Dissertations

The Effect of Vesicle Shape, Line Tension, and Lateral Tension on Membrane-Binding Proteins

Jaime Bosart Hutchison, *University of Massachusetts - Amherst*

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First Advisor
Anthony D. Dinsmore

Second Advisor
Robert M. Weis

Third Advisor
Lori Goldner

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Abstract

Model membranes allow for the exploration of complex biological phenomena with simple, controllable components. In this thesis we employ model membranes to determine the effect of vesicle properties such as line tension, lateral tension, and shape on membrane-binding proteins. We find that line tension at the boundary between domains in a phase separated vesicle can accumulate model membrane-binding proteins (green fluorescent protein with a histidine tag), and that those proteins can, in turn, alter vesicle shape. These results suggest that domains in biological membranes may enhance the local concentration of membrane-bound proteins and thus alter protein function. We also explore how membrane mechanical and chemical properties alter the function of the N-BAR domain of amphiphysin, a membrane-binding protein implicated in endocytosis. We find that negatively charged lipids are necessary for N-BAR binding to membranes at detectable levels, and that, at least for some lipid species, binding may be cooperative. Measurements of N-BAR binding as a function of vesicle tension reveal that modest membrane tension of around 2 mN/m, corresponding to a strain of around 1%, strongly increases N-BAR binding. We attribute this increase in binding with tension to the insertion of N-BAR's N-terminal amphipathic helix into the membrane which increases the membrane area. We propose that N-BAR, which was previously described as being able to sense membrane curvature, may be sensing strain instead. Measurements of membrane deformation by N-BAR as a function of membrane tension reveal that tension can hinder membrane deformation. Thus, tension may favor N-BAR binding yet suppress membrane deformation/tubulation, which requires work against tension. These results suggest that membrane tension, a parameter that is often not controlled in model membranes but is tightly controlled in biological cells, may be important in regulating protein binding and assembly and, hence, protein function.