

The Department of Electrical Engineering

nkrol

Mentors: Dr. Mohammad Imtiaz, Dr. Jing Wang & Dr. In Soo Ahn

AN ELECTRICAL ENGINEERING PERSPECTIVE OF THE HUMAN HEART

This research project investigates heart physiology from an electrical engineering perspective. The goal of this project is to help medical professionals gain a better understanding of the human heart and to investigate cardiac interactions with specific drugs and irregularities. By defining the cell as an electrical system, it is possible to simulate how membrane potential oscillations, called action potentials, occur in cardiomyocytes, and then propagate to stimulate heart contractions. To achieve this, the project uses the Hodgkin-Huxley based mathematical model as a building block to represent the ionic mechanisms underlying the initiation and sustenance of action potentials in a cell. The specific aim of this project is to investigate a one dimensional cardiac muscle cell system under different conditions, such as drug interactions and physical defects within part of the heart.

Contents

Acknowledgements.....	3
Table of Figures.....	4
Introduction	5
Heart Physiology	5
Heart as an Electrical System	6
Cable Model	7
Heart Abnormalities and Drug Interaction	8
Project Scope	8
Methods.....	9
Partial Differential Equations and Reaction-Diffusion System	9
Numerical Method: Forward-Difference	9
Framework	9
Results.....	10
Single Cell.....	10
Heat Equation	13
Multi-cell cable model	26
Defects and Drug Interaction.....	29
Conclusion.....	32
Main Conclusion.....	32
Future Work.....	32
References	33

Acknowledgements

This project would not have been possible without the aid and guidance of my senior project advisor Dr. Mohammad Imtiaz, whose encouragement and support drove my interest for this project.

I would also like to show my gratitude to Dr. In Soo Ahn, Dr. Aleksander Malinowski, Mr. Christopher Mattus, and to everyone else who supported me in any respect during the completion of my project.

Table of Figures

Figure 1: The Electrical System of the Heart.....	5
Figure 2: Excitable Cell as an Electrical Circuit.....	6
Figure 3: Action Potential of Cardiac Muscles.....	7
Figure 4: Cable Model of Excitable Cells.....	8
Figure 5: Cable Model with Differential Equations.....	9
Figure 6: Single Cell Membrane Voltage over Time.....	11
Figure 7: Single Cell Gate Value over Time.....	12
Figure 8: Gate m.....	12
Figure 9: Heat Flow Visual.....	13
Figure 10: Standard Heat Source.....	15
Figure 11: Temperature-Space Plot of Standard Heat Source.....	15
Figure 12: Standard Heat Source with Increased K Coefficient.....	16
Figure 13: Temperature-Space Plot with Increased K Coefficient.....	16
Figure 14: Standard Heat Source with Small K Coefficient.....	17
Figure 15: Temperature-Space Plot with Small K Coefficient.....	17
Figure 16: Oscillating Heat Source without Initial Condition.....	18
Figure 17: Temperature-Space Plot with Oscillating Heat Source.....	19
Figure 18: Oscillating Heat Source with Large K Value.....	19
Figure 19: Temperature-Space Plot with Oscillating Source and Large K Value.....	20
Figure 20: Oscillating Heat Source with Small K Value.....	20
Figure 21: Temperature-Space Plot with Oscillating Heat Source and Small K Value.....	21
Figure 22: Oscillating Heat Source with Increased Frequency.....	21
Figure 23: Temperature-Space plot with Oscillating Source and High Frequency.....	22
Figure 24: Oscillating Heat Source with Low Frequency.....	22
Figure 25: Temperature-Space Plot with Oscillating Source and Low Frequency.....	23
Figure 26: Oscillating Heat Source with Low Frequency placed at $x = 51$	24
Figure 27: Temperature-Space Plot of Oscillating Heat Source with Low Frequency @ $x = 51$	24
Figure 28: Oscillating Heat Source with High Frequency placed at $x = 51$	25
Figure 29: Temperature-Space Plot of Oscillating Heat Source with Low Frequency @ $x = 51$	25
Figure 30: Voltage Potential Colormap.....	26
Figure 31: Multi-cell Model Voltage over Time.....	27
Figure 32: Multi-cell Model Plot of h Gate.....	28
Figure 33: Multi-cell Model Plot of m Gate.....	28
Figure 34: Multi-cell Model Plot of n Gate.....	28
Figure 35: Voltage Potential Colormap with Increasing Capacitance.....	29
Figure 36: Drug and Defect Interaction with the Heart's Electrical System.....	31

Introduction

Heart Physiology

The human heart is a muscular organ which pumps blood throughout the body ensuring every cell receives enough oxygen and nutrients to function. The heart is divided into four chambers, including the upper left and right atria; and the lower left and right ventricles. In order for the heart to pump blood correctly throughout the body, the heart must contract in a specific and organized manner which begins with a group of pace-making cells within the sinoatrial node. The sinoatrial node is located in the right atrium and activates a focal event with the initial depolarization occurring due to a difference between the voltages inside the cell compared to outside the cell. From this initial action potential within the sinoatrial node, the signal propagates throughout the heart through purkinje fibers which eventually lead to the muscle of the heart and start the contraction to push blood from the ventricles out to the pulmonary artery and the aorta.

Electrical System of the Heart

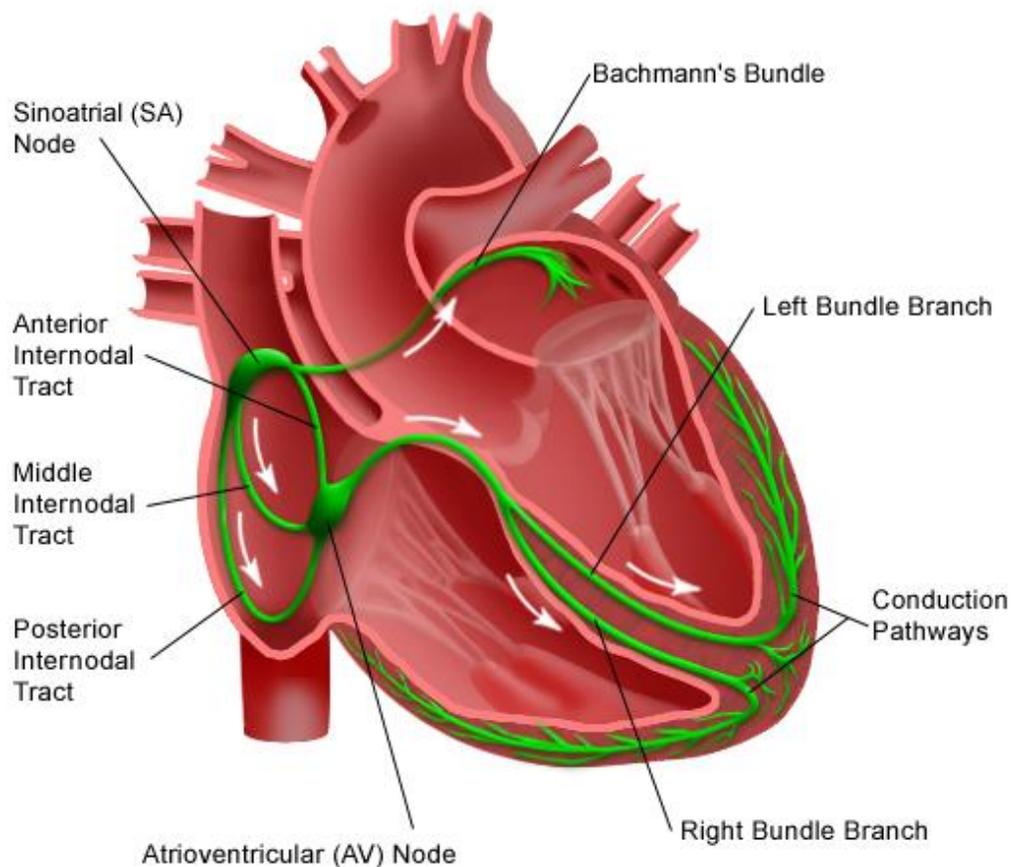


Figure 1: The Electrical System of the Heart

Heart as an Electrical System

In 1963 Alan Lloyd Hodgkin and Andrew Fielding Huxley received the Nobel Prize in Physiology & Medicine for their mathematical model which describes the initiation and propagation of action potentials in a giant squid axon. The Hodgkin-Huxley mathematical model, which is made up of nonlinear differential equations approximate the electrical characteristics of excitable cells such as cardiac myocytes (cardiomyocyte). This is essential to the study of biology from an electrical engineering perspective because each cardiomyocyte can be drawn as an electrical circuit. In figure 2, the basic circuit represents an excitable cell. The capacitor C_m represents the capacitance of the cell membrane. The voltage-gated and leak ion channels are represented by nonlinear g_n and linear g_L conductances. The electrochemical gradients driving the flow of ions are represented by batteries (E_n and E_L), and the ion exchangers are represented as current sources (I_p). Using the Hodgkin-Huxley mathematical model as a building block, it is possible to investigate heart function and dysfunction through the computerized simulations of these electrical propagations. Each cardiac action potential is due to a brief change in voltage (membrane potential) across the cell membrane of the cardiomyocytes. This is caused by ions flowing in and out of the cell through ion channels (shown in detail in Figure 3). All cardiac muscle cells are electrically linked to one another by structures known as gap junctions, which allow the action potentials to propagate throughout the heart and cause contractions which pump blood throughout the body.

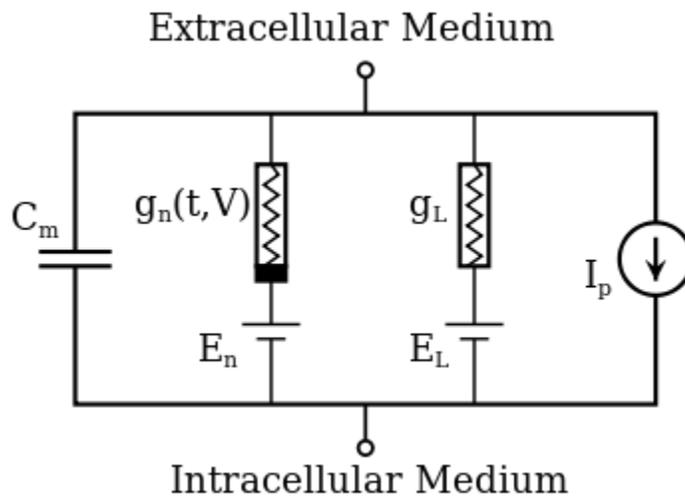


Figure 2: Excitable Cell as an Electrical Circuit

Action potential of cardiac muscles

Grigoriy Ikonnikov and Eric Wong

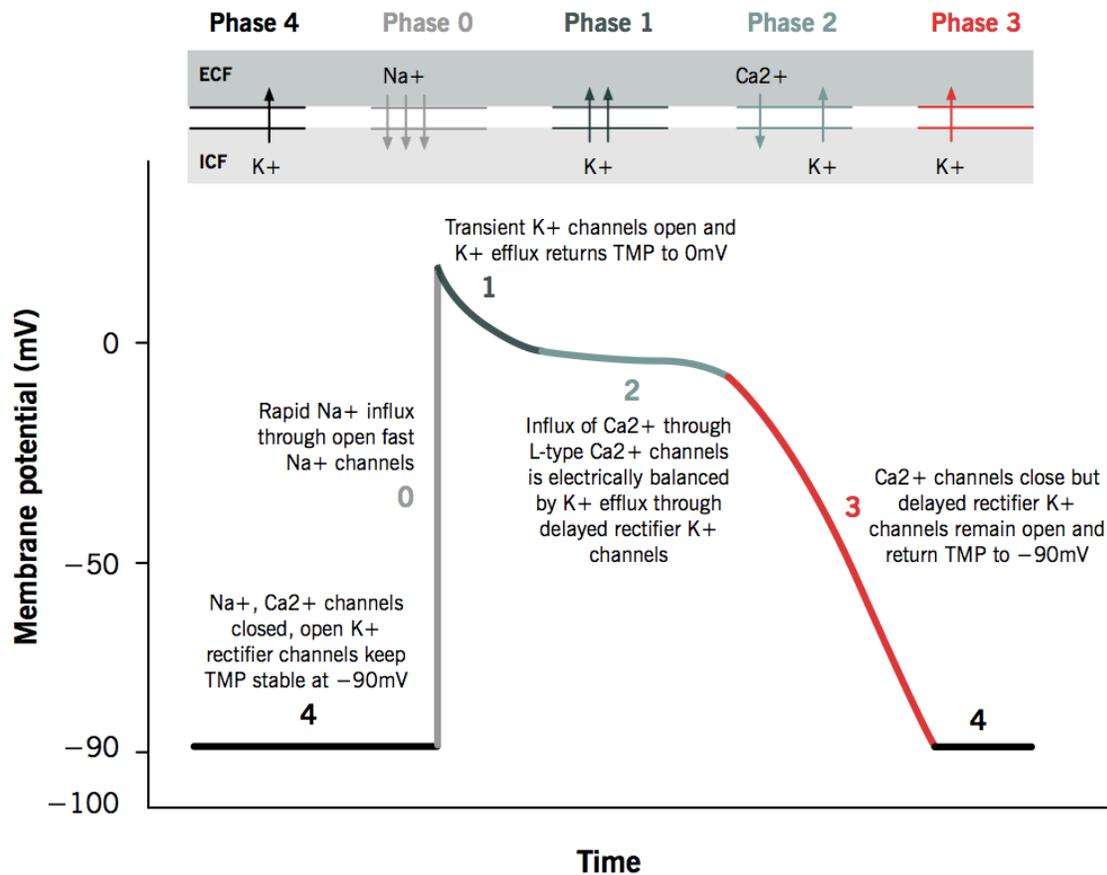


Figure 3: Action Potential of Cardiac Muscles

Cable Model

Since an individual cell can be represented as an electrical circuit and simulated through means of computer software, multi-cell models can be created due to the fact that each cardiomyocyte is linked to each other. The next stage of investigating excitable heart cells is to develop a one-dimensional system called a cable model. A simplified one-dimensional version of a cable model is shown in Figure 4. In order to develop the electrical cable model, an investigation of heat diffusion is helpful. Heat flow and diffusion is very similar to the propagation of current in a cable. Heat flow is an example of a parabolic partial differential equation, where the temperature in time and space are not represented directly, but through its derivative. There are two derivatives time and space, therefore the heat equation is a partial differential equation rather than an ordinary differential equation with only one derivative. The purpose of studying heat flow is due to the numerous similarities to electrical current flow, therefore this is a perfect stepping stone to better understanding electrical current in the human heart.

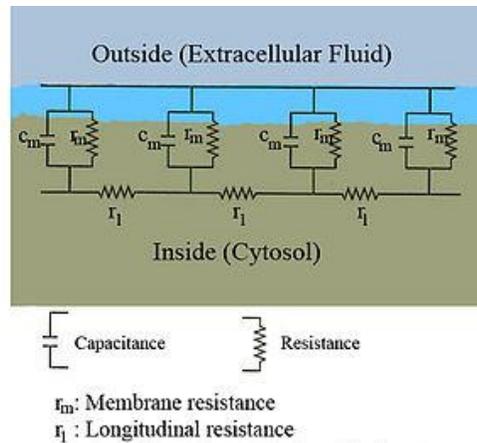


Figure 4: Cable Model of Excitable Cells

Heart Abnormalities and Drug Interaction

The cardiac conduction system is the foundation of both normal and abnormal heart rhythms. Understanding the normal conduction process allows the investigation of abnormal conduction patterns and provides the capability of unraveling the mechanisms contributed to heart arrhythmias of all types. Additionally, by understanding the foundation of the heart's conduction system, drug interaction can be investigated and simulated before testing on humans.

Project Scope

The scope of this project involves several major topics which have been researched and investigated throughout two semesters. The beginning of the project was mostly research based. Most of the initial time dedicated to working on the project went into understanding the Hodgkin-Huxley mathematical model, then taking their research to develop Matlab scripts in order to simulate the excitation of cardiac cells. The next major step was to investigate a single cell's action potential caused by ions flowing in and out of the cell in Matlab. The next phase of the project involved understanding and investigating the heat diffusion equation and simulating the process in Matlab. The final stage of the project involved expanding the programs to simulate a one-dimensional cable of excitable cells and to then vary the parameters representing different heart dysfunction and defects.

Methods

Partial Differential Equations and Reaction-Diffusion System

The matlab programs used to investigate excitable heart cells contain four ordinary differential equations to simulate the individual cell's membrane potential, followed by a partial differential equation which links each cell to each other. The programs resemble a reaction-diffusion system which is a mathematical model which corresponds to several physical phenomena; in this case the change is in space and time while looking at the concentration of specific ions within a cell.

Numerical Method: Forward-Difference

The forward difference method was chosen to estimate the differential equations making up the cell's action potentials. The reason for choosing this method was due to the simplicity of being able to create a matlab program to estimate the four differential equations that were being solved simultaneously. However, the forward difference method is not the most efficient form within the finite difference approximation arsenal. The forward difference method is an explicit method for solving the action potentials in a cell and simulating a cable model between many cells. It is difficult to maintain a numerically stable and convergent explicit method in this scenario due to the fact that the convergence factor $r \leq \frac{1}{2}$. In order to achieve this, the time step in our program needs to be very small with a larger distance x . With these values, the matlab program can become very tedious and will take a long time to process the differential equations over many time steps.

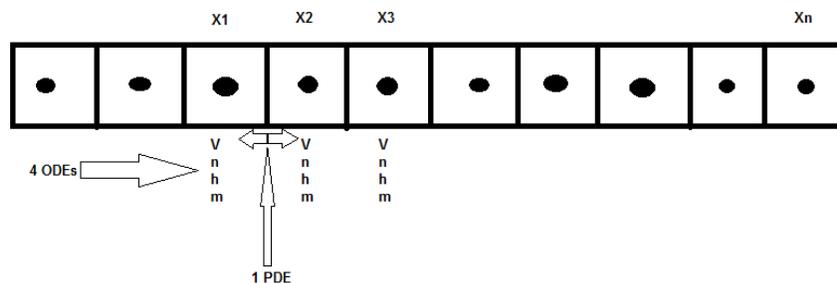


Figure 5: Cable Model with Differential Equations

Framework

All Matlab simulations were run on version R2015a. The computer specifications are as follows: Intel Core i5-4670K CPU @ 3.40 GHz. 8.00GB Installed memory (RAM). 64-bit Windows 8.1 Pro Operating System.

Results

Single Cell

The Hodgkin-Huxley model defines the current flowing through the cell membrane in equation 1 where C_m is the capacitance of the cell membrane and V_m is the membrane voltage.

$$I_C = C_m \frac{dV_m}{dt}$$

Equation 1

Additionally, the current through a given ion channel is the product shown in equation 2 where V_i is the reverse voltage potential of the i -th ion channel.

$$I_i = g_n(V_m - V_i)$$

Equation 2

A cell with sodium and potassium ion channels (excluded calcium channel for simplicity), the total current through the membrane is shown in equation 3.

$$I = C_m \frac{dV_m}{dt} + g_K(V_m - V_K) + g_{Na}(V_m - V_{Na}) + g_l(V_m - V_l)$$

Equation 3

According to the Hodgkin-Huxley mathematical model, I is the total membrane current, C_m is the membrane capacitance, g_K and g_{Na} are the potassium and sodium conductances, V_K and V_{Na} are the ion reversal voltage potentials and g_l and V_l are the leak conductance and leak reversal potential. Furthermore, Hodgkin-Huxley research led to modeling the properties of an excitable cell with a set of four ordinary differential equations. In addition to equation 3, they developed equations 4, 5 and 6 to represent gates within the ion channels which allow the flow of ions in and out of the cell.

$$\frac{dn}{dt} = \alpha_n(V_m)(1 - n) - \beta_n(V_m)n$$

Equation 4

$$\frac{dm}{dt} = \alpha_m(V_m)(1 - m) - \beta_m(V_m)m$$

Equation 5

$$\frac{dh}{dt} = \alpha_h(V_m)(1 - h) - \beta_h(V_m)h$$

Equation 6

Using Hodgkin and Huxley's research as a building block, a Matlab function was created to simulate the influx and efflux of ions in a single cell based on three gates (n , m and h). The final result is shown in figure 6, which resembles the ideal action potential of a cardiac cell (figure 3).

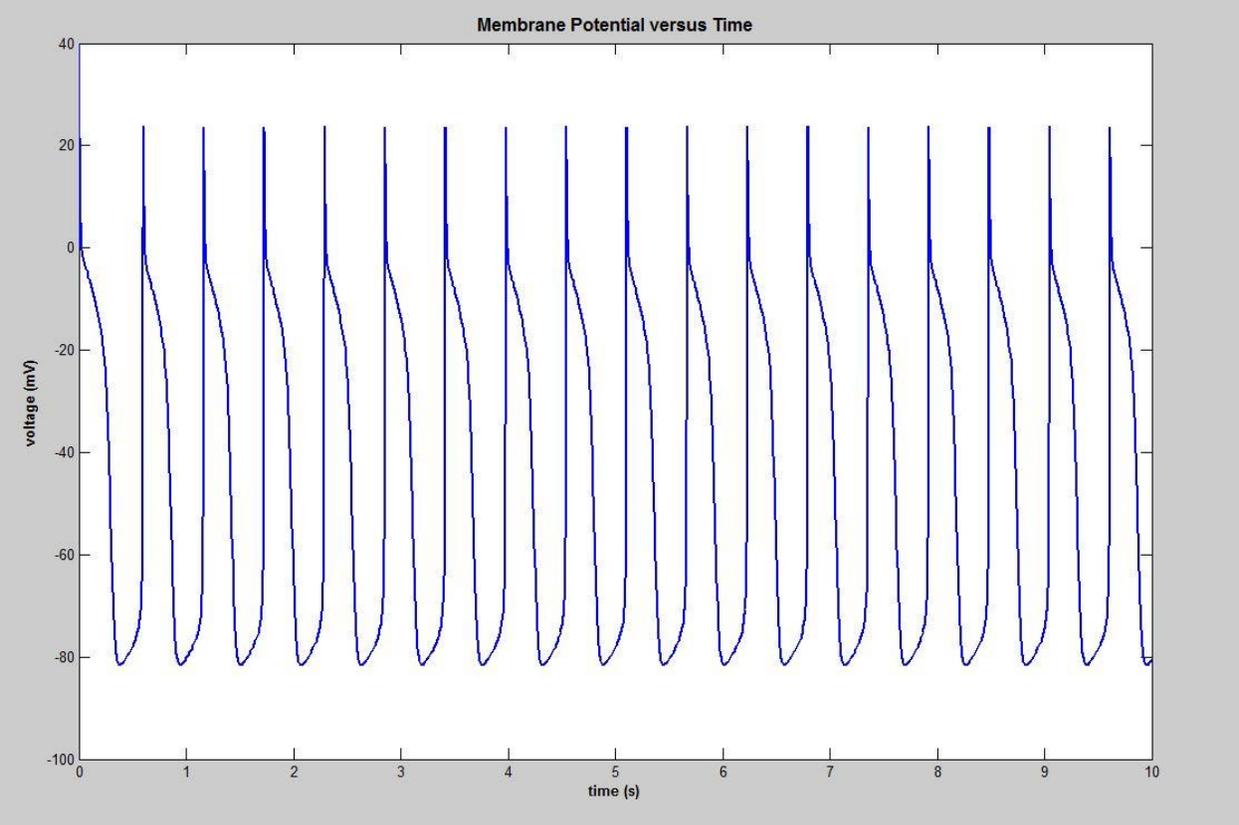


Figure 6: Single Cell Membrane Voltage over Time

Investigating the process further, each gate can be plotted over time to determine their effect of the action potential. In figure 7, each gate opens and closes the same amount of times as the membrane potential spikes to a positive value. The gates oscillate at nearly the same frequency as the voltage membrane potential in figure 6, with a slight offset which gives the membrane potential its unique shape.

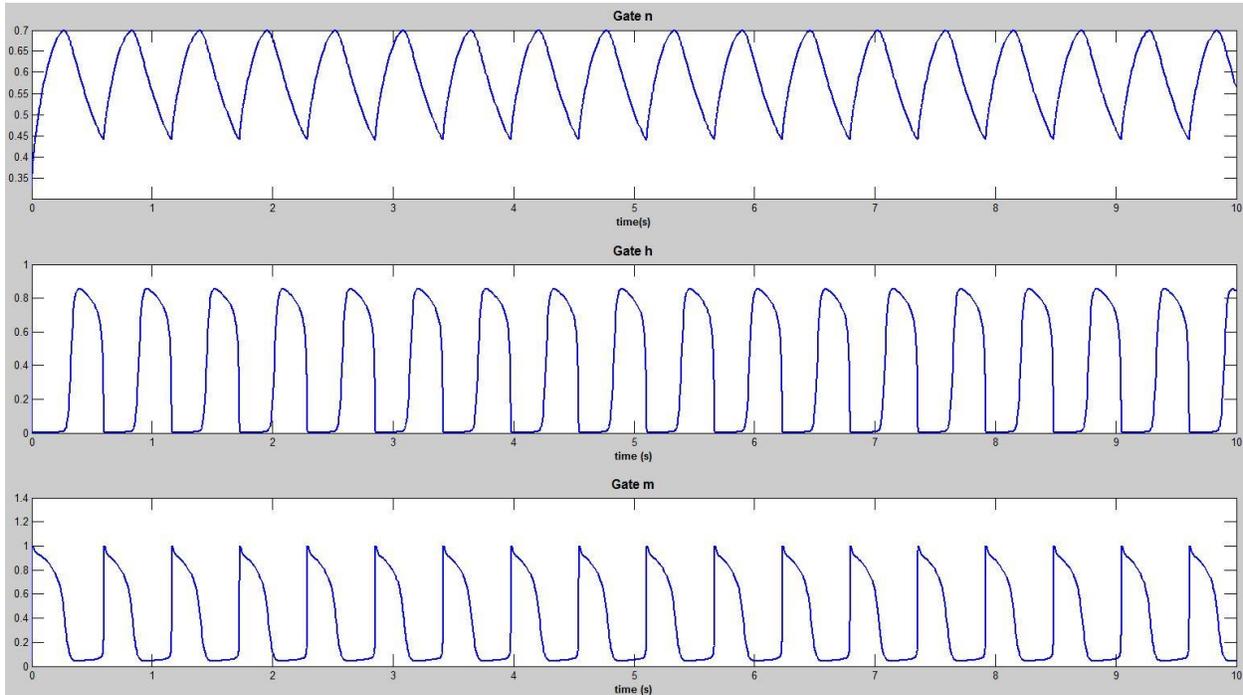


Figure 7: Single Cell Gate Value over Time

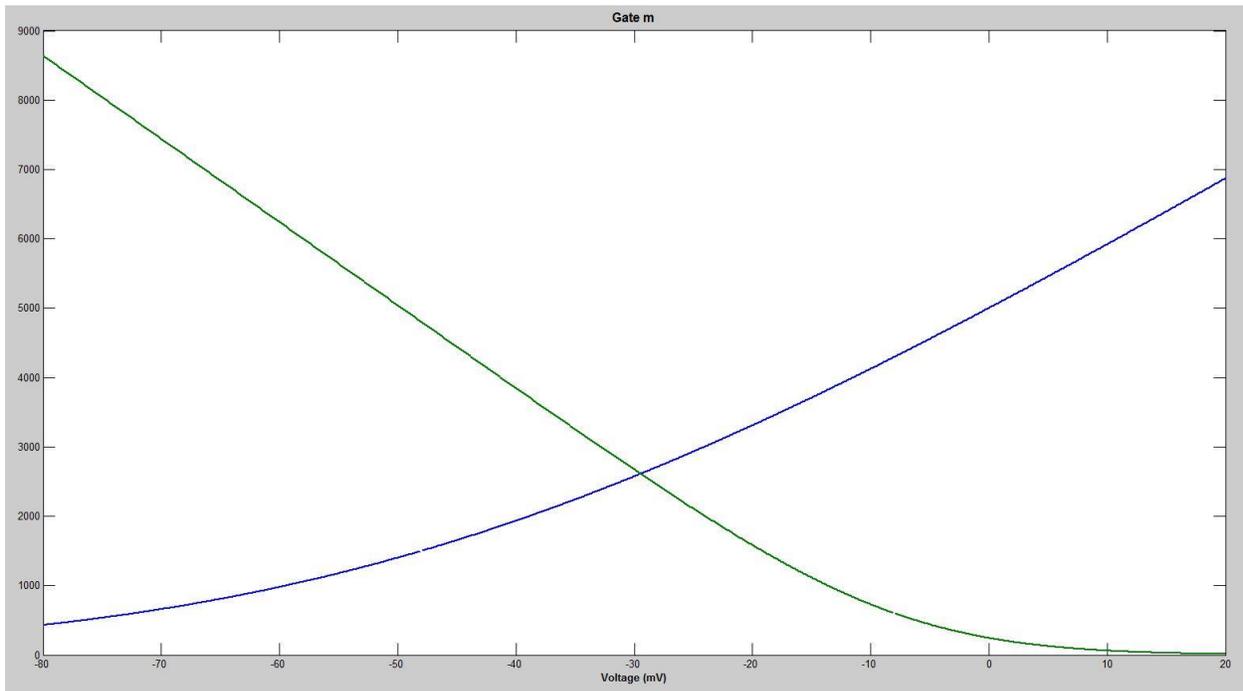


Figure 8: Gate m

Heat Equation

The investigation on heat flow and diffusion helped understand the propagation of current in cardiac cells. Heat flow is an example of a parabolic partial differential equation. In figure 9, a graphic depicts the basic theory behind the heat equation. Assume the red arrow is a heat source, heating a rod of X length. The heat will diffuse through the rod from the flame, in an exponentially decreasing manner as shown in the graph. Depending on the material, the heat will diffuse further in the length of the rod, or may not diffuse at all. The graph shows the heat decaying over the distance from the heat source, eventually reaching a steady-state value which usually represents the ambient temperature.

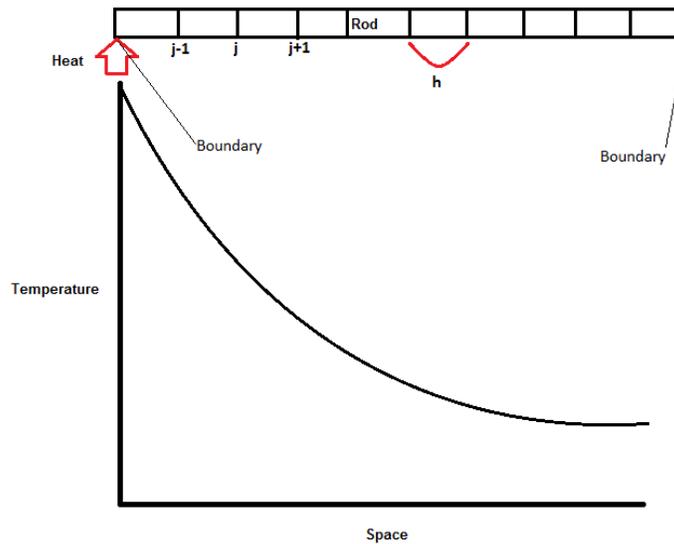


Figure 9: Heat Flow Visual

The heat equation is shown as equation 7. The alpha value is a constant which is specific to the material of the object under experimentation. Equation 9 represents the main formula for estimating the heat diffusion at a given point in a one-dimensional object. At the given point, the heat is calculated by taking the previous and following points and subtracting two times the point under observation. The resulting quantity is multiplied by a coefficient K which depends on the material of the object, and then dividing everything by the squared space between each point. The boundary conditions are represented in equations 10, 11 and 12. In equation 10 and 11, the initial point of the one dimensional system is calculated by subtracting the initial point from the next and dividing by the space between each segment. Similarly, equation 11 calculates the same initial temperature, but adds a sinusoidal waveform which will simulate an oscillating heat source. The frequency for the sinusoid in equation 11 was arbitrarily chosen. In equation 12, the ending temperature is calculated by using the last two points in the one dimensional system.

$$\frac{\partial u}{\partial t} = \alpha \nabla^2 u$$

Equation 7

$$\nabla^2 = \frac{\partial^2 u}{\partial x^2}$$

Equation 8

$$\nabla^2 U = K(U_{j-1}^n + U_{j+1}^n - 2U_j^n)/h^2$$

Equation 9

$$temp(initial) = (K((j + 1) - j))/h$$

Equation 10

$$temp(initial) = (K((j + 1) - j + 11\sin(0.001\pi t)))/h$$

Equation 11

$$temp(final) = (K(j - (j - 1)))/h$$

Equation 12

Working with Dr. Imtiaz, a Matlab script was created in order to simulate the propagation of heat through one dimension. The primary figure of the script yielded a color map of the heat diffusion in the nodes created in a matrix. The following figures represent dimensionless time on the x-axis, and dimensionless space on the y-axis. Figure 10 shows the standard, non-oscillating heat source at the starting point (t=0). An arbitrary value of 50 was chosen to be the initial condition. An arbitrary value of 13 was chosen for the K coefficient. In this figure it is seen that the initial condition starts as a bright yellow point and slightly diffuses. In Figure 11, a plot shows the temperature change through the one dimensional system at different time iterations. The step size of the timing was chosen to be 0.01 units ending at an arbitrary final time of 511; therefore there are 51,100 (511/0.01) iterations to calculate the heat diffusion through the entire system. The first blue line shows the change in temperature through the space of the material at the initial iteration. In reference to the blue line, one will see the initial condition of 50 at the start then an immediate drop to zero because there was no time for the heat to diffuse through the one dimensional system. The second, red, line shows the heat diffusion through space at iteration 15. Similar to the blue line, the red line barely has a curve because not much time has passed for the heat to diffuse. The yellow and purple lines are the 2,555th and 5,110th iterations respectively. Both yellow and purple lines decay exponentially, resembling figure 9 which describes the basic theory behind the heat equation and how heat diffuses. The green line plots the final time iteration and shows that the temperature at t=0 has already decayed to roughly half of the initial condition of 50.

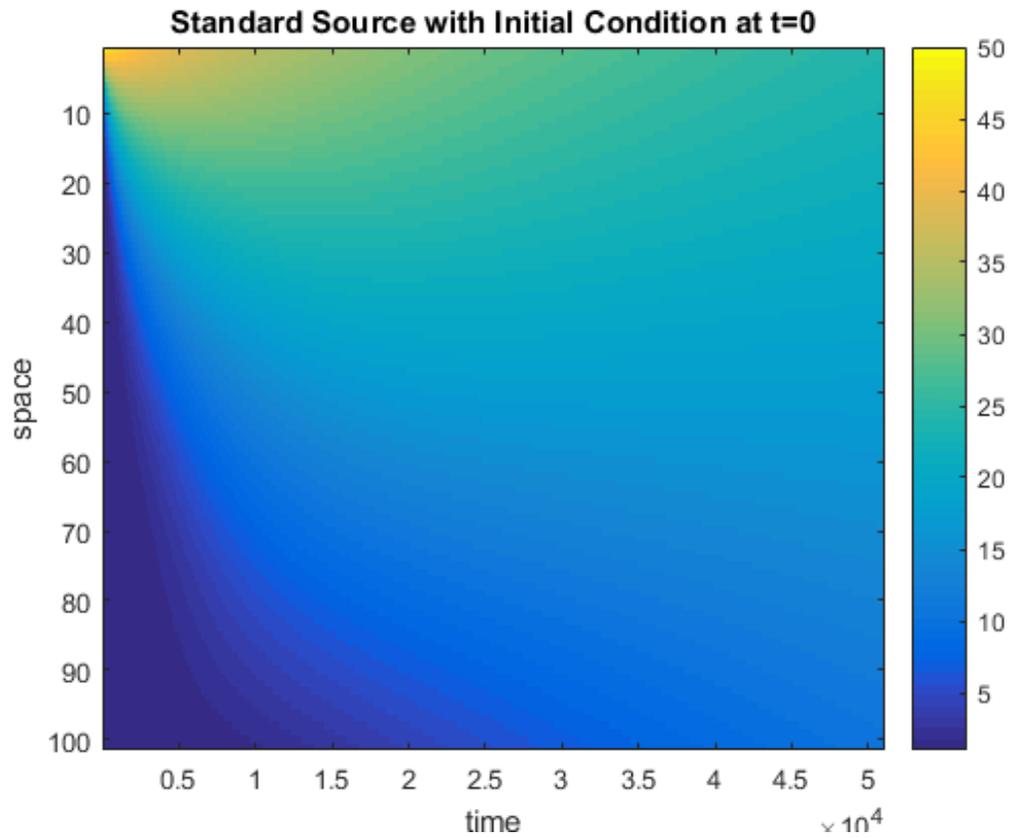


Figure 10: Standard Heat Source

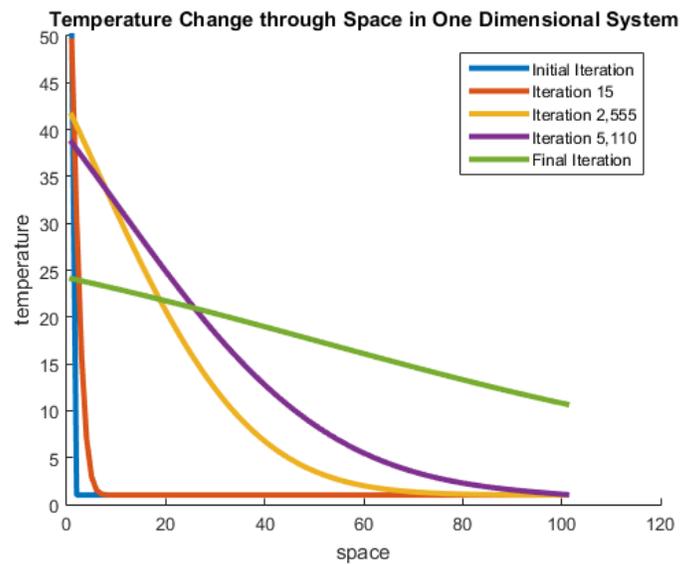


Figure 11: Temperature-Space Plot of Standard Heat Source

Figure 12 is the same non-oscillating source with initial condition of 50. The difference in this figure is that the coefficient of K was greatly increased to a value of 50 (originally 13). The figure shows that with a higher coefficient, the heat diffuses in more space than with a lower value of K.

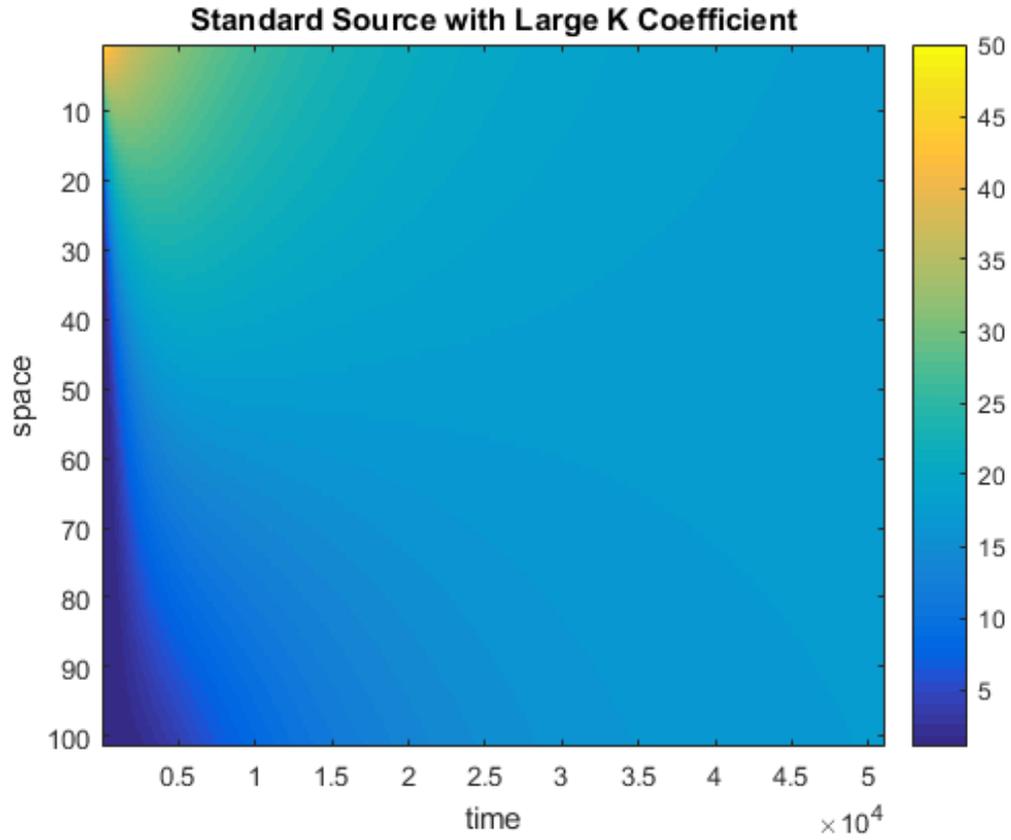


Figure 12: Standard Heat Source with Increased K Coefficient

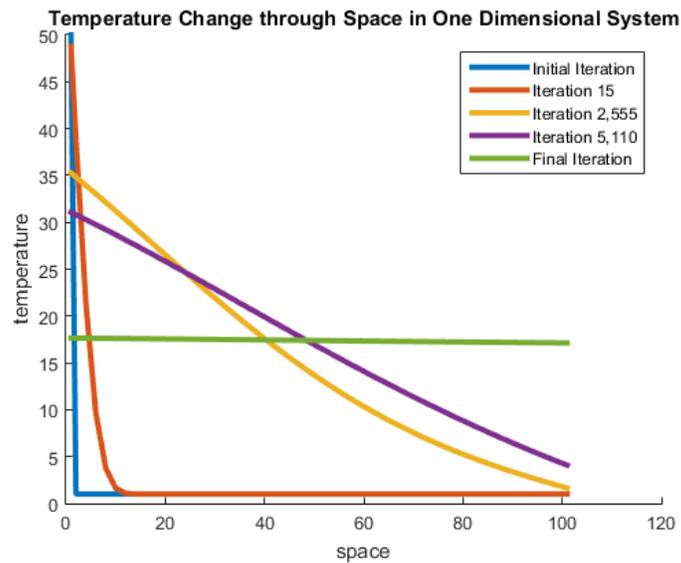


Figure 13: Temperature-Space Plot with Increased K Coefficient

Contrary to figure 12, figure 14 shows the same heat source with a value of 1.3 for the K coefficient instead of the original value of 13. From both of these figures, we can conclude that this coefficient relates to how easily heat diffuses through the material.

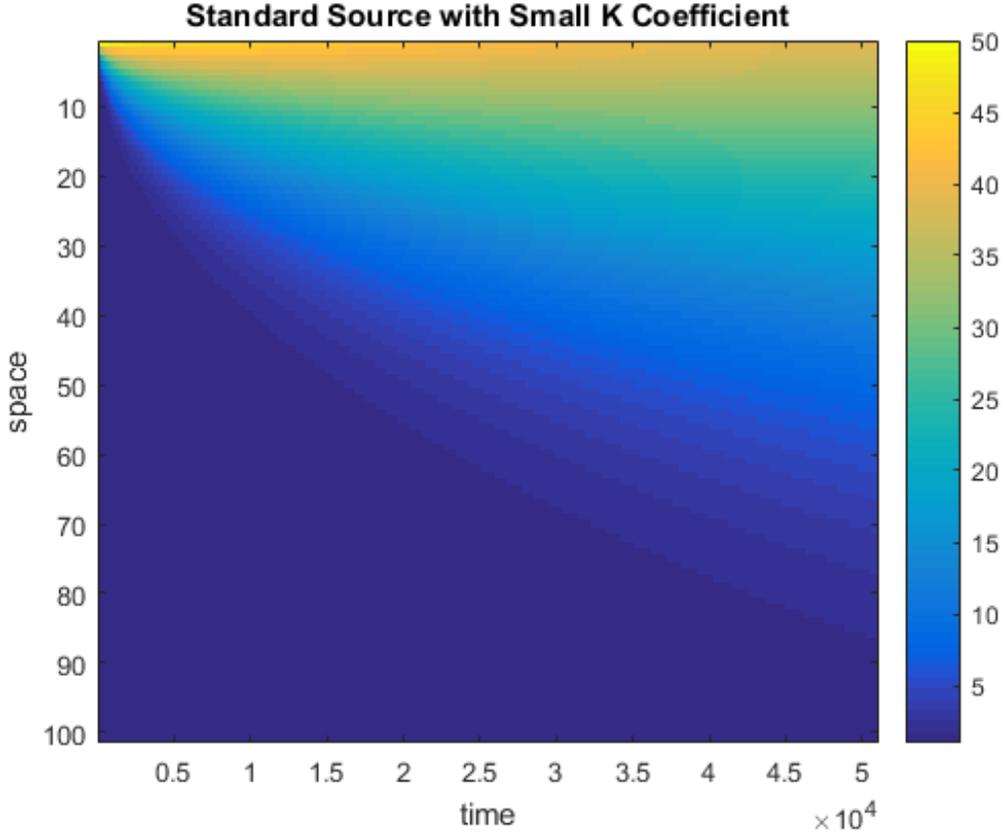


Figure 14: Standard Heat Source with Small K Coefficient

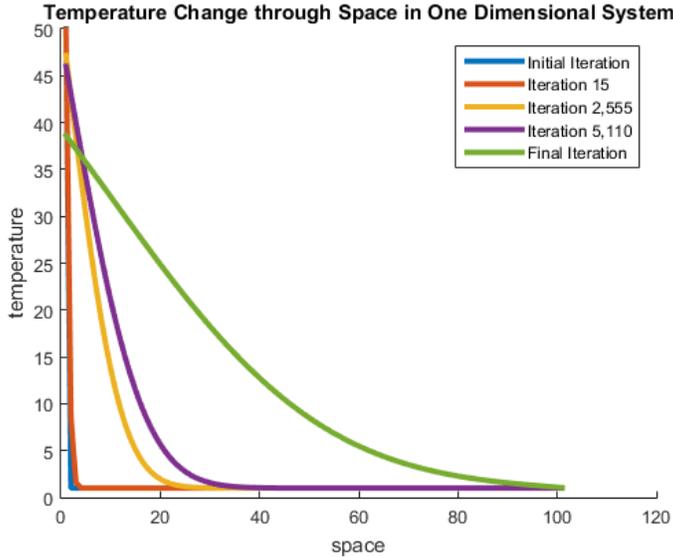


Figure 15: Temperature-Space Plot with Small K Coefficient

In figure 16, a sinusoidal waveform is added to show the oscillation of the heat. To help visualize the oscillation of the source, no initial condition was implemented. The sinusoidal waveform was arbitrarily chosen to be $11\sin(0.001\pi t)$. The amplitude and frequency of the sinusoid were arbitrary values. As seen in figure 16, the heat briefly diffuses during each oscillation. This is an ideal case of a heat source oscillation because the source is brought back to zero very quickly, which is difficult to replicate in a real experiment.

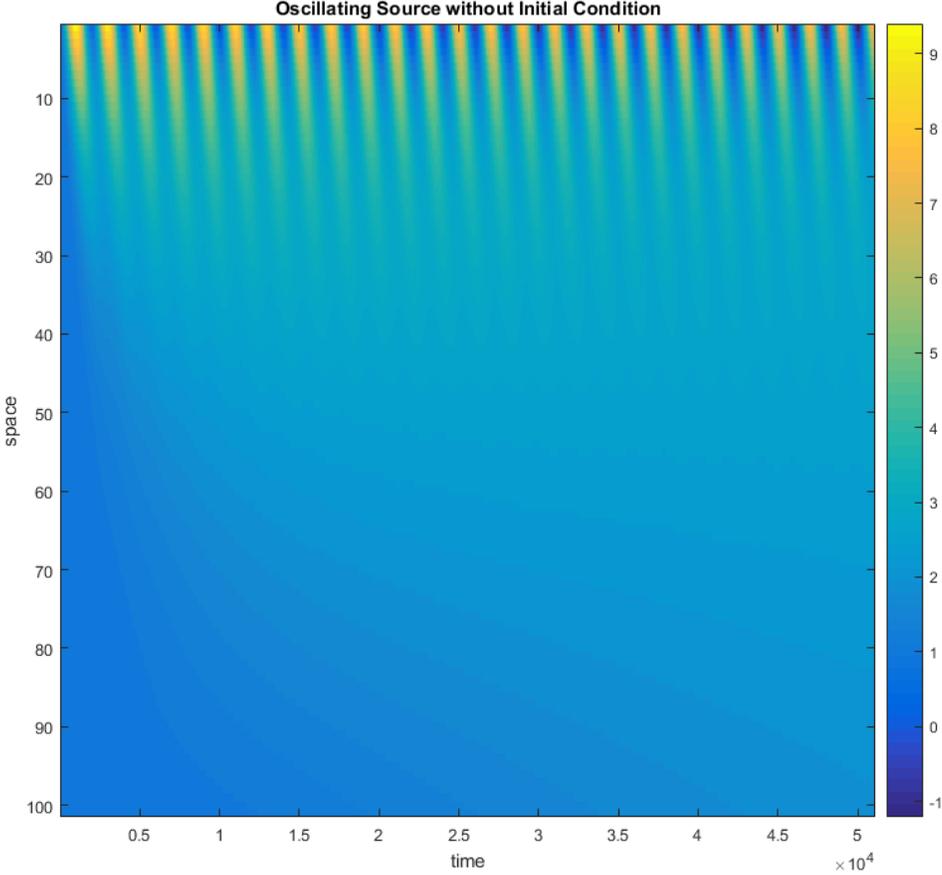


Figure 16: Oscillating Heat Source without Initial Condition

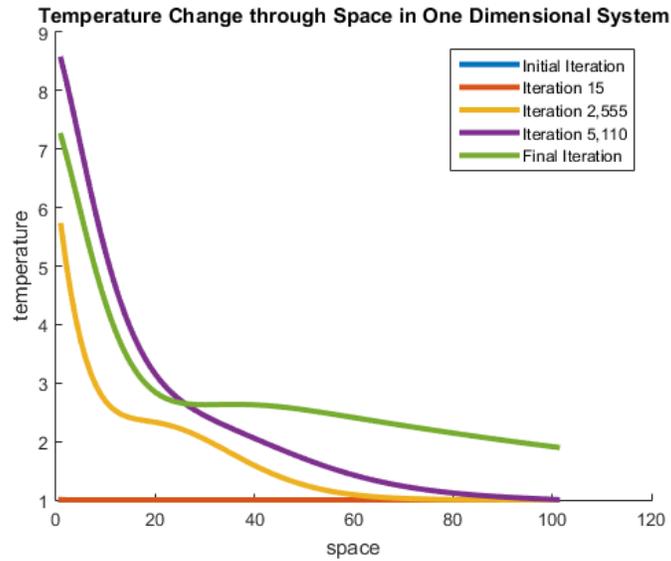


Figure 17: Temperature-Space Plot with Oscillating Heat Source

Similar to the standard source simulation in figure 12, the value of K was increased in figure 18 with the oscillating heat source. As in figure 12, the value of K was increased to the same value of 50. Again, we see the heat diffuse in more space (down the y-axis) compared to the smaller value of K.

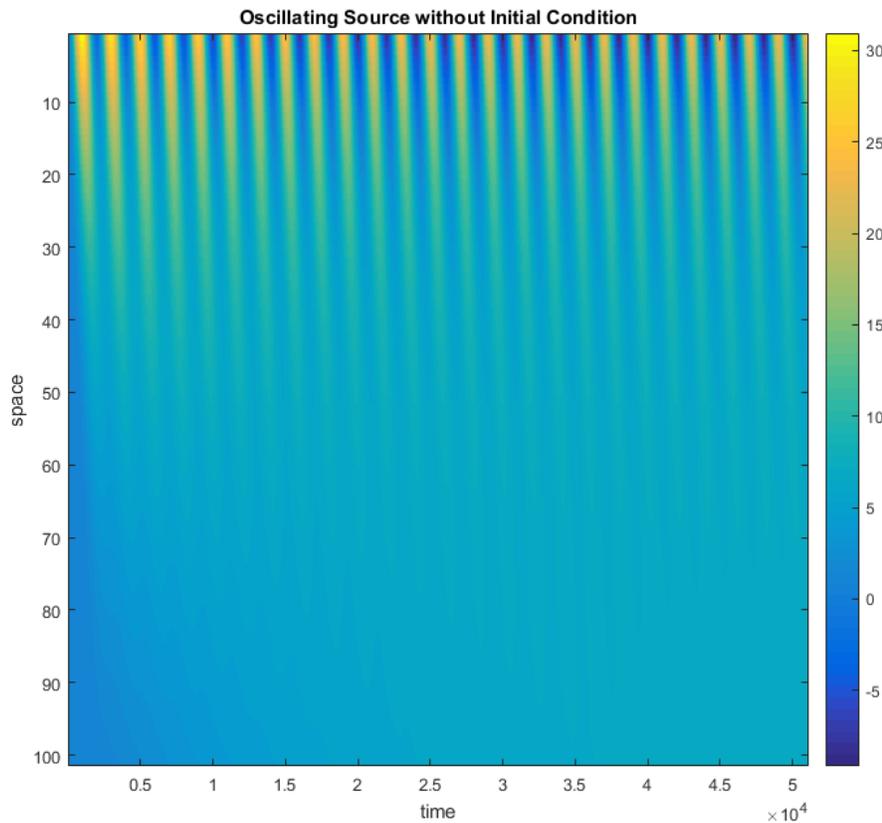


Figure 18: Oscillating Heat Source with Large K Value

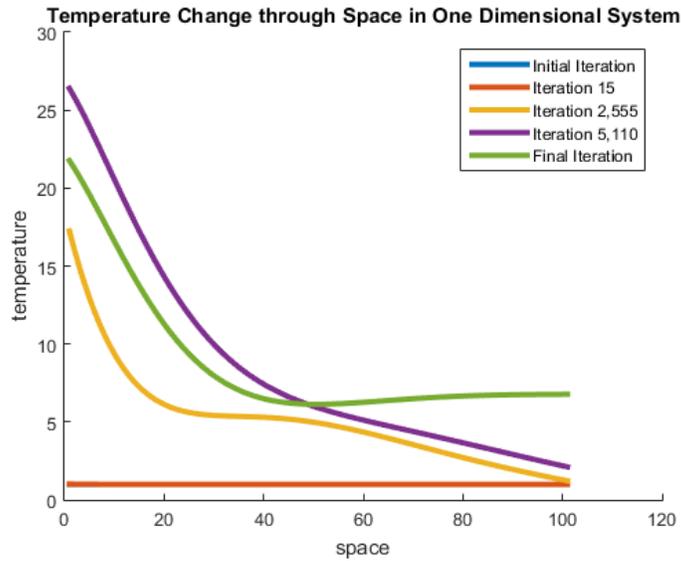


Figure 19: Temperature-Space Plot with Oscillating Source and Large K Value

To show contrast, in figure 20, the value of K was also decreased to the same value as in figure 14 (K value of 1.3). With the smaller K coefficient, it is noticeable that the oscillations barely extend into the y-axis. In order to visualize the oscillations, the color map legend was adjusted.

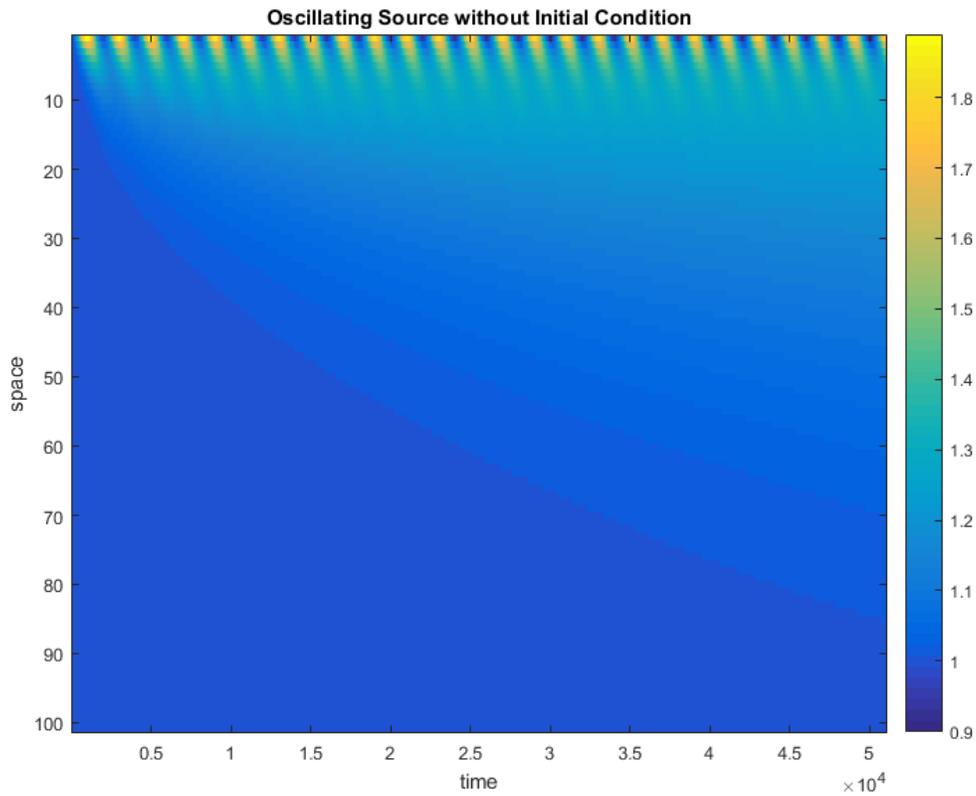


Figure 20: Oscillating Heat Source with Small K Value

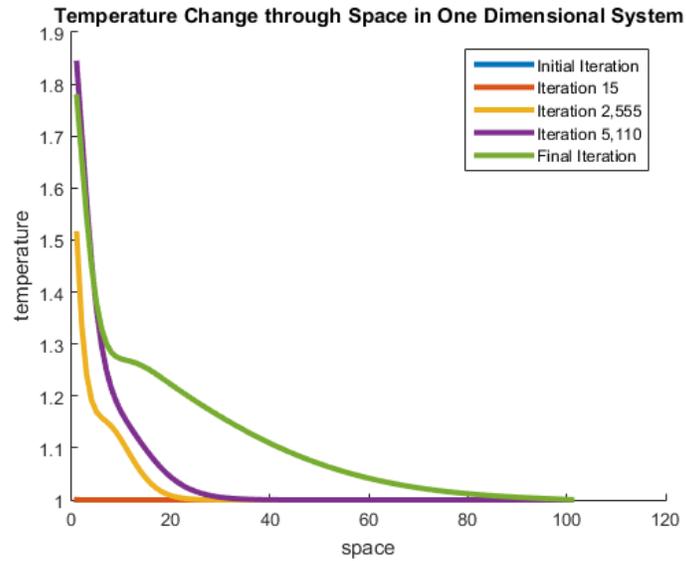


Figure 21: Temperature-Space Plot with Oscillating Heat Source and Small K Value

Figure 22 shows the same oscillating source as in the previous three figures; however the frequency was greatly increased from 0.001 to 0.01 in the sinusoid. The oscillations are barely noticeable with a high frequency which helps generate the hypothesis that a high frequency source will have a difficult time diffusing through a material.

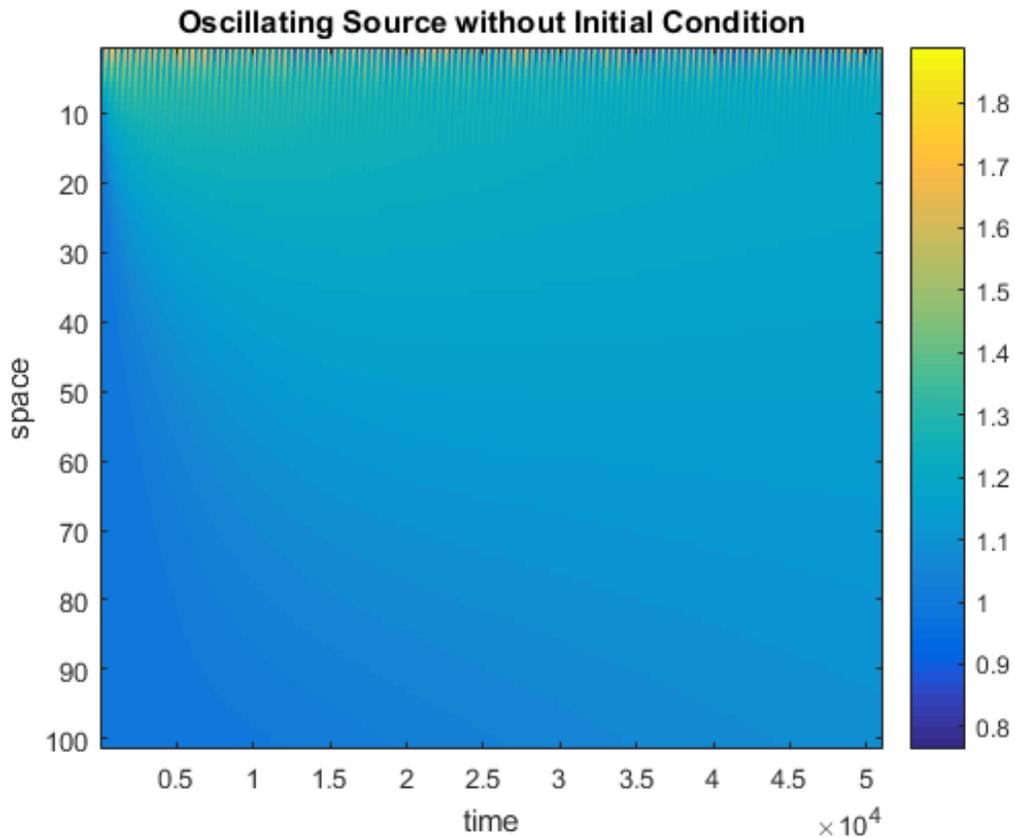


Figure 22: Oscillating Heat Source with Increased Frequency

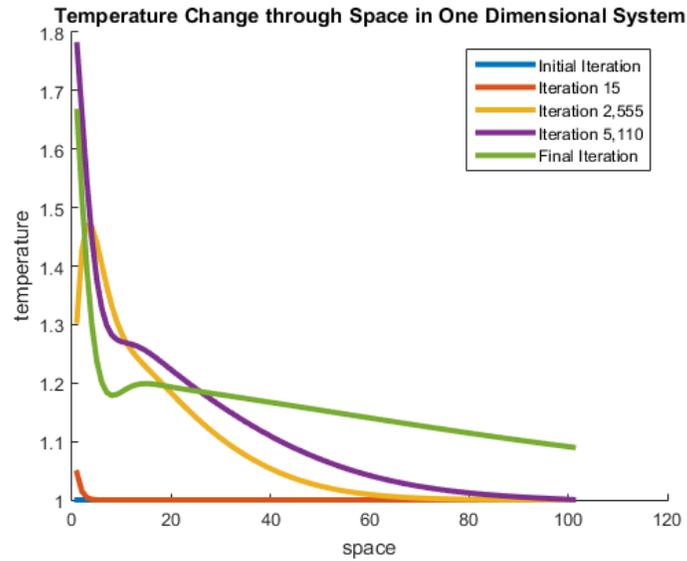


Figure 23: Temperature-Space plot with Oscillating Source and High Frequency

In Figure 24, the frequency of the sinusoid was decreased from 0.001 to 0.0001. With the low frequency, the heat diffuses into a much greater distance in space. This confirms the hypothesis that high frequencies have difficult diffusing into space, while lower frequency oscillations are able to penetrate much further through materials.

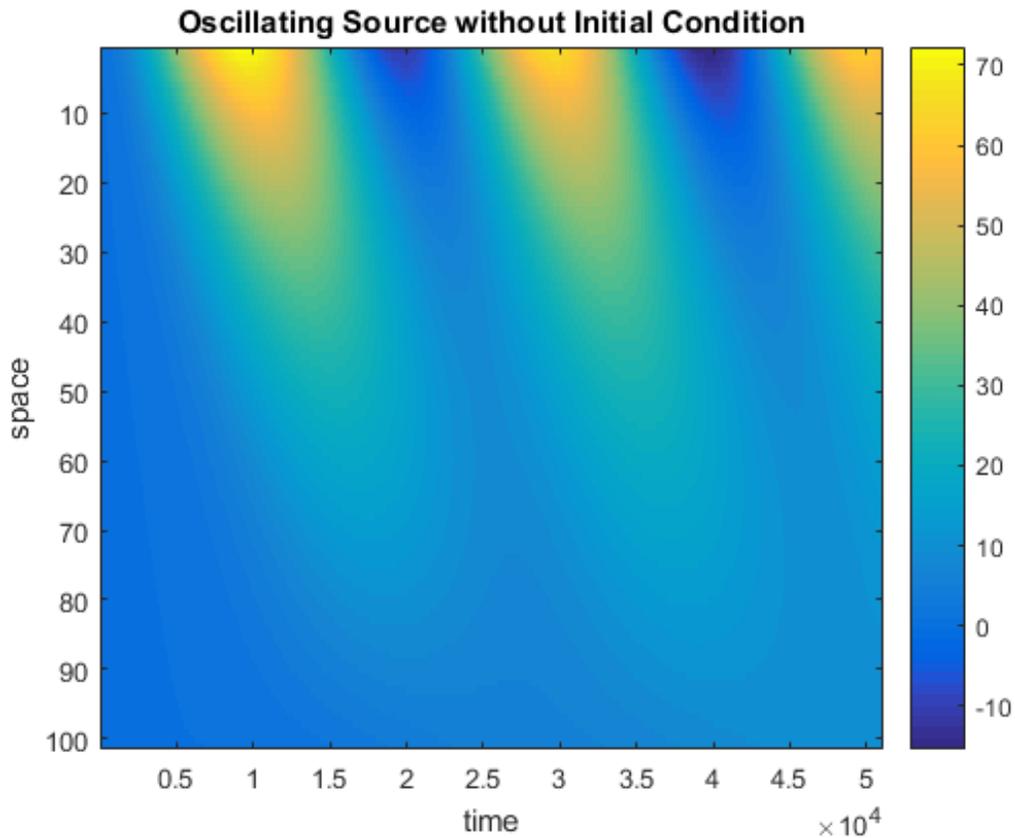


Figure 24: Oscillating Heat Source with Low Frequency

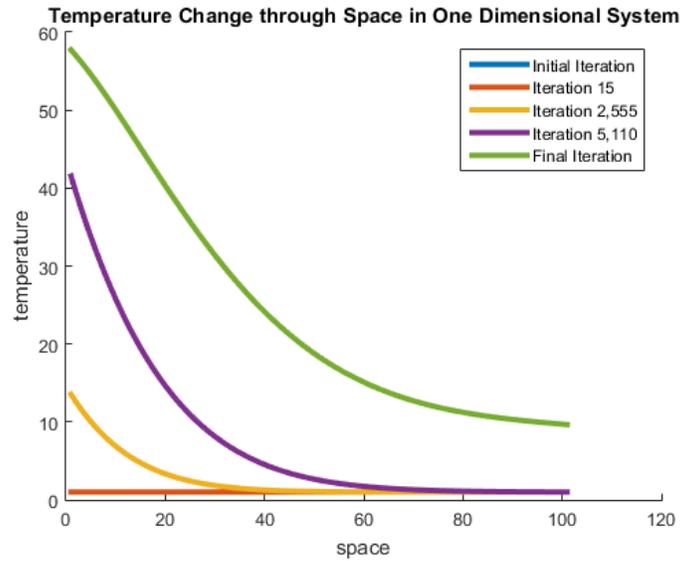


Figure 25: Temperature-Space Plot with Oscillating Source and Low Frequency

To better help confirm the hypothesis about low and high frequencies diffusing through materials, the oscillating source was placed in the middle of the one dimensional system (at space $x = 51$) in figure 26. It can be seen that the low frequency source is able to cover much more space than its high frequency counterpart. This is an ideal case of oscillation due to the fact that the source comes back to a zero value instantaneously.

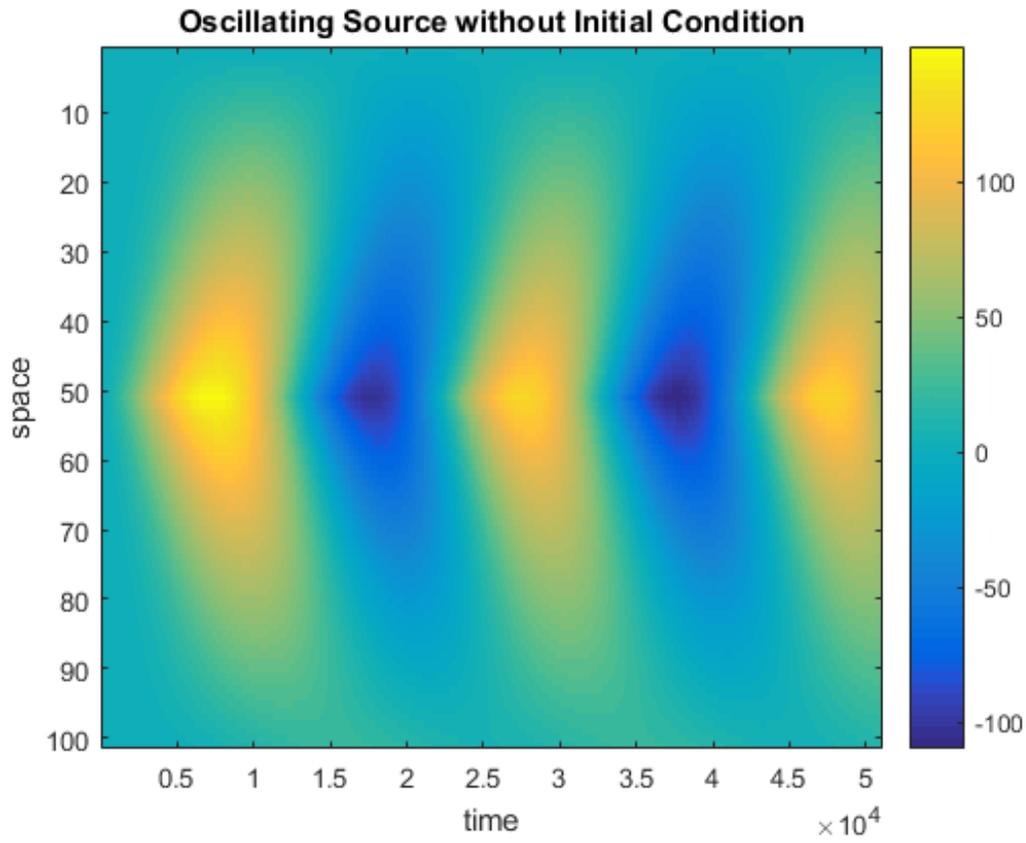


Figure 26: Oscillating Heat Source with Low Frequency placed at $x = 51$

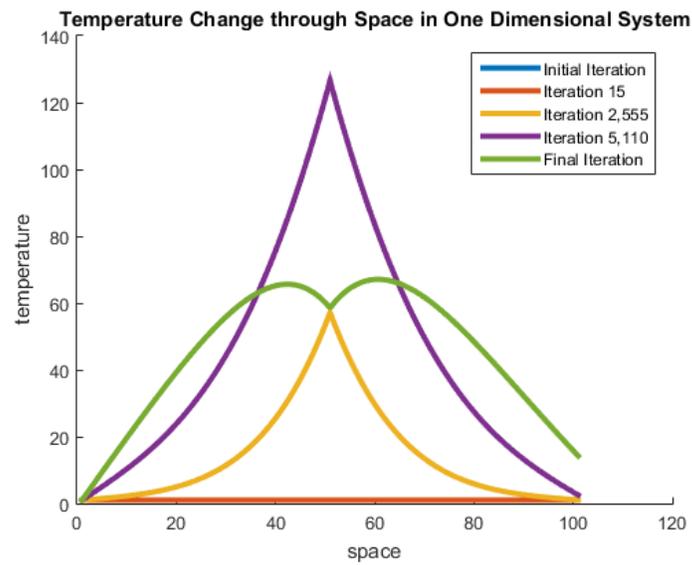


Figure 27: Temperature-Space Plot of Oscillating Heat Source with Low Frequency @ $x = 51$

Similar to figure 22, in figure 28 the frequency of the sinusoid was increased to 0.01 to show that higher frequencies do not propagate through space compared to lower frequencies. Again this is an ideal case because the source instantaneously returns to a zero value, which is cause for the spiky look.

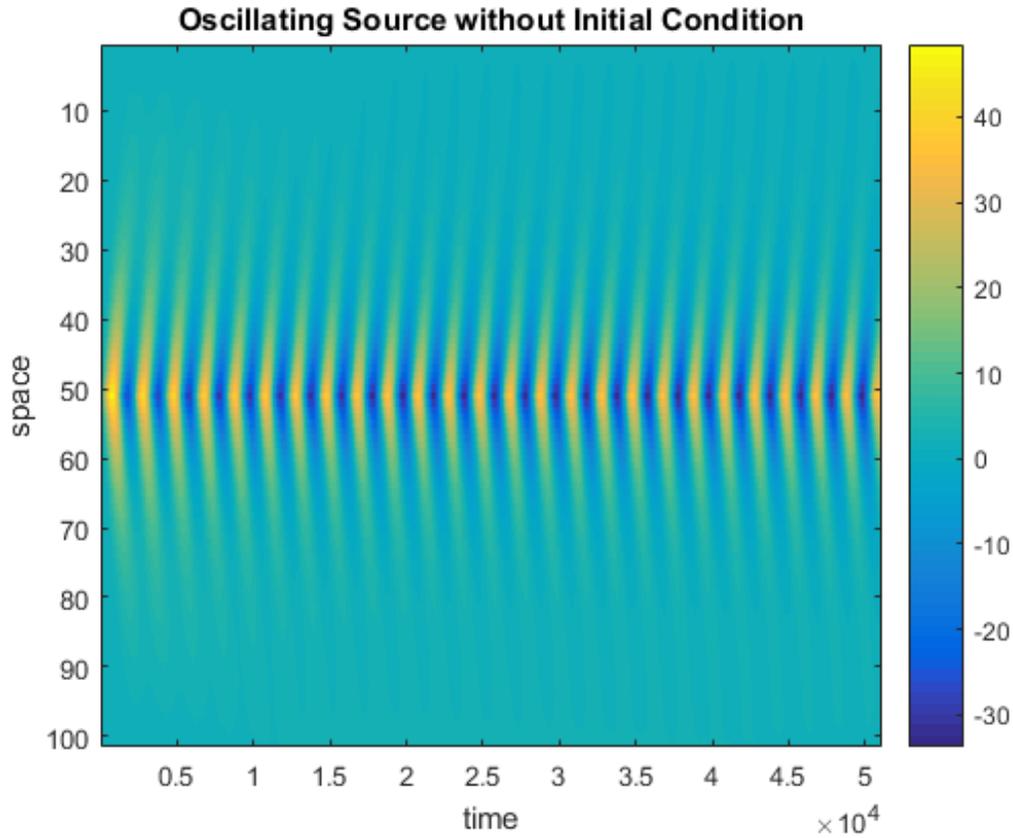


Figure 28: Oscillating Heat Source with High Frequency placed at $x = 51$

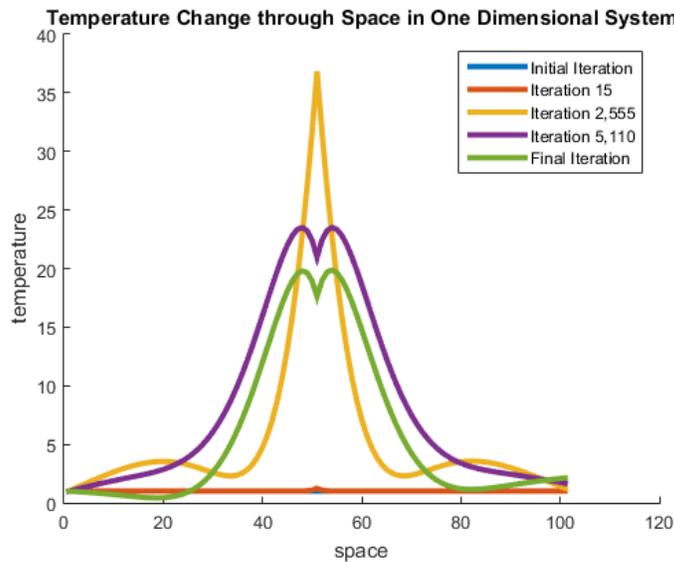


Figure 29: Temperature-Space Plot of Oscillating Heat Source with Low Frequency @ $x = 51$

After experimenting with the variables associated with the one-dimensional heat diffusion equation, a better understanding of the equation was obtained. First, the K coefficient has a very impactful role when simulating heat propagation in a material. Adjusting the coefficient helps observe the differences in varying materials. For example, a metal rod would have a much higher value of K than a rod made from wood because heat would easily diffuse through a metal rod as opposed to one made completely out of a wood. Similar to heat, a coefficient is tied to specific conductive materials for electrical current to travel. The higher the conductivity of the material would result in a higher value of the coefficient. Secondly, when dealing with a source that has oscillation, frequency is a significant factor in the resulting propagating waves. Higher frequency oscillators will not propagate or diffuse through a material as much as a lower frequency oscillator. This hypothesis was concluded in figures 22 and 24 above.

Multi-cell cable model

Similar to the equations in which heat diffusion was investigated in matlab, the multi-cell cable model expands on the solver to include four variables being solved simultaneously as opposed to the single temperature variable changing over time and space. Just as we simulated heat diffusion, the goal was to use a forward difference method to simulate the action potential in a cell and ultimately notice the signal decay over a one-dimensional system. In figure 30, a colormap of the propagating action potentials are shown. All of the variables are kept constant as a control, which is why the voltage is the same at all points in space. For these simulations, the elapsed time was doubled in order to clearly see the effect of adjusting the variables.

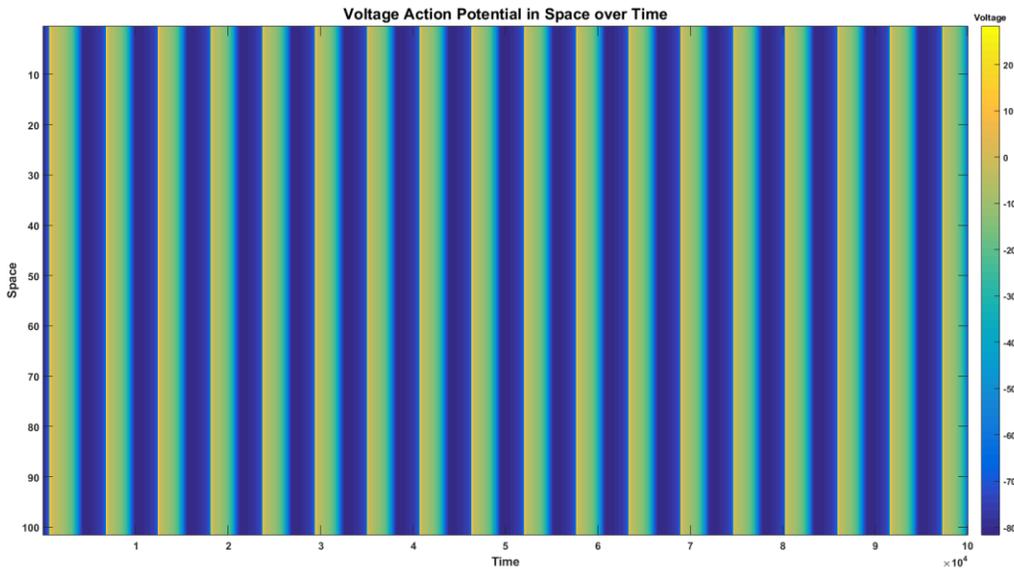


Figure 30: Voltage Potential Colormap

In addition to the colormap shown in figure 30, the Matlab script also plotted out the voltage of every action potential over time. The voltage over time plot in figure 31 shows 100 action potentials all firing

at the exact same time with the same frequency. The purpose of this is to make sure the program was simulating correctly and to have a control to compare and contrast with. The plot follows the ideal fire of the cell's action potential, starting at -80mV and firing up to around 20mV with the correct shape modeling the phases of the cardiac cell action potential.

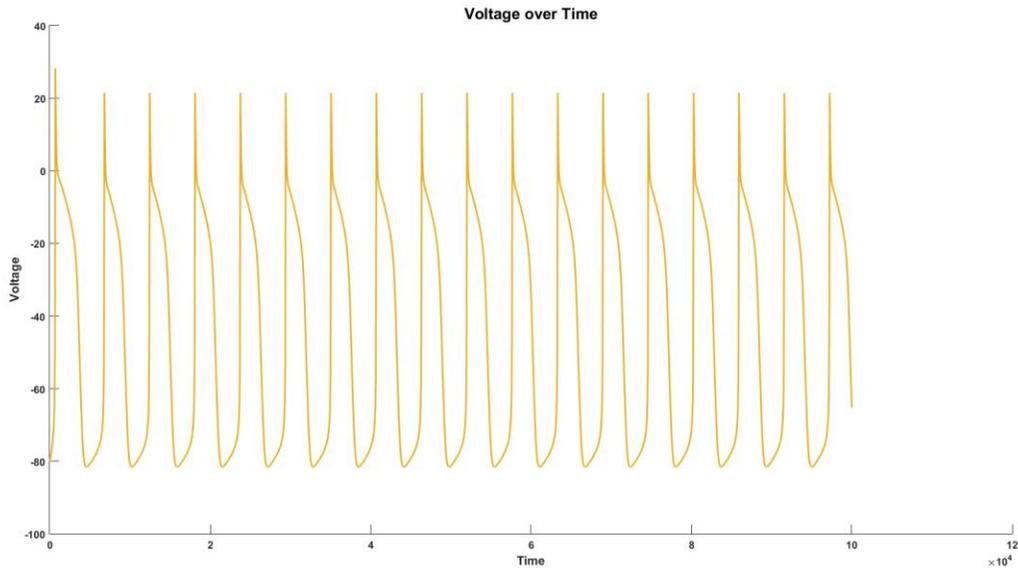


Figure 31: Multi-cell Model Voltage over Time

Furthermore, the plots of gates h, m and n are also plotted for all cells. These plots show the normal action for the gates to allow the influx and efflux of ions in order for the action potentials to properly propagate through a one-dimensional system. Similar to the voltage over time plot in figure 31, all 100 cells are plotted and opening and closing at the same time which is why it appears the plots only have one curve.

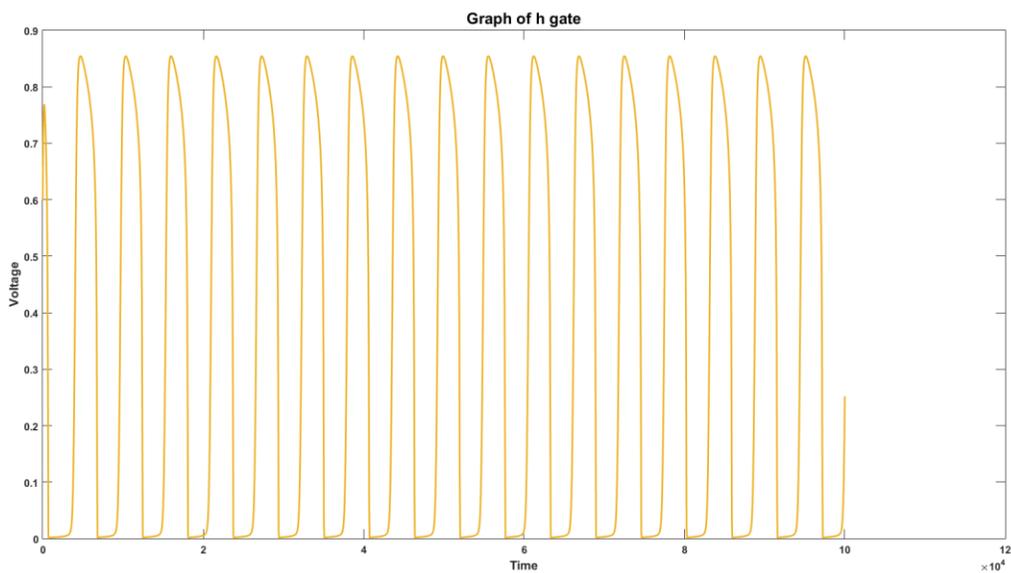


Figure 32: Multi-cell Model Plot of h Gate

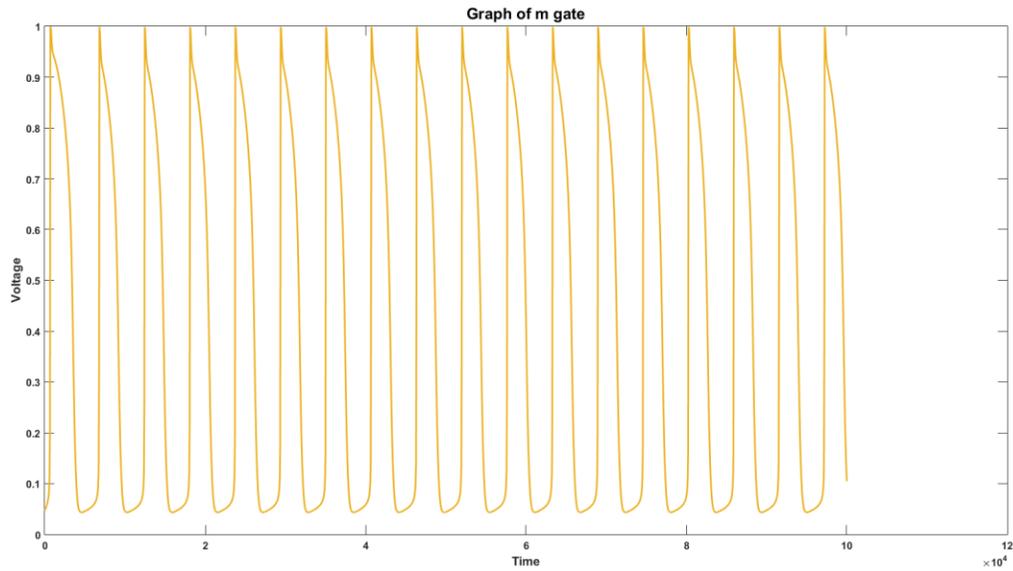


Figure 33: Multi-cell Model Plot of m Gate

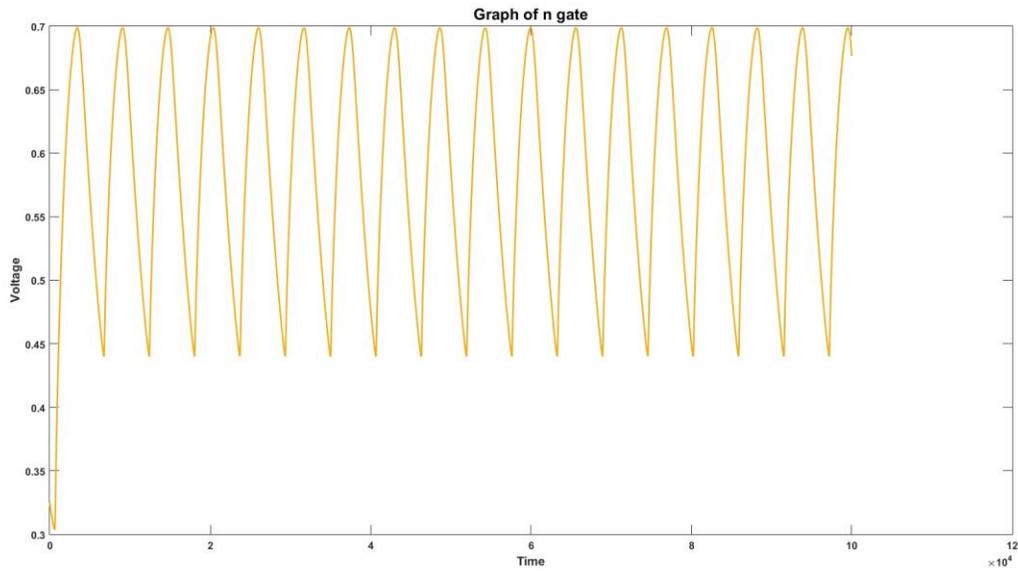


Figure 34: Multi-cell Model Plot of n Gate

In order to represent cardiac cell voltage potentials propagating in a one-dimensional system properly, the capacitance needs to gradually increase for each cell. The purpose of increasing the capacitance is because the cells in the sinoatrial node are very small and gradually growing in size as the signal is propagated through the heart. Since the cells are becoming larger, the cell membrane is also larger which needs to be represented with increased capacitance. After enabling the C_m as a vector in the

program, it is clearer to see the propagation of the signal. Since the larger cells have a bigger cell membrane resulting in a higher capacitance, the frequency in which they oscillate are slower compared to the smaller cell. This concept is depicted in figure 35 where the action potential begins to shift in an angled manner. This is due to the larger cells oscillating slower over time compared to the smaller, initial cells.

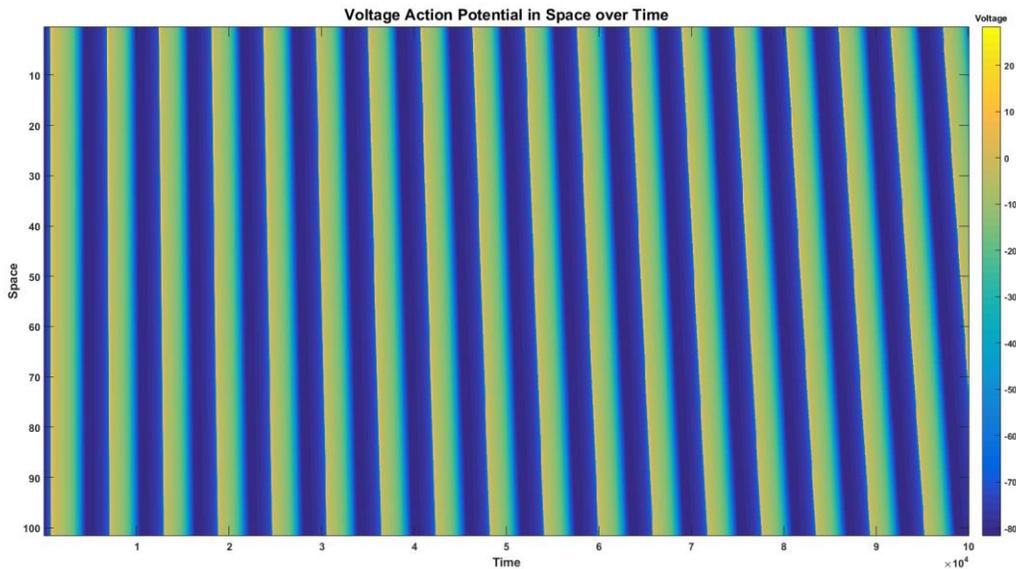


Figure 35: Voltage Potential Colormap with Increasing Capacitance

With the successful simulation of cells propagating through a one-dimensional system, manipulations can be made to investigate different interactions, such as drugs and physical heart defects on the propagating signal.

Defects and Drug Interaction

Human heart defects and the effect of specific drugs can be observed on the heart's electrical system by manipulating the ion gate variables, capacitance vector and the K coefficient which represents the structural coupling of the cells. Certain heart defects and drugs can inhibit specific ion gates within the heart, affecting the amount of sodium, potassium or calcium flowing in and out of the cell. To observe the effect of the ion gates being tampered with, the variables were multiplied to only allow a certain percentage of maximum ions entering and leaving the cell. These variables were modified until the system broke down and would not correctly oscillate to emphasize the importance of the ion gates in the cardiac cells. In order to clearly see the results of the ion channels being manipulated, the voltage initial condition was set to be more random than the typical uniform initial condition. Originally, all cells were set to start at a membrane potential of -80mV. To be more realistic, a random number generator set the initial condition of the cells to start anywhere from -115mV to -50mV. In reality, the cells would be at different phases of their action potential, so the initial condition would resemble the random

number generator as opposed to all cells starting at the exact same resting voltage. Figure 36 shows the effect of inhibiting the ion gates with and without a pre-existing structural defect within the heart. For these figures, the structural defect was placed at cells 40-60. It is noticeable that the propagating signals have difficult time synchronizing due to the structural defect. To imitate a structural heart defect, the coupling coefficient was reduced which disturbs the propagating waves and makes the signal more difficult to synchronize. In the drug interaction portion of the figure, 80% of the sodium (Na) ions were allowed to be present, and 95% of the potassium (K) ions were present. By interfering with the sodium ion channels, a slower voltage potential oscillation and lower peak potential was present. The signals also had a difficult time recovering from the structural defect with the sodium gates inhibited. Manipulating the potassium ion channels caused a major problem when there was an underlying heart defect. With just the potassium channels inhibited, there was not much of an issue with the heart's electrical system, but if there is a structural defect within the heart, there is a much higher chance the heart will have a severe arrhythmia as shown in the bottom right graph. In the graph with potassium inhibited and a structural defect, the propagating waves could not synchronize properly and began acting as the pace-making cells, which cause an electrical storm. For example, some jellyfish have a toxin which blocks certain ion channels including potassium in the heart's cardiac cells. To most people, a sting from the jellyfish would not be life-threatening, but individuals with a structural defect in the heart could have serious health consequences including death.

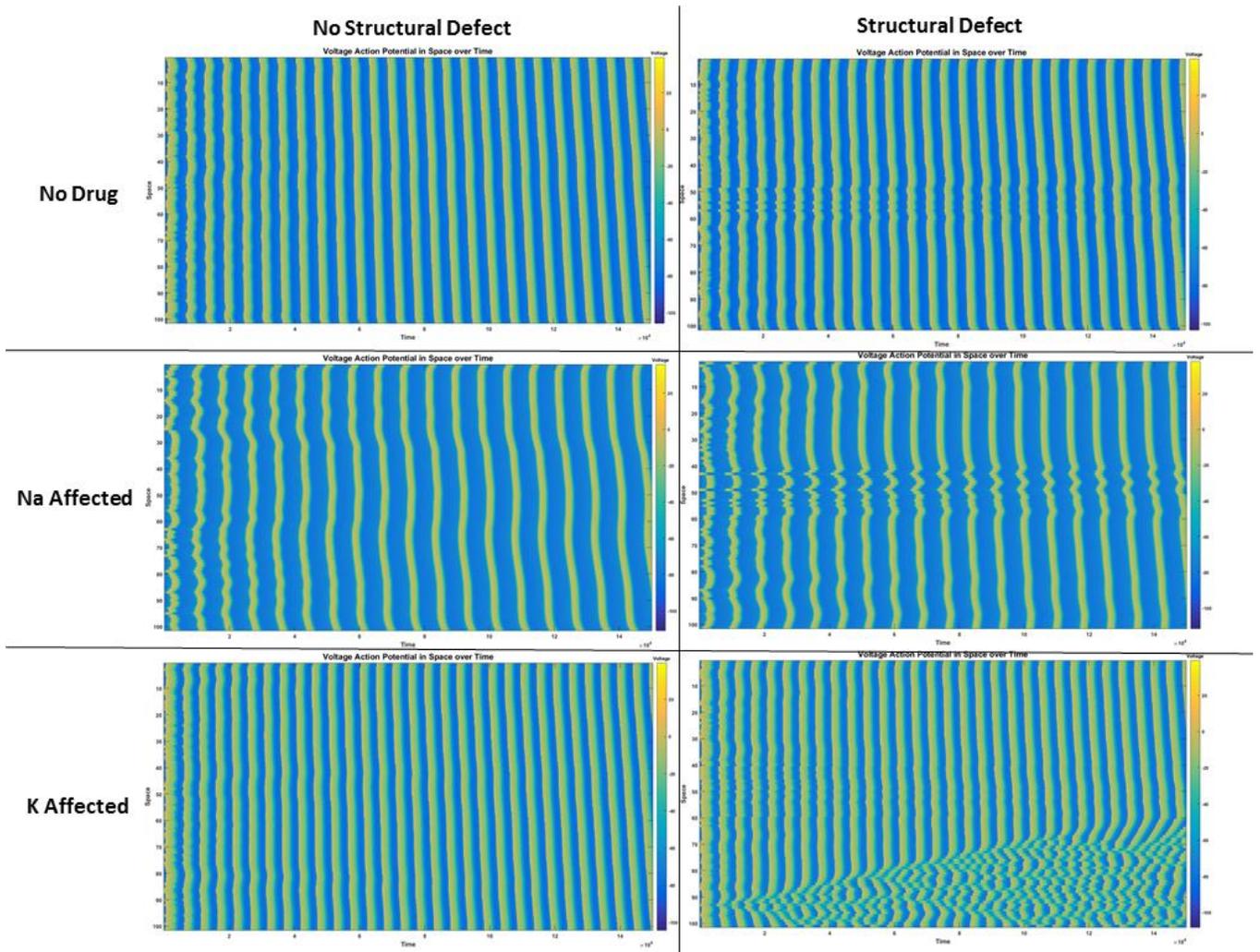


Figure 36: Drug and Defect Interaction with the Heart's Electrical System

Conclusion

Main Conclusion

Heart disease is the number one leading cause of death in the United States. There are still many heart diseases and disorders that are not fully understood. By taking a different approach, such as investigating the heart's electrical system from an electrical engineering perspective, a more well-rounded understanding of the human heart will be developed. With this greater understanding of the heart's electrical system, disorders can be remedied and defects can be fixed. This kind of research is already the frontier for many hospitals, including OSF Saint Francis in Peoria. With additional investigation and research, electrical heart issues will hopefully be a problem of the past.

Future Work

Moving forward there are numerous features to extend on. First, the simulations need to be expanded to show a two-dimensional system. With a sheet of cells, it is easier to see the propagation of the signal over time. After a two-dimensional system has been successfully investigated, the next step would be to create a three-dimensional simulation and use the form of a human heart. This is a big jump in the process but would be incredibly beneficial to medical professionals because they could see the propagations throughout the entire heart. Another reason why this step is incredibly difficult is due to the complexity of the simulation. A supercomputer would be necessary in order to simulate the hundreds of thousands of differential equations and provide a visual of the signal. The final stage of this research would be to combine the three-dimensional modeling with patient specific data in order to investigate the cause of their electrical heart dysfunction. The data can be retrieved via MRI or CT scans and properly modeled in a CAD program to create a mesh of the patient's heart. This would be incredibly helpful because medical professionals would be able to pinpoint the area of problem within the heart's electrical system. This would also expedite the surgery process since medical professionals would have a visual of exactly where the issue is located on the patient's heart.

References

1. <http://www.gwheartandvascular.org/education/cardiovascular-diseases/anatomy-and-function-of-the-hearts-electrical-system/>
2. <https://en.wikipedia.org/wiki/Heart>
3. <http://www.theeplab.com/index.php>
4. https://en.wikipedia.org/wiki/Cardiac_action_potential
5. https://en.wikipedia.org/wiki/Cable_theory
6. https://en.wikipedia.org/wiki/Partial_differential_equation
7. https://en.wikipedia.org/wiki/Reaction%E2%80%93diffusion_system
8. https://en.wikipedia.org/wiki/Hodgkin%E2%80%93Huxley_model
9. https://en.wikipedia.org/wiki/Finite_difference