Prof. Jürgen M. Plitzko
Dept Struct Biol, Max Planck Institute of Biochemistry, Martinsried, Germany

3 dimensional cryo-electron microscopy (3DEM): Voyages to uncharted molecular territories

Cryo-electron tomography (cryo-ET) of whole cells allows us to investigate the structure-function relationship of molecular complexes and supramolecular assemblies in their native environment. It thus makes a fundamental change in the way we approach biochemical processes that underlie and orchestrate higher cellular functions. In the past, molecular interactions were studied mostly in a collective manner, whereas now we have the tools to visualize the interactions between individual molecules in their unperturbed functional environments. Although they share common underlying principles, no two cells or organelles are identical, owing to the inherent stochasticity of biochemical processes in cells as well as their functional diversity. Therefore, it will be a major challenge to extract generic features from the three dimensional maps, such as the modes of interaction between molecular species. However, the ultimate goal, the discovery of general rules that underlie cellular processes, has to go beyond observing qualitative features and has to be based on stringent analytical criteria combining the information gathered from different methods for a complete integrative analysis.
Merging the power of identification (e.g. by quantitative mass spectrometry or correlative light microscopy) with advanced preparation techniques (e.g. focused ion beam milling) while utilizing the power of visualization techniques (by cryo-ET/EM approaches) is definitely a 'nouvelle route' with a great potential in the field of molecular structural biology that promises to provide a non-invasive and deep insight into the functional organization of cellular proteomes).