Analyzing Field Effects in Cardiac Models

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Introduction

Gap junctions (GJ) are thought of as the main mode of action potential (AP) propagation; however, inconsistencies from past studies demonstrate this is not always the case in cardiac tissue with reduced GJ [2]. Such cases can be explained through ephaptic coupling: an effect in which charge congregated between cells proceeds AP propagation, even with reduced GJ. This study focuses on the effects of ephaptic coupling (EpC) and its behavior in different parameters.

Objective

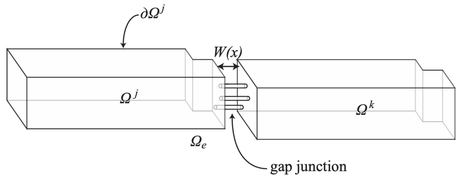
We want to understand the effects of EpC by studying how cellular geometry, ion channel distribution, and GJ affects AP behavior in two directions.

The Model

In this study, we are using a model developed in 2010 by Lin and Keener [1]. The model shown below utilizes a system of nonlinear differential equations of current conservation in both extracellular (Eq. 1) and intracellular (Eq. 2) space:

$$\nabla\dot{(}W(X)C_e\nabla\phi_e) = \sum_{j\in E(x)}\left(C_m\frac{\partial}{\partial t}(\phi_i^j-\phi_e)+I_{\text{ion}}^j(\phi_i^j-\phi_e x)\right) \tag{1}$$

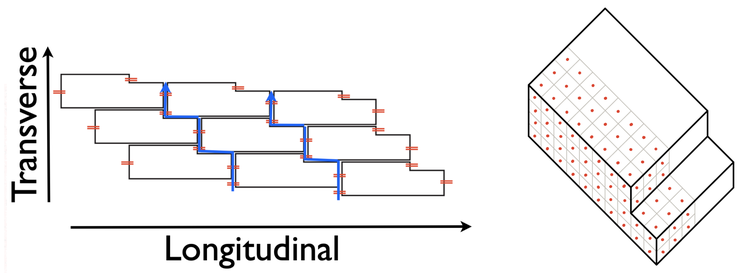
$$\begin{aligned}\chi^j Cm\frac{\partial\phi_i^j}{\partial t} - C_m\frac{\partial}{\partial t}\int_{\partial\Omega^j} I_{\text{ion}}^j(\phi_i^j-\phi_e x)dx \\ = \sum_{k\in I^j}\int_{\partial\Omega^j} g_{jk}(x)(\phi_i^k-\phi_i^j)dx\end{aligned} \tag{2}$$



This system is rearranged and numerically solved for Φ, a collection of potential values ϕ spaced around the cell.

Methodology

To emulate the organically shaped cardiac tissue, we represent cells as indented bricks and arrange periodically, end-to-end. We form the cells such that it can be arranged in two directions: longitudinal and transverse. GJs will appear between cells in the longitudinal direction as shown:



Next, we will activate current to travel in one of the two directions of the tissue. Each individual cell will have nodes ϕ along its membrane divided into three layers. These nodes will store the membrane's potential on that point every 2×10^{-4} ms. These simulations will run for different values of GJ, perinexal widths, ion channel distribution, and current direction. Cell size and both intracellular and extracelluar conductance are held constant.

Data Analysis

The figures below depict maximum AP upstroke (measured as dV/dt_{max}) on different GJ values for tissues with even sodium ion distribution (left) and end-to-end sodium ion distribution (right).

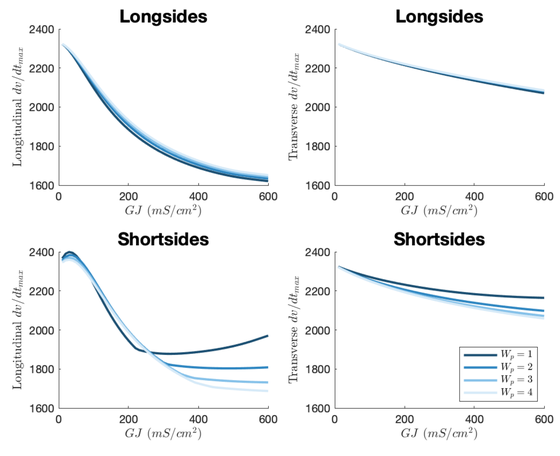


Figure: dV/dt_{max} vs. GJ for tissues with sodium ion channels distributed evenly around the cell membrane.

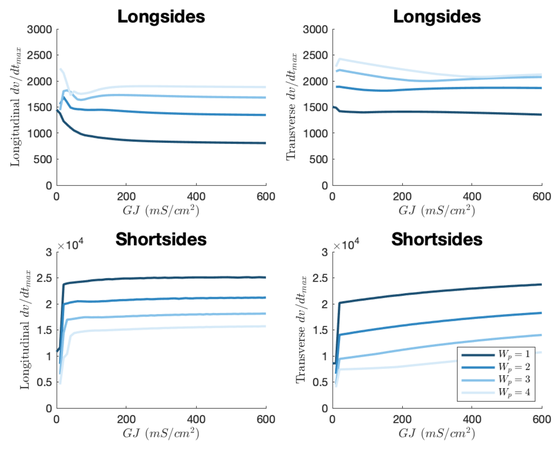


Figure: dV/dt_{max} vs. GJ for tissues with sodium ion channels distributed at the ends of the cell membrane.

The decreasing dV/dt_{max} with reduced junctional width or reduced GJ suggests EpC to further propagate AP. On the other hand, increasing dV/dt_{max} suggests charge accumulation.

A Closer Look

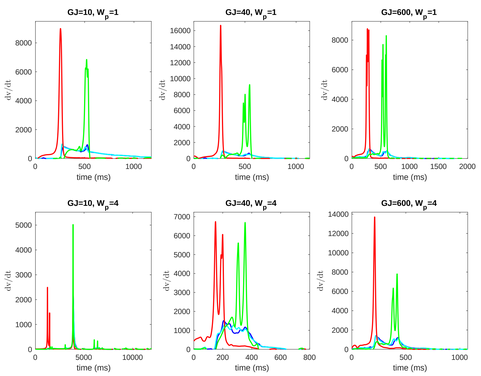


Figure: Average rate of change in AP for different areas of the tissue corresponding to the colors from the top figure of cell (longitudinal direction, Na ends distribution).

Further Discussion

We want to further investigate the cell as a 3D model and incorporate the other layers of the membrane nodes in some visualizations. We also want to investigate the trends of tissues with reduced GJ and understand its patterns.

References

[1] Joyce Lin and James P. Keener.
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[2] Jian-An Yao, David E. Gutstein, Fangyu Liu, Glenn I. Fishman, and Andrew L. Wit.
Cell coupling between ventricular myocyte pairs from connexin43-deficient murine hearts.
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