In situ Structures of Macromolecular Assemblies by CryoFIB and CryoET

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Recent development in cryo-electron microscopy (cryoEM) has revolutionized the field of structural biology, allowing protein structures to be determined at the atomic resolution in a close-to-native, frozen-hydrated state, especially using cryoEM SPA method. For studying macromolecular complexes that are intrinsically flexible and dynamic, and often function in higher-order assemblies that are difficult to purify, cryoET and subtomogram averaging (cryoET STA) has emerged as a potent tool to obtain structures of these at near-atomic resolution. The study of such complexes and assemblies in situ using cryoET STA, coupled with cryoFIB/SEM and correlative imaging, opens a new frontier in structural cell biology. I will present our recent studies on the infection of SARS-CoV-2, architecture of native chromatin fibers in intact cells and particulate methane monooxygenase (pMMO) in methanotrophic bacteria, to demonstrate the power of high-resolution in situ structural biology using cell lamellae-based cryoET STA.