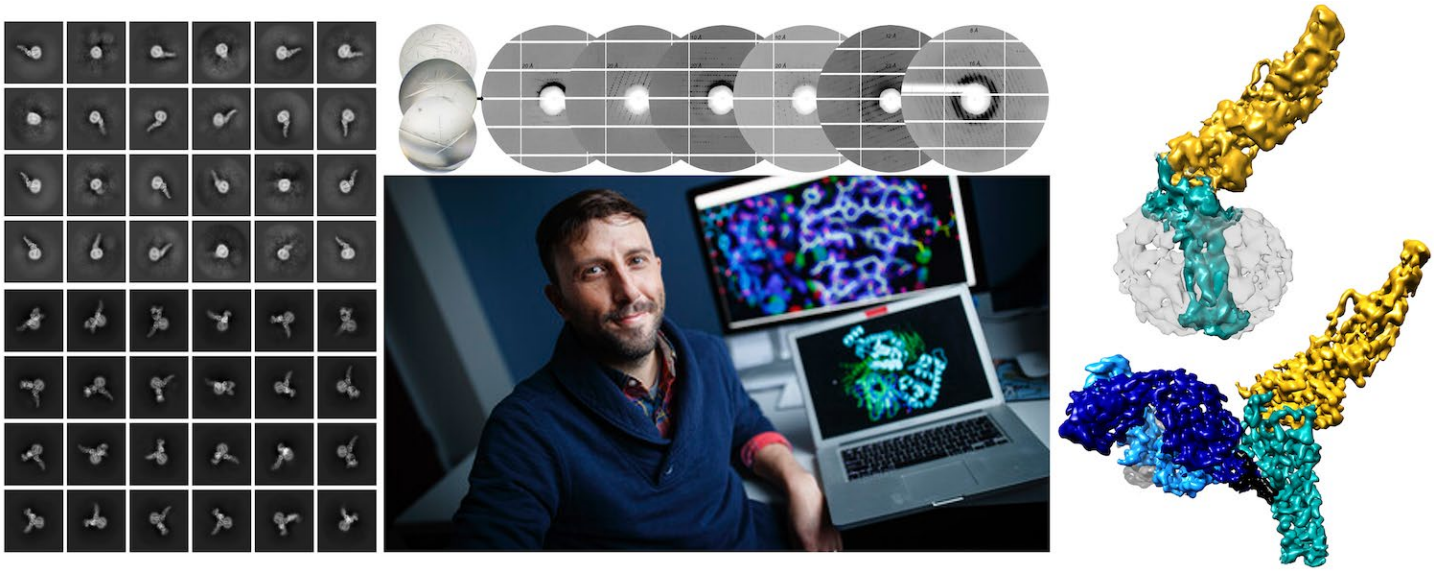
CryoEM Current Practices Webinar

Cryo-EM and fiducial marks as fail-safes for structural studies of very small membrane proteins



Alex J. Vecchio, Ph.D.

Assistant Professor

Department of Structural Biology
Jacobs School of Medicine & Biomedical Sciences, University of Buffalo

12PM EDT / 9AM PDT Thursday, December 12th, 2024

Proteins smaller than 100 or 50 kDa remain a challenge for structure determination by cryo-EM. This is markedly true for membrane proteins, which require detergents of equivalent mass to the protein to be bound during biochemical preparation. For very small membrane proteins (<50 kDa) with little to no extracellular or intracellular mass that do not oligomerize, detergents mask signal contributions by the protein and prevent protein/protein interactions required for crystallization—making them intractable for cryo-EM and X-ray crystallography. In this webinar, I will discuss a brief history of structural work on our biological targets as a backdrop to rationalize our need to develop a platform that enables higher throughput structures of <25 kDa membrane proteins. Using cryo-EM and synthetic antibody fragments (sFabs), which act as fiducial marks and stabilizers of these proteins, I will highlight one case where this strategy yielded high-resolution structures where X-ray crystallography and non-sFab-assisted cryo-EM both stalled. The platform's associated workflows can be input into both structural methods, establishing a fail-safe approach for structural studies of very small membrane proteins. Importantly, we will also reveal how sFabs can be much more than fiducials—capable of modulating protein structure, tissue function, or inhibiting cellular events.

All are welcome to attend. Registration is at no-cost, but sign-up is required:
https://us02web.zoom.us/webinar/register/WN_L6EJDD-GSX-B5KxzQROymA

This webinar series is jointly hosted by the NIH Transformative High Resolution CryoEM Program Service Centers: the National Center for CryoEM Access and Training (NCCAT), the Pacific Northwest Center for CryoEM (PNCC), and the Stanford-SLAC CryoEM Center (S2C2) who provide no-cost access to cryoEM instrumentation and training. In this monthly series, we will highlight cryoEM methods and use the Q&A session after the seminar to stimulate discussion of best practices and interesting challenges that will be helpful to researchers new to the field. Representatives from all three service centers will also be on hand to answer questions about the cryoEM resources available to biomedical researchers and how to access them.