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Lipid Corralling and Polymer Squeeze-out in Membranes[1]

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Victims of electrical trauma suffer extensive loss of structural integrity of cell membranes. Stable structural defects – "pores" in the range of 0.1 mm – have been demonstrated in electroporated cell membranes. Poloxamer 188, a triblock copolymer of the form poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) is known to help seal electroporated cell membranes, arresting the leakage of intracellular materials of the damaged cell. Using a monolayer to mimic the outer leaflet of the cell membrane, we have examined the interaction between the poloxamer and zwitterionic and anionic phospholipid monolayers. With synchrotron x-ray reflectivity and grazing-incidence x-ray diffraction, both the out-of-plane and in-plane structures of mixed phospholipid-poloxamer 188 monolayers were investigated at the air-water interface. P188 selectively inserts into low lipid-density regions of the membrane and "corrals" lipid molecules to pack tightly, leading to unexpected Bragg peaks at low nominal lipid density and inducing the film to separate into P188-rich and -poor phases. At tighter lipid packing, the once inserted P188 is squeezed out, providing a route for the poloxamer to gracefully exit when the membrane integrity is restored. Cryo-electron microscopy shows that the poloxamer can associate with the lipid in a reversible two-state fashion, depending on the physical state of the lipid. At temperatures above the main transition temperature (T_M) where the lipid is fluid, the poloxamer can incorporate itself into lipid vesicles, resulting in a more monodispersity vesicle population. At temperatures below T_M,the poloxamer cannot penetrate into the gel-like lipid layer, but instead corrals the lipid molecules to self-assemble into bilayer disks with the edges stabilized by the poloxamer.

[1]This work is mainly that of Guohui Wu (U of Chicago), and is done in collaboration with Canay Ege (U of Chicago), Jaroslaw Majewski (Los Alamos National Laboratory), Markus Weygand and Kristian Kjaer (Riso National Laboratory, Denmark)