

Title:

The long and winding road to in situ structural biology with cryo-ET

Abstract:

In situ structural biology, as we know it today, is the study of molecular machines at their original setting, i.e., inside the cell in which they reside. Cryo-electron tomography has provided the first insights into molecular details of various cell types. However, the route has been long and winding with many technical and methodological advances that have made this possible. Yet, along with the progress, challenges remain, and a key step still is sample preparation, especially for larger cells and tissues.

This lecture will take us to the beginnings of tomography, from the early days of contemplation to today's technical achievements and the latest methodology that is still evolving. Historical and theoretical aspects are not unimportant, but the view from the practitioner's perspective is maybe the most appealing and avoids glossiness in the structures and slides presented. It is worth noting that with some cutting-edge technologies, less than a handful of scientists have even been able to perform in situ cryo-ET at all. However, with the advent of new, streamlined, and simplified instruments and practices in recent years, that handful has grown to several dozen, and their numbers continue to grow.

We will showcase our latest workflow for in situ structural biology, from correlated light microscopy, integrated approaches, to lamellar milling of cells (on-the-grid) and of course tissues or whole organisms (lift-out) - and give you an up-close look at large-scale production of lamellae and tomograms. With regard to the latter, a perspective on revisiting visual proteomics will be given in light of having "1001+" tomograms readily at hand.