Supporting Information for

Surface Ligand Rigidity Modulates Lipid Raft Affinity of Ultra-small Hydrophobic Nanoparticles: Insights from Molecular Dynamics Simulations

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1. Encapsulation of Hydrophobic NPs Shows Little Effects on the Lipid Raft Dynamics.

As shown in **Fig. S1**, the phase separation processes of DPPC/DUPC/CHOL bilayers are not significantly affected by ultra-small hydrophobic NPs. We analyzed lipid chain order parameters (**Fig. S2**) and cholesterol preferences (**Fig. S3**) in these systems, which are tightly correlated with the lipid raft dynamics. Generally, there are no obvious differences among membrane systems with or without embedded hydrophobic NPs. Moreover, the ligand-modified NPs were embedded in the phase separated membrane, which hardly affect the diffusion coefficients of either saturated (DPPC) or unsaturated lipids (DUPC) as shown in **Fig. S4** and **Table S1**.

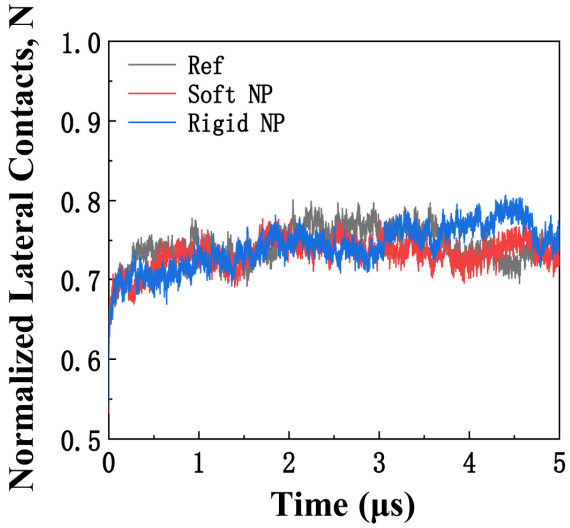

Figure S1. Time evolution of normalized lateral contact N of unsaturated lipids for NP-embedded lipid membrane systems (ligand rigidity: soft and rigid, ligand density: 66%) and the NP-free membrane system (Ref).

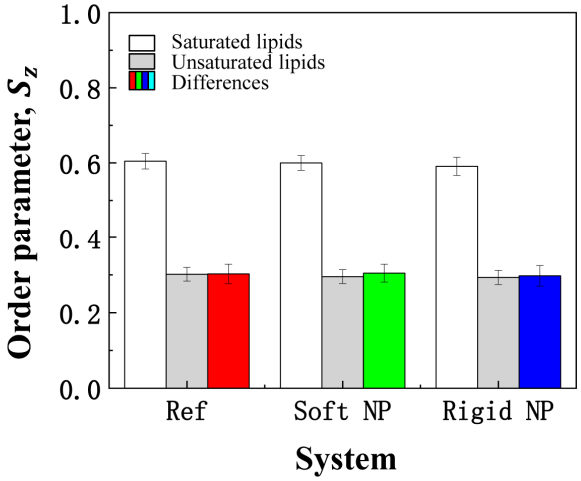

Figure S2. Lipid chain order parameter for NP-embedded lipid membrane systems (ligand rigidity: soft and rigid, ligand density: 66%) and the NP-free membrane system (Ref).

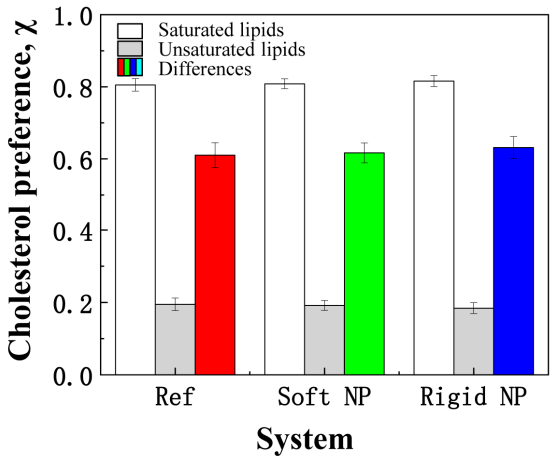

Figure S3. Percentage contact with cholesterol, χ, of saturated lipids, unsaturated lipids, and their differences for NP-embedded lipid membrane systems (ligand rigidity: soft and rigid, ligand density: 66%) and the NP-free membrane system (Ref).

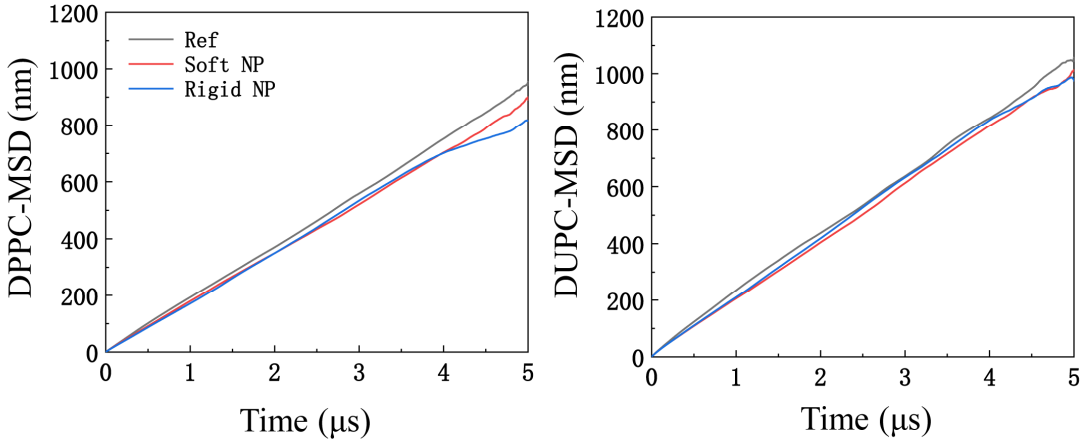

Figure S4. Time evolution of mean square displacement of saturated lipids and unsaturated lipids for NP-embedded lipid membrane systems (ligand rigidity: soft and rigid, ligand density: 66%) and the NP-free membrane system (Ref).

Table S1. The diffusion coefficients of saturated lipids (DPPC) and unsaturated lipids (DUPC).

	Diffusion coefficient	
	DPPC (1e-5 cm^2/s)	**DUPC** (1e-5 cm^2/s)
Ref	0.0465 (+/- 0.0034)	0.0508 (+/- 0.0004)
Soft NP	0.0434 (+/- 0.0021)	0.0371 (+/- 0.0027)
Rigid NP	0.0437 (+/- 0.0039)	0.0431 (+/- 0.0018)

2. Local Disturbance of Embedded NPs on the Phase-separated Lipid Membranes.

In order to further validate the results shown in **Fig. 4**, the same analysis was performed for systems with soft NP (**Fig. S5**). We can find that, soft NP's disturbance to the surrounding lipids was less obvious as rigid NP. In addition, lipid chain order differences between saturated (DPPC) and unsaturated (DUPC) lipids became more obvious when the lipid bilayer was fully phase-separated (**Fig. S6**).

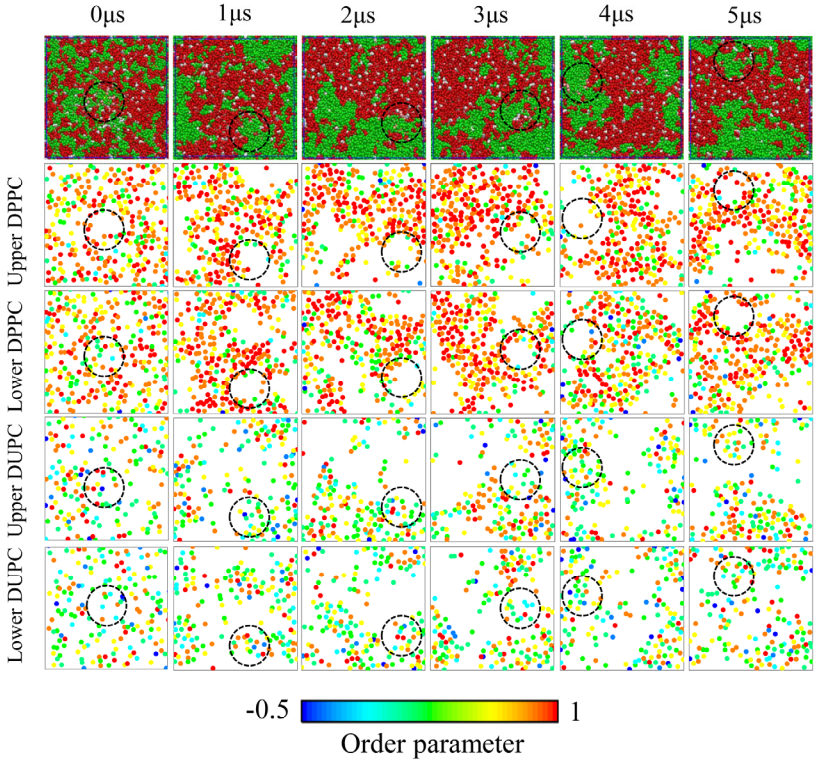

Figure S5. System snapshots and time evolutions of lipid order parameters for each lipid of NP-embedded lipid membrane systems (ligand rigidity: soft, ligand density: 66%). Each point represents one DPPC/DUPC molecule, and its color shows the averaged chain order parameters. The dashed black circle indicates the localization of the ligand-modified NP.

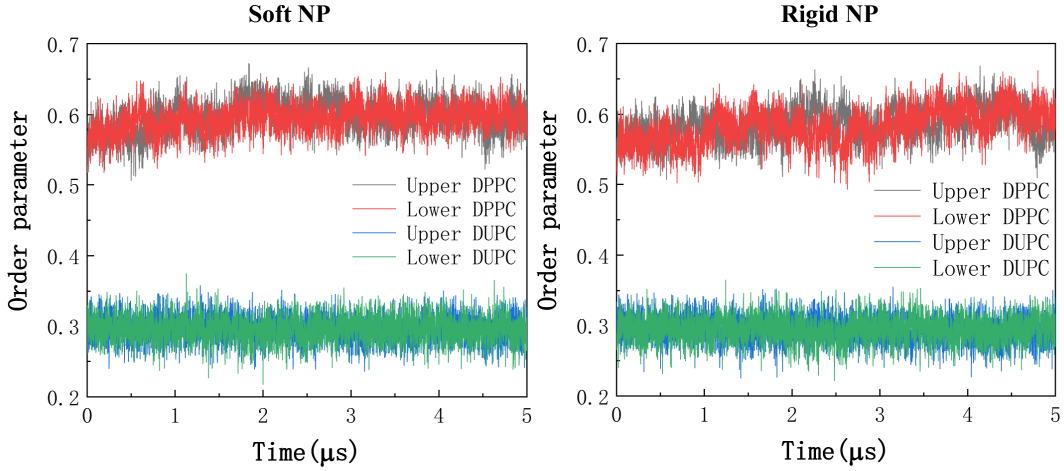

Figure S6. Time evolution of lipid chain order parameters for NP-embedded lipid membrane systems (ligand rigidity: soft and rigid, ligand density: 66%).