Transdermal Cellular Membrane Penetration of Protein with Gold Nanoparticle: A Molecular Dynamics Study

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Supporting Information

S1 Projected area on XY plane per lipid and over all order parameter

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

$$APL = 2\frac{Lx\,Ly}{Nlipid} \quad (1)$$

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:

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

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.

The overall order parameter was calculated using following relationship:

$$S = \frac{\sum_{i=1}^{n} Sz(i)}{n} \quad (3)$$

Where n is number of beads in the ceramide molecules and Sz is order parameter for i^{th} bead of ceramide chain.

S2. **Area compressibility**

The Area compressibility of a bilayer whose normal is oriented along the Z axis is calculated as:

$$K_A = k_b T \frac{<A>}{<A^2>-<A>^2} \qquad \text{(S1)}$$

$$A = (APL)\frac{N_{lipids}}{2} \qquad \text{(S2)}$$

Where, A is projected area on XY plane, N_{lipids} is number of lipids, k_b is the Boltzmann constant, and T is the temperature. The angular brackets denote the ensemble averages taken over the course of the simulation.

S3. Interaction of Au-protein with skin lipid bilayer.

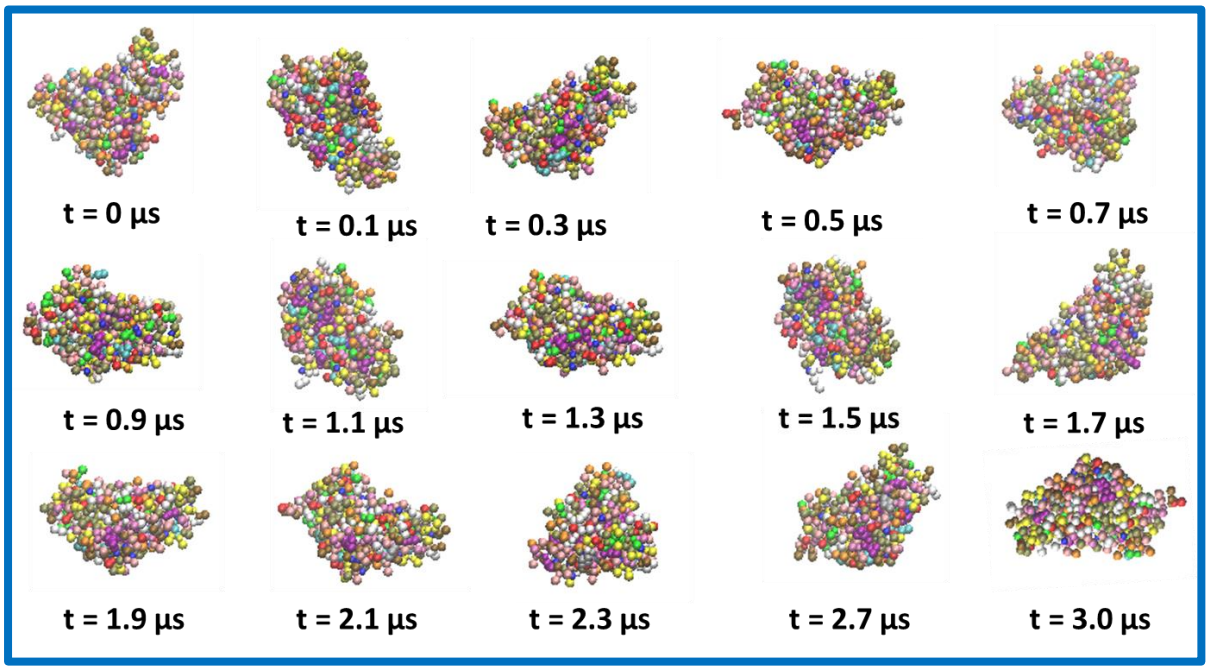

Figure S1. Snapshot of the conformation of HRP protein in the skin lipid bilayer in the presence of AuNP (bulk). The protein is shown in vdW style of VMD software. The snapshot were created using the VMD software.[1]

S4. Evolution of distance between the center of mass of lipid, AuNP and protein.

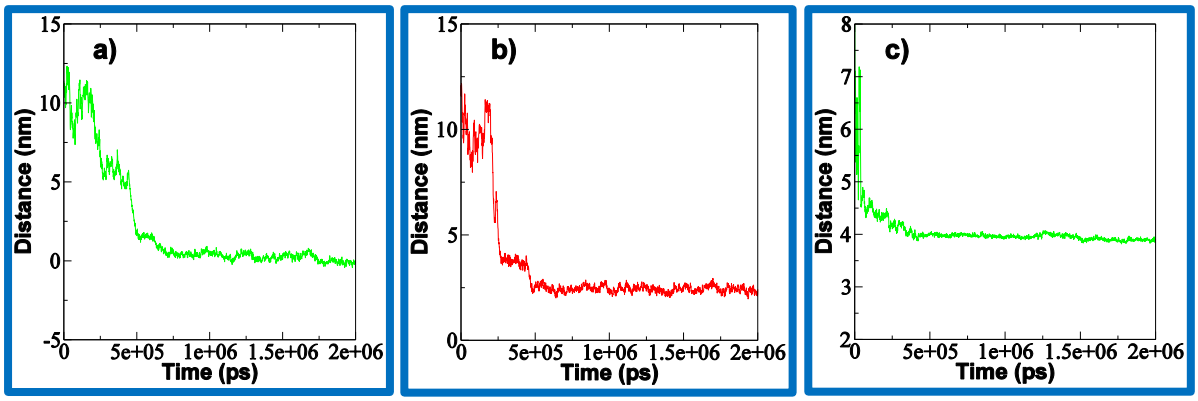

Figure S2. Evolution of distance between the center of the mass of a) AuNP-lipid b) Protein-lipid and c) AuNP-Protein in first 2 μs of unconstrained simulation in case (iii).

S5. Radial Distribution function

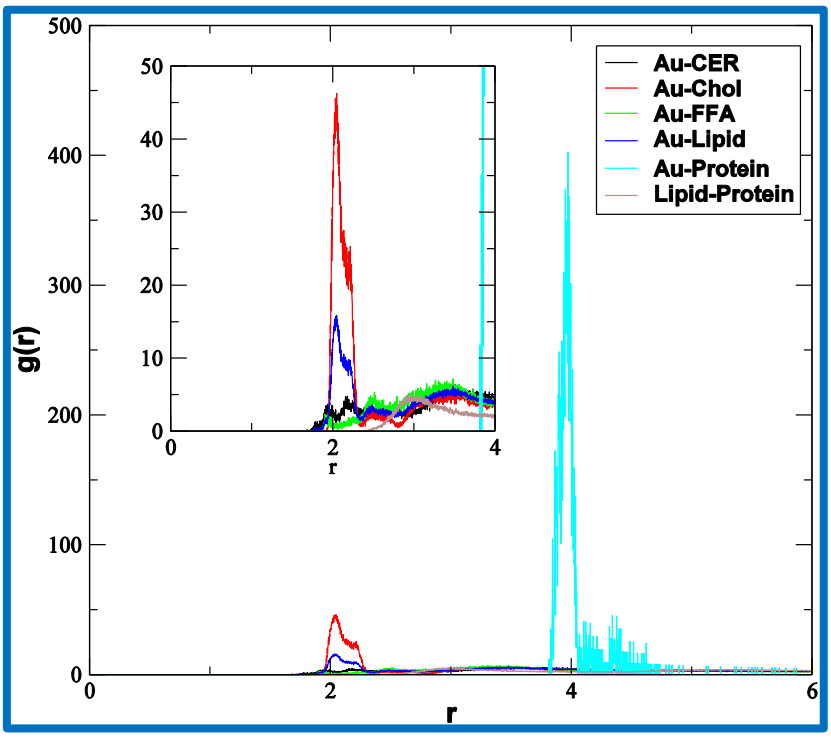

Figure S3. Radial Distribution function g(r) of CER, CHOL and FFA, lipid and protein with respect to AuNP calculated in 3 μs unconstrained simulation. For the purpose of the clarity, small peaks of CER, FFA, CHOL and lipid are shown in the inset of figure.

S6. Evolution of potential energy of the system

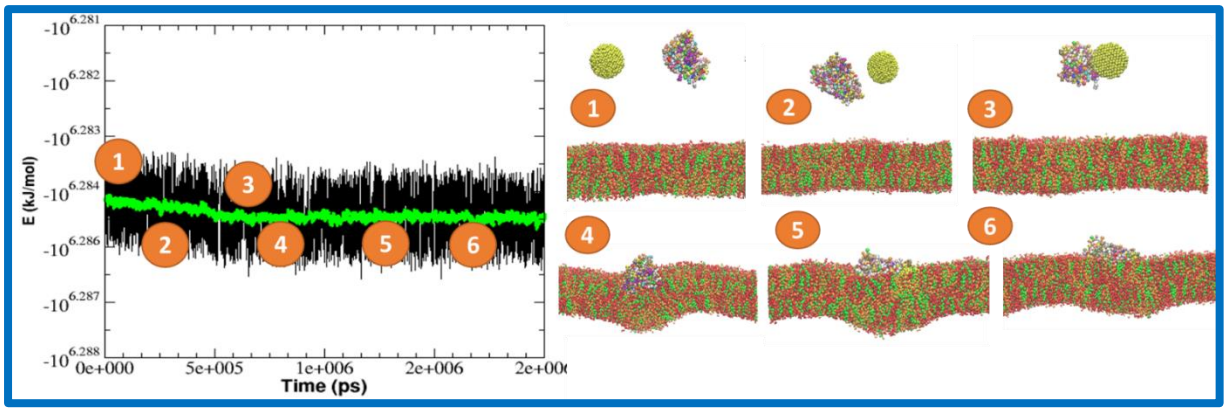

Figure S4. Evolution of the potential energy of the AuNP-Protein bilayer system (case iii) during the unconstrained simulation run (left). The changes in the potential energy are marked with points and corresponding snapshot of the system is also shown (right). The snapshots were created using the VMD software.[1]

S7. Order parameter

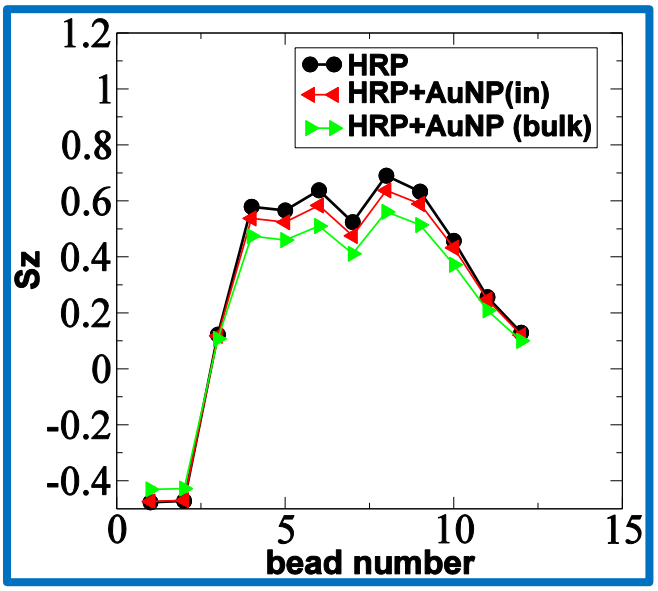

Figure S5. Order parameter of chain sn1 and chain sn2 of ceramide in each simulated system, calculated in unconstrained MD run.

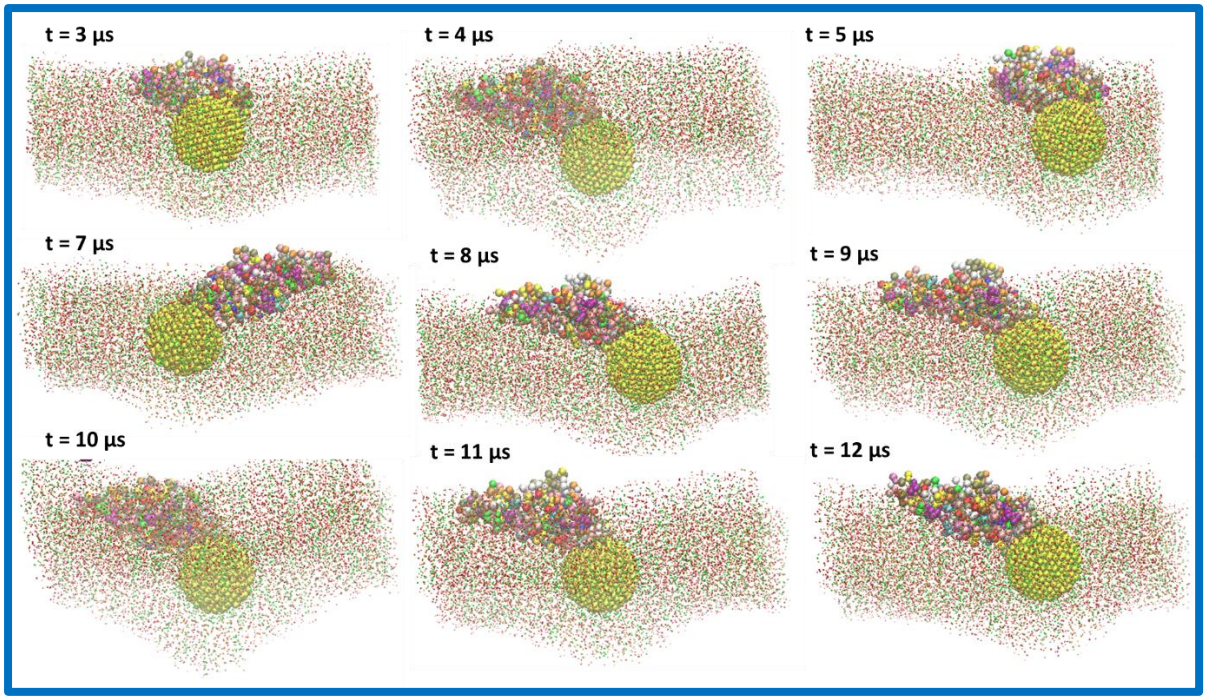

Figure S6. Interaction of HRP protein with the skin lipid bilayer in the presence of AuNP (bulk) during extended 12 µs simulation. The water molecules has been removed for the purpose of clarity. The Ceramide, cholesterol, free fatty acid are shown in point style and protein and gold nanoparticle are shown in vdW style of VMD software. The snapshot were created using the VMD software.[1]

S8. Interaction of Au-protein with skin lipid bilayer in constrained simulation.

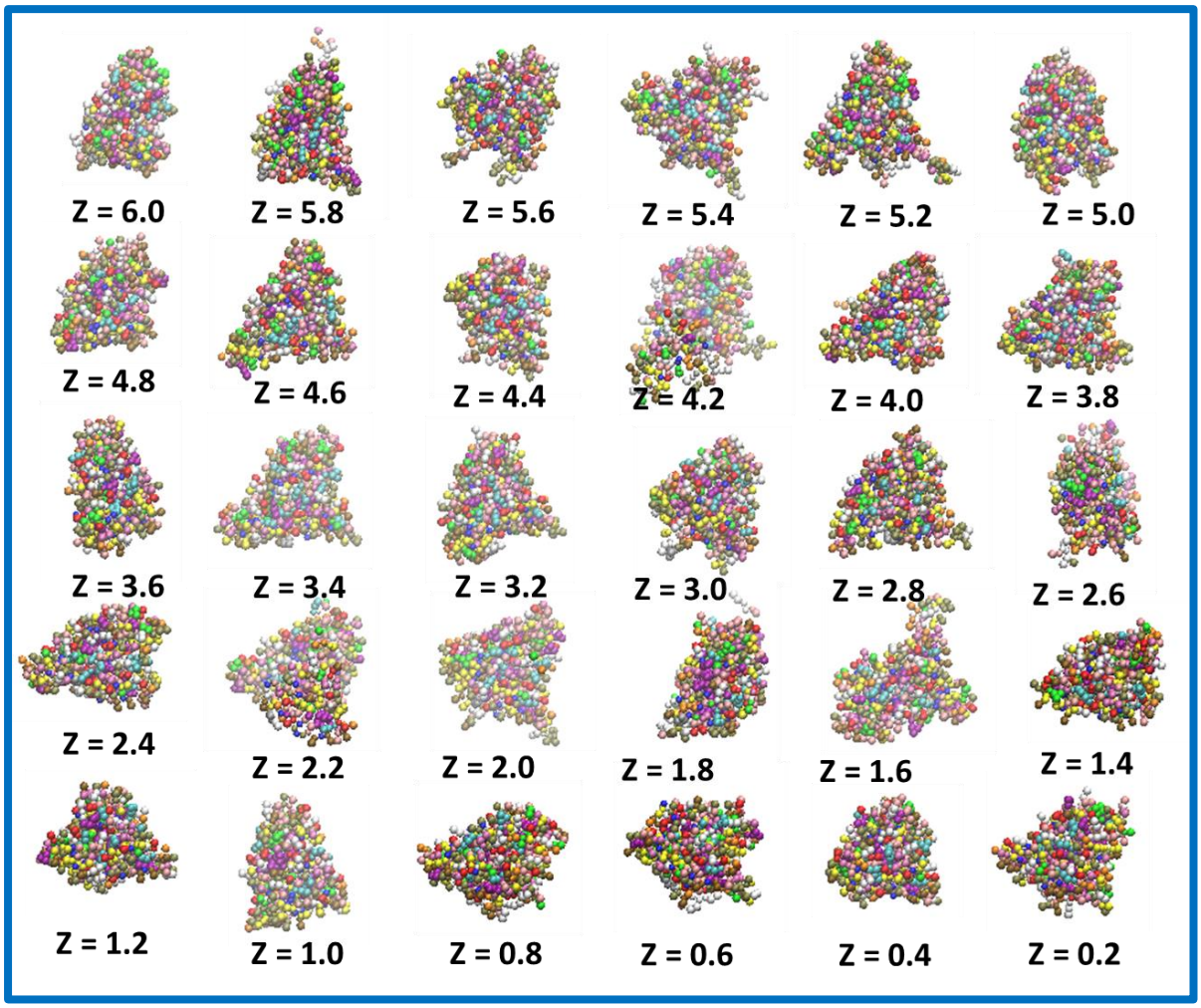

Figure S7. Snapshot of the conformation of HRP protein in the skin lipid bilayer in the presence of AuNP (bulk) during the constrained simulation run. The protein is shown in vdW style of VMD software. The snapshot were created using the VMD software.[1]

S9. Potential energy of the system calculated along the bilayer normal in constrained simulation.

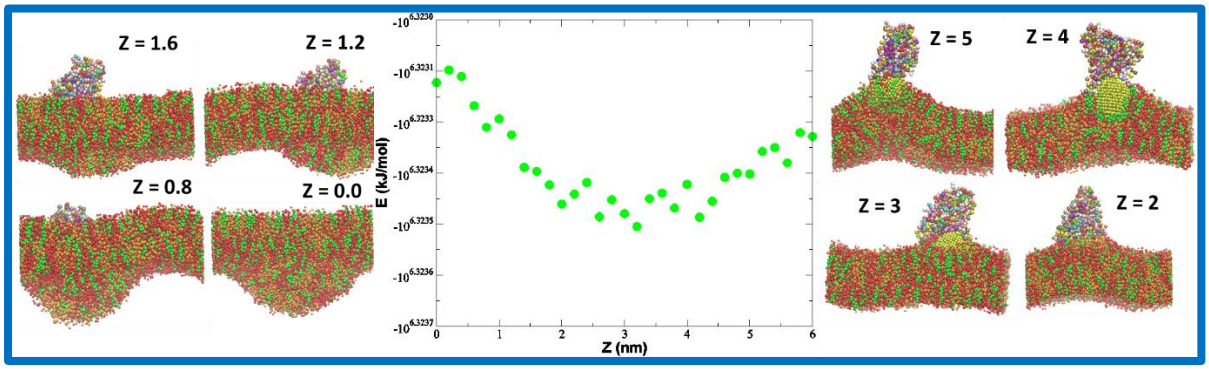

Figure S8. Potential energy of protein HRP-AuNP and bilayer system along the bilayer normal (z) calculated from constrained CG MD simulations. Here, z=0 correspond to the bilayer centre. The profile is shown only for upper bilayer leaflet. For colour code refer to web version of the article. The snapshots were created using VMD software.[1]

S10. Comparison between umbrella sampling and constrained simulation.

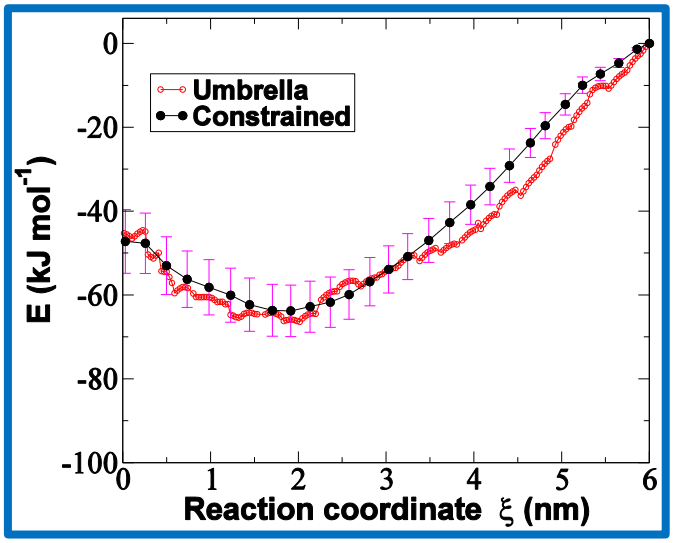

Figure S9. Potential of mean force or free energy of permeation of HRP-AuNP along the bilayer normal (z) calculated from umbrella sampling and constrained CG MD simulations. Here, z=0 correspond to the bilayer centre. The profile is shown for upper bilayer leaflet. For colour code refer to web version of the article.

Reference

1. Humphrey, W.; Dalke, A.; Schulten, K. VMD - Visual Molecular Dynamics. *J. Molec. Graphics.* 1996, 14.1, 33-38.