Giant unilamellar vesicles as model systems to probe the interaction of cytochrome *c* with mitochondria-mimetic biomembranes

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Abstract

Lipid membranes mimic the structural matrix of natural cell membranes and have found extensive applications as a minimal model system to study fundamental structural and dynamic processes in biology. The interaction of extraneous matter with biomembranes can have significant impact on the structure and mechanics of the lipid bilayer, leading to process such as membrane budding, adhesion, fusion and permeabilization. Numerous experimental systems for lipid bilayer reconstruction have been reported; one of the closest mimics to natural cells are giant unilamellar vesicles (GUVs), with their similar microscale dimensions, spherical morphology and unsupported membrane. GUVs are large enough to be probed by optical imaging techniques, allowing experiments to be conducted at the single vesicle level. This has advantages over ensemble experiments by permitting sensitivity to the distribution of vesicle behaviours and transient intermediate states.

Here I will present experiments on GUVs containing the lipid cardiolipin (CL) at compositions similar to those found in mitochondria, the energy producing powerhouses of eukaryotic cells. We investigate the interaction of these membranes with the peripheral membrane protein cytochrome *c*, which is normally found localized in the intermembrane space of a mitochondrion. We find that cytochrome *c* can cause CL-containing membranes to become permeable to passive leakage markers in a process that we interpret as the formation of lipid pores. We also find that cytochrome *c* can induce fascinating morphology changes in CL-rich regions of membrane that leads to their eventual collapse into a crumpled state. I will discuss the physical mechanisms by which we believe these processes are driven and their possible implications in native mitochondria.