Impact of geometry changes in the channel pore by the gating movements on the channel's conductance

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Abstract

Kv 1.2 are voltage-dependent potassium channels of great biological importance. Despite the existence of many reports considering structure – function relations of the Kv 1.2 channel's quantitative domains, some details of the voltage gating remain ambiguous, or even unknown. One of the examples is the range of the S4 - S6 domains motions involved in channel activation and gating. Another important question is to what extent the channel geometry influences the observable channel conductance at different voltages, and what mechanism stands behind. Does the narrowing of the pore reduce the conductance by ohmic resistance growth? The answer is surprisingly negative. But it can be explained in an alternative way by considering the fluctuations.

To address these problems, we formulate geometric models that mimic the generic features of voltage sensor movement and trigger the movement of the other domains involved in gating. We carry out a complete simulation of S4 - S6 domains translations and tilts. The obtained pore profiles allow to estimate the (ohmic) conductance dependency on the voltage. From a family of analysed models, we choose the one most concurring with the experimental data. The results allow to suggest the most probable scenario of S4 - S6 domains movement during channel activation by membrane depolarization.

Key words: geometric modelling, Kv 1.2 channels, voltage activation, channel subdomains' movement, channel pore geometry