Supporting Information

Small-angle neutron scattering reveals the nanostructure of liposomes with embedded OprF porins of *Pseudomonas Aeruginosa*

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Power expansion coefficients of normalization factors

$$a_{0,g,\mathrm{in}} = ((\nu_{g,\alpha}\mathrm{n}_{g,\alpha}D_{\mathrm{h,in}})/(\nu_{\mathrm{h,in}}w_{g,\alpha}))/2$$

$$a_{1,g,\mathrm{in}} = -((\nu_{g,\alpha}\mathrm{n}_{g,\alpha}(D^2_{\mathrm{h,in}}\xi^2_{\mathrm{h,in}} + 24D^2_{\mathrm{h,in}} + 48r_{g,\alpha}D_{\mathrm{h,in}} - 4\sigma^2_{\mathrm{term}}))/(\nu_{\mathrm{h,in}}w_{g,\alpha}))/48$$

$$a_{2,g,\mathrm{in}} = ((\nu_{g,\alpha}\mathrm{n}_{g,\alpha}(D^3_{\mathrm{h,in}}\xi^2_{\mathrm{h,in}}$$
$$+ 2r_{g,\alpha}D^2_{\mathrm{h,in}}\xi^2_{\mathrm{h,in}} - 4w^2_{g,\alpha}D_{\mathrm{h,in}}\xi^2_{g,\alpha} + 8D^3_{\mathrm{h,in}} + 48r_{g,\alpha}D^2_{\mathrm{h,in}} - 8w^2_{g,\alpha}D_{\mathrm{h,in}} + 72r^2_{g,\alpha}D_{\mathrm{h,in}}$$
$$- 8r_{g,\alpha}\sigma^2_{\mathrm{term}}))/(\nu_{\mathrm{h,in}}w_{g,\alpha}))/48$$

$$a_{3,g,\mathrm{in}} = ((\nu_{g,\alpha}\mathrm{n}_{g,\alpha}(w^2_{g,\alpha}D^2_{\mathrm{h,in}}\xi^2_{g,\alpha}\xi^2_{\mathrm{h,in}} - 12r_{g,\alpha}D^3_{\mathrm{h,in}}\xi^2_{\mathrm{h,in}} + 2w^2_{g,\alpha}D^2_{\mathrm{h,in}}\xi^2_{\mathrm{h,in}}$$
$$- 18r^2_{g,\alpha}D^2_{\mathrm{h,in}}\xi^2_{\mathrm{h,in}} + 24w^2_{g,\alpha}D^2_{\mathrm{h,in}}\xi^2_{g,\alpha} + 96r_{g,\alpha}w^2_{g,\alpha}D_{\mathrm{h,in}}\xi^2_{g,\alpha} - 4\sigma^2_{\mathrm{term}}w^2_{g,\alpha}\xi^2_{g,\alpha}$$
$$- 96r_{g,\alpha}D^3_{\mathrm{h,in}} + 48w^2_{g,\alpha}D^2_{\mathrm{h,in}} - 432r^2_{g,\alpha}D^2_{\mathrm{h,in}} + 192r_{g,\alpha}w^2_{g,\alpha}D_{\mathrm{h,in}} - 576r^3_{g,\alpha}D_{\mathrm{h,in}} - 8\sigma^2_{\mathrm{term}}w^2_{g,\alpha}$$
$$+ 72r^2_{g,\alpha}\sigma^2_{\mathrm{term}}))/(\nu_{\mathrm{h,in}}w_{g,\alpha}))/288$$

$$a_{0,g,\mathrm{out}} = ((\nu_{g,\alpha}\mathrm{n}_{g,\alpha}D_{\mathrm{h,out}})/(\nu_{\mathrm{h,out}}w_{g,\alpha}))/2$$

$$a_{1,g,\mathrm{out}} = ((\nu_{g,\alpha}\mathrm{n}_{g,\alpha}(D^2_{\mathrm{h,out}}\xi^2_{\mathrm{h,out}} + 24D^2_{\mathrm{h,out}} - 48r_{g,\alpha}D_{\mathrm{h,out}} - 4\sigma^2_{\mathrm{term}}))/(\nu_{\mathrm{h,out}}w_{g,\alpha}))/48$$

$$a_{2,g,\mathrm{out}} = ((\nu_{g,\alpha}\mathrm{n}_{g,\alpha}(D^3_{\mathrm{h,out}}\xi^2_{\mathrm{h,out}} - 2r_{g,\alpha}D^2_{\mathrm{h,out}}\xi^2_{\mathrm{h,out}} - 4w^2_{g,\alpha}D_{\mathrm{h,out}}\xi^2_{g,\alpha}$$
$$+ 8D^3_{\mathrm{h,out}} - 48r_{g,\alpha}D^2_{\mathrm{h,out}} - 8w^2_{g,\alpha}D_{\mathrm{h,out}} + 72r^2_{g,\alpha}D_{\mathrm{h,out}} + 8r_{g,\alpha}\sigma^2_{\mathrm{term}}))/(\nu_{\mathrm{h,out}}w_{g,\alpha}))/48$$

$$a_{3,g,\mathrm{out}} = -((\nu_{g,\alpha}\mathrm{n}_{g,\alpha}(w^2_{g,\alpha}D^2_{\mathrm{h,out}}\xi^2_{g,\alpha}\xi^2_{\mathrm{h,out}} + 12r_{g,\alpha}D^3_{\mathrm{h,out}}\xi^2_{\mathrm{h,out}} + 2w^2_{g,\alpha}D^2_{\mathrm{h,out}}\xi^2_{\mathrm{h,out}}$$
$$- 18r^2_{g,\alpha}D^2_{\mathrm{h,out}}\xi^2_{\mathrm{h,out}} + 24w^2_{g,\alpha}D^2_{\mathrm{h,out}}\xi^2_{g,\alpha} - 96r_{g,\alpha}w^2_{g,\alpha}D_{\mathrm{h,out}}\xi^2_{g,\alpha} - 4\sigma^2_{\mathrm{term}}w^2_{g,\alpha}\xi^2_{g,\alpha}$$
$$+ 96r_{g,\alpha}D^3_{\mathrm{h,out}} + 48w^2_{g,\alpha}D^2_{\mathrm{h,out}} - 432r^2_{g,\alpha}D^2_{\mathrm{h,out}} - 192r_{g,\alpha}w^2_{g,\alpha}D_{\mathrm{h,out}} + 576r^3_{g,\alpha}D_{\mathrm{h,out}} - 8\sigma^2_{\mathrm{term}}w^2_{g,\alpha}$$
$$+ 72r^2_{g,\alpha}\sigma^2_{\mathrm{term}}))/(\nu_{\mathrm{h,out}}w_{g,\alpha}))/288 \tag{S1}$$

Excess SLD profile

The excess SLD profile, according to Eqs. 11, 8, 9 and 10 is

$$\begin{aligned}
\varrho(r)-\rho_0 \quad = \quad & \sum_{\alpha=\mathrm{in,out}} \left\{ (\rho_{1,\alpha}-\rho_0)\left[\varphi_{\mathrm{h},\alpha}(r)-\sum_{g=2}^{N_{\mathrm{h},\alpha}}\varphi_{g,\alpha}(r)\right] \right. \\
& + \sum_{g=2}^{N_{\mathrm{h},\alpha}+N_{\mathrm{p},\alpha}} (\rho_{g,\alpha}-\rho_0)\varphi_{g,\alpha}(r) \\
& +(\rho_{N_{\mathrm{h},\alpha}+N_{\mathrm{p},\alpha}+1,\alpha}-\rho_0)\left[\mathrm{rect}\left(\frac{r-R}{R+(D_{\mathrm{out}}-R)(\alpha-1)}-(-1)^{\alpha}\frac{1}{2}\right\}\right) \\
& \left.\left. -\bar{\varphi}_{\mathrm{h},\alpha}(r)-\sum_{g=N_{\mathrm{h},\alpha}+1}^{N_{\mathrm{h},\alpha}+N_{\mathrm{p},\alpha}}\varphi_{g,\alpha}(r)\right]\right\}. \qquad \text{(S2)}
\end{aligned}$$

This expression can be can be re-written as

$$\begin{aligned}
\varrho(r)-\rho_0 \quad = \quad & (\rho_{N_{\mathrm{h,in}}+N_{\mathrm{p,in}}+1,\mathrm{in}}-\rho_0)\mathrm{rect}\left(\frac{r-R}{R}+\frac{1}{2}\right) \\
& +(\rho_{N_{\mathrm{h,out}}+N_{\mathrm{p,out}}+1,\mathrm{out}}-\rho_0)\mathrm{rect}\left(\frac{r-R}{D_{\mathrm{out}}}-\frac{1}{2}\right) \\
& + \sum_{\alpha=\mathrm{in,out}} \left\{ (\rho_0-\rho_{N_{\mathrm{h},\alpha}+N_{\mathrm{p},\alpha}+1,\alpha})\bar{\varphi}_{\mathrm{h},\alpha}(r) \right. \\
& +(\rho_{1,\alpha}-\rho_0)\varphi_{\mathrm{h},\alpha}(r) \\
& + \sum_{g=2}^{N_{\mathrm{h},\alpha}} (\rho_{g,\alpha}-\rho_{1,\alpha})\varphi_{g,\alpha}(r) \\
+ \quad & \left. \sum_{g=N_{\mathrm{h},\alpha}+1}^{N_{\mathrm{h},\alpha}+N_{\mathrm{p},\alpha}} (\rho_{g,\alpha}-\rho_{N_{\mathrm{h},\alpha}+N_{\mathrm{p},\alpha}+1,\alpha})\varphi_{g,\alpha}(r) \right\} \qquad \text{(S3)}
\end{aligned}$$

Fourier transform of $f(r)$

The isotropic Fourier transform of $f(r)$ is defined as

$$\tilde{f}(q) = 4\pi \int_{R+r_0-w-\xi_l w}^{R+r_0+w+\xi_r w} f(r) r^2 \frac{\sin(qr)}{qr} dr \qquad \text{(S4)}$$

It is convenient to introduce the new integration variable $u = r - R$ and to work in the complex space by exploiting the identity $\sin x = \frac{\imath}{2}(e^{-\imath x} - e^{\imath x})$. Accordingly, we obtain

$$
\begin{aligned}
\tilde{f}(q) &= \frac{2\pi\imath}{q}\int_{r_0-w-\xi_l w}^{r_0+w+\xi_r w} f(R+u)(R+u)[e^{-\imath(q(R+u)} - e^{\imath(q(R+u)}]du \\
&= \frac{2\pi\imath}{q}\{e^{-\imath qR}[R\tilde{f}_1^*(q) + \tilde{f}_2^*(q)] - e^{\imath qR}[R\tilde{f}_1(q) + \tilde{f}_2(q)]\} \\
&= \frac{4\pi}{q}\Im\{e^{\imath qR}[R\tilde{f}_1(q) + \tilde{f}_2(q)]\}
\end{aligned} \tag{S5}
$$

where $\Im(z)$ stands for the imaginary part of the complex variable z. Notice that we have introduced the two following Fourier transformed functions, which we have analytically solved

$$
\begin{aligned}
\tilde{f}_1(q) &= \int_{r_0-w-\xi_l w}^{r_0+w+\xi_r w} f(R+u)e^{\imath qu}du \\
&= \imath\frac{e^{\imath q r_0}}{q^3 w^2}\left(\frac{1}{\xi_r^2}e^{\imath qw(1-\xi_r)}(e^{\imath qw\xi_r} - 1)^2\right. \\
&\quad \left. -\frac{1}{\xi_l^2}e^{-\imath qw(1+\xi_l)}(e^{\imath qw\xi_l} - 1)^2\right)
\end{aligned} \tag{S6}
$$

$$
\begin{aligned}
\tilde{f}_2(q) &= \int_{r_0-w-\xi_l w}^{r_0+w+\xi_r w} f(R+u)ue^{\imath qu}du \\
&= \frac{e^{\imath q r_0}}{q^4 w^2}\left(\frac{1}{\xi_r^2}e^{\imath qw-\imath qw\xi_r}(e^{\imath qw\xi_r} - 1)\right. \\
&\quad (e^{\imath qw\xi_r}(\imath q(w(\xi_r+1) + r_0) - 3) \\
&\quad +\imath q(w(\xi_r - 1) - r_0) + 3) \\
&\quad -\frac{1}{\xi_l^2}e^{-\imath qw-\imath qw\xi_l}(e^{\imath qw\xi_l} - 1) \\
&\quad (e^{\imath qw\xi_l}(\imath q(w(\xi_l - 1) + r_0) - 3) \\
&\quad \left. +\imath q(w(\xi_l + 1) - r_0) + 3)\right)
\end{aligned} \tag{S7}
$$

It is important to consider that both $\tilde{f}_1(q)$ and $\tilde{f}_2(q)$ do not depend on the vesicle radius R. In the limit $q = 0$, the two functions read

$$\tilde{f}_1(0) = 2w \tag{S8}$$

$$\tilde{f}_2(0) = \frac{w(24r_0 + w(\xi_r^2 - \xi_l^2))}{12} \tag{S9}$$

Since the hydrophobic domain volume fraction $\varphi_{\mathrm{h},\alpha}(r)$ is expressed through the parabolic peak function $f(r)$, Eqs. S5, S6 and S7 are exploited to calculate the Fourier transform of $\varphi_{\mathrm{h},\alpha}(r)$,

$$\tilde{\varphi}_{\mathrm{h},\alpha}(q) = \frac{4\pi}{q}\Im\{e^{\imath qR}[R\tilde{\varphi}_{\mathrm{h},\alpha,1}(q) + \tilde{\varphi}_{\mathrm{h},\alpha,2}(q)]\} \tag{S10}$$

In particular, $\tilde{\varphi}_{\mathrm{h,in},1}(q)$ and $\tilde{\varphi}_{\mathrm{h,in},2}(q)$ are calculated with Eq. S6 and S7, respectively, by taking $r_0 = -D_{\mathrm{h,in}}/2$, $w = D_{\mathrm{h,in}}/2$, $\xi_l = \xi_{\mathrm{h,in}}$ and $\xi_r = \sigma_{\mathrm{term}}/(D_{\mathrm{h,in}}/2))$; likewise, $\tilde{\varphi}_{\mathrm{h,out},1}(q)$ and $\tilde{\varphi}_{\mathrm{h,out},2}(q)$ are calculated with Eq. S6 and S7, respectively, by taking $r_0 = D_{\mathrm{h,out}}/2$, $w = D_{\mathrm{h,out}}/2$, $\xi_l = \sigma_{\mathrm{term}}/(D_{\mathrm{h,out}}/2)$ and $\xi_r = \xi_{\mathrm{h,out}}$.

In parallel, Eqs. S5, S6 and S7 are exploited to calculate the Fourier transform of $\bar{\varphi}_{\mathrm{h},\alpha}(r)$,

$$\tilde{\bar{\varphi}}_{\mathrm{h},\alpha}(q) = \frac{4\pi}{q}\Im\{e^{\imath qR}[R\tilde{\bar{\varphi}}_{\mathrm{h},\alpha,1}(q) + \tilde{\bar{\varphi}}_{\mathrm{h},\alpha,2}(q)]\} \tag{S11}$$

where $\tilde{\bar{\varphi}}_{\mathrm{h,in},1}(q)$ and $\tilde{\bar{\varphi}}_{\mathrm{h,in},2}(q)$ are calculated with Eq. S6 and S7, respectively, by taking $r_0 = -D_{\mathrm{h,in}}/2$, $w = D_{\mathrm{h,in}}/2$, $\xi_l = \xi_{\mathrm{h,in}}$ and $\xi_r = 0$; likewise, $\tilde{\bar{\varphi}}_{\mathrm{h,out},1}(q)$ and $\tilde{\bar{\varphi}}_{\mathrm{h,out},2}(q)$ are calculated with Eq. S6 and S7, respectively, by taking $r_0 = D_{\mathrm{h,out}}/2$, $w = D_{\mathrm{h,out}}/2$, $\xi_l = 0$ and $\xi_r = \xi_{\mathrm{h,out}}$.

Concerning the group volume fractions, $\varphi_{g,\alpha}(r)$, we recall that they are expressed via Eq. 4 on the basis of normalized parabolic peaks $f_{g,\alpha}(r)$. Their Fourier transform read

$$\tilde{\varphi}_{g,\alpha}(q) \quad = \quad \frac{4\pi}{q}\sum_{k=0}^{K}\frac{a_{k,g,\alpha}}{R^k}\Im\{e^{\imath qR}[R\tilde{f}_{g,\alpha,1}(q) + \tilde{f}_{g,\alpha,2}(q)]\} \tag{S12}$$

Clearly the functions $\tilde{f}_{g,\alpha,1}(q)$ and $\tilde{f}_{g,\alpha,2}(q)$ are calculated via Eqs. S6 and S7, respectively, with with $r_0 = r_{g,\alpha}$, $w = w_{g,\alpha}$ and $\xi_l = \xi_r = \xi_{g,\alpha}$.

Calculation of $F(q)$ and $F^2(q)$

On the basis of Eq. 12 and S3, the vesicle form factor $F(q)$ can be written as

$$
\begin{aligned}
F(q) &= \frac{4\pi}{q^3}(\rho_{N_{\mathrm{h,in}}+N_{\mathrm{p,in}}+1,\mathrm{in}} - \rho_0)\Im\{e^{\imath qR}(1-\imath qR)\} \\
&+ \frac{4\pi}{q^3}(\rho_{N_{\mathrm{h,out}}+N_{\mathrm{p,out}}+1,\mathrm{out}} - \rho_0)[\Im\{e^{\imath qR}e^{\imath qD_{\mathrm{out}}}(1-\imath q(R+D_{\mathrm{out}})\} - \Im\{e^{\imath qR}(1-\imath qR)\}] \\
&+ \sum_{\alpha=\mathrm{in,out}} \Bigg\{(\rho_0 - \rho_{N_{\mathrm{h},\alpha}+N_{\mathrm{p},\alpha}+1,\alpha})\frac{4\pi}{q}\Im\{e^{\imath qR}[R\tilde{\tilde{\varphi}}_{\mathrm{h},\alpha,1}(q) + \tilde{\tilde{\varphi}}_{\mathrm{h},\alpha,2}(q)]\} \\
&+ (\rho_{1,\alpha} - \rho_0)\frac{4\pi}{q}\Im\{e^{\imath qR}[R\tilde{\varphi}_{\mathrm{h},\alpha,1}(q) + \tilde{\varphi}_{\mathrm{h},\alpha,2}(q)]\} \\
&+ \sum_{g=2}^{N_{\mathrm{h},\alpha}}(\rho_{g,\alpha} - \rho_{1,\alpha})\frac{4\pi}{q}\Im\{\sum_{k=0}^{K}\frac{a_{k,g,\alpha}}{R^k}e^{\imath qR}[R\tilde{f}_{g,\alpha,1}(q) + \tilde{f}_{g,\alpha,2}(q)]\} \\
&+ \sum_{g=N_{\mathrm{h},\alpha}+1}^{N_{\mathrm{h},\alpha}+N_{\mathrm{p},\alpha}}(\rho_{g,\alpha} - \rho_{N_{\mathrm{h},\alpha}+N_{\mathrm{p},\alpha}+1,\alpha})\frac{4\pi}{q}\Im\{\sum_{k=0}^{K}\frac{a_{k,g,\alpha}}{R^k}e^{\imath qR}[R\tilde{f}_{g,\alpha,1}(q) + \tilde{f}_{g,\alpha,2}(q)]\}\Bigg\} \qquad \text{(S13)}
\end{aligned}
$$

where we have introduced the isotropic Fourier transform of the rectangular function

$$
4\pi\int_0^\infty \mathrm{rect}\left(\frac{1}{2} - \frac{r-B}{A-B}\right)\frac{\sin(qr)}{qr}r^2dr = \frac{4\pi}{q^3}\Im\{e^{\imath qB}(1-\imath qB) - e^{\imath qA}(1-\imath qA)\} \qquad \text{(S14)}
$$

with $A < B$. Eq. S13 can be rearranged in a much compact form, according to

$$
F(q) = \frac{4\pi}{q}\sum_{k=-1}^{K}\Im\left\{e^{\imath qR}\frac{F_k(q)}{R^k}\right\} \qquad \text{(S15)}
$$

where the following intermediate functions, all independent on R, have been introduced

$$
\begin{aligned}
F_{-1}(q) &= -\frac{\imath}{q}(\rho_{N_{\mathrm{h,in}}+N_{\mathrm{p,in}}+1,\mathrm{in}} - \rho_0) \\
&\quad -\frac{\imath}{q}(\rho_{N_{\mathrm{h,out}}+N_{\mathrm{p,out}}+1,\mathrm{out}} - \rho_0)[e^{\imath qD_{\mathrm{out}}} - 1] \\
&\quad + \sum_{\alpha=\mathrm{in,out}}\Bigg\{(\rho_0 - \rho_{N_{\mathrm{h},\alpha}+N_{\mathrm{p},\alpha}+1,\alpha})\tilde{\tilde{\varphi}}_{\mathrm{h},\alpha,1}(q) \\
&\quad +(\rho_{1,\alpha} - \rho_0)\tilde{\varphi}_{\mathrm{h},\alpha,1}(q) \\
&\quad + \sum_{g=2}^{N_{\mathrm{h},\alpha}}(\rho_{g,\alpha} - \rho_{1,\alpha})a_{0,g,\alpha}\tilde{f}_{g,\alpha,1}(q) \\
&\quad + \sum_{g=N_{\mathrm{h},\alpha}+1}^{N_{\mathrm{h},\alpha}+N_{\mathrm{p},\alpha}}(\rho_{g,\alpha} - \rho_{N_{\mathrm{h},\alpha}+N_{\mathrm{p},\alpha}+1,\alpha})a_{0,g,\alpha}\tilde{f}_{g,\alpha,1}(q)\Bigg\} \qquad \text{(S16)}
\end{aligned}
$$

$$
\begin{aligned}
F_0(q) &= \frac{1}{q^2}(\rho_{N_{\mathrm{h,in}}+N_{\mathrm{p,in}}+1,\mathrm{in}} - \rho_0) \\
&+ \frac{1}{q^2}(\rho_{N_{\mathrm{h,out}}+N_{\mathrm{p,out}}+1,\mathrm{out}} - \rho_0)[e^{\imath q D_{\mathrm{out}}}(1 - \imath q D_{\mathrm{out}}) - 1] \\
&+ \sum_{\alpha=\mathrm{in,out}} \{(\rho_0 - \rho_{N_{\mathrm{h},\alpha}+N_{\mathrm{p},\alpha}+1,\alpha})\tilde{\tilde{\varphi}}_{\mathrm{h},\alpha,2}(q) \\
&\quad +(\rho_{1,\alpha} - \rho_0)\tilde{\varphi}_{\mathrm{h},\alpha,2}(q) \\
&\quad + \sum_{g=2}^{N_{\mathrm{h},\alpha}}(\rho_{g,\alpha} - \rho_{1,\alpha})[a_{0,g,\alpha}\tilde{f}_{g,\alpha,2}(q) + a_{1,g,\alpha}\tilde{f}_{g,\alpha,1}(q)] \\
&+ \left.\sum_{g=N_{\mathrm{h},\alpha}+1}^{N_{\mathrm{h},\alpha}+N_{\mathrm{p},\alpha}}(\rho_{g,\alpha} - \rho_{N_{\mathrm{h},\alpha}+N_{\mathrm{p},\alpha}+1,\alpha})[a_{0,g,\alpha}\tilde{f}_{g,\alpha,2}(q) + a_{1,g,\alpha}\tilde{f}_{g,\alpha,1}(q)]\right\}
\end{aligned} \tag{S17}
$$

For $1 \leq k \leq K-1$

$$
\begin{aligned}
F_k(q) &= \sum_{\alpha=\mathrm{in,out}} \left\{ \sum_{g=2}^{N_{\mathrm{h},\alpha}}(\rho_{g,\alpha} - \rho_{1,\alpha})[a_{k,g,\alpha}\tilde{f}_{g,\alpha,2}(q) + a_{k+1,g,\alpha}\tilde{f}_{g,\alpha,1}(q)] \right. \\
&+ \left. \sum_{g=N_{\mathrm{h},\alpha}+1}^{N_{\mathrm{h},\alpha}+N_{\mathrm{p},\alpha}}(\rho_{g,\alpha} - \rho_{N_{\mathrm{h},\alpha}+N_{\mathrm{p},\alpha}+1,\alpha})[a_{k,g,\alpha}\tilde{f}_{g,\alpha,2}(q) + a_{k+1,g,\alpha}\tilde{f}_{g,\alpha,1}(q)] \right\}
\end{aligned} \tag{S18}
$$

for $k = K$

$$
\begin{aligned}
F_K(q) &= \sum_{\alpha=\mathrm{in,out}} \left\{ \sum_{g=2}^{N_{\mathrm{h},\alpha}}(\rho_{g,\alpha} - \rho_{1,\alpha})a_{K,g,\alpha}\tilde{f}_{g,\alpha,2}(q) \right. \\
&+ \left. \sum_{g=N_{\mathrm{h},\alpha}+1}^{N_{\mathrm{h},\alpha}+N_{\mathrm{p},\alpha}}(\rho_{g,\alpha} - \rho_{N_{\mathrm{h},\alpha}+N_{\mathrm{p},\alpha}+1,\alpha})a_{K,g,\alpha}\tilde{f}_{g,\alpha,2}(q) \right\}
\end{aligned} \tag{S19}
$$

It can be shown that the squared form factor can be expressed by the following equation

$$
F^2(q) = \frac{8\pi^2}{q^2} \sum_{k_1,k_2=-1}^{K} \Re \left\{ \frac{F_{k_1}(q)F^*_{k_2}(q)}{R^{k_1+k_2}} - e^{\imath 2qR}\frac{F_{k_1}(q)F_{k_2}(q)}{R^{k_1+k_2}} \right\} \tag{S20}
$$

where $\Re(z)$ stands for the real part of the complex variable z.

Average of of $F(q)$ and $F^2(q)$ over the Schulz distribution function

We assume that the vesicle radius R is polydispersed according to the Schulz distribution function

$$
p(R) = \frac{s^{sR_0}}{\Gamma(sR_0)} R^{sR_0-1} e^{-sR} \tag{S21}
$$

which is characterized by two parameters, the average radius $R_0 \equiv <R>$, with

$$<R> \; = \; \int_0^\infty R\, p(R)\, dR \tag{S22}$$

and $s = \frac{1}{R_0 \xi_R^2}$, being ξ_R the dispersion of R, defined as

$$\xi_R^2 = (<R^2> - <R>^2)/ <R>^2 \tag{S23}$$

In particular, the following other two averages can be derived

$$<R^2> \; = \; \frac{R_0(1+sR_0)}{s} \tag{S24}$$

$$<R^3> \; = \; \frac{R_0(1+sR_0)(2+sR_0)}{s^2} \tag{S25}$$

By using the compact forms of of $F(q)$ and $F^2(q)$ (Eqs. S15 and S20) we have been able to derive the two following analytic expression for their averages over the Schulz distribution,

$$\begin{aligned} < F(q) > &= s^{sR_0} \frac{1}{\Gamma(sR_0)} \int_0^\infty F(q) R^{sR_0-1} e^{-sR}\, dR \\ &= \frac{4\pi}{q} \sum_{k=-1}^{K} \frac{s^{sR_0}\Gamma(sR_0-k)}{(q^2+s^2)^{\frac{sR_0-k}{2}}\Gamma(sR_0)} \\ &\times[\Im(F_k)\cos\left(\tan^{-1}\left(\frac{q}{s}\right)(sR_0-k)\right) + \Re(F_k)\sin\left(\tan^{-1}\left(\frac{q}{s}\right)(sR_0-k)\right)] \end{aligned} \tag{S26}$$

$$\begin{aligned} < F^2(q) > &= s^{sR_0} \frac{1}{\Gamma(sR_0)} \int_0^\infty F^2(q) R^{sR_0-1} e^{-sR}\, dR \\ &= \frac{8\pi^2}{q^2} \sum_{k_1,k_2=-1}^{K} \frac{\Gamma(sR_0-k_2-k_1)s^{k_1+k_2}}{\Gamma(sR_0)} [\Im(F_{k_1})\Im(F_{k_2}) + \Re(F_{k_1})\Re(F_{k_2})] \\ &+\{[\Im(F_{k_1})\Im(F_{k_2}) - \Re(F_{k_1})\Re(F_{k_2})]\cos\left(\tan^{-1}\left(\frac{2q}{s}\right)(sR_0-k_2-k_1)\right) \\ &+[\Re(F_{k_1})\Im(F_{k_2}) + \Im(F_{k_1})\Re(F_{k_2})]\sin\left(\tan^{-1}\left(\frac{2q}{s}\right)(sR_0-k_2-k_1)\right)\} \\ &\times\frac{\Gamma(sR_0-k_2-k_1)s^{sR_0}}{(4q^2+s^2)^{\frac{sR_0-k_1-k_2}{2}}\Gamma(sR_0)} \end{aligned} \tag{S27}$$

Volume of the solution inside the vesicle

According to the definition of the volume fraction distribution within the vesicle, reported in Eq. 9, it is simple to calculate the volume of the hydration solution inside the vesicle,

$$\begin{aligned}
V_{N_{\mathrm{h,in}}+N_{\mathrm{p,in}}+1} &= 4\pi \int_0^\infty \varphi_{N_{\mathrm{h,in}}+N_{\mathrm{p,in}}+1,\mathrm{in}}(r) r^2 dr \\
&= \frac{4}{3}\pi R^3 - 4\pi \int_0^\infty \bar{\varphi}_{\mathrm{h,in}}(r) r^2 dr - 4\pi \sum_{g=N_{\mathrm{h,in}}+1}^{N_{\mathrm{h,in}}+N_{\mathrm{p,in}}} \int_0^\infty \varphi_{g,\mathrm{in}}(r) r^2 dr \\
&= \frac{4}{3}\pi R^3 - \tilde{\bar{\varphi}}_{\mathrm{h,in}}(0) - \sum_{g=N_{\mathrm{h,in}}+1}^{N_{\mathrm{h,in}}+N_{\mathrm{p,in}}} \tilde{\varphi}_{g,\mathrm{in}}(0) \\
&= \frac{4}{3}\pi R^3 - \tilde{\bar{\varphi}}_{\mathrm{h,in}}(0) - \sum_{g=N_{\mathrm{h,in}}+1}^{N_{\mathrm{h,in}}+N_{\mathrm{p,in}}} \tilde{f}_{g,\mathrm{in}}(0) \sum_{k=0}^{K} \frac{a_{k,g,\mathrm{in}}}{R^k}
\end{aligned} \tag{S28}$$

Considering the expressions of $a_{k,g,\mathrm{in}}$ (Eq. S1), the ones reporting the value at $q = 0$ of the Fourier transform of $f(r)$ (Eqs. S8-S9) and recalling the average values of the k-th momentum of R under the Schulz distribution function,

$$< R^k > = \int_0^\infty R^k \, p(R) \, dR = \frac{\Gamma(sR_0 + k)}{s^k \Gamma(sR_0)}, \tag{S29}$$

with $sR_0 + k > 0$ and k positive or negative, we have been able to calculate the average value of the volume inside the polydispersed vesicle, as it follows

$$
\begin{aligned}
<V_{N_{\mathrm{h,in}}+N_{\mathrm{p,in}}+1}> \quad = \quad & 4\pi\{[-2s^2 {w_{\mathrm{h,in}}}^3 - s^2 {w_{\mathrm{h,in}}}^3 {\xi_{\mathrm{h,in}}}^2 + (s^2 {w_{\mathrm{h,in}}}^2 {\xi_{\mathrm{h,in}}}^2 \\
& +6s^2 {w_{\mathrm{h,in}}}^2 - 6sw_{\mathrm{h,in}} + 4)R_0 + (6s - 6s^2 w_{\mathrm{h,in}}){R_0}^2 + 2s^2 {R_0}^3]/[6s^2] \\
& - \sum_{g=N_{\mathrm{h,in}}+1}^{N_{\mathrm{h,in}}+N_{\mathrm{p,in}}} a_{0,g,\mathrm{in}}[w_{g,\mathrm{in}}(6{r_{g,\mathrm{in}}}^2 s \\
& +2s{w_{g,\mathrm{in}}}^2 + s{w_{g,\mathrm{in}}}^2 {\xi_{g,\mathrm{in}}}^2 + 6R_0 + 12r_{g,\mathrm{in}} sR_0 + 6s{R_0}^2)]/[3s] \\
& +a_{1,g,\mathrm{in}}[w_{g,\mathrm{in}}(-12r_{g,\mathrm{in}} + 6{r_{g,\mathrm{in}}}^2 s \\
& +2s{w_{g,\mathrm{in}}}^2 + s{w_{g,\mathrm{in}}}^2 {\xi_{g,\mathrm{in}}}^2 \\
& -6R_0 + 12r_{g,\mathrm{in}} sR_0 + 6s{R_0}^2)]/[3(sR_0 - 1)] \\
& +a_{2,g,\mathrm{in}}[w_{g,\mathrm{in}}(12 - 24r_{g,\mathrm{in}} s \\
& +6{r_{g,\mathrm{in}}}^2 s^2 + 2s^2 {w_{g,\mathrm{in}}}^2 + s^2 {w_{g,\mathrm{in}}}^2 {\xi_{g,\mathrm{in}}}^2 + 18sR_0 + 12r_{g,\mathrm{in}} s^2 R_0 \\
& +6s^2 {R_0}^2)]/[3(sR_0 - 2)(sR_0 - 1)] \\
& -a_{3,g,\mathrm{in}}[sw_{g,\mathrm{in}}(36 - 36r_{g,\mathrm{in}} s \\
& +6{r_{g,\mathrm{in}}}^2 s^2 + 2s^2 {w_{g,\mathrm{in}}}^2 + s^2 {w_{g,\mathrm{in}}}^2 {\xi_{g,\mathrm{in}}}^2 - 30sR_0 + 12r_{g,\mathrm{in}} s^2 R_0 \\
& +6s^2 {R_0}^2)]/[3(sR_0 - 3)(sR_0 - 2)(sR_0 - 1)]\} \qquad \text{(S30)}
\end{aligned}
$$

Mass balance

We assume that the molecular units of the two monolayers are formed by N_S compounds (lipids, proteins, carbohydrates, nucleic acids, drugs, etc.) and that their total molar concentration is C_k, with $k = 1, N_S$. Each of these compounds could be differently distributed in the two distinct monolayers, according to a molar ratio $x_{k,\alpha}$, with $\sum_{\alpha=\mathrm{in}}^{\mathrm{out}} x_{k,\alpha} = 1$. Let us assume that the first compound (labelled with $k = 1$) is present in both monolayers ($x_{1,\alpha} \neq 0$ for $\alpha = \mathrm{in}, \mathrm{out}$). The nominal stoichiometry of the α-molecular unit can be defined through the ratios of the concentration of the k-compound and the concentration of the first compound

$$\zeta_{k,\alpha} = \frac{x_{k,\alpha} C_k}{x_{1,\alpha} C_1} \qquad \text{(S31)}$$

so that we get $\zeta_{1,\alpha} = 1$. Hence, the molar concentration of the α-molecular unit is $C_{\mathrm{MB},\alpha} = x_{1,\alpha} C_1$. The molar concentration of the vesicles will be $C_{\mathrm{ves}} = C_{\mathrm{MB},\alpha} / < N_{\mathrm{sa},\alpha} >$. So we have $C_{\mathrm{ves}}(< N_{\mathrm{sa,in}} > + < N_{\mathrm{sa,out}} >) = C_{\mathrm{MB,in}} + C_{\mathrm{MB,out}}$. As a consequence, we find

$$C_{\mathrm{ves}} = \frac{C_1}{< N_{\mathrm{sa,in}} > + < N_{\mathrm{sa,out}} >}. \tag{S32}$$

We noticed that, on the basis of Eqs. 5 and 6 together with Eq. S24, the average self-assembling numbers are

$$\begin{aligned} < N_{\mathrm{sa,in}} > &= \frac{\pi}{6\nu_{\mathrm{h,in}}}(8D_{\mathrm{h,in}}^3 + D_{\mathrm{h,in}}^3 \xi_{\mathrm{h,in}}^2 + R_0(24 D_{\mathrm{h,in}}(1 + sR_0)/s \\ &\quad -24 D_{\mathrm{h,in}}^2 - D_{\mathrm{h,in}}^2 \xi_{\mathrm{h,in}}^2 + 4\sigma_{\mathrm{term}}^2)) \qquad \text{(S33)} \\ < N_{\mathrm{sa,out}} > &= \frac{\pi}{6\nu_{\mathrm{h,out}}}(8D_{\mathrm{h,out}}^3 + D_{\mathrm{h,out}}^3 \xi_{\mathrm{h,out}}^2 + R_0(24 D_{\mathrm{h,out}}(1 + sR_0)/s \\ &\quad +24 D_{\mathrm{h,out}}^2 + D_{\mathrm{h,out}}^2 \xi_{\mathrm{h,out}}^2 - 4\sigma_{\mathrm{term}}^2)) \qquad \text{(S34)} \end{aligned}$$

Area per molecular unit

The average area associated to each molecular unit can be defined by the ratio between the average vesicle surface and the average number of sf-assembled molecular unit. In detail

$$a_{\mathrm{in}} = \frac{4\pi < (R - D_{\mathrm{in}})^2 >}{< N_{\mathrm{sa,in}} >} = \frac{4\pi (R_0(1 + sR_0)/s + D_{\mathrm{in}}^2 - 2R_0 D_{\mathrm{in}})}{< N_{\mathrm{sa,in}} >} \tag{S35}$$

$$a_{\mathrm{out}} = \frac{4\pi < (R + D_{\mathrm{out}})^2 >}{< N_{\mathrm{sa,out}} >} = \frac{4\pi (R_0(1 + sR_0)/s + D_{\mathrm{out}}^2 + 2R_0 D_{\mathrm{out}})}{< N_{\mathrm{sa,out}} >} \tag{S36}$$

In the limit of large R_0, by considering Eqs. S33-S34, we obtain $a_\alpha = \nu_{\mathrm{h},\alpha} / D_{\mathrm{h},\alpha}$, as expected for flat monolayers.

Table S1: Third class of fitting parameters obtained by the global-fit analysis of SANS curves. Validity ranges of fitting parameters: [a] ±20% of nominal x_D; [b] $(0-3)\cdot 10^{-2}$ cm^{-1}; [c] fixed value.

L		PL	
x_D [a]	B [b]	x_D [a]	B [b]
0 [c]	1.8±0.2	0 [c]	0.9±0.2
0.0965±0.0008	1.49±0.08	0.0734±0.0005	0.7±0.1
0.141±0.001	0.3±0.1	0.098±0.001	0.5±0.1
0.197±0.001	2.30±0.07	0.420±0.008	0.55±0.02
0.294±0.002	2.46±0.05		
0.399±0.002	2.18±0.03		

Third class fitting parameters

SLD profiles obtained from SANS data

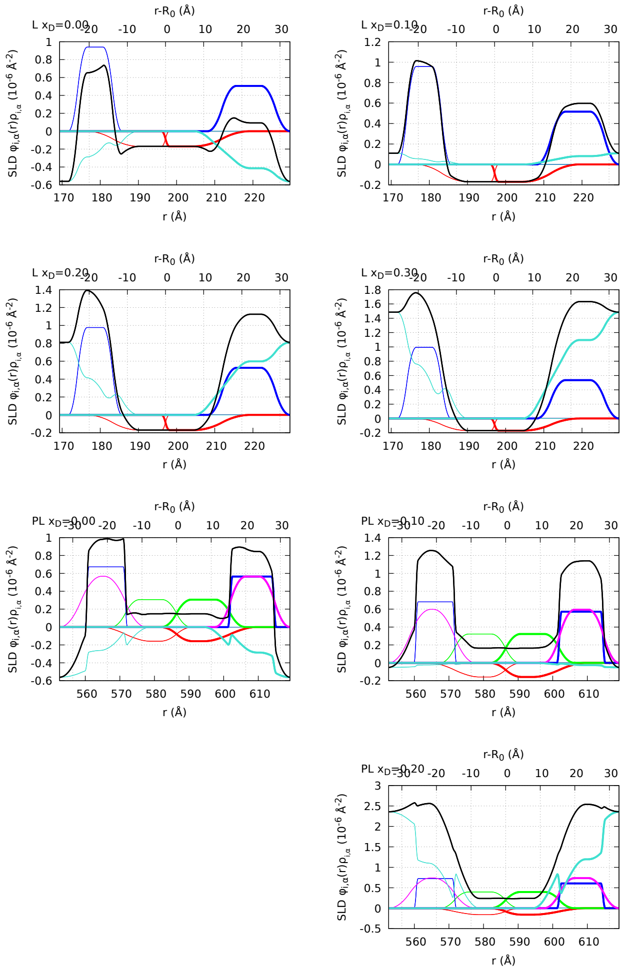

Figure S1: SLD of united groups derived from the analysis of SANS data at different solvent deuteration grade x_D for liposomes (L panels) and proteoliposomes (PL panels) reported as a function of the radial distance r from the vesicle center (bottom horizontal axis) and as a function of the radial distance from the average vesicle radius R_0 (top horizontal axis). Thin and thick lines refer to inner ($\alpha = \text{in}$) and outer ($\alpha = \text{out}$) monolayer, respectively. Red, blue and turquoise distributions refer to lipid hydrophobic group, lipid polar group and water, respectively. In PL panels, green and magenta colors refer to hydrophobic protein group and polar protein group, respectively. In all panels, the black line is the total SLD of the system.