Electronic Supplementary Information

Chirality-Dependent Interaction of d- and l-Menthol with Biomembrane Models

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NMR Spectroscopy

The 13C-NMR spectrum of DOPC titrated with d- or l-menthol at 15 °C is shown in Figure S3. As the concentration of d-menthol increased, the peak at 70.4 ppm, corresponding to the carbon at the g2 position of DOPC, remained unchanged. On the other hand, this peak became less intense as the l-menthol concentration was increased. In addition, the peak at 71.57 ppm, which corresponds to C1 of menthol, intensified compared to when d-menthol was added. Since the carbon at the g2 position is located in the hydrophilic region of DOPC, there is a hydrophilic interaction between l-menthol and DOPC.

Figure S1. Systematic numbering of the chemical structures of (a) Chol, (b) l-menthol, and (c) d-menthol.
Table S1. $^1$H chemical shift values for DOPC, Chol, and menthol at 15 °C. Since there are no significant differences in chemical shifts between d- and l-menthol, only the results for l-menthol are shown.

| Component | $^1$H-site | Chemical Shift (ppm) |
|-----------|------------|----------------------|
| DOPC      | C18        | 0.895                |
|           | $\alpha$   | 3.42                 |
|           | C9 and C10 | 1.90                 |
|           | (CH$_2$)$_n$ | 1.30                 |
|           | C1         | 2.01                 |
| Chol      | C26-27     | 0.88                 |
|           | C25        | 1.56                 |
| Menthol   | C1         | 3.41                 |
|           | C6         | 1.96                 |
|           | C7         | 2.16                 |
|           | C8         | 0.93                 |
|           | C9         | 0.809                |
|           | C10        | 0.90                 |
|           | C5         | 1.41                 |

Figure S2. $^1$H-NMR spectra of (a) DOPC, (b) Chol, and (c) menthol.
Figure S3. $^{13}$C-NMR spectra of DOPC titrated with d- or l-menthol at 15 °C.
Phase-separated Structures at Room Temperature

Figure S4. Typical microscopic image of reverse domain formation. Scale bar = 10 μm.