POSTER ABSTRACT PRESENTATIONS

SESSION TITLE: STRUCTURE OF MEMBRANE PROTEINS

DOI: 10.21103/IJBM.9.Suppl_1.P2

**Abstract P-2: Modeling Encapsulated Lipid Molecules in Cryo-EM Maps of
Membrane Complexes**

Olga Novitskaia, Pavel Buslaev, Ivan Gushchin

Moscow Institute of Physics and Technology, Dolgoprudny, Russia

Background: Membrane complexes are of great importance for cell functioning. Among the best studied complexes are rotor ATPases which create ATP from ADP, or vice versa (J.E. Walker, *Biochem. Soc. Trans.* 41, pp. 1-16, 2013). Generally, rotor ATPases consist of a soluble part and a membrane-embedded part. The membrane part includes a c-ring – a symmetric oligomer of subunits c, which is rotating in the membrane during the protein operation. The inside pore of the c-rings in some cases is plugged by phospholipids.

While the protein components are well ordered in the structures, the surrounding lipid molecules, including those trapped inside the c-ring, usually are not resolved. Most probably this is due to the great flexibility of lipids (P. Buslaev *et al.*, *J. Chem. Theory Compyt.* 12, pp. 1019-1028, 2017) and lack of specific lipid-protein interactions, or due to techniques used for sample preparation.

Recently, a Cryo-EM structure of spinach chloroplast ATPase with recognizable densities in the membrane region has become available, providing an opportunity to compare the modeled lipid positions with the experimental data (A. Hahn *et al.*, *Science* eaat4318, 2018).

Methods: We introduce nature-inspired approach to model the lipids inside the c-ring. It uses a biasing force to assemble the whole ring, essentially by incorporating experimental restraints into the coarse grained (CG) molecular dynamics (MD) simulation. The numerical comparison of modeled lipid densities with the EM maps was performed using the real space correlation coefficient (RSCC).

Results: The structures converged into an assembled ring. The numbers of lipids trapped at the loop side and the NC-side were consistent in different runs: 9 to 11 and 13 to 15, respectively. However, RSCC of modeled lipid densities with the EM map was poor. Thus, we conducted short CG simulations where lipids were removed one-by-one to maximize RSCC (Fig. 1). The best fit (RSCC > 0.8) was observed for a system with 6 lipids at the loop side and 9 lipids at the NC side. The obtained systems were converted to atomistic models and were stable for several hundreds of nanoseconds. The atomistic models also correlated with experimental data well (RSCC > 0.8) and showed the same trend as densities for coarse grained simulations.

Fig. 1. (A) Experimental densities for c-ring of rotor ATPase. Lipid densities are shown in grey, protein densities in black. (B) Comparison of experimental and modeled densities. Experimental densities are shown in grey; modeled densities for 6 lipids at the loop side and 9 lipids at the NC side are shown in black.

Conclusion: We expect that the approach will be helpful for modelling of the lipids encapsulated within membrane protein and for studies of assembly of membrane complexes.

Key Words: molecular dynamics simulations • rotor ATPase • CryoEM

Sources of Funding: This work was supported by RFBR according to the research project №18-34-00986

International Journal of Biomedicine. 2019;9 Suppl 1: S17. doi: 10.21103/IJBM.9.Suppl_1.P2

©2019 International Medical Research and Development Corporation