Membrane traffic, an essential cellular process that plays a role in many human diseases, requires key biophysical steps including formation of membrane buds, loading of these buds with specific molecular cargo, separation from the parent membrane, and fusion with the target membrane. The prevailing view has been that structured protein motifs such as wedge-like amphipathic helices, crescent-shaped BAR domains, curved coats and constricting dynamin rings drive these processes. However, many proteins that contain these structural motifs also contain large intrinsically disordered protein (IDP) domains of 300-1500 amino acids, including many clathrin and COPII coat components. While these IDP domains have been regarded primarily as flexible biochemical scaffolds, we have recently discovered that IDPs are highly efficient physical drivers of membrane budding. Further, our work demonstrates that IDP domains serve as strong drivers of membrane fission. How can molecules without a defined structure drive membrane budding and fission? Our results support the idea that disordered domains generate entropic pressure at membrane surfaces, which is critical to overcoming key biophysical barriers to membrane traffic. IDPs are particularly efficient generators of entropic pressure owing to their very large hydrodynamic radii, potential for electrostatic repulsion owing to high net charge, and the substantial entropic cost of extending them. More broadly our findings suggest that any protein, regardless of structure, can contribute to membrane remodeling by increasing entropic pressure, and paradoxically, that proteins that lack a defined secondary structure, IDPs, may be among the most potent drivers of membrane traffic. Our ongoing work focuses on understanding how entropic pressure influences membrane traffic, and designing biophysical tools for manipulating receptor recycling and signaling.

For information regarding her research, visit https://www.bme.utexas.edu/about-us/faculty-directory/stachowiak

Refreshments will be available prior to seminar at 10:45 a.m. in the Shain Atrium

Graduate Students can meet with the speaker in Room 8305F at 1:00 pm