

# Effectiveness of Ca<sup>2+</sup> clearance by PMCA pumps

Barbara Schmidt<sup>1</sup>, Cristina Constantin<sup>2</sup>, Bernd Fakler<sup>2</sup> and Heiko Rieger<sup>1</sup>

<sup>1</sup>*Center for Biophysics & Dep. Theoretical Physics, Saarland University, 66123 Saarbrücken, Germany*

<sup>2</sup>*Institute of Physiology, University of Freiburg, 79104 Freiburg, Germany*

Ca<sup>2+</sup> influx through voltage-gated (Cav) channels leads to an increase in the intracellular Ca<sup>2+</sup>-concentration ([Ca<sup>2+</sup>]<sub>i</sub>) that can be monitored by BK-type Ca<sup>2+</sup>-activated K<sup>+</sup> channels. Due to their large-conductance and their particular gating kinetics BK-channels may be used as fast and reliable sensors for [Ca<sup>2+</sup>]<sub>i</sub> underneath the plasma membrane, thus contrasting the commonly used FURA sensors (sensing [Ca<sup>2+</sup>]<sub>i</sub> in the entire cell). In this project, K<sup>+</sup> currents through BK channels were used to determine the Ca<sup>2+</sup> transport activity of Ca<sup>2+</sup>-ATPases of the plasma membrane (PMCA), the classical Ca<sup>2+</sup> pumps that were recently shown to be complexes from two PMCA-subunits and two Neuroplastin or Basigin proteins.

Experimentally we monitored PMCA-mediated Ca<sup>2+</sup> clearance (or transport) by the decay of BK-currents following their activation by a short (0.8 ms) period of Ca<sup>2+</sup>-influx through Cav2.2 channels. Our theoretical model describes the Ca<sup>2+</sup> diffusion within a spherical cell. Time- and Ca<sup>2+</sup> concentration- dependent boundary conditions model the initial Ca<sup>2+</sup> influx by the Cav channels and the following outflow via the PMCA pumps. The time scale of this diffusion process is used to predict the strength of the PMCA pumps. Based on the experimentally determined density of Cav channels and PMCA pumps within the membrane we predict a PMCA pump strength that is at least 1.5 orders of magnitude larger than what has been assumed so far.