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The Role of Protein Crowding in Shaping and Organizing Cellular Membranes

The health of cells, tissues, and organisms relies on communication of biochemical instructions across membrane interfaces. Perturbation of membrane structure and organization play a role in diverse diseases. Using quantitative molecular-scale measurements, research in our laboratory aims to understand the physical principles of cellular membrane organization and utilize these principles for the design of biomimetic materials. Curved membrane surfaces are an essential feature of dynamic cellular structures including endocytic pits, filopodia protrusions, viral buds, and most organelles. Specialized proteins capable of inducing membrane curvature are being identified, yet we lack an understanding of how these proteins function in the complex cellular environment. Based on studies of proteins involved in clathrin-mediated endocytosis, as well as engineered protein-lipid interactions, we propose that protein-protein crowding can strongly influence membrane shape and organization. Specifically, by correlating shape and structure with quantitative measurements of protein density on membrane surfaces, we demonstrate that lateral pressure generated by collisions between membrane-bound proteins can drive membrane curvature and influence the process of membrane phase separation. These findings demonstrate an efficient mechanism by which the crowded protein environment on the surface of cellular membranes can be manipulated to alter membrane organization and structure.