Structural Analysis of Artificial Macromolecular Membrane Proteins by Contrast-Matching Neutron Scattering

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Membrane proteins in living organisms exhibit a wide range of functions, including signal transduction, ion transport, and catalysis, all of which are essential for maintaining cellular homeostasis. Incorporating membrane proteins with specific functions into cells can thus enable precise regulation of cellular behavior. However, the direct integration of native membrane proteins into cellular membranes is often hindered by their intrinsic instability and synthetic complexity. To overcome these challenges, increasing attention has been directed toward engineering synthetic membrane proteins to endow cells with novel functionalities [1].

Previously, we demonstrated that amphiphilic polymers containing poly(propylene oxide) (PPO) as a hydrophobic segment can self-assemble into highly permeable polymer vesicles in aqueous environments. Moreover, when incorporated into phospholipid liposomes to form hybrid vesicles, these polymers act as artificial molecular channels. These findings suggest that PPO-based polymers functionalized with metal catalysts could serve as synthetic membrane proteins with both channel and catalytic capabilities.

To explore this possibility, we developed an amphiphilic random copolymer composed of oligo(ethylene glycol) (OEG) as the hydrophilic segment, PPO as the hydrophobic segment, and bipyridine units as metal-coordinating ligands. When added to model lipid membranes, such as phospholipid liposomes, the polymer was successfully incorporated into the bilayer. However, the in-membrane structural organization of the polymer—which is critical for its functionality—remains poorly understood.

In this study, we employed contrast-matching small-angle neutron scattering to elucidate the structure of the copolymer within the liposomal membrane. The polymer was incorporated into DMPC-d54 liposomes at 0.5 mol%, and measurements were performed under lipid contrast-matching conditions to selectively visualize the polymer domains. The results revealed that the copolymer assembles into short rod-like domains with an approximate diameter of 5 nm and length of 10 nm.

Moving forward, we will explore the tuning of domain size by varying the polymer composition, aiming to optimize both the catalytic and channel functions of these synthetic membrane proteins.

[1] Yugang et al., J. Am. Chem. Soc., **145**, 1262 (2023).

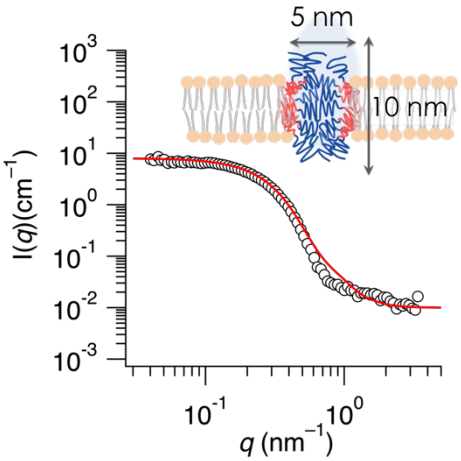

Fig. 1. SANS profile of the random polymer/DMPC-d_{54} hybrid vesicles at 37 °C in 84 : 16 D_2O : H_2O (open circles) and theoretical curves obtained from the core-shell cylinder model (red line). The 84 : 16 D_2O : H_2O ratio corresponds to the contrast-matching condition for DMPC- d_{54}.