Supporting Information

Penetration of DPPC Monolayer by Nanoparticles: Insights from Molecular Dynamics Simulation

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Supporting Information

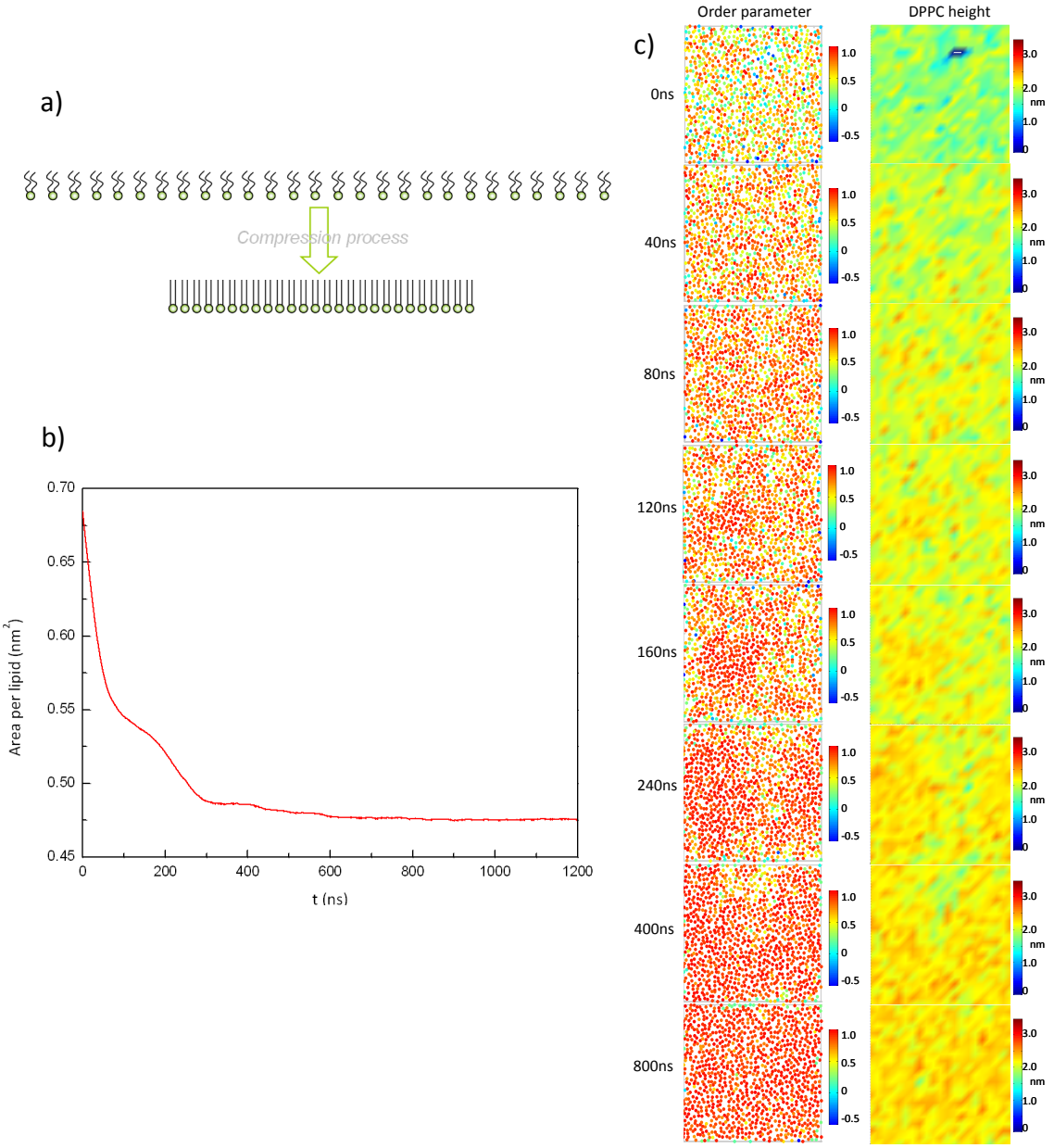

Figure S1. a) Scheme of the compression process of the DPPC monolayer; b) Time evolution of averaged area per lipid (A_{av}) of the interfacial DPPC molecules during the compression process of the DPPC monolayer (LE→LC-LE→LC); c) Two dimensional maps for the phase behavior (order parameter) and thickness of interfacial DPPC molecules. These two maps are perfectly consistent, which validates the reliability of two-dimensional phase map used in our work.

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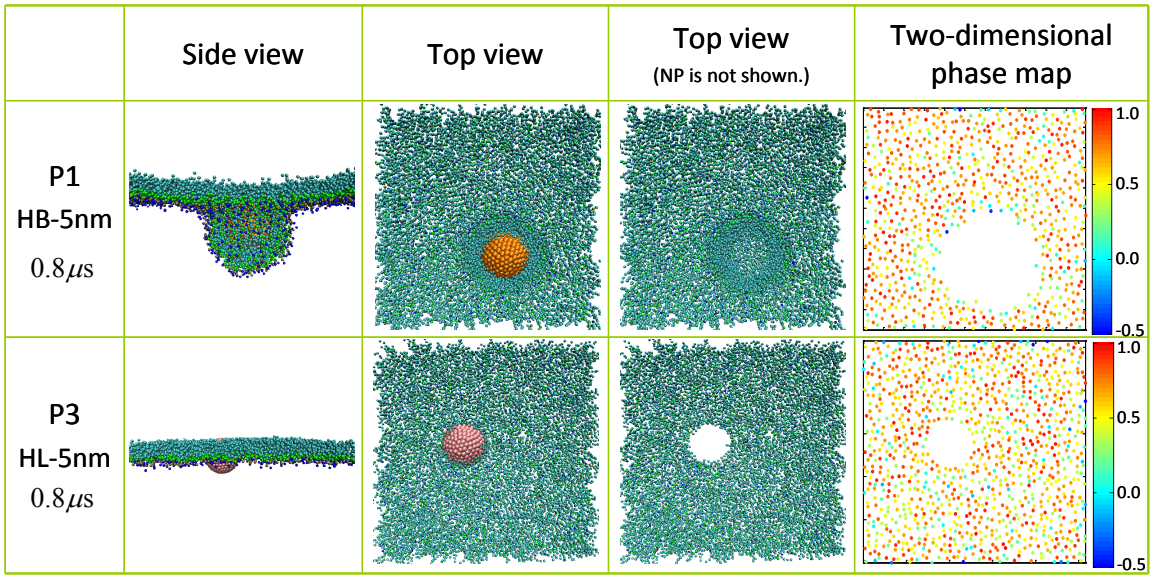

Figure S2. Illustrations of the blank regions in the two-dimensional phase maps in Figure 4. Here, we just show two typical cases: t=0.8μs of the compression process (HB-5nm) and the expansion process (HL-5nm). The blank regions of the maps correspond to the situations that the large structural disruption is induced by NPs and the DPPC monolayer is embedded by NPs.

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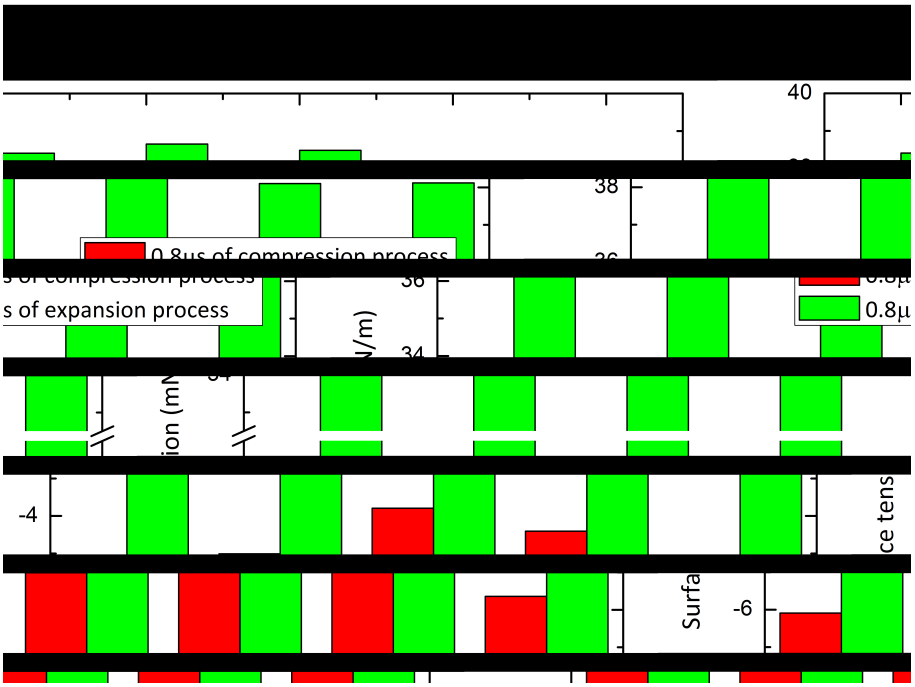

Figure S3. The surface tension of the DPPC monolayer for the equilibrium states (t=0.8μs) of all simulation systems. Both hydrophobic NPs and hydrophilic NPs show little effects on the surface tension of the DPPC monolayer.

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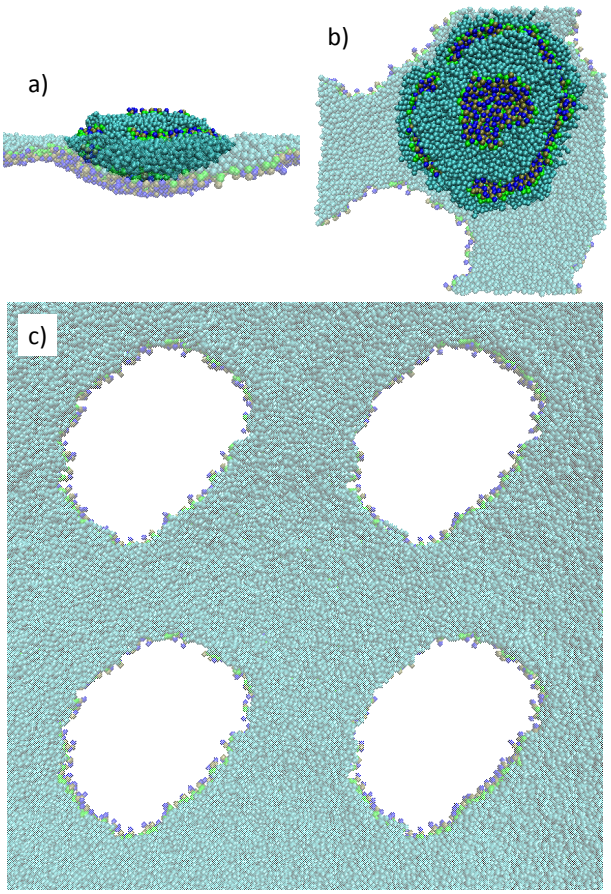

Figure S4. a) The side-view of the snapshot of liposome-DPPC monolayer at the end of the expansion simulation; b) Top-view of the snapshot in (a); c) Top-view of the DPPC monolayer with pbc condition of the snapshot in (a). Obviously, the liposome promotes pore formation of the DPPC monolayer during the expansion process.

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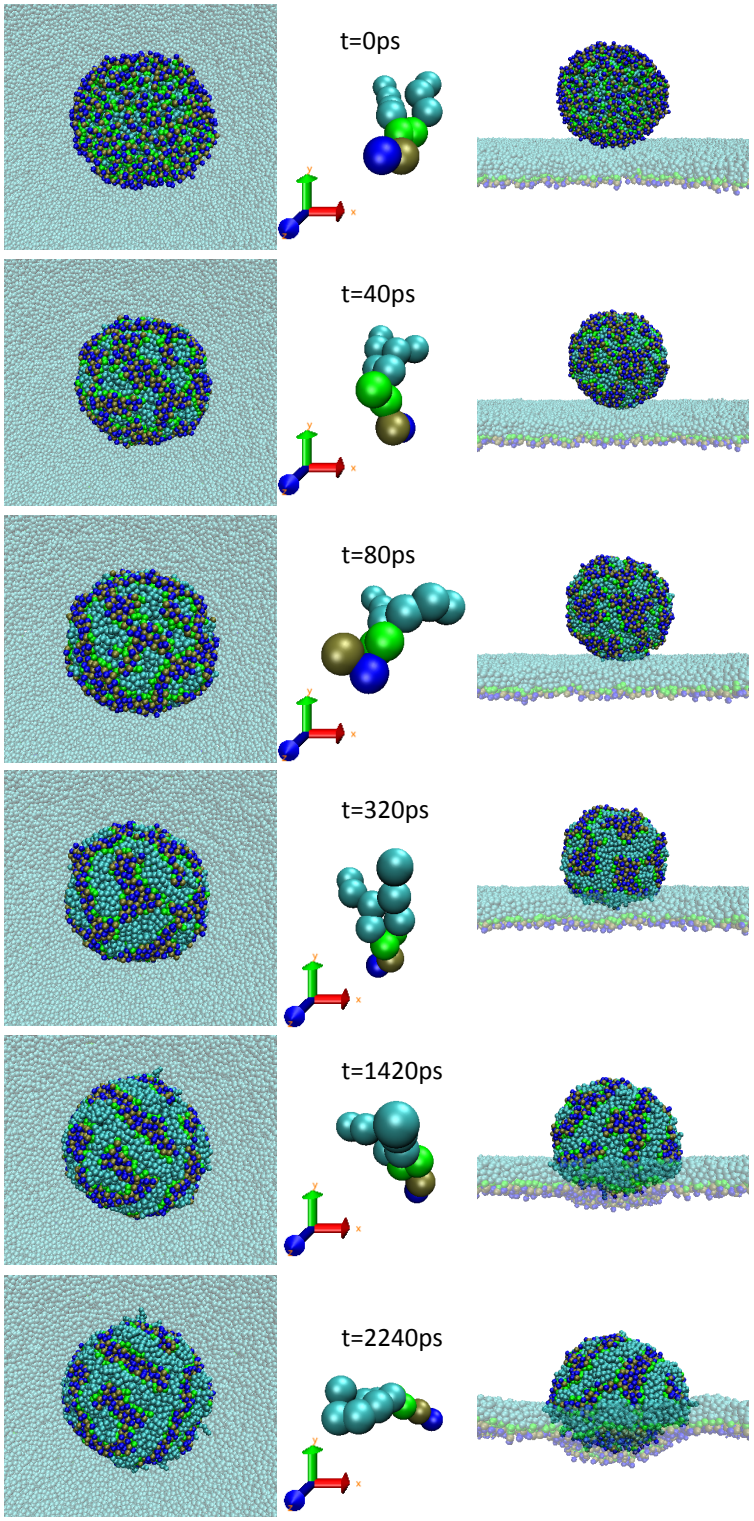

Figure S5. DPPC molecules in the liposome can easily flip-flop to keep their hydrophobic tails facing the gas phase. The left column is the top-view of the liposome-DPPC monolayer system; the right column is the side-view of the liposome-DPPC monolayer system; the middle column is flip-flop process of a single molecule selected from the liposome. Water molecules are not shown for clarity.

Supporting Information

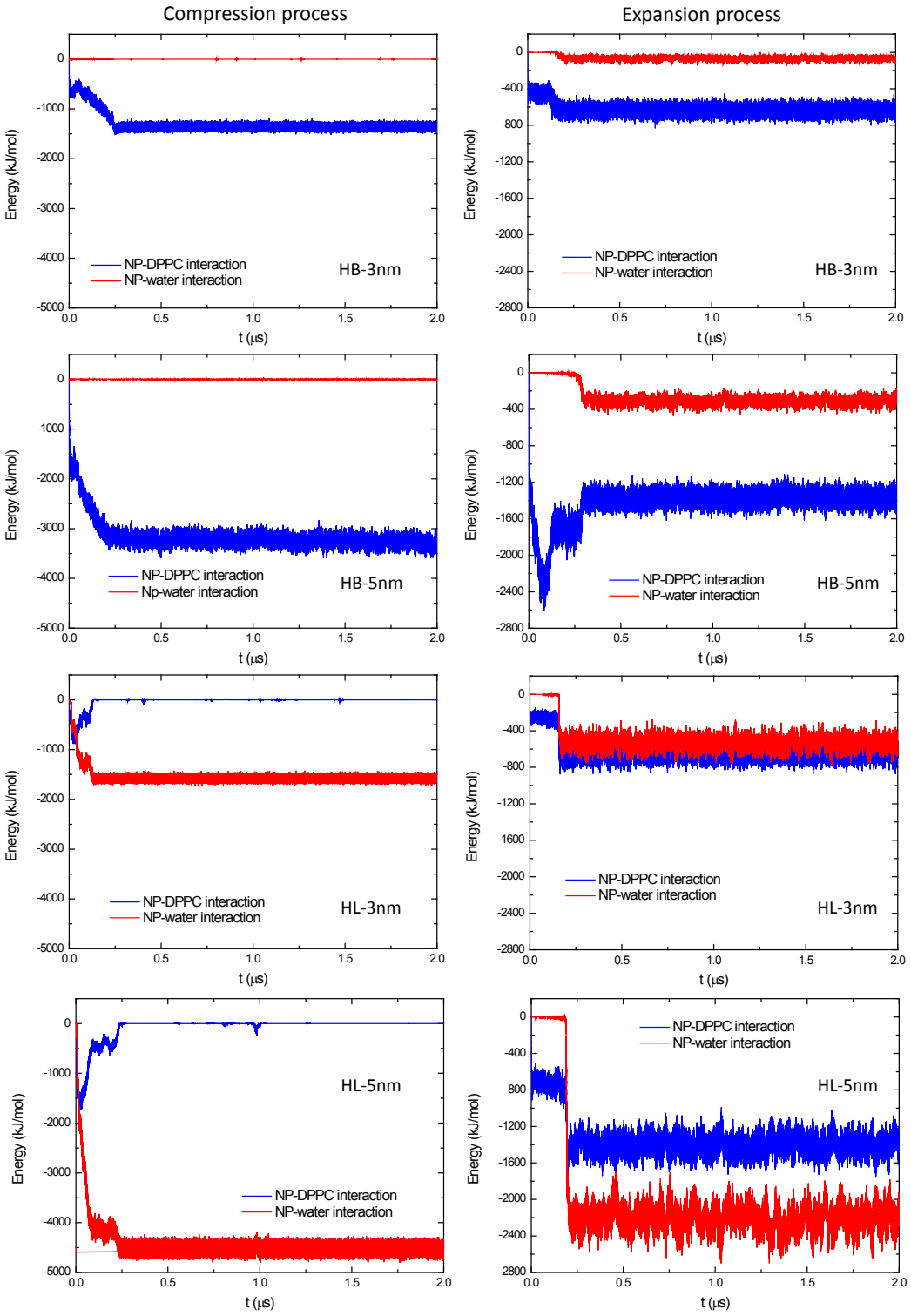

Figure S6. The interaction energy between NP and DPPC, water during the compression and expansion process.

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To circumvent the limitation of MD simulations, we have performed the pulling simulation recommended by the reviewer. We think this is a very interesting idea and a useful alternative to tackle the time limitation of MD simulations. As shown in Figure S7, we performed pulling simulation of HB-5nm system. The system at t=2μs was used as the initial conformation for pulling simulation (t_0=2μs). Hydrophobic NP was pulled from the DPPC monolayer with the velocity (0.2nm/ns). At t=2.16μs, hydrophobic NP, surrounded in lipids (252 DPPC molecules), has completely detached the monolayer. Then we fixed the NP, and monitored the changes of the interfacial DPPC molecules. The results show that the phase behavior of the interfacial DPPC molecules could return to normal (similar to the state of the pure DPPC monolayer at the end of compression process) at about 150ns after detaching the lipid-coated NP from the monolayer. In other words, the normal phase transition inhibition of the interfacial DPPC molecules caused by hydrophobic NP only occurred during the NP's translocation process across the lipid monolayer.

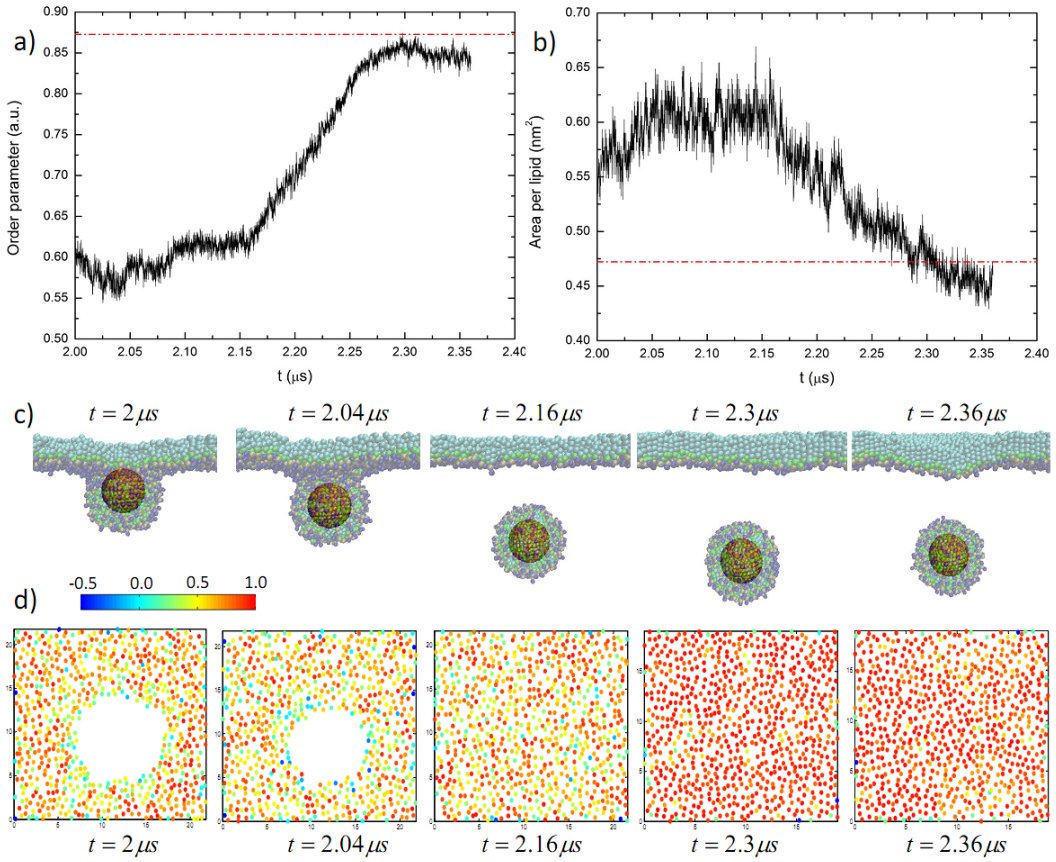

Figure S7. HB-5nm was firstly pulled away from the lipid monolayer (2μs-2.16μs; At t=2.16μs, NP had detached from the lipid monolayer.) and then fixed to monitor the changes of the interfacial molecules (2.16μs-2.36μs). a) Time evolution of order parameter of the interfacial DPPC molecules during this process, red line corresponds to order parameter of pure DPPC monolayer at the end of compression process; b) Time evolution of the averaged area per lipid of the interfacial DPPC

molecules, red line corresponds to the averaged area per lipid of pure DPPC monolayer at the end of compression process; c) Section view of the simulation system at t=2, 2.04, 2.16, 2.3, 2.36μs, coloring for the molecules are the same as Figure 2 in the manuscript, and water molecules are not shown for clarity; d) 2D phase maps of the interfacial DPPC molecules at 2, 2.04, 2.16, 2.3, 2.36μs. Compared to Figure 4 in the manuscript, we can conclude that the phase behavior of the interfacial DPPC molecules could return to normal soon after the detachment of hydrophobic NP.