# Fusion, fission, and pore formation –
# Computer simulation of collective phenomena that alter the topology of membranes

Marcus Müller,[1] Israel A. Barragan-Vidal,[1] H. Jelger Risselada,[1] Yuliya Smirnova,[1] Christina L. Ting,[2] and Guojie Zhang[1]

[1]Institut für Theoretische Physik, Georg-August-Universität, Friedrich-Hund-Platz 1. 37077 Göttingen, Germany

[2]*Sandia National Laboratories P.O. Box 5800 MS-1315 Albuquerque, NM 87185-1315, U.S.A.*

mmueller@theorie.physik.uni-goettingen.de

## Abstract

Using computer simulation and self-consistent field theory of coarse-grained models for lipid membranes, we study the free-energy landscape of collective phenomena that alter the topology of lipid membranes.[1,2] These processes – pore formation, fusion and fission – often involve time scales of tens of nanometres and milliseconds that are large for atomistic simulation. Frequently, they involve transition states with high curvatures that are difficult to describe by Helfrich-like models. Coarse-grained models can access the relevant time and length scales, allow for a systematic exploration of parameters like the lipid architecture or membrane tension, and they are well suited to study collective phenomena that alter the topology of membranes because they capture the lipid self-assembly.

The talk will discuss different computational techniques – Wang-Landau sampling, field-theoretic umbrella sampling,[3] and the string method[4] – to investigate metastable intermediates (like the stalk in the course of membrane fusion – see Fig. 1) and transition states of pore formation, membrane fusion and fission.[5] Using coarse-grained models – implicit-solvent model and the MARTINI model – we explore the universal aspects of topology-altering processes and additionally comment on the extent to which coarse-grained model capture specific effects of protein-mediated processes.[6]

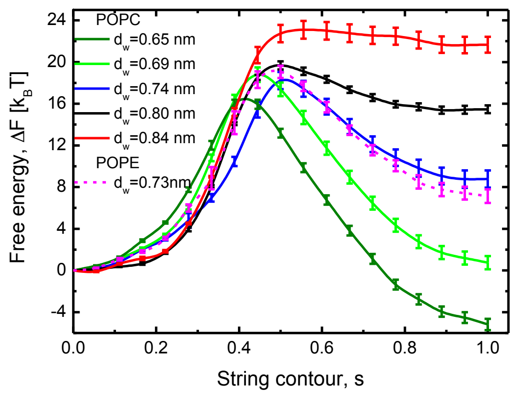


**Fig. 1** Minimum free-energy path from two planar, apposing bilayer membranes to a stalk – an hourglass-shaped hydrophobic connection between the two membranes – as a function of the distance, $d_w$, between the two membranes. Whereas the free-energy barrier is rather insensitive to de-hydration, the excess free energy of the stalk rapidly decreases with decreasing hydration and stalk may even become more stable than the two apposing membranes.

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[1] M. Fuhrmans, G. Marelli, Y.G. Smirnova, and M. Müller, Chem. Phys. Lipids **185**, 109–128 (2015)
[2] Y.G. Smirnova, M. Fuhrmans, I.A. Barragan Vidal, and M. Müller, J. Phys. D: Appl. Phys. **48**, 343001 (2015)
[3] Y.G. Smirnova and M. Müller, J. Chem. Phys. **143**, 243155 (2015)
[4] M. Müller, Y.G. Smirnova, G. Marelli, M. Fuhrmans, and A.C. Shi, Phys. Rev. Lett. **108**, 228103 (2012)
[5] M. Fuhrmans and M. Müller, Soft Matter **11**, 1464 (2015)
[6] H.J. Risselada, G. Marelli, M. Fuhrmans, Y.G. Smirnova, H. Grubmüller, S.J. Marrink, and M. Müller, PLoS ONE **7**, e38302 (2012)