CeMMP Centre for Cryo-electron Microscopy of Membrane Proteins

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Rado Danev graduated solid-state physics at the University of Sofia in Bulgaria. During his Ph.D., and in the following years, he worked on the development of phase plates for electron microscopy in the laboratory of Prof. Nagayama in Okazaki, Japan. He published the first phase plate applications in cryo-EM single particle analysis and cryo-tomography. In 2011 he became a group leader at the Max Planck Institute of Biochemistry in Martinsried, Germany, and in the same year was awarded the Burton Medal of the Microscopy Society of America. Thereafter, he led an academia-industry collaboration that resulted in the development of the Volta phase plate (VPP). For this research, in 2017 he was awarded the Ernst Ruska prize of the German Society for Electron Microscopy. Since November 2018, Rado is a professor at the Graduate School of Medicine, The University of Tokyo. His current projects involve cryo-EM studies of GPCRs in collaboration with the GPCR team at Monash University, first forays into cryo-tomography, and more generally methods development for cryo-EM.

Pushing the boundaries of cryo-EM for GPCRs

Cryo-electron microscopy (cryo-EM) continues to grow as a powerful method for structural studies of biomolecules and their complexes. Nowadays, it can routinely determine molecular structures with resolutions in the 2.5 – 3.5 Å range. Such results are adequate for modelling of the protein but lack fidelity for confident localization of water molecules and hydrogen atoms. Unambiguous elucidation of the biochemistry behind protein function and pharmacology of drugs would require atomic resolution structures, at levels below 1.5 Å. Last year, several groups worldwide demonstrated atomic resolution cryo-EM with a test sample comprising the “easy” soluble protein apoferritin. This was an important technological milestone showcasing the best-case-scenario capabilities of cryo-EM. However, membrane proteins, and other real-world samples, impose numerous experimental challenges, such as small size, heterogeneity, flexibility, preferential orientation, etc. The talk will be about optimizing the performance of cryo-EM for challenging membrane proteins, and particularly in studies of the structure, pharmacology, and dynamics of G protein-coupled receptors.