# MODULATION OF VOLTAGE GATED ION CHANNELS BY LIPIDS

Marina KASIMOVA,[1,2] Lucie DELEMOTTE[3] and Mounir TAREK[1,4]

[1] *Biological Faculty, Moscow State University, Moscow, Russian Federation*
[2] *University of Lorraine, Nancy, France*
[3] *Temple University, Philadelphia, PA, USA*
[4] *CNRS, UMR 7565, Nancy, France*

Mounir.tarek@univ-lorraine.fr

Voltage-gated potassium channels are ubiquitous transmembrane (TM) proteins, enabling the passive flow of ions across the cell membrane upon changes in the TM voltage. Their modulation by lipids is a widespread mechanism in living cells. The lipid content influences indeed the amplitude of the ionic current and changes the probability of the channel being open and conducting or closed. Experimental findings inferred from a variety of techniques as well as Molecular Dynamics (MD) simulations studies have revealed direct interactions between the lipid headgroups of the membranes and ion channel residues, suggesting an influence of the local lipid environment on the channel's function. Alteration of the lipids may in principle modify also the overall electrostatic environment of the channel, and hence the transmembrane potential, leading to an indirect modulation, i.e. a global effect. We reveal here based on out recent atomistic MD simulations of several voltage-gated potassium (Kv) channels several scenarios that seem to highly depend on the characteristics of the channels. Our findings rationalize the apparently different potentiation of Kv channels by lipids.

[1] Kasimova, M. A., Tarek, M., Shaytan, A. K., Shaitan, K. V., & Delemotte, L. (2014). Voltage-gated ion channel modulation by lipids: Insights from molecular dynamics simulations. Biochimica et Biophysica Acta (BBA) – Biomembranes, 1838, 1322–1331

[2] Tarek, M., & Delemotte, L. (2013). Omega Currents in Voltage-Gated Ion Channels: What Can We Learn from Uncovering the Voltage-Sensing Mechanism Using MD Simulations? Acc. Chem. Res., 46, 2755–2762

[3] Abderemane-Ali, F., Es-Salah-Lamoureux, Z., Delemotte, L., Kasimova, M. A., Labro, A. J., Snyders, D. J., Fedida, D., Tarek, M., Baro, I., & Loussouarn, G. (2012). Dual effect of PIP2 on Shaker potassium channels. J. Biol. Chem. 287, 36158-36167

[4] Delemotte, L., Tarek, M., Klein, M. L., Amaral, C., & Treptow, W. (2011). Intermediate states of the Kv1.2 voltage sensor from atomistic molecular dynamics simulations. Proc. Natl. Acad. Sci., 108, 6109–6114.