



BiophysTO Lunchtime Seminar Series

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Date

Thursday, April 15th,
2020
12:00 – 1:00 pm

The Role of Intrinsically Disordered Proteins in Sensing Membrane Curvature

We have recently discovered that intrinsically disordered proteins (IDPs) can also be potent sensors of membrane curvature. This ability of IDPs to sense curvature arises from two key physical features – a high degree of conformational entropy and a high net negative charge. Binding of such IDPs to membrane surfaces results simultaneously in a decrease in conformational entropy and an increase in electrostatic repulsion by anionic lipids. Here we show that each of these effects gives rise to a distinct mechanism of curvature sensing. Specifically, as the curvature of the membrane increases, the steric constraint that it imposes on the conformation of the IDP is reduced, leading to an entropic preference for curved membranes. At the same time, increasing membrane curvature increases the average separation between anionic amino acids and anionic lipids, leading to an electrostatic preference for curved membranes. To examine curvature sensitivity by IDPs, we engineered various truncation and chimeric mutants that were derived from the endocytic proteins AP180, Epsin1, and Amphiphysin1. Using Monte Carlo simulation and quantitative in vitro fluorescence techniques, our results demonstrate that long IDP chains with relatively low net charge sense membrane curvature predominately through the entropic mechanism, while shorter, more highly charged IDP chains rely largely on the electrostatic mechanism. We also demonstrate that IDPs can sense membrane curvature in live cells. Finally, we show that full-length endocytic proteins, which contain both structured curvature sensors and disordered regions, are more than twice as curvature sensitive as their respective structured domains alone. **Host: James Otis** **Zoom Link:**

<https://us02web.zoom.us/j/89407663380?pwd=OFBMczlhWVZKbUswQzk3VXNkLzhGdz09>



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