Electronic Supplementary Information

Partitioning of nanoscale particles on a heterogeneous multicomponent lipid bilayer

Kai Yang, #ab Ran Yang, #a Xiaodong Tian, #c Kejie He, #a Seth Leon Filbrun, #d Ning Fang, #d Yuqiang Ma #e and Bing Yuan #ab

# Center for Soft Condensed Matter Physics and Interdisciplinary Research & School of Physical Science and Technology, Soochow University, Suzhou, 215006, P. R. China. E-mail: yuanbing@suda.edu.cn

b Jiangsu Key Laboratory of Thin Films, Soochow University, Suzhou, 215006, P. R. China

c Department of Thoracic Surgery, Chinese PLA General Hospital, Beijing, 100853, P. R. China

d Department of Chemistry, Georgia State University, Atlanta, Georgia, 30303, USA

e National Laboratory of Solid State Microstructures and Department of Physics, Nanjing University, Nanjing, 210093, P. R. China

# These authors contribute equally to this work.
Fig. S1 Time-lapse phase separation behavior of a ternary bilayer under the perturbation of NPs (top and bottom views). (A) $N = 3$, $R = 3.0 \text{ nm}$, $\varepsilon = S$. (B) $N = 1$, $R = 3.0 \text{ nm}$, $\varepsilon = W$. (C) $N = 1$, $R = 1.0 \text{ nm}$, $\varepsilon = S$. $N$ and $R$ refer to the quantity and radius of the NPs, respectively. $\varepsilon = S$ (or $W$) represents a strong (or weak) NP-lipid affinity. The time of each snapshot is labeled on top of each column. The composition of the bilayer is DPPC/DUPC/CHOL = 0.35/0.35/0.3 in mol.
Fig. S2 Time-lapse phase separation behavior of a ternary bilayer with varying composition under the perturbation of a NP (\( R = 3.0 \, \text{nm}, \, \varepsilon = 5 \)) and partitioning of the NP on the membrane surface (top view). (A) The bilayer composition is DPPC/DUPC/CHOL = 0.42/0.28/0.3 in mol. (B) The bilayer composition is DPPC/DUPC/CHOL = 0.28/0.42/0.3 in mol. The NP is omitted in the bottom Fig. for clarification. Initially, the lipid components are randomized laterally.
Fig. S3 Sketch of registration condition of lipid domains between the two leaflets of a lipid bilayer. (A) registered; (B) partially registered; (C) antiregistered. The registration degree A>B>C.
Fig. S4 Pair correlations of Lo-Lo and Ld-Ld phases under the perturbation of the NP ($N = 1$, $R = 3.0 \text{ nm}$, $\epsilon = S$) under various initial membrane conditions. (A) The Intraleaflet Pair Correlation function, $g(r)$, of the Lo/Ld phase (the upper leaflet). (B) The Interleaflet Pair Correlation function, $g'(r)$, of the Lo/Ld domains. Here, a “phase-bilayer” means a phase-separated lipid bilayer, and a “random-bilayer” refers to a bilayer with the randomized lateral distribution initially; “NP@Lo” stands for the initial location of the NP at the Lo domain of a phase-separated bilayer, and the similar is for “NP@Ld”. Note, no matter where the NP is located initially (Lo or Ld), it is recruited by the Ld domain finally.
Fig. S5 Interaction energy between the NP and the lipid bilayer in various conditions. Left: NP-Lo molecules; Right: NP-Ld molecules. For $N = 3$, the profile represents the average energy for one NP. The lipid bilayers used here have laterally random distribution of lipids and cholesterol initially.
Fig. S6 Time-lapse partitioning behavior of a NP ($R = 3.0 \text{ nm}$, $\varepsilon = S$) on a phase-separated ternary lipid bilayer. The initial location of the NP is at (A) Ld phase domain or (B) Lo phase domain. From top to bottom: side view and top view respectively. The time of each snapshot is labeled on top of each column. The bilayer composition is DPPC/DUPC/CHOL = 0.35/0.35/0.3 in mol.
Fig. S7 Radial distribution function (RDF) of Lo/Ld phase around a NP (R = 3.0 nm, $\varepsilon = S$) under various initial membrane conditions (phase-separated or not). Here, “phase-bilayer” means a phase-separated lipid bilayer and “random-bilayer” refers to the bilayer with laterally randomized distribution initially. “NP@Lo” stands for the initial location of the NP at the Lo domain of a phase-separated bilayer, and the similar is for “NP@Ld”.
Here the bending modulus, $\kappa$, of the membrane is estimated based on the fluctuation spectrum of a lipid bilayer.\(^1\)\(^3\) Generally, a fluctuating lipid bilayer could be described with the Helfrich theory as:

$$E\{h(X)\} = \frac{1}{2} \kappa \int |\nabla^2 h(X)|^2 \, dX + \frac{1}{2} \gamma \int |\nabla h(X)|^2 \, dX.$$  

Herein, the first term refers to a bending energy with the modulus of $\kappa$, the second term is a surface tension term with the coefficient $\gamma$, and $h(X)$ is a Monge representation of the bilayer. In the Fourier space, the fluctuations with different wave vectors decouple; thus, we have

$$h(q) = \frac{i}{A} \int e^{i q \cdot X} h(q)dq$$  

or

$$h(q) = \frac{1}{A} \int e^{-i q \cdot X} h(X)dX,$$

where $q = (q_x, q_y) = (\frac{2\pi}{\lambda_x}, \frac{2\pi}{\lambda_y})$, $\lambda_x$ and $\lambda_y$ are the wavelength along $x$ and $y$ directions, $A$ is the projected area of the membrane. Accordingly, the system energy becomes

$$E\{h(q)\} = \frac{A}{8\pi^2} \int (\kappa q^4 + \gamma q^2) h(q)h^*(q)dq$$  

(* denotes the complex conjugate, $q = \sqrt{q_x^2 + q_y^2}$). Based on the equipartition theorem, we obtain $S(q) = \langle |h(q)|^2 \rangle = \langle h(q)h^*(q) \rangle = \frac{\kappa gT}{A(\kappa q^4 + \gamma q^2)}$. When surface tension $\gamma = 0$, this relation further becomes $S(q) = \langle |h(q)|^2 \rangle = \frac{\kappa gT}{A\kappa q^4}$. Therefore, if the undulation structure factor $S(q)$ or Mean square amplitude $\langle |h(q)|^2 \rangle$ in the Fourier space can be measured from the simulations, the bending modulus $\kappa$ could be estimated by fitting the relation of $S(q) = \langle |h(q)|^2 \rangle = \frac{\kappa gT}{A\kappa q^4}$. 

---

**Fig. S8** The fluctuation spectra of the lipid bilayers. (A) The bilayer in Lo phase. The composition of the bilayer is DPPC/DUPC/CHOL = 0.7/0/0.3 in mol. (B) The bilayer in Ld phase. The composition of the bilayer is DPPC/DUPC/CHOL = 0.10/0.85/0.05 in mol.
In the simulations, we built two lipid bilayers to estimate the bending modulus $\kappa$ of Lo domain and Ld domain respectively. One is a Lo bilayer with the composition of DPPC/DUPC/CHOL = 0.7/0/0.3 in mol and the other is a bilayer in Ld phase with the composition of DPPC/DUPC/CHOL = 0.10/0.85/0.05 in mol.\(^4\) A large bilayer size of 45 nm $\times$ 45 nm and a long simulation time of 5 $\mu$s are chosen to ensure the undulation modes of the bilayers to fully develop.\(^3\) All lipid bilayers are simulated in the semi-isotropic pressure ensembles to maintain the tensionless states. The last 4 $\mu$s simulations are used to calculate the fluctuation spectrum (Fig. S7, blue circles) and the data with low $q$ is used to fit the bending modulus $\kappa$, according to the relation of $S(q) = \langle|h(q)|^2\rangle = \frac{k_BT}{\kappa q^4}$ (Fig. S7, red lines).

In addition, the compositions of DPPC/DUPC/CHOL for the Lo bilayer and Ld bilayer used for the calculation of $\kappa$ are chosen roughly based on the phase-separated ternary bilayer which is used for the investigation of NP’s partitioning behavior (See Fig. 3 in the text). The estimated $\kappa$ from the two bilayers mentioned above are used as the moduli of the Lo and Ld phases.
Fig. S9 (A) Schematic representation of free volume (yellow shaded area) available to a lipid chain without or with the interaction of a NP. The free volume available to lipid tails in a pure bilayer (top) is larger than that under the interaction of the NP (bottom). (B) Average order parameters for lipid sn-1 carbon beads under the perturbation of a NP ($R = 3.0$ nm, $\varepsilon = S$). The lipid bilayer is well phase separated at initial with the composition of DPPC/DUPC/CHOL = 0.35/0.35/0.3 in mol. Data ($S_{CD}$) is collected when the NP is located at a specific domain (Lo or Ld). For the comparison, the order parameters of lipids in a bilayer without the perturbation of the NP are also shown. Compared with a pure lipid bilayer, the changing degree of $S_{CD}$ of DUPC under the perturbation of a NP is greater than that of DPPC: $\Delta S_{CD} = \frac{S_{CD, pure bilayer} - S_{CD, with- NP}}{S_{CD, pure bilayer}} = 17\%$ for DUPC, while 4\% for DPPC.
Fig. S10 Time-lapse motions of lipids near a NP in the membrane (colored in purple, within 1.2 nm from the NP center initially, top view). Snapshots are obtained (A) before or (B) after the full phase separation of the bilayer. \( N = 1, \ R = 3.0 \text{ nm}, \ \varepsilon = S \). For comparison, the corresponding snapshot without the NP is also shown below. These lipids include DPPC (~38%), DUPC (~52%) and CHOL (~10%) in (A) or are mostly DUPC (>90%) in (B). The composition of the bilayer is DPPC/DUPC/CHOL = 0.35/0.35/0.3 in mol.
Fig. S11 Time dependent distribution of the mean square displacement (MSD) of lipids in the lateral plane of the lipid bilayer under the perturbation of a NP with $R = 3.0 \text{ nm}$ and $\varepsilon = S$. Two starting time points, before or after the full phase separation, are chosen, respectively. The lipids near the NP initially (those within $R_d = 1.2 \text{ nm}$ from the NP center) are especially examined, whose diffusion is compared with the lipids in the whole bilayer.

References


