Permeation of Nanoparticles across Intestinal Lipid Membrane: Dependence on Shape and Surface Chemistry studied through Molecular Simulations

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Supporting Information

S1. Translocation barrier, rate constant and translocation time

The rate constants (k) for nanoparticle penetration was calculated by transition state theory rate constant equation:

$$k = \frac{k_B T}{h} exp\left[-\frac{\Delta G}{k_B T}\right]$$

Where, k_B is Boltzmann constant, T is temperature, h is planks constant, and ΔG is energy difference between maxima and minima in the PMF curve. Under the assumption that the translocation is the first order reaction, the half-life of the translocation can be given as

$$t_{1/2} = \frac{0.693}{k}$$

S2 Projected area on XY plane per lipid, lateral area and over all order parameter

In a molecular dynamics simulation of lipid bilayer, which has normal along the z direction, the area per lipid can be calculated using the following equation:

$$Area/N\_lipids = 2\frac{Lx\ Ly}{Nlipid}$$

$$Lateral\ Area = Lx\ Ly$$

Where L_x , L_y is the box length in X and Y direction, respectively and N_{lipid} is total number of lipids in the bilayer.

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

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

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

The overall order parameter was calculated using following relationship:

$$< S >= \frac{1}{nl}\sum_{i=1}^{nl}\sum_{j=1}^{n} Sz_i(j)\ /n$$

Where nl is number of lipid types in the system, n is number of beads in a lipid molecule and Sz (j) is order parameter for jth bead of lipid.

S3. Model apical lipid bilayer

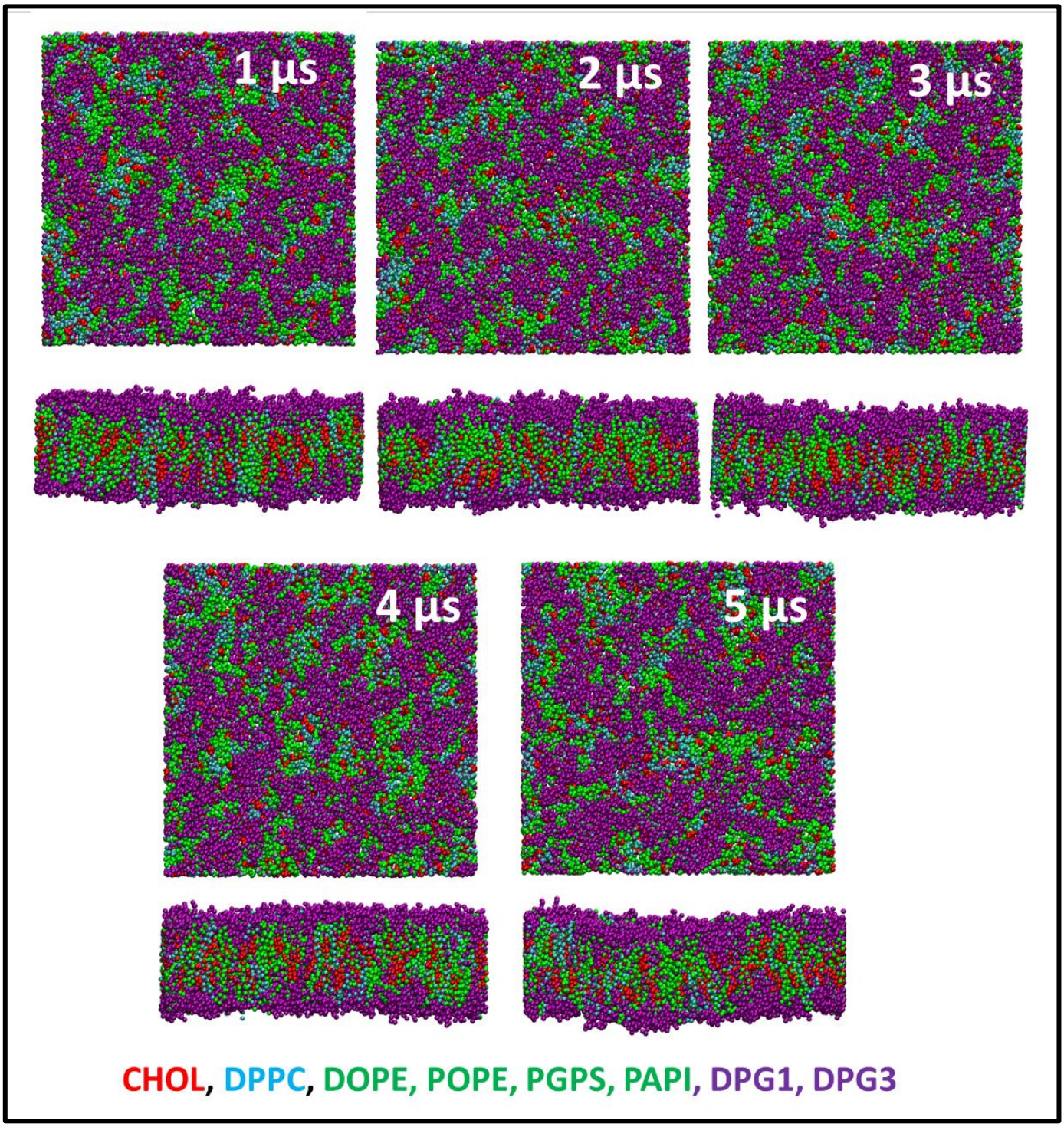

Figure S1. Structural evolution of model intestinal lipid bilayer. Water and ions were removed for visual clarity. The lipids are represented in vdw style. Images and snapshots were created using the VMD software.

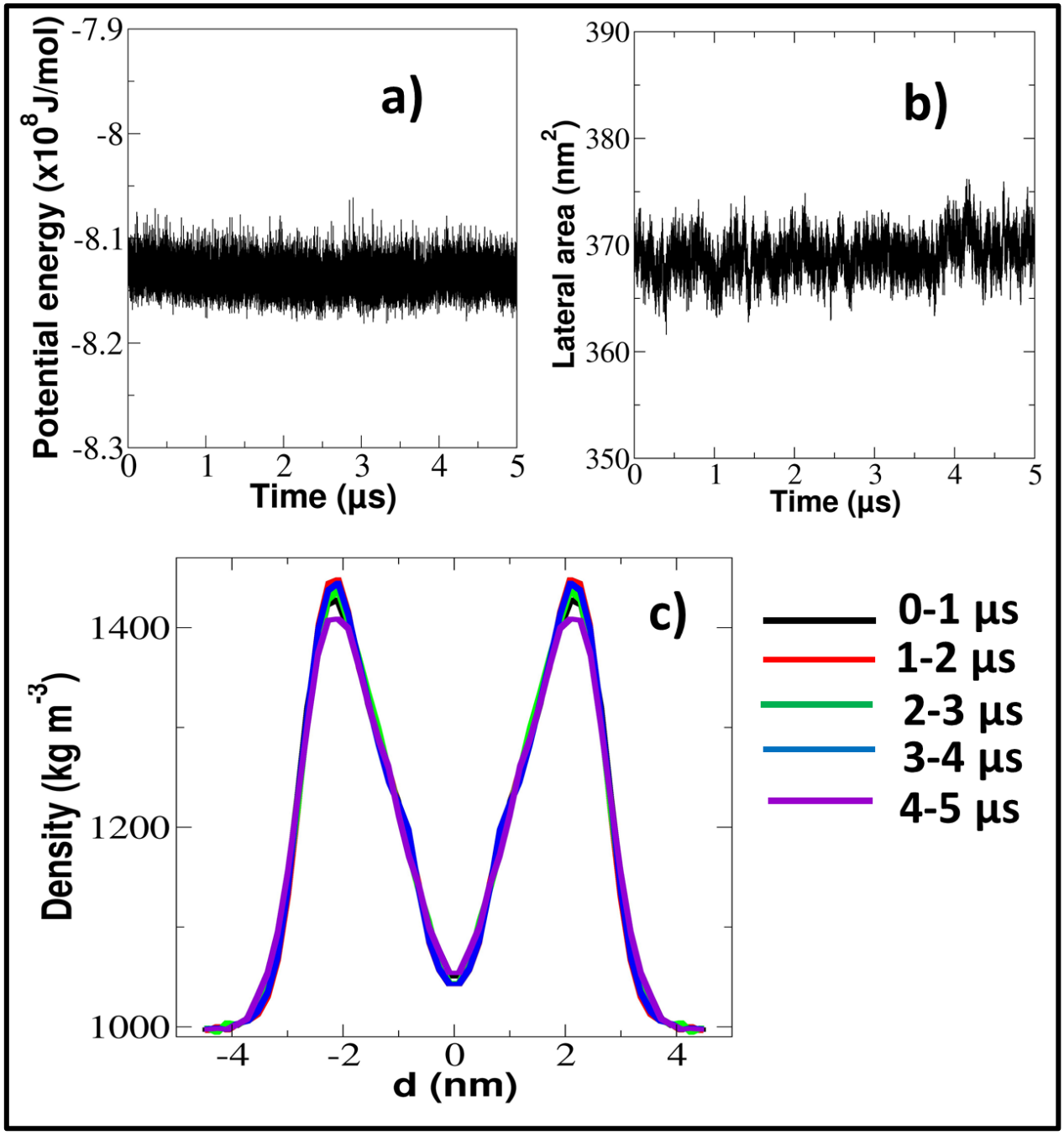

Figure S2. Strucutral properties of model lipid bilayer a) Evolution of potential energy b) lateral area of simulation box c) in last 5 μs simulation run c) density of biayer constituents along the bilayer normal calcualted in various simualtion time intervel.

S4. Convergence of free energy profile

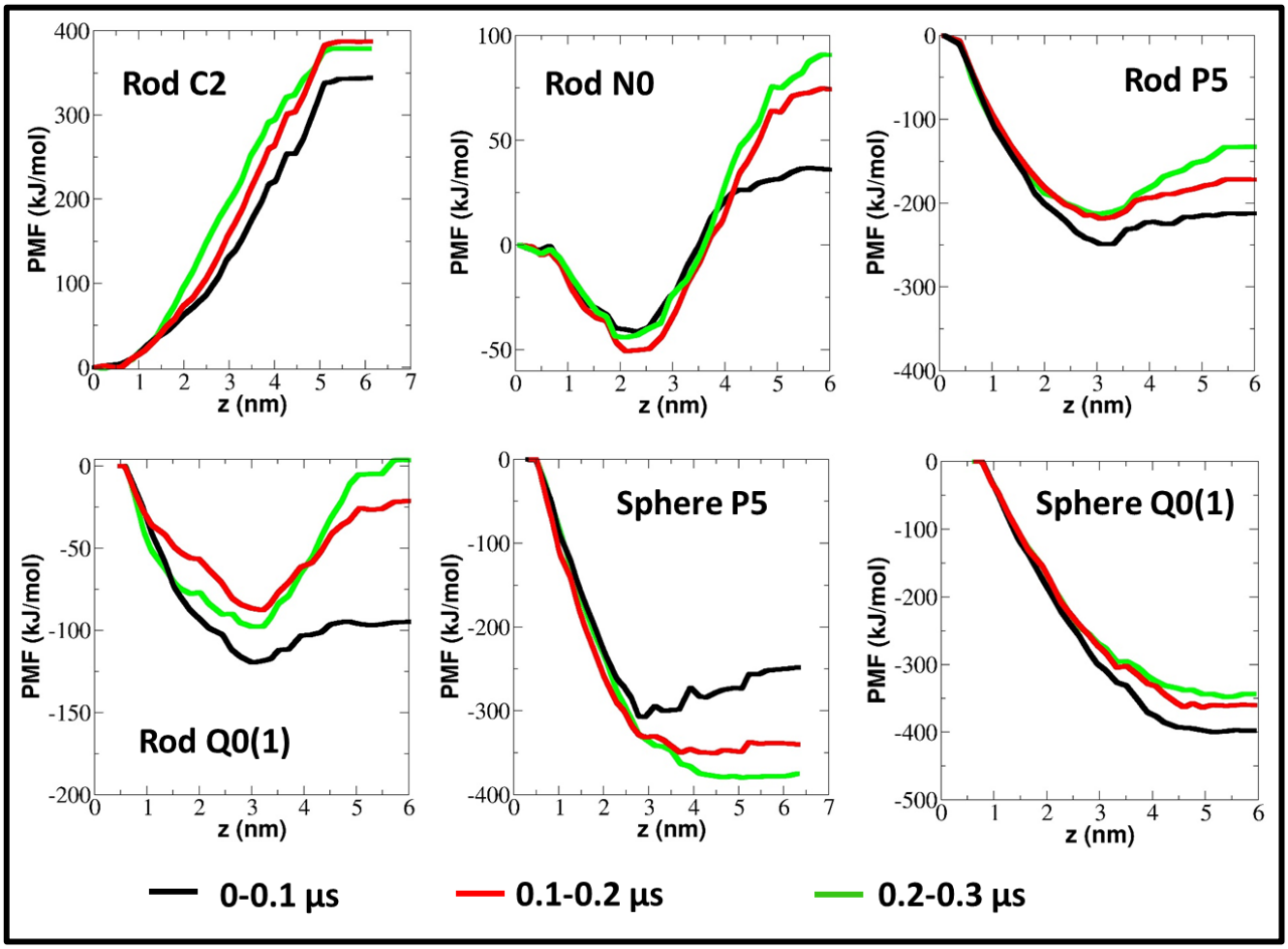

Figure S3. Convergence of potential of mean force profile of permeation of nanoparticle of various shapes and surface chemistry across model apical lipid layer calculated using umbrella sampling simulations. Here, z=0 correspond to the bilayer center.

S5. Radial distribution plot of rod, disc and spherical nanoparticles

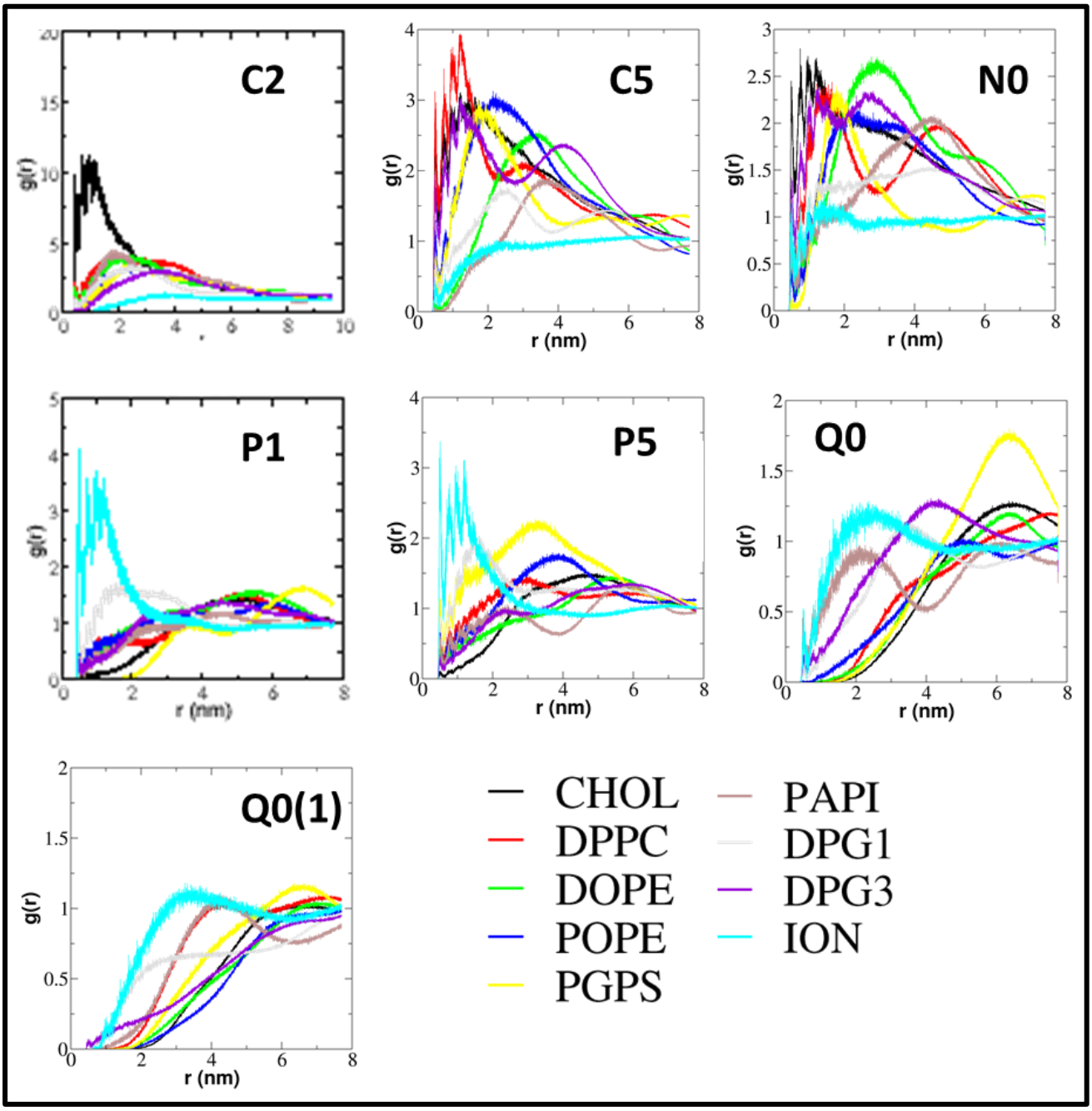

Figure S4. Radial distribution plot of rod-shaped nanoparticles having different surface chemistry calculated in last 0.3 µs simulation run.

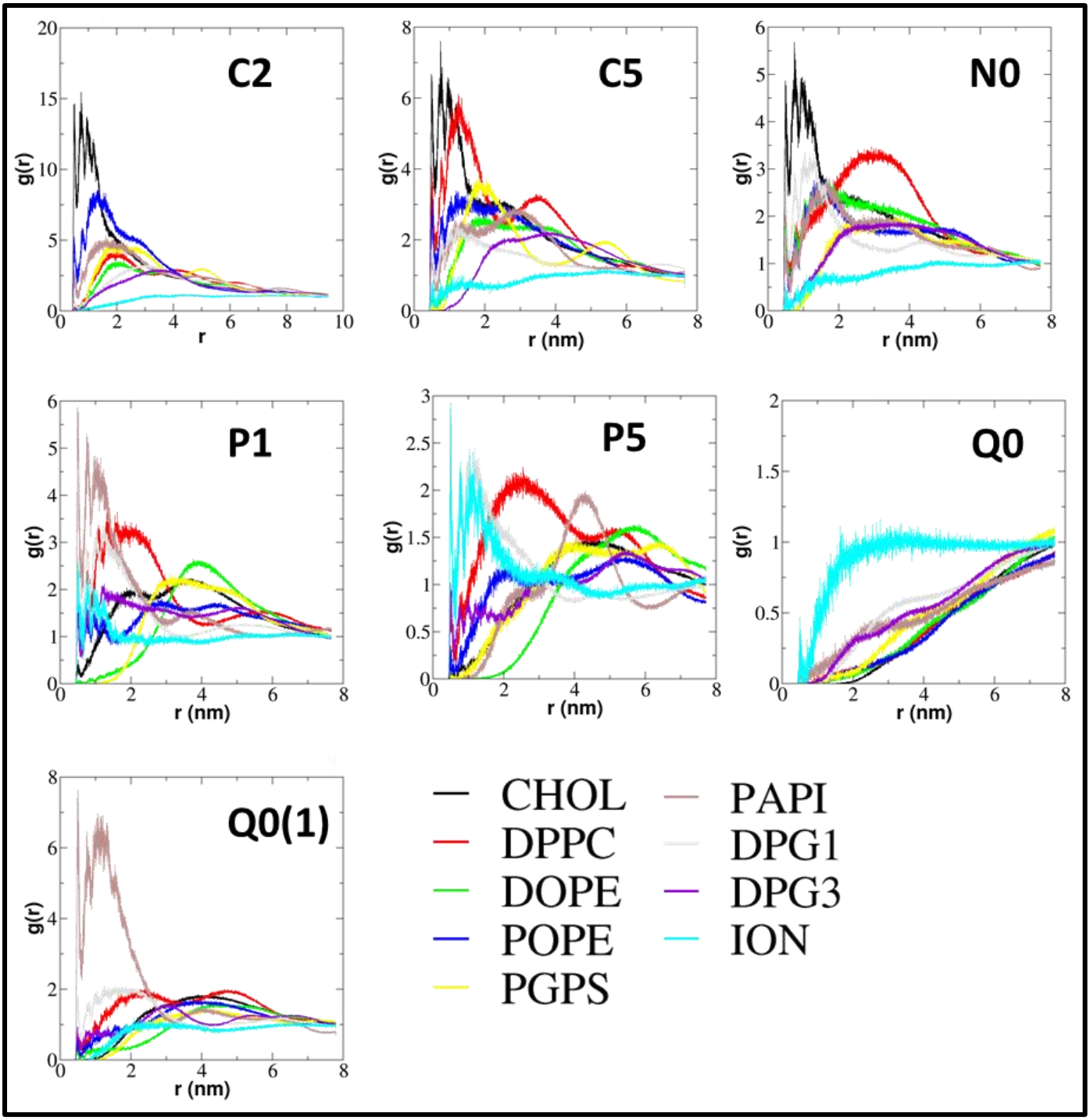

Figure S5. Radial distribution plot of disc shaped nanoparticles having different surface chemistry calculated in last 0.3 μs simulation run.

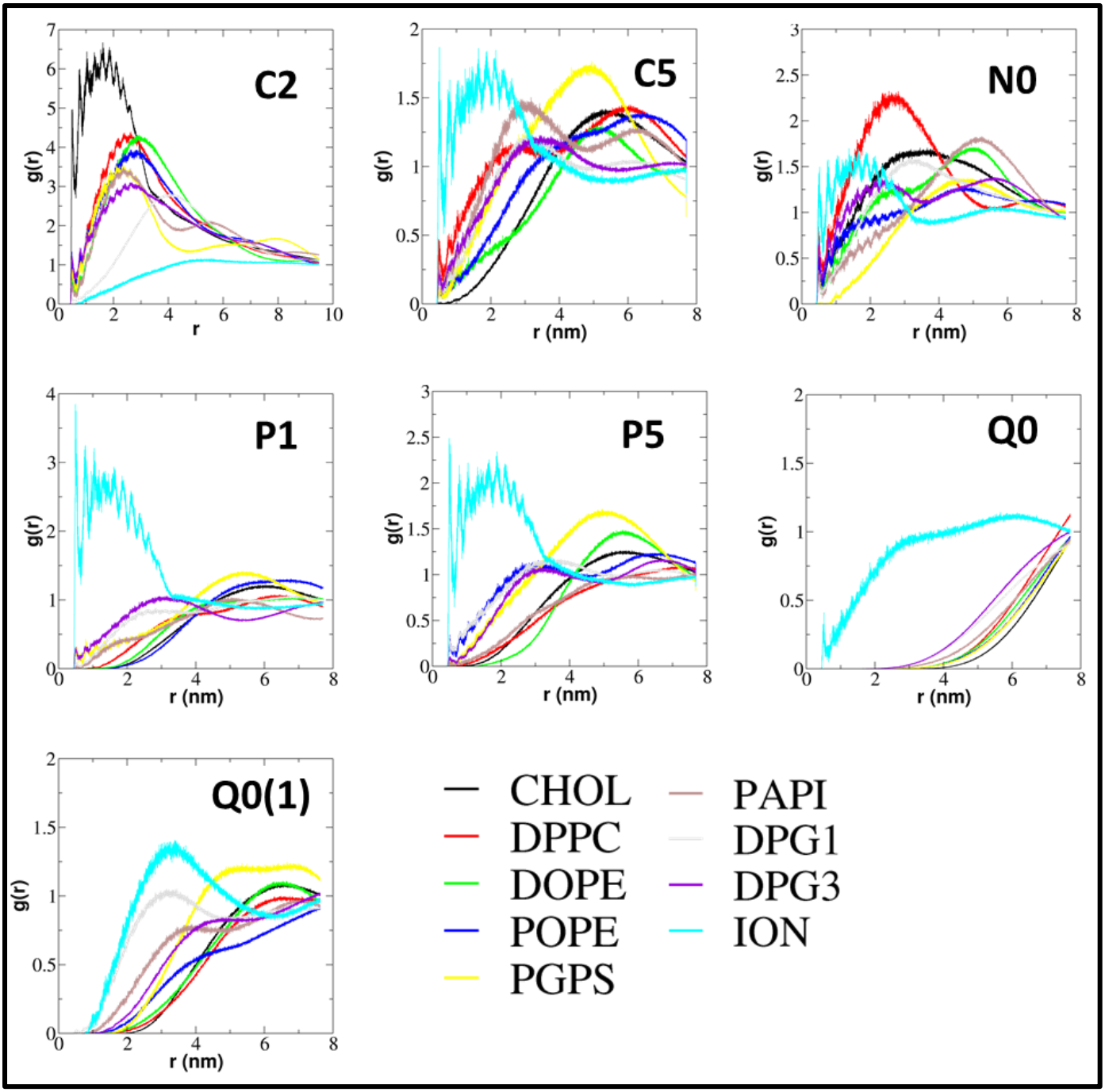

Figure S6. Radial distribution plot of sphere-shaped nanoparticles having different surface chemistry calculated in last 0.3 μs simulation run.

S6. Interaction of nanoparticles with apical lipid bilayer at high concentration

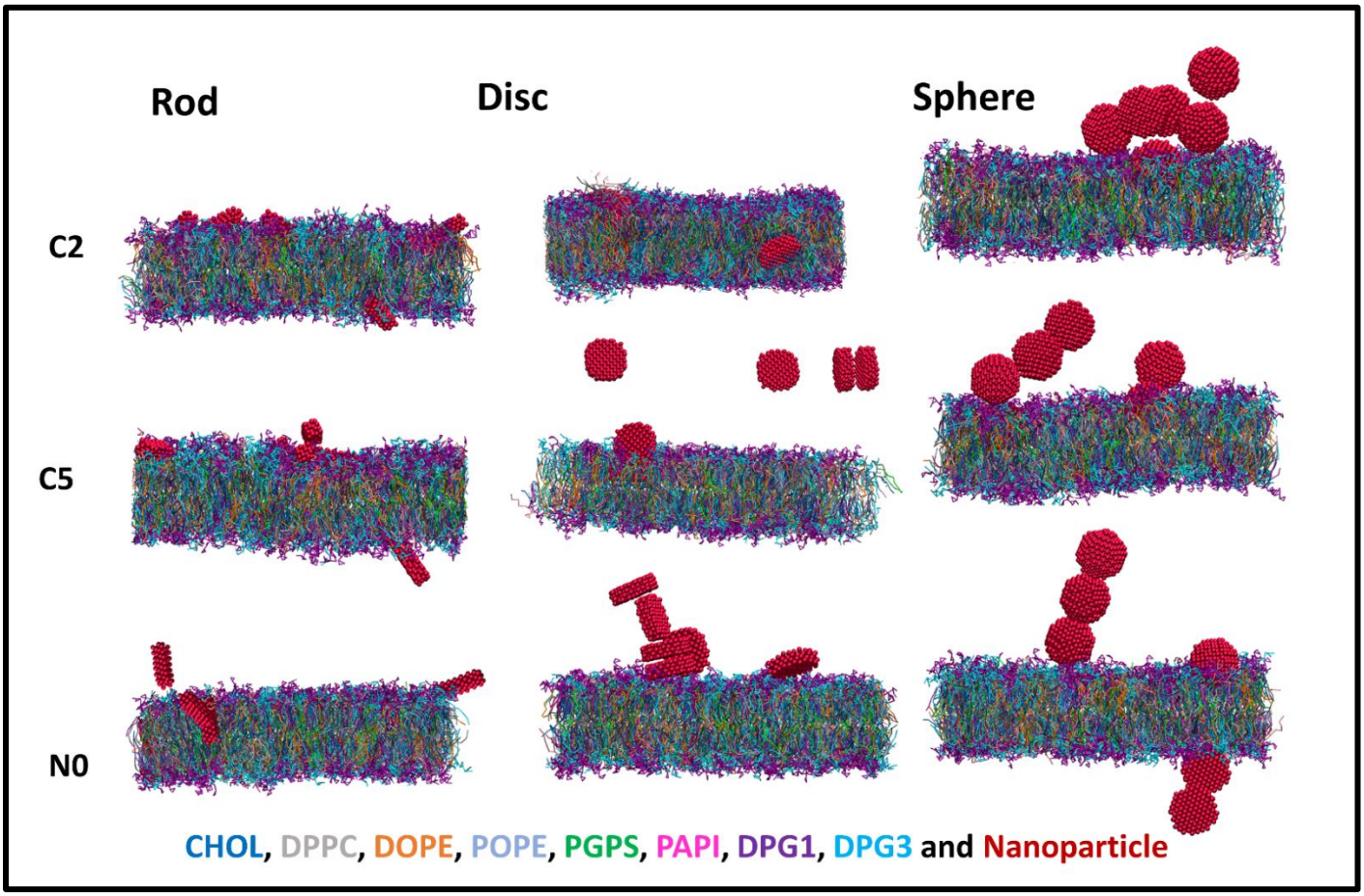

Figure S7. Snapshots of model apical bilayer systems in presence of nanoparticles of various shapes and surface chemistries at high concentrations (N=6) obtained at the end of 3 μs unrestrained simulation. The surface bead type is shown for each system (left). The lipids and nanoparticles are represented in the line and vdw style, respectively. The nanoparticles are shown in red color. Water and ions were removed for clarity. Images/snapshots were created using the VMD software.

S7. Protein corona formation on nanoparticles

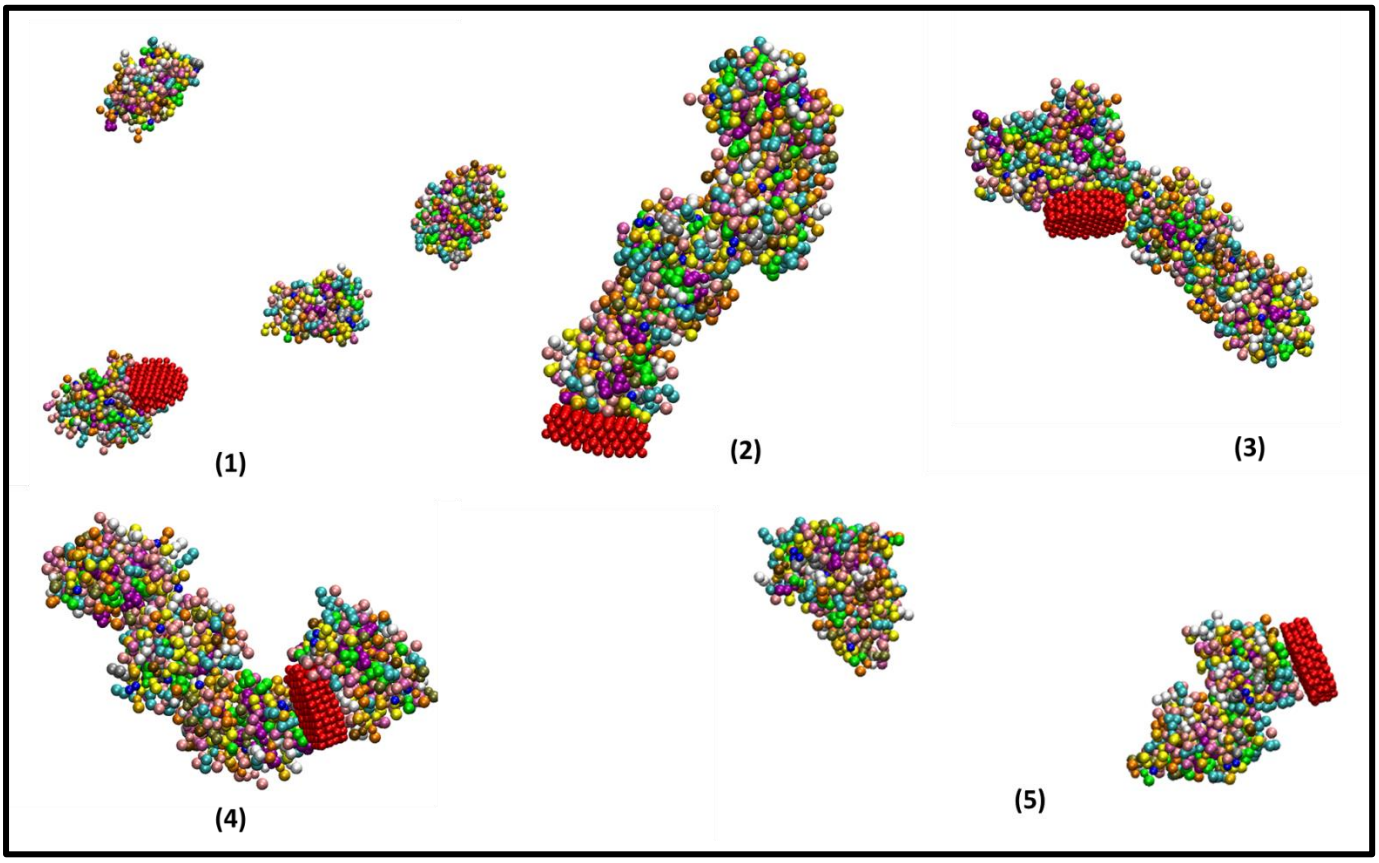

Figure S8. Snapshots of disc shaped C2(1) nanoparticle in presence of multiple proteins obtained in the end of 1 μs unrestrained simulation. Five different initial configurations were used for these simulations. The protein forms corona around the nanoparticle. The proteins and nanoparticles are represented in vdw style. The nanoparticles are shown in red color. Water and ions were removed for clarity. Images/snapshots were created using the VMD software.

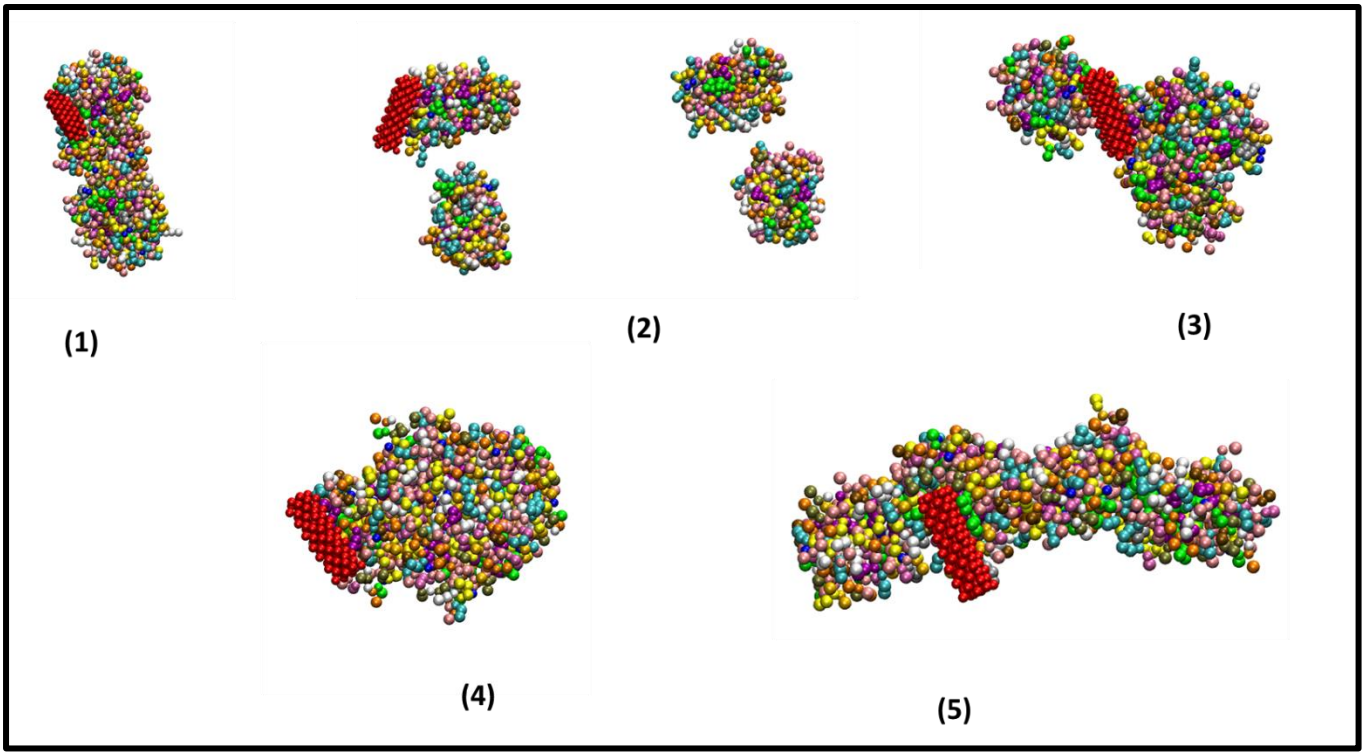

Figure S9. Snapshots of rod shaped C2(1) nanoparticle in presence of multiple proteins obtained in the end of 1 μs unrestrained simulation. Five different initial configurations were used for these simulations. The protein forms corona around the nanoparticle. The proteins and nanoparticles are represented in vdw style. The nanoparticles are shown in red color. Water and ions were removed for clarity. Images/snapshots were created using the VMD software.

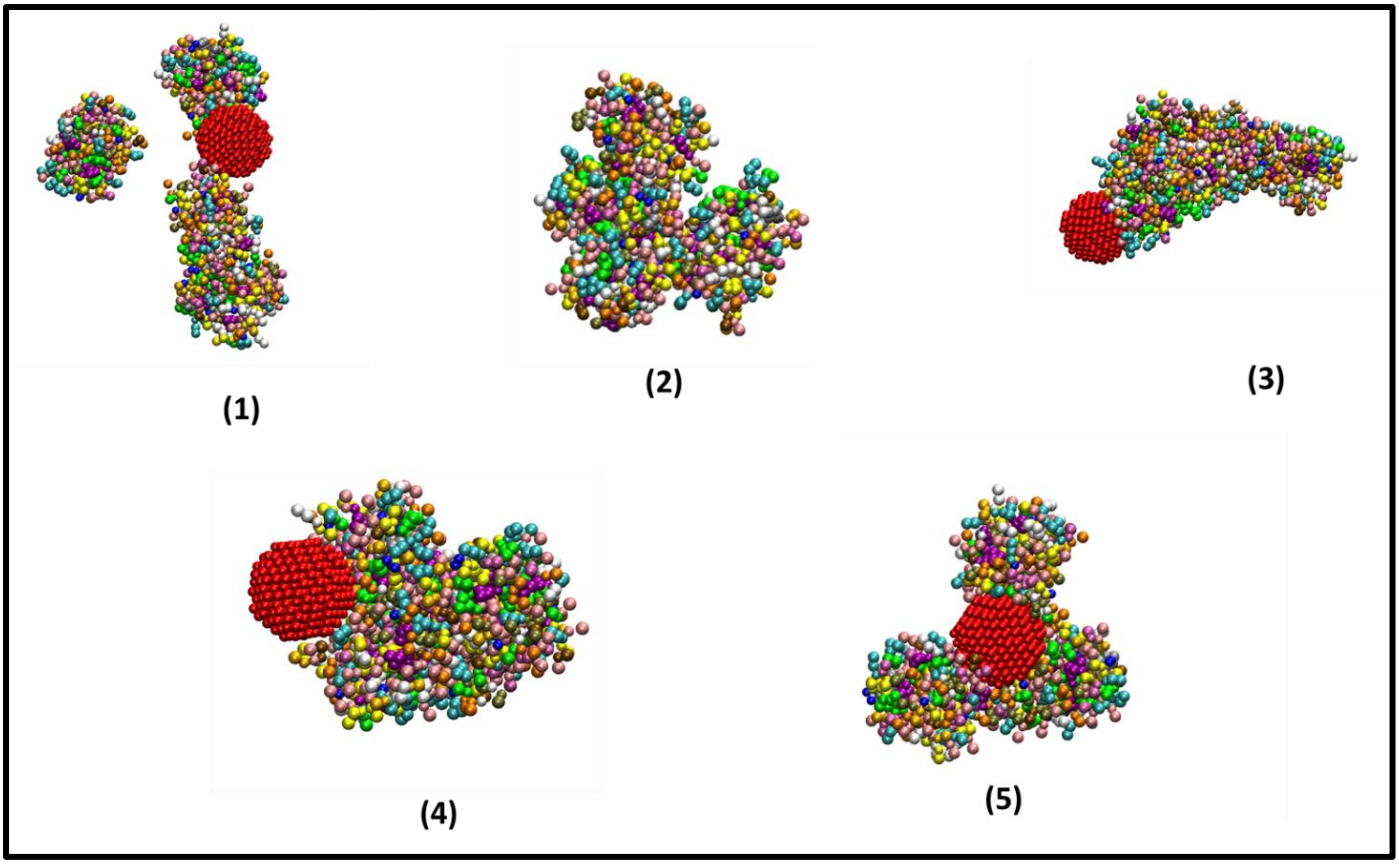

Figure S10. Snapshots of sphere shaped C2(1) nanoparticle in presence of multiple proteins obtained in the end of 1 μs unrestrained simulation. Five different initial configurations were used for these simulations. The protein forms corona around the nanoparticle. The proteins and nanoparticles are represented in vdw style. The nanoparticles are shown in red color. Water and ions were removed for clarity. Images/snapshots were created using the VMD software.