

Supplementary information

A Simple Method for Continuous Synthesis of Bicelles in Microfluidic Systems

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S1. Comparison of bicelles prepared by microfluidic and conventional method

To evaluate the quality of the synthesized bicelle through the microfluidic chip, the physicochemical properties were investigated by comparing the bicelles prepared by microfluidic and conventional method. Under 5 mM DMPC and 20 mM DHPC condition ($q=0.25$), the conventionally prepared sample has smaller size and liquid-crystalline phase membrane, indicating that it was mixed micelles, on the contrary to the sample prepared by the microfluidic method (Figure S1). In a thin-film hydration method, the hydration of DMPC and DHPC occurs simultaneously. However, in the microfluidic method, DMPCs were assembled first and DHPCs were constituted the rim area, so that the bicelles can be formed. Meanwhile, the samples prepared under 10 mM DMPC and 20 mM DHPC condition ($q=0.5$) have similar physicochemical properties as shown in Figure S1.

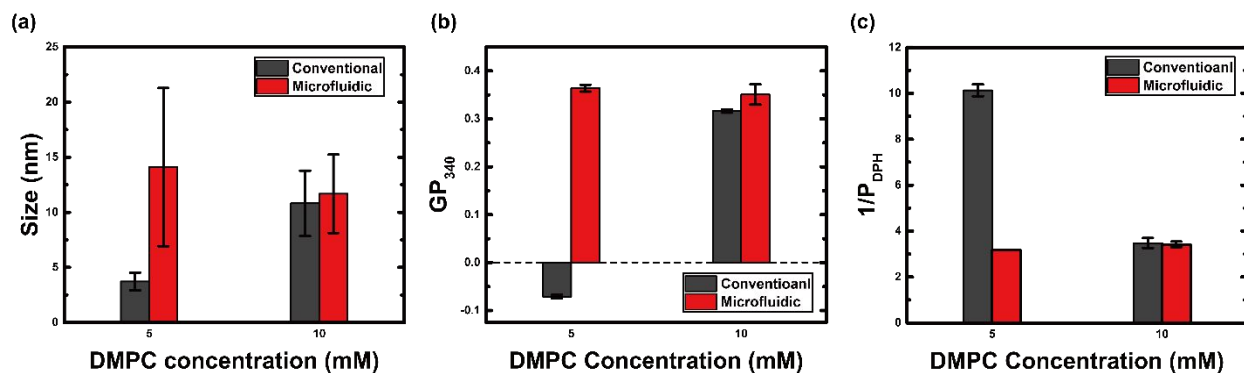


Figure S1. (a) The size, (b) membrane polarity, and (c) membrane fluidity of assemblies prepared by conventional and microfluidic methods. DMPC concentration were 5 mM and 10 mM while DHPC concentration was fixed as 20 mM.

S2. Mixing time

As stated in the manuscript, the mixing time was obtained from the analytical model for the stream width of inner phase. Each value to obtain the mixing time was depicted as shown in Table S1.

Table S1. Parameters for the mixing time

V_f of ethanol ($V_{\text{ethanol}}/V_{\text{total}}$)	Mixture viscosity (η_{mixture} , mPa·s)	Viscosity ratio ($\chi: \eta_{\text{mixture}}/\eta_{\text{buffer}}$)	Stream width (δ , μm)	Diffusion coefficient ($10^{-10}\text{m}^2\text{s}^{-1}$)	Mixing time (sec)
0	0.522	0.588	11.076	18.147	0.034
0.25	0.627	0.706	11.978	15.007	0.048
0.5	0.753	0.848	12.944	12.887	0.065
0.75	0.906	1.020	13.976	11.599	0.084
1	1.090	1.228	15.078	10.713	0.106

S3. Residual solvent after sample preparation

The residual solvent might affect the physicochemical properties of final products so that the solvent was evaporated under a low vacuum condition (80 kPa) for 3 hours at room temperature, as stated in section 2.3. After the solvent evaporation process, the residual solvent was investigated via ^1H NMR. As shown in Figure S2, it was confirmed that the solvent was mostly evaporated.

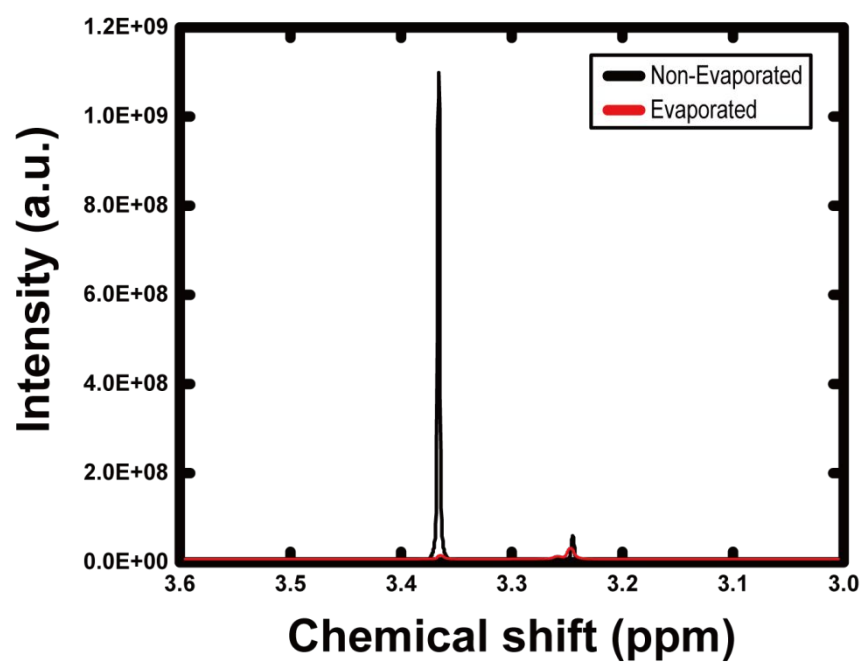


Figure S2. The chemical shift value of samples (a) before evaporation, and (b) after evaporation.

The area under ^1H NMR signals at 3.36 ppm where the methanol peak occurred was reduced from 101.95 to 2.017 after evaporation.