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ORAL ABSTRACT PRESENTATIONS

SESSION TITLE: NEW METHODS OF SAMPLE PREPARATION AND DATA PROCESSING FOR CRYO-ELECTRON MICROSCOPY

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Abstract OR-17: High Resolution Studies of Biocomplexes by Cryo-Electron Microscopy, Basis for High Throughput Studies

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Background: The last decade has witnessed an extremely impressive rise in the role of cryo-electron microscopy (cryo-EM) for structural studies of biocomplexes. For many years, EM was not considered as a structural method and was mainly used for visualization of shapes of large biocomplexes or organelles in cells. However, the decades of laborious efforts of many scientists to fulfil theoretical promises in usage of electrons for imaging of biological molecules at the level of atomic resolution were not in vain and the best representatives of the EM community were recognized in 2017 by the Nobel prize awarded to *J. Dubochet, J. Frank, and R. Henderson* (Henderson R. *Angew Chem Int Ed Engl.* 2018 Aug 20;57(34):10804-10825. doi: 10.1002/anie.201802731; Dubochet J. *Angew Chem Int Ed Engl.* 2018 Aug 20;57(34):10842-10846. doi: 10.1002/anie.201804280. Frank J. *Angew Chem Int Ed Engl.* 2018 Aug 20;57(34):10826-10841. doi: 10.1002/anie.201802770).

Methods: Cryo-electron microscopy, cryo sample preparations, direct detectors, computational methods (Dubochet J. 2012 Mar;245(3):221-4; McMullan G, Faruqi AR, Henderson R. *Methods Enzymol.* 2016;579:1-17. doi: 10.1016/bs.mie.2016.05.056; Kaledhonkar S, Fu Z, White H, Frank J. *Methods Mol Biol.* 2018;1764:59-71. doi: 10.1007/978-1-4939-7759-84),

Results: The last five years in EM were manifested by crucial technical advances in micro technology, improving the electron sources and systems for digital registration of images. It is important to acknowledge the role of improvements in sample preparation where they allowed the retrieval of high-resolution structural information from two-dimensional images. The progress in technology was accompanied by the development of mathematical approaches describing image formation in microscopes, algorithms for the fast and efficient processing of recorded images and automation of processing, where subsequent analysis facilitated the determination of structures at near-atomic resolution. During the last years, success of cryo-EM was highlighted by a large number of structures resolved at a resolution better than 4Å, where one can recognize the interface of protein-protein interactions, reveal different conformations of complexes and understand their function through their dynamic properties, and now we witness new achievements such as structures at a resolution better as 2

Å. Now we need to fully automate the data collection on electron microscopes, increase the dimensions of digital detectors (whilst reducing at the same time the sizes of individual sensors) and to get powerful computers that will allow us to do statistical analysis of data to distinguish variations in structures. The next important step would be to resolve functional changes of complexes in time.

Key Words: cryo-EM • biological complexes • structure • image processing

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