

Enhanced Computer Modeling of Cardiac Action Potential Dynamics using Experimental Data-Based Feedback

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Mathematical models of cardiac action potential (AP) dynamics are useful for studying the formation of dynamically significant patterns such as alternans and conduction block. A closed-loop observer is an augmented version of a mathematical model, in which experimental data, such as microelectrode measurements of membrane potential, are supplied to the model through a feedback algorithm. An observer can reconstruct unmeasured quantities, such as AP durations (APDs) at locations away from sensing electrodes. These reconstructed quantities can be used to gain insight into AP behavior within an experiment, or provide enhanced information to anti-tachyarrhythmic stimulus protocols that depend on real-time measurements. In this study, tools for observer analysis and design were applied to a two-variable Karma model of AP dynamics. Observability Grammians were computed for a single-cell Karma model, and it was determined that the membrane potential variable, rather than the refractory variable, is the better choice for reconstructing the initial state of the model. Next, a two-cell Karma model was augmented with Luenberger observer feedback, and a restricted search of stabilizing observer gain values was used to determine gains that were optimal in the sense of minimizing the 2-norm of the closed-loop eigenvalues. A practical extension of these results is presented, in which a 106-cell Luenberger observer was used with membrane-potential data from microelectrodes at 0.3, 0.9, and 1.5 cm from the proximal end of a 2.1-cm in vitro canine Purkinje fiber. Compared with the Karma model by itself, the observer was able to reduce the mean absolute APD error from 69.5 ms to 12.9 ms, averaged over three locations (0.6, 1.2, and 1.8 cm) where the observer was not supplied with electrode data. This shows that observer feedback can help the Karma model to reproduce measured APDs, even when the correct model parameters are not known precisely.