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Analysis of Heterogeneous Cardiac Pacemaker Tissue Models and Traveling Wave Dynamics

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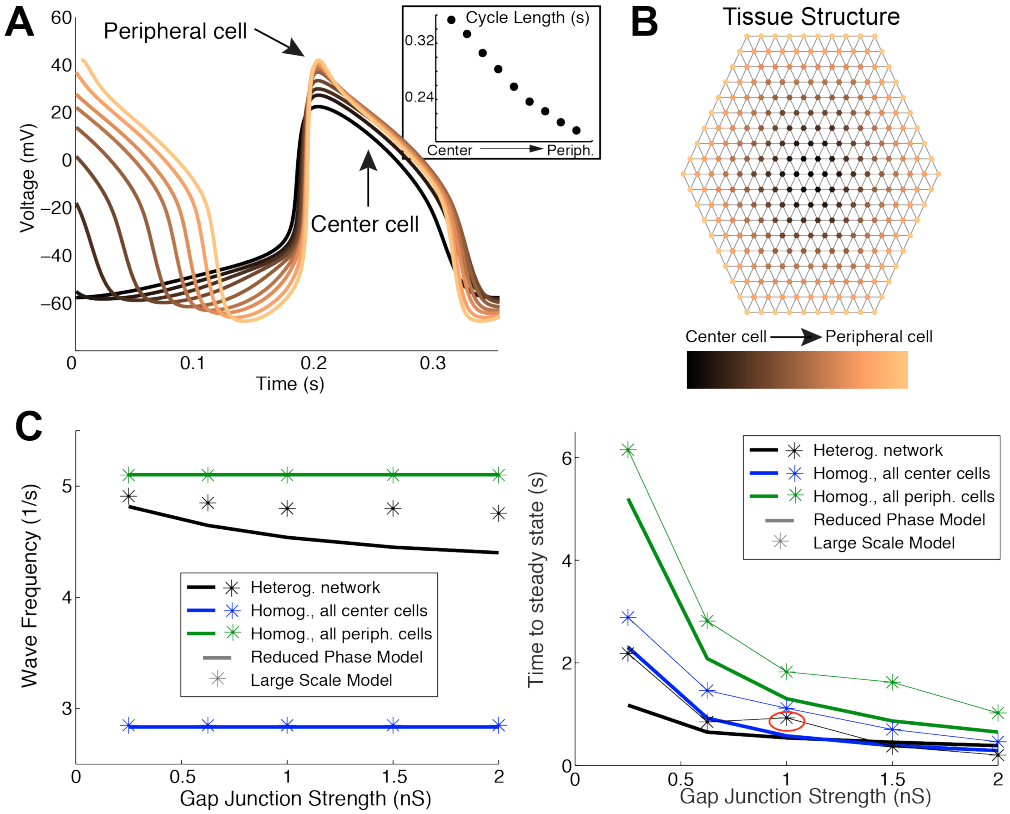
Abstract

The sinoatrial-node (SAN) is a complex heterogeneous tissue that generates a stable rhythm in healthy hearts, yet a general mechanistic explanation for when and how this tissue remains stable is lacking. Computational and theoretical analyses have rarely been used in realistic (large-dimensional) gap-junction coupled heterogeneous pacemaker tissue models. In this study, we adapt a recent model of pacemaker cells (Severi et al. 2012), incorporating biophysical representations of ion channel and intracellular calcium dynamics, to capture physiological features of a heterogeneous population of pacemaker cells, in particular ``center" and ``peripheral" cells with distinct intrinsic frequencies and action potential morphology. We use phase reduction methods that do not require fully simulating the large-scale model to capture dynamics in the large-scale models, including: complete synchrony, traveling waves of activity originating from periphery to center, and transient traveling waves originating from the center. Moreover, the phase reduced models accurately predict key properties of the tissue electrical dynamics, including wave frequencies, synchrony, and wave propagation direction. Thus, we demonstrate that phase reduced oscillator models applied to realistic pacemaker tissue is a useful tool for investigating the spatial-temporal dynamics of cardiac pacemaker activity. We also discuss ongoing work that includes coupling SAN to the atrium where physiological behavior appears to be more robust but analogous analyses are currently elusive.



Caption: A) Uncoupled heterogeneous SAN cells. B) 2D network with nearest neighbor gap junction coupling. C) left: predicted wave frequency (lines) for 3 networks qualitatively matches large-scale simulations (stars); right: predicted transient time, 1 discrepancy (red circle). See Ly & Weinberg *Journal of Theoretical Biology* 2018
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