



Prof. Michael M. Kozlov, Ph.D.

Department of Physiology and Pharmacology
Sackler Faculty of Medicine



E-mail: michk@post.tau.ac.il

Theoretical Biophysics of Membranes and Cytoskeleton

Position

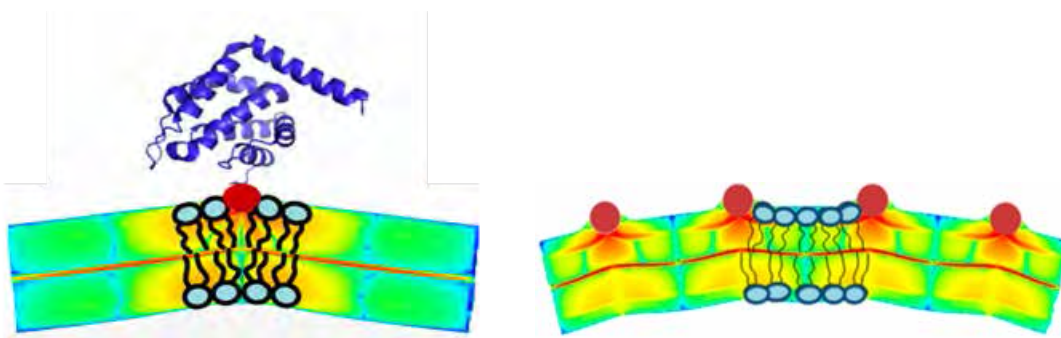
Professor, Sackler Faculty of Medicine
Joseph Klaffer Chair in Biophysics

Research

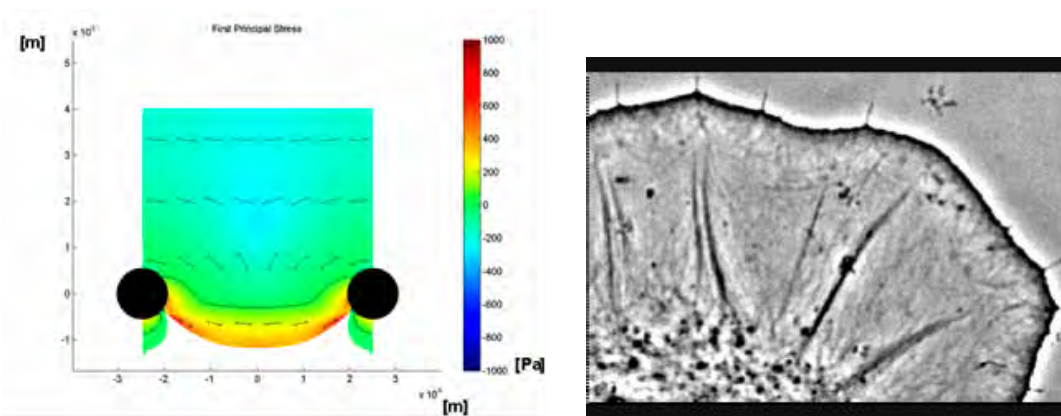
We model the mechanisms of shaping and remodeling of intracellular membranes by specialized proteins that includes generation of large membrane curvatures, membrane fission and fusion. Our goal is to reveal the common mechanistic themes in the function of membrane shaping proteins acting in different intracellular systems. In this way, we hope to be able to understand whether every stage of membrane

shaping needs a special protein or the same protein machinery can enable both membrane curvature generation and fission and/or fusion. Specifically, we model the action of BAR domain proteins, Epsins and Dynamins in endocytosis, Reticulons and their partners in shaping the Endoplasmic Reticulum, and ESCRT-III complexes in fission of cytokinetic tubes.

We model the mechanisms underlying the dynamic organization of the actin cytoskeleton and the system of cell adhesion in polarizing and moving cells. Our major goal is to understand the mechanosensitivity of the cytoskeletal systems and its role in the system temporal rearrangements and steady-state structures.



Computational results for membrane curvature generation by amphipathic N-terminal helices of N-BAR domains, ENTH domains and small G-proteins.



Computational modeling of lamellipodium boundary formation resulting from actin-focal adhesion interaction (left), the phenomenon observed in moving fibroblasts (right, courtesy of A. Verkhovsky).

Publications

Buzon, V., Natrajan, G., Schibli, D., Campelo, F., **Kozlov, M.M.**, Weissenhorn, W., Crystal structure of HIV-1 gp41 including both fusion peptide and membrane proximal external regions. *PLoS Pathog*, 2010. 6: e1000880.

Shibata, Y., Shemesh, T., Prinz, W.A., Palazzo, A.F., **Kozlov, M.M.**, Rapoport, T.A., Mechanisms determining the morphology of the peripheral ER. *Cell*, 2010. 143: 774-88.

Richard P., Leikina E., Langen R., Henne W.M., Popova M., Balla T., McMahon H.T., **Kozlov M.M.**, L.V. Chernomordik. Intracellular curvature generating proteins in cell-to-cell fusion. *Biochem J.*, 2011. 440:185-93.

Bershinsky A.D., **Kozlov M.M.** Crawling cell locomotion revisited. *Proc Natl Acad Sci USA*. 2011. 108: 20275-20276.

Boucrot E., Pick A., Camdere G., Liska N., Evergren E., McMahon H.T., **Kozlov M.M.** Hydrophobic insertions promote, while crescent BAR scaffolds limit vesicle membrane fission. *Cell*. 2012. 149: 124-136.

Elia N., Fabrikant G., **Kozlov M.M.** Lippincott-Schwartz J. Computational model for cytokinetic abscission driven by ESCRT-III polymerization and remodeling. *Biophys J*. 2012. 102: 2309-2320

Shemesh T., Bershinsky A.D., **Kozlov M.M.** Physical model for self-organization of actin cytoskeleton and adhesion complexes at the cell front. *Biophys J*. 2012 ;102:1746-56

Leikina E., Melikov K., Sanyal S., Verma S.K., Eun B., Gebert C., Pfeifer K., Lizunov V.A., **Kozlov M.M.**, Chernomordik L.V. Extracellular annexins and dynamin are important for sequential steps in myoblast fusion. *J Cell Biol*. 2013. 200:109-23.

Schweitzer Y, **Kozlov M.M.** Cell motion mediated by friction forces: understanding the major principles. *Soft Matter*. 2013. 9:5186-5195

Terasaki M., Shemesh T., Kasthuri N., Klemm R.W., Schalek R., Hayworth K.J., Hand A.R., Yankova M., Huber G., Lichtman J.W., Rapoport T.A., **Kozlov**

M.M. Stacked endoplasmic reticulum sheets are connected by helicoidal membrane motifs. *Cell*. 2013;154:285-96.

G. Fabrikant, S. Gupta, G.V. Shivashankar, **M.M. Kozlov**. Model of T-cell nuclear deformation by the cortical actin layer. *Biophys J*. 105:1316-23, 2013

F. Campelo, **M.M. Kozlov**. Sensing membrane stresses by protein insertions. *PLoS Comp Biol*. 10: e1003556, 2014.

Y. Schweitzer, A.D. Lieber, K. Keren, **M.M. Kozlov**. Theoretical analysis of membrane tension in moving cells. *Biophys J*.106:84-92, 2014.

Reviews

Graham, T.R. and **Kozlov, M.M.**, Interplay of proteins and lipids in generating membrane curvature. *Curr Opin Cell Biol*, 2010. 22: 430-6.

Kozlov, M.M., Biophysics: Joint effort bends membrane. *Nature*, 2010. 463: 439-40.

Kozlov, M.M., H.T. McMahon, and Chernomordik, L.V., Protein-driven membrane stresses in fusion and fission. *Trends Biochem Sci*, 2010. 35: 699-706.

McMahon, H.T., **M.M. Kozlov**, and Martens, S., Membrane curvature in synaptic vesicle fusion and beyond. *Cell*, 2010. 140: 601-5.

Chernomordik, L.V. and **Kozlov, M.M.**, eds. Current Topics in Membranes. Vol. 68. 2011, Elsevier.

M.M. Kozlov, F. Campelo, N. Liska, L.V. Chernomordik, S.J. Marrink, H.T. McMahon. *Curr Opin Cell Biol*. Mechanisms shaping cell membranes. 29:53-60, 2014

F. Campelo, C. Arnarez, S.J. Marrink, **M.M. Kozlov**. Helfrich model of membrane bending: From Gibbs theory of liquid interfaces to membranes as thick anisotropic elastic layers. *Adv Colloid Interface Sci*. 208: 25-33, 2014

Grants

2011-2015 The Israel Science Foundation (ISF), Membrane Shaping by Proteins