



# BIOLOGY COLLOQUIUM

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Hosted by Dr Lu Gan

## Phase plate imaging in electron cryo-microscopy



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The Volta phase plate (VPP) is a remarkably simple device comprising a thin (~10 nm) amorphous carbon film positioned at the back focal plane of the objective lens. The film is continuously heated at ~250°C to prevent beam-induced contamination and enable the Volta potential effect. The strong central diffraction beam of unscattered electrons interacts with the film and modifies its surface properties leading to the creation of a Volta potential difference between the central spot and the surrounding areas. This in turn leads to a three-dimensional electrostatic potential distribution above and below the film which when integrated along the beam path results in a phase shift difference between the central beam and the scattered beams.

Single particle applications of the VPP are still in their early days, but the results thus far are very encouraging. The improved contrast was instrumental in the near-atomic cryo-EM structure determination of peroxiredoxin-3, the nucleosome, a calcitonin class-B GPCR, a biased agonist-bound human GLP-1 receptor-Gs complex and hemoglobin. The VPP has the capability to extend the applicability of cryo-EM towards smaller particles and it is not unreasonable to expect that in the near future we will be able to solve structures under 50 kDa.

*Rado Danev graduated solid-state physics at Sofia University, Bulgaria in 1997. During his Ph.D. (1998-2001) in the laboratory of Prof. Nagayama in Okazaki, Japan he worked on the development of phase plates for electron microscopy. He continued work at NIPS on the application of phase plates in cryo-EM and published the first successful phase plate applications in single particle analysis and cryo-tomography. In 2011 he became a group leader at the Max Planck Institute of Biochemistry, Martinsried, Germany. In the same year he was awarded the Burton Medal of the Microscopy Society of America. Rado was the project leader of an academia-industry collaboration which led to the invention of the Volta phase plate (VPP). The VPP is now commercially available and is being used in cryo-electron tomography and single particle analysis. In 2017 Rado was awarded the Ernst Ruska prize of the German Society for Electron Microscopy.*