Curvature dependence of SNARE TMD mediated membrane fusion

Matthias Pöhnl[1] and Rainer A. Böckmann[1]

[1]*Computational Biology, FAU Erlangen-Nürnberg, Germany*

Membrane fusion is a key event in a wide range of biological processes like exocytosis, fertilization and intracellular trafficking. Soluble N-ethylmaleimide-sensitive factor attachment protein receptor (SNARE) proteins are thought to be involved in all steps of the fusion process, e.g. docking the membranes, initializing hydrophobic contacts, and reducing bending energies [1]. However, microscopic details and the role of the specific domains of the SNARE proteins remain elusive.

Mutating the primary structure of the SNARE transmembrane domain (TMD) was shown to alter vesicle fusion by altering the initiation and pore opening [2]. Molecular dynamics (MD) simulations of flat membranes were used to obtain a molecular description of these effects. The TMD regulates lipid mobility, and hence lipid protrusion events leading to first hydrophobic contacts between the merging membranes [3]. Furthermore the specific TMD primary structure regulates the oligomerization propensity [4], which is key for efficient membrane fusion.

However, previous studies neglect effects of membrane curvatures involved in fusion. Hence, we extend previous work on the properties of SNARE TMDs and SNARE TMD mutants using coarse-grained MD simulations allowing for strongly curved membrane geometries. In a first step we investigate the curvature dependence of the localization of SNARE TMDs and their oligomers.

[1] Jahn R. and Fasshauer D., Nature, 2012

[2] Dhara M., Yarzagaray A., Makke M., Schindeldecker B., Schwarz Y., Shaaban A., et al., eLife, 2016

[3] Han J., Pluhackova K., Bruns D., Böckmann R., BBA, 2016

[4] Han J., Pluhackova K., Wassenaar T., Böckmann R., Biophys. J., 2015