

## A Complete Micro-Electron Diffraction (MicroED) Solution for Fast Structure Determination for Macromolecules and Small Molecules

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X-ray diffraction on synchrotrons is a traditional method for determining atomic structure; however, these experiments require large, well-ordered protein crystals (50-100  $\mu\text{m}$ ). Growing large protein crystals is a critical bottleneck that is either time-consuming or challenging to overcome, and often smaller crystals are more attainable. Although, special beamlines can analyze crystals as small as 10-50  $\mu\text{m}$ , they are prone to radiation damage destroying the crystal before a diffraction pattern can be obtained. Electrons are more advantageous than X-rays for the analysis of very small crystals (well below 1  $\mu\text{m}$  in size) because their interaction with matter is stronger, resulting in a stronger signal. Micro electron diffraction (MicroED) is thus well suited for the analysis of small nanocrystals, producing high-resolution 3D structures of small chemical compounds or biological macromolecules. MicroED can be used in a variety of fields, including structural biology, medicinal chemistry, and other organic and inorganic chemistry disciplines like catalyst research.

MicroED experiments do not require a specialized synchrotron facility; instead, cryo-EM equipment that fits in a standard laboratory can be used. MicroED experiments are carried out in a vacuum, which reduces background scatter. The use of cryogenic temperatures protects the sensitive crystal sample from radiation damage, which would otherwise result in rapid degradation. Because only nanometer-sized crystals must be grown, this method significantly shortens the sample preparation process. Furthermore, intermediate-sized crystals that are too large for MicroED but too small for X-ray crystallography can be solved by physically breaking up the crystals or thinned with a cryo-focused ion beam (cryo-FIB).

In this session, we will talk about our complete workflow, innovations and improved workflow for MicroED preparation and analysis. You will learn how MicroED allows for the rapid determination of the 3D structure of small chemical compounds and biological macromolecules. How our cryo-TEM is outfitted with a specially designed diffraction package to efficiently collect diffraction datasets of nanocrystals. Also, we will highlight all of the required hardware components, as well as optimized optical settings and specialized software for automated data collection. Together, showing how our data collection is fully automated and can be completed in a matter of minutes that allows for high-resolution structure determination.