# Study of a multilipid receptor-embedded cell membrane in different ensembles

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Nowadays, a widely adopted approach for construction of a targeted drug delivery system (DDS) is the *active targeting*. It is based on including in the DDS a ligand, which is specifically recognized by cell surface receptors overexpressed in neoplastic membranes. Such a protein is the α-folate receptor (α-FR) with folic acid as its natural ligand. One of the initial steps of the study aimed at understanding the ligand-receptor interactions is to obtain a credible model of a receptor-embedded cell membrane. This includes selection of an appropriate thermodynamic ensemble for adequate description of the receptor and membrane properties. The model neoplastic membrane is constructed in accordance with available experimental data [1, 2] and 35 different lipids are used. The X-ray structure of the receptor is taken and embedded into the membrane by a GPI anchor [3]. Classical atomistic molecular dynamics simulations of the system immersed in saline are carried out at physiological conditions. The calculations are done in three ensembles – NPT with isotropic or with semi-isotropic pressure scaling and NPγT.

The properties in the three ensembles are compared in terms of RMSD evolution and mass density profiles of the components. Order parameter of the lipid tails and average area per lipid are also calculated. The secondary structure of the protein is evaluated, too.

Similarity in the profiles of all characteristics computed in semi-iso NPT and NPγT is found. The largest difference between the three ensembles is in the RMSD and mass density profiles of the membrane. Overall, the membrane is in liquid disordered state in iso NPT, while in the other two ensembles the lipid tails adopt partial order corresponding to liquid ordered state. The latter is in correspondence with the experimentally expected behaviour. The average areas per lipid in NPγT match very well available experimental data.

The NPγT ensemble is selected for further simulations of ligand-receptor-membrane interactions.

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