Electronic Supplementary Material (ESI) for Soft Matter.

Supplementary Information

Rapid leakage from PEGylated liposomes triggered by bubbles

Tetsuya Fujie, Makoto Yoshimoto*

Department of Applied Chemistry, Yamaguchi University, Tokiwadai 2-16-1, Ube 755-8611, Japan

*Corresponding author: *E-mail address:* yosimoto@yamaguchi-u.ac.jp (M. Yoshimoto).

Contents

1. Determination of concentrations of 5(6)-carboxyfluorescein in liposomes

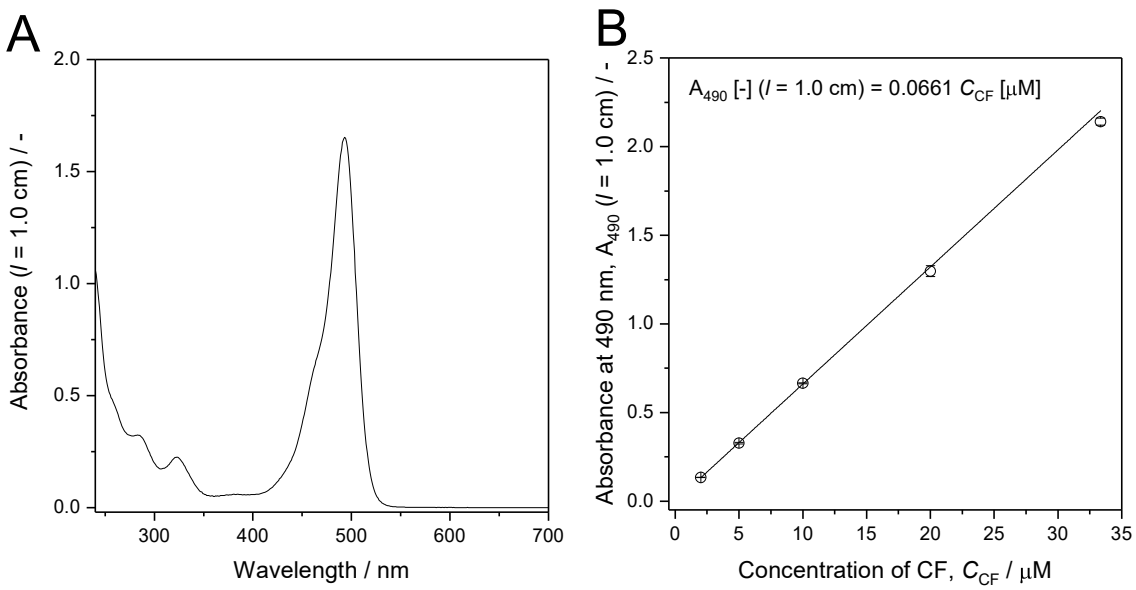

Fig. S1 (A) UV/vis spectrum of the mixture of lipids, sodium cholate and CF prepared by solubilizing CFL-PEG$_{5000}$ (f_P = 0.01) at the concentrations of lipids and cholate of 0.1 mM and 40 mM, respectively. (B) Relationship between the absorbance at 490 nm and concentration of CF. The measurements were performed in the absence of sodium cholate. Data represent mean value ± standard deviation (n = 2). The presence of 40 mM cholate showed negligible effect on the A_{490} value as confirmed at [CF] = 10 and 20 μM.

For CFL-PEG$_{5000}$ (f_P = 0.01), the concentration of CF in liposomes, $C_{CF,in}$ was determined as follows. The concentration of CF, $C_{CF,overall}$ in the lipid/cholate micellar solution ([lipid] = 0.1 mM) can be determined as $C_{CF,overall}$ = 24.3 μM with Fig. S1A and B above. The number of lipid molecules per liposomes can be estimated as 1.40×10^5 with D_h = 131 nm, assumed bilayer thickness of 3.7 nm, and assumed head group area of 0.73 nm^2. Therefore, the concentration of liposomes in the liposome suspension ([lipid] = 0.1 mM) can be determined as 0.717 nM. The volume of a water pool of a liposome can be calculated as 9.88×10^{-22} m^3. Accordingly, the fractional volume of the total water pool of liposomes in the suspension can be calculated as 4.26×10^{-4}. The $C_{CF,in}$ value is determined as 24.3 μM/(0.000426) = 57 mM.

2. External loop airlift bubble column and viscometer

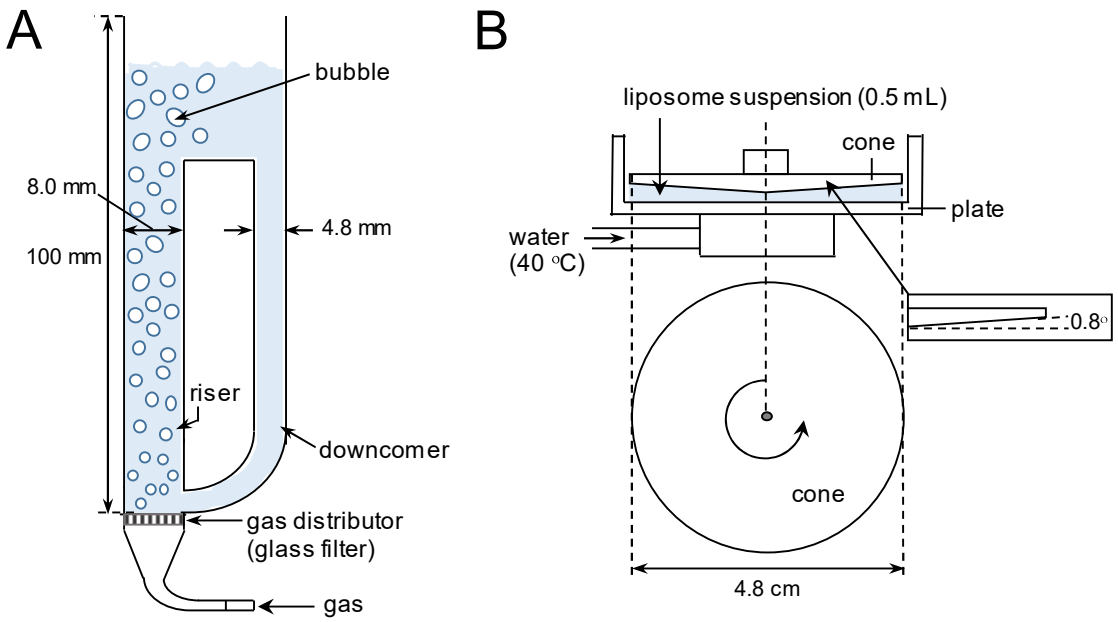

Fig. S2 Schematic illustration of (A) external loop airlift bubble column and (B) cone-and-plate viscometer.

3. Normal bubble column

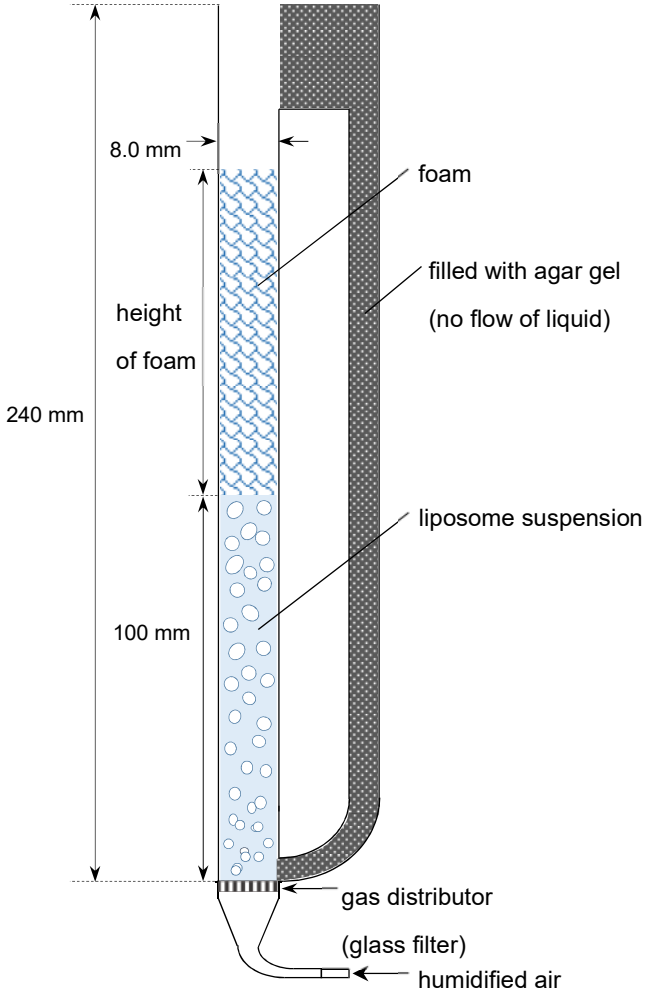

Fig. S3 Schematic illustration of a normal bubble column. The liquid flow in the downcomer of an airlift bubble column (240 mm in total height) was blocked with 3 wt% agar gel.

4. Storage stability of 5(6)-carboxyfluorescein-containing liposomes

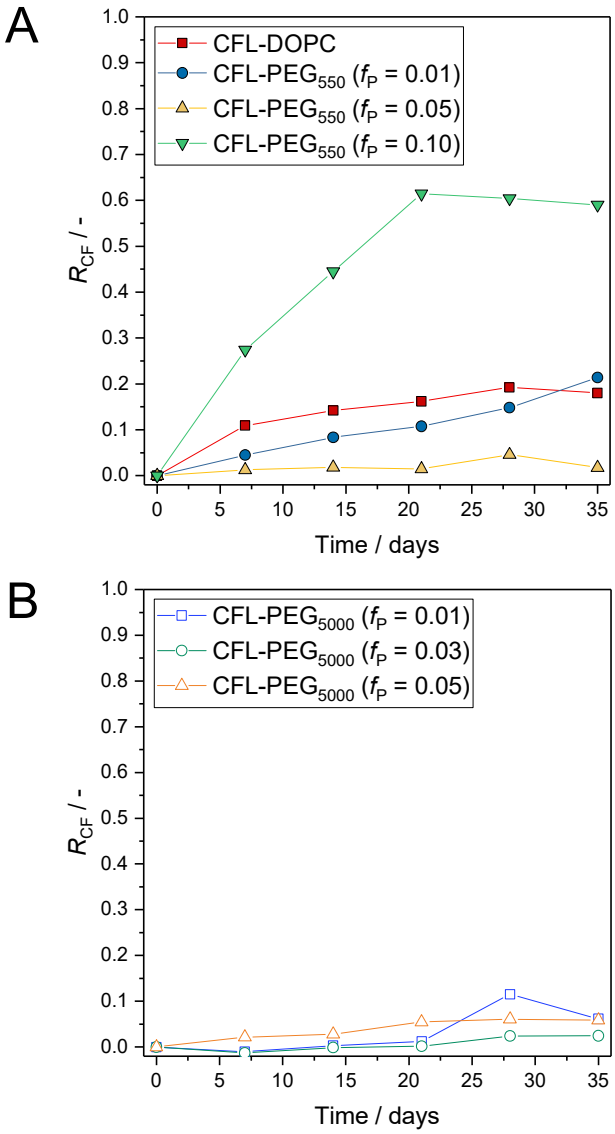

Fig. S4 Effect of storage time at 4 °C on the fractional amount of 5(6)-carboxyfluorescein (CF) released, R_{CF} from (A) dye-containing 1,2-dioleoyl-*sn*-glycero-3-phosphocholine liposomes (CFL-DOPC) and dye-containing liposomes composed of DOPC and DSPE-PEG_{550} (CFL-PEG_{550}), and from (B) dye-containing liposomes composed of DOPC and DSPE-PEG_{5000} (CFL-PEG_{5000}). The values of f_P represent mole fraction of the PEGylated lipid in liposome membranes. The liposome suspension was stored in a 2.0-mL polypropylene tube at the total concentrations of lipids of 10-15 mM. For the measurements, each CFL prepared in a single batch was used and the R_{CF} value was calculated with a single set of the fluorescent intensity measured with and without sodium cholate for solubilization of liposomes.

5. Effects of U_G and temperature on the release of CF from liposomes

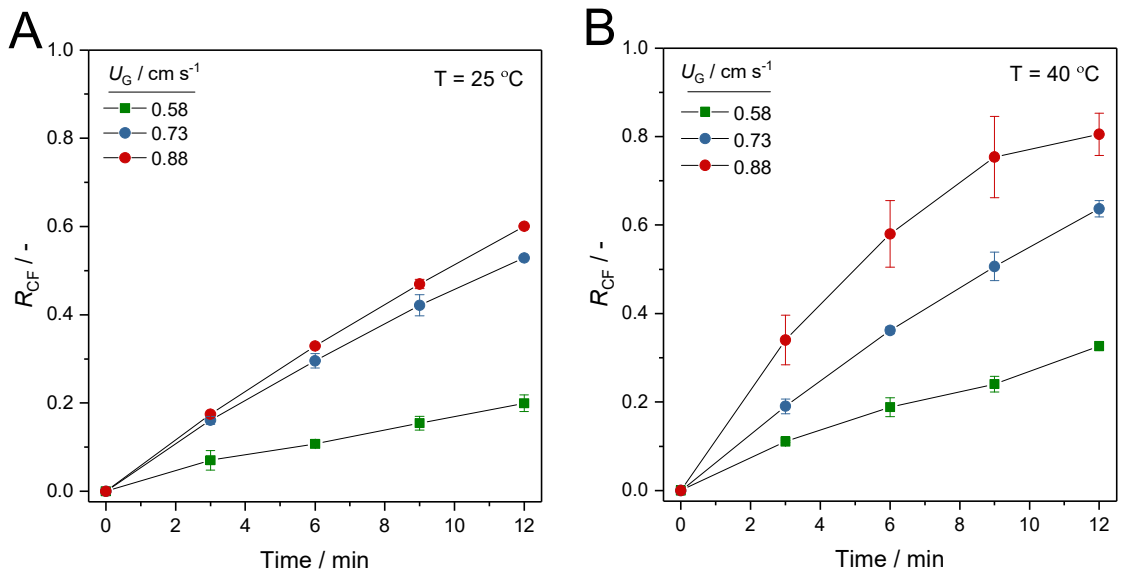

Fig. S5 (A) Time course of the fractional amount of CF released from CFL-PEG$_{5000}$ (f_P = 0.01) at 25 °C (A) and 40 °C (B) at various superficial gas velocities, U_G. The concentration of total lipids was 0.1 mM. Data represent mean value ± standard deviation (n = 3 for the data at 40 °C and U_G = 0.88 cm/s being the same as the data shown in Fig. 3B in the main text, and n = 2 for other conditions).

6. Effect of gas-liquid flow on size distribution of liposomes

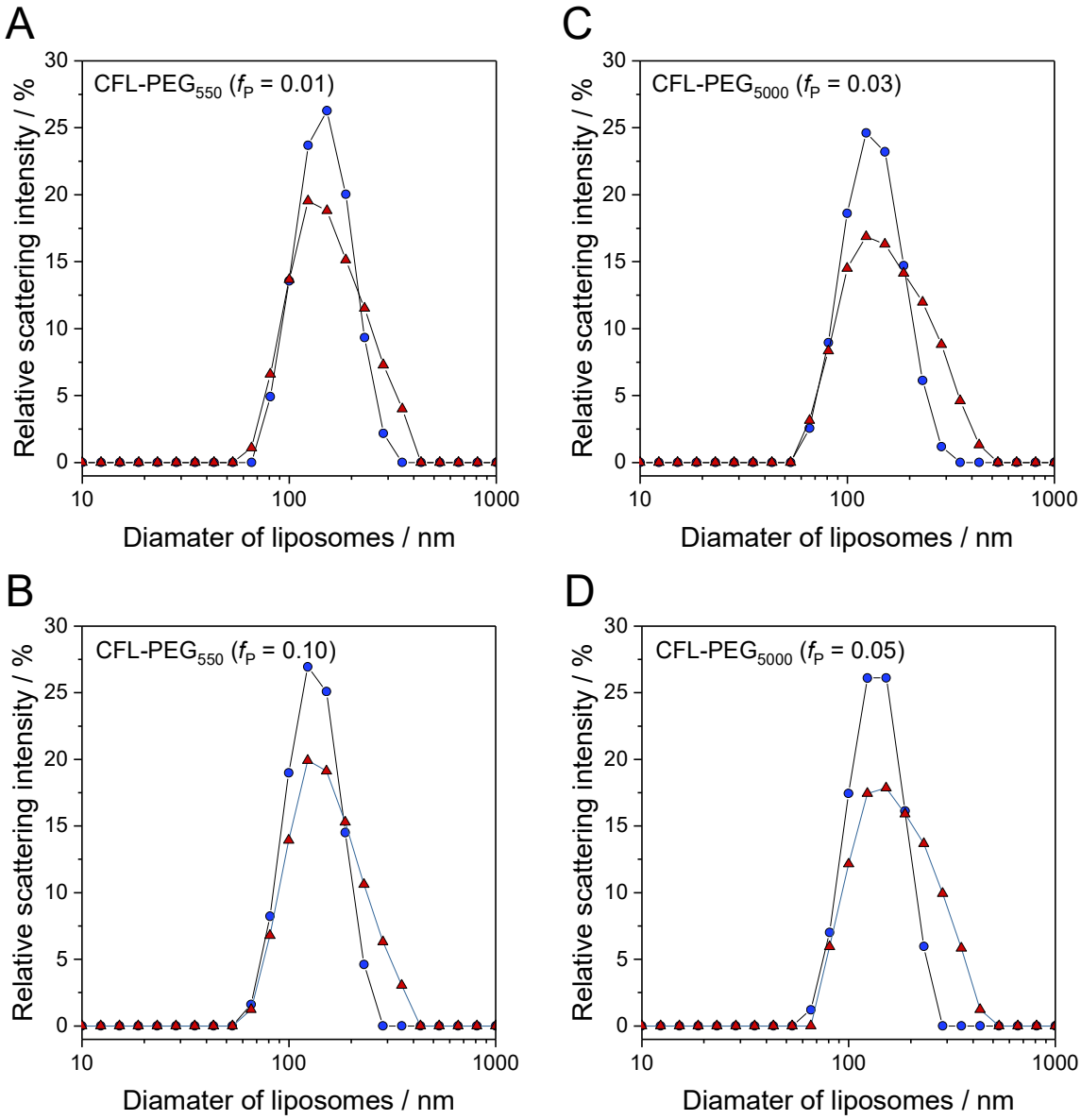

Fig. S6 Size distribution of CFL-PEG without (blue circles) and with (red triangles) being suspended at 40 °C in the airlift bubble column. The measurements were performed with the DLS method at 25 °C. The superficial gas velocity U_G of the airlift was U_G = 0.88 cm/s. For the operation time of the airlift suspending each CFL-PEG, see Fig. 4C and 4D in the main text.

7. Release kinetics of CF from liposomes in the viscometer

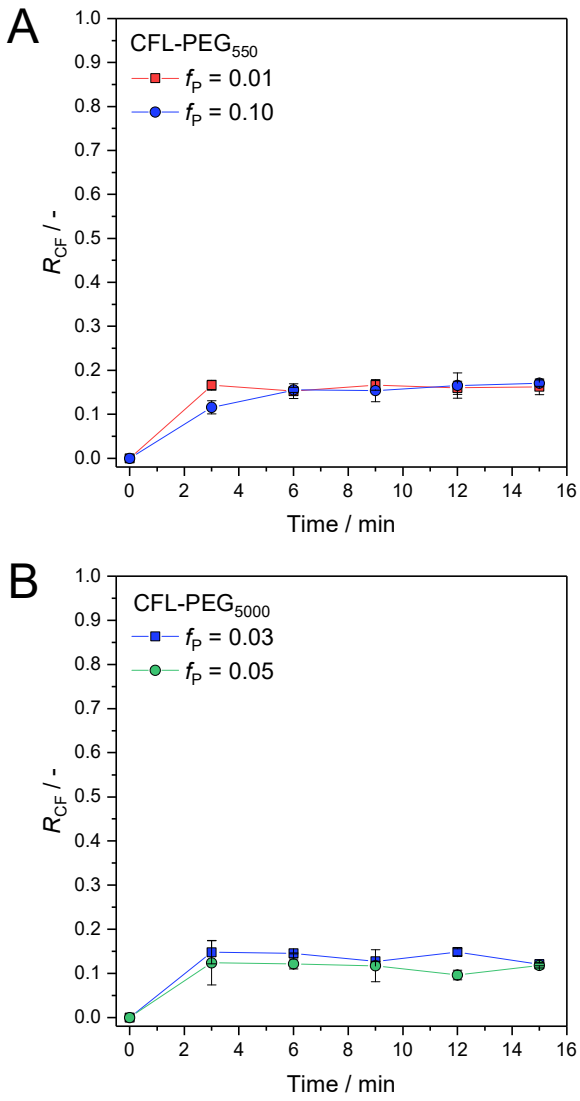

Fig. S7 Time courses of the R_{CF} value for (A) CFL-PEG$_{550}$ and (B) CFL-PEG$_{5000}$ being suspended at 40 °C in liquid shear flow in the cone-and-plate viscometer. Data represent mean value ± standard deviation (n = 2).