New methods to directly identify sub-micron domains in membranes


Fluorescence micrographs that capture the sizes, shapes, and distributions of liquid domains in model membranes have provided high standards of evidence to prove (and disprove) theories of how micron-scale domains form and grow. Some theories about smaller domains have remained untested, partly because experimental methods of identifying submicron domains in vitrified, hydrated vesicles have not been available. In this paper, we introduced two such methods; both leverage cryo-electron tomography to observe membrane features far smaller than the diffraction limit of light. The first method is probe-free and identifies differences in thicknesses between liquid domains and their surrounding membranes. The second method identifies membrane regions labeled by an electron-dense, fluorescent protein, which enables direct comparison of fluorescence micrographs with cryo-electron tomograms. Partly based on this paper, the first author, Caitlin Cornell, was awarded the 2020 Anna Louise Hoffman Award for Outstanding Achievement in Graduate Research.