Multi-physics Simulation of the Biomedical Process- Heart Electrophysiology

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Research Plan

- Goal
- Utilize a set of computer programs to study and simulate   the multi-physics phenomena of the heart.
- Steps
  - Study and understand the governing equations for simulating the heart: Monodomain Model and Beeler-Reuter Model.
  - Develop the geometry and mesh of the heart.
  - Program the electrical models: Beeler-Reuter and Monodomain model.
  - Examine the interaction between the electrical and physiological effects of the heart.
- Medical Applications
  - Test drug use on heart failures such as cardiac arrhythmia.

Phase 1: Beeler-Reuter Model

Potential and Current Equations

$$V^{n+1} = V^n + \frac{dV}{dt}\Delta t + O(\Delta t)^2$$

$$\frac{dV}{dt} = -\frac{(i_{k1} + i_{x1} + iNa + iCa - i_{external})}{Cm}$$

$$i_{k1} = \left\{ \frac{4\{\exp[0.04(V+85)]-1\}}{\exp[0.08(V+53)] + \exp[0.04(V+53)]} \right.$$
$$\left. + \frac{0.2(V+23)}{1 - \exp[-0.04(V+23)]} \right\}$$

$$i_{x1} = x_1 \cdot 0.8 \cdot \frac{\{\exp[0.04(V+77)]-1\}}{\exp[0.04(V+35)]}$$

$$\frac{dCa}{dt} = -10^{-7} \cdot iCa + 0.07 \cdot (10^{-7} - [Ca])$$

$$iNa = (gNa \cdot m^3 \cdot h \cdot j + gNaCa)(V - ENa)$$

Gates Equations (ODE)

$(dx\_1)/dt = \alpha\_x1\ (1-x\_1\ ) - \beta\_x1\ x\_(1\ )$

$(dm\_1)/dt = \alpha\_m1\ (1-m\_1\ ) - \beta\_m1\ m\_1$

$(dh\_1)/dt = \alpha\_h1\ (1-h\_1\ ) - \beta\_h1\ h\_1$

$(dj\_1)/dt = \alpha\_j1\ (1-j\_1\ ) - \beta\_j1\ j\_1$

$(dd\_1)/dt = \alpha\_d1\ (1-d\_1\ ) - \beta\_d1\ d\_1$

$(df\_1)/dt = \alpha\_f1\ (1-f\_1\ ) - \beta\_f1\ f\_(1\ )$
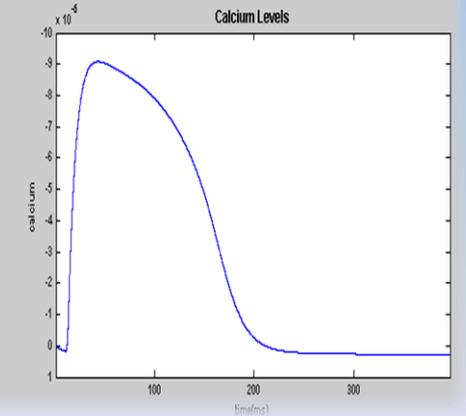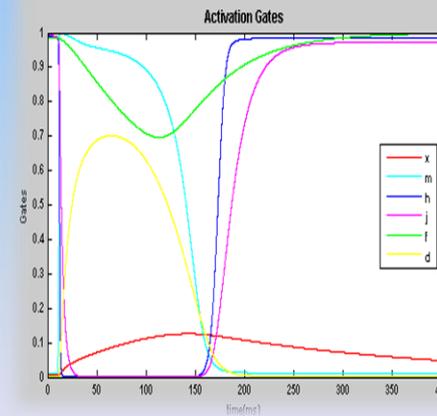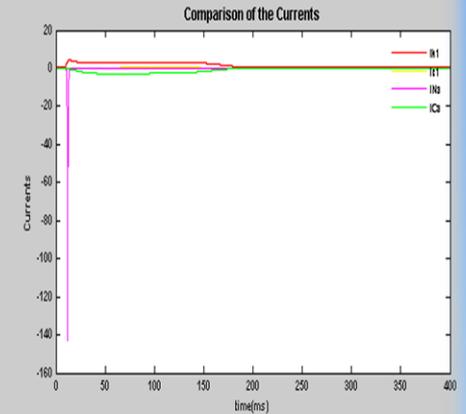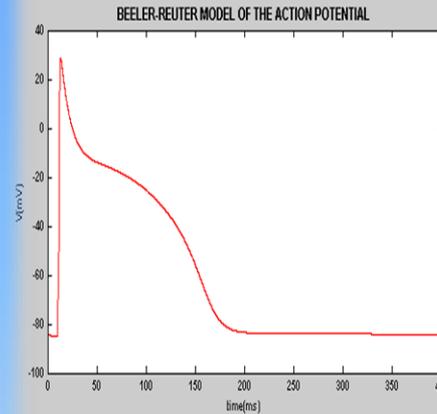
Bidomain and Monodomain Model

- Bidomain Model

$$\nabla \cdot (M_{(i)} \nabla v) + \nabla \cdot (M_i \nabla u_e) = \partial v / \partial t + I\_ion(v,s)$$

After assumptions of homogeneity between the intracellular and extracellular components of the heart the model is simplified into

- Monodomain Model

$$\wedge/(1+\wedge) \nabla \cdot (M_i \nabla v) = \partial v/\partial t + I\_ion(v,s)$$

- Using the operator splitting schemes, the Monodomain model can be split into a set of equations which can be solved simultaneously at different time steps

$$\partial v/\partial t = -I\_ion(v,s), \quad v(t_{(n)}) = v^\wedge n$$

$$\partial s/\partial t = f(v,s), \quad s(t_{(n)}) = s^\wedge n$$

- The partial differential equation below can then be solved linearly at different time steps

$$\partial v/\partial t = \wedge/(1+\wedge) \nabla \cdot (M_i \nabla v), \quad v(t_{(n)}) = v\_\theta^\wedge n$$

Phase 2- CUBIT Meshing

- CUBIT is a full-featured software toolkit for robust generation of two- and three-dimensional finite element meshes (grids) and geometry preparation.
- Choose geometry and dimensions from options in Cubit
- Manipulate geometry into desired shape through cutting and merging
- Apply mesh from Cubit options
- Apply the boundary conditions to the chosen region

Phase 3: Programming

- Export the model from Cubit as a Patran file

- Upload the file into the program remotely on Star1. Star 1 has 12 cores and is located in Perkins

- Average number of cores used ranged between 2-6

- C++ program consists of ODE, PDE and diffusion model, solvers and libraries

- Calculate the voltage of each node

- Visualized results using Paraview

Screenshots of the code being run remotely on Star 1

Programming (B)

- Trilinos is a collection of open source software libraries, called packages, intended to be used as building blocks for application
- The libraries used were Aztec00 for the sparse matrix solver and Epetra for distributing the matrices and vectors to the parallel solver
- METIS is used for partitioning

Time Log

| Input Data
Read and distribute data | → | Newton Solver
Trilinos
Epetra
Electrical module
Aztec00 | → | Convergence in the Newton iteration | Yes → | Output file
Tec plot File | → | Paraview |

No
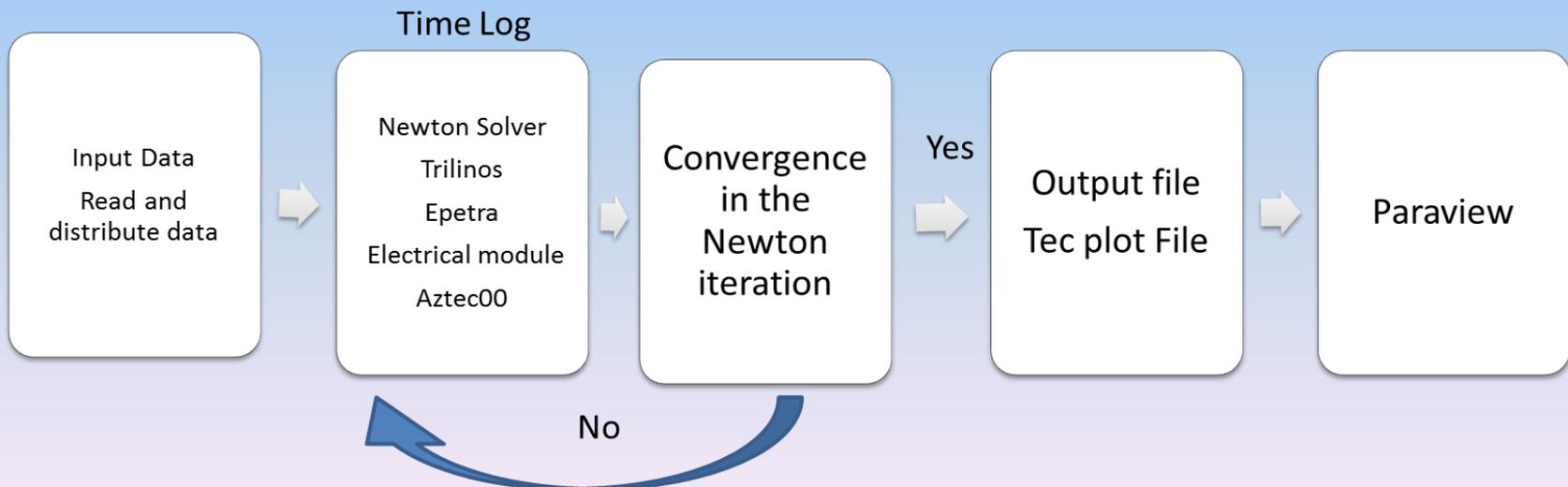
1Beat

- Thin membrane model
  - 10x10x1cm
  - Node interval: approximately 0.2
  - Hexahedral mesh
- Cubic model
  - 10x10x10 cm
  - Node interval: approximately 0.2
  - Hexahedral mesh
- Heart model
  - Tetrahedral mesh

Thin Membrane

- Thin membrane model with boundary conditions applied to 1/16th of node
- Upload file into program
- Solutions saved as Tec plot file were uploaded into Paraview and visualized
- Results are uploaded into Paraview and visualized
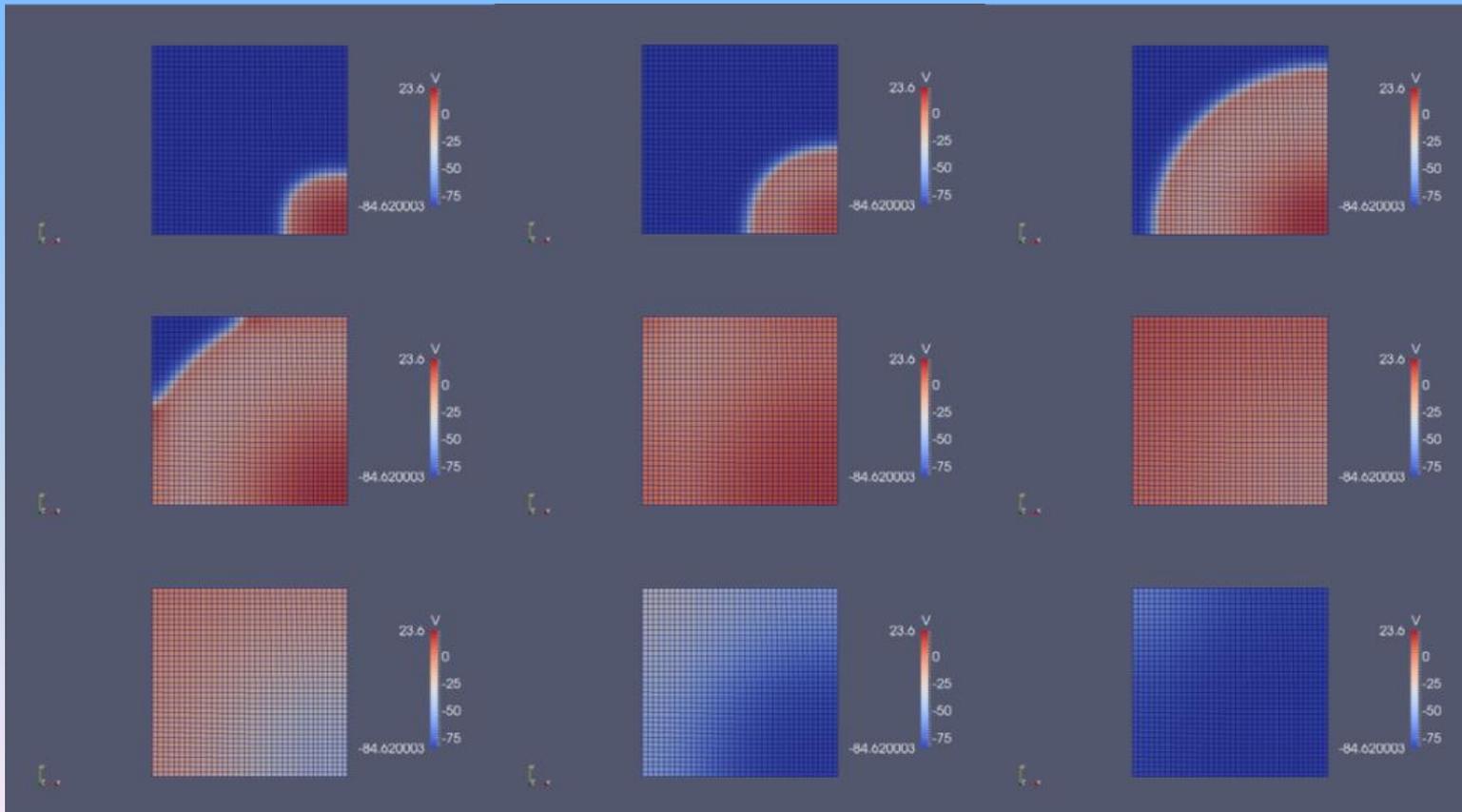
Propagation of the wave in thin membrane. Diffusion value: 0.01 Runtime: 400ms

Cubic model

- 1/16th of nodes of model simulated
- Boundary condition was applied on the 1/16 nodes of the model to simulate it

Parameters:
Diffusion- 0.1
Runtime -400ms
Time step- 1ms
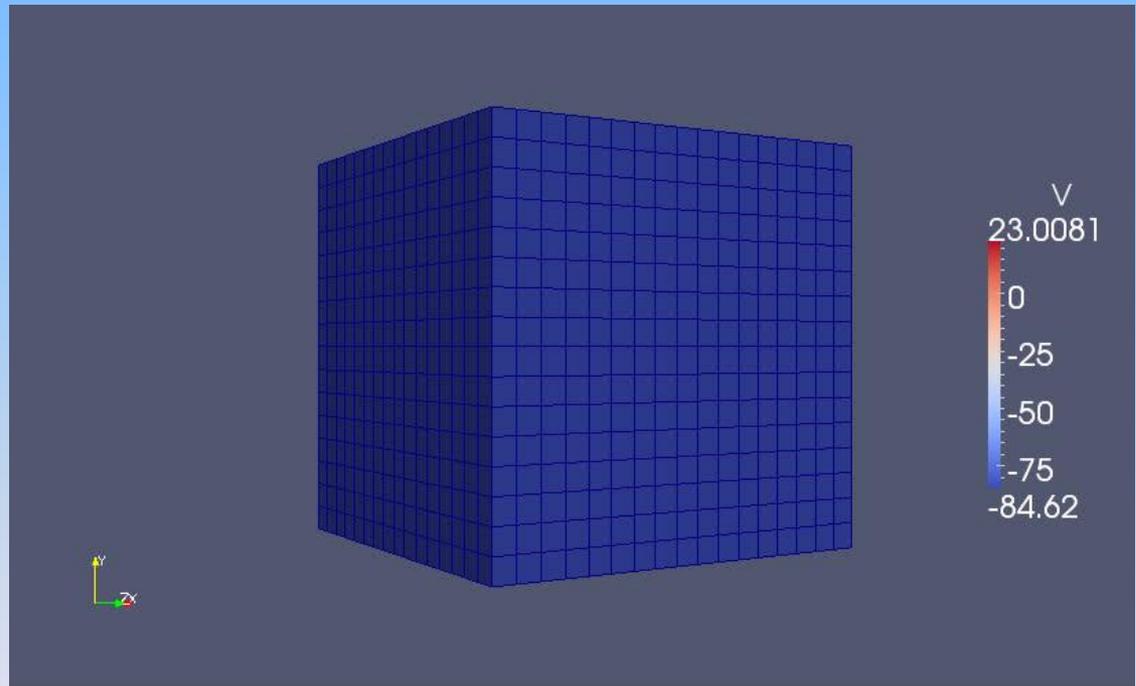
Heart Model

- Boundary condition was applied to simulate the region

- Simulated region is the first region to turn red upon visualization

Propagation of voltage during a single heartbeat

Diffusion value : 0.001

Runtime: 400ms

Time step: 0.1ms
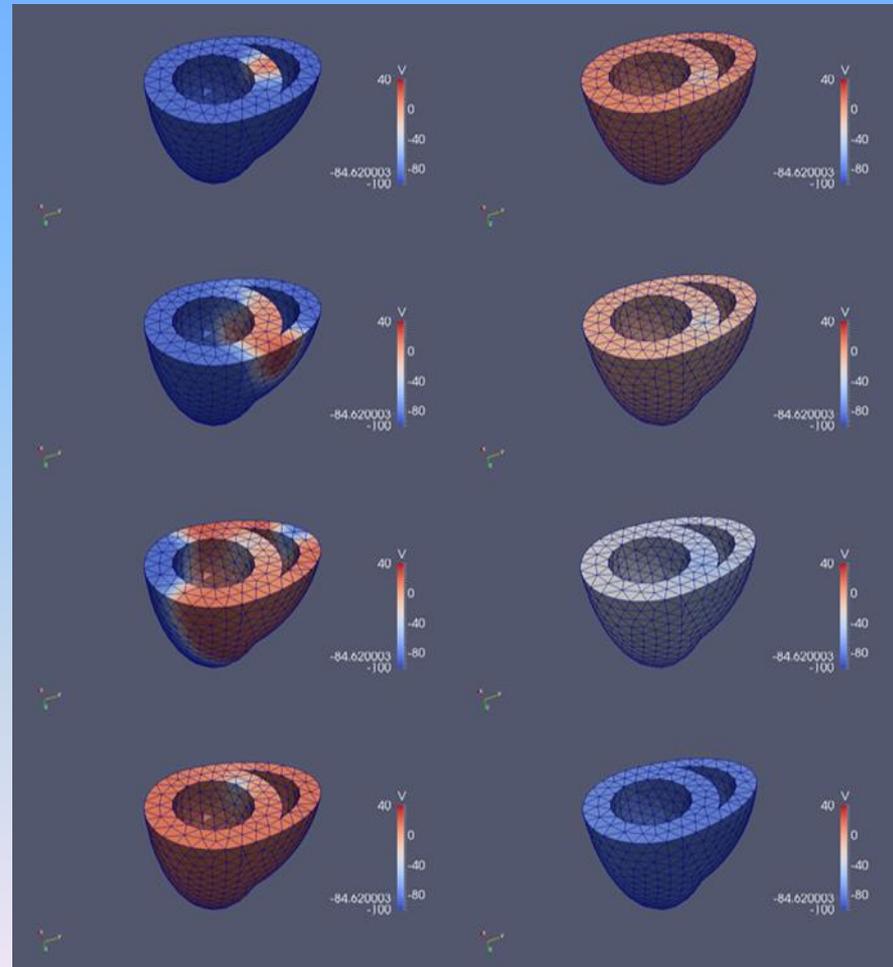
Analysis :1 Beat

- Thin membrane
  - The wave front and wave back propagated as expected
- Cubic Model
  - A range of diffusion values were tested and the range that seemed to work for this model was 0.07 to 0.13
  - The wave front propagated as expected
  - The wave back propagated but the propagation differed within the ranges
- Heart Model
  - Wave front propagated as expected
  - The voltage uniformly diffused across the whole model during the wave back.

2 Beats: Thin Membrane

- The program was modified to run multiple beats
- 1/16th of model is simulated
- 2nd heart beat was programmed to begin simulation after 400ms with a run time of 800ms as the Beeler-Reuter model showed that the first beat ended by 400ms
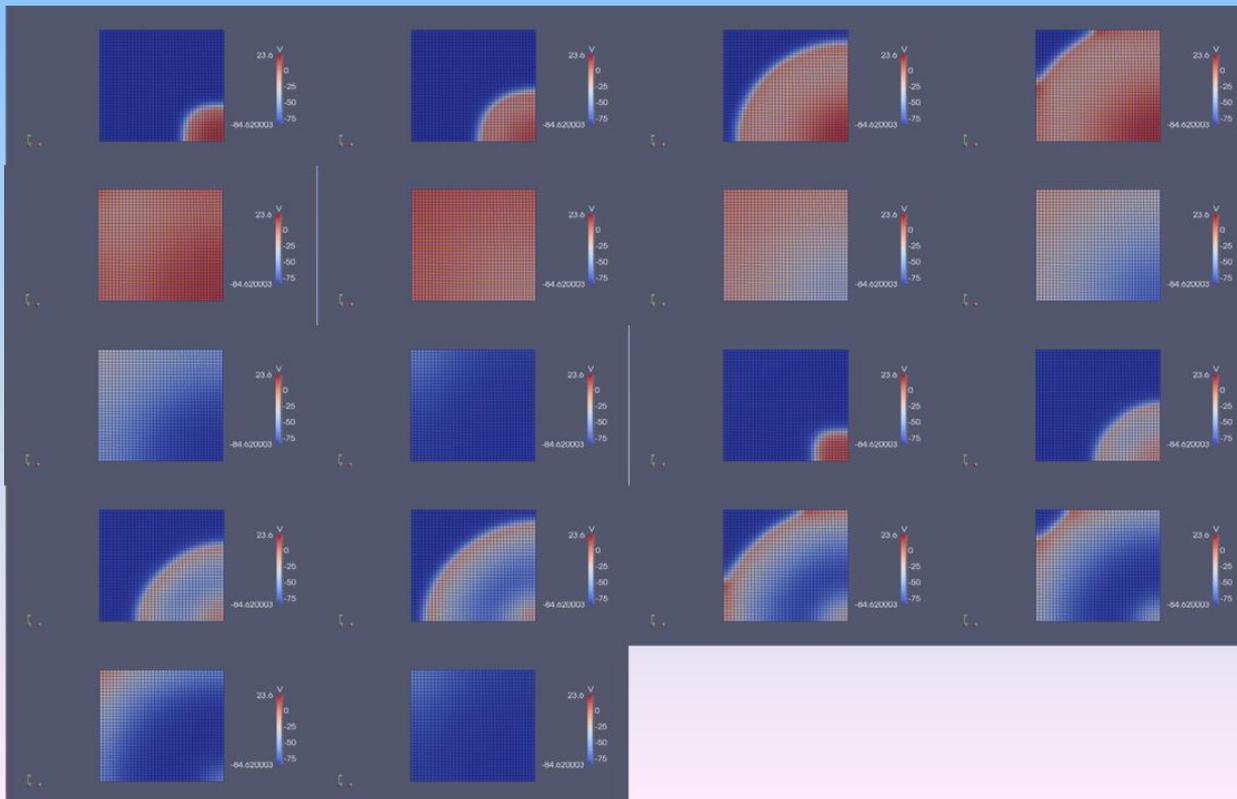
Simulation in Paraview of 2 beats using thin membrane model

Diffusion value: 0.01

Runtime: 400ms

Time step: 1ms

Cubic Model

- The same nodes simulated in the 1 beat model where simulated in the two beat model
- The second heart beat was programmed to begin after 600ms with a runtime of 1200ms
    - This was to ensure that the model there was enough time between the end of the first beat and second simulation
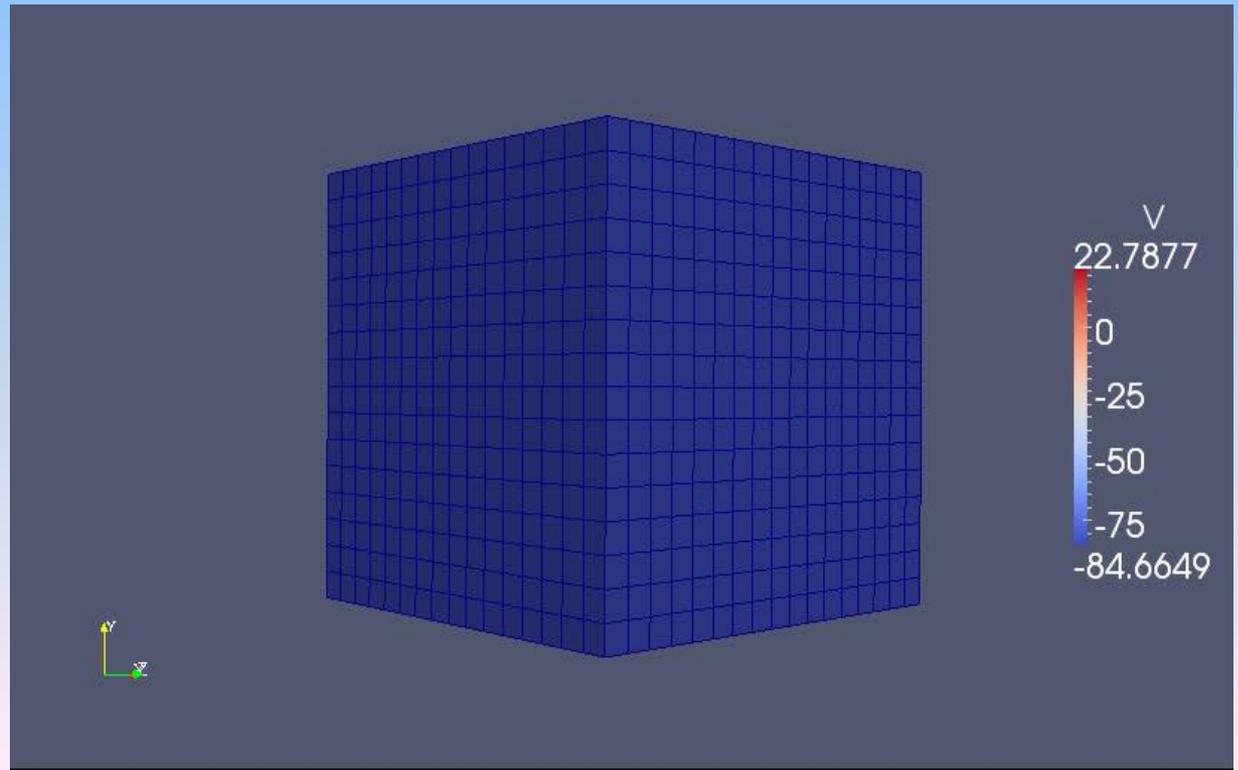
Heart Model

- Second heart beat was programmed to begin after 400ms and the runtime was 600ms
  - Since the time step for this model was 0.1, the runtime of 600ms was used to speed up computation results for the initial test
  - Upon successful completion of the initial test the runtime would have been increase to the replicate any desired number of beats
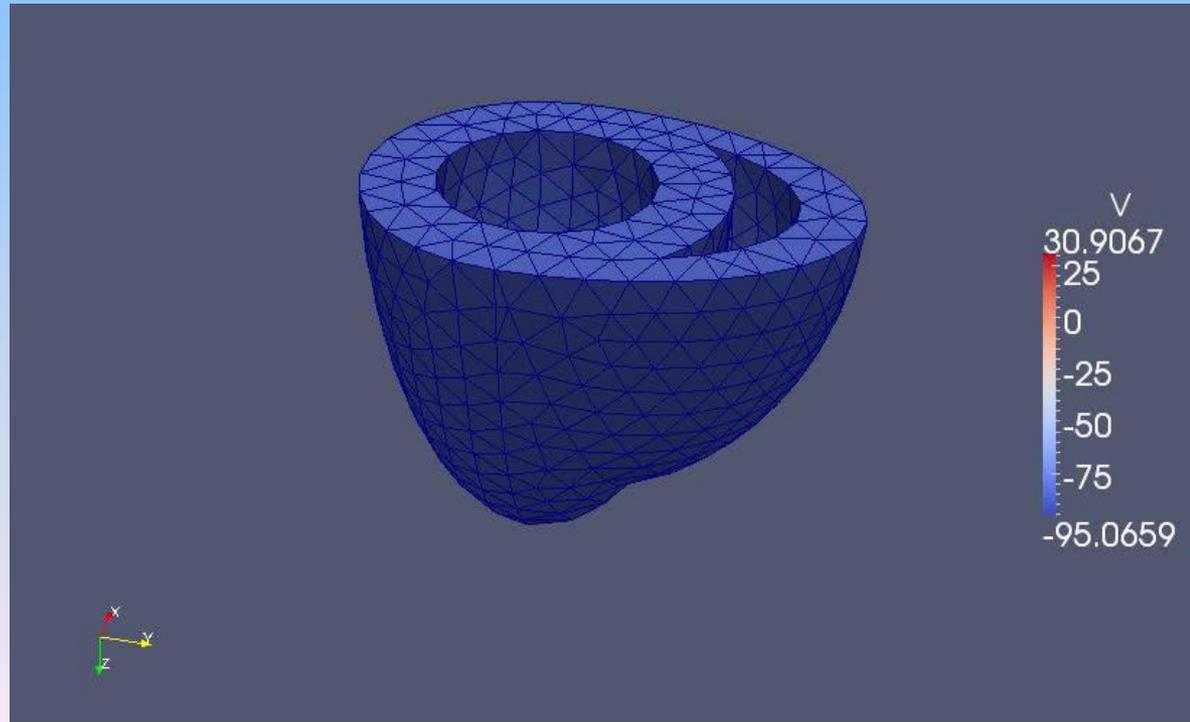
Analysis of 2 Beat

- Propagation of second beat occurred on thin membrane.

- Propagation of second beat did not occur on either the cubic model or the heart model.

- Various test were run to determine why the second beat was not propagating

Entire Nodes Simulated Test

- Thin membrane with all nodes simulated
- This test was to give confirmation if it worked that our program was working well. Since it did not give the desired results it confirmed that there was indeed something wrong with the program
- The irregular pattern developed in this simulation were reduced to two conclusions.
  - There was an issue with either the ode model or
  - There was an issue with the diffusion model of the program
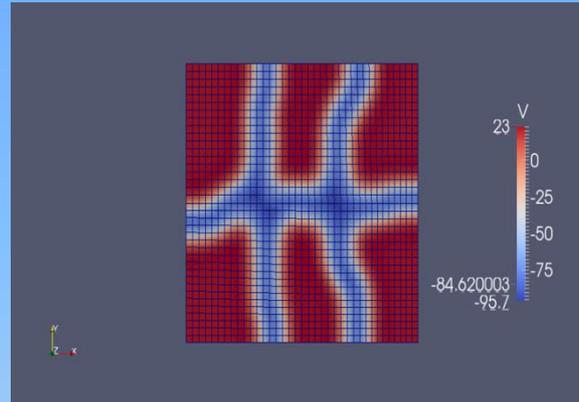
Simulation in Paraview with all nodes simulated
Diffusion value: 0.01
Runtime: 400ms
Time step: 1ms
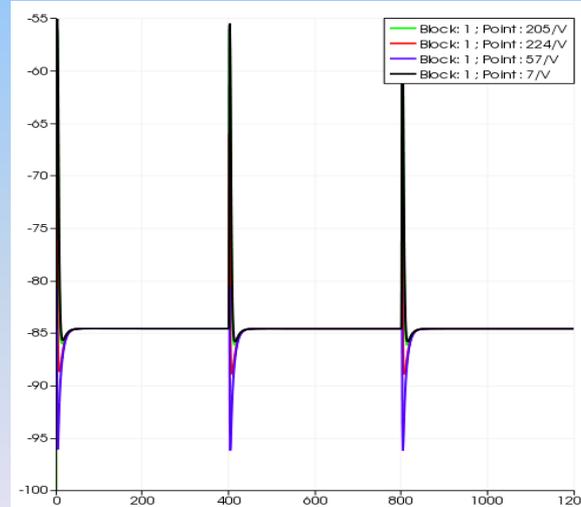
Plot in Paraview with all nodes simulated

Diffusion Test

- The first test to determine the problem with the code was the diffusion test
- All the other models of the program were turned of and the diffusion model was tested using the thin membrane model
- The Boundary condition applied to nodes in along the edge of the model
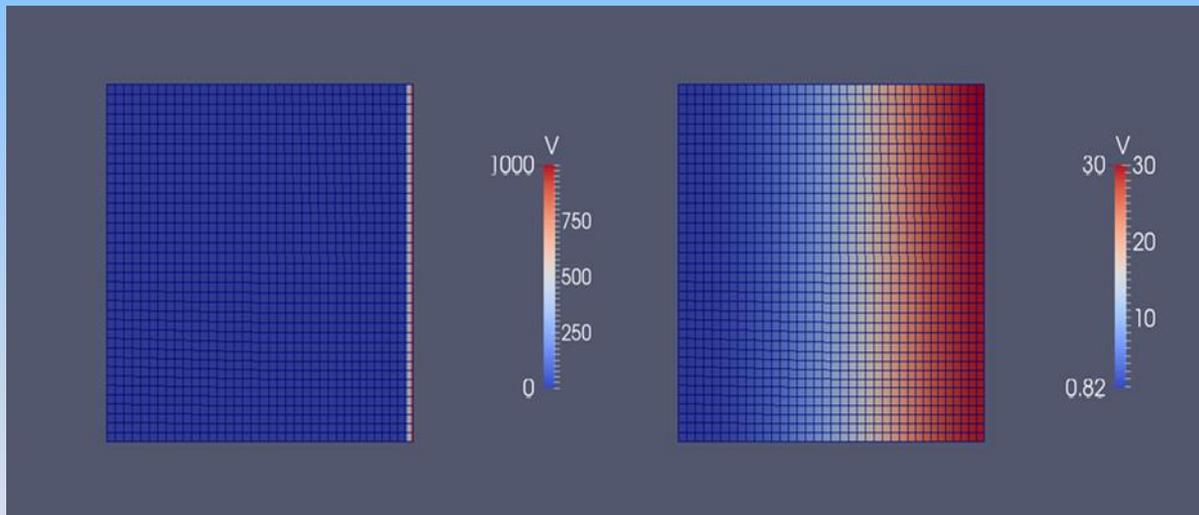
Simulation in Paraview of diffusion model
  Diffusion value: 0.01
  Runtime: 400ms
   Time step: 1ms

- The diffusion seemed to be working well although the propagation of the wave is not exactly parallel to the edge. This may be due to resolution

ODE Model Test

- The ode model was tested to determine if it was the reason behind the failed second beat
- The Plot generated was expected to be made up of multiple identical Beeler-Reuter model figures
- The initial beat was stimulated higher than the remaining beats
- It was determined that this was a physiological effect and therefore correct representation of the heart
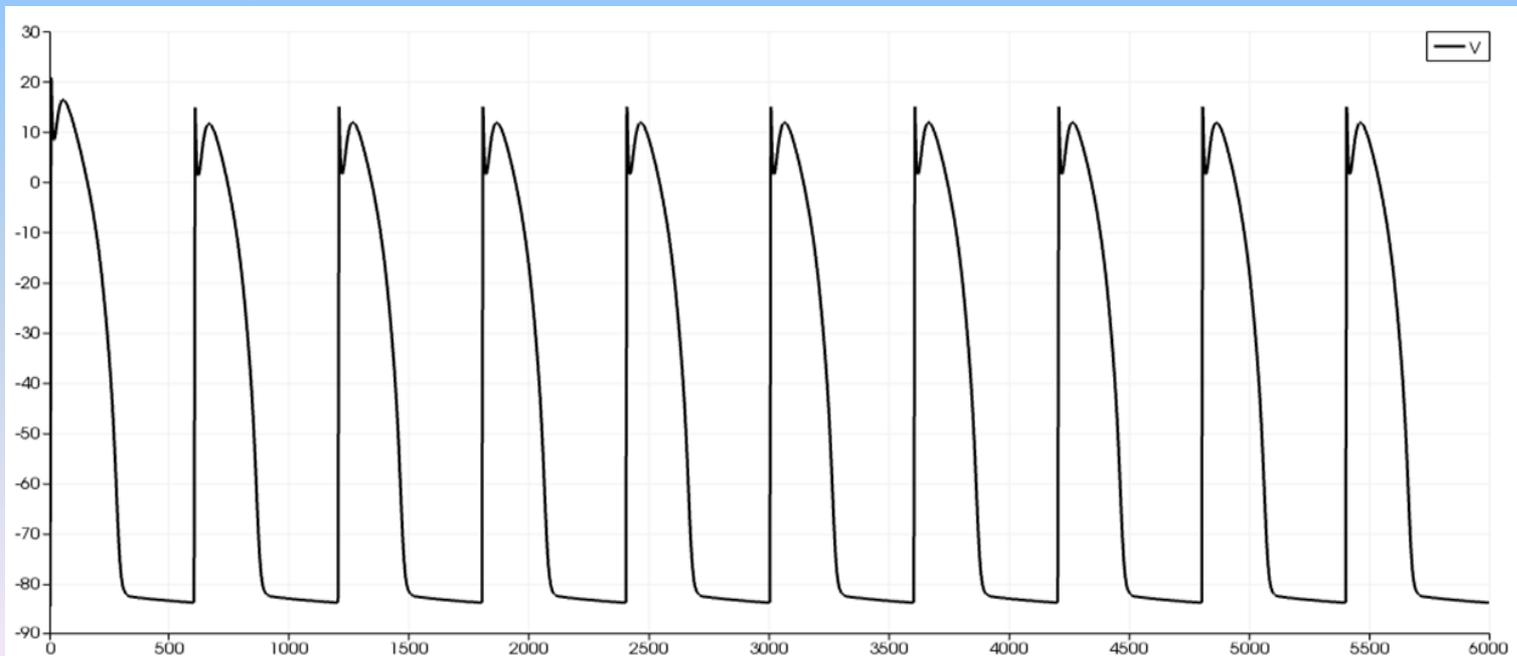
Plot of ten heart beats

Cubic Model Comparison Test

- The cubic model displayed slight difference in the wave propagation during the first and second beat depending on the diffusion value used from the determined ranges

- A comparison test of the second beat between both extremes of the range that is 0.07 and 0.13 showed the following results
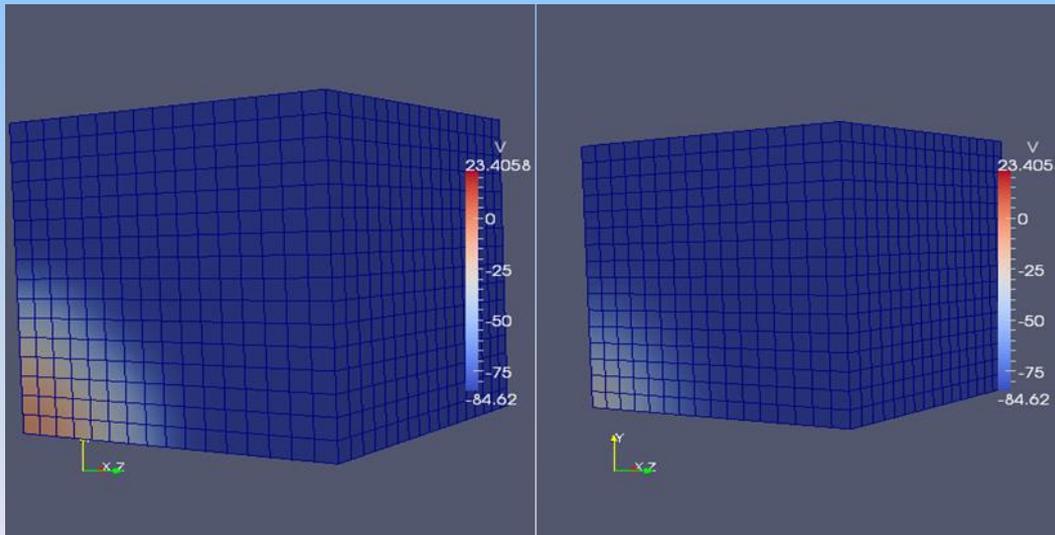
Simulation in Paraview of two beats of diffusion terms 0.07 and 0.13

Diffusion value: 0.01
Runtime: 400ms
Time step: 1ms

- The diffusion value of 0.07 was more efficient than that of 0.13 in wave propagation during the second beat although both propagations where incomplete

Plot of Nodes

- Three heart beats where simulated
- A plot of three nodes, one in the simulated region , another in the mid region and one at the other end was made
- Analysis of this plot showed that only the first beat in the stimulated region produced the desired graph. The remaining nodes portrayed wrong results and the remaining beats where totally different from what was expected
- The graph expected was to be similar to the graph obtained from the ODE mode for all the nodes
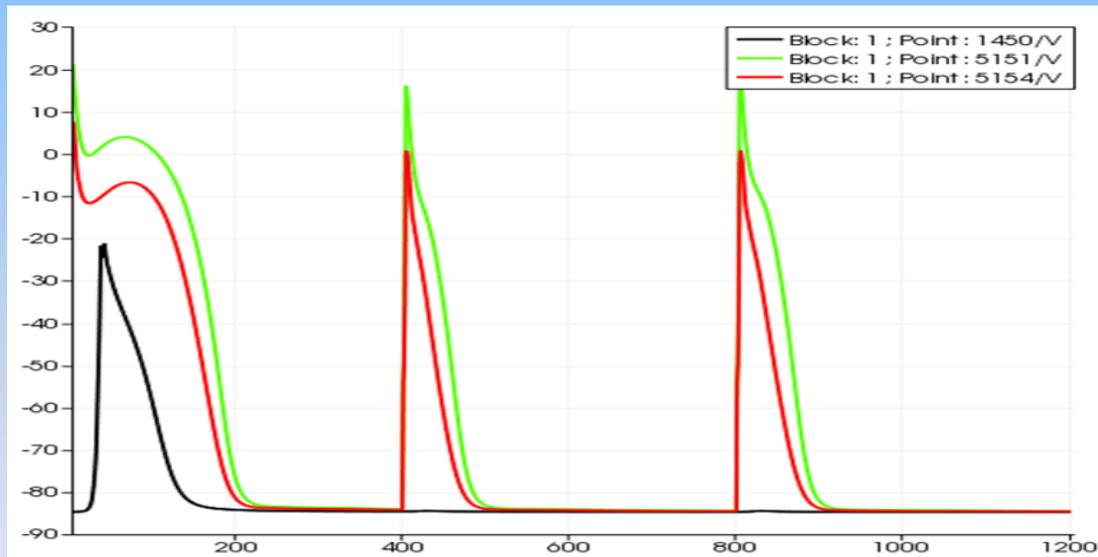
Plot of three nodes on cubic model in ParaView
Diffusion: 0.07
Runtime: 1200ms
Time step-1ms

- The results show that the program is not working as expected and that the discrepancy may be due to the diffusion model

Plot of Diffusion Test

- To confirm our conclusions a plot was made of a set of vertical nodes in the diffusion test
- The graph expected was uniform
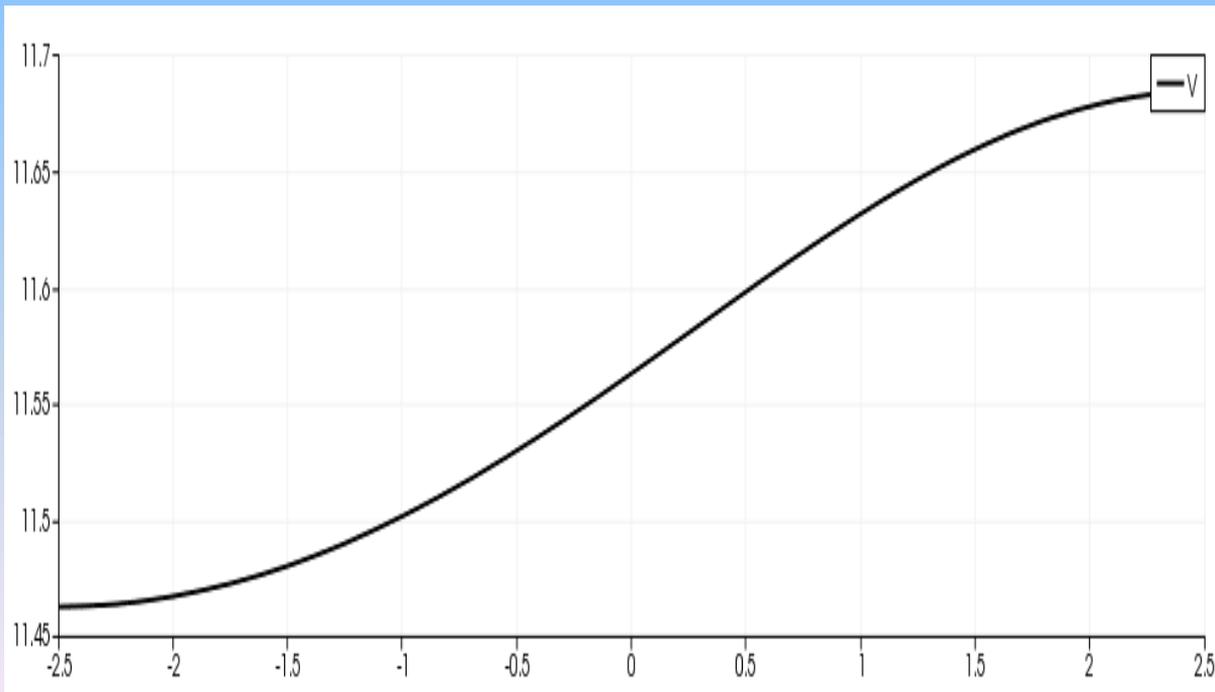
Plot of nodes on cubic model in ParaView
Diffusion: 0.01
Runtime: 400ms
Time step-1ms

Summary and Future Work

- Address and fix the diffusion model
- Work on the program to be able to solve and simulate the electrical model of the heart in multiple beats on both the thin membrane, cubic and heart model
- Adapt the model to test drugs and perform research useful to the Biomedical field

References

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- Fenton, Flavio H., Elizabeth M. Cherry, Harold M. Hastings, and Steven J. Evans. "Multiple Mechanisms of Spiral Wave Breakup in a Model of Cardiac Electrical Activity." Chaos: An Interdisciplinary Journal of Nonlinear Science 12.3 (2002): 852. Print.

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Questions?