Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supporting Information

Caffeine Destabilizes Preformed Aβ Protofilament: Insights from All Atom Molecular Dynamics Simulations

Shivani Gupta[1] and Ashok Kumar Dasmahapatra[1,2*]

[1]Department of Chemical Engineering and [2]Center for Nanotechnology, Indian Institute of Technology Guwahati, Guwahati - 781039, Assam, India.

[*] Corresponding author: Phone: +91-361-258-2273; Fax: +91-361-258-2291; Email address: akdm@iitg.ac.in

Table S1- CFF.itp as obtained from SWISS-PARAM

nr	type	resnr	resid	atom	cgnr	charge	mass
1	NPYL	1	LIG	N1	1	0.0476	14.0067
2	C5A	1	LIG	C2	2	0.0365	12.011
3	N5B	1	LIG	N2	3	-0.5653	14.0067
4	C5B	1	LIG	C3	4	0.2902	12.011
5	C5A	1	LIG	C4	5	-0.2366	12.011
6	C=O	1	LIG	C5	6	0.715	12.011
7	NC=O	1	LIG	N3	7	-0.4201	14.0067
8	C=O	1	LIG	C6	8	0.69	12.011
9	NC=O	1	LIG	N4	9	-0.4231	14.0067
10	CR	1	LIG	C1	10	0.2556	12.011
11	O=C	1	LIG	O1	11	-0.57	15.9994
12	O=C	1	LIG	O2	12	-0.57	15.9994
13	CR	1	LIG	C7	13	0.3001	12.011
14	CR	1	LIG	C8	14	0.3001	12.011
15	HCMM	1	LIG	H1	15	0	1.0079
16	HCMM	1	LIG	H2	16	0	1.0079
17	HCMM	1	LIG	H3	17	0	1.0079
18	HCMM	1	LIG	H4	18	0.15	1.0079
19	HCMM	1	LIG	H5	19	0	1.0079
20	HCMM	1	LIG	H6	20	0	1.0079
21	HCMM	1	LIG	H7	21	0	1.0079

22	HCMM	1	LIG	H7	22	0	1.0079
23	HCMM	1	LIG	H9	23	0	1.0079
24	HCMM	1	LIG	H10	24	0	1.0079

The topology file for the ligand has been retrieved from SWISS-PARAM which is readable by GROMACS. This helps in combining coordinates of protein and ligand together in one topology file for the simulation of Protein-Ligand complex.

Figure S1: Correlation between the theoretical and experimental NMR chemical shifts for Cα and Cβ atoms of Aβ42 protofibril structure is shown in panel a, and b, respectively. The unit of NMR chemical shift is ppm

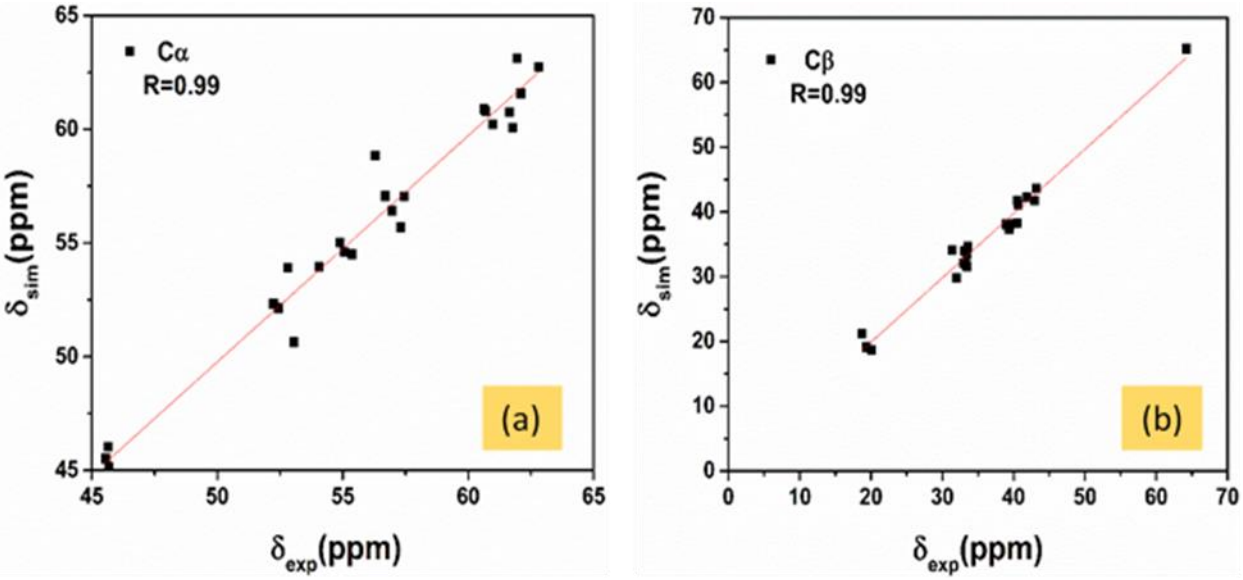

Figure S2: Comparison of simulated 3JHN-Hα coupling constants of the Aβ42 residues (red) with experimental measurements

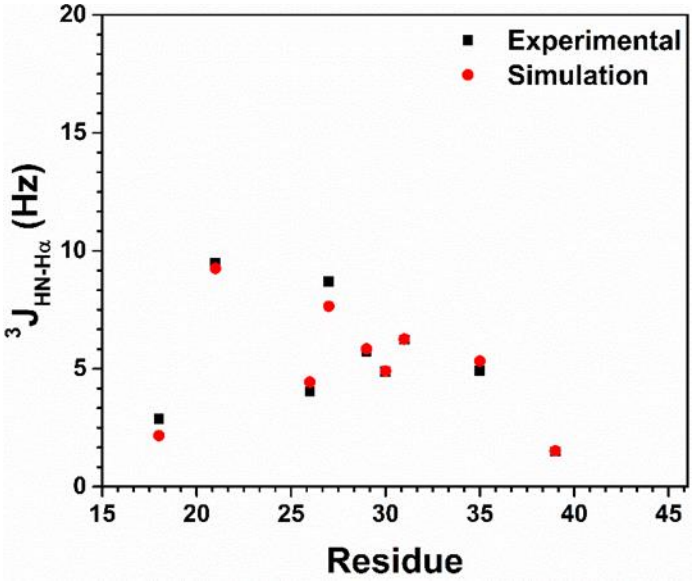

Figure S3: Statistical significance of all three simulation runs by Mean and standard deviation across R_g for all three sets in Aβ-CFF for 100 ns.

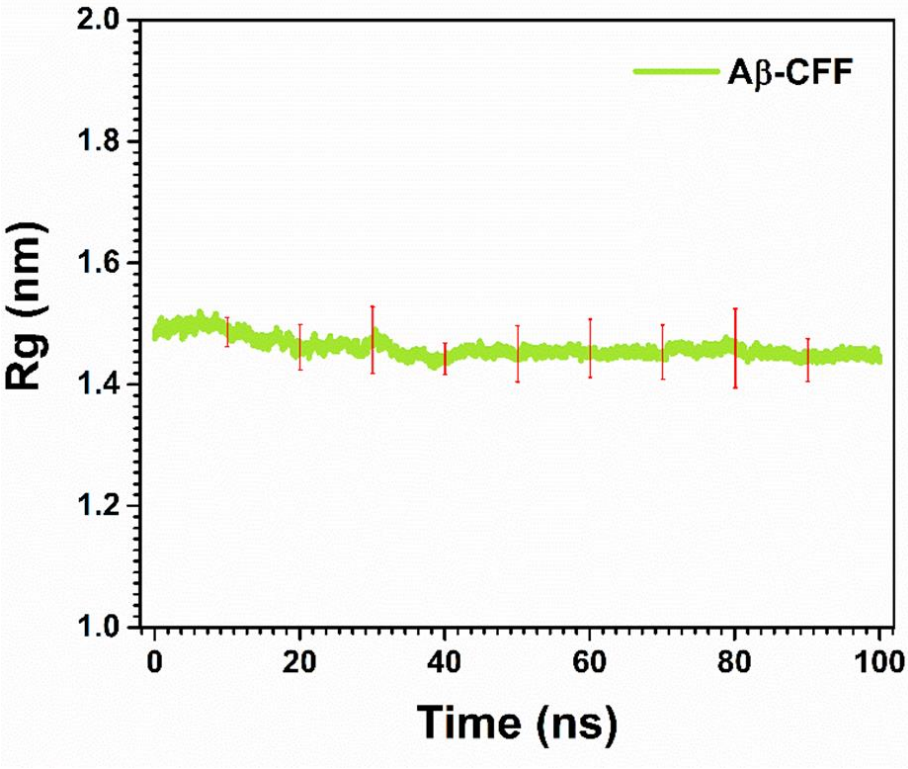

Table S2: Secondary structure component statistics for $A\beta_{17-42}$ protofibril–Caffeine complex with three sets of simulations

The helix$^{\alpha}$ is the sum of α– and 3_{10}– helices

Secondary structure component(%)	$A\beta_{17-42}$ protofibril-Water (Average over 3 Sets)	$A\beta_{17-42}$ protofibril-CFF complex (simulation 1)	$A\beta_{17-42}$ protofibril-CFF complex (simulation 2)	$A\beta_{17-42}$ protofibril-CFF complex (simulation 3)
Coil	31	37	38	44
β-Sheet	51	33	44	37
β-Bridge	1	4	3	3
Bend	12	17	11	11
Turn	2	5	1	2
Helix$^{\alpha}$	0	2	0	0
Chain_Separator	3	3	3	3

A movie showing destabilization effect of caffeine on Aβ protofibril