## Supporting Information

# Morphology-Induced Defects Enhance Lipid Transfer Rates 

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## S1 Contrast matched solvents

Neutron scattering length densities (NSLDs) of contrast-matched (CM) solvents are calculated based on the initial equal molar mixtures of $h$ - and $d$ - bicelles (i.e., $\rho_{C M}=\frac{\rho_{h-B i c}+\rho_{d-B i c}}{2}$ ("Bic" refers to bicelle), where $\rho_{C M}, \rho_{h-B i c}$ and $\rho_{d-B i c}$ are the NSLDs of CM solvent bicelles containing protiated and deuterated DPPC, respectively). The molar ratios of $\mathrm{H}_{2} \mathrm{O}$ to $\mathrm{D}_{2} \mathrm{O}$ are determined by the calculated $\rho_{C M}$, based on $\rho_{H_{2} O}=-5.8 \times 10^{-7} \AA^{-2}$ and $\rho_{D_{2} O}=6.38 \times 10^{-6} \AA^{-2}$. Table S1 tabulates the CM water for each case.

Table S1. Calculated values of $\rho_{C M}$ and molar ratios of $\mathrm{H}_{2} \mathrm{O}: \mathrm{D}_{2} \mathrm{O}$

| -/d-DPPC bicelle | $\rho_{\mathrm{CM}}\left(\AA^{-2}\right)$ | $\mathrm{H}_{2} \mathrm{O}: \mathrm{D}_{2} \mathrm{O}$ at CM condition |
| :---: | :---: | :---: |
| $(\mathrm{Q}=2.5)$ | $1.97 \times 10^{-6}$ | $0.635: 0.365$ |
| $h$-/d-DPPC bicelle |  |  |
| $(\mathrm{Q}=3)$ | $2.04 \times 10^{-6}$ | $0.624: 0.376$ |
| $h$-/d-DPPC bicelle | $2.10 \times 10^{-6}$ | $0.616: 0.384$ |
| $(\mathrm{Q}=3.5)$ | $0.643: 0.357$ |  |
| PEGlyated $h$-/d-DMPC | $1.91 \times 10^{-6}$ |  |
| bicelle $(\mathrm{Q}=3)$ | $1.96 \times 10^{-6}$ | $0.636: 0.364$ |
| PEGlyated $h$-/d-DPPC |  |  |
| bicelle $(\mathrm{Q}=3)$ |  |  |

## S2 Time-Resolved Small Angle Neutron Scattering

## S2.1. SANS Fitting Results

SANS data of bicellar mixtures were best fit using a polydisperse radius discoidal model, where the size averaged form factor $P_{\text {disc }}(q)$ and scattering amplitude $A_{\text {disc }}(q, \alpha)$ are expressed as:

$$
\begin{gather*}
P_{\text {disc }}(q)=\frac{1}{V_{\text {disc }}} \int_{0}^{\infty} f(r) d r \int_{0}^{\pi / 2} A_{\text {disc }}^{2}(q, \alpha) \sin \alpha d \alpha,  \tag{S1}\\
A_{\text {disc }}(q, \alpha)=2 V_{\text {disc }}\left(\rho_{\text {disc }}-\rho_{C M}\right) j_{0}\left(\frac{q t}{2} \cos \alpha\right) \frac{J_{1}(q r \sin \alpha)}{(q r \sin \alpha)}, \tag{S2}
\end{gather*}
$$

where $V_{\text {disc }}$ is the average disc volume, $f(r)$ is the Schulz distribution, $\alpha$ is the angle between the bilayer normal and the scattering vector, $q$, and $t$ is the disc thickness. The polydispersity, $p$, of the bicelle radius, $r$, in the Schulz distribution function is defined as the ratio of the standard deviation, $\sigma$, of $r$ to the average of $r,\left\langle R_{i}\right\rangle$, i.e. $p=\frac{\sigma}{\left\langle R_{i}\right\rangle}$. Then the Schultz distribution function can be expressed as:

$$
\begin{equation*}
f(r)=\frac{p^{-2 / p^{2}}}{\left\langle R_{i}>\Gamma\left(1 / p^{2}\right)\right.}\left(\frac{r}{\left\langle R_{i}\right\rangle}\right)^{\frac{\left(1-p^{2}\right)}{p^{2}}} \exp \left(-\frac{r}{\left.p^{2}<R_{i}\right\rangle}\right) \tag{S3}
\end{equation*}
$$

where $\Gamma(x)$ is the Gamma function. The functions $J_{1}(x)$ and $j_{0}(x)$ are the first order Bessel and first spherical Bessel functions $\left(\frac{\sin (x)}{x}\right)$, respectively. Eqn (S1) includes the average overall possible orientations and different size of discs. The average volume for the disc can be approximated as $V_{\text {disc }}=\pi r^{2} t\left(\frac{z+2}{z+1}\right)$, based on $r$ following the Schulz distribution, and z is related to the polydispersity, $\mathrm{p}\left(z=\frac{1}{p^{2}}-1\right)$. The radius and thickness of the bicelles used in the model were chosen based on the values obtained from the best fit to the data from the highest-contrast sample (i.e., the initial condition). The value of $\rho_{C M}$ was also calculated based on the $\mathrm{H}_{2} \mathrm{O} / \mathrm{D}_{2} \mathrm{O}$ composition. Therefore, the only variable parameter as a function of time is the NSLD of the
bicelles, $\rho_{\text {disc }}$. Tables S 2 to S 4 summarize the best fit data of $\rho_{\text {disc }}$ from the time-resolved SANS data of DPPC bicelles at different temperatures. The NSLD contrast $(\Delta \rho)$ between CM solvent $\left(\rho_{s}\right)$ and bicelles were then calculated at different times. The lipid transfer kinetics in bicelle can be characterized using a single exponential decay ${ }^{1}$

$$
\begin{equation*}
\left|\rho(t)-\rho_{s}\right|=\Delta \rho_{0} e^{-k t} \tag{S4}
\end{equation*}
$$

where $\Delta \rho_{0}$ is the SLD difference between the CM solvent and the bicelles at $t=0$, and $k$ is the apparent spontaneous lipid transfer rate constant.

Table S2. Best fit values of $\rho_{\text {disc }}$ from time-resolved SANS data of $Q=3 \mathrm{~h}$-/d- DPPC bicellar mixtures at $20^{\circ} \mathrm{C}$, with a radius and thickness of $64-67 \AA$ and $34.6-36.7 \AA$, respectively, and a fixed $\rho_{S}$ of $2.04 \times 10^{-6} \AA^{-2}$.

|  | 0.6 hrs | 52 hrs | 77 hrs | 101 hrs | 150 hrs |
| :--- | :---: | :---: | :---: | :---: | :---: |
| $\rho_{\text {disc }}\left(\AA^{-2}\right)$ | $4.94 \times 10^{-6}$ or | $4.75 \times 10^{-6}$ | $4.64 \times 10^{-6}$ or | $4.58 \times 10^{-6}$ or | $4.44 \times 10^{-6}$ or |
|  | $-8.6 \times 10^{-7}$ | or $-6.7 \times 10^{-7}$ | $-5.6 \times 10^{-7}$ | $-5.0 \times 10^{-7}$ | $-3.6 \times 10^{-7}$ |
|  | $2.90 \times 10^{-6} \pm$ | $2.71 \times 10^{-6} \pm$ | $2.60 \times 10^{-6} \pm$ | $2.54 \times 10^{-6} \pm$ | $2.4 \times 10^{-6} \pm$ |
| $\Delta \rho\left(\AA^{-2}\right)$ | $9 \times 10^{-9}$ | $6.2 \times 10^{-8}$ | $5.1 \times 10^{-8}$ | $6.2 \times 10^{-8}$ | $1.04 \times 10^{-7}$ |
|  |  |  |  |  |  |

Table S3. Best fit values of $\rho_{\text {disc }}$ from time-resolved SANS data of $Q=3 h$-/d- DPPC bicellar mixtures at $25^{\circ} \mathrm{C}$, with a radius and thickness of $65-69 \AA$ and $31-36 \AA$, respectively, and a fixed $\rho_{S}$ of $2.04 \times 10^{-6} \AA^{-2}$.

|  | 0.45 hrs | 11 hrs | 16 hrs | 26 hrs | 42 hrs |
| :---: | :---: | :---: | :---: | :---: | :---: |
| $\rho_{\text {disc }}\left(\AA^{-2}\right)$ | $\begin{aligned} & 4.95 \times 10^{-6} \text { or } \\ & -8.7 \times 10^{-7} \end{aligned}$ | $\begin{aligned} & 4.86 \times 10^{-6} \text { or } \\ & -7.8 \times 10^{-7} \end{aligned}$ | $\begin{gathered} 4.82 \times 10^{-6} \text { or } \\ -7.4 \times 10^{-7} \end{gathered}$ | $\begin{gathered} 4.75 \times 10^{-6} \text { or } \\ -6.7 \times 10^{-7} \end{gathered}$ | $\begin{gathered} 4.61 \times 10^{-6} \text { or } \\ -5.3 \times 10^{-7} \end{gathered}$ |
| $\Delta \rho\left(\AA^{-2}\right)$ | $\begin{gathered} 2.91 \times 10^{-6} \pm \\ 3.65 \times 10^{-9} \end{gathered}$ | $\begin{gathered} 2.82 \times 10^{-6} \pm \\ 3.32 \times 10^{-9} \end{gathered}$ | $\begin{gathered} 2.78 \times 10^{-6} \pm \\ 4.21 \times 10^{-9} \end{gathered}$ | $\begin{aligned} & 2.71 \times 10^{-6} \pm \\ & 3.46 \times 10^{-8} \end{aligned}$ | $\begin{gathered} 2.57 \times 10^{-6} \pm \\ 5.17 \times 10^{-9} \end{gathered}$ |
|  | 50 hrs | 56 hrs | 82 hrs | 108 hrs | 159 hrs |
| $\rho_{\text {disc }}\left(\AA^{-2}\right)$ | $\begin{aligned} & 4.56 \times 10^{-6} \text { or } \\ & -4.8 \times 10^{-7} \end{aligned}$ | $\begin{aligned} & 4.49 \times 10^{-6} \text { or } \\ & -4.1 \times 10^{-7} \end{aligned}$ | $\begin{gathered} 4.35 \times 10^{-6} \text { or } \\ -2.7 \times 10^{-7} \end{gathered}$ | $\begin{gathered} 4.17 \times 10^{-6} \text { or } \\ -9 \times 10^{-8} \end{gathered}$ | $\begin{gathered} 3.98 \times 10^{-6} \text { or } \\ 1.0 \times 10^{-7} \end{gathered}$ |
| $\Delta \rho\left(\AA^{-2}\right)$ | $\begin{aligned} & 2.52 \times 10^{-6} \pm \\ & 3.69 \times 10^{-9} \end{aligned}$ | $\begin{gathered} 2.45 \times 10^{-6} \pm \\ 3.76 \times 10^{-9} \end{gathered}$ | $\begin{gathered} 2.31 \times 10^{-6} \pm \\ 3.77 \times 10^{-9} \end{gathered}$ | $\begin{gathered} 2.13 \times 10^{-6} \pm \\ 2.71 \times 10^{-9} \end{gathered}$ | $\begin{aligned} & 1.94 \times 10^{-6} \pm \\ & 3.18 \times 10^{-9} \end{aligned}$ |
|  | 184 hrs | 233 hrs | 259 hrs | 356 hrs | 407 hrs |
| $\rho_{\text {disc }}\left(\AA^{-2}\right)$ | $\begin{gathered} 3.78 \times 10^{-6} \text { or } \\ 3.0 \times 10^{-7} \end{gathered}$ | $\begin{aligned} & 3.71 \times 10^{-6} \text { or } \\ & 3.7 \times 10^{-7} \end{aligned}$ | $\begin{gathered} 3.62 \times 10^{-6} \text { or } \\ 4.6 \times 10^{-7} \end{gathered}$ | $\begin{gathered} 3.39 \times 10^{-6} \text { or } \\ 6.9 \times 10^{-7} \end{gathered}$ | $\begin{gathered} 3.20 \times 10^{-6} \text { or } \\ -8.8 \times 10^{-7} \end{gathered}$ |
| $\Delta \rho\left(\AA^{-2}\right)$ | $\begin{gathered} 1.74 \times 10^{-6} \pm \\ 3.40 \times 10^{-9} \end{gathered}$ | $\begin{aligned} & 1.67 \times 10^{-6} \pm \\ & 3.58 \times 10^{-9} \end{aligned}$ | $\begin{aligned} & 1.58 \times 10^{-6} \pm \\ & 4.28 \times 10^{-9} \end{aligned}$ | $\begin{gathered} 1.35 \times 10^{-6} \pm \\ 5.01 \times 10^{-9} \end{gathered}$ | $\begin{gathered} 1.16 \times 10^{-6} \pm \\ 1.21 \times 10^{-9} \end{gathered}$ |

Table S4. Best fit values of $\rho_{\text {disc }}$ from time-resolved SANS data of $Q=3 \mathrm{~h}-/ \mathrm{d}-$ DPPC bicellar mixtures at $30^{\circ} \mathrm{C}$, with a radius and thickness of $66-70 \AA$ and $32-36 \AA$, respectively, and a fixed $\rho_{S}$ of $2.04 \times 10^{-6} \AA^{-2}$.

|  | 0.4 hrs | 7 hrs | 12 hrs | 14 hrs | 23 hrs |
| :---: | :---: | :---: | :---: | :---: | :---: |
| $\rho_{\text {disc }}\left(\AA^{-2}\right)$ | $\begin{gathered} 4.98 \times 10^{-6} \text { or } \\ -9.0 \times 10^{-7} \end{gathered}$ | $\begin{gathered} 4.83 \times 10^{-6} \text { or } \\ -7.5 \times 10^{-7} \end{gathered}$ | $\begin{gathered} 4.74 \times 10^{-6} \text { or } \\ -6.6 \times 10^{-7} \end{gathered}$ | $\begin{aligned} & 4.73 \times 10^{-6} \text { or } \\ & -6.5 \times 10^{-7} \end{aligned}$ | $\begin{aligned} & 4.56 \times 10^{-6} \text { or } \\ & -4.8 \times 10^{-7} \end{aligned}$ |
| $\Delta \rho\left(\AA^{-2}\right)$ | $\begin{gathered} 2.94 \times 10^{-6} \pm \\ 3.73 \times 10^{-9} \end{gathered}$ | $\begin{gathered} 2.79 \times 10^{-6} \pm \\ 3.61 \times 10^{-9} \end{gathered}$ | $\begin{gathered} 2.70 \times 10^{-6} \pm \\ 3.51 \times 10^{-9} \end{gathered}$ | $\begin{gathered} 2.69 \times 10^{-6} \pm \\ 3.84 \times 10^{-9} \end{gathered}$ | $\begin{gathered} 2.52 \times 10^{-6} \pm \\ 4.95 \times 10^{-9} \end{gathered}$ |
|  | 34 hrs | 60 hrs | 85 hrs | 109 hrs | 146 hrs |
| $\rho_{\text {disc }}\left(\AA^{-2}\right)$ | $\begin{aligned} & 4.34 \times 10^{-6} \text { or } \\ & -2.6 \times 10^{-7} \end{aligned}$ | $\begin{gathered} 3.79 \times 10^{-6} \text { or } \\ 2.9 \times 10^{-7} \end{gathered}$ | $\begin{gathered} 3.53 \times 10^{-6} \text { or } \\ -5.5 \times 10^{-7} \end{gathered}$ | $\begin{gathered} 3.4 \times 10^{-6} \text { or } \\ 6.8 \times 10^{-7} \end{gathered}$ | $\begin{gathered} 3.37 \times 10^{-6} \text { or } \\ 7.1 \times 10^{-7} \end{gathered}$ |
| $\Delta \rho\left(\AA^{-2}\right)$ | $\begin{gathered} 2.30 \times 10^{-6} \pm \\ 7.62 \times 10^{-9} \end{gathered}$ | $\begin{gathered} 1.75 \times 10^{-6} \pm \\ 3.81 \times 10^{-9} \end{gathered}$ | $\begin{gathered} 1.49 \times 10^{-6} \pm \\ 3.85 \times 10^{-9} \end{gathered}$ | $\begin{gathered} 1.36 \times 10^{-6} \pm \\ 7.27 \times 10^{-9} \end{gathered}$ | $\begin{gathered} 1.33 \times 10^{-6} \pm \\ 4.45 \times 10^{-9} \end{gathered}$ |
|  | 184 hrs | 233 hrs | 283 hrs |  |  |
| $\rho_{\text {disc }}\left(\AA^{-2}\right)$ | $\begin{aligned} & 3.11 \times 10^{-6} \text { or } \\ & 9.7 \times 10^{-7} \end{aligned}$ | $\begin{gathered} 3.07 \times 10^{-6} \text { or } \\ 1.01 \times 10^{-6} \end{gathered}$ | $\begin{gathered} 2.99 \times 10^{-6} \text { or } \\ 1.09 \times 10^{-7} \end{gathered}$ |  |  |
| $\Delta \rho\left(\AA^{-2}\right)$ | $\begin{gathered} 1.07 \times 10^{-6} \pm \\ 2.06 \times 10^{-8} \end{gathered}$ | $\begin{aligned} & 1.03 \times 10^{-6} \pm \\ & 7.15 \times 10^{-9} \end{aligned}$ | $\begin{gathered} 9.52 \times 10^{-7} \pm \\ 2.87 \times 10^{-8} \end{gathered}$ |  |  |

## S3 Time-Resolved Differential Scanning Calorimetry

## S3.1. TR-DSC data



Figure S1 TR-DSC data of lipid transfer between bicelles of different $Q$ values.
Figure S 1 shows the TR-DSC data collected for lipid transfer experiments of different $Q$. The two distinct peaks are clearly visible in each DSC endotherm at early mixing periods,
corresponding to the melting transition of $d$ - bicelles (lower $T_{M}$ ) and $h$ - bicelles (higher $T_{M}$ ). As the lipid transfer between $h$ - and $d$ - bicelles takes place, these peaks move toward each other. the DSC endotherm contains other minor peaks, possibly due to the presence of $d$ - and $h$ - vesicles with increasing $T .^{2}$ The difference in $T_{M}$ between bicelles and vesicles of the same molecular make up is presumably due to their distinct cooperative units. ${ }^{3,4}$ All the $T_{M} \mathrm{~S}$, including those of $d$ - and $h$ - bicelles and vesicles, were identified using a sum of four independent Gaussian curves. $\Delta T_{M}$ between $h$-rich and $d$-rich bicelles can then be calculated at each $t$ using the lipid transfer rate equation (S5)

$$
\begin{equation*}
T_{M, h}-T_{M, d}=\Delta T_{M, o} e^{-k t} \tag{S5}
\end{equation*}
$$

where $T_{M, h}$ and $T_{M, d}$ is the $T_{M}$ of $h$-rich and $d$-rich bicelles, respectively. $\Delta T_{M, o}$ is the initial $\Delta T_{M}$ $\left(T_{M, h}-T_{M, d}\right)$ at $t=0$.

## S3.2. Gaussian Fitting Results

DSC scans were fit using four Gaussians ( $d$ - an $h$ - DPPC associated with bicelles and vesicles are shown in Tables S5-S13).

Table S5. DSC peak positions obtained by Gaussian fits of $Q=2.5$ DPPC bicelles at $20^{\circ} \mathrm{C}$ and as a function of time

|  | $d$-vesicle | $d$-bicelle | $h$-vesicle | $h$-bicelle | $\Delta T_{\text {bicelle }}$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 0.4 hr | $37.44 \pm 0.18$ | $40.32 \pm 0.35$ | $41.74 \pm 0.08$ | $44.45 \pm 0.03$ | $4.13 \pm 0.38$ |
| 24 hrs | $37.50 \pm 0.05$ | $40.71 \pm 0.16$ | $41.81 \pm 0.08$ | $44.55 \pm 0.05$ | $3.84 \pm 0.20$ |
| 47 hrs | $37.84 \pm 0.18$ | $40.62 \pm 0.39$ | $41.88 \pm 0.10$ | $44.41 \pm 0.03$ | $3.79 \pm 0.42$ |
| 104 hrs | $37.81 \pm 0.11$ | $40.61 \pm 0.37$ | $41.66 \pm 0.06$ | $44.08 \pm 0.06$ | $3.47 \pm 0.43$ |
| 148 hrs | $37.76 \pm 0.06$ | $40.70 \pm 0.33$ | $41.60 \pm 0.06$ | $44.07 \pm 0.06$ | $3.37 \pm 0.38$ |
| 193 hrs | $38.04 \pm 0.18$ | $40.64 \pm 1.18$ | $41.54 \pm 0.26$ | $43.84 \pm 0.06$ | $3.21 \pm 1.24$ |
| 338 hrs | $38.08 \pm 0.08$ | $41.08 \pm 0.10$ | $40.75 \pm 0.03$ | $43.45 \pm 0.03$ | $2.70 \pm 0.06$ |

Table S6. DSC peak positions obtained by Gaussian fits of $Q=2.5$ DPPC bicelles at $25^{\circ} \mathrm{C}$ and as a function of time

|  | $d$-vesicle | $d$-bicelle | $h$-vesicle | $h$-bicelle | $\Delta T_{\text {bicelle }}$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 0 hr | $37.95 \pm 0.19$ | $40.78 \pm 0.13$ | $42.15 \pm 0.07$ | $44.61 \pm 0.04$ | $3.832 \pm 0.17$ |
| 26.5 hrs | $38.35 \pm 0.19$ | $40.88 \pm 0.07$ | $42.16 \pm 0.07$ | $44.11 \pm 0.05$ | $3.23 \pm 0.12$ |
| 48 hrs | $38.30 \pm 0.15$ | $40.79 \pm 0.03$ | $42.17 \pm 0.05$ | $43.80 \pm 0.04$ | $3.01 \pm 0.07$ |
| 72.8 hrs | $38.57 \pm 0.18$ | $40.89 \pm 0.06$ | $42.22 \pm 0.06$ | $43.72 \pm 0.04$ | $2.83 \pm 0.09$ |

Table S7. DSC peak positions obtained by Gaussian fits of $Q=2.5$ DPPC bicelles at $30^{\circ} \mathrm{C}$ and as a function of time

|  | $d$-vesicle | $d$-bicelle | $h$-vesicle | $h$-bicelle | $\Delta T_{\text {bicelle }}$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 0.3 hr | $38.25 \pm 0.29$ | $40.92 \pm 0.19$ | $42.44 \pm 0.14$ | $44.98 \pm 0.27$ | $4.06 \pm 0.22$ |
| 6.3 hrs | $38.17 \pm 0.40$ | $40.75 \pm 0.56$ | $42.11 \pm 0.29$ | $44.59 \pm 0.35$ | $3.84 \pm 0.59$ |
| 18.9 hrs | $38.61 \pm 0.37$ | $40.99 \pm 0.87$ | $42.07 \pm 0.38$ | $44.24 \pm 0.05$ | $3.25 \pm 0.92$ |
| 27.1 hrs | $38.80 \pm 0.30$ | $41.01 \pm 0.41$ | $42.09 \pm 0.32$ | $43.95 \pm 0.04$ | $2.94 \pm 0.45$ |
| 46.3 hrs | $37.94 \pm 0.02$ | $41.52 \pm 0.02$ | $42.88 \pm 0.03$ | $44.23 \pm 0.02$ | $2.71 \pm 0.04$ |

Table S8. DSC peak positions obtained by Gaussian fits of $Q=3.0$ DPPC bicelles at $20^{\circ} \mathrm{C}$ and as a function of time

|  | $d$-vesicle | $d$-bicelle | $h$-vesicle | $h$-bicelle | $\Delta T_{\text {bicelle }}$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 0 hr | $37.99 \pm 0.16$ | $40.90 \pm 0.31$ | $42.42 \pm 0.12$ | $45.13 \pm 0.03$ | $4.23 \pm 0.34$ |
| 27.5 hrs | $38.99 \pm 0.16$ | $41.00 \pm 0.42$ | $42.33 \pm 0.13$ | $44.98 \pm 0.04$ | $3.98 \pm 0.46$ |
| 48.4 hrs | $38.13 \pm 0.16$ | $41.06 \pm 0.36$ | $42.41 \pm 0.15$ | $44.96 \pm 0.03$ | $3.90 \pm 0.39$ |
| 96.5 hrs | $38.17 \pm 0.15$ | $41.10 \pm 0.34$ | $42.34 \pm 0.16$ | $44.70 \pm 0.04$ | $3.61 \pm 0.38$ |
| 174 hrs | $38.45 \pm 0.06$ | $41.20 \pm 0.40$ | $42.36 \pm 0.22$ | $44.61 \pm 0.04$ | $3.41 \pm 0.44$ |
| 263 hrs | $38.66 \pm 0.15$ | $41.26 \pm 0.22$ | $42.51 \pm 0.21$ | $44.48 \pm 0.03$ | $3.21 \pm 0.25$ |

Table S9. DSC peak positions obtained by Gaussian fits of $Q=3.0$ DPPC bicelles at $25^{\circ} \mathrm{C}$ and as a function of time

|  | $d$-vesicle | $d$-bicelle | $h$-vesicle | $h$-bicelle | $\Delta T_{\text {bicelle }}$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 0 hr | $37.50 \pm 0.15$ | $40.66 \pm 0.65$ | $41.94 \pm 0.20$ | $44.80 \pm 0.06$ | $4.14 \pm 0.71$ |
| 7 hrs | $37.52 \pm 0.21$ | $40.53 \pm 0.68$ | $41.83 \pm 0.31$ | $44.57 \pm 0.04$ | $4.05 \pm 0.72$ |
| 27 hrs | $37.75 \pm 0.11$ | $40.78 \pm 0.12$ | $42.10 \pm 0.08$ | $44.36 \pm 0.04$ | $3.59 \pm 0.16$ |
| 50.5 hrs | $37.98 \pm 0.12$ | $40.84 \pm 0.08$ | $42.21 \pm 0.08$ | $44.20 \pm 0.03$ | $3.36 \pm 0.11$ |
| 96 hrs | $37.68 \pm 0.12$ | $41.29 \pm 0.06$ | $42.61 \pm 0.08$ | $44.24 \pm 0.03$ | $3.10 \pm 0.11$ |

Table S10. DSC peak positions obtained by Gaussian fits of $Q=3.0$ DPPC bicelles at $30^{\circ} \mathrm{C}$ and as a function of time

|  | $d$-vesicle | $d$-bicelle | $h$-vesicle | $h$-bicelle | $\Delta T_{\text {bicelle }}$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 0 hr | $38.41 \pm 0.25$ | $41.23 \pm 0.31$ | $42.77 \pm 0.15$ | $45.47 \pm 0.02$ | $4.24 \pm 0.33$ |
| 6.5 hrs | $37.64 \pm 0.06$ | $39.11 \pm 0.20$ | $41.46 \pm 0.03$ | $45.14 \pm 0.04$ | $3.67 \pm 0.24$ |
| 26.7 hrs | $38.68 \pm 0.12$ | $41.33 \pm 0.03$ | $\mathrm{~N} / \mathrm{A}$ | $44.36 \pm 0.03$ | $3.03 \pm 0.06$ |

Table S11. DSC peak positions obtained by Gaussian fits of $\mathrm{Q}=3.5$ DPPC bicelles at $20^{\circ} \mathrm{C}$ and as a function of time

|  | $d$-vesicle | $d$-bicelle | $h$-vesicle | $h$-bicelle | $\Delta T_{\text {bicelle }}$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 0.4 hr | $37.11 \pm 0.04$ | $40.28 \pm 0.16$ | $41.67 \pm 0.02$ | $44.43 \pm 0.04$ | $4.15 \pm 0.21$ |
| 24.5 hrs | $37.25 \pm 0.05$ | $40.32 \pm 0.21$ | $41.72 \pm 0.02$ | $44.44 \pm 0.04$ | $4.12 \pm 0.25$ |
| 74 hrs | $37.29 \pm 0.07$ | $40.18 \pm 0.32$ | $41.57 \pm 0.04$ | $44.20 \pm 0.05$ | $4.02 \pm 0.36$ |
| 141.6 hrs | $37.62 \pm 0.09$ | $40.30 \pm 0.29$ | $41.69 \pm 0.05$ | $44.21 \pm 0.02$ | $3.91 \pm 0.32$ |
| 214.3 hrs | $37.60 \pm 0.05$ | $40.27 \pm 0.07$ | $41.52 \pm 0.02$ | $43.96 \pm 0.05$ | $3.70 \pm 0.12$ |

Table S12. DSC peak positions obtained by Gaussian fits of $\mathrm{Q}=3.5$ DPPC bicelles at $25^{\circ} \mathrm{C}$ and as a function of time

|  | $d$-vesicle | $d$-bicelle | $h$-vesicle | $h$-bicelle | $\Delta T_{\text {bicelle }}$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 0 hr | $37.54 \pm 0.08$ | $40.66 \pm 0.32$ | $42.12 \pm 0.09$ | $44.92 \pm 0.04$ | $4.26 \pm 0.36$ |
| 19.8 hrs | $37.64 \pm 0.10$ | $40.67 \pm 0.47$ | $42.07 \pm 0.13$ | $44.76 \pm 0.04$ | $4.09 \pm 0.51$ |
| 46.3 hrs | $37.84 \pm 0.11$ | $40.74 \pm 0.62$ | $42.09 \pm 0.17$ | $44.62 \pm 0.04$ | $3.88 \pm 0.66$ |
| 69.5 hrs | $37.73 \pm 0.13$ | $40.65 \pm 1.34$ | $41.81 \pm 0.33$ | $44.32 \pm 0.07$ | $3.68 \pm 1.41$ |
| 136.5 hrs | $37.91 \pm 0.01$ | $41.40 \pm 0.02$ | $42.97 \pm 0.08$ | $44.38 \pm 0.02$ | $2.98 \pm 0.04$ |
| 210.5 hrs | $38.20 \pm 0.05$ | $40.85 \pm 0.02$ | $42.43 \pm 0.06$ | $43.66 \pm 0.03$ | $2.81 \pm 0.05$ |

Table S13. DSC peak positions obtained by Gaussian fits of $\mathrm{Q}=3.5$ DPPC bicelles at $30^{\circ} \mathrm{C}$ and as a function of time

|  | $d$-vesicle | $d$-bicelle | $h$-vesicle | $h$-bicelle | $\Delta T_{\text {bicelle }}$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 0.3 hr | $37.13 \pm 0.07$ | $40.26 \pm 0.89$ | $41.53 \pm 0.12$ | $44.64 \pm 0.06$ | $4.38 \pm 0.94$ |
| 6.0 hrs | $37.55 \pm 0.10$ | $40.57 \pm 0.84$ | $41.78 \pm 0.15$ | $44.65 \pm 0.06$ | $4.08 \pm 0.90$ |
| 23.9 hrs | $37.52 \pm 0.17$ | $40.45 \pm 2.17$ | $41.52 \pm 0.69$ | $44.12 \pm 0.02$ | $3.67 \pm 2.19$ |
| 50.0 hrs | $37.80 \pm 0.05$ | $40.71 \pm 0.02$ | $42.14 \pm 0.05$ | $43.67 \pm 0.03$ | $2.95 \pm 0.05$ |
| 70.4 hrs | $37.76 \pm 0.03$ | $40.65 \pm 0.02$ | $42.12 \pm 0.03$ | $43.49 \pm 0.01$ | $2.84 \pm 0.02$ |
| 94.3 hrs | $38.10 \pm 0.07$ | $40.51 \pm 0.03$ | $42.15 \pm 0.05$ | $43.29 \pm 0.03$ | $2.78 \pm 0.06$ |

## S4 Determination of the Morphology of Different-Q Bicelles Using SANS



Figure S2. SANS data of initial DPPC/DPPG/DHPC bicelles with different $Q$ values and constant charged lipid ratio $R=0.05$ at $10^{\circ} \mathrm{C}$ at initial stage of lipid transfer.
SANS measurements were conducted at NCNR to determine the bicelle size at different $Q$ s. Fig. S2 shows examples of SANS data of different $Q$ (2.5, 3.0 and 3.5) DPPC bicelles. The solid lines are the best fits to the data using a discoidal model, as described in S2. Although there is a strong charge effect, the structure factor did not appear in the SANS curves because of the contrast-matched condition. We were therefore able to fit the data using only the discoidal form factor. Table S14 lists the best fit parameters, indicating that bicelle radii decrease with increased amounts of DHPC (i.e., increased fraction of interface in a bicelle). This is the most likely explanation for the observed enhanced lipid transfer rate constants observed as a function of increased amounts of DHPC.

TABLE S14. Best fit parameters from SANS data of DPPC bicelles

|  | Radius $(\AA)$ | Thickness $(\AA)$ |
| :--- | :---: | :---: |
| $\mathrm{Q}=2.5$ | $73.2 \pm 0.8$ | $38.0 \pm 0.4$ |
| $\mathrm{Q}=3.0$ | $81.7 \pm 0.7$ | $38.8 \pm 0.4$ |
| $\mathrm{Q}=3.5$ | $95.0 \pm 0.6$ | $38.3 \pm 0.4$ |

## S5 DSC Endotherms of h-, d- and h-/d- Bicelles



Figure S3. DSC data of $Q=2.5$ (a), 3 (b) and 3.5 (c) $h$-, $h / d$ - and $d$ - DPPC bicelles.

## S5.1. DSC data of pure $h$-, $d$ - and intimate mixed equal molar $h$-/d- DPPC bicelles

Fig S2 shows DSC scans of $h$-, $h / d$ - and $d$-DPPC bicelles, where $h / d$-DPPC bicelles were prepared through mixing equal molar deuterated and protiated DPPC lipids. Each curve has a major peak and a shoulder, most likely corresponding to the $T_{M}$ of DPPC associated with vesicles, whose $T_{M}$ is known to be lower than that of bicelles. Table S 14 shows that the $T_{M}$ difference $\left(\Delta T_{M}\right)$ between $h$-bicelles and $d$-bicelles is $\sim 4^{\circ} \mathrm{C}$, providing sufficient separation to differentiate between peaks. The $T_{M}$ for $h / d$ bicelles is similar to the average of $T_{M, h}$ and $T_{M, d .}$

Table S15. $T_{M}$ summary of DPPC bicelles

|  | $Q=2.5$ | $Q=3$ | $Q=3.5$ |
| :---: | :---: | :---: | :---: |
| $T_{M, h}$ | 45.66 | 45.42 | 44.99 |
| $T_{M, d}$ | 41.03 | 41.13 | 40.98 |
| $T_{M, h / d}$ | 43.02 | 43.03 | 43.07 |
| $\Delta T_{M}$ | 4.63 | 4.19 | 4.01 |

## S5.2. Phase Transition Enthalpy

In order to compare phase transition enthalpies at different $Q$ values, we integrated each phase transition peak to obtain the phase transition enthalpy $\left(\Delta H_{f_{u}}\right)$, summarized in Table S 16 . It should be noted that the transition enthalpy was normalized based on the amounts of DPPC and DPPG, and not DHPC, since DHPC does not undergo a phase transition over the temperature range studied. It was found that $\Delta H$ is smallest for $Q=2.5$. The decrease in $\Delta H$ is most likely the result of increased DPPC/DHPC fraction at the interfacial region between domains, allowing DPPC to melt from the gel to the liquid crystalline phase at lower energy cost. This interface between domains is thought to enhance the transfer rate of DPPC.

Table S16. Phase transition enthalpies of DPPC bicelles $\left(\Delta H_{f u}, \Delta H_{f u, d}\right.$ and $\Delta H_{f u, h / d}$ are the enthalpies for $h-, d$ - and $h / d$ - bicelles, respectively.)

|  | $Q=2.5$ | $Q=3$ | $Q=3.5$ |
| :---: | :---: | :---: | :---: |
| $\Delta H_{f u, h}$ | 16.18 | 18.54 | 19.54 |
| $\Delta H_{f u, d}$ | 14.84 | 19.87 | 18.64 |
| $\Delta H_{f u, h / d}$ | 15.3 | 19.2 | 18.51 |

## S6 Lipid Exchange between PEGylated Bicelles



Figure S4. TR-SANS data of the lipid transfer on the PEGylated bicelles at $10{ }^{\circ} \mathrm{C}$. (a) DMPC/DMPG/DHPC/DSPE-PEG2000, $Q=3, R=0.05$, and DSPE-PEG2000 ratio of 5.0 $\mathrm{mol} . \%$ (b) DPPC/DPPG/DHPC/DSPE-PEG2000, $Q=3, R=0.05$, and DSPE-PEG2000 ratio of $5.0 \mathrm{~mol} . \%$. The solid lines are the best fits using a disk model with polydispersed radii to generate the neutron scattering length density (NSLD) of bicelle.

Tables S17 and S18 tabulate the best fit parameters for DMPC and DPPC bicelles containing DSPE-PEG2000.

Table S17. Best fit results from SANS data of DMPC/DMPG/DHPC/PEG2000-DSPE bicelles at $10^{\circ} \mathrm{C}$ with a radius of $\sim 58 \AA$, a thickness of $\sim 29 \AA$, and a fixed $\rho_{s}$ of 1.91 $\times 10^{-6} \AA^{-2}$.

|  | 0.32 hrs | 2.32 hrs | 5.80 hrs | 9.48 hrs |
| :--- | :---: | :---: | :---: | :---: |
|  |  |  |  |  |
| $\rho_{\text {disc }}\left(\AA^{-2}\right)$ | $2.69 \times 10^{-6}$ or | $2.48 \times 10^{-6}$ or | $2.29 \times 10^{-6}$ or | $2.20 \times 10^{-6}$ or |
|  | $1.13 \times 10^{-6}$ | $1.34 \times 10^{-6}$ | $1.53 \times 10^{-7}$ | $1.62 \times 10^{-7}$ |
|  | $7.79 \times 10^{-7} \pm$ | $5.70 \times 10^{-7} \pm$ | $3.77 \times 10^{-6} \pm$ | $2.86 \times 10^{-7} \pm$ |
| $\Delta \rho\left(\AA^{-2}\right)$ | $4.28 \times 10^{-9}$ | $5.93 \times 10^{-10}$ | $7.31 \times 10^{-10}$ | $9.16 \times 10^{-10}$ |
|  |  |  |  |  |

TABLE S18. Best fit results from SANS data of DPPC/DPPG/DHPC/PEG2000DSPE bicelles at $10^{\circ} \mathrm{C}$ with a radius of $\sim 57 \AA$, a thickness of $\sim 33 \AA$, and a fixed $\rho_{s}$ of $1.96 \times 10^{-6} \AA^{-2}$.

|  | 0.27 hrs | 1.54 hrs | 784 hrs | 2197 hrs |
| :--- | :---: | :---: | :---: | :---: |
|  |  |  |  |  |
| $\rho_{\text {disc }}\left(\AA^{-2}\right)$ | $4.54 \times 10^{-6}$ or | $4.41 \times 10^{-6}$ or | $4.25 \times 10^{-6}$ or | $4.16 \times 10^{-6}$ or |
|  | $-6.2 \times 10^{-7}$ | $-4.9 \times 10^{-7}$ | $-3.3 \times 10^{-7}$ | $5.2 \times 10^{-7}$ |
|  | $2.58 \times 10^{-6} \pm$ | $2.45 \times 10^{-6} \pm$ | $1.88 \times 10^{-6} \pm$ | $1.44 \times 10^{-6} \pm$ |
| $\Delta \rho\left(\AA^{-2}\right)$ | $8.58 \times 10^{-9}$ | $8.20 \times 10^{-9}$ | $7.32 \times 10^{-9}$ | $2.67 \times 10^{-9}$ |
|  |  |  |  |  |



Figure. S5. The time evolution NSLD contrast, $\Delta \rho$ of (a) DMPC/DMPG/DHPC and (b) DPPC/DPPG/DHPC bicelles in the absence and presence of DSPE-PEG2000. The solid lines are the best fits using eq (S4). The non-PEGlyated bicelle data were obtained from previous report. ${ }^{1}$

The derived values for $k_{\text {inter }}$ are $(4.13 \pm 0.15) \times 10^{-4}$ and $0.233 \pm 0.003 \mathrm{hr}^{-1}$ for $10^{\circ} \mathrm{C}$ DSPE-PEG2000-associated DPPC and DMPC bicelles, respectively.

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