A Bottom-up Synthetic Biology Approach to Origin, Structure, and Dynamics of Biological Membranes

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Compartmentalization is a defining feature of all forms of life. Amphiphilic lipid molecules are the primary building blocks of cellular membrane compartments. Numerous processes like signaling, transport, and biosynthesis take place in cells through the interplay between structure and dynamics of cellular membranes. Here we take a bottom-up synthetic biology approach to developing a fundamental understanding of cellular processes involving lipid membranes. Various lipid architectures were used to build functional models of the membranous structures found in cells. We utilized giant vesicles to recapitulate the basic membrane-bound structure of cells. To model membrane-rich organelles such as the endoplasmic reticulum, we used bicontinuous sponge phase lipid droplets. To understand the origins of cellular compartmentalization, we explored various minimal chemoenzymatic pathways for *de novo* generation of lipid membranes. We further demonstrated a few primitive modes of growth and division of such membrane compartments to provide a hint at how earliest cells may have proliferated. Given their central role in cellular physiology, lipid membranes are also key to understanding the fundamentals of many infectious diseases. For example, pathogens like viruses hijack the dynamical processes of the cellular membrane systems to gain entry. We describe the application of surface-immobilized lipid vesicles to experimentally model the events concerning cellular attachment, endosomal membrane fusion, and genome transfer of enveloped viruses such as influenza.