TOWARDS THE DEVELOPMENT OF AN IN SILICO MODEL FOR THE ZEBRAFISH ACTION POTENTIAL

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In recent years, the zebrafish use for cardiac electrophysiology studies has exponentially grown. One of the most peculiar aspects are the similarities in action potential (AP) morphology due to the presence of human gene orthologues, leading to functional similarities in cardiac ion channels. Despite this interest, no efforts have been made to develop a mathematical model of the zebrafish AP. In addition, developing such a numerical model will open new potential applications, such as studying the underlying ionic mechanisms behind known pathologies or the response of a new drug. Further, this will also help in reducing the number of animals used for experimental studies and refine the experimental procedures. This work aims at developing a mathematical model of the zebrafish AP, which can adequately reproduce the AP morphology and restitution properties. The TenTusscher model was reparametrized and adapted to the zebrafish. For 1D computations, the forward Euler method was used. A space discretization of $\Delta x = 0.01$ mm and a time step of $\Delta t = 0.02$ ms were used, with $\sigma = 0.249$ μS. To integrate the Hodgkin-Huxley type equations for the gating variables of the various time-dependent currents, the Rush and Larsen scheme was used. Also, a sensitivity analysis was performed on the newly developed AP model to fit AP recordings from the ventricle of adult zebrafish. The figure shows the numerical and experimental APs recordings and their APD_{90} restitution curve. The model accounts for the main transmembrane currents that have been characterized in zebrafish and generally reproduce measured AP morphology.

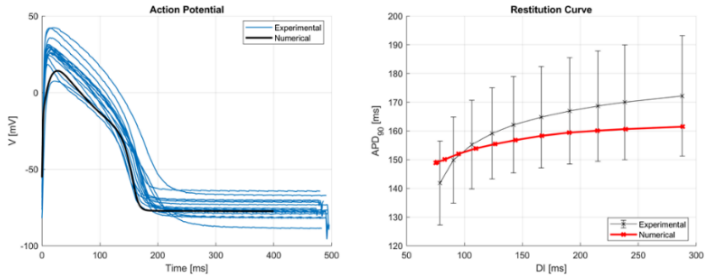

Figure 1: Comparison of ventricular experimental and numerical APs (left) and APD_{90} restitution curve (right).