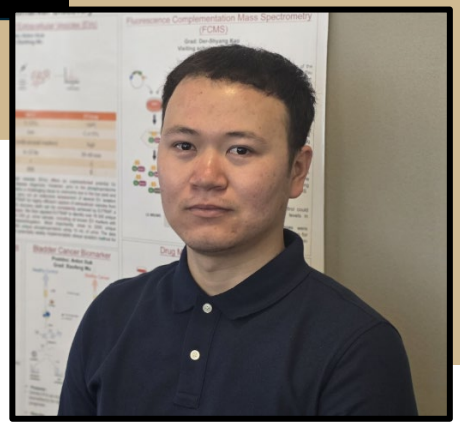
ANALYTICAL SEMINAR



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"When Crystals Are Too Small: MicroED for Pharmaceutical Structure Determination"

Determining atomic-level structures of small molecules remains a central challenge when crystals are too small for conventional single-crystal X-ray diffraction. Many pharmaceutical compounds and polymorphs form only micro- or nanocrystalline powders, limiting the applicability of traditional crystallographic methods. Microcrystal electron diffraction (MicroED), a cryo-electron microscopy–based technique, overcomes this limitation by enabling high-resolution structure determination from nanometer-scale crystals.

MicroED employs a transmission electron microscope operated in diffraction mode, where continuously rotating nanocrystals are exposed to a low-dose electron beam to collect three-dimensional diffraction data. Owing to the strong interaction between electrons and matter, complete datasets can be obtained from crystals hundreds of nanometers in size, often within hours and without crystal growth optimization. This seminar will describe the MicroED workflow, including sample preparation, crystal identification, continuous-rotation data collection, and structure solution. Applications to pharmaceutical solids will be highlighted, along with practical advantages and current limitations such as beam damage, crystal thickness requirements, and dynamical scattering effects. Together, MicroED represents a powerful addition to the structural characterization toolbox for small molecules when conventional approaches fail.

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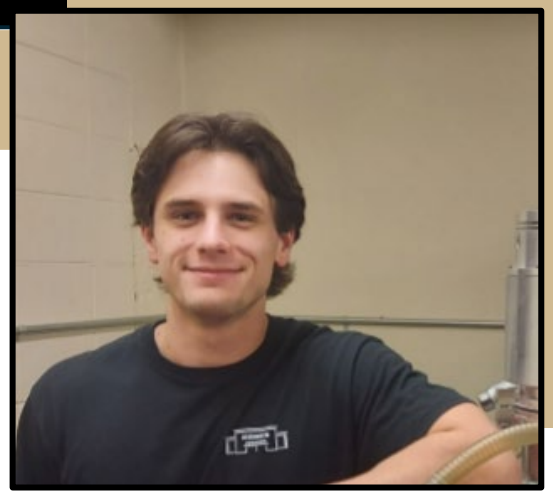

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"Atomic Force Microscopy in Combination with Infrared Spectroscopy (AFM-IR) Investigations in Protein Aggregation"

Protein aggregation plays a central role in many neurodegenerative diseases, but its structural characterization remains analytically challenging due to nanoscale heterogeneity and the coexistence of multiple aggregation states. Spectroscopic techniques such as Fourier transform infrared (FTIR) spectroscopy provide valuable information on protein secondary structure but lack the spatial resolution required to resolve individual aggregates, while atomic force microscopy (AFM) offers high-resolution morphology without chemical specificity. Atomic force microscopy–infrared spectroscopy (AFM-IR) is an analytical technique that bridges these limitations by enabling nanoscale, chemically specific measurements of protein aggregates. AFM-IR combines the spatial resolution of AFM with localized infrared absorption spectroscopy, allowing correlation of morphology and secondary structure at the level of single oligomers and fibrils.