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In Situ Synthesis of Lipid Membranes

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Introduction: We have a strong interest in applying covalent coupling reactions to the formation and modification of lipid membranes. We have utilized chemoselective reactions, such as copper-catalyzed triazole formation or the native chemical ligation, to drive the *de novo* synthesis of phospholipid membranes. To interface synthetic membranes with proteins, we have shown that in situ lipid synthesis enables spontaneous incorporation of integral membrane protein. Living organisms carry out the *de novo* synthesis and subsequent remodeling of phospholipid membranes. The development of comparatively dynamic artificial lipid membranes will require simple methods to mimic how native phospholipid membranes are synthesized and remodeled. Using reversible coupling reactions, we have been able to sequentially form and remodel artificial lipid membranes. Interestingly, *in situ* remodeling of phospholipids is capable of controlling micrometer scale changes in vesicle spatial organization, composition and morphology. These studies could shed light and provide important models for the prebiotic emergence of phospholipid based membranes.

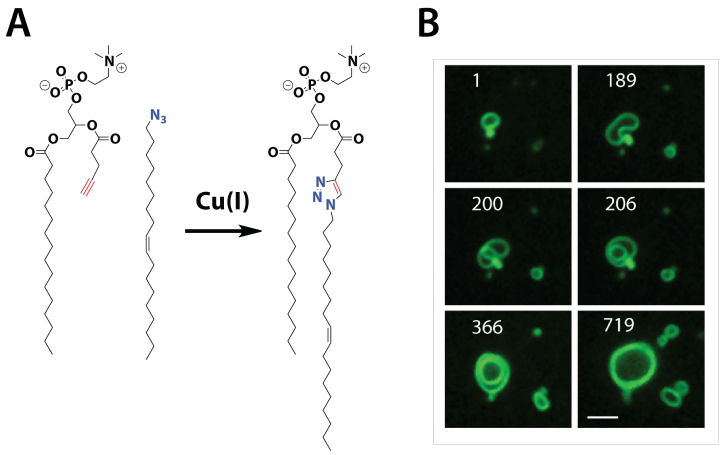

Figure 1 – A) Copper catalyzed azide-alkyne cycloaddition leads to the synthesis of a membrane forming phospholipid from non-membrane forming single-chain precursors. B) Continual phospholipid synthesis can be achieved by utilizing an oligotriazole autocatalyst. The constant production of phospholipids leads to vesicle growth. Numbers indicate elapsed time, in minutes, from start of imaging. Scale bar, 3 microns.