

# **Cryo-electron tomography and subtomogram averaging for high-resolution structure determination of macromolecules**

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Cryo-electron tomography and subtomogram averaging are rising and fast-evolving imaging techniques to study biological events, providing structural information at an unprecedented resolution while preserving spatial correlation in their native contexts. The latest technology and methodology development ranging from sample preparation to data collection and data processing, has enabled significant advancement in its applications to various biological systems. I will present an overview of the current technology development enabling high-resolution structural study *in situ*, highlighting the use of *a priori* information of biological samples to assess the quality of subtomogram averaging pipeline. I will exemplify the applications of this technique to understanding viruses and principles of macromolecule assembly using different biological systems, ranging from *in vitro* to *in situ* samples, which provide structural information at different resolutions and contexts. Finally, the challenges of cellular cryo-electron tomography will be discussed.