Structural analysis of the polymer domains in the hybrid vesicles by contrast-matching neutron scattering measurements

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Molecularly permeable vesicles have attracted interest as compartments for nanoreactors or artificial cells, as they can allow the transport of molecules from the exterior to the interior of the vesicles [1]. One strategy to increase vesicle permeability is the incorporation of amphiphilic copolymers that contain thermoresponsive poly(propylene oxide) into phospholipid vesicles [2]. However, the nanostructures of these polymers, which are directly related to the molecular permeability, remain to be elucidated. The permeability of the hybrid vesicles can be expected to be influenced by the distribution of the polymer on the hybrid membranes, for example, by a homogeneous polymer distribution or the formation of polymer-rich domains, as well as the nanostructures of the polymer domains, such as bilayer formation or a state of simple insertion in the phospholipid membranes. Thus, gaining a deeper understanding of the structural characteristics of these hybrid membranes could potentially be useful for controlling their permeability and designing PPO-based polymers that act as synthetic channels.

Here, we studied the nanostructures of polymers incorporated in such membranes by using contrast-matching SANS measurements. We then subjected the polymer/DMPC-d_{54} hybrid vesicles in 86 vol% D_2O (i.e., the contrast matching point of DMPC-d_{54}) at 30 °C, which is above the phase transition temperature of DMPC, to SANS measurements (Fig. 1). The SANS profile of the hybrid vesicle solution does not show a distinct minimum like that seen in the SANS profile of the DMPC-d_{54} liposome solution, indicating that the scattering profile does not reflect the spherical vesicular structures. We then attempted to fit the SANS profile using a core–shell disk model to obtain information about the polymer-rich domains. The model fitted the SANS profile well over the entire q-range and was consistent with a disk radius of 38

nm, a hydrophobic layer thickness of 9.5 nm, and an overall thickness of 13.5 nm; these results clearly suggest that the polymer-rich phase forms disk-like bilayer structures. The thicknesses of the polymer-rich domains were found to be very similar to those of the bilayer membranes when the polymers alone are self-assembled into spherical vesicles. We have also demonstrated that the polymer-rich domains act as synthetic molecular channels for water-soluble PEG with an average molecular weight of 550, transporting the molecules into the inner phase of the hybrid vesicles. These findings provide valuable insights into the design of novel polymers for synthetic channels and the preparation of permeable vesicles.

[1] J.-F. Le Meins *et al.*, J. Colloid. Interface. Sci. **604**, 575 (2021).
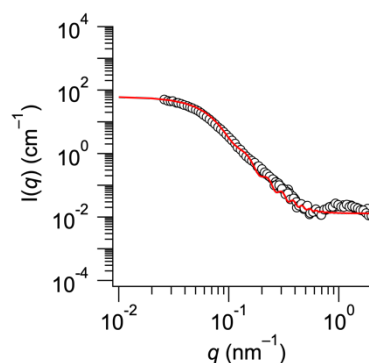[2] T. Nishimura *et al.*, J. Am. Chem. Soc. **142**, 154 (2020).

Fig. 1. SANS profile of the maltopentaose-*b*-PPO$_{2.5K}$/DMPC-d_{54} hybrid vesicles at 30 °C in 86 : 14 D_2O : H_2O (open circles) and theoretical curves obtained from the core–shell disk model (red line).