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Cryo-TEM Observation of the Effect of Grafted PEG on Fluctuating Membranes

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The formation of spontaneous surfactant bilayer vesicles is observed in a few chemical systems, most widely in mixtures of cationic and anionic surfactants. While PEG-lipids have been studied as stabilizers of rigid phospholipid vesicles (in applications including drug delivery), the effect of grafted polymers on the micro-mechanical properties of a *thermally fluctuating* vesicle membrane is not well understood either theoretically or experimentally [1-3].

The common starting point of describing membrane mechanics is the Helfrich curvature energy expansion, Eqn. 1. For spherical vesicles, this leads to the form of Eqn. 2. The thermodynamic relationship between curvature energy and the actual vesicle size distribution is predicted in Eqn 3 (details in ref [3]). Thus, by direct experimental observation of the spontaneous vesicle size distribution as a function of PEG-lipids, we can better understand the effect of grafted polymers on fluctuating membranes, assisting in the development of new nano-structured materials.

The best technique for determining surfactant vesicle size distributions is cryogenic transmission electron microscopy (Cryo-TEM). By directly visualizing thin films of vitrified vesicles in their native state, cryo-TEM averts the ambiguities of scattering methods or other indirect measurements. Furthmore, one may visualize vesicle shape transitions that are out of the realm of scattering. The core catanionic vesicle system of interest comprises mixtures of CTAT (Cetyl trimethylammonium tosylate) and SDBS (Sodium Dodecylbenzene sulfonate) in water. The microstructure and stability of this system is well-studied. Changes in vesicle size and shape upon incorporation of Brij700, a polyoxyethylene-stearate having a 4500 Mw PEG moiety ($C_{18}E_{100}$), were systematically observed as decreases in the mean vesicle size as well as polydispersity (Fig 1). In terms of membrane curvature energy theory, a 3 mole % grafting of 4500 Mw PEG yields a 3-fold increase in the bending rigidity, K, and a 40% increase in the spontaneous curvature, $1/R_O$ (Table 1). At higher PEG graftings, a nearly monodisperse population of vesicles is possible, as curvature deviations from the spontaneous radius, R_O, become energetically prohibited. However, at extremely high PEG-lipid grafting levels (above ~20 mole %), the surfactant membranes become micellized -as is also observed with phospholipid membranes. This represents a situation where we are able to *a priori* control the average size and polydispersity of spontaneous vesicle system simply by varying the amount of grafted polymers. Such a scheme is useful not only as a test for prevailing theories, but also as a practical tool for nano-structured materials synthesis.

References

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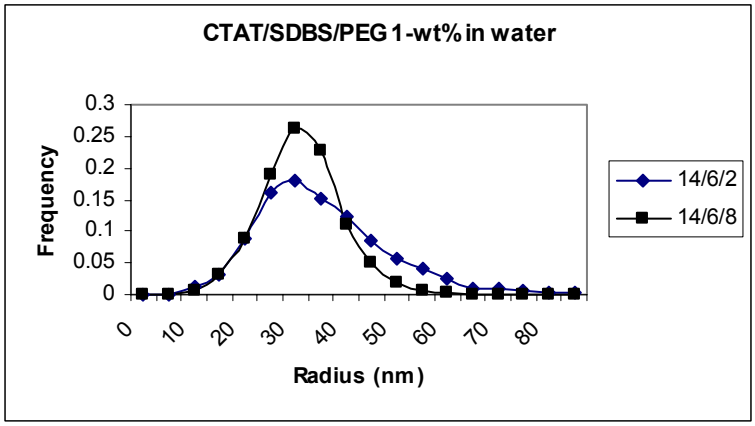

FIG 1. Size distributions from Cryo-TEM of CTAT/SDBS/PEG.

TABLE 1. CTAT/SDBS/PEG

CTAT/SDBS/Brij700 weight ratio (at 1 wt% in water)	K (k_BT)	R_O (nm)
14/6/0	0.15	55
14/6/2	0.38	44
14/6/8	0.50	40

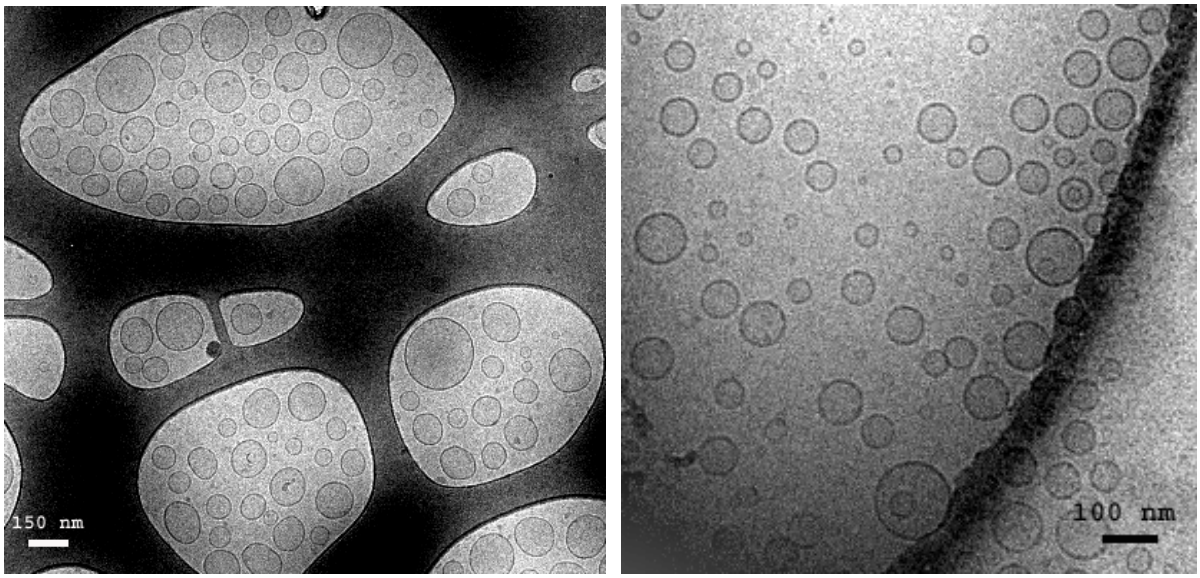

FIG 2. Cryo-TEM micrograph of A) CTAT/SDBS/PEG 14/6/2 and B) 14/6/8 vesicles @ 1-wt% in water. The dark areas are the lacey carbon support film.

(1) $f_c = \frac{1}{2}\kappa\left(\frac{1}{R_1}+\frac{1}{R_2}-\frac{2}{\overline{R_0}}\right)^2 + \overline{\kappa}\left(\frac{1}{R_1 R_2}\right)$ where R_1 and R_2 are the principle radii of curvature, $\overline{R_0}$ is the spontaneous curvature, κ is the curvature modulus, $\overline{\kappa}$ is the saddle-splay modulus

(2) $f = 2K\left(\frac{1}{R}-\frac{1}{R_0}\right)^2$ where $2K = 2\kappa + \overline{\kappa}$ and $R_0 = \frac{2\kappa+\overline{\kappa}}{2\kappa}\overline{R_0}$

(3) $C_N = \left\{C_M \exp\left[-\frac{8\pi K}{k_b T}\left(1-\frac{R_0}{R}\right)^2\right]\right\}^{\frac{R^2}{R_0^2}}$

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