A Novel Computational Model of the Zebrafish Atrial Action Potential and Intracellular Calcium Transient

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Introduction: The zebrafish is an increasingly popular experimental model for the study of cardiac electrophysiology, due to its electrophysiological similarity to human. Yet, while computational modelling of the cardiac action potential (AP) and calcium (Ca^{2+}) transient is highly advanced for many model species and has contributed to important pathophysiological insight, there currently exists no zebrafish-specific computational model. To address this, we have recently developed a novel model of the zebrafish ventricular AP and Ca^{2+} transient. Here we present the development of a similar model for the zebrafish atrium.

Methods: The 2004 TenTusscher and Panfilov computational AP and Ca^{2+} transient model was reparametrized based on the existing ventricular model given the lack of patch-clamp data, under the assumption that the underlying currents are consistent between chambers. This involved the addition of the T-type Ca^{2+} current (I_{CaT}) and removal of the transient outward current (I_{to}). Using new experimental data of the zebrafish atrial AP and Ca^{2+} transient generated from microelectrode and optical mapping recordings in the isolated heart, the model was reparametrized using MATLAB. Parameter estimation and sensitivity analysis were conducted to refine the model and simulations were run under various conditions to validate it against additional experimental data.

Results: After formulating the behaviour of the gating variables for the various currents, the model was integrated using the Rush-Larsen scheme with a fixed time-step of 0.02 ms. The Monte Carlo method was used to select which of the 11,000 combinations of 34 parameters best fit the experimental AP and Ca^{2+} transient, while keeping the model stable (Fig 1).

Conclusion: Our novel computational model is the first zebrafish-specific model of the atrial AP and Ca^{2+} transient. It represents a valuable tool for future wet-dry investigations of cardiac pathophysiology and pharmacological interventions.

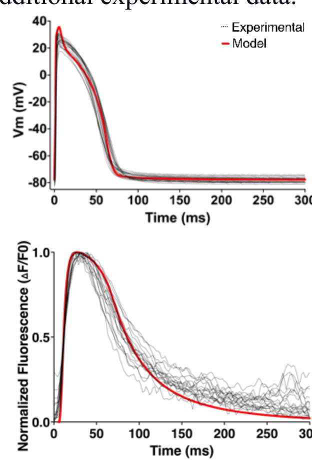

Fig 1. Model of zebrafish atrial AP (top) and Ca^{2+} transient (bottom).