Cryo electron tomography of in vitro membrane systems

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Structure - function relationship studies in molecular membrane biology have so far with very few exceptions stayed separate. This stems from the regretable circumstance that techniques for functional studies that use in vitro membrane systems, such as proteoliposomes, planar bilayer electrophysiology, nano-well technology or supported membranes, are not compatible with methods of structure determination. This severely impedes a true understanding of the so important structure-function relationship.

Cryo electron tomography (cryoET) has been developed in the last few decades mainly with the aim to study the structure or spatial relationship of macromolecular complexes and cellular compartments of the cell in situ. With the in recent years by new direct electron detectors and new image analysis tools started and ongoing resolution revolution in cryo electron microscopy not only single particle cryoEM, but also cryoET experienced a great leap foward in problems that can be addressed by cryoEM.

Here I would like to make the case that cryoET harbours the potential to open up completely new possibilities in combining functional studies with structural studies employing the same experimental set-up. To illustrate this potential I would like show some published data on reconstituted mammalian FoF1 ATP synthase and explain how new techniques of auto membrane insertion could be very helpful to study important questions in mitochondrial biology.