

Analysis of correlation effects in the activity of the TRPM8 cold and menthol receptor

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Transient receptor potential (TRP) channels play significant roles in cell signaling by responding to various environmental physical and chemical factors and translating them into cell membrane potential changes that modulate calcium influx. The TRPM8 cation channel has been extensively studied as a major neuronal cold sensor. TRPM8 is also activated by membrane depolarisation, calcium store depletion, and some lipids as well as by compounds that produce cooling sensations, such as menthol or icilin. Despite a large progress has been made in understanding the molecular mechanisms of its activation, the underlying TRP channel kinetics at the single channel level are still incompletely understood.

In this study, we propose a general mathematical approach for fast express analysis of the existence of correlation effects (possibly of non Markov type of behavior) in the activity of single TRP channels. The novelty of our approach consists in statistical evaluation of distribution function for difference of duration of two subsequent pairs of adjacent open and close states with the distribution function for the chain of open-close-open-close events. Experimental observations are then compared to the theoretical predictions for non-correlation behavior. In the framework of our approach we found pronounced correlation effects present in the activity of the TRPM8 cation channel.