Stable Disk-fused Vesicle in DMPC/DHPC Lipid Mixture System

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長鎖/短鎖リン脂質混合系では、温度上昇によって平板ミセルが融合し、単層膜ベシクルが自発的に形成されることが最近の研究で明らかになってきた。この構造相転移は温度に対して可逆過程であるが、低脂質濃度領域では相転移温度以下でも単層膜ベシクルがそのまま維持される。本研究では、低温でも安定に存在する単層膜ベシクルの形成メカニズムを解明するために、中性子小角散乱による構造観測を行った。その結果、融合前の平板ミセルサイズと融合後のベシクルサイズの関係が、低温で単層膜ベシクルが維持されるために本質的な役割を果たしていることが明らかになった。

For phospholipid mixture system consisting of long- and short-chain lipids, it was reported that small uni-lamellar vesicles (ULVs) were spontaneously formed [1]. Recently, Nieh *et al.* have carried out small-angle neutron scattering (SANS) experiments on aqueous solutions of dimyristoyl-phosphatidylcholine (DMPC) and dihexanoylphosphatidylcholine (DHPC) mixture [2]. The experimental results showed that disk micelles at low temperature fuse into ULVs above the chain melting temperature, T_c, of DMPC molecules (about 24°C) in an adequate condition. Although disk-fused ULVs usually fissure into small disk micelles below T_c, it was shown that the ULVs were stable even below T_c at very low lipid concentration [3]. However, the mechanism of the stable ULV formation has not been clarified yet.

In this study, we investigated the structural change on a disk-fusion and vesicle-fission by SANS to understand the mechanism of the stable vesicle formation at low lipid concentration. The SANS experiment was performed with changing lipid concentration, c_L, the molar ratio of DMPC to DHPC, q', and temperature. The sample temperature was increased from 20°C to 50°C on a disk-fussion process, and decreased to 20°C again on a vesicle-fission process. Figure 1 shows the c_L-dependence of SANS profiles with changing temperature in case of $q' = 3.2$. From the SANS profiles, it was shown that the disk size increased with decreasing c_L at 20°C before heating, and the vesicle size increased with increasing c_L at 50°C. On the other hand, the SANS profiles at 20°C after heating were irreversible in case of low c_L, and large disk micelles were observed. Moreover, stable ULV were observed in case of $q' = 4.6$ as shown by Nieh *et al.*

For the quantitative discussion, the relation between the disk radius at 20°C and the vesicle radius at 50°C for were shown in Fig. 2. In the disk-fusion process, the relation between the

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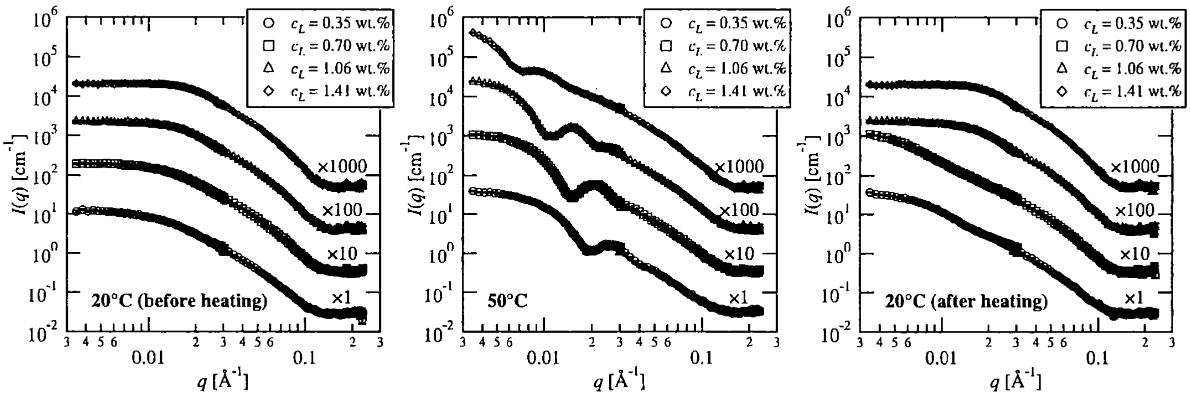

Figure 1: Dependence of SANS profiles on lipid concentration, c_L, with changing temperature, when the ratio of DMPC to DHPC, q', is 3.2.

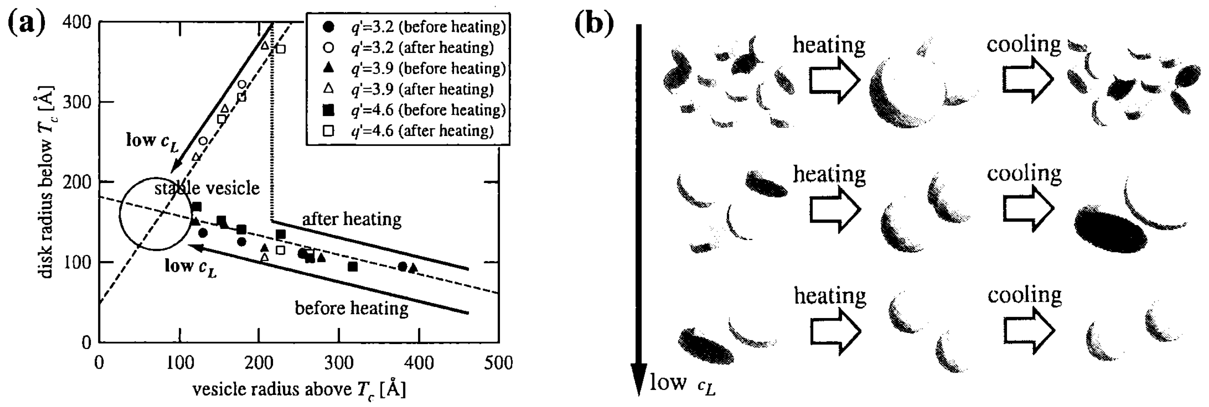

Figure 2: (a) The relation between the disk radius at 20°C and the vesicle radius at 50°C. (b) Schematic illustration of disk-fusion and vesicle-fission process suggested by the experimental results.

disk- and vesicle-size is roughly on a master curve for all c_L and q'. Whereas, the relation in the disk-fission process was different from that in the heating process: small disks and large disks were observed with decreasing c_L. Remarkably, the relation between large disk- and vesicle-size was on another master curve, and the stable ULVs were observed in the crossover region of the two master curves at low c_L. From these results, it can be said that the relation between disk- and vesicle-size is essential to understand the stability of disk-fused ULVs. The detailed discussion will be shown in the conference.

References

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