Effects of Optogenetic Defibrillation on Cardiac Electrophysiology

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Introduction: Optogenetic defibrillation offers a new approach for terminating cardiac arrhythmias based on timed activation of light-gated ion channels known as channelrhodopsins (ChR). So far, studies mainly used cation non-selective ChR, such as ChR2, or anion non-selective ChR, such as GtACR1. However, both terminate arrhythmias by membrane depolarisation, and thus, their activation may contribute to intracellular Ca^{2+} and Na^{+} overload. In contrast, K^{+}-selective ChR (KChR) may be better alternatives, as their activation will keep cardiomyocytes (CM) close to their natural resting potential. Experiments indicate that WiChR, a predominantly K^{+}-selective ChR, presents a promising target for optical defibrillation.

Methods: Employing the O'Hara model of a human ventricular CM, we incorporated ChR2, GtACR1 or a KChR. For ChR2 and GtACR1, we used existing models and simulated illumination with 470 nm or 515 nm light at intensities of 5 mW/mm^2. For KChR we used a simple model including only a K^{+}-conductance (1.4 mS/cm^2) during light-activation. To assess CM behaviour without optogenetic manipulation, we paused the electrical pacing during the illumination period as a control scenario. Moreover, we are currently parameterising a computational model of WiChR to achieve a more realistic representation of KChR functionality.

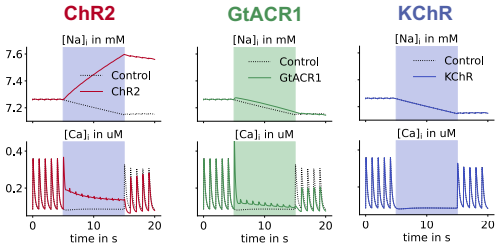

Fig. 1: ChR effects on intracellular ion levels.

Results: The simulations predict an increase in intracellular Ca^{2+} and Na^{+} during activation of ChR2 and GtACR1. In the case of KChR, the results do not indicate significant differences in these ion concentrations compared to control (see Fig. 1).

Outlook: We will test our hypothesis that ChR ion selectivity determines the efficacy and safety of optogenetic defibrillation in 2D and 3D simulations.