Electronic Supplementary Material (ESI) for Nanoscale.

Molecular Dynamics Simulation Study of Translocation of Fullerene C_{60} through Skin Bilayer: Effect of Concentration over Barrier Properties

Rakesh Gupta and Beena Rai*

Physical Science Research Area, TCS Research

Tata Research Development and Design Centre, Tata Consultancy Services,

54B, Hadapsar Industrial Estate, Pune – 411013, INDIA

*Corresponding author: beena.rai@tcs.com

Fax: 91-20-66086399

Tel: 91-20-66086203

Supporting Information

S1 Projected area on XY plane

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

$$A = 2\frac{Lx\,Ly}{Nlipid} \qquad \text{(S1)}$$

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.

S2 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.

S3. Overall order parameter along the bilayer axis Z

The overall order parameter was calculated using following relationship:

$$S = \frac{\sum_{i=1}^{n} Sz(i)}{n} \quad \text{(S3)}$$

Where n is number of beads in the ceramide molecules and Sz is order parameter for i^{th} bead of ceramide chain as shown in the figure 1.

S4. Order parameter script

The order parameter script (orderpy) is attached with the supplementary information.

S5. Bilayer Width

The volume per lipid (vpl) could be calculated by subtracting volume of water molecule from the total volume,

$$V = L_x L_y L_z \quad \text{(S4)}$$

$$V_{lipid} = \frac{V - N_W V_W}{N_{lipid}} \quad \text{(S5)}$$

where, V_{lipid} is volume per lipid, V is total volume of box calculated by simulation, N_W is number of water molecule, V_W is volume span by single water molecule at similar simulation conditions such as temperature, van der Waals and columbic cutoffs.

The average thickness of a bilayer is calculated based on volume and area per lipid using the following equation.

$$d = \frac{2 \times vpl}{apl} \quad \text{(S6)}$$

Where vpl and apl are calculated using equation S5 and S1 respectively.

S6. Evolution of potential energy

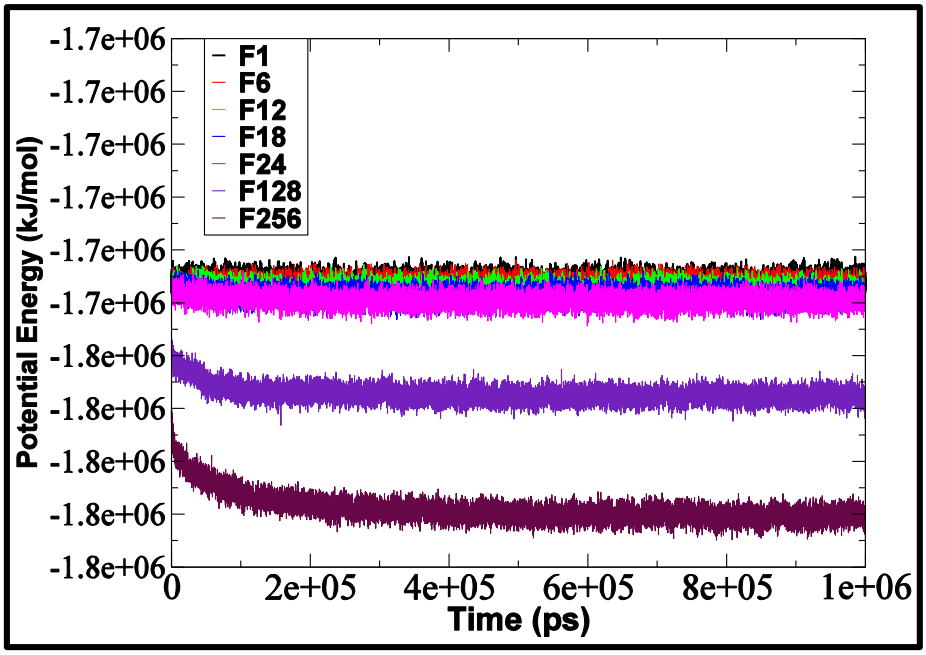

Figure S1. Evolution of potential energy of each fullerene-bilayer system in the course of first 1μs unconstrained MD simulation run.

S7. Evolution of box volume and projected area on xy plane

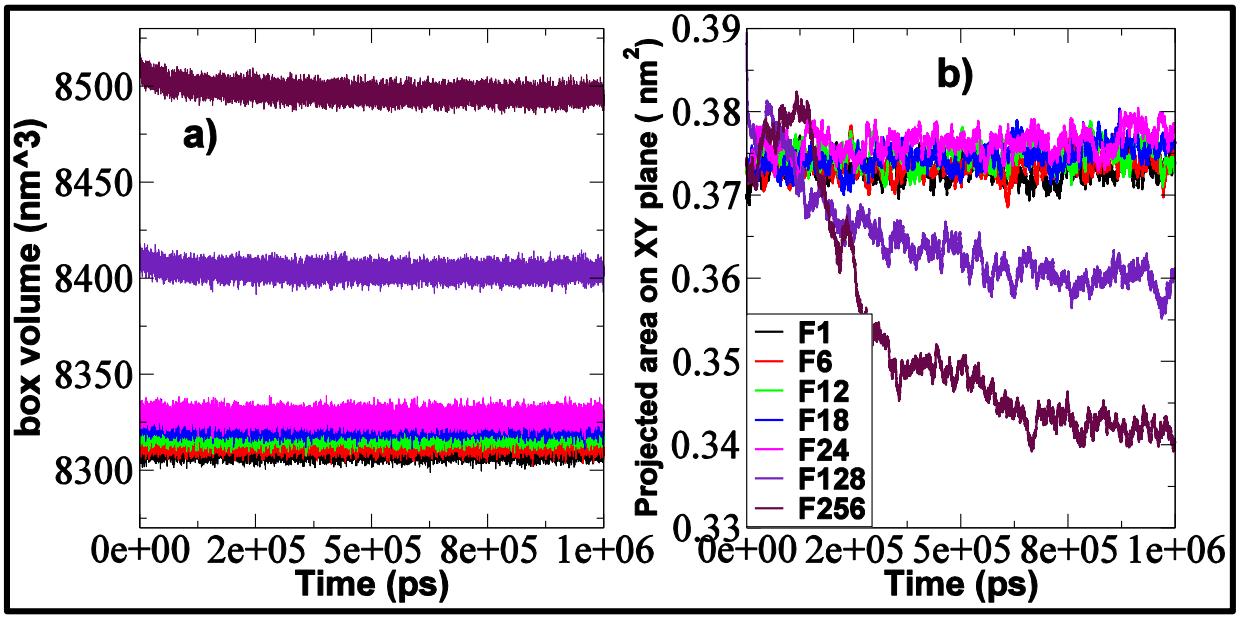

Figure S2. Evolution of a) box volume and b) projected area on XY plane per lipid of each fullerene-bilayer system in the course of first 1μs unconstrained MD simulation run.

S8. Evolution of center of mass distance between fullerene and bilayer.

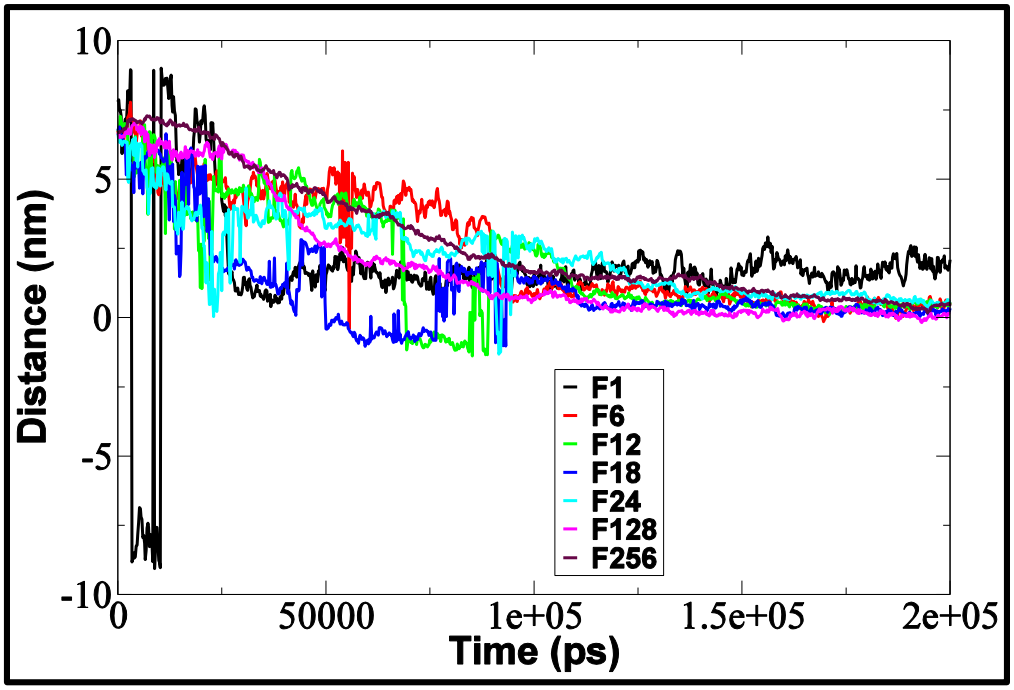

Figure S3. Evolution of distance between the center of mass of lipid and center of mass of fullerene in each fullerene-bilayer system in the course of first 200ns unconstrained MD simulation run.

S9. Evolution of density of individual skin lipid component and fullerene along the bilayer normal.

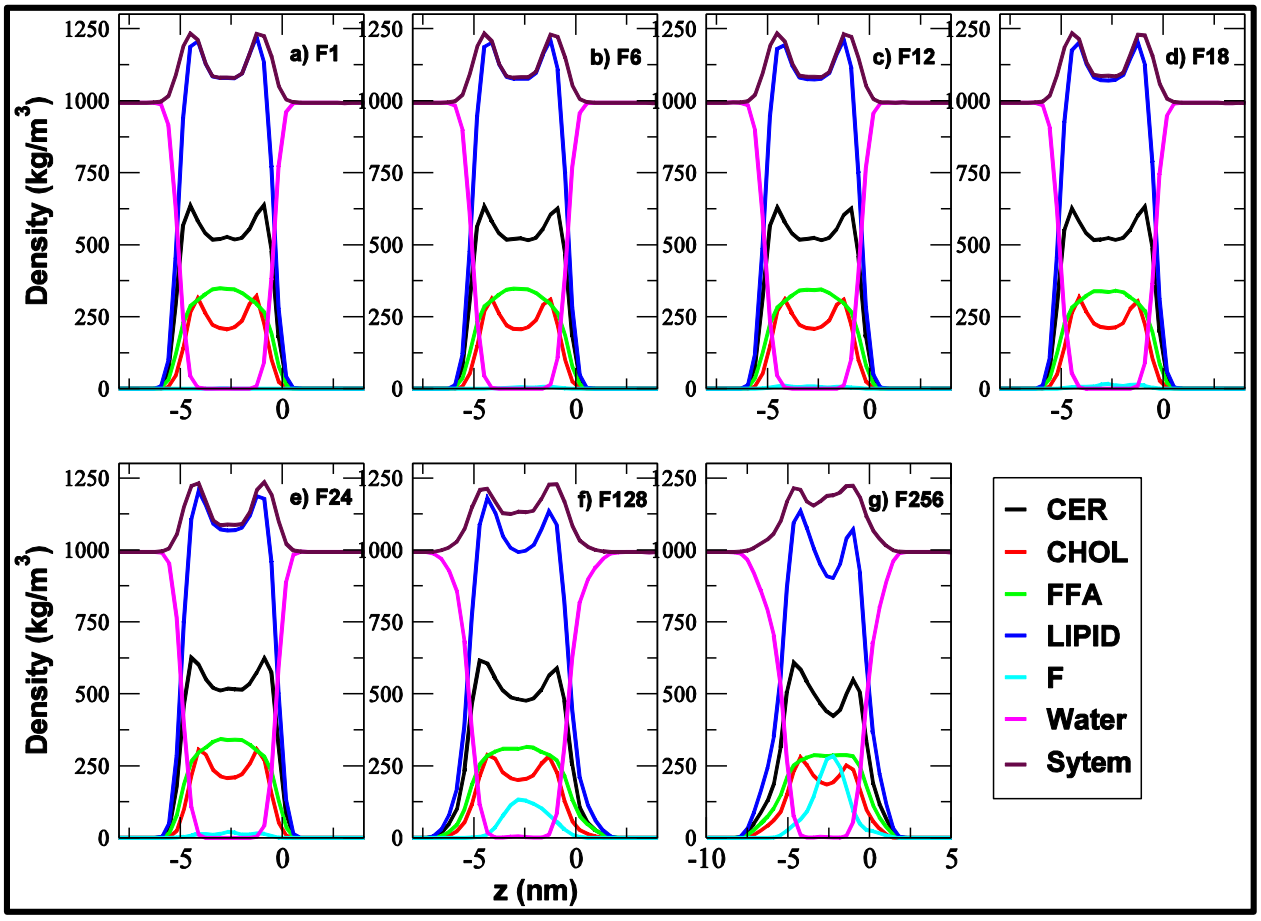

Figure S4. Evolution of density of individual component of bilayer along the bilayer normal (z) in each fullerene-bilayer system in the course of final 2 μs unconstrained MD simulation run.

S10. Effect of intermediate fullerene concentration on skin lipid bilayer: F48 and F60 system

In main text we have described the effect of fullerene concentration on bilayer structural properties both at lower and higher concentration of fullerenes. We have also performed additional simulations at intermediate concentration of fullerenes (system F48 and F60). These simulations have been carried out for 3 μs.

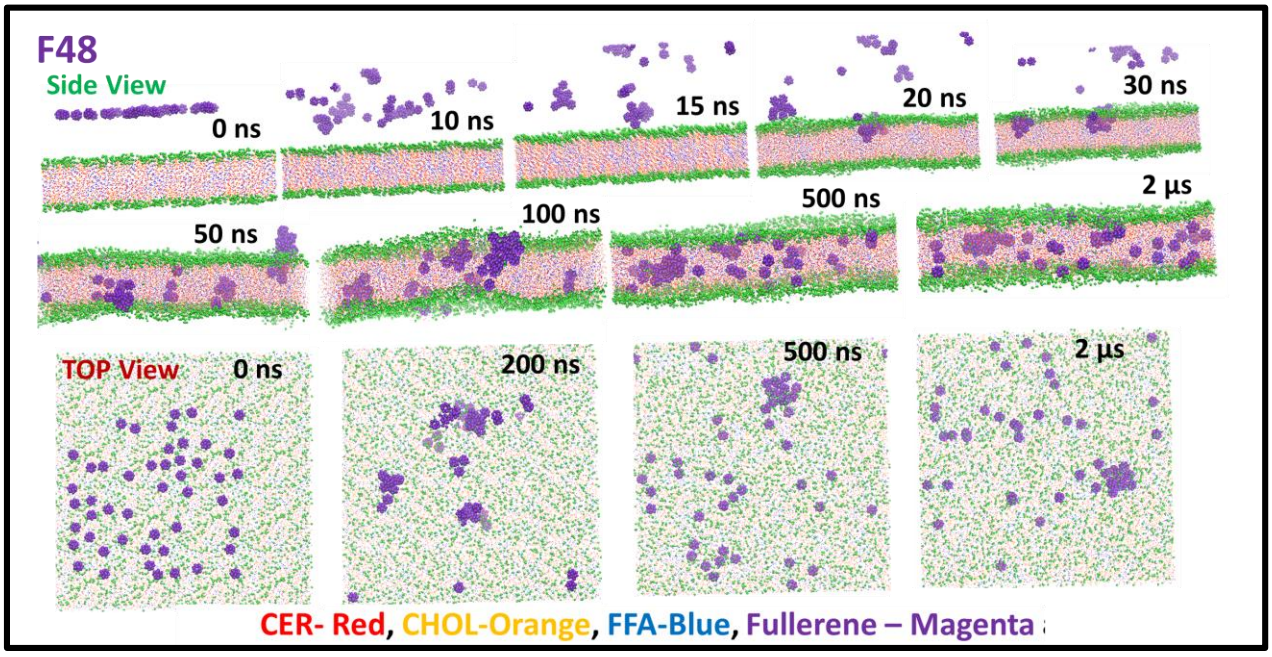

Figure S5. Structural changes induced by the fullerene molecules in skin lipid bilayer (F48 system) with simulation time. The head groups of lipids (CER, CHOL and FFA), CER tail, CHOL aromatic rings, FFA tail and fullerenes are shown in green, red, orange, blue and magenta respectively. Water molecules have been removed for the purpose of clarity. Images/snapshots were created using the VMD software.[1]

The interaction of the fullerenes at concentration of F48 and F60 with skin lipid bilayer are shown in the Figure S5 and Figure S6 respectively. In both of the cases, the fullerene molecules formed small (2 and 3 fullerenes) and bigger clusters (> 5 fullerenes). These cluster penetrated in the interior of the bilayer with in first 100 ns of simulation as observed in both lower and higher concentration cases (Figure 2).

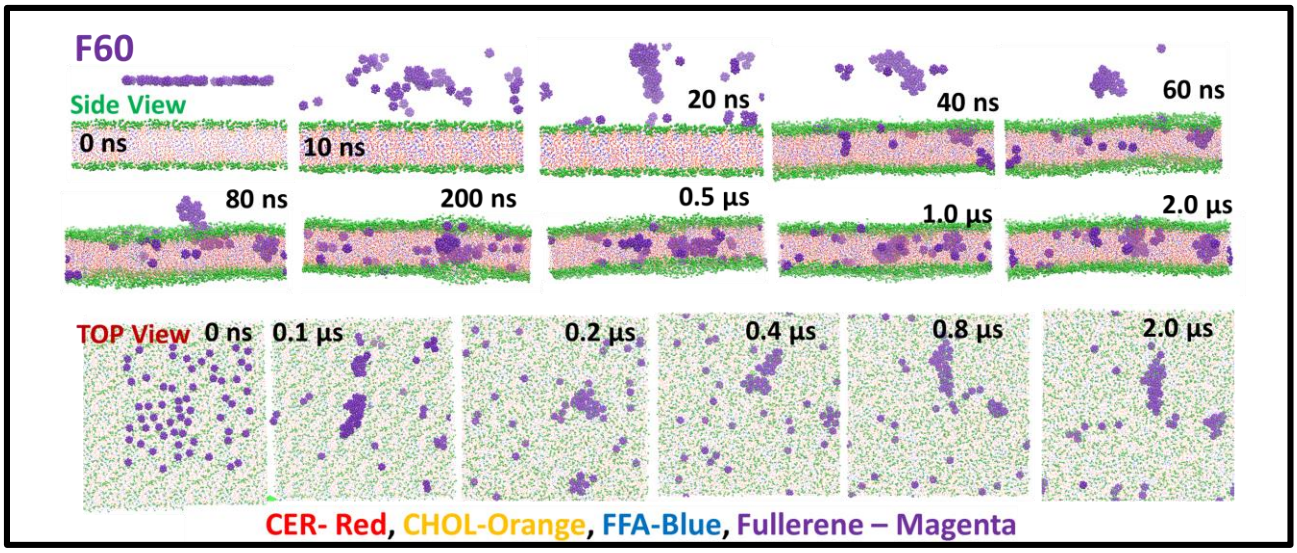

Figure S6. Structural changes induced by the fullerene molecules in skin lipid bilayer (F60 system) with simulation time. The head groups of lipids (CER, CHOL and FFA), CER tail, CHOL aromatic rings, FFA tail and fullerenes are shown in green, red, orange, blue and magenta respectively. Water molecules have been removed for the purpose of clarity. Images/snapshots were created using the VMD software.[1]

The interesting point to note that, at lower concentration (up to F24) the fullerenes formed small cluster in water layer and remained dispersed and penetrated as it is in the bilayer interior. In contrast, at higher concentration of fullerene (F128 and F256), the fullerenes aggregated in the water layer and penetrated inside the bilayer in the aggregated form (Figure 2). Here, at intermediate concentration fullerene were present both in small and big cluster and they penetrated in the bilayer interior spontaneously. The small cluster disintegrated in the bilayer interior in both F48 and F60 system. While large cluster did not disintegrate with in the simulation time frame of 3 µs. The cluster disintegration may take up to many microsecond, which was not possible to simulate with current computational capabilities.

S11. Effect of initial configuration of fullerenes on its permeation mechanism.

The unconstrained simulations were performed at lower and higher fullerene concentrations. The fullerene molecules were inserted in the upper layer of the bilayer. The fullerene molecules were significantly far apart in water layer and they did not aggregate in the simulation at lower concentration (Figure 2).

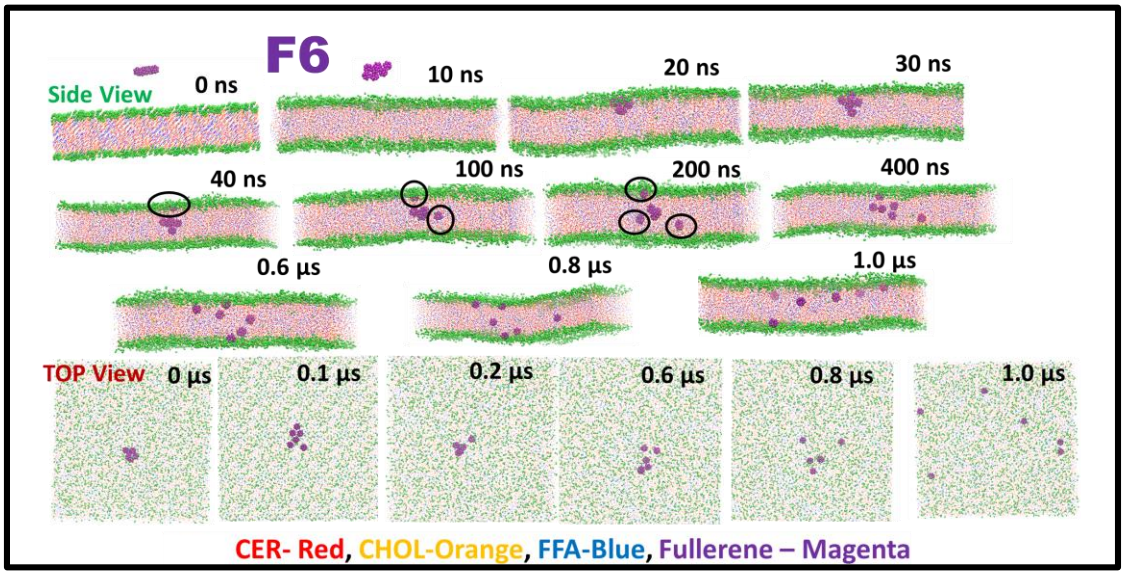

Figure S7. Structural changes induced by the fullerene molecules in skin lipid bilayer (F6 system) with simulation time. The head groups of lipids (CER, CHOL and FFA), CER tail, CHOL aromatic rings, FFA tail and fullerenes are shown in green, red, orange, blue and magenta respectively. The black circles shows the dispersed fullerene molecules in lipid interior. Water molecules have been removed for the purpose of clarity. Images/snapshots were created using the VMD software.[1]

To check the effect of initial fullerene packing, the additional simulations were performed at lower concentration range (F6 to F24). In these simulation the fullerene were kept very near to each other in the upper water layer. The simulation snapshots of interaction of fullerene with bilayer in F6, F12, F18 and F24 system are shown in Figure S7, Figure S8, Figure S9 and Figure S10 respectively. The simulation of F6 and F12 were ran for 1 µs, while F18 and F24 were ran for 3 µs.

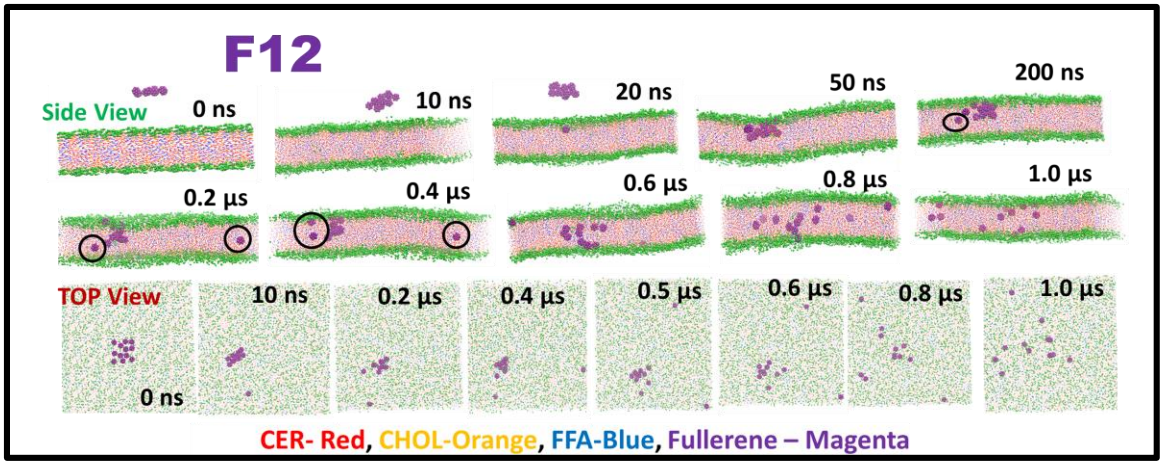

Figure S8. Structural changes induced by the fullerene molecules in skin lipid bilayer (F12 system) with simulation time. The head groups of lipids (CER, CHOL and FFA), CER tail, CHOL aromatic rings, FFA tail and fullerenes are shown in green, red, orange, blue and magenta respectively. The black circles shows the dispersed fullerene molecules in lipid interior. Water molecules have been removed for the purpose of clarity. Images/snapshots were created using the VMD software.[1]

It is interesting to note that, in each case fullerene molecules aggregated in the water layer spontaneously. The aggregated fullerene penetrated in the lipid interior with in first ~50 ns of simulation time. The aggregated fullerene started disintegrating in the bilayer interior for each case, but the rate at which it disintegrated was concentration dependent. In both F6 and F12 system, the fullerene aggregate was completely disintegrated within 1 µs simulation run and each fullerene molecule was dispersed in the bilayer interior (Figure S7, S8). On the other hand, the fullerene aggregate in both (F18 and F24) of the cases was much more stable. The disintegration process was very slow in both F18 and F24 system, even after 3 µs, only 5 and 6 fullerene molecules were dispersed in F18 and F24 system respectively (Figure S9, S10). The complete disintegration may take up to several microseconds.

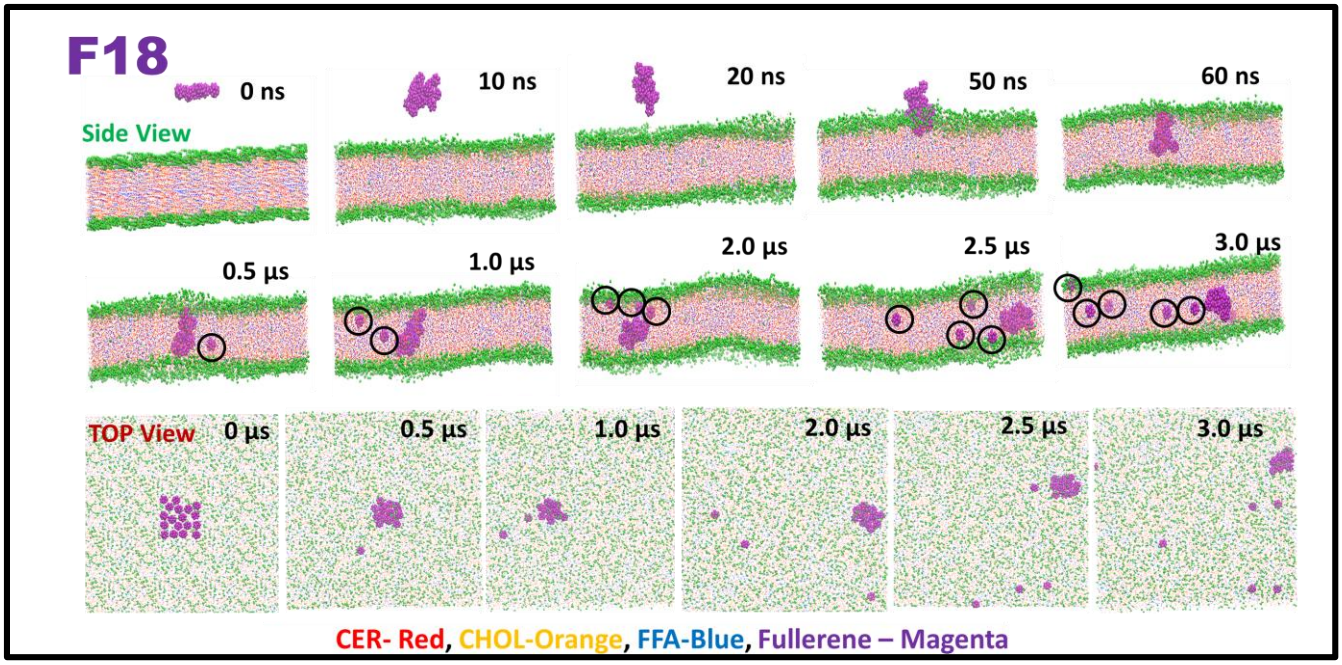

Figure S9. Structural changes induced by the fullerene molecules in skin lipid bilayer (F18 system) with simulation time. The head groups of lipids (CER, CHOL and FFA), CER tail, CHOL aromatic rings, FFA tail and fullerenes are shown in green, red, orange, blue and magenta respectively. The black circles shows the dispersed fullerene molecules in lipid interior. Water molecules have been removed for the purpose of clarity. Images/snapshots were created using the VMD software.[1]

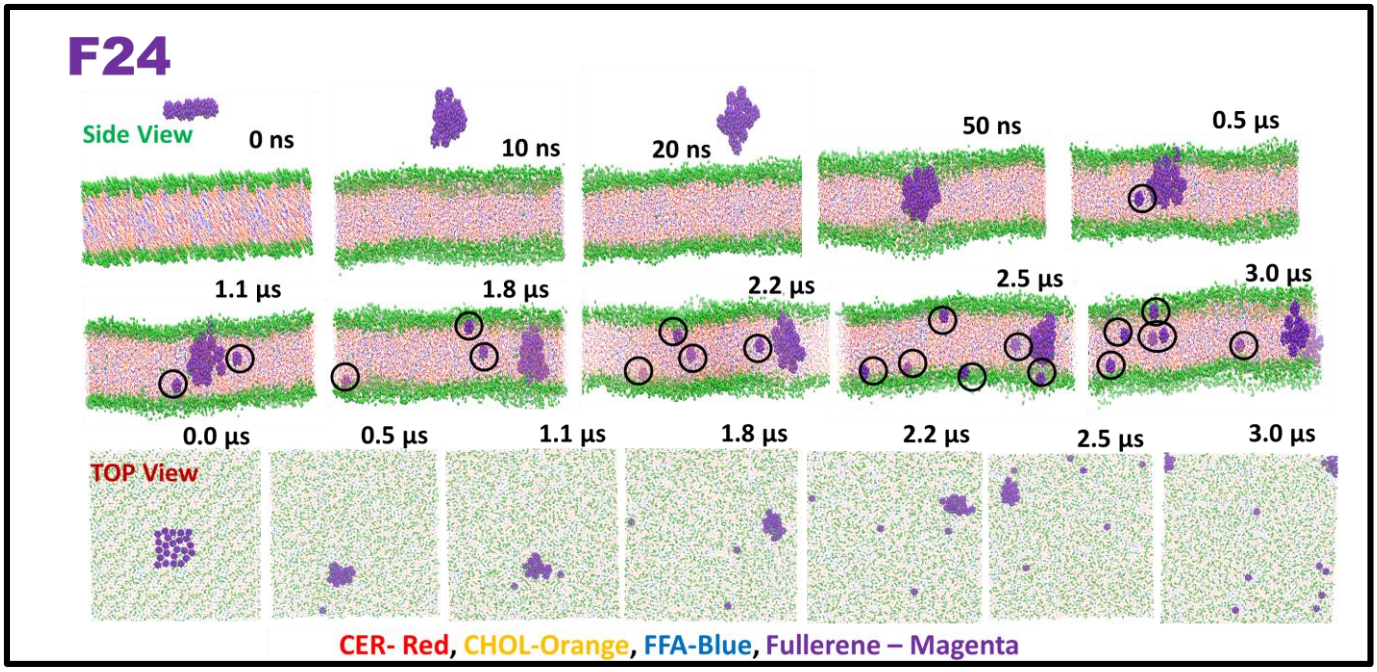

Figure S10. Structural changes induced by the fullerene molecules in skin lipid bilayer (F24 system) with simulation time. The head groups of lipids (CER, CHOL and FFA), CER tail, CHOL aromatic rings, FFA tail and fullerenes are shown in green, red, orange, blue and magenta respectively. The black circles shows the dispersed fullerene molecules in lipid interior. Water molecules have been removed for the purpose of clarity. Images/snapshots were created using the VMD software.[1]

References

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