

Future possibilities for MicroED in studying IDRs

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Growing large and well-ordered crystals is often prohibited for structural disordered and flexible proteins. Conversely, molecules with a dynamic nature preferably form tiny crystals which are suitable for analysis by the cryo-electron microscopy (cryoEM) method microcrystal electron diffraction (MicroED).

MicroED has been successfully used to determine atomic resolution structures from crystals that are vanishingly small. In MicroED electron diffraction patterns are collected from continuously rotated three dimensional micro- and nanocrystals using a transmission electron microscope. The samples are prepared on cryoEM grids which are vitrified by plunging into liquid ethane before data collection.

By circumventing the crystal size limitations, MicroED has the potential to enable structural studies of new targets such as intrinsically disordered proteins (IDPs) and in particular proteins containing intrinsically disordered regions (IDRs), and their flexible binding partners.

Since its initial demonstration in 2013, MicroED has proved to overcome the crystal size limitations and structures have been determined for a variety of proteins, peptides and small molecules. Future directions involve investigations on dynamic systems, including the determination of active state structures and flexible ligands.