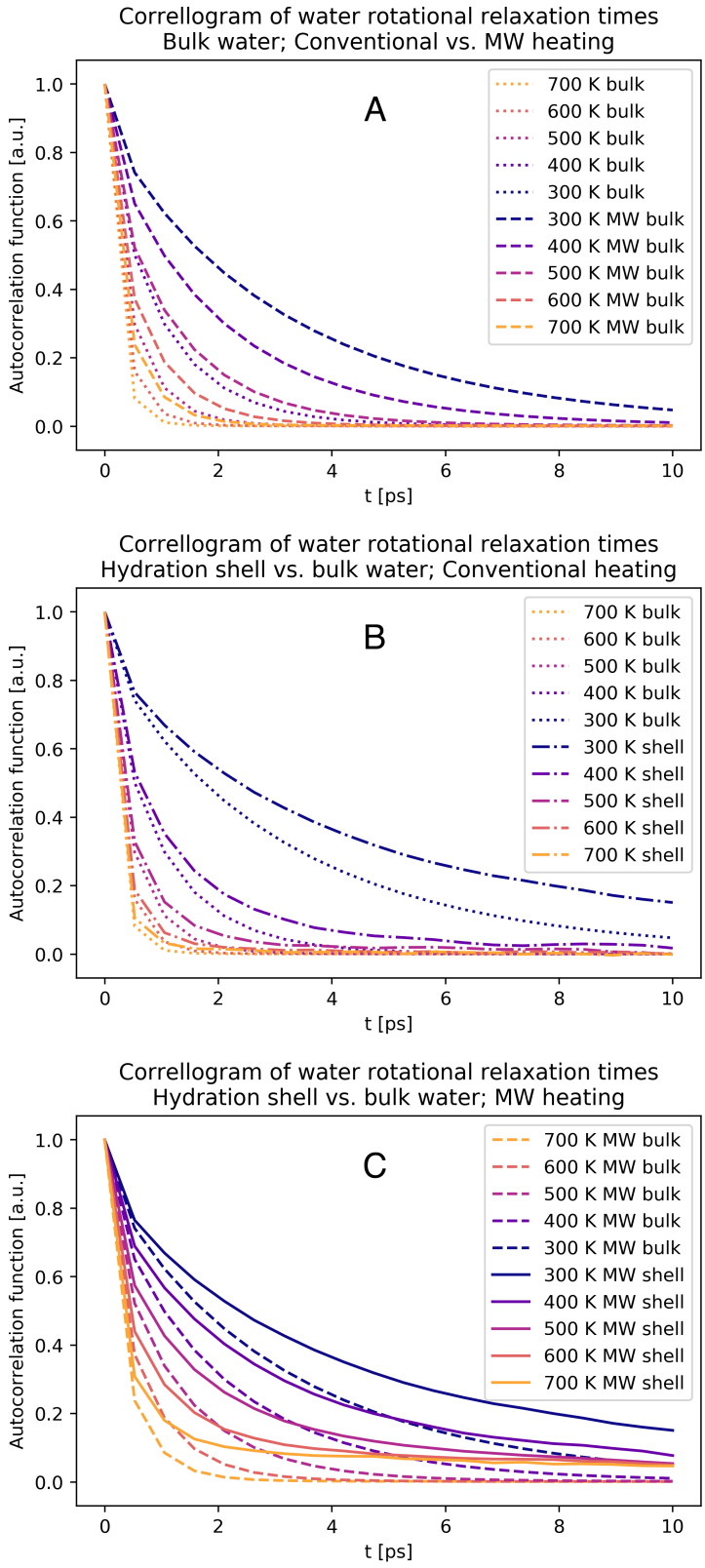

Figure S4: Correllograms of the rotational relaxation times of water molecules. The autocorrelation functions were calculated using the first-order Legendre polynomial of molecular axis aligned with the water molecule's dipole vector[1]. A (top): Comparison of the bulk solvent using conventional heating and microwave heating. B (middle): Comparison of the hydration shell and the bulk solvent using conventional heating. C (bottom): Comparison of the hydration shell and the bulk solvent using MW heating.

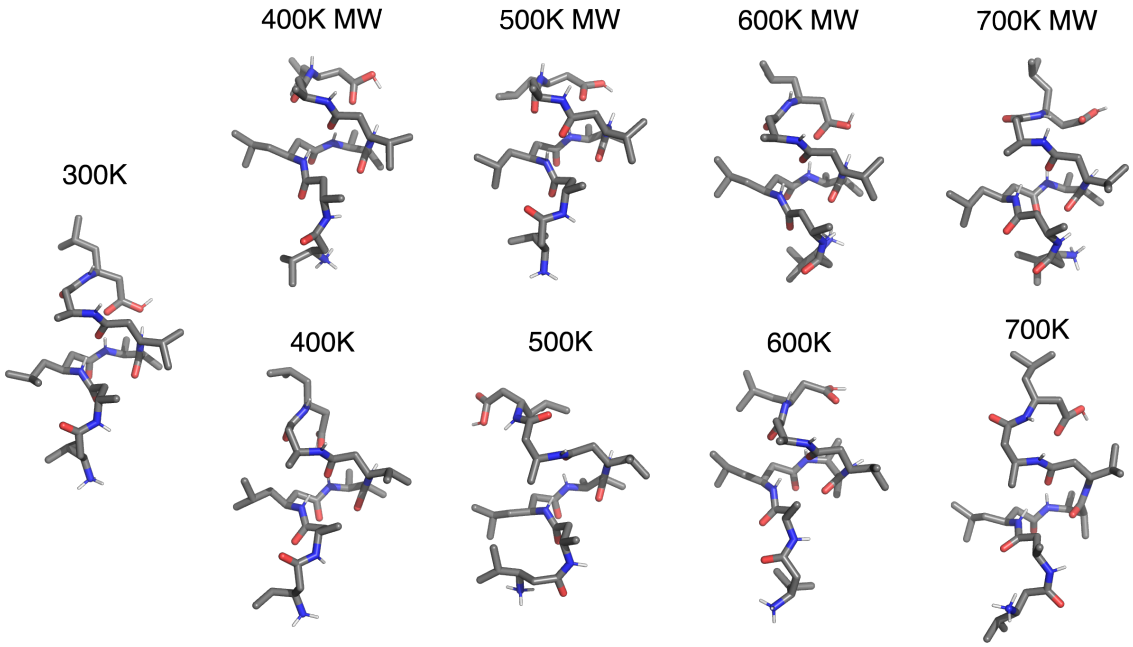

Figure S5: Central member structures of the most stable cluster for each simulation. The temperature labels 300 K – 700 K denote the systems at equilibrium temperature while the labels 400 K MW – 700 K MW denote rotationally heated systems.

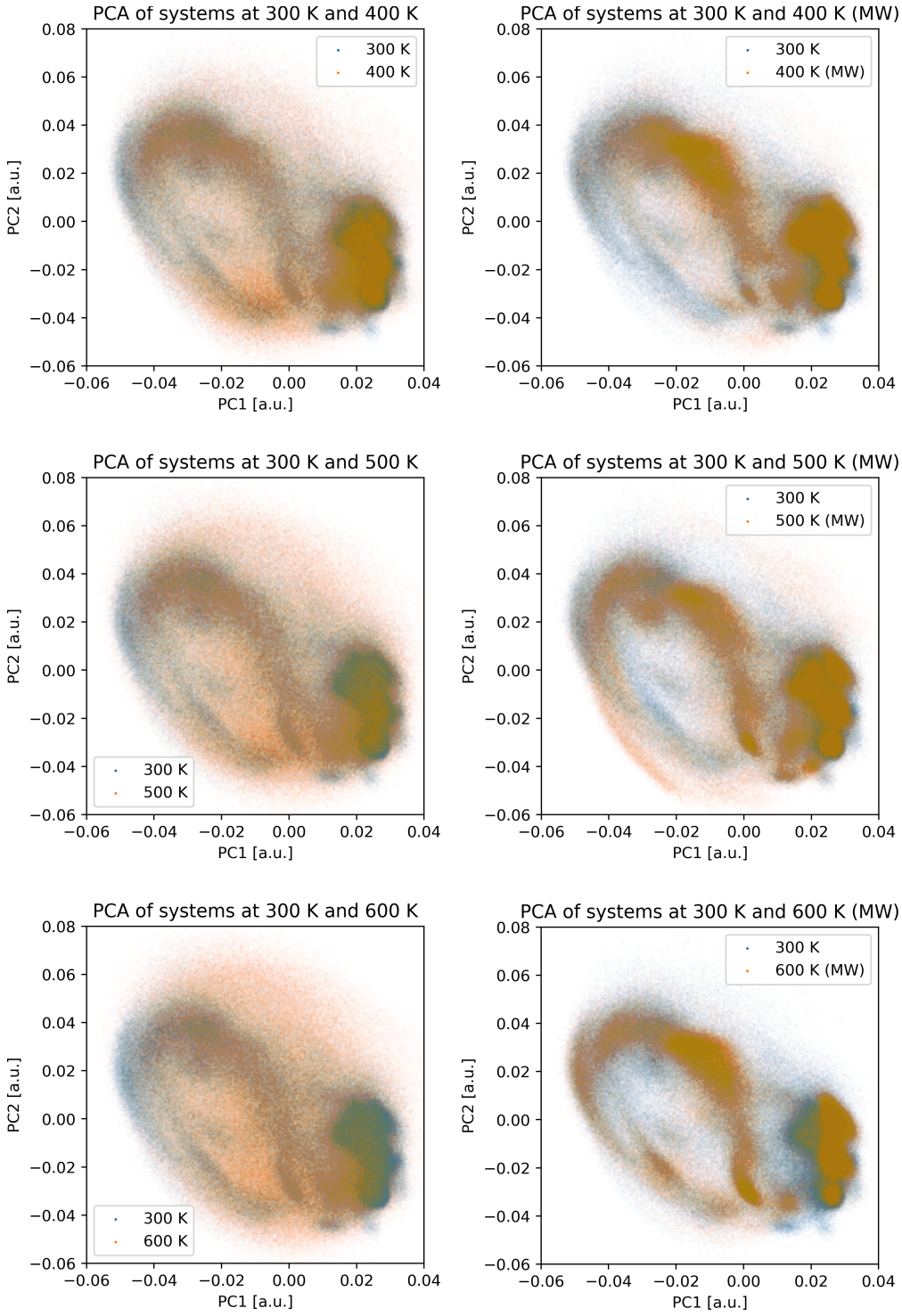

Figure S6: Principal component analysis of the combined clustering of systems at equilibrium temperature of 300 K, conventionally and MW heated up to 400 K (top row), 500 K (middle row) and 600 K (bottom row). The first and second principal component form the x and y axis of the scatter plots, respectively. On each plot, the trajectory at equilibrium 300 K is depicted with blue dots and the trajectory at an elevated temperature is depicted with orange dots.

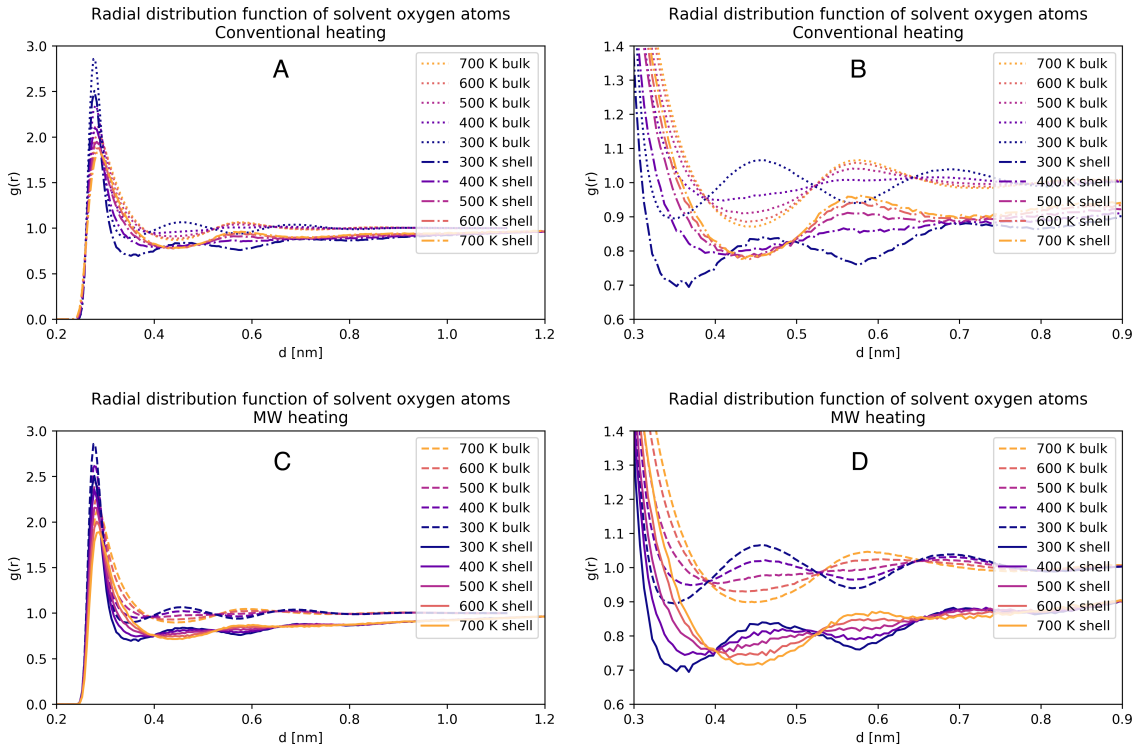

Figure S7: Radial distribution functions (RDFs) of the water oxygen atoms. A, B (top): Comparison of RDFs between the hydration shell and bulk water for the simulations of conventional heating. C, D (bottom): Comparison of RDFs between the hydration shell and bulk water for the simulations of MW heating.

Tables

Table S1: Relative lifetimes of the most stable cluster

T_T / T_R [a] [K]	rel. lifetime [%] [b]
700 / 700	1.1
600 / 600	2.1
500 / 500	4.6
400 / 400	9.6
300 / 300	20.6
300 / 400	19.1
300 / 500	17.7
300 / 600	32.0
300 / 700	29.7

[a] Translational (T_T) and rotational (T_R) temperature of the solvent during MD simulation.
[b] Relative lifetime of the most stable cluster, calculated as the ratio of the number of cluster members to the total number of trajectory snapshots.

Table S2: Relative occurrences of peptide intramolecular hydrogen bonds

donor residue	acceptor residue	relative occurrence [%] [a]	helix-forming
Cluster 1			
1	3	6.9	*
2	4	55.6	*
3	5	86.1	*
4	6	40.4	*
4	7	31.5	
5	7	20.9	*
Cluster 2			
1	3	13.2	*
1	4	8.2	
4	5	5.1	
4	6	64.9	*
4	7	9.9	
5	7	42.6	*
Cluster 3			
1	6	8.1	*
3	1	5.1	
3	6	10.3	
3	7	20.7	
4	6	6.6	
4	6	70.7	
Cluster 4			
1	3	13.5	*
1	4	29.2	
1	5	36.7	
2	5	5.9	
2	6	19.3	
3	6	61.3	
3	7	6.8	
4	7	5.7	
Cluster 5			
1	3	58.8	*
4	5	55.6	

[a] Calculated as a ratio between the snapshots containing the particular hydrogen bond and the total number of snapshots. Only the hydrogen bonds present in at least 5% of the snapshots are reported.

References

(1) Eichenberger, A. P.; Allison, J. R.; Dolenc, J.; Geerke, D. P.; Horta, B. A.; Meier, K.; Oostenbrink, C.; Schmid, N.; Steiner, D.; Wang, D.; Van Gunsteren, W. F. GROMOS++ software for the analysis of biomolecular simulation trajectories. *J. Chem. Theory Comput.* **2011**, *7*, 3379–3390.