3. The influence of phospholipid composition on membrane interaction with amyloid beta peptides within molecular dynamics simulations

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At the present time there is a hypothesis about the key role of amyloid beta peptide in the onset of Alzheimer's disease. It is considered that its interaction with cell membranes causes a disruption of their permeability and integrity, which may trigger further neurodegenerative processes [1]. The experimental study showed that the peptide takes part in the morphological changes of the phospholipid membrane during its transition through the main lipid phase transition temperature [2]. However, this research did not allow us to look into the processes and resulting structures at the atomic level. The latter results are better achieved in theoretical studies that we have carried out recently.

It has been suggested that different phase states within one membrane may play a key role in the process of phospholipid membrane destruction in the presence of amyloid beta peptides. In order to shed some light on this, the interaction of Aβ(25-35) with DPPC and DOPC phospholipids, which have different tail lengths and might form rafts, at different temperatures was simulated using the coarse-grained and all-atom molecular dynamics method in the GROMACS 2019.3 software package. Using the coarse-grained approach, we have obtained the type of structures that are formed from a box of randomly distributed components at different temperatures below and above the main transition. Whereas all-atom consideration has allowed us to determine the influence of rafts on the internal location of peptides in the membrane.

References:

1. Martel A., et al. Membrane permeation versus amyloidogenicity: a multitechnique study of islet amyloid polypeptide interaction with model membranes. Journal of the American Chemical Society, 2017, 139, 137-148.
2. Ivankov O., et al. Amyloid-beta peptide (25–35) triggers a reorganization of lipid membranes driven by temperature changes. Scientific Reports, 2021, 11(1), 21990.