Mathematical Modelling of Electrical Activity of Cardiac Tissue by Finite Element Method

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Abstract— The main objective of this research is to simulate the electrical activity of cardiac tissue by finite element method. Electrical activity is responsible for the periodic contraction and relaxation cycle of the human heart. Mathematical modeling of heart provides a better understanding for the complex biophysical phenomena related to electrical activity in the heart. Various electro-physical models have been developed to simulate electrical properties of cardiac tissue. In this research work monodomain model which is coupled with the single cell FitzHugh-Nagumo model is used to simulation the electrical activities. Two dimensional monodomain model equations on a general domain with equal isotropy and no fiber orientation are considered. Finite element method which has been widely used as an analysis and design tool is used to deal with the complex monodomain model equations. The single cell simulation represents the behavior system by changing the parameters of single cell model. The outcome of the simulation represents the effect of applied current and threshold value on the model behavior.

Index Terms— Cardiac Action Potential, Electrical Activity of Heart, FitzHugh-Nagumo model, Finite Element Method, Hodgkin–Huxley model, Monodomain Model, Transmembrane Potential.

1 INTRODUCTION

The Electrical activity of cardiac tissue is an important part of bio-medical science. Computer simulation is becoming an important tool in cardiovascular research. We are on the brink of a revolution in cardiac research, one in which computational modeling of proteins, cells, tissues, and the organ permit linking genomic and proteomic information to the integrated organ behavior, in the quest for a quantitative understanding of the functioning of the heart in health and diseases. Mathematical model of cardiac electrical activity has been recognized as one of the significant approaches capable of revealing diagnostic information about the heart. The electrical activity of the heart is an important tool for the primary diagnosis of the heart diseases; it shows the electrophysiology of the heart and the ischemic changes may cause myocardial infection, conduction defects and arrhythmia [1].The aim of the study is to simulate the Electrical activity of cardiac tissue by finite element method. Here monodomian model is used. In case of single cell simulation modified FitzHugh-Nagumo model (FHN) is used.

The human body is a complex system made up of many intricate processes. For example, the heart has four different compartments that each has different purposes. It pumps blood throughout the body so that we can obtain the oxygen we need to survive. This process occurs through the contractions of the heart. Each cell contributes to the heart's contractions by sending out small electrical impulses called action potentials. Mathematical models can be used to better understand the dynamics of these action potentials in a surprisingly accurate way.

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The models in which we are interested consist of systems of differential equations. Models of the electrophysiology of one cell are governed by systems of ordinary differential equations (ODEs), and models of the electrophysiology of more than one cell are governed by one or more partial differential equations (PDEs). Typically, a PDE model is coupled with an ODE model to simulate heart tissue consisting of a network of cells; the ODEs model the electrical activity in the cells, and the PDEs model propagation of the electrical activity across the network as a whole. Cardiac electrophysiological models are often based on the Nobel prize-winning work of Hodgkin and Huxley modeled neural tissue mathematically as a circuit. Modern cardiac electrophysiological models adapt the work of Hodgkin and Huxley to describe electrical activity in the heart and include data gathered from experiments to form models with increasing physiological accuracy. In this research work the modified FHN model is used for single cell simulation. This model represents action potential at different conditions of a single cell. This model consists of two differential equations. So it is less complicated o simulate.

In order to describe electrical activity in the whole heart, a single cell model with the Partial differential equations model that describes how electricity flows across a network of cells [2]. The most complete model of such a complex setting is the anisotropic bidomain model that consists of a system of two degenerate parabolic reaction diffusion equations describing the intracellular and extracellular potentials in the cardiac muscle, coupled with a system of ordinary deferential equations describing the ionic currents flowing through the cellular membrane [3]. But this model requires a long simulation time, large computer memory. So in this research monodomain model is used. The technique of finite element method has been used to build a computer program to solving the phenomena propagation of excitations. The finite element method (FEM) has been widely used as an analysis and design tool in many engineering disciplines like structures and computational fluid mechanics. The FEM method is a powerful tool for

solving differential equations. The method can easily deal with complex geometries and higher-order approximations of the solution [4]. A domain of interest is represented as an assembly of finite elements.

2 SINGLE CELL MODELS

The single cell models of cardiac tissue are capable of facilitating insights into the mechanisms underlying cardiac electrical dynamics. A model begins with a mathematical description of electrical events at the cellular level that give rise to cardiac action potentials. In particular, models incorporate formulations of transmembrane ionic currents along with the voltage, ionic concentrations, and ion channel kinetics responsible for the currents. The advantage of using those models is that they can simulate an action potential with the lowest possible computational cost. In neurons, action potential transfers inside the single cell and participate in neuron-to-neuron communication. Since neural and cardiac cells have many similarities, much of the mathematics of cardiac cell modeling is drawn from the pioneering work of Hodgkin and Huxley.

2.1 Hodgkin Guxley Model

The Hodgkin–Huxley model (HH), or conductance-based model, is a mathematical model that describes how action potentials in neurons are initiated and propagated. It is a set of nonlinear differential equations that approximates the electrical characteristics of excitable cells such as neurons and cardiac myocytes. Alan Lloyd Hodgkin and Andrew Huxley described the model to explain the ionic mechanisms underlying the initiation and propagation of action potentials in the squid giant axon [5].

This model usually represents the biophysical characteristic of the cell membrane. The lipid layer is represented by the capacitance C_m. Voltage-gated and leak ion channels are represented by nonlinear (g_n) and linear (g_L) conductances, respectively. The voltage source E_n whose voltage is determined by the ratio of the intracellular and extracellular concentrations of the ionic species of interest [5]. The capacitive current I_c is defined by the rate of change of charge q at the transmembrane surface and

The charge q (t) is related to the instantaneous membrane voltage $V_m(t)$ and membrane capacitance C_m by the relationship $q = C_m.V_m$. Thus the capacitive current can be rewritten as

$$I_c = C_m \frac{dv_m}{dt}$$

In the Hodgkin-Huxley model of the squid axon, the ionic current I_{ion} is subdivided into three distinct components, a sodium current I_{Na}, a potassium current I_K, and a small leakage current I_L that is primarily carried by chloride ions. So the differential equation is given by

$$C_m \frac{dv_m}{dt} + I_{ion} = I_{appl} \quad (1)$$

Where I_{appl} is an externally applied current, such as might be introduced through an intracellular electrode.

The individual ionic currents I_{Na}, I_K and I_L represent the macroscopic currents flowing through a large population of individual ion channels. In HH-style models, the macroscopic current is assumed to be related to the membrane voltage through an Ohm's law relationship of the form V=IR. In many cases Ohm's law described by I=GV, where G is the conductance. So the total ionic current I_{ion} is the algebraic sum of the individual contributions from all participating channel types found in the cell membrane is given by

$$I_{ion} = \sum I_k = \sum G_k (v_m - E_k) \quad (2)$$

This expands to the following expression for the Hodgkin-Huxley model of the squid axon

$$I_{ion} = G_{Na}(v_m - E_{Na}) + G_k(v_m - E_k) + G_L(v_m - E_L) \quad (3)$$

In general, the conductances are not constant values, but they can depend on other factors like membrane voltage or the intracellular calcium concentration. In order to explain their experimental data, Hodgkin and Huxley postulated that G_{Na} and G_K were voltage-dependent quantities, whereas the leakage current G_L was taken to be constant. Although Hodgkin and Huxley did not describe about the properties of individual membrane channels when they developed their model, it will be convenient for us to describe the voltage-dependent aspects of their model in those terms.

2.2 The FitzHugh–Nagumo Model

The HH model proved to be very accurate and useful in further research into action potentials. However, the formula was rather complicated and relied heavily on empirical equations fit from the data. A simpler formulation was needed to analyze such systems with mathematical rigor. Richard Fitzhugh rose to the task and helped formulate an approximation of the HH Model which is known as the FHN model [6], [7]. This is the simplest cell model. The motivation for the FHN model was to isolate conceptually the essentially mathematical properties of excitation and propagation from the electrochemical properties of sodium and potassium ion flow [6], [7]. The model consists of a voltage-like variable having cubic nonlinearity that allows regenerative self-excitation via a positive feedback and a recovery variable having a linear dynamics that provides a slower negative feedback.

It is known that the cell membrane carries a potential across the inner and outer surfaces, hence a basic model for a cell membrane is that of a capacitor and resistor in parallel [7]. The model equation takes the form

$$C_m \frac{dv}{dt} = -\left(\frac{v - v_{eq}}{R}\right) + I_{appl}$$

Here where C_m is the membrane capacitance, R the resistance, V_{eq} the rest potential the potential across the inner and outer surfaces and I_{appl} is known as the applied current.A key part of their model assumptions was that the membrane contains channels for potassium and sodium ion flow.

In the mid-1950's, FitzHugh-Nagumo thought to reduce the Hodgkin-Huxley model to a two variable model for which phase plane analysis applies .His general observation was that the gating variables n and h have slow kinetics relative to m. Moreover, for the parameter values selected by Hodgkin and Huxley, n + h is approximately 0.8 [7].This led to a two varia-

ble model, called the fast-slow phase plane model, of the form

$$C_m \frac{dv}{dt} = gkn^4(v - v_k) - gNam^3h(v - v_{Na}) - gL(v - v_L) + I_{appl}$$

$$n_w(v)\frac{dn}{dt} = n\infty(v) - n \quad (4)$$

In effect this provides a phase space qualitative explanation of the formation and decay of the action potential .A further observation due to FitzHugh was that the V null-cline had the shape of a cubic function and the null-cline could be approximated by a straight line, both within the physiological range of the variables. This suggested a polynomial model reduction of the form is given below

$$\frac{dv}{dt} = v(v - \alpha)(1 - v) - w + I_{appl} \quad (5)$$

$$\frac{dv}{dt} = \varepsilon(v - \gamma w) \quad (6)$$

3 MONODOMAIN MODEL

The monodomain model is a simplification of the bidomain model that is easier to analyze. It is also notable that computational cost of using the monodomain model is about one-half to one-tenth the cost of using the bidomain model, depending on the complexity of the cell model used [8].This model helps to understand the patterns of electrical conduction and propagation from the scale of a single tissue to whole heart. In this physical model the cell membrane is viewed as an electrical network with the fibers of myocardial cells constituting a cable [8]. In this analysis, it is assumed that the anisotropy of the intracellular, D_i and extracellular spaces, D_e is the same, i.e. that the conductivity in the extracellular space is proportional to the intracellular conductivity.

$$D_e = \lambda D_i$$

Here λ is a scalar, which representing the ratio between the conductivity of the intercellular and extracellular spaces. The choice of the value of λ can determines physiological accuracy, but it is important to select a suitable value that gives the satisfactory results [1, 7]. Since an effective conductivity

$$D = \frac{1}{1+\lambda} D_i$$

Then by the monodomain model for cardiac tissue is given by

$$\nabla.(D\nabla V_m) = C_m(\frac{\partial V_m}{\partial t}) + I_{ion} + I_{appl}$$

The conductivity of the tensor D, in the above equation is defined largely by the orientation of the tissue. Cardiac cells are grouped into muscle fibers, and the muscle fibers are grouped into sheets of fibers. The structure of the heart influences the flow of electricity. Conductivity is usually greater along the fibers rather than across them.

3.1 Solution of Monodomain Model by FEM

In this research work the FEM is used to solve the monodomain model. FEM has been widely used as an analysis and design tool in many engineering disciplines. The method can easily deal with complex geometries and higher-order approximations of the solution. Galerkin method is used to discretize the monodomian model. Galerkin methods are a class of methods for converting a continuous operator problem (such as a differential equation) to a discrete problem [4]. In principle, it is the equivalent of applying the method of variation of parameters to a function space, by converting the equation to a weak formulation. Typically one then applies some constraints on the function space to characterize the space with a finite set of basis functions.

The monodomain equation which is coupled the modified FitzHugh-Nagumo model is given below

$$\nabla.D(D_i\nabla V_m) = C_m(\frac{\partial V_m}{\partial t}) + I_{ion} + I_{appl}$$

From the above equation we can write

$$C_m(\frac{\partial V_m}{\partial t}) + I_{ion} + I_{appl} = D_x(\frac{\partial^2 V_m}{\partial x^2}) + D_y(\frac{\partial^2 V_m}{\partial y^2})$$

We can apply the Euler method in the above equation for time derivative and the application of Galerkin method to the diffusion term only over the entire domain Ω of equation. Now we can write

$$C_m \int_\Omega W\frac{\partial V_m}{\partial t}d\Omega + \int_\Omega W(I_{ion} + I_{appl})d\Omega = \int_\Omega W[D_x(\frac{\partial^2 V_m}{\partial x^2}) + D_y(\frac{\partial^2 V_m}{\partial y^2})]d\Omega$$

Where, W is the weighting function. Now applying the Euler method for time derivative the resulting algebraic equation in matrix form is following equation

$$(\frac{C_m}{\Delta t}M + k)v^{n+1} = \frac{C_n}{\Delta t}Mv^n + MI_{ion} + MI_{appl}$$

Here M is the FEM lumped mass matrix and K is stiffens matrix.

4 SIMULATIOON RESULT AND DISCUSSION

4.1 Single Cell Simulation

In order to explain the excitability of cardiac cells with modified FitzHugh-Nagumo model researchers use null-clines and phase plots (w, v plot).To find the null-clines of the FHN model, the necessary condition of the two ODEs are

$$\frac{dv}{dt} = 0$$

$$\frac{dw}{dt} = 0$$

From equation (5) and (6) we get

$$w_1 = v(v-\alpha)(1-v)$$

$$w_2 = v\gamma$$

i. Simulation with changing applied current, I_{appl} Keeping α=0.1; ε=0.01; γ=0.5 constant

Figure 1(a) shows the variation of transmembrane potential for I_{appl} =0.1. We can see that the oscillation die out, not stimuli. The phase plane plot shows in the figure 1(b). We can see there is no close loop in the phase plane plot. The figure 1(c) shows the null-clines. We can see the null clines are intersected at point which represents a stable state. So no oscillation occurred.

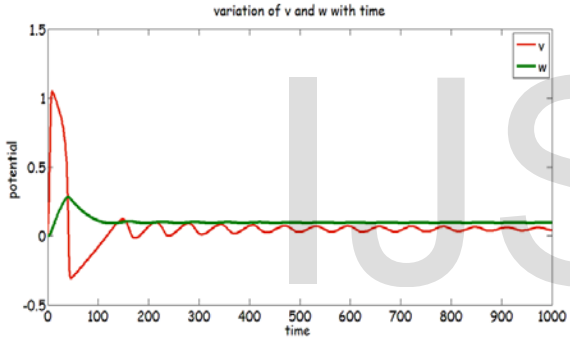

Fig.1(a). I_{appl}=0.1

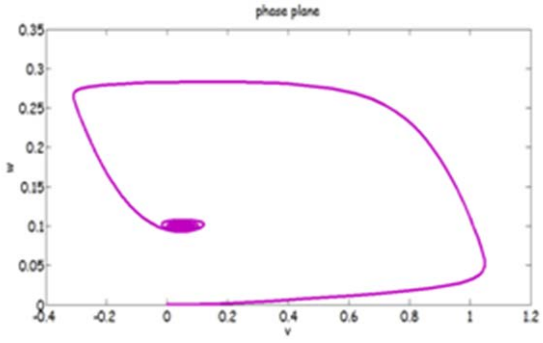

Fig.1(b).Phase Plane for I_{appl}=0.1

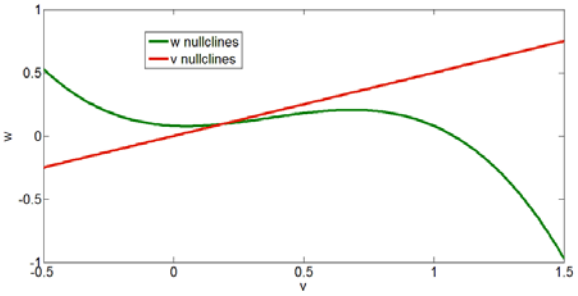

Fig.1(c).Null-Clines of the FHN model for I_{appl}=0.1

Figure 2(a) shows the variation of transmembrane potential for I_{appl} =0.8. We can see that there is a constant oscillation. The phase plane plot shows in the figure 2(b). Due to this value of I_{appl} we can see a close loop in the phase plane. Figure 2(c) shows the null- the null clines are intersected at point which represents an unstable state.So periodic oscillation is occurred.

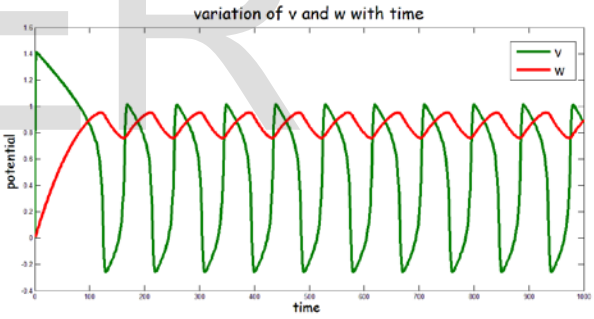

Fig.2(a). I_{appl}=0.8

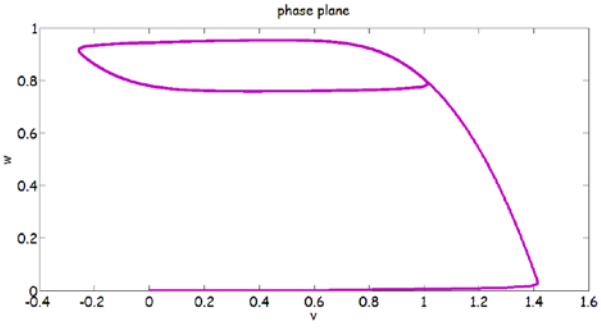

Fig.2(b).Phase Plane for I_{appl}=0.8

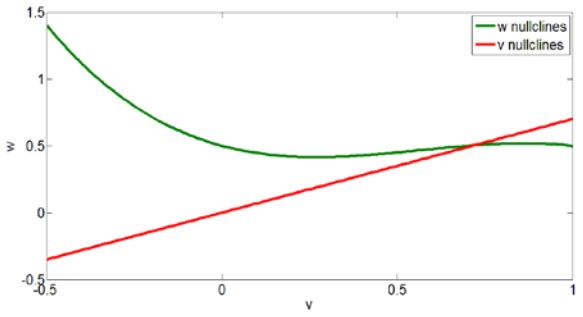

Fig.2(c).Null-Clines of the FHN model for I_{appl}=0.8

ii. Ii. Simulation with threshold value, α Keeping I_{app}I=0.4; ε=0.01; γ=0.5 constant

Figure 3 shows the effects of α on model behavior. The figure 3(a) shows there is no oscillation, only one spike. The value of α is this case is α=0.82. Action potential is not generated for this value of α.

Now if α is set just above the value of applied current i.e. α=0.42, the oscillation is die out as illustrated in the figure 3 (b). Furthermore, if α is set just below the applied current, we can see continuous oscillation by the figure 3(c). Lastly, if the value of α is substantially below the applied current again we see contentious oscillation by the figure 3(d). At the same time the excitation propagation rate also increases.

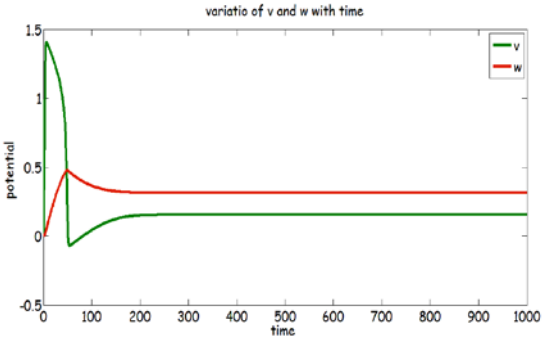

Fig.3(a). α=0.82

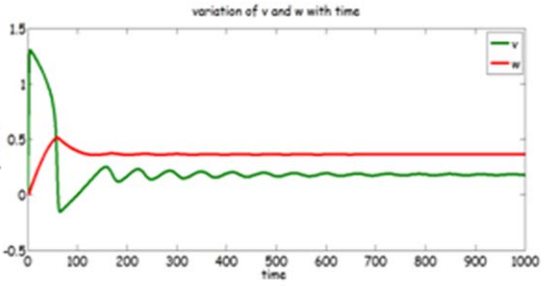

Fig.3(b). α=0.42

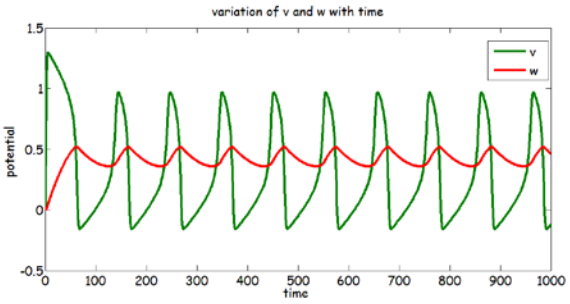

Fig.3(c). α=0.38

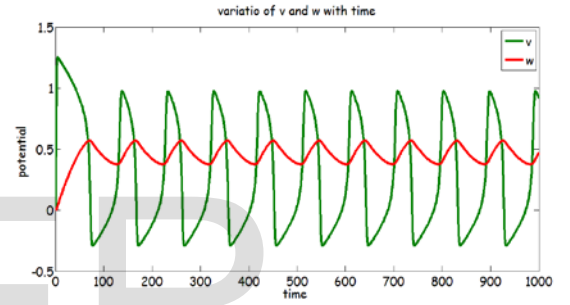

Fig.3(d). α=0.1

From the above study, we can understand the effect of α on the system behavior. If α is above the applied current then no oscillation occurs but if α is below the applied current oscillation occurs and the propagation excitation rate also increases.

4.2 Monodomain Model Simulation

The simulation result is obtained by the MATLAB code to generate the uniform mesh for the heart tissue as a triangular element. The first step in the finite element method is to divide the structure or solution region into subdivisions or elements. Hence, the structure is to be modeled with suitable finite elements. The number, type, size, and arrangement of the elements are to be decided.Although the implementation supports both two dimensional and three-dimensional problems, for the simplicity only two dimensional equations are used. The Intel dual core processor computer with 4GB RAM also used for simulation.

In simulation purpose cardiac tissue is considered as a uniform mesh for triangle elements for 25 × 25 nodal elements. A MATLAB code for 625 nodes and 1152 elements is build up. The simulation work is done about 5 hours. We can observe the propagation of excitations in the heart tissue by the figure 4 for 625nodes and 1152 elements.

The surface plots show the propagation of excitations. Since

the current above the threshold value is applied to the initial node of the square mesh grid and less than threshold value to other nodes. The diffusion coefficient d_x along the fibers and d_y perpendicular to the fibers but not in the plane. From the initial nodes the excitations are propagated to the nearby horizontal and vertical nodes. Since the value of diffusion coefficient along the horizontal axis is more than vertical. So the propagation of excitations along the horizontal axis is more than the vertical. Gradually the excitations propagate from initial nodes to the middle nods. The potential of those nodes changes consequently .After a uniform time interval the excitations reached at the end of the nodes. Then the process started from the initial condition. Figure 4 consequently shows the process.

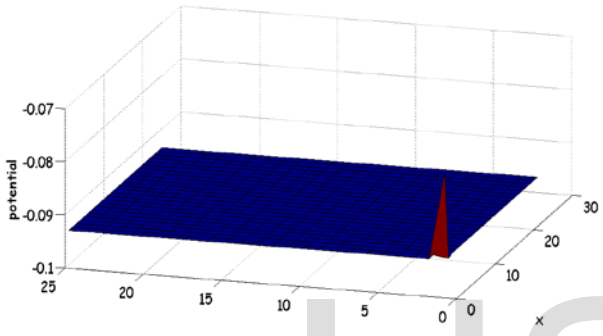

Fig.4(a). Surface plot for the propagation of excitations in the heart tissue at a uniform time step for 25×25 nodal elements.

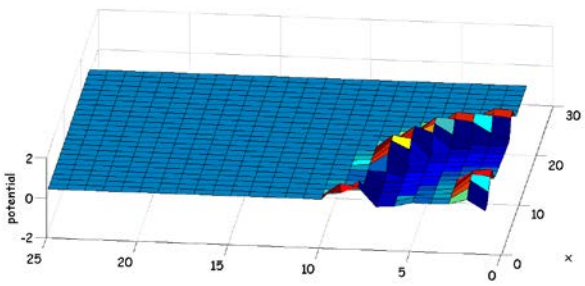

Fig.4(b). Surface plot for the propagation of excitations in the heart tissue at a uniform time step for 25×25 nodal elements.

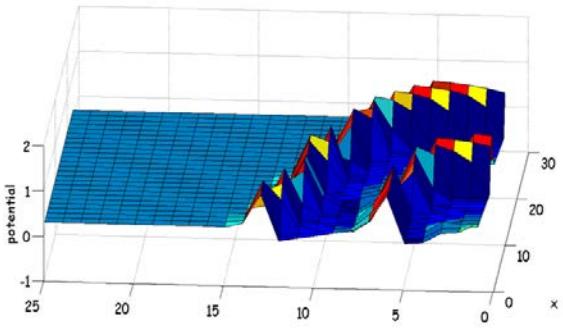

Fig.4(c). Surface plot for the propagation of excitations in the heart tissue at a uniform time step for 25×25 nodal elements.

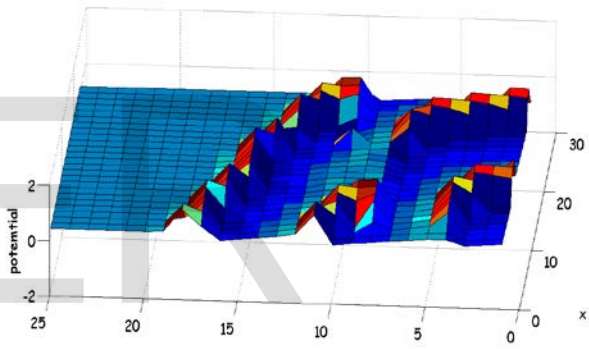

Fig.4(d). Surface plot for the propagation of excitations in the heart tissue at a uniform time step for 25×25 nodal elements.

5 Conclusion

In this research work propagation of excitation in the cardiac tissues is simulated, based on electro-physical monodomain model. The action potential in a single cell is simulated by modified FHN model, especially designed for human cardiac tissues. This research work has been able to create some insights about the electrical behavior of human heart, revealing the nature of the excitation, propagation pattern in the cardiac tissue.

In case of single cell simulation, the modified FHN model is used because it is easy to simulate than other biophysical models. The model consists of two ODEs. Single cell simulation showed that cardiac action potential could be significantly affected by variation of the parameters. We observed the variation of potential, phase plane, phase plane and null-clines plots for different applied current. The phase plane represented the physical properties of the model. Periodic oscillation

occurred only if the null clines intersected at an unstable point. At the same time a close loop forms in the phase plot. We also observed the effect of different threshold values on the system. The oscillation only occurred if the threshold value is less than applied current. Simultaneously the propagation excitation rate also increases.

The two dimensional monodomain equations solved to study the behavior of excitation propagation. The surface plots showed how excitation propagated in the cardiac tissue. node. The model is solved for two dimensional equations for less complicity. If we want to increase more elements and nodes number then the simulation process becomes difficult. Because the simulation process need more time, computer memory and computational power. In future the models can be updated with patient-specific geometry and body surface potentials. At the same time more detailed cell models can be used and eventually the model can be improved by coupling with other electro-mechanical and blood flow models.

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