Technology Development for *In Situ* Structural Study of Macromolecular Machinery

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With the mature and rapid development of single particle electron cryo-microscopy, structural biology has gone into a new era with more and more supra macromolecular complexes and membrane protein complexes whose structures are well resolved and studied. A new direction has emerged to study the structures of these complexes *in situ* without purifying them from their native environment. The development of cryo-electron tomography has provided such opportunity for high resolution *in situ* structural study. However, there are still various bottlenecks including specimen preparation, data collection and image processing that need to be solved to improve the throughput, efficiency, and resolution. Here I will talk about our past effects in this direction, which include the development of site-specific cryo-focused ion beam (cryo-FIB) technique, the workflow to prepare cryo-lamella of tissue specimen and reconstruction algorithms to deal with missing-wedge problem.

References:

1. ***J Struct Biol.*** 194(2): 218-223, (2016)
2. ***J Struct Biol.*** 195(1): 100-112, (2016)
3. ***J Struct Biol.*** 195(1): 49-61, (2016)
4. ***Biophys Rep.*** 3(1):36-42, (2017)
5. ***J Struct Biol.*** 201(1): 63-75, (2018)
6. ***J Struct Biol.*** 213(3): 107763, (2021)
7. ***Nature Methods*** 20(2): 276-83, (2023)
8. ***Communications Biology*** (in press), 2023