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A tale of two lipids: small chemical changes that shape cell membranes

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Dr. Itay Budin is an Assistant Professor in the Department of Chemistry & Biochemistry UC San Diego. His lab leverages biophysical, cell biology, and chemical biology approaches to investigate the interplay between lipid chemistry and cell membrane biology. Before arriving at UC San Diego, he completed PhD studies at Harvard University and postdoctoral research as a Miller Fellow at UC Berkeley. He is the recipient of the Walter Shaw Young Investigator Award in lipid biology from the American Society for Biochemistry and Molecular Biology, a Distinguished Investigator Award from the Paul Allen Foundation, and early career awards from the National Science Foundation and Department of Energy.

Abstract

Our lab investigates how – and why – cells control the composition of their lipid membranes. In this talk, I will focus on a pair of recent biophysical studies that shed light on this overall question. First, I will describe how sterols like cholesterol or ergosterol allow the formation of fluid membrane domains in cells. Through a systematic analysis of ergosterol synthesis, we tested a 50-year-old model for the evolution of sterol metabolism through a combination of in vivo, in vitro, and in silico approaches. Second, I will show how the shape of lipids – described by their spontaneous curvature – is a biophysical parameter that has driven adaptations in phospholipid chemistry. I will describe a wide-ranging investigation into the membranes of marine animals that led us to discover how high-pressure environments act on lipid curvature and, in turn, how cells can maintain this property. This study identified linkage chemistry as a key modulator of phospholipid shape, which carries implications for class of ether-linked lipids that have emerging functions in our own tissues.

Selected publications

Juarez-Contreras I, Lopes LJS, Holt J, Yu-Liao L, O'Shea K, Ruiz-Ruiz J, Sodt A, and Budin I. Structural dissection of ergosterol metabolism reveals a pathway optimized for membrane phase separation. *Science Advances* 11: eadu7190 (2025). https://pubmed.ncbi.nlm.nih.gov/40267201/

Winnikoff J, Milshteyn D, Vargas-Urbano SJ, Perdaza MA, Armando AM, Quehenberger O, Sodt A, Gillilan RE, Dennis EA, Lyman E, Haddock SHD and Budin I. Homeocurvature adaptation of phospholipids to pressure in deep-sea invertebrates. *Science* 384: 1482-1488 (2024). https://pubmed.ncbi.nlm.nih.gov/38935710/

Budin I, de Rond T, Chen Y, Chan LJG, Petzold CJ, Keasling JD. Viscous control of cellular respiration by membrane lipid composition. *Science* 362: 1186-1189 (2018). https://pubmed.ncbi.nlm.nih.gov/30361388/

Budin I, Szostak JW. Expanding roles for diverse physical phenomena during the origin of life. *Annu Rev Biophys* 39:245-263 (2010). https://pubmed.ncbi.nlm.nih.gov/20192779/