中央大學物理學系

Department of Physics, National Central University

Colloquium

Recent progress and future perspective of electron cryomicroscopy for structural life sciences

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Abstract :
CryoEM image analysis has become a powerful tool for life/medical sciences and drug design. Single particle image analysis can easily determine a macromolecular structure beyond 2 Å resolution from a few ml drop of sample solution within a few days. With a transmission electron cryomicroscope (cryoTEM) we have been developing with JEOL over the last decade (CRYO ARM), we solved the structure of apoferritin at 1.53 Å from about 900 images collected in one day in early 2019 using a GATAN K2 camera. With a new TEM control software that we developed for multi-hole imaging and a GATAN K3 camera, nearly 30,000 images can be collected. We determined the structure of apoferritin at 1.29 Å from about 7,500 images collected over 15 hours in late 2020, but this data collection could be completed in a few hours now. We also developed an epoxidized graphene grid (EG-grid) to solve difficult problems in cryo-grid preparation, such as denaturation and preferred orientation that occur at the air-water interface. We were able to solve the structure of GroEL at 1.99 Å from only about 500 images collected within 1 hour. Successful use of the EG-grid with advanced cryoTEM allows high-throughput data collection without sacrificing high resolution. Recent development of high-resolution cellular tomography workflow with a combination of cryoFIB-SEM and cryoTEM and in-situ structural analysis of macromolecular complexes by subtomogram averaging is also becoming a powerful tool that allows visualization of intracellular localization and interaction networks of macromolecules for us to deeply investigate cellular physiology in many biologically important contexts. I will discuss future potential of cryoEM technology for life sciences as well as drug discovery.