PHYS 6260 Project Proposal: Finite Differencing Simulation of Myocardial Tissue

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1 Cardiac Tissue Simulation

1.1 Field of Study

Studies of the heart at the scale of contractile tissue have advanced rapidly in the last 50 years with the simultaneous advent of two critical technologies. One is the development of fluorescent ion indicators and potentiometric dyes that allow experiments to directly measure electrophysiological parameters with exceptional spatiotemporal resolution[1]. The other is the implementation of increasingly large parallel computational capabilities to solve large systems of differential equations at high speeds, allowing researchers to develop detailed, anatomically scaled models of cardiac cells and tissue.

At the same time, developments in protein-scale studies have produced models of the individual contributions of ion channels and membrane mechanisms that have informed the dynamics of models at the tissue level[2]. As a result, it is becoming more feasible to develop detailed, quantitative models of cardiac tissue which can be validated by currently employed experimental techniques.

1.2 Research Question

The development of models of defibrillation and anti-arrhythmia therapies relies on accurate modeling of the underlying electrophysiology governing the propagation of action potentials, and in particular modeling the response of tissue to external voltages. One of the key mechanisms responsible for the success of defibrillation by external electric shocks is the formation of *virtual electrodes* within the bulk tissue. It is widely hypothesized that spatial heterogeneity in the conductance of the cardiac tissue gives rise to local maxima in the membrane potential that develops in response to an external shock voltage[3][4]. The goal of this project is to simulate a model of cardiac cells using a finite differencing approach, and to observe the effects of spatially heterogeneous conductivity on the solution for the membrane potential.

2 Background

To date, the model that has been the most successful at reproducing the electrical behavior of myocardial tissue is the *bidomain model*[5]. The quantities simulated in the model represent the voltages of the extracellular space and the transmembrane potential, i.e. the difference in potential between the cell interior and the extracellular space.

The basis of the bidomain model is that source charges generate fields in accordance with standard E&M theory. The electric field is defined in terms of a scalar potential,

$$\mathbf{E} = -\nabla\Phi, \tag{1}$$

and by Ohm's Law, the E-field induces a current density

$$\mathbf{J} = \sigma\mathbf{E}, \tag{2}$$

where σ denotes the conductance of the medium. More generally, in cases where the conductance is spatially heterogeneous, the conductance may be represented as the tensor $\mathbf{\Sigma}$. The potentials of interest are the interior and the extracellular potentials, with the transmembrane potential defined as

$$V_m = V_i - V_e. \tag{3}$$

The evolution of these potentials is derived by taking the divergence of the current to get expressions for the source terms, which are constrained by physiological parameters. The dynamics of the two potentials V_m and V_e are modeled by two PDE's,

$$C_m\frac{\partial V_m}{\partial t} = -I_{ion}(v,w) + \nabla\cdot\left[\mathbf{\Sigma_i}\nabla\left(V_m + V_e\right)\right]\chi^{-1} \tag{4}$$

$$-\nabla\cdot\left(\mathbf{\Sigma_i}\nabla V_m\right) = \nabla\cdot\left[\left(\mathbf{\Sigma_i} + \mathbf{\Sigma_e}\right)\nabla V_e\right]. \tag{5}$$

Equation (4) is a time-dependent reaction diffusion equation that dictates the evolution of the transmembrane potential, where the right hand side contains two source terms. The first is an ion current that is itself a nonlinear function of the transmembrane potential, and this term is scaled by the membrane capacitance (C_m) and the cellular surface-to-volume ratio (χ). The second term accounts for diffusion across the membrane, and is proportional to the surface to volume ratio χ. The second equation relates the evolution of the transmembrane potential to the extracellular potential.

Table 1: List of Symbols

Variable	Symbol
Transmembrane Potential	V_m
Extracellular Potential	V_e
Membrane Capacitance	C_m
Cell Ion Current	I_{ion}
Internal Conductance	Σ_i
External Conductance	Σ_e
Surface to Volume Ratio	χ
Current Gating Variable	w

3 Simulation

In order to simulate the response of cardiac tissue to external source charges, I will use the Crank-Nicholson method discussed in chapter 9 of *Computational Physics*[6] to evolve the reaction diffusion equation while solving the time-independent boundary value problem in equation (5) using the updated values of V_m. My basis for choosing Crank-Nicholson for this problem is that it is stable for the reaction-diffusion equation[7].

I will begin by modeling a 1D filament of cardiac cells discretized uniformly in space, simulating the boundary using ghost points. This simplifies the conductance terms in (4) and (5) so that there is only conduction coaxial and transverse to the muscle fiber. Limiting the simulation to 1D is still somewhat physiologically useful, as cardiac cells do organize into cylindrical syncytial structures.

After successfully simulating cells in 1D using the full bidomain formulation, there are three potential avenues to expand on the technique.

1. Extending the model to higher dimensions. It is possible to scale the system up incrementally by imposing symmetry conditions on the orientation and homogeneity of the fibers as the dimension of the system increases.

2. Heterogeneous conductance. It would be informative to observe the effect of non-uniform conductivity in the bidomain model to determine whether virtual electrodes do indeed emerge due to these defects within the constraints of this model.

3. Comparison of defibrillation shock simulations between bidomain model and simplified model. Simpler models are sometimes used to simulate cardiac tissue dynamics, and it would be useful to verify whether sufficient phenomenological models can replicate the necessary features of tissue with regard to defibrillation.

The initial conditions for the simulation will be defined by implementing low-level random noise in the internal points and imposing various configurations and amplitudes of shock voltage at defined portions of the boundaries. For initial test runs, small domains of $N = 10$ grid points will be used. As the simulation is expanded in to 2 and 3D, the computations involved with solving the two PDE's will become expensive, and the simulation scale will depend on computational speeds. For physiologically relevant timescales, the simulation will run for order 1s, with timesteps of 10^{-3}s as a starting point.

References

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