Virtual DANDRITE Lecture

(Followed by a student encounter from 15:10-16:00)

Thursday 17 November 2022

14.00 – 15.00

Location: Online via zoom. Find the link in the outlook invitation or write Astrid Munk (asmu@dandrite.au.dk) to get it.

Silvio Rizzoli

Director at the Department of Neuro- and Sensory Physiology, University Medical Center Göttingen, Germany.

Expansion microscopy at one nanometer resolution

Link to Silvio Rizzoli's manuscript on bioRxiv.

Fluorescence imaging is one of the most versatile and widely-used tools in biology. Although techniques to overcome the diffraction barrier were introduced more than two decades ago, and the nominal attainable resolution kept improving to reach single-digit nm, fluorescence microscopy still fails to image the morphology of single proteins or small molecular complexes, either purified or in a cellular context. Here we report a solution to this problem, in the form of one-nanometer expansion (ONE) microscopy. We combined the 10-fold axial expansion of the specimen (1000-fold by volume) with a fluorescence fluctuation analysis to achieve resolutions down to 1 nm or better. We have successfully applied ONE microscopy to image cultured cells, tissues, viral particles, molecular complexes and single proteins. At the cellular level, using immunostaining, our technology revealed detailed nanoscale arrangements of synaptic proteins, including a quasi-regular organisation of PSD95 clusters. At the single molecule level, upon main chain fluorescent labelling, we could visualise the shape of individual membrane and soluble proteins. Moreover, conformational changes undergone by the ~17 kDa protein calmodulin upon Ca2+ binding were readily observable. We could also image and classify molecular aggregates in cerebrospinal fluid samples from Parkinson's Disease (PD) patients, which represents a promising new development towards an improved PD diagnosis. ONE microscopy is compatible with conventional microscopes and can be performed with the software we provide here as a free, open-source package. This technology bridges the gap between high-resolution structural biology techniques and light microscopy, and provides a new avenue for discoveries in biology and medicine.

Host: Poul Henning Jensen