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Abstract

The overarching goal of the proposed research program is to design synthetic membrane systems to provide a platform for a self-reproducing artificial cell. Lipid membranes are required to organize cellular reactions and regulate the exchange of matter and energy with the environment. State-of-the-art approaches to mimic cell membranes in synthetic cells have relied on using static lipid structures that are at thermodynamic equilibrium, formed from hydrating dried lipid films or using microfluidic techniques. We currently do not understand the rules for reconstituting and maintaining lifelike lipid membranes that function far from equilibrium. We will leverage our lab's previous experience in designing biomimetic synthetic membranes, along with a range of interdisciplinary approaches, to engineer the following fundamental functions in artificial cells: 1) Growth – we will develop revolutionary methods for sustained lipid synthesis in artificial cells and determine how lipid curvature affects membrane morphology; 2) Division – we will determine how growth can be coupled to controlled fission by optimizing membrane lipid compositions and employing simple protein components that affect curvature; 3) Transport and Signaling – given that artificial cells will require mechanisms to import nutrients and respond to stimuli, we will design innovative strategies for transport and communication in artificial membranes; 4) Mesophase Transitions – the plasma membrane is well-modeled by planar membranes; however, some organelles can form dense 3-dimensional networks of lipids and proteins. We will examine whether non-lamellar lipid phases provide functional mimics of organelles that are capable of growth and division. Combining these approaches will result in an organizational framework for an artificial cell that is hierarchically organized and capable of self-reproduction. Understanding and utilizing reliable mechanisms to produce artificial cells with synthetic lipid membranes could lead to the development of biomimetic materials with greater complexity and function than those currently available. The proposed studies could enhance our understanding of how to interface synthetic and biological systems and redefine what constitutes living matter. Ultimately, a substantial impact will be the ability to engineer artificial cells, resulting in lifelike materials with the ability to grow, metabolize, and reproduce. Engineering dynamic artificial cell membranes could lead to modular and programmable biomaterials with revolutionary applications in synthetic biology and materials science research. Synthetic cells could have a substantial impact on biomanufacturing and sensing by moving past the limitations imposed by existing biochemical systems. Potential transformative applications of the proposed research that could impact Department of Defense capabilities include the detection and neutralization of chemical or biochemical warfare agents, environmental decontamination, wound repair, biomanufacturing, and the creation of more robust biological sensors.