Mathematical Modeling of Non-Selective Channels: Estimating Ion Current Fractions and their Impact on Pathological Simulations

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Currents through non-selective ion channels are often mathematically modeled as an Ohmic current. In such models, quantifying the contributions of different contributing ion species is not possible.

We present a method to adapt Ohmic descriptions using the Goldman-Hodgkin-Katz equation in order to describe every ion species' contribution to the total channel current. We apply our method to an Ohmic model of Channelrhodopsin-2, a light-gated cation non-selective channel. We test our adaption in single cell and 1-dimensional tissue strand simulations using the ten Tusscher & Panfilov human ventricular myocyte model. In the tissue strands, we simulated ventricular tachycardia by rapid pacing and using model variants with reduced g_{Kr} (long-QT syndrome), elevated g_{CaL}, and reduced τ_f to elicit early afterdepolarizations.

Resulting contribution ratios of sodium, potassium and proton currents of the adapted channel model match expectations and correlate well with previously published data. Contrary to the original model, our modification results in a rising intracellular sodium concentration upon long-term (>100s) pacing and during continuous illumination in single cells. Simulations of optical defibrillation for ventricular tachycardia show that our model predicts a potentially detrimental outcome in ischaemia-like pathological settings; these are missed by the original (Ohmic) model.

We conclude that modeled changes in ion concentrations by non-selective channels are affected significantly by the choice of channel model and that consideration of ion concentration changes may give rise to different outcomes in VT defibrillation studies. Our simulations also indicate that optical defibrillation would be improved by using a truly repolarizing (e.g., potassium selective) channel rather than a depolarization-based approach to silencing electrical activity.