Exploring Molecular Landscapes Inside Cells with *In-Situ* Cryo-ET

Dr. Benjamin David ENGEL
Helmholtz Center Munich, Germany

Cells accomplish the biochemical reactions of life by concentrating their proteins into a variety of subcellular compartments called organelles. Our group explores the relationship between the *form* of the organelle and the *function* of its resident macromolecules. How does organelle architecture direct molecular function, and reciprocally, how do macromolecules sculpt and shape organelles? To investigate these questions, we use focused ion beam (FIB) milling of frozen cells followed by cryo-electron tomography to image macromolecules within their native cellular environment. Through a combination of nanometer-precision localization and high-resolution structural analysis, we aim to chart the molecular landscapes of organelles. Thanks to its superb cryo-EM contrast and textbook organelle architecture, the unicellular green alga *Chlamydomonas* is an ideal specimen for this approach. We have taken a holistic approach to survey the whole integrated "planimal", with *in situ* molecular studies of the nuclear envelope, ER, Golgi, centrioles, and chloroplast. In this talk, I will provide an overview of some of these studies, touching on proteasome-rich degradation centers (Albert et al., 2017), the nuclear pore complex (Mosalaganti et al., 2018), COPI coats (Bykov et al., 2017), IFT train assembly, centriole structure, and the molecular organization of chloroplast's thylakoid membranes and pyrenoid (Freeman Rosenzweig et al., 2017).

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