Denver

CHEMISTRY

Spring 2022
Seminar Series

11am-12pm
Feb. 11th
NC 1130

Crystal Vander Zanden, Ph.D.

Assistant Professor, Chemistry & Biochemistry
University of Colorado, Colorado Springs

"Assessing Membrane Protein Structure Using Liquid Surface X-Ray Scattering"

Technologies for membrane protein structure determination have lagged behind those available for aqueous proteins, and it is especially difficult to determine the interplay between protein interactions and membrane structure. Liquid surface X-ray reflectivity (XR) and grazing incidence diffraction (GID) are powerful tools for elucidating the structure and interactions of peripheral membrane proteins. Here, we applied XR and GID to study two biological systems: amyloidogenic proteins involved in Alzheimer's disease, and glycolipid-binding proteins involved in cell communication. Amyloid-beta (Aβ) is an amyloidogenic protein that is hypothesized to promote neuronal cell death through toxic interactions with the cell membrane. Using XR and GID, we characterized β-sheet rich fibrillar binding interactions with the membrane, finding that different Aβ oligomer forms caused differences in lipid organization. We also applied XR and GIXD to determine the structure of galectin-3 (Gal-3) interacting with the glycolipid ganglioside GM1. Gal-3 interacts with GM1 on the extracellular leaflet of the plasma membrane to regulate downstream cell-signaling cascades involved in neuronal growth and adhesion. We observed that the carbohydrate recognition domain interacts with the GM1 glycans, while the N-terminal domain is pointed away from the membrane, likely to facilitate protein-protein interactions. A molecular dynamics simulation was used to build an atomistic model of membrane-bound Gal-3, which, coupled with the experimental data, supports an atomistic model for Gal-3 bound to a membrane. In conclusion, XR and GID are powerful techniques to study interactions of peripheral membranes proteins and determine their impacts on lipid phase composition.

Graphical abstract: