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

Supporting Material

Microsecond molecular dynamics simulation of guanidinium chloride induced unfolding of ubiquitin

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Running Title: Guanidinium chloride induced unfolding of ubiquitin.

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Supporting Material Text

We performed another independent simulation of ubiquitn in ~ 6 M Gdmcl solutions upto ~600ns. The solution contains one ubiquitin molecule in the centre along with 2632 water and 710 guanidinium chloride molecules with a box size of nearly 58 Å × 58 Å × 58 Å. All other simulation processes are same as mentioned in main manuscript. Time evolution plots of R_g and RMSD(shown in figure S3 and figure S4) and visual inspection through VMD confirms unfolding process through several intermediate structures like microsecond simulation in main manuscript.

Control simulation:

Control Molecular dynamics simulation of ubiquitin was performed using similar box size as mentioned in main manuscript and 3701 water molecules. Further we calculated time evolution plot of Backbone root mean square deviation (RMSD) [shown in fig. S1], Radius of gyration (R_g) of backbone alpha carbon atoms (shown in fig. S2) and Solvent accessible surface area (SASA)[shown in fig. S3] but did not found any significant change. RMSD plot shows only little fluctuation (average value ~2.5Å) probably due to temperature effect. Almost no change in R_g value (average value ~11.35Å) shows no change in compactness and also reflected from SASA value plot. We have calculated the salt-bridge distance between nitrogen (N) atom of Lys11 and oxygen(OE2) atom Glu34 and shown in fig. S4 which shows salt – bridge interaction is maintained, although distance plot shows fluctuation which signifies that this salt – bridge interaction is weak in nature which is also shown in main text. Our results signify that guanidinium ion induced unfolding of ubiquitin is not due to artifacts of force – field.

R_g of hydrophobic core:

Ubiquitin contains a hydrophobic core which is defined by the hydrophobic residues M1, I3, V5, T13, L15, V17, and V26. To study the time evolution conformational change of hydrophobic core of ubiquitin, we have calculated R_g value of backbone alpha carbons of these residues of ubiquitin .Plot shows only little fluctuation but no sharp change before ~350ns of simulation but large change after ~350ns and further time evolution shows harmonic behavior i.e. alternating unfolding and folding of hydrophobic core. Visualization of the trajectory indicates that the N-terminal beta hairpin gets separated from the alpha helix and C – terminal regions after ~400ns and again comes closer and goes far away such phenomenon occurs for several times after unfolding which is reflected in time evolution R_g plot of hydrophobic core [fig. 1.c) in main test]. R_g plot hydrophobic core also confirms the probability of existence of a pre-folding state of ubiquitin just before sudden jump of R_g value.

Supporting Information Figure Legends

FIGURE S1. Free-energy landscape constructed from R_g (Y-axix) vs RMSD (X-axix). The color is scaled by Kcal/mol and shown in right-side.

FIGURE S2. One dimensional free energy plot constructed from RMSD values.

FIGURE S3. Time evolution plot of Radius of gyration (R_g) for second independent simulation of ubiquitin in ~6M Gdmcl solution.

FIGURE S4. Time evolution plot of Backbone root mean square deviation (RMSD) for second independent simulation of ubiquitin in ~6M Gdmcl solution.

FIGURE S5. Time evolution plot of Backbone root mean square deviation (RMSD) for ubiquitin - pure water system.

FIGURE S6. Time evolution plot of Radius of gyration (R_g) for ubiquitin - pure water system.

FIGURE S7. Time evolution plot of Solvent accessible surface area (SASA) for ubiquitin - pure water system.

FIGURE S8. Time evolution plot of salt-bridge distance between N atom of Lys11 and OE2 atom of Glu34 for ubiquitin - pure water system.

FIGURE S9. Radial distribution functions between backbone hydrogen atom (H_B) of ubiquitin and chloride ions where solid black line, dashed red line and dotted green line represents plot from first 20ns, 410 to 430ns and last 20ns of simulation respectively.

FIGURE S10. Radial distribution functions between acidic oxygen (OE2) atom of Glutamic acids (O_E) and guanidiniums hydrogen atom (H_G) and water hydrogen (H_W) where black solid line, red dashed line and green dotted line represents H_W for first 20ns, 410 to 430ns and last 20ns of simulation respectively and solid blue line, cyan dashed line and magenta dotted line represents H_G for first 20ns, 410 to 430ns and last 20ns respectively.

FIGURE S11. The distance plot between backbone oxygen(O) of Ile44 and carbon atom of one specific guanidinium ion.

FIGURE S12. Radial distribution functions between CG atom of Lys11 (CG_{K11}) and guanidiniums carbon atom (C_G) and water oxygen (O_W) where solid black line, dashed red line, dotted green line and dashed – dotted blue line represents plot for C_G from first 5ns, 10 – 20ns, 370 – 380ns and last 20ns respectively and solid cyan line, dashed magenta line, dotted purple

line and dashed – dotted dark yellow line represents plot for H_W from first 5ns, 10 – 20ns, 370 – 380ns and last 20ns respectively.

FIGURE S13. The hydrogen bond distance plot between backbone oxygen(O) of Ilu36 and amide hydrogen(HH11) of Gln41.

FIGURE S14. Radial distribution functions between OE1 atom of Gln41 ($OE1_{Q41}$) and guanidiniums carbon atom (C_G) and water oxygen (O_W) where solid black line, dashed red line, dotted green line and dashed – dotted blue line represents plot for C_G from first 20ns, 300 – 320ns, 370 – 380ns and last 20ns respectively and solid cyan line, dashed magenta line, dotted purple line and dashed – dotted dark yellow line represents plot for H_W from first 20ns, 300 – 320ns, 370 – 380ns and last 20ns respectively.

FIGURE S15. Radial distribution functions between CB atom of Val70 (CB_{V70}) and guanidiniums carbon atom (C_G) and water oxygen (O_W) where solid black line, dashed red line and dotted green line represents plot for C_G from 300 – 320ns, 370 – 380ns and last 20ns respectively and dashed – dotted blue line, solid cyan line and dashed magenta line represents plot for H_W from from 300 – 320ns, 370 – 380ns and last 20ns respectively.

Figures

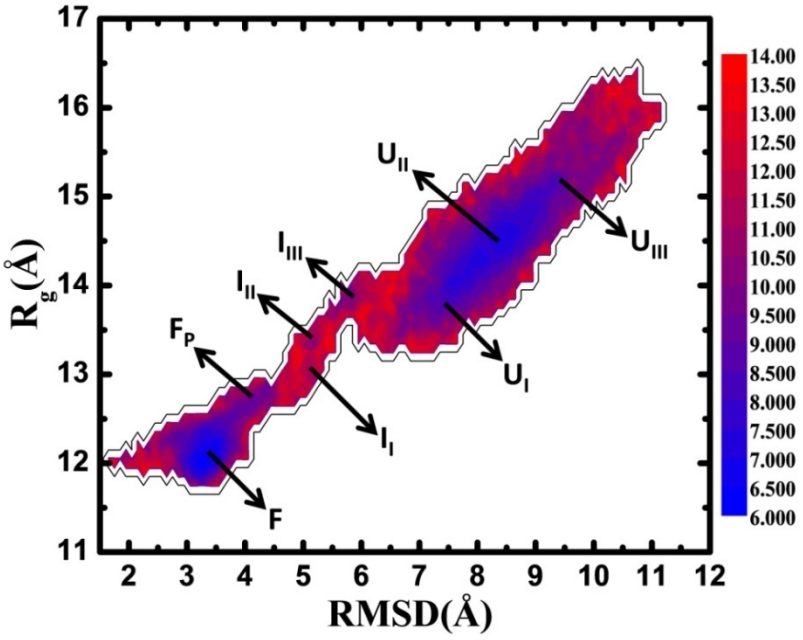
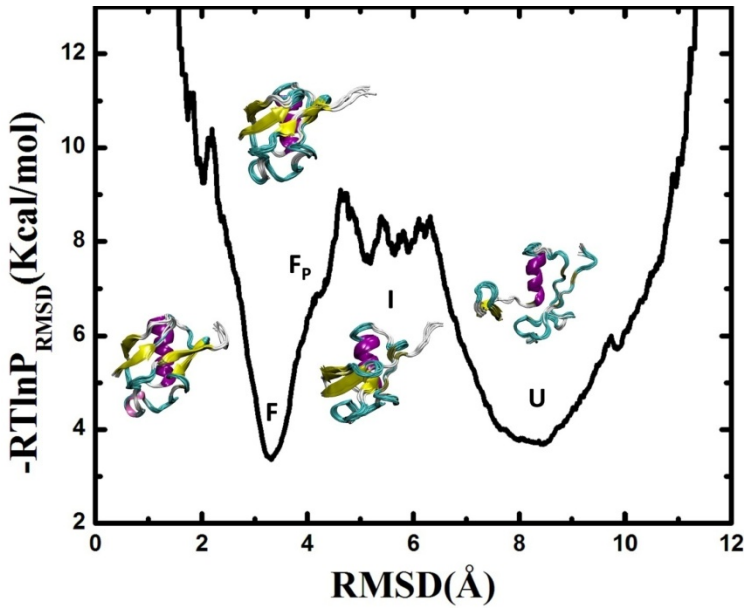


FIGURE S1.



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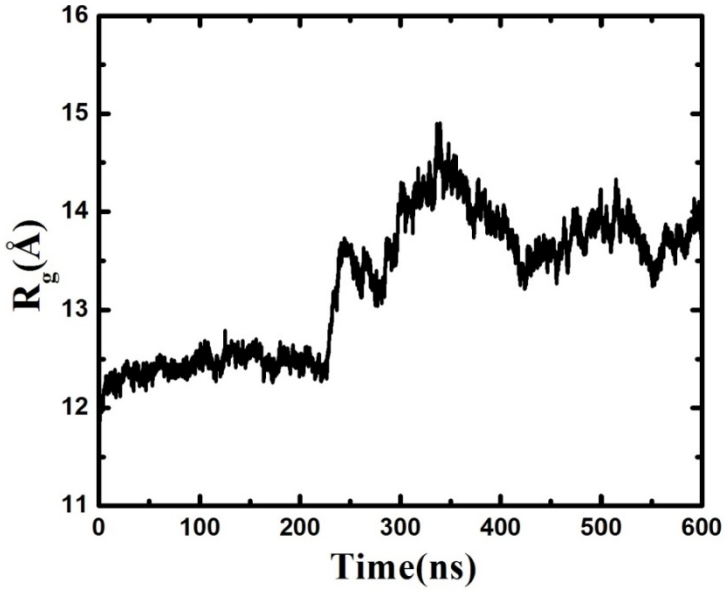
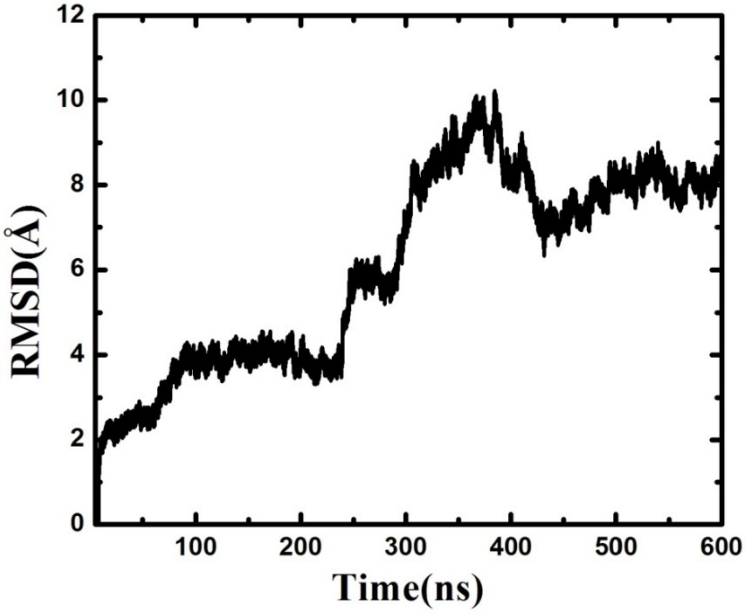


FIGURE S3.



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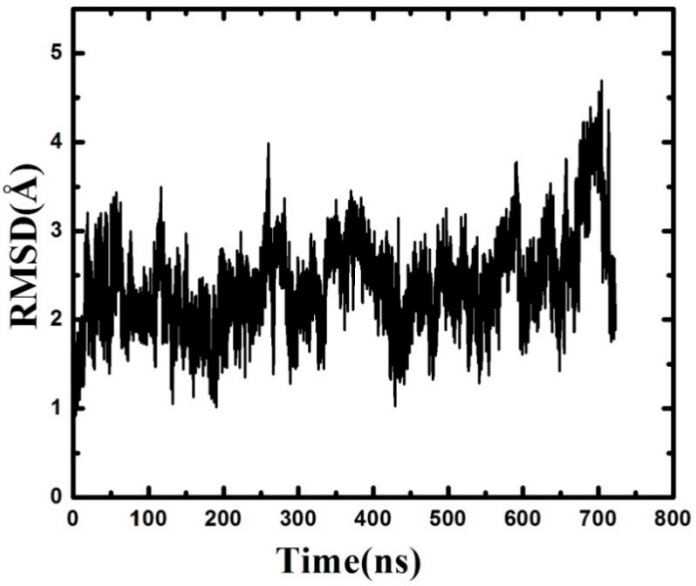

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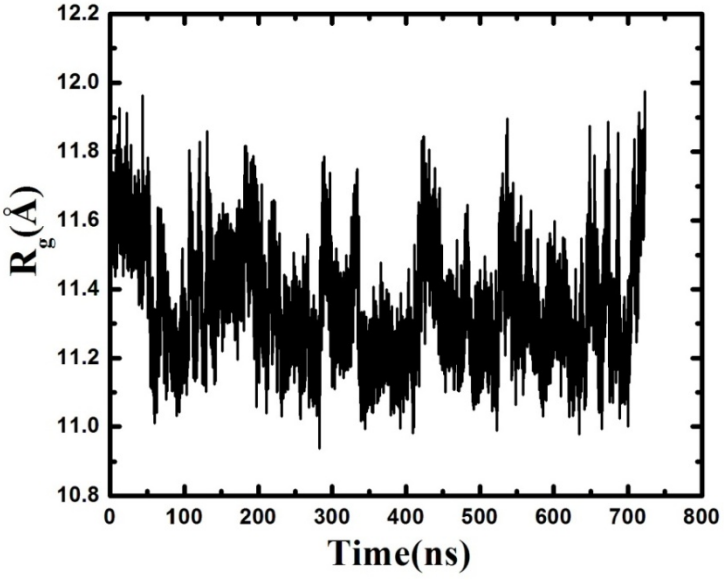

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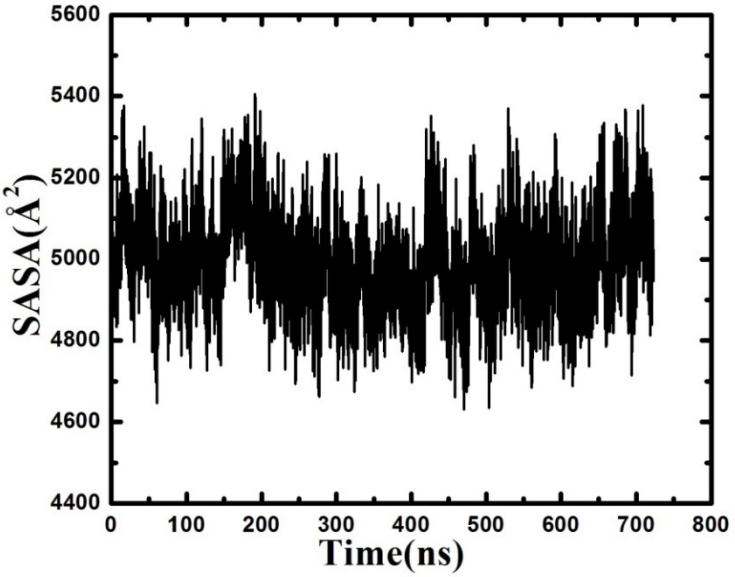

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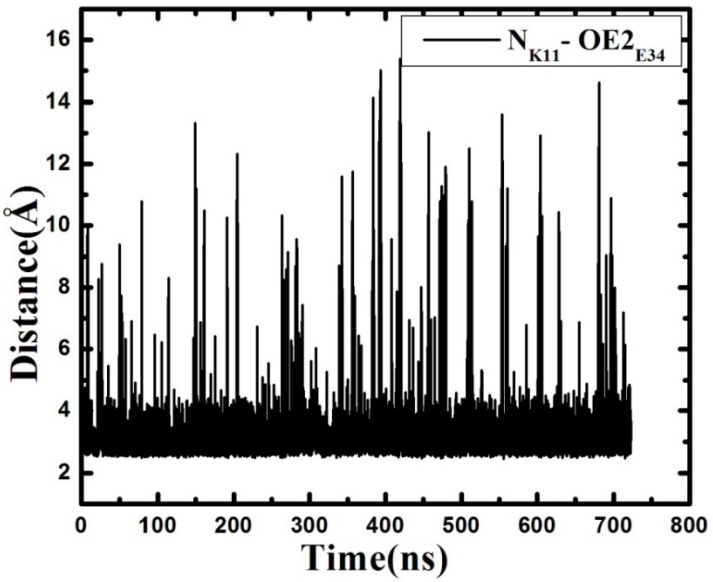

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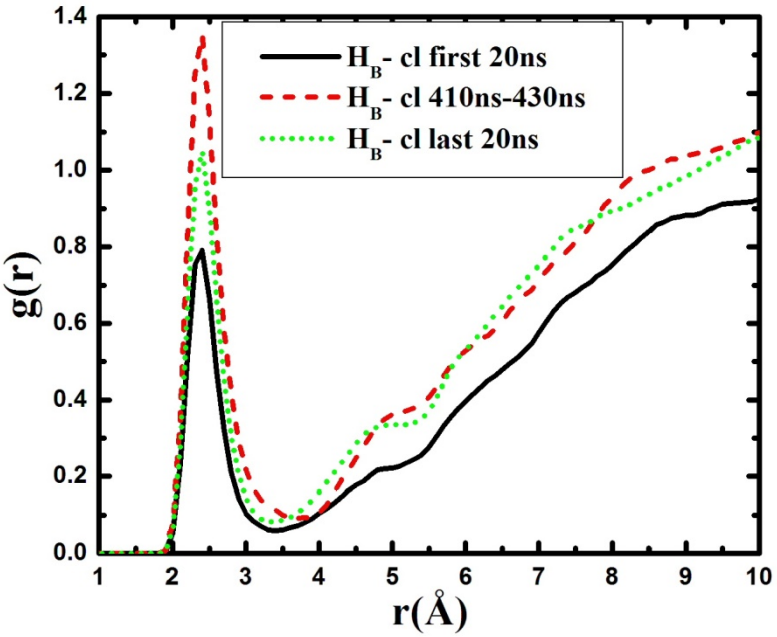
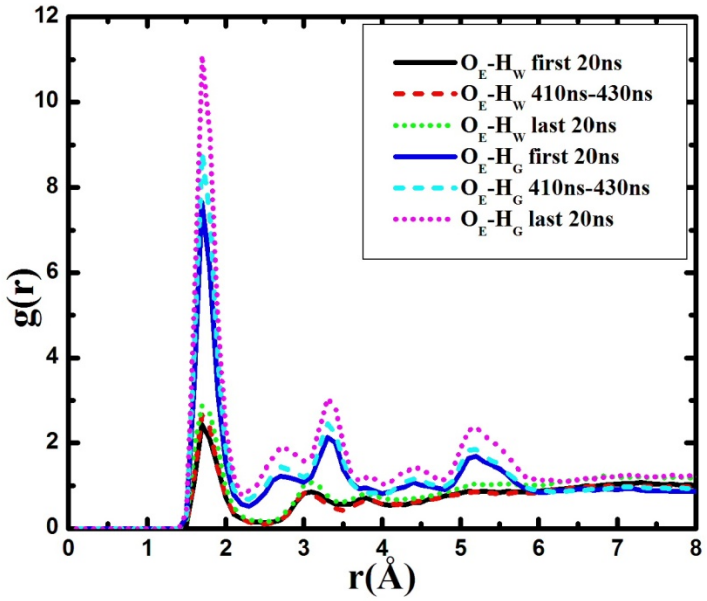

H_B- cl first 20ns
H_B- cl 410ns-430ns
H_B- cl last 20ns
g(r)
r(Å)
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
1
2
3
4
5
6
7
8
9
10

FIGURE S9.



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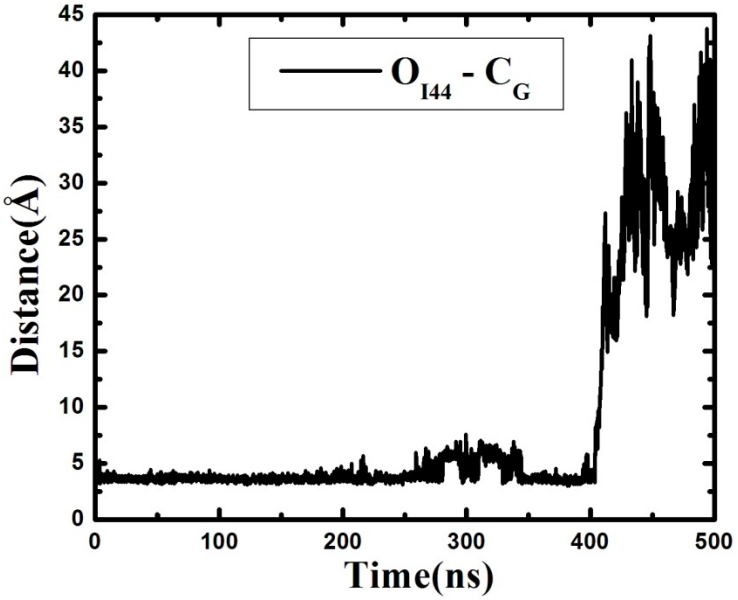
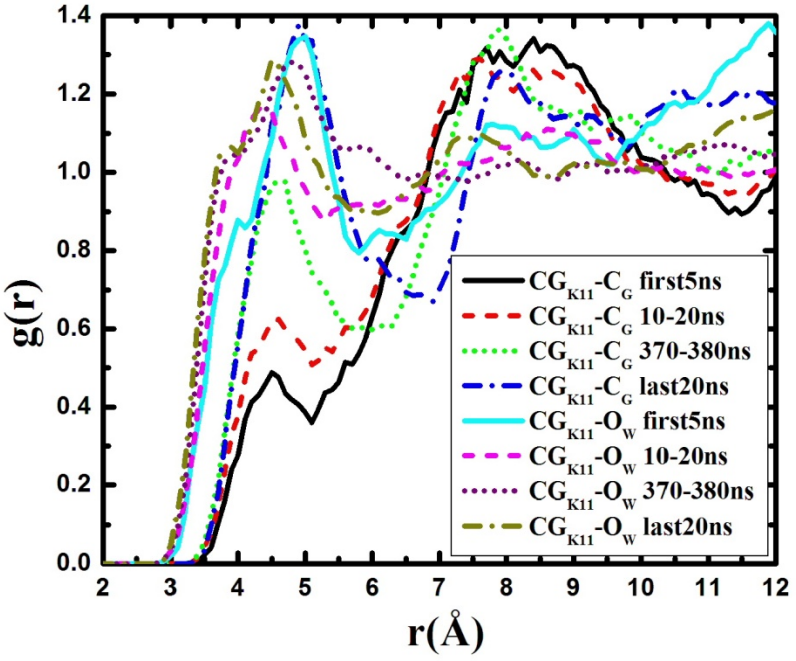


FIGURE S11.



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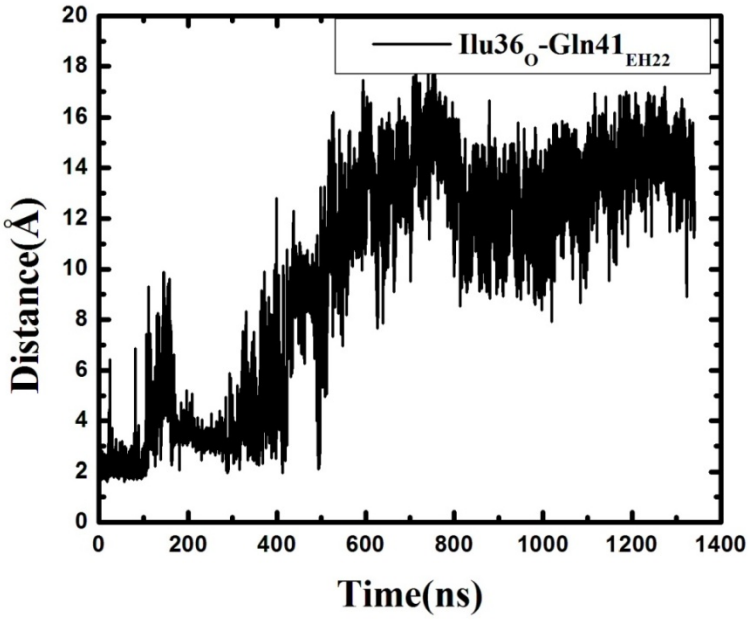

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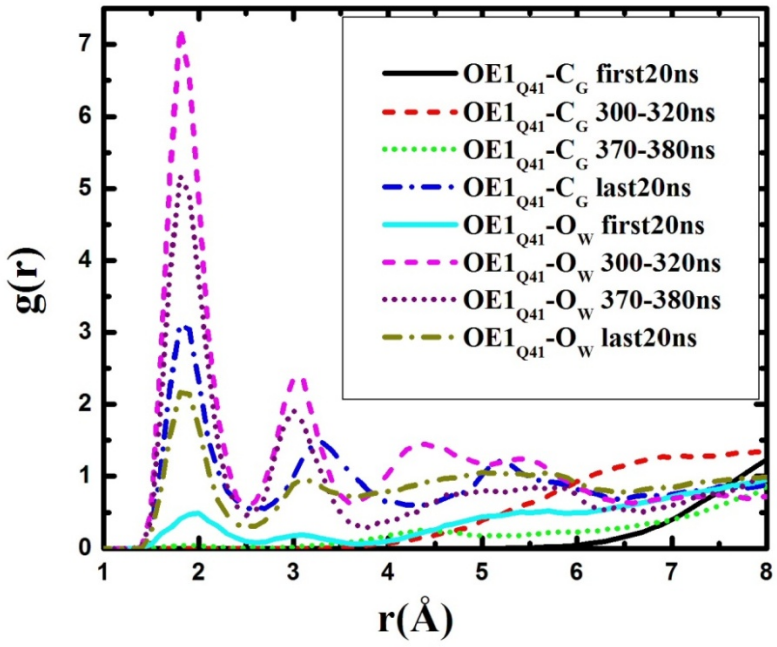

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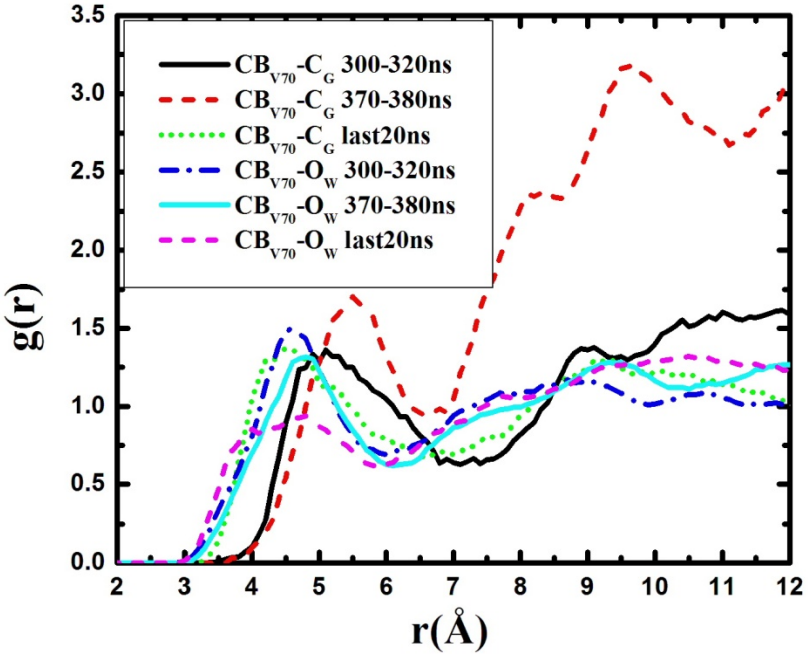

FIGURE S15.