

MS04-03 | A NEW AND SIMPLE METHOD FOR CRYO-EM SPECIMEN PREPARATION

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Cryo-electron microscopy (cryo-EM), including single-particle cryo-EM and micro-crystal electron diffraction (MicroED), has made great impacts on structural biology. Specimen preparation remains as one of the major bottlenecks. The pipetting-blotting-plunging routine has been the most widely used method for preparing cryo-EM specimen. The main drawback of the method is that 99.9% of the particles ends up on the blotting paper^{1,2}. On the other hand, the method is not optimized for preparing specimen of micro-crystals used in MicroED, an emerging method for structure determination of small- and macro-molecules. Here, we present a novel method for preparing cryo-EM specimen (in manuscript). The new method can be implemented in two simple setups, one for single particles and the other for micro-crystals. Using the method, protein consumption can be reduced by at least one order of magnitude compared to the blotting method, offering biologists new opportunities to work with samples of low concentration. Furthermore, the method is able to handle protein crystals grown in viscous mother liquid, allowing MicroED to be applied to a large variety of micro-crystals³.

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[3] Xu, H. *et al.* Solving the first novel protein structure by 3D micro-crystal electron diffraction. *bioRxiv* (2019)
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