Electronic Supplementary Material (ESI) for Nanoscale Advances.

Elucidating Collective Translocation of Nanoparticles Across the Skin Lipid Matrix: A Molecular Dynamics Study

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Supporting information

1. Single bilayer

1.1 Snapshots

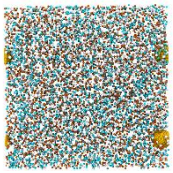
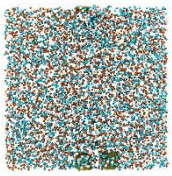
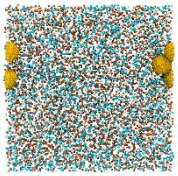
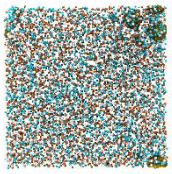
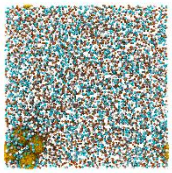
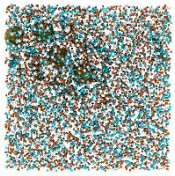
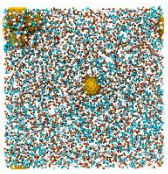
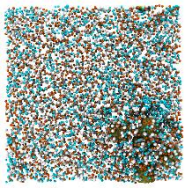
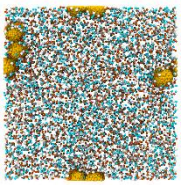
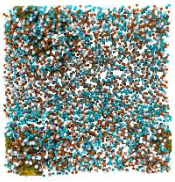
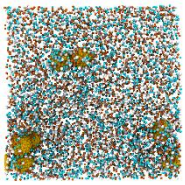
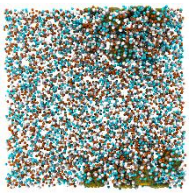
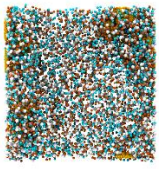
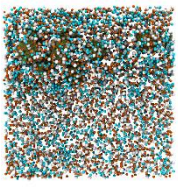
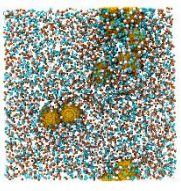
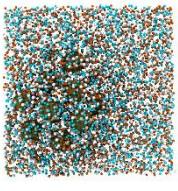
Bare		Coated	
B2		C2	
B3		C3	
B4		C4	
B5		C5	
B6		C6	
B7		C7	
B8		C8	
B9		C9	

Figure S1. Final snapshots of single bilayer-NP system after 1 μs simulation run.

1.2 Trajectories

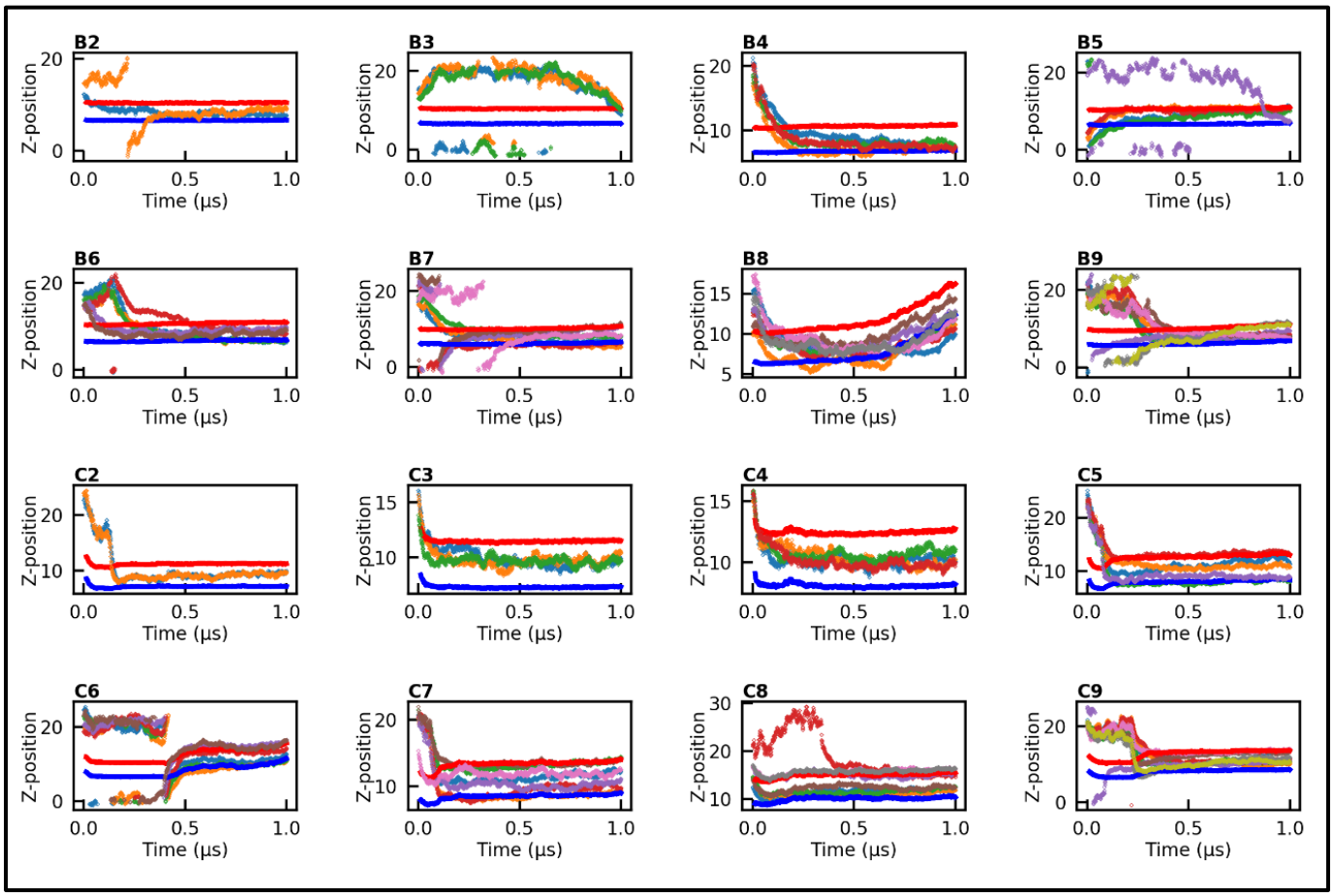


Figure S2. Time trajectories of bilayer headgroup atoms and NPs along the z direction calculated over 1 μs simulation time. The head group data for upper and lower leaflet are shown in red and blue color respectively. Individual NP trajectories are shown in other colors.

1.3 Fluctuations

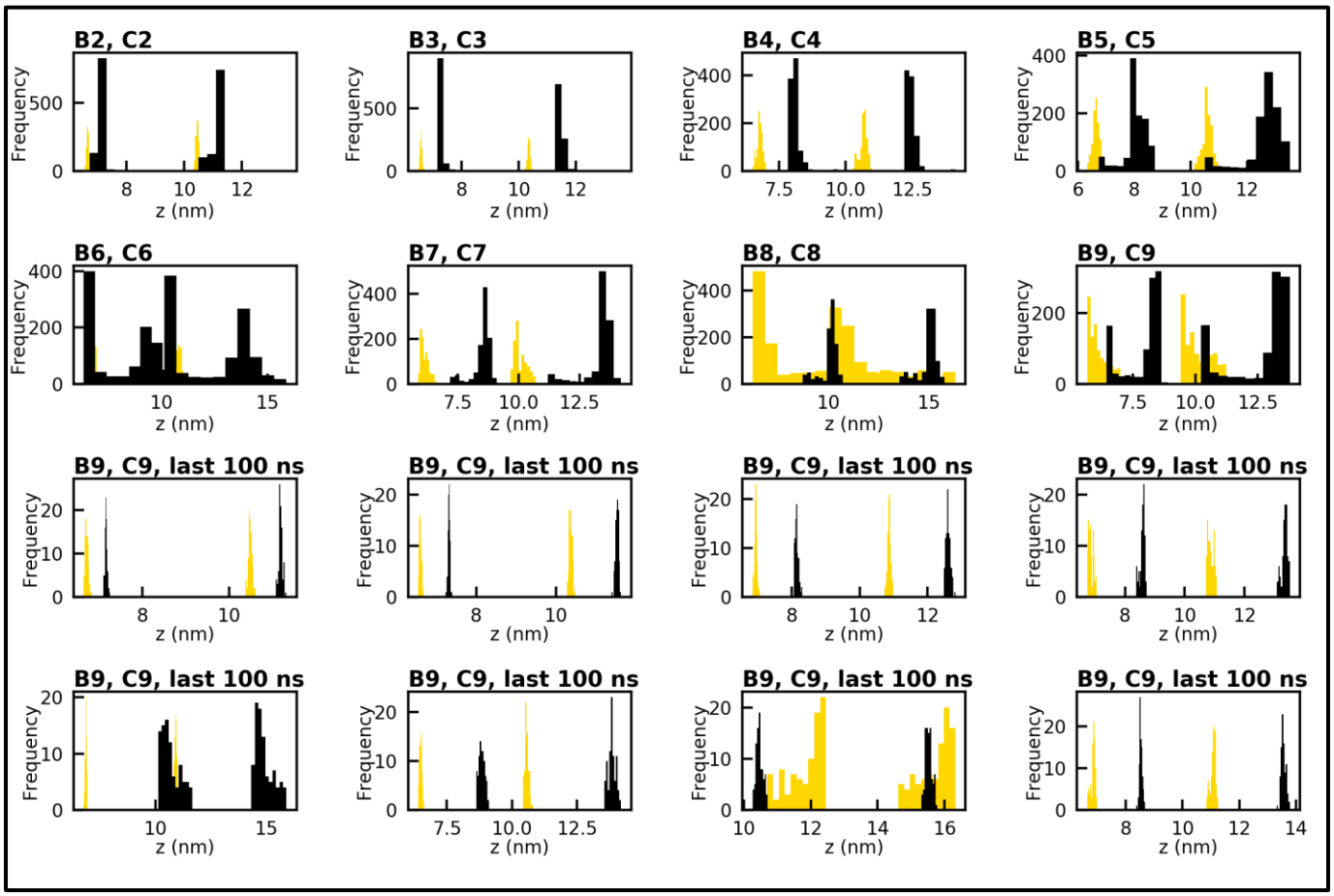


Figure S3. Histograms of time trajectories given in Figure S2. The narrower histograms for last 100 ns trajectory signify stable bilayers as compared to entire 1 μs trajectory. Bare and coated NPs are shown in gold and black color respectively.

1.4 Projected are on XY Plane

The projected area on xy plane per lipid calculated using the following equation:

$$A = \frac{c\ Lx\ Ly}{Nlipid} \qquad \text{(S1)}$$

Where L_x, L_y is the box length in X and Y direction, respectively, the C takes value of two and four for single a double bilayer respectively, and N_{lipid} is total number of lipids in the bilayer.

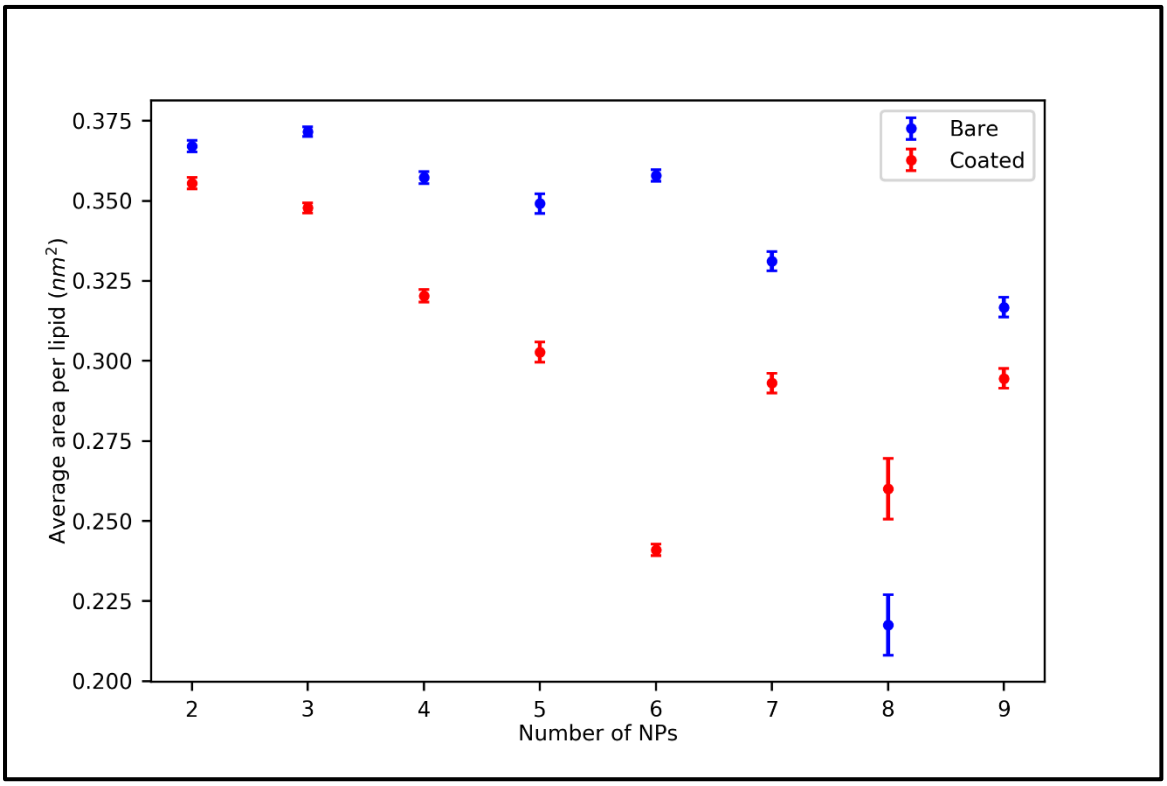


Figure S4. Projected area on XY plane of bilayer calculated in last 0.1 µs production run.

1.5 Bilayer density along bilayer normal (z axis)

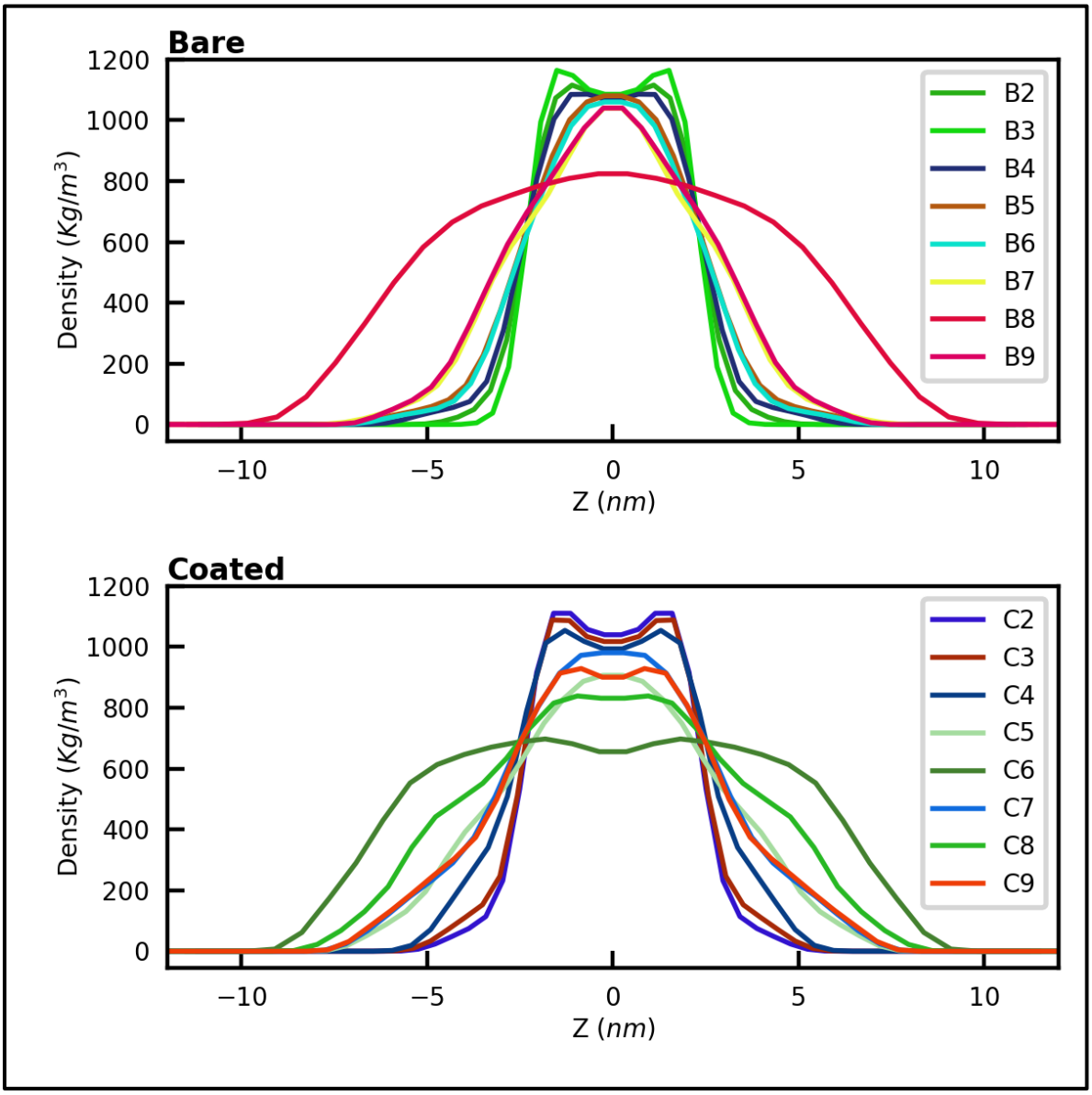


Figure S5. Bilayer density along z axis (last 100 ns)

1.6 Lipid order parameter

The second rank order parameter for the bilayer, which has normal in z direction, could be defined as:

$$Sz = \frac{1}{2}(3cos^2\theta - 1) \qquad \text{(S2)}$$

where θ is the angle between the bond and the bilayer normal. Sz = 1 means perfect alignment with the bilayer normal, Sz = −0.5 anti-alignment, and Sz = 0 random orientation of the lipid chains.

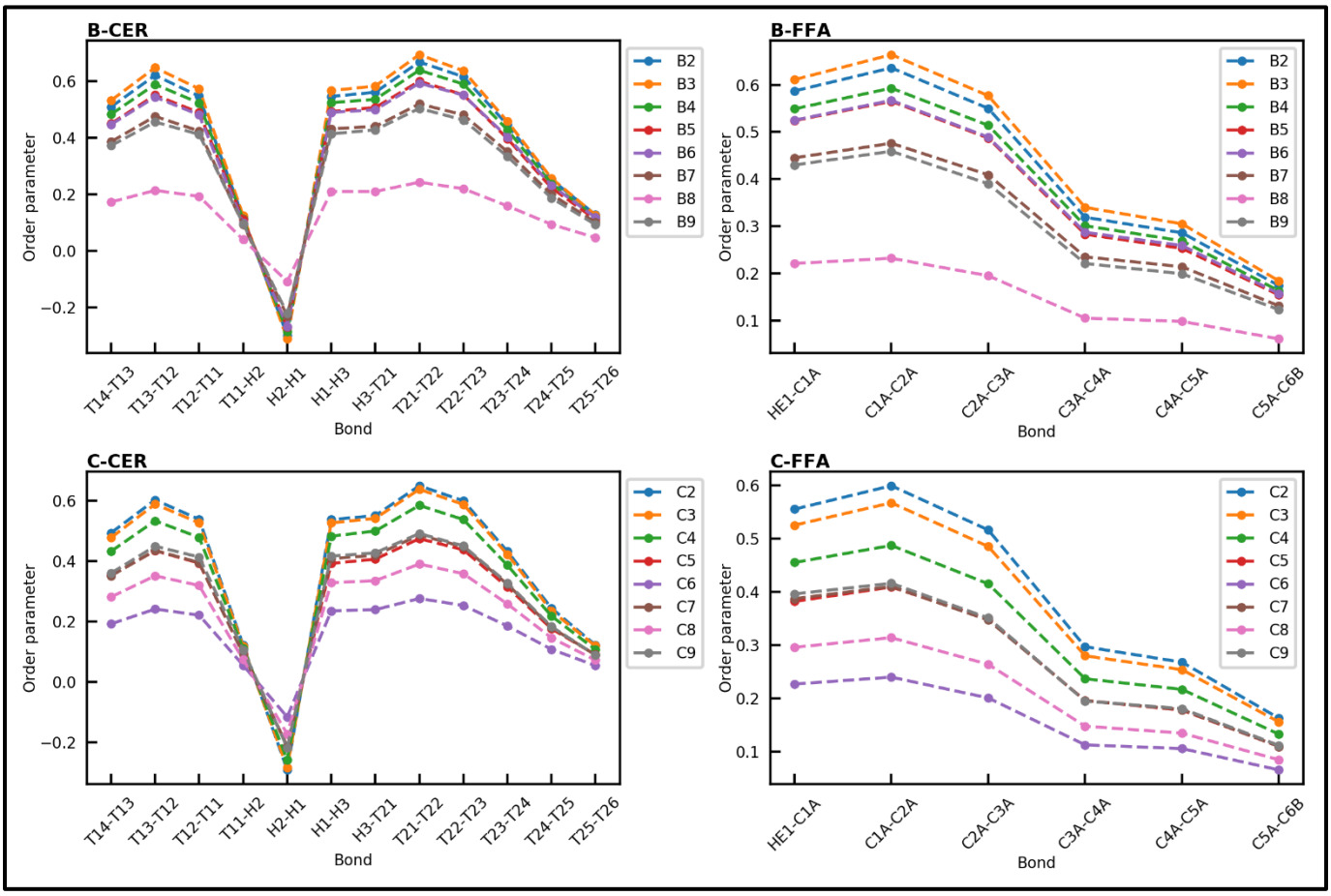


Figure S6. Tail order parameter of CER and FFA chains. B and C corresponds to bare and coated nanoparticle system respectively.

1.7 Density maps

1.7.1 Bare

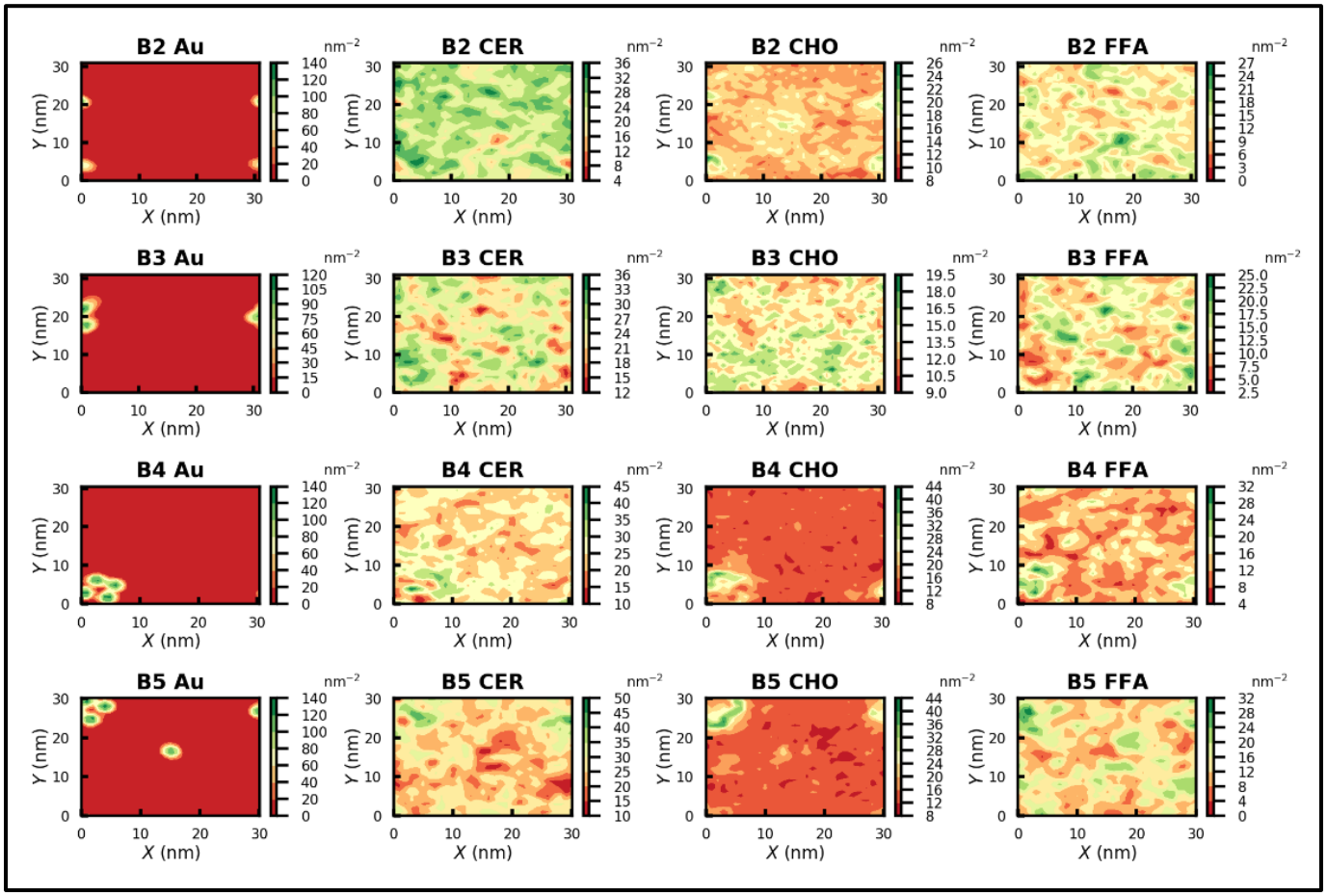


Figure S7. Density maps of nanoparticles, ceramide, cholesterol, and free fatty acid for B2 to B5 systems.

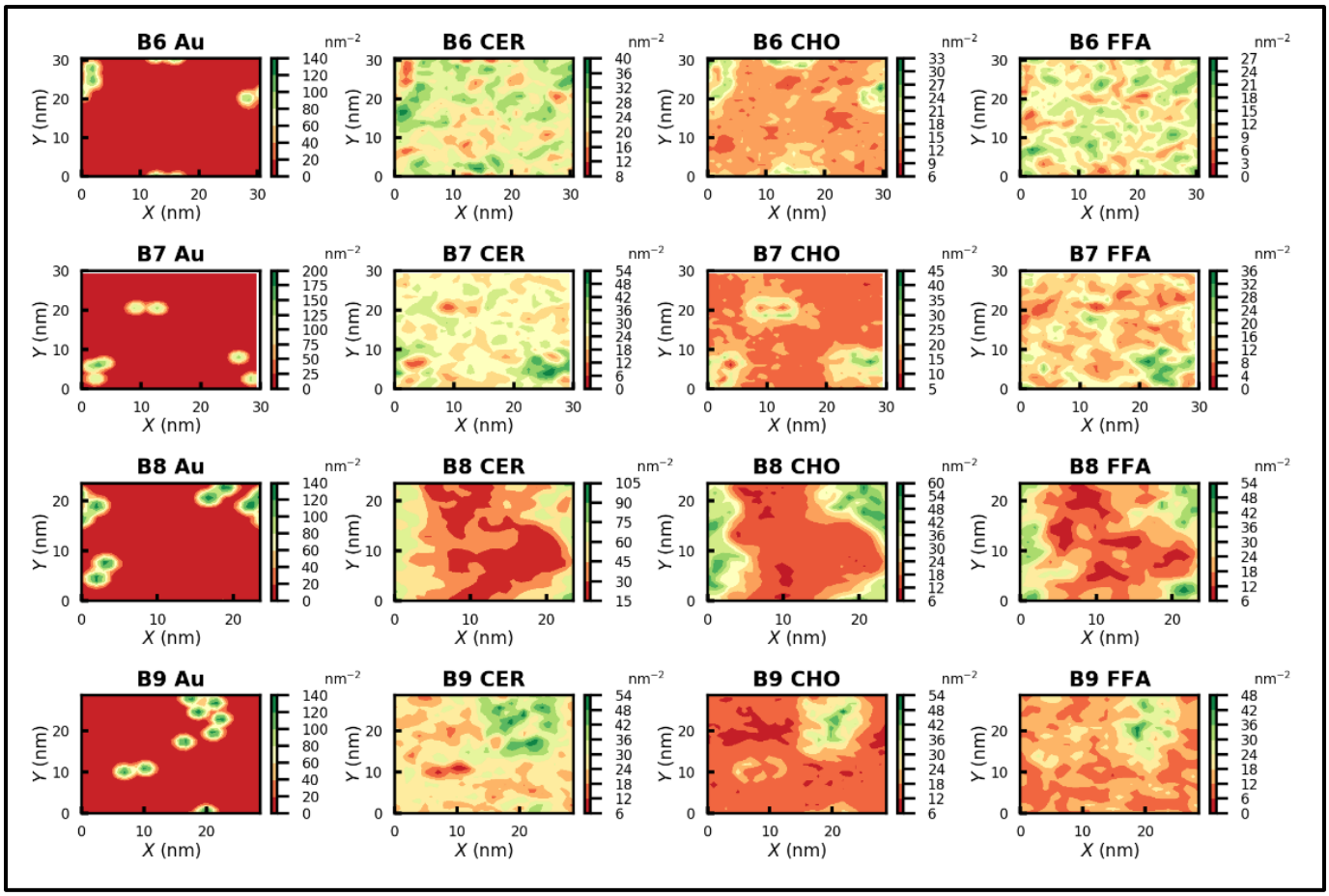


Figure S8. Density maps of nanoparticles, ceramide, cholesterol, and free fatty acid for B6 to B9 systems.

1.7.2 Coated

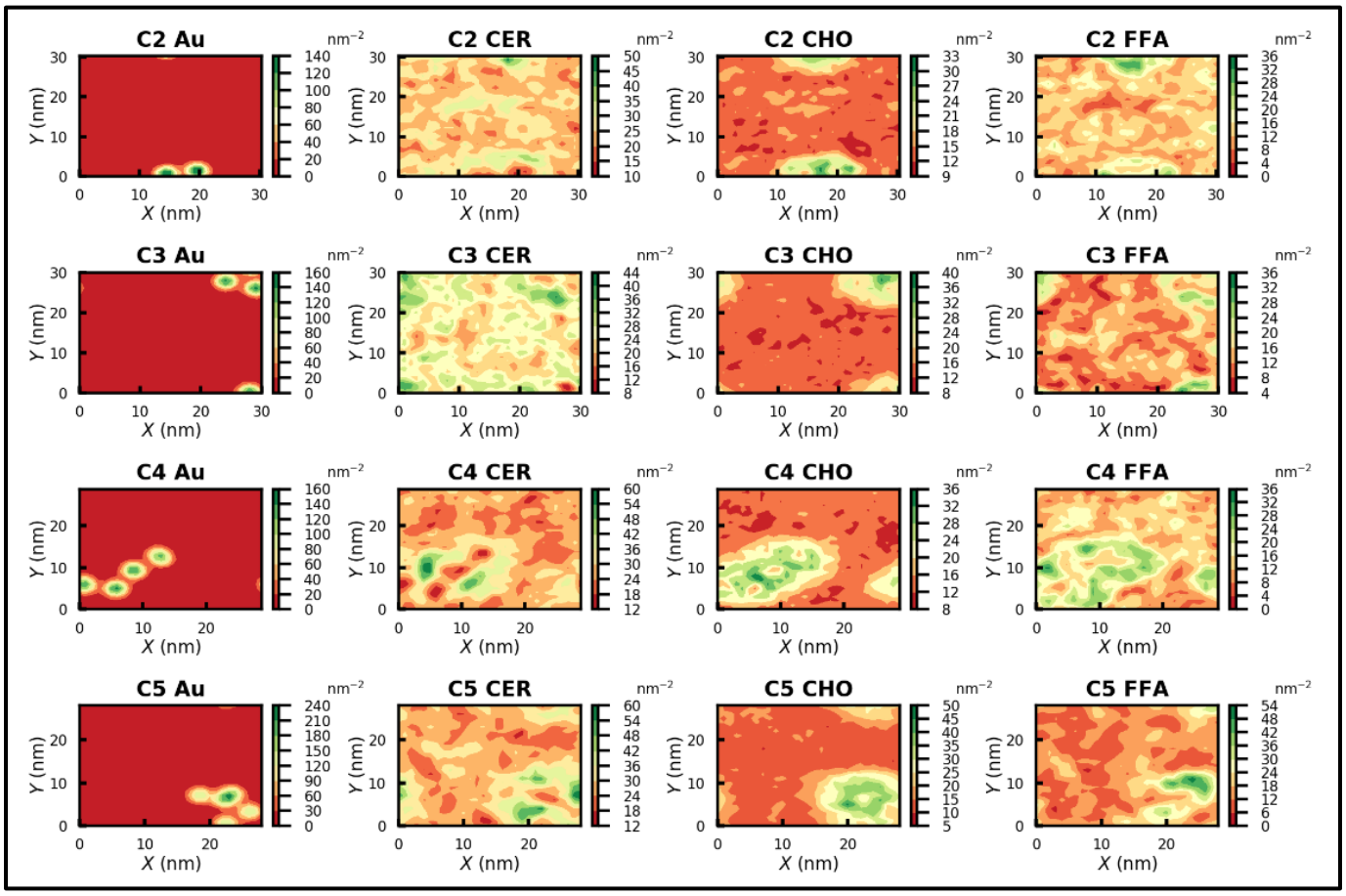


Figure S9. Density maps of nanoparticles, ceramide, cholesterol, and free fatty acid for C2 to C5 systems.

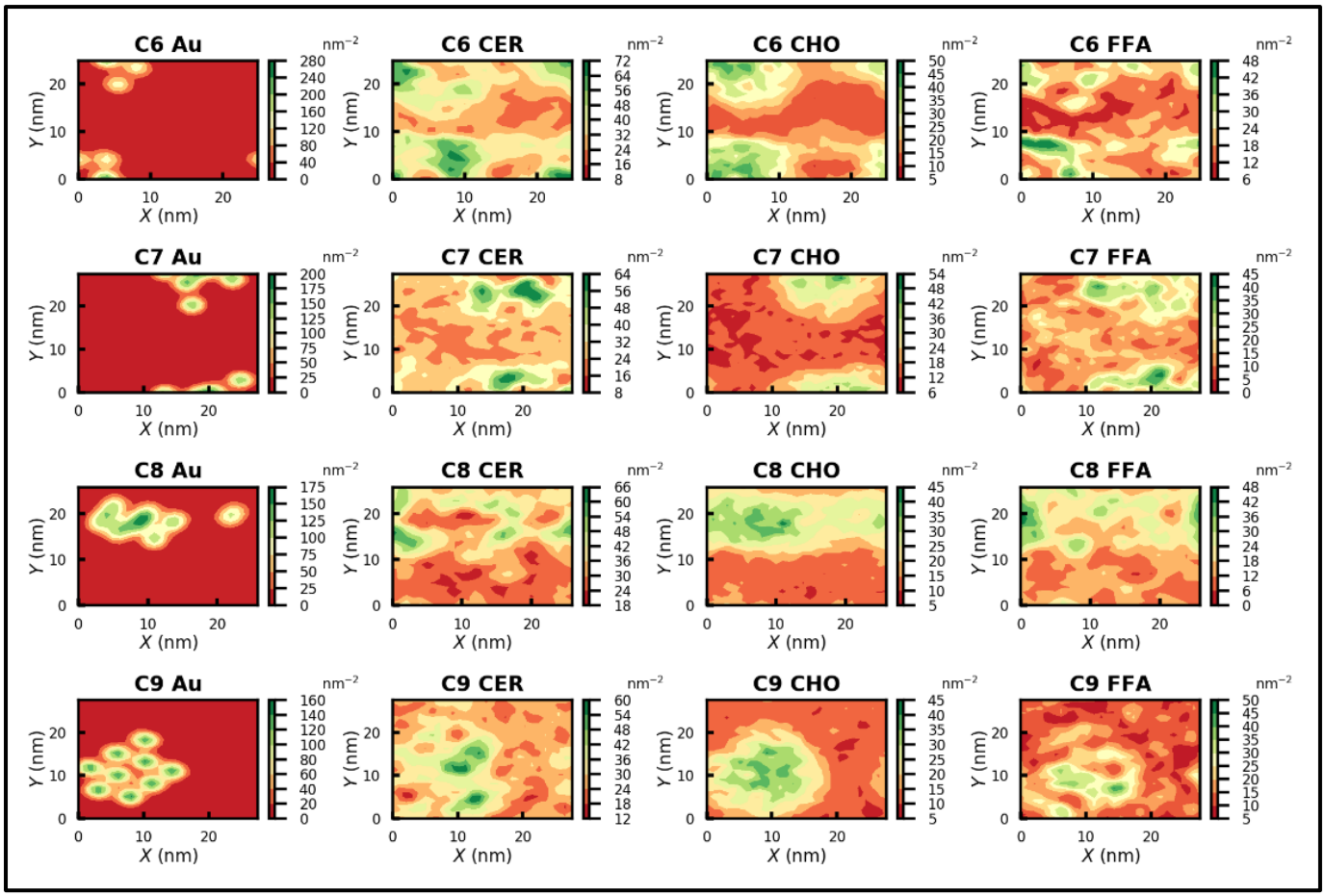


Figure S10. Density maps of nanoparticles, ceramide, cholesterol, and free fatty acid for C6 to C9 systems.

1.8 Radial distribution function

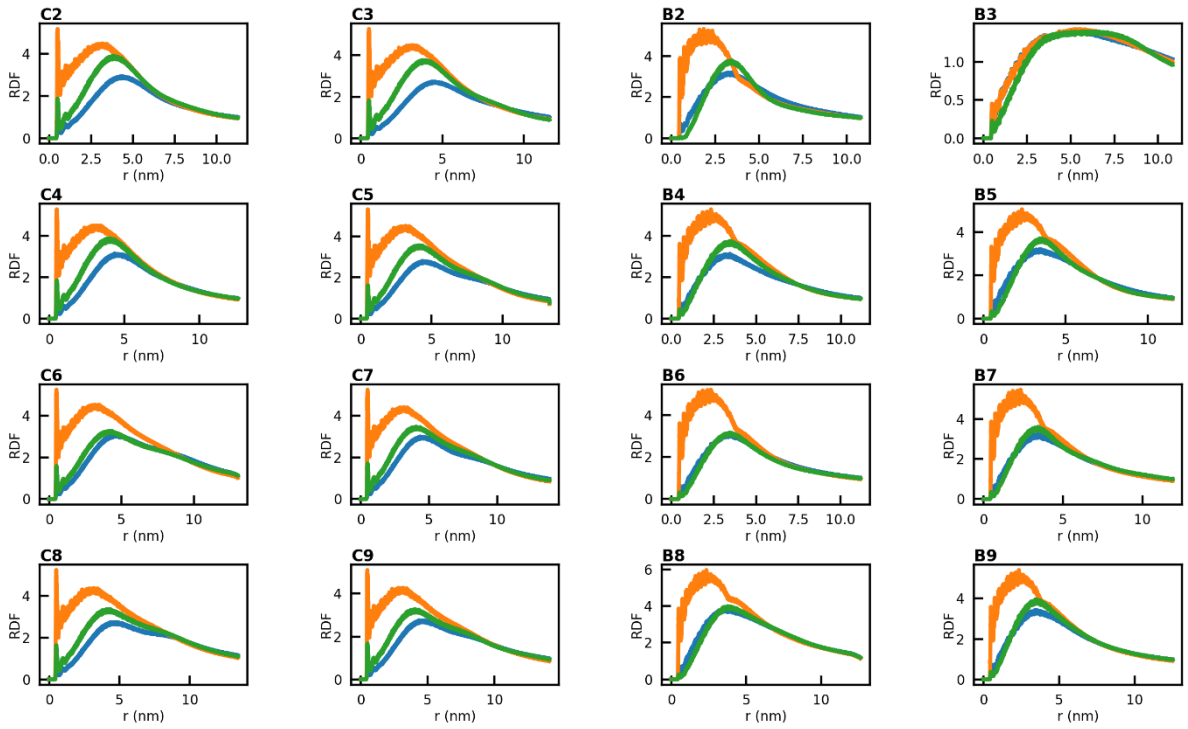


Figure S11. Radial distribution function of CER (green), CHO (orange) and FFA(blue) with nanoparticles.

2. Double membrane

2.1 Snapshots

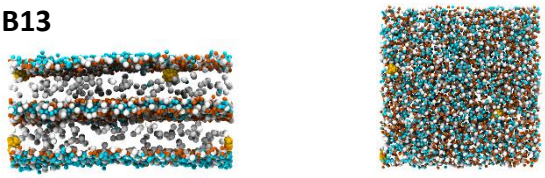
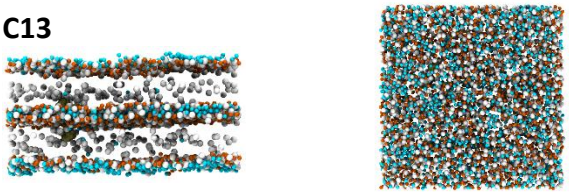
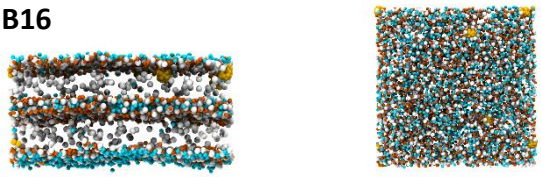
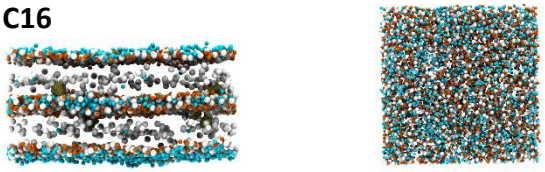
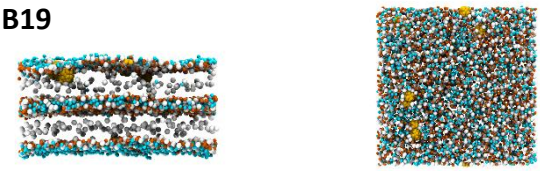
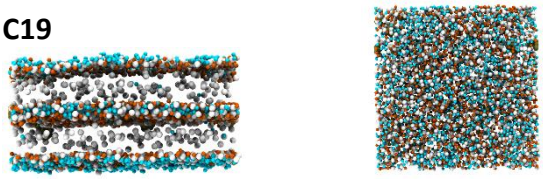
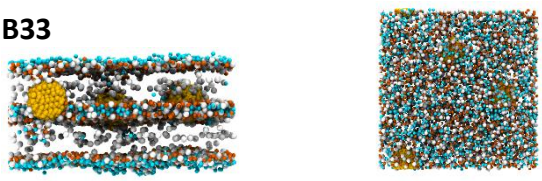
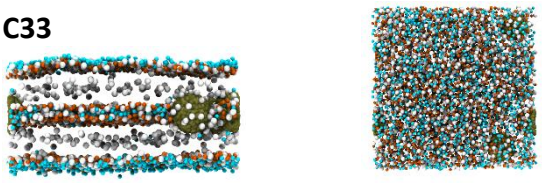
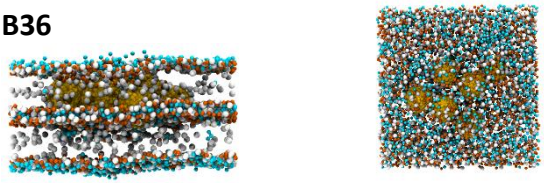
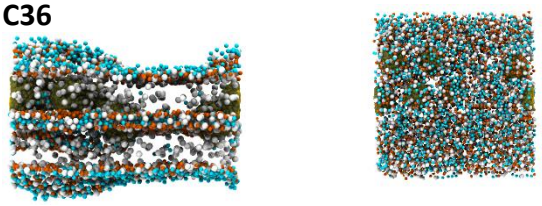
Bare	Coated
B13 	C13 
B16 	C16 
B19 	C19 
B33 	C33 
B36 	C36 

Figure S12. Final snapshots of double bilayer-NP system after 3 μs simulation.

2.2 Trajectories

2.2.1 1 µs trajectory

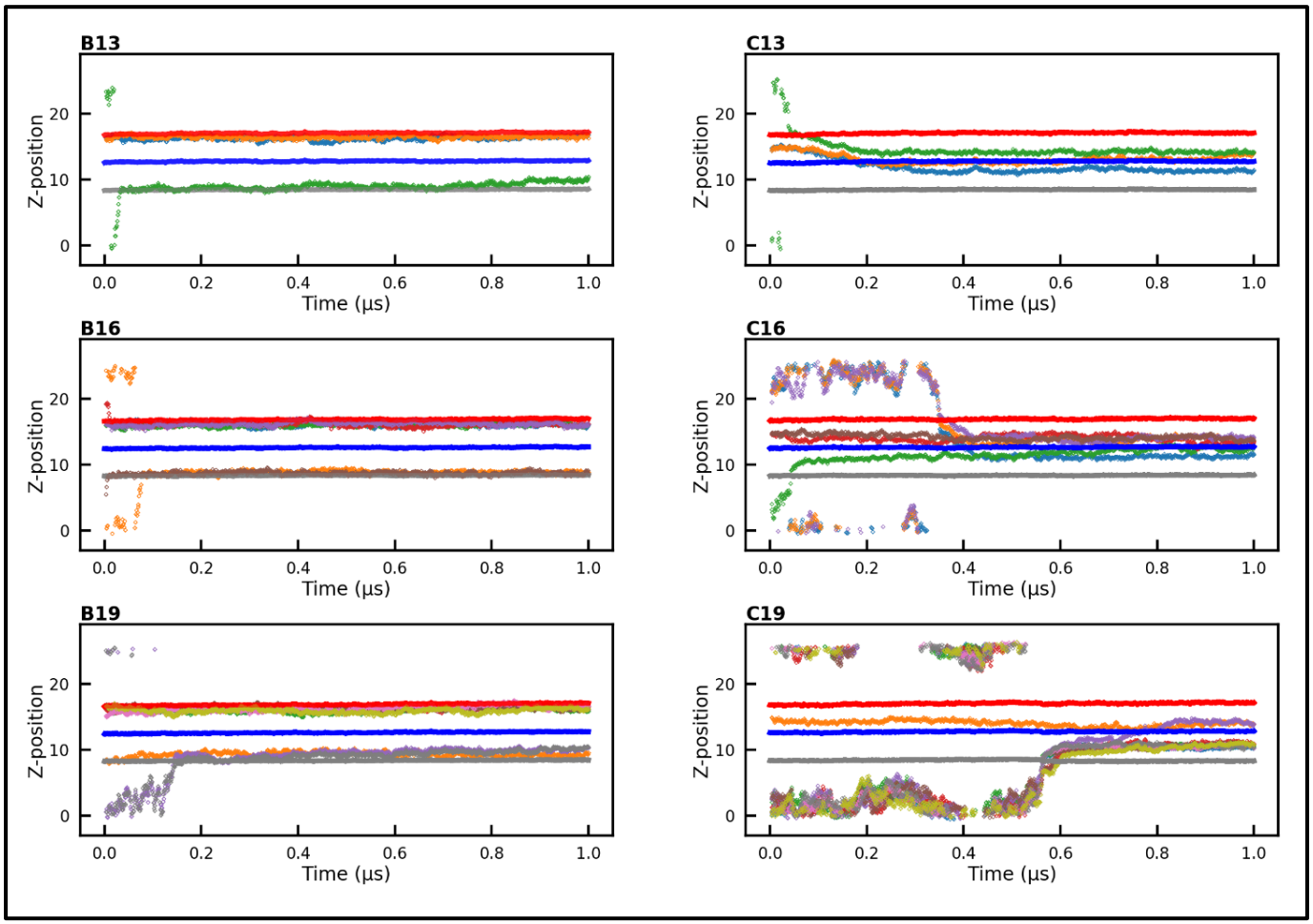


Figure S13. Time trajectories of double bilayer headgroup atoms and NPs (of 1 nm size) along the Z direction calculated over 1 µs simulation time. The head group data for upper, middle, and lower leaflet are shown in red, blue, and grey color respectively. Individual NP trajectories are shown in other colors.

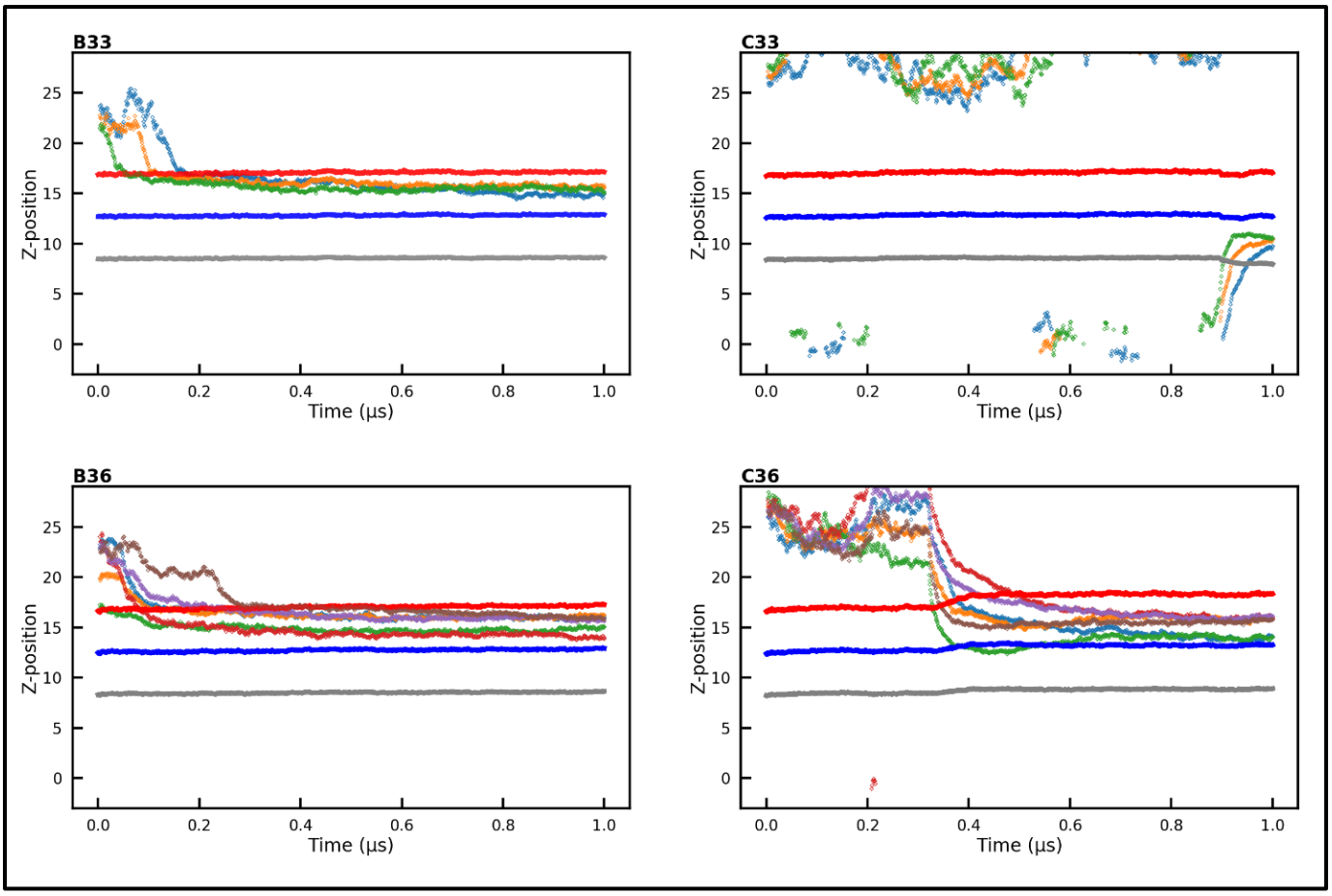


Figure S14. Time trajectories of double bilayer headgroup atoms and NPs (of 3 nm size) along the Z direction calculated over 1 μs simulation time. The head group data for upper, middle, and lower leaflet are shown in red, blue, and grey color respectively. Individual NP trajectories are shown in other colors.

2.2.2 3 µs trajectory

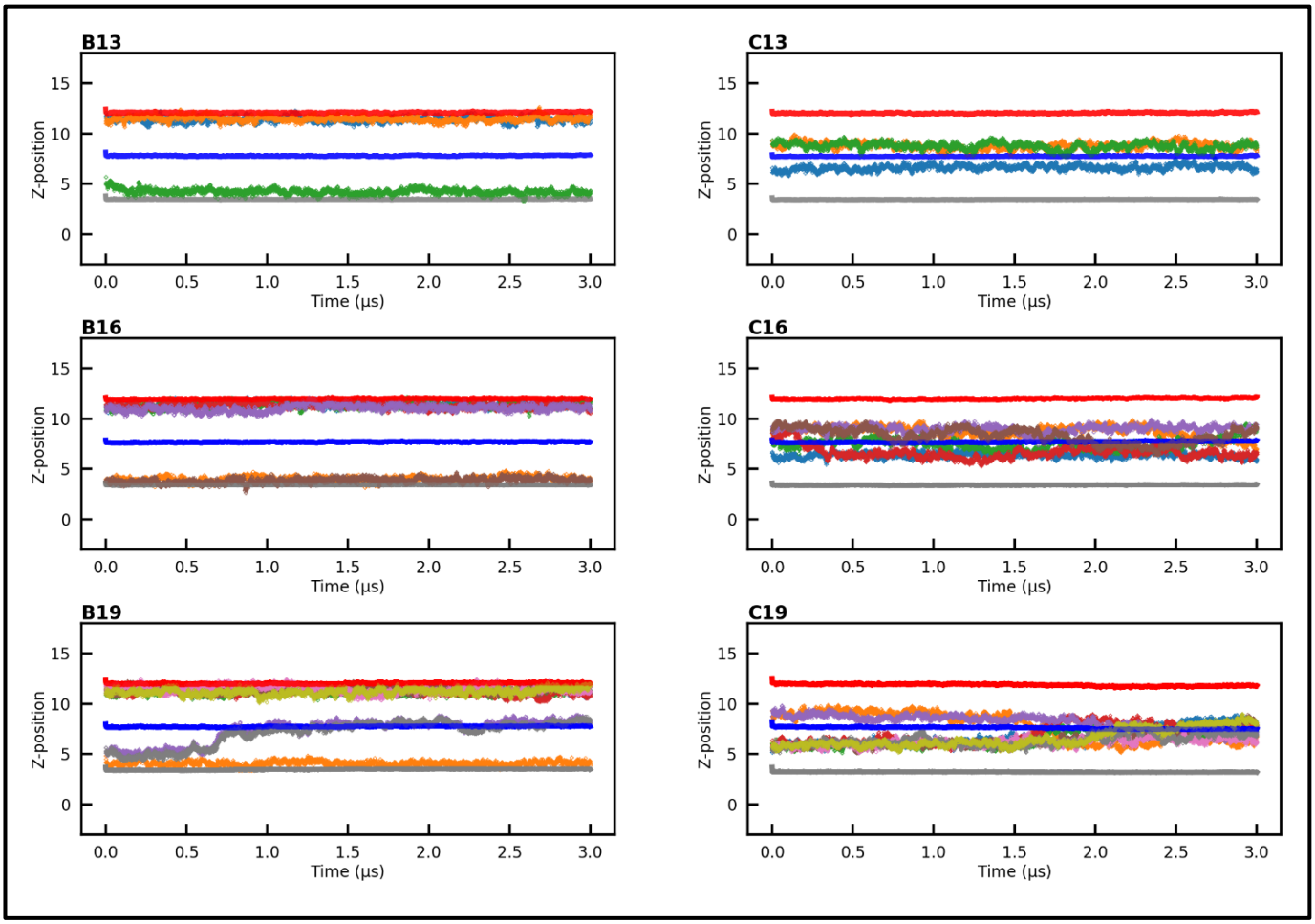


Figure S15. Time trajectories of double bilayer headgroup atoms and NPs (of 1 nm size) along the Z direction calculated over 3 µs simulation time. The head group data for upper, middle, and lower leaflet are shown in red, blue, and grey color respectively. Individual NP trajectories are shown in other colors.

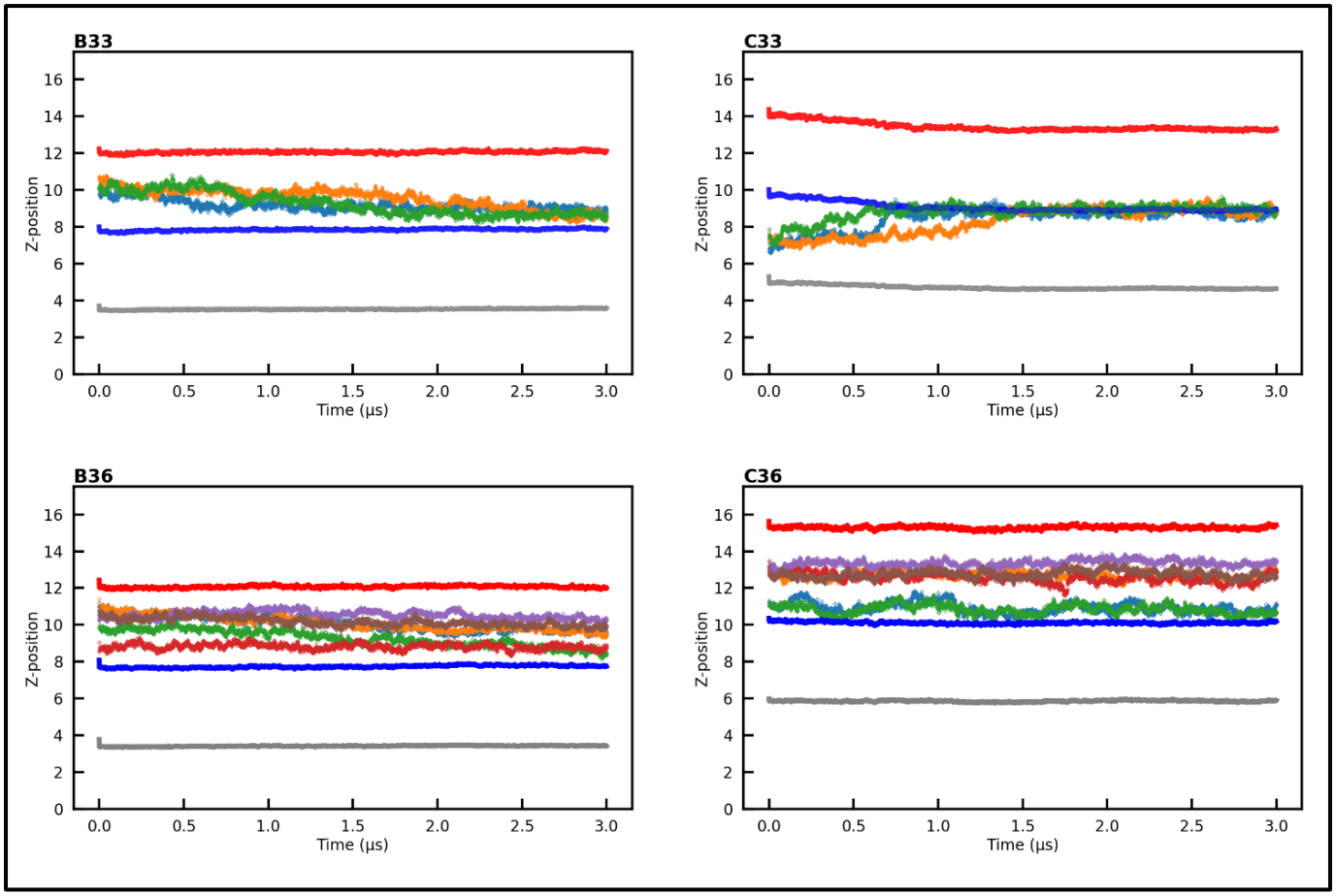


Figure S16. Time trajectories of double bilayer headgroup atoms and NPs (of 3 nm size) along the Z direction calculated over 1 μs simulation time. The head group data for upper, middle, and lower leaflet are shown in red, blue, and grey color respectively. Individual NP trajectories are shown in other colors.

2.3 Fluctuations

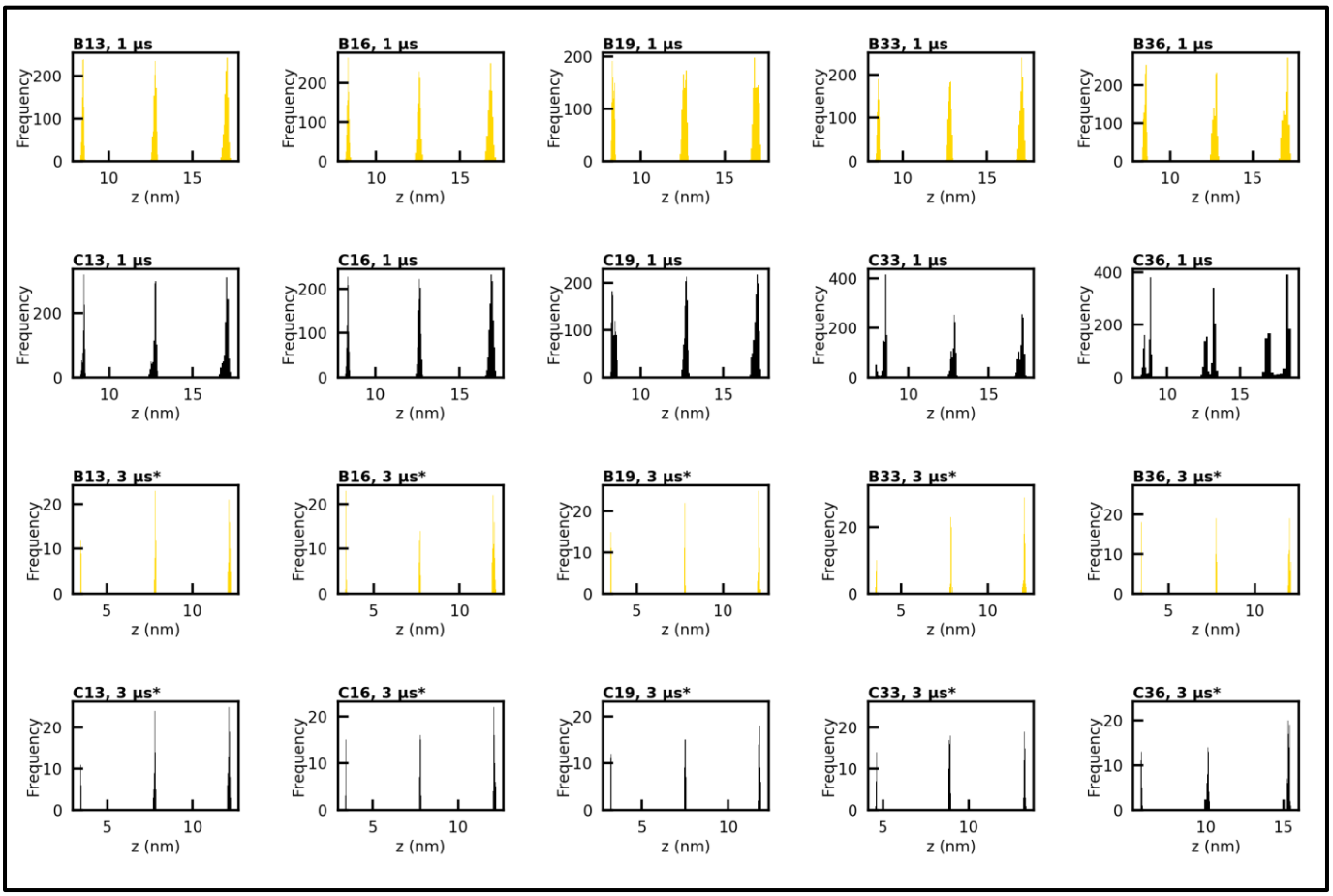


Figure S17. Histograms of time trajectories given in Figures S9 to S10. * Corresponds to data for last 100 ns time trajectory of 3 µs simulation. The narrower histograms for last 100 ns trajectory signify stable bilayers as compared to earlier time of simulation. Histograms for bare and coated NPs are shown in gold and black color respectively.

2.4 Bilayer density along bilayer normal (z axis)

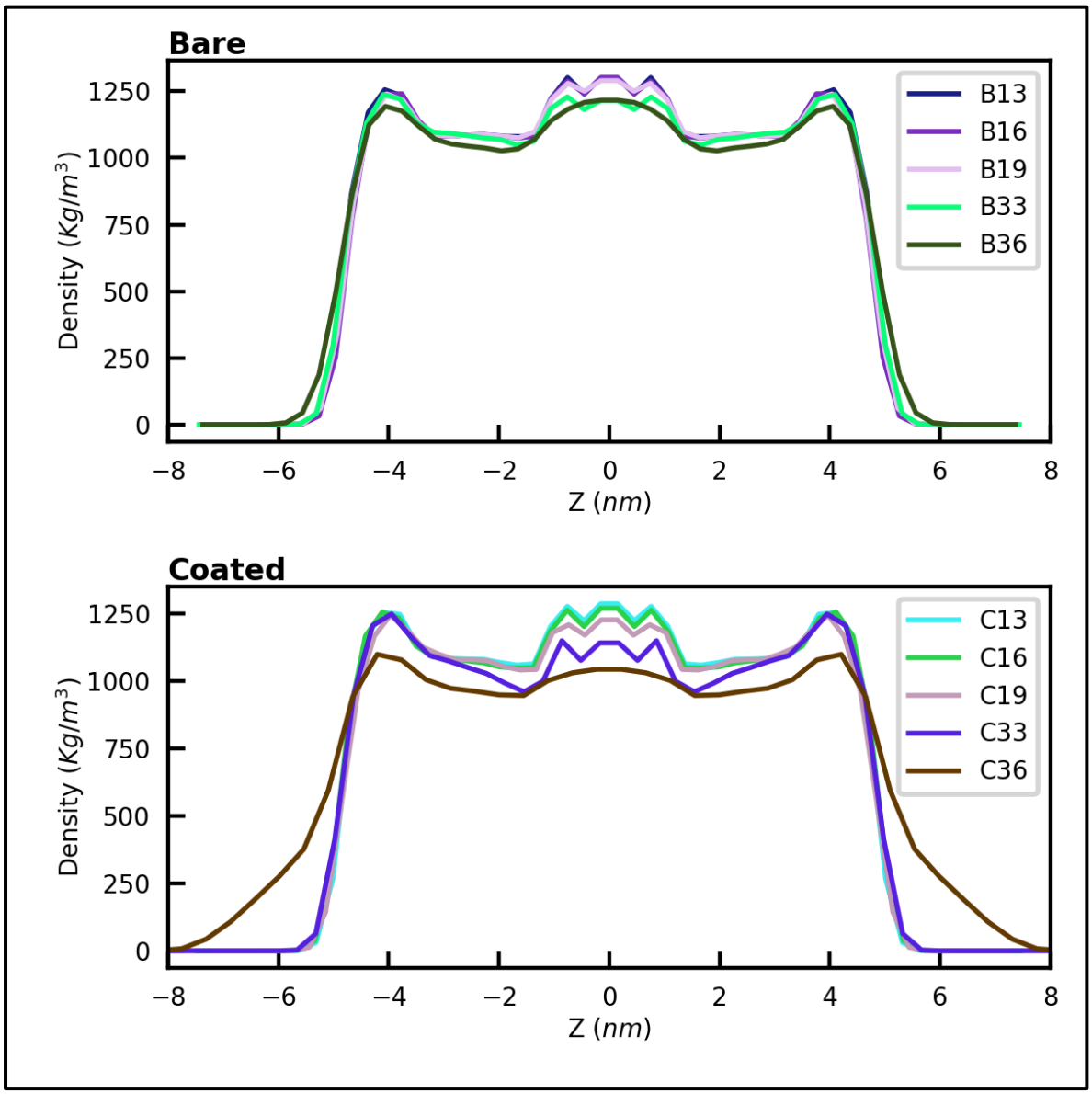


Figure S18. Bilayer density along z axis (last 100 ns)

2.5 Lipid order parameter

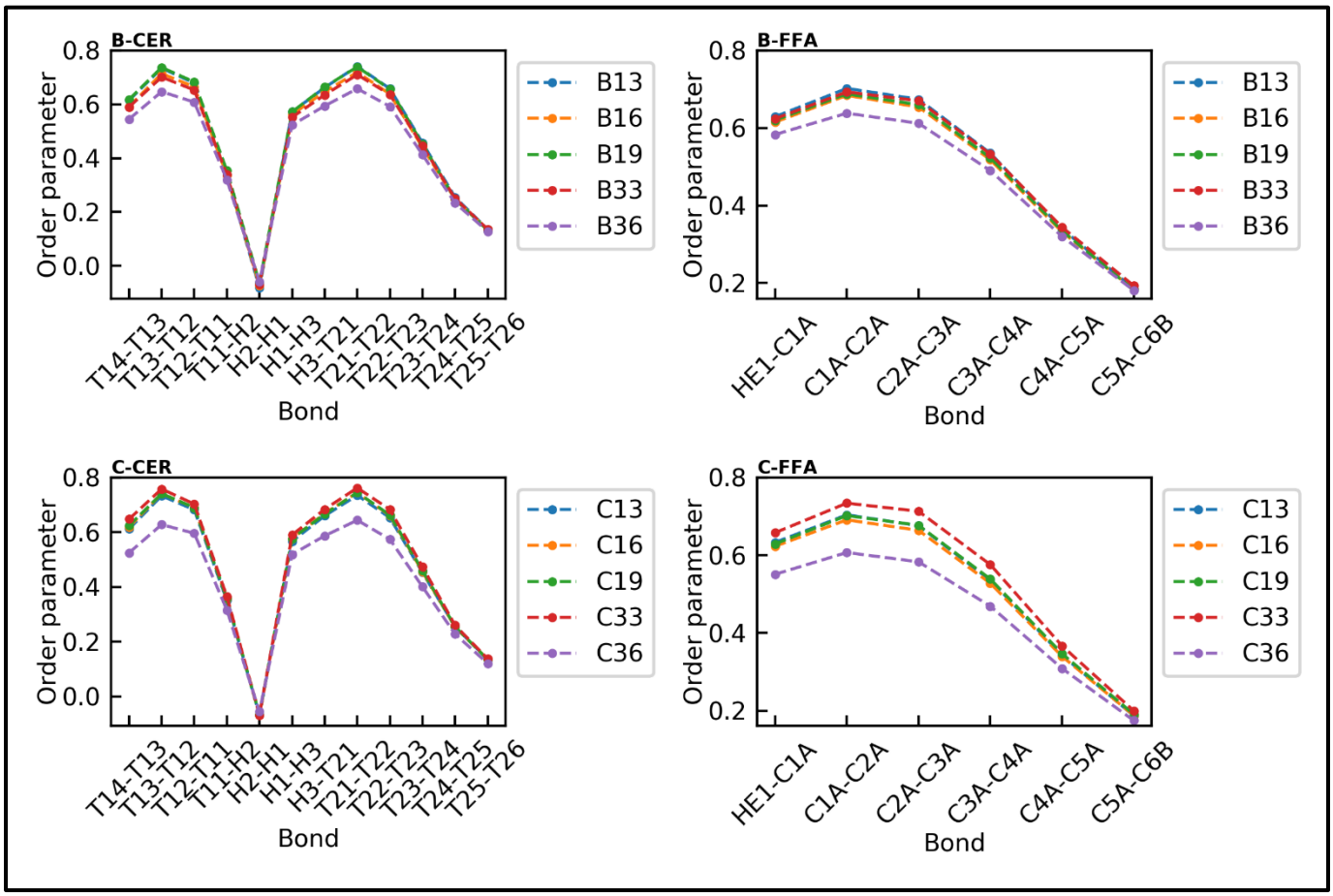


Figure S19. Tail order parameter of CER and FFA chains. B and C corresponds to bare and coated nanoparticle system respectively.

2.6 Density maps

2.6.1 Bare NP, size 1 nm

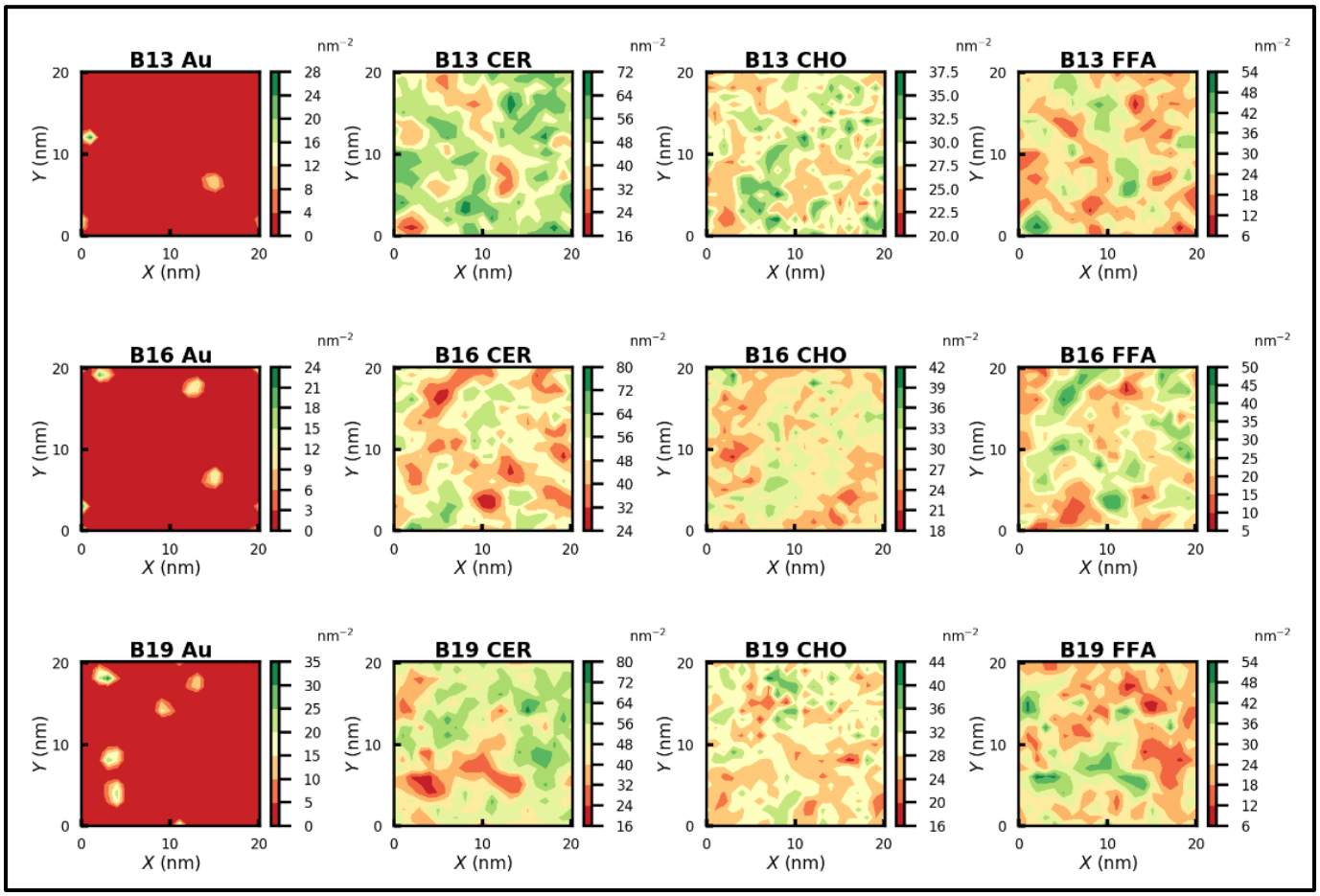


Figure S20. Density maps of nanoparticles, ceramide, cholesterol, and free fatty acid for B13 to B19 systems.

2.6.2 Coated NP, size 1 nm

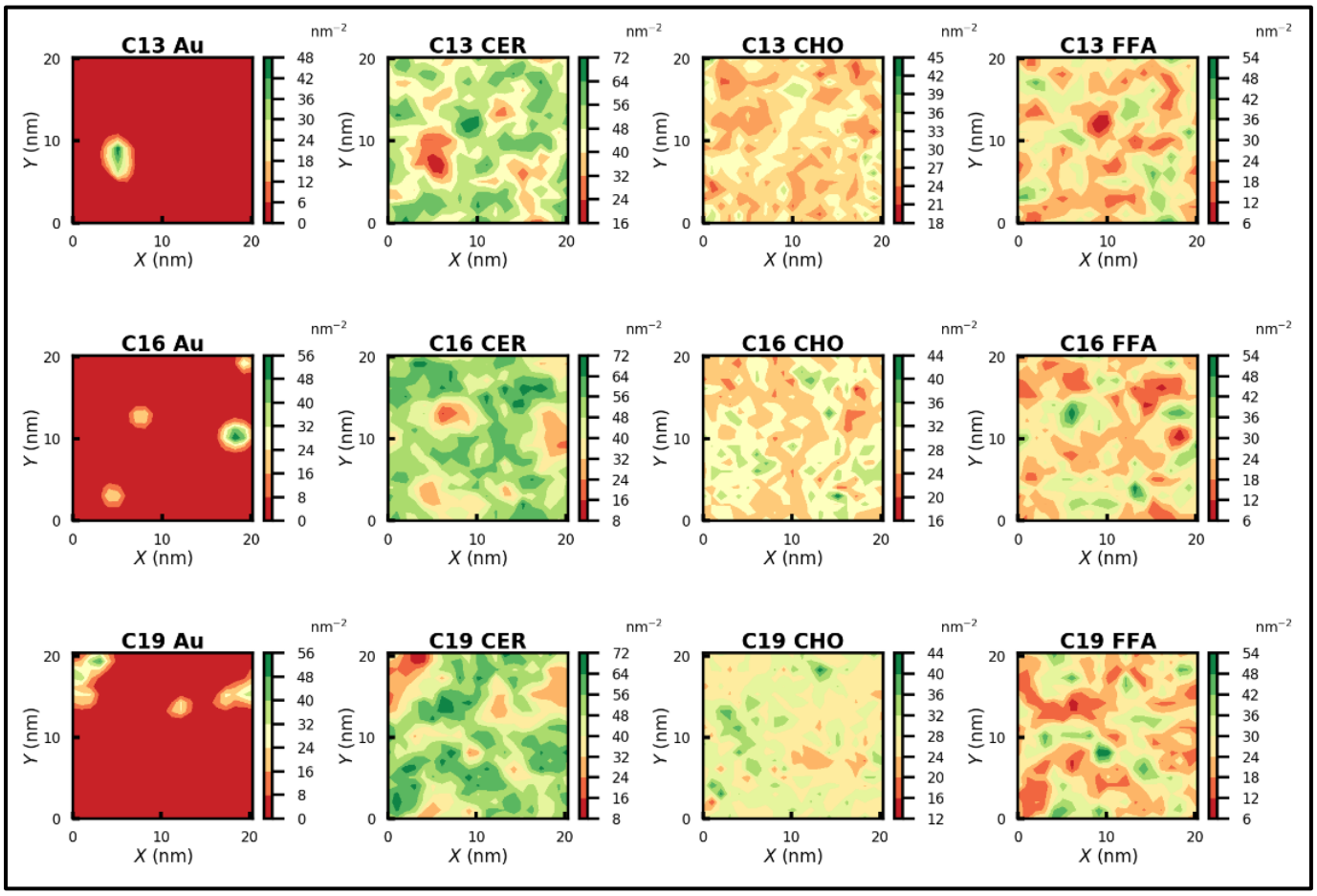


Figure S21. Density maps of nanoparticles, ceramide, cholesterol, and free fatty acid for C13 to C19 systems.

2.6.3 Bare & Coated NP, size 3 nm

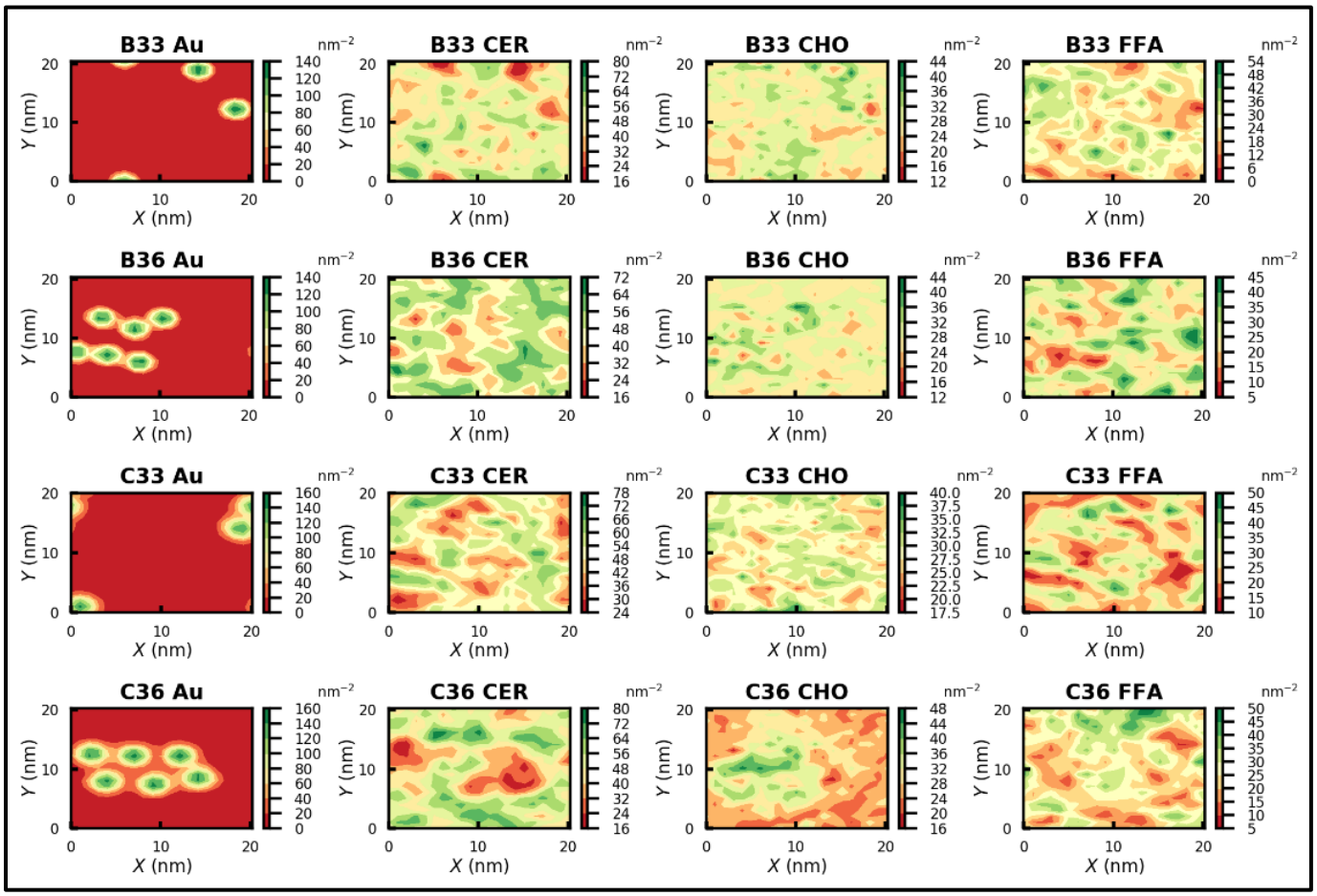


Figure S22. Density maps of nanoparticles, ceramide, cholesterol, and free fatty acid for B33, B36, C33 and C36 systems.

2.7 Radial distribuion function

2.7.1 NP size 1 nm

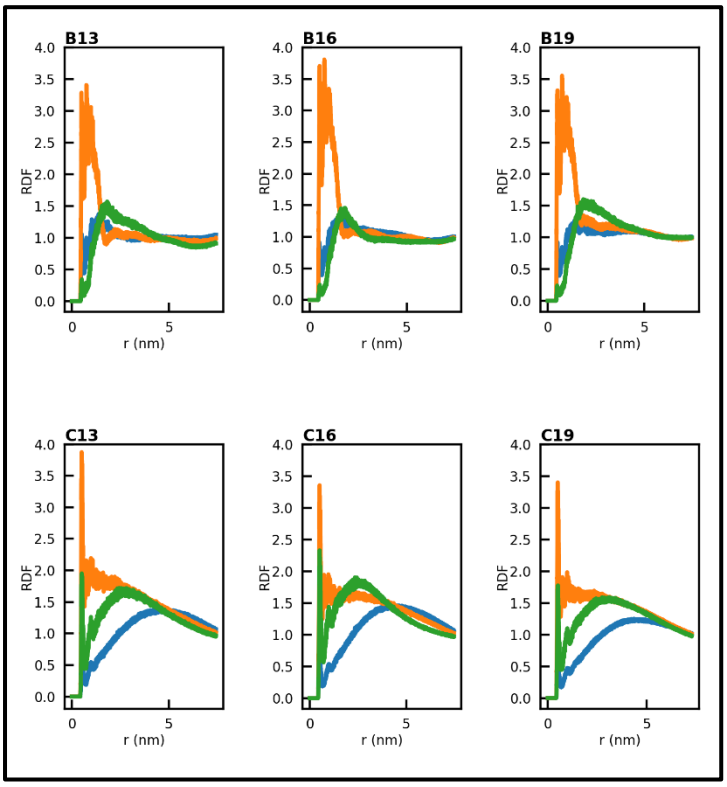


Figure S23. Radial distribution function of CER, CHO and FFA with nanoparticles.

2.7.2 NP size 3 nm

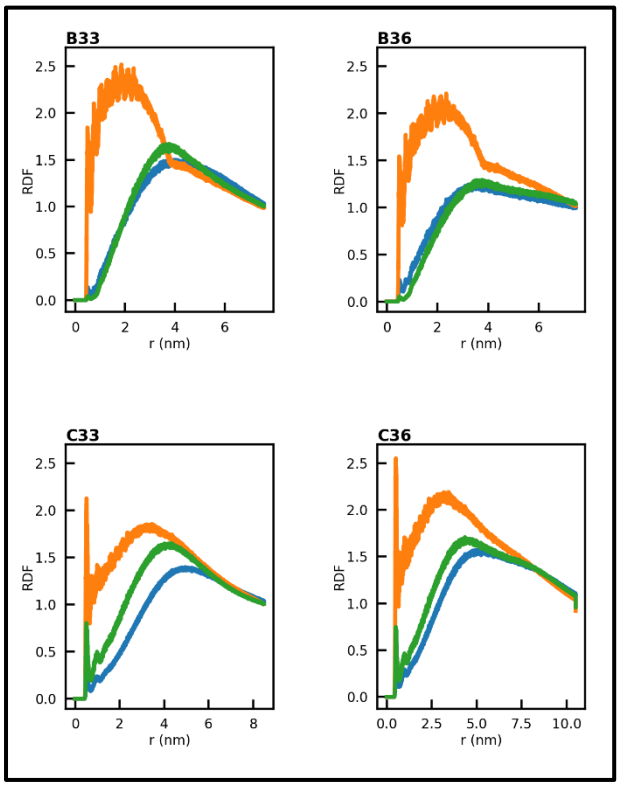


Figure S24. Radial distribution function of CER (green), CHO (orange) and FFA (blue) with nanoparticles

2.8 Cluster analysis

2.8.1 Single Bilayer

2.8.1.1 Bare

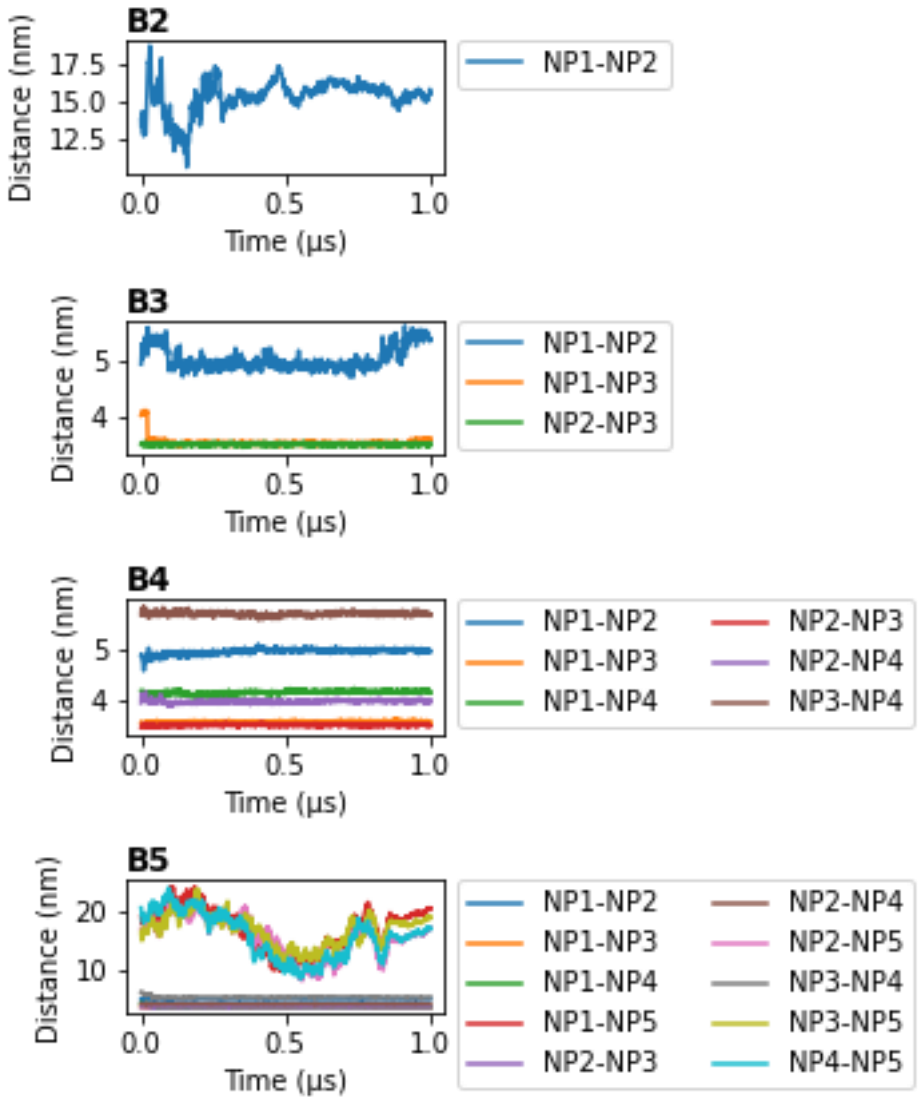


Figure S25. NP-NP pair distance for B2 to B5 system.

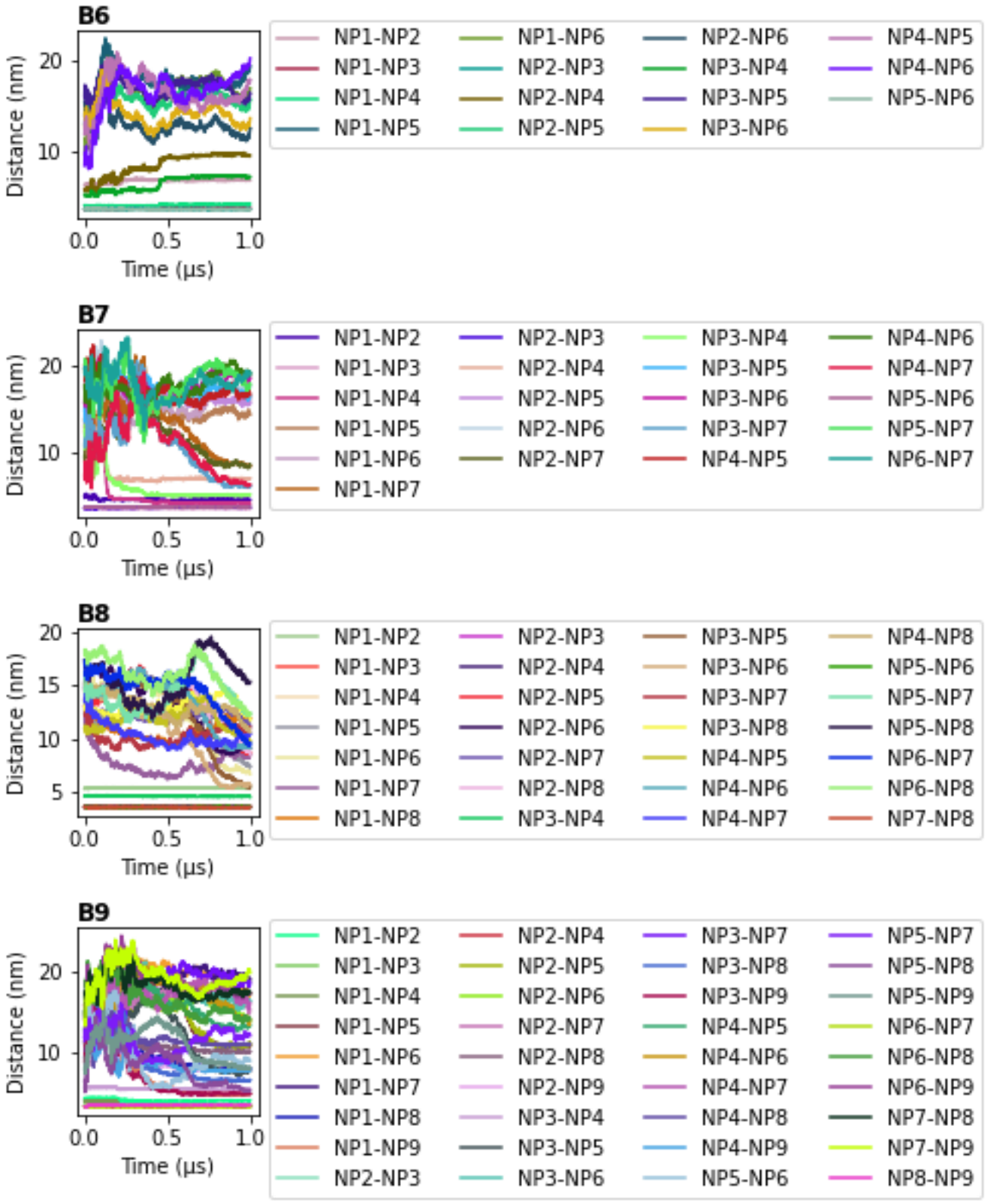


Figure S26. NP-NP pair distance for B6 to B9 system.

2.8.1.2 Coated

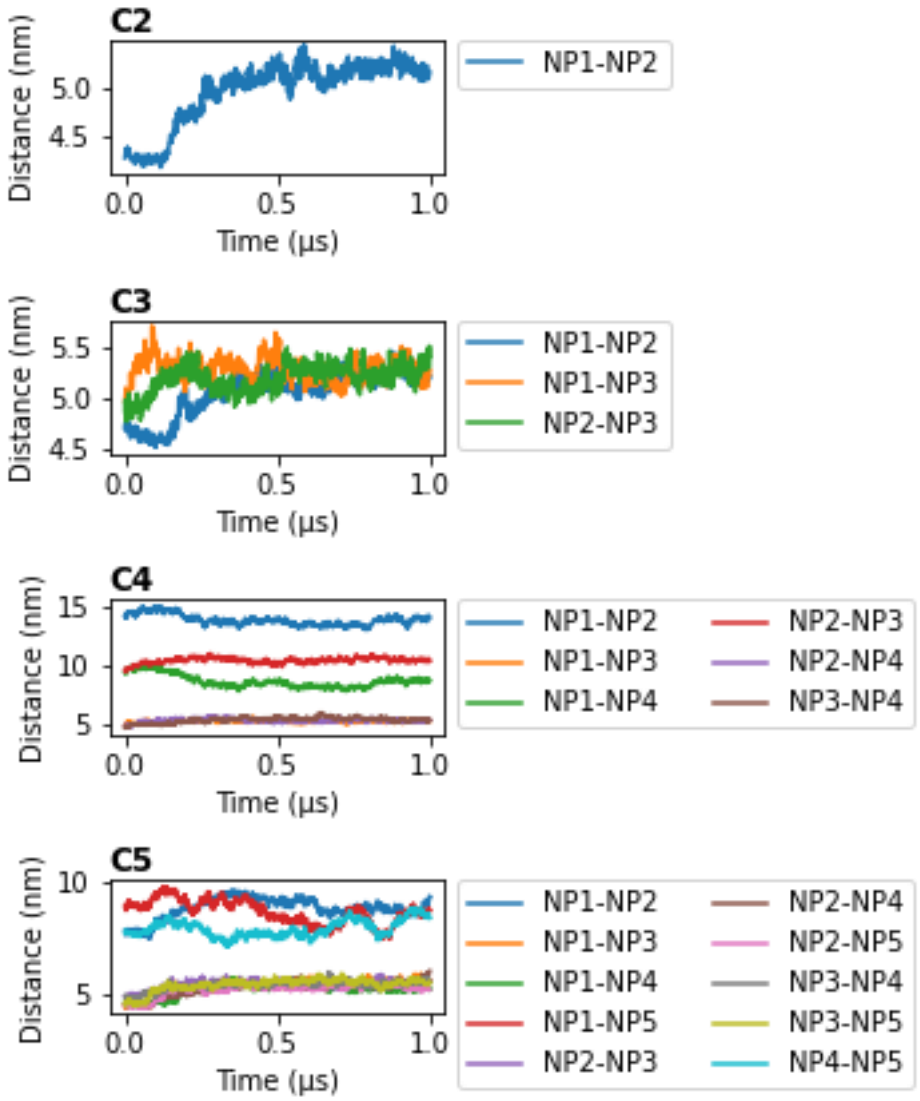


Figure S27. NP-NP pair distance for C2 to C5 system.

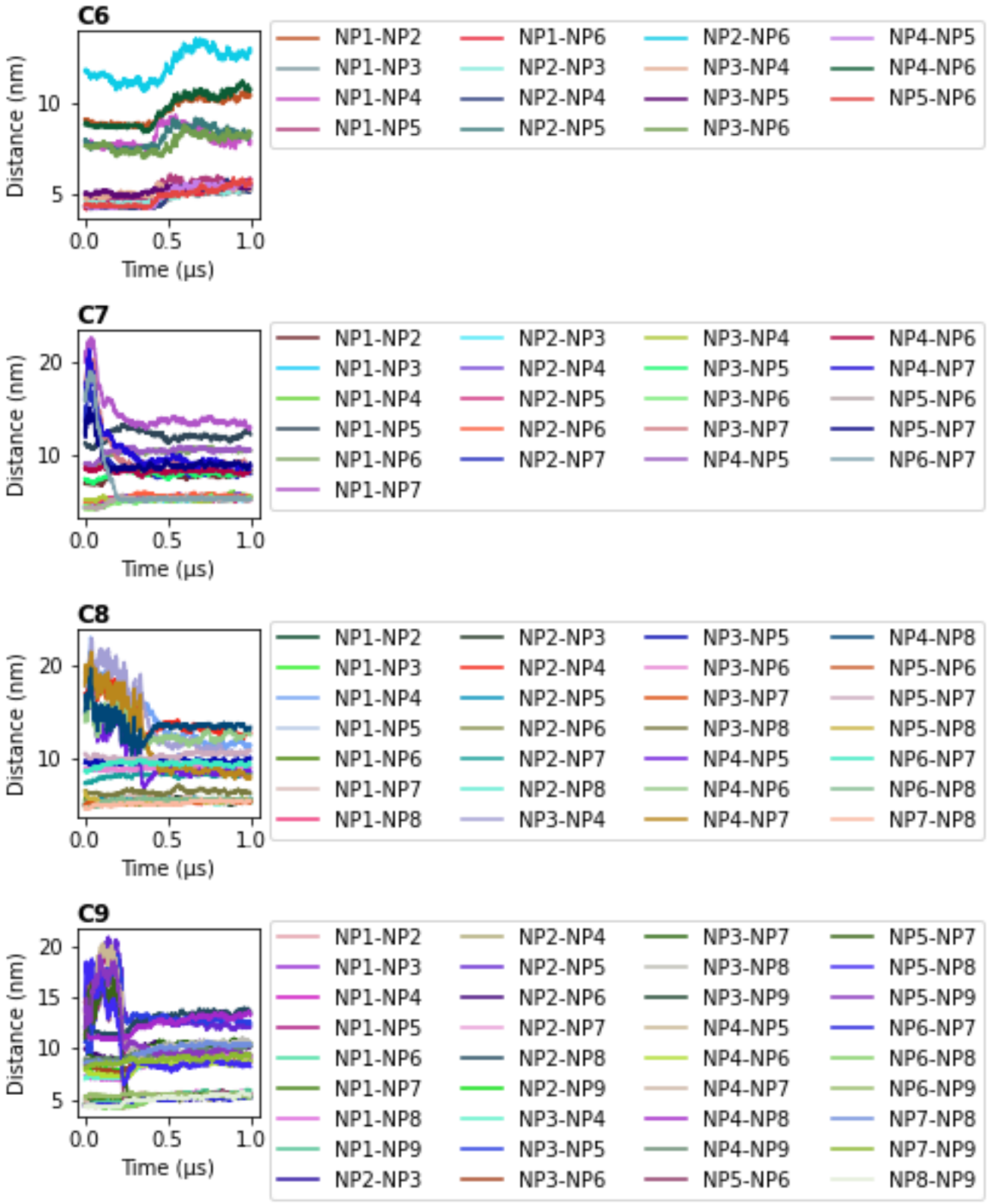


Figure S28. NP-NP pair distance for C6 to C9 system.

2.8.2 Double Bilayer

2.8.2.1 Bare

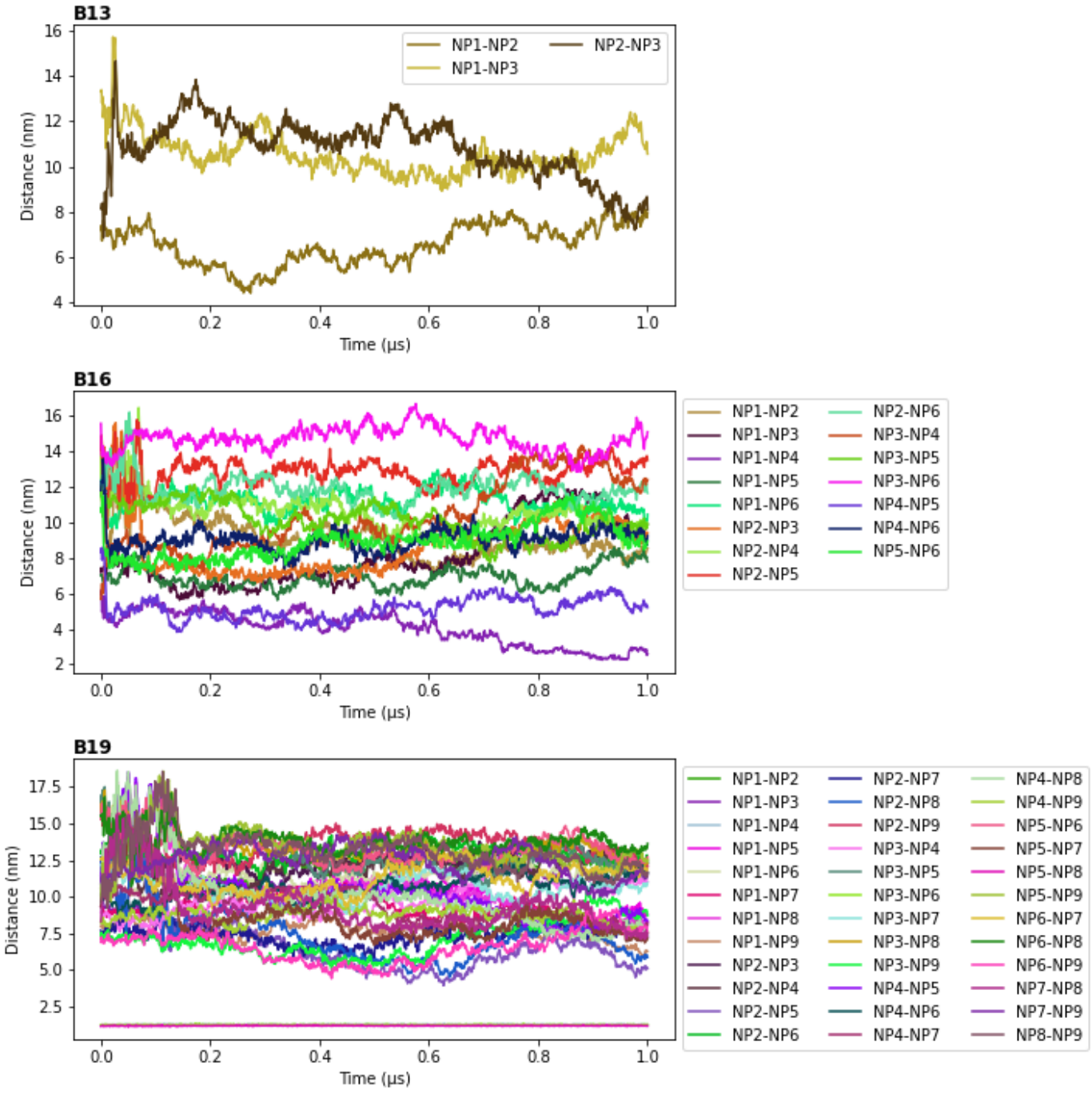


Figure S29. NP-NP pair distance for bare 1 nm NP.

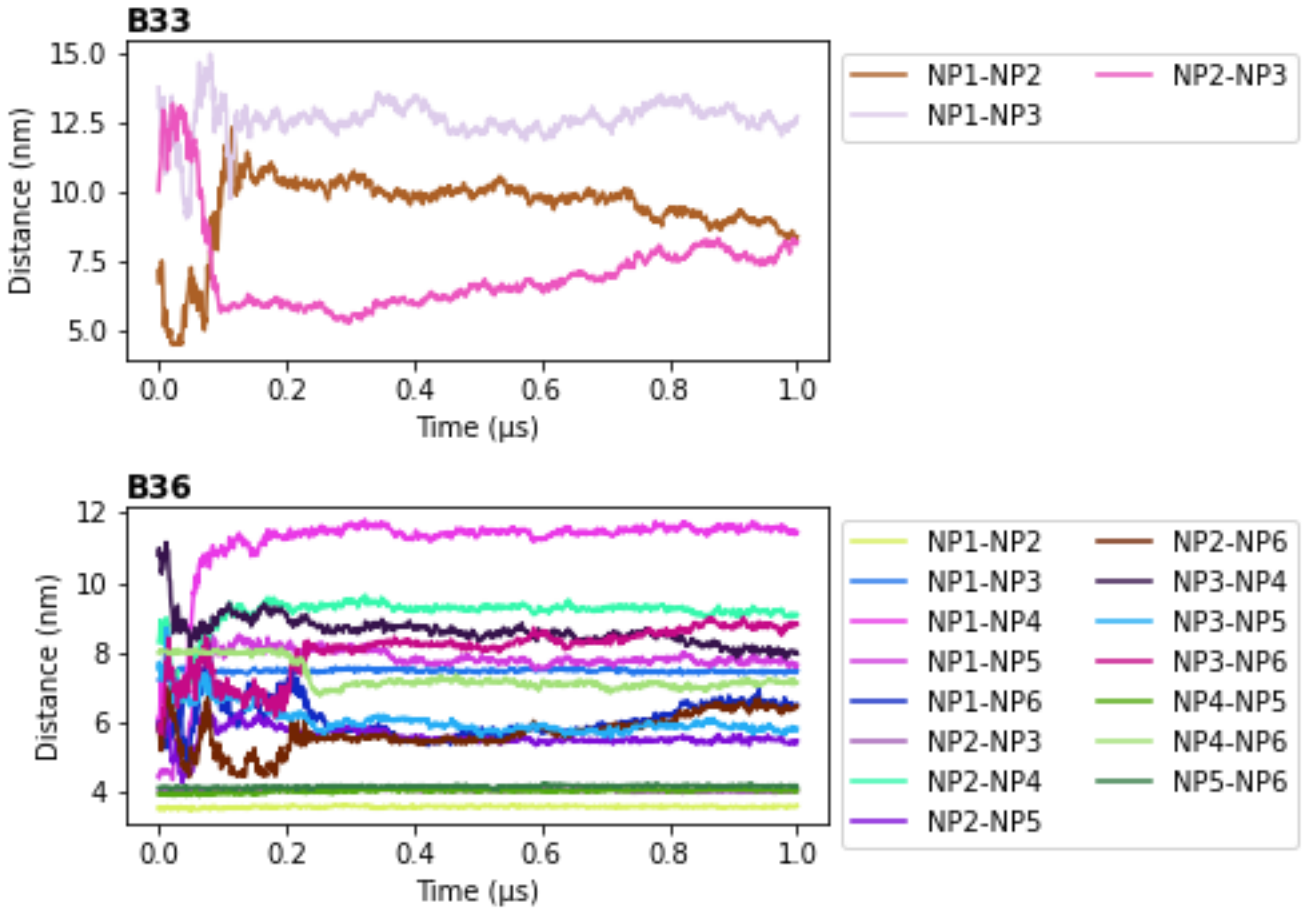


Figure S30. NP-NP pair distance for bare 3 nm NP.

2.8.2.2 Coated

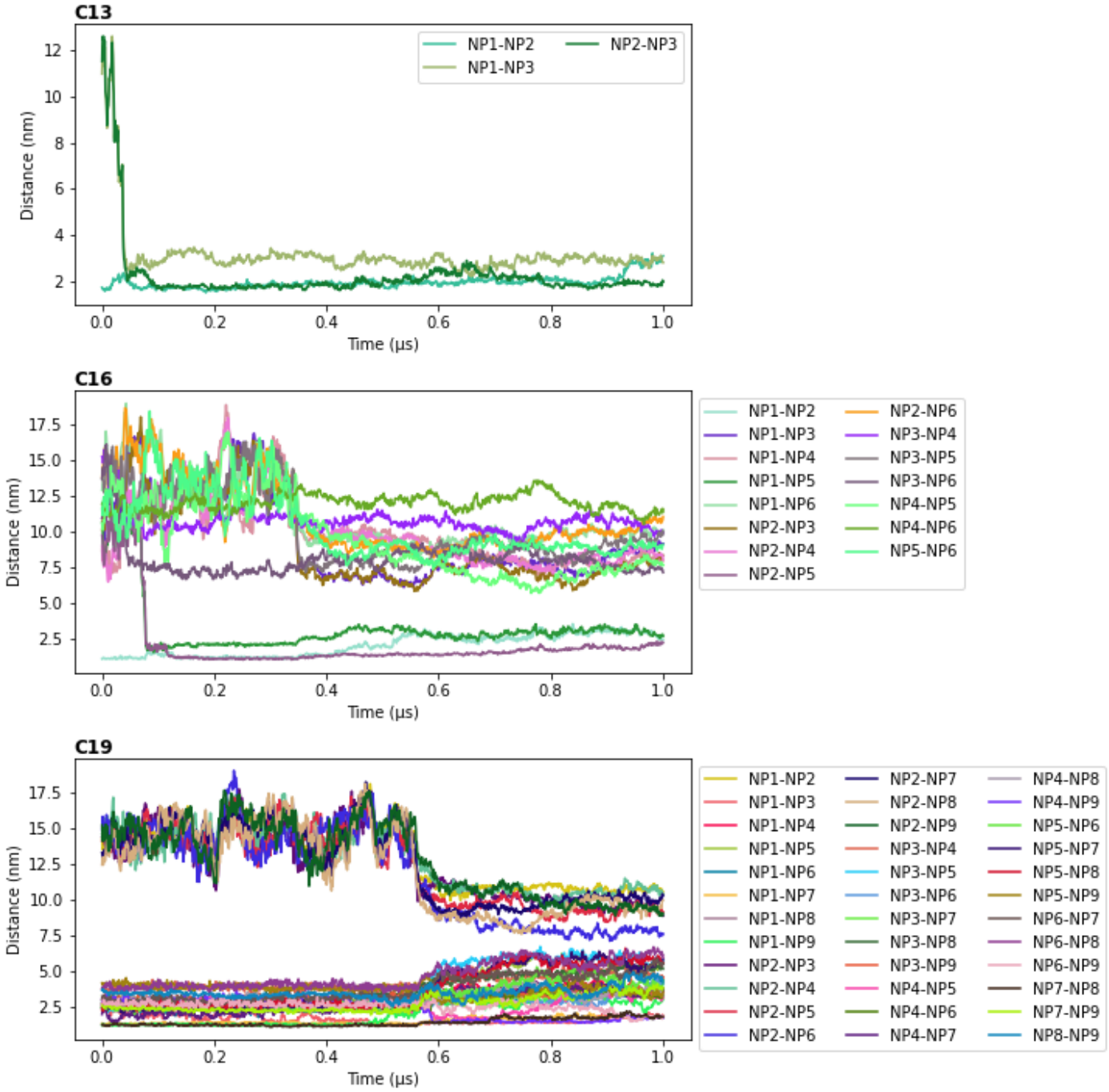


Figure S31. NP-NP pair distance for coated 1 nm NP.

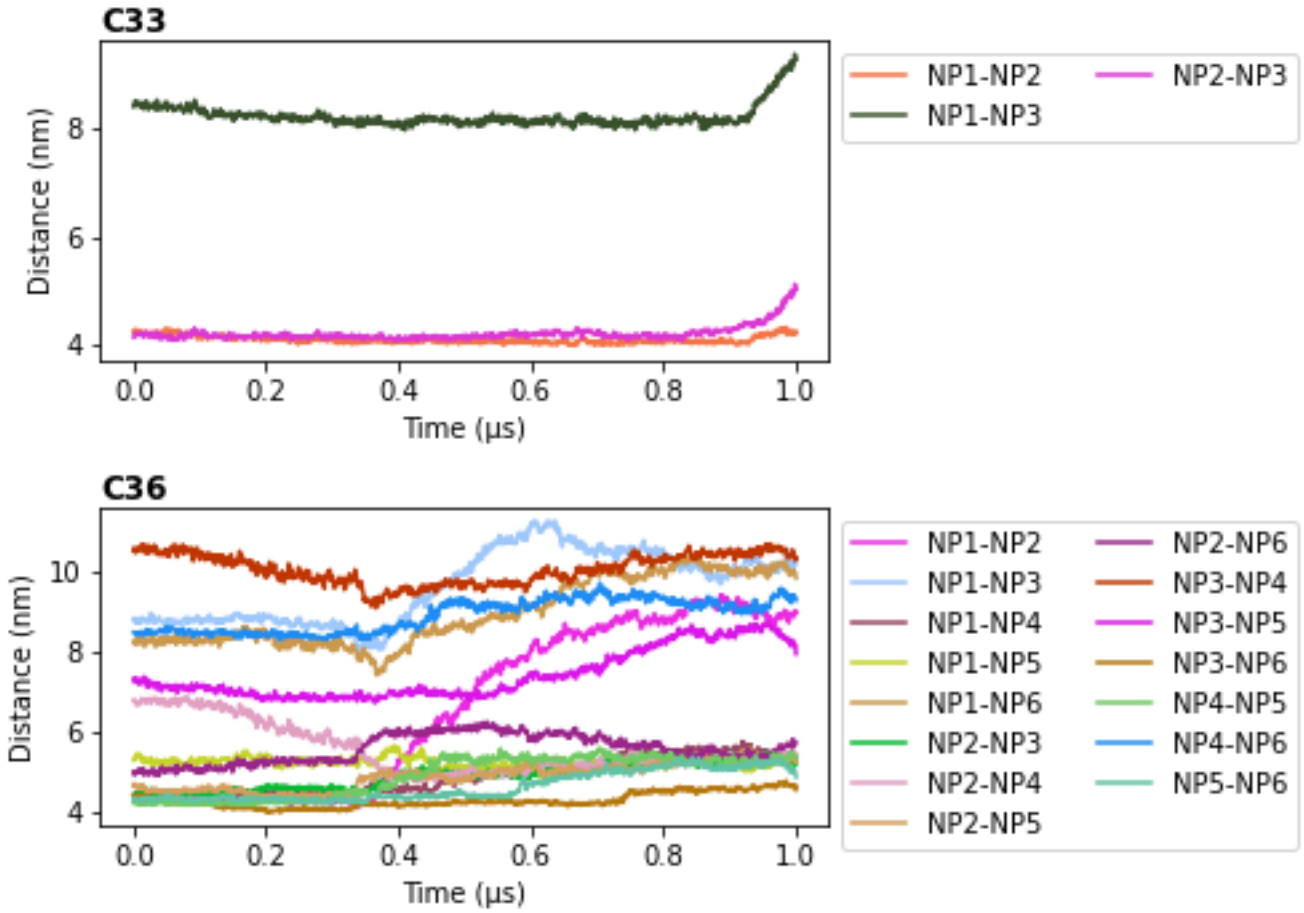


Figure S32. NP-NP pair distance for coated 3 nm NP.

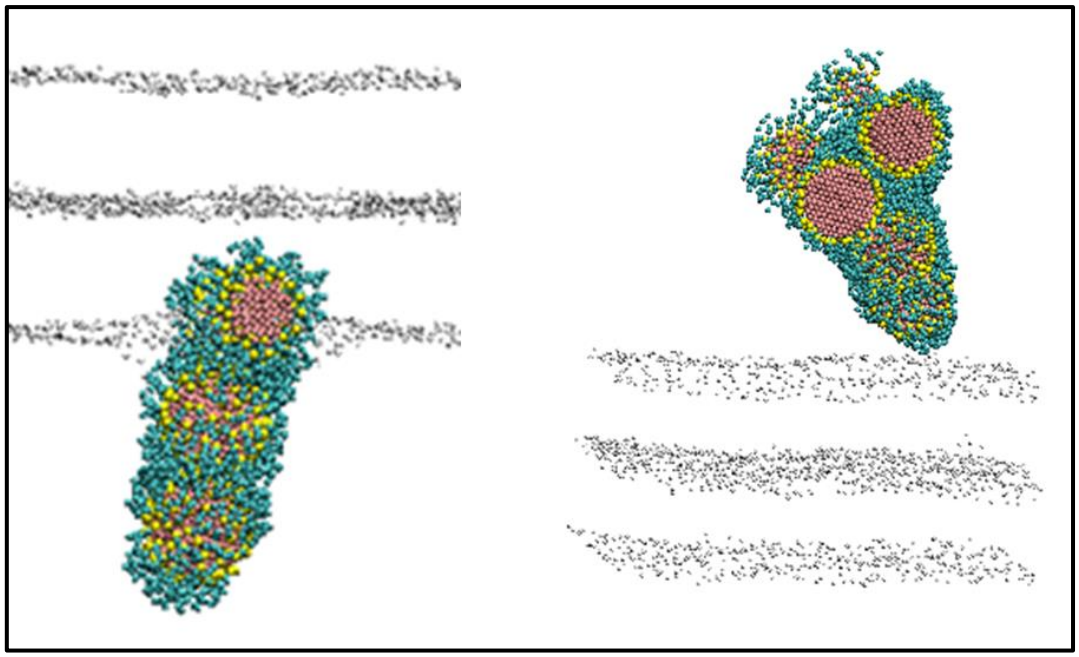


Figure S33. The penetration of trimer (left) and 6-mer (right) of coated NPs (3 nm) inside double bilayer system. The headgroup atom of CER is shown in white color. For coated NP, the Au, and thiol chains is colored pink, yellow, and cyan color respectively.