“Advances and Developments in Cryo-Electron Tomography for In Situ Structural Biology”

Juergen PLITZKO

Cryo-electron microscopy (cryo-EM) has become the most versatile method in structural biology due to recent advances in instrumentation, automation and image processing. It is used to determine the structure of isolated and purified macromolecular structures, i.e. ex situ. But biological functions are rarely performed by individual molecules. They are based on the interactions of the many molecular species occurring in the cells. Cryo-electron tomography (cryo-ET) is the method of choice to investigate these in situ, i.e. in an undisturbed cellular context. In tomography, however, several different high-end devices are involved and many different tasks are chained to a complex, but not yet fully integrated and optimized workflow. The fragile and sensitive sample must be prepared, the information from different steps passed on and above all the sample (safely and reliably) from one system to another. In order to exploit the full potential of such a workflow and routinely apply it to many different sample materials (e.g. from the cell to the tissue), there is an urgent need for further technology and method development across the entire workflow range.

This lecture presents our current work in the area of cryo-ET and in situ structural biology and shows technological developments, limits and their possibilities. In addition, a perspective is given on how "anatomical" details can be obtained on a molecular level from larger cells or tissues with the aid of cryo-electron tomography.