Fast Ca^{2+}-transport by PMCA-Neuroplastin complexes

by Bernd Fakler, Inst. of Physiology, University of Freiburg

Plasma membrane Ca^{2+}-ATPases (PMCA), or Ca^{2+}-pumps, terminate Ca^{2+}-signals in any type of cell by extruding Ca^{2+} ions from the cytosol to the extracellular space. In neurons and epithelial cells, Ca^{2+}-extrusion occurs within tens of milliseconds, a speed that is not compatible with current knowledge on PMCA activity.

Based on our recent identification of native PMCAs being assembled from ATPase subunits and the auxiliary proteins Neuroplastin or Basigin, we have revisited the transport velocity of these Ca^{2+}-pumps in the plasma membrane of in intact cells. We found that PMCA2-Neuroplastin complexes, the most abundant Ca^{2+}-transporters in the mammalian brain, provide Ca^{2+}-clearing in the low millisecond-range. Freeze-fracture derived immuno-EM data on densities of Ca^{2+}-source(s) and Ca^{2+}-transporters translated these kinetics into transport rates for PMCA2-Neuroplastin complexes of more than 6000 cycles/s. Direct comparison with the Na^{+}/Ca^{2+}-exchanger NCX2, an alternate-access transporter with fast kinetics, indicated similar efficiencies in Ca^{2+}-transport. Thus, our results unveiled PMCA-Neuroplastin complexes as Ca^{2+}-transporters with unanticipated high transport rates and demonstrate that under cellular conditions ATPases may operate in the kHz range.