

A simple pressure-assisted method for MicroED specimen preparation

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Micro-crystal electron diffraction (MicroED) has shown great potential for structure determination of macromolecules from nano- and micron-sized crystals which are too small for X-ray diffraction. However, specimen preparation remains a major bottleneck. Here, we report a simple method for preparing MicroED specimens, named Preassis, in which excess liquid is removed through an EM grid with the assistance of pressure. The ice thicknesses can be controlled by tuning the pressure in combination with EM grids with appropriate carbon hole sizes. Importantly, Preassis can handle a wide range of protein crystals grown in various buffer conditions including those with high viscosity, as well as samples with low crystal concentrations. Preassis is simple and easy to implement, making it widely accessible to cryoEM labs at very low cost.