![PULSE - Postdoc Upskilling in Laboratory & Specialized Expertise. A Professional Development Initiative for Postdoctoral Scholars at UNC Core Facilities]

Title of Proposed Project

Advancing MicroED through CryoEM Method Development

Name of Core Facility

Chemistry X-ray Crystallography Core Laboratory (XCL)

Core Director Name *Official contact for the program*

Chun Hsing (Josh) Chen

Project Description

This project focuses on developing and optimizing Microcrystal Electron Diffraction (MicroED) carried out as a joint collaboration between the XCL and the CryoEM Core. By refining sample preparation, data collection protocols, and processing workflows, the goal is to expand MicroED's applicability to challenging microcrystalline materials by 1) using test sample benchmark microED package to determine an atomic structure of small molecules (e.g. acetaminophen/ibuprofen/biotin), 2) writing SOP's for sample preparation, data collection, and data processing, 3) making a flyer highlighting microED capabilities of the XCL core to attract customers, and 4) giving a 40 min PowerPoint presentation over zoom to spread awareness of the microED capabilities of the university.

The work aims to establish robust, reproducible pipelines that improve resolution, throughput, and overall structure-determination success.

Expected Skill Development

What skills, tools, or technologies will the postdoc gain experience with? Include technical, analytical, or professional competencies.
This project will develop advanced skills in MicroED including micro-/ nanocrystal preparation, cryogenic grid handling, and low-dose electron diffraction data collection. The postdoc will gain experience in data processing, structure determination, and method optimization, while learning to operate Thermo Fisher Talos Arctica Cryo-TEM instrument in collaboration with the CryoEM Core. Additional skills include cross-facility workflow coordination, troubleshooting, and communicating methodologies to diverse scientific audiences.

Scheduling Considerations

The postdoc will dedicate approximately one day per week collecting data at the CryoEM Core, focusing on high-impact research samples, with additional time to process data and document results. The project will begin in February 2026 and is anticipated to be concluded by May 2026.

Estimated Time Commitment

8 hours/week

Expected Project Duration

12 weeks

Designated Mentor(s)

Chun Hsing Chen, Director of XCL, will mentor the postdoc in crystal selection, data-quality evaluation, and structure solution and refinement. Joshua Strauss, Director of the CryoEM Core, will oversee training in cryo-EM sample preparation, instrument operation, and data-collection software.

How often will the mentor meet with the participating postdoctoral scholar?

Bi-weekly

Required Background or Skills

The postdoc should have intermediate or advanced knowledge of crystallography, including diffraction theory, unit cells, and basic structure solution and refinement. Basic experience operating cryo-TEM instrumentation is required, and prior exposure to MicroED is highly desirable. Strong attention to detail, experience with handling small crystals, and familiarity with cryogenic techniques are also beneficial.

Onboarding Plan

The postdoc will begin by familiarizing themselves with all required University safety protocols, including laboratory safety training, chemical handling, and cryogenic safety procedures. In parallel, they will review the foundational crystallography concepts needed for MicroED, including diffraction theory, reciprocal space, and basic structure refinement principles. The postdoc will also receive guided training in handling micro- and nanoscale crystals, including crystal harvesting, dispersion, and grid preparation, as well as safe and confident operation of cryogenic equipment.

While many of these skills traditionally require years of experience, the UNC core-specific operational requirements, such as facility access procedures, equipment checklists, grid-

handling protocols, and data-logging standards, are expected to be acquired within approximately one week.

Additional onboarding will include introductions to XCL and CryoEM Core workflows, instrument scheduling systems, and coordinated expectations between the two mentoring facilities. A biweekly collaborative meeting will take place every other Monday afternoon to review progress and align next steps.

Training Plan

The postdoc will receive hands-on training in MicroED method development using the ThermoFisher Talos Arctica at the UNC CryoEM Core. Training will cover cryogenic sample handling and grid preparation, low-dose diffraction data collection using EPU-D, and electron diffraction data reduction and processing with DIALS and PETS. Structure solution and refinement will be performed using Oxford CRYSTALS. Through this training, the postdoc will develop the skills to independently operate the Talos Arctica for MicroED experiments, optimize data quality, and establish reproducible workflows in collaboration with the XCL and CryoEM Core.

Potential Deliverables/Outcomes

Method development
Training or outreach materials
Quality improvement documentation
Skill Development