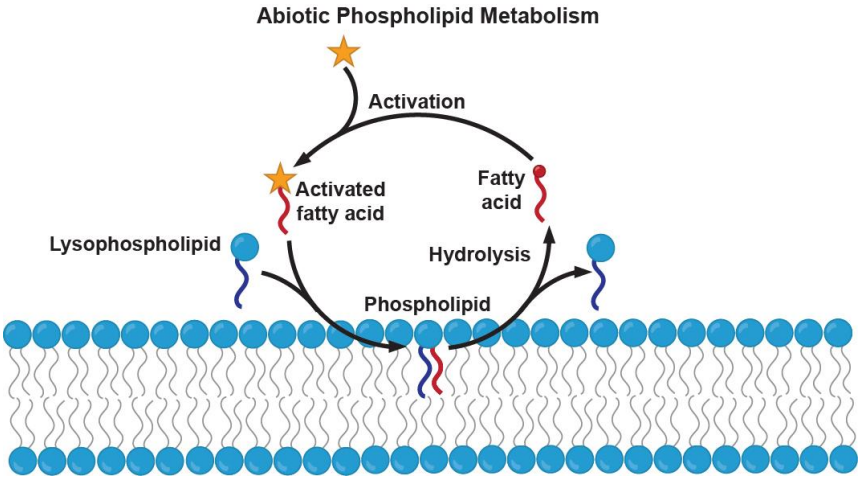
Artificial Lipid Metabolism as a Tool for Membrane Design



Lipid membranes are dynamic structures that undergo continuous synthesis, remodeling, fusion, and division, allowing cells to adapt to environmental changes and maintain complex internal organization. Central to this dynamic behavior is lipid metabolism, which regulates membrane composition and enables key cellular processes such as growth, transport, and signaling. Mimicking these dynamics is critical for constructing synthetic cells capable of growth, adaptation, and communication. We developed an artificial lipid metabolic network that drives the in situ synthesis of non-canonical phospholipids, enabling membranes to grow, and allowing selective lipid enrichment, reversible phase transitions, and lipid mixing across vesicle populations. We also demonstrate that minimal metabolic pathways can drive the de novo formation of lipid membranes from simple chemical precursors, providing a possible pathway to address the longstanding challenge of how the first membranes could have formed in the absence of pre-existing membrane templates. Using acetate and cysteine as building blocks, soluble enzymes catalyze the formation of fatty-acyl chains from acetate that spontaneously couple to cysteine backbones, yielding diacyl lipids that self-assemble into bilayer vesicles. Pore-forming peptides import fresh precursors, enabling sustained vesicle growth and proton-gradient maintenance. Together, these metabolism-driven approaches establish minimal routes for membrane generation and remodeling, providing a foundation for building synthetic cells with increasingly complex and functional behaviors.

Biographical overview

Dr. Alessandro Fracassi is a Postdoctoral Research Fellow working with Prof. Neal K. Devaraj in the Department of Chemistry and Biochemistry at the University of California San Diego (UCSD). He earned his B.S. and M.S. in Chemistry from the University of Rome Sapienza, where he focused on the preparation of glycosylated lipid vesicles under the mentorship of Dr. Giovanna Mancini. He completed his Ph.D. in chemistry at ETH Zurich in the lab of Prof. Yoko Yamakoshi, where he developed synthetic analogs of low-density lipoprotein (LDL) as MRI contrast agent carriers to diagnose early-stage atherosclerosis. At UCSD, his research focuses on engineering artificial lipid compartments that emulate the dynamic behavior of natural membranes, with the aim of uncovering general principles for building synthetic biological systems.