

**MS25-1-1 Structure determination of a protein-peptide complex using microcrystal electron diffraction**  
**#MS25-1-1**

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**Abstract**

Developments in microcrystal electron diffraction (MicroED) allow the determination of protein structures from crystals that are too small to be analyzed by conventional X-ray crystallography [1]–[3]. Although the method has been used to determine novel protein structures, it is limited to micro/submicron ultra-thin protein crystals [4], [5]. Due to the limited rotation range of the sample stage in a MicroED setup, completeness of the collected data is restricted by crystal shape, symmetry and orientation on the grid [4], [6]. Here we applied MicroED to determine the structure of a novel complex between an enzyme regulatory domain and an intrinsically disordered peptide. Needle-like crystals in the space group  $P2_12_12_1$  were grown using the hanging drop vapour diffusion method. Diffraction data were collected on a 200 kV Thermo Scientific Glacios Cryo-TEM equipped with a CetaD detector. Data were collected along multiple sections of several crystal needles within the limiting rotation range of the sample stage. The performed collection strategy allowed data processing from only two crystals that were oriented perpendicular to each other on the grid, resulting in a 3.2 Å resolution dataset with a merged completeness of 89.3%. Our work represents an effective workflow for obtaining a complete electron diffraction dataset from needle-like protein crystals.

**References**

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