

Mathematical Modelling of Cardiac Electrical Activity Using Bidomain Approach

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Abstract

In recent times, mathematical model of cardiac electrical activity has been recognized as one of the significant approaches capable of revealing diagnostic information about the heart. However, an efficient and accurate mathematical technique required for this modelling is one of the major problems in the field of biomedical research. This work presents mathematical modelling of cardiac electrical activity using bidomain approach. The cardiac electrical activity is best mathematically modelled coupled systems of ordinary differential equations and partial differential equations which are non-linear, stiff, and therefore difficult to solve numerically and implement. Hence, the bidomain model was adopted due to

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its ability to reflect the actual cardiac wave propagation. Explicit forward Euler method and 2-D network modelling were respectively used for time- and space-discretisation of the derived bidomain equations coupled with FitzHugh-Nagumo's ionic equations to obtain linearized equations for transmembrane potential V_m , extracellular potential ϕ_e and gating variable w which are the main variables of interest. We implemented the linearized equations using code developed from Java 6.0 version to obtain the time characteristic of transmembrane potential V_m . The results of this work provide some insights into the nature of electrical wave propagation pattern in the normal cardiac tissue.

Mathematics Subject Classification: 97N40

Keywords: Mathematical model, Cardiac electrical activity, Bidomain model, Transmembrane potential

1 Introduction

Globally, cardiovascular disease has been recognised as the major source of cardiac deaths. According to the global status report on non-communicable diseases by World Health Organisation (WHO) in 2008 [1], 80% of the 17 million deaths due to cardiovascular disease occurs in low and middle income countries like Nigeria. This therefore calls for immediate attention to address the problem.

Cardiac electrophysiology is the science of the mechanisms, functions and performance of the electrical activities of specific regions of the heart [2]. The normal intrinsic electrical conduction of the cardiac tissue (heart) allows electrical propagation to be transmitted throughout the whole cardiovascular system. The main cause of sudden cardiac death has been attributed to cardiac electrical abnormalities, preventing blood circulation to various compartments of the body. In diagnosing these disastrous cardiac electrical abnormalities, mathematical

modelling of cardiac electrical activities plays a vital role, revealing baseline diagnostic information about the functional status of heart.

The models of cardiac electrophysiology are usually governed by differential equations [3, 4] consisting of systems of partial differential equations (PDEs) coupled to ordinary differential equations (ODEs). The PDEs give the description of electrical wave propagation across the cardiac tissue whereas the ODEs give the description of electrochemical reaction of the cardiac cells.

This work presents mathematical modelling of cardiac electrical activity using bidomain approach with the main focus on cardiac action potential, an important basic electrical property of the heart.

1.1 Bidomain Model

Bidomain model is one of the two differential equation based models for cardiac electrical activity. The model is considered as the mathematical equations that have been used for simulating cardiac electrophysiological waves for years taking into account the non-linear dynamic nature of the cardiac signal and giving realistic simulation. This model gives the representation of the cardiac tissue at a macroscopic scale by relating the transmembrane potential, the extracellular potential and the ionic currents [3, 5]. It consists of a system of two non-linear partial differential equations coupled to a system of ordinary differential equations. However, the major difficulties with this model are the computational grids size that must be very fine to get a realistic simulation of cardiac tissue. The action potential is a wave with sharp depolarization and repolarization fronts and this wave travels across the whole computational domain requiring a very fine uniform mesh. One of the remedies to these computational challenges is the use of the monodomain model. This model consists of a single non-linear partial differential equation coupled with the same system of ordinary differential equations for the

ionic currents. Although, it has been reported that the central processing unit requirements are reduced when simplifying the bidomain model to a monodomain model, but both models still encounter computational difficulties because of the need for fine meshes and small time-steps [5].

2 Mathematical Equations Governing Cardiac Electrical Activity

For complete modelling of the cardiac electrical activity, it is essential to derive a system of governing equations, discretising them into appropriate forms and then solve the discretised equations using suitable techniques.

The electrical wave propagation in the thoracic volume is governed by three fundamental electrical laws [3, 4, 6] which include:

- The electrical charge conservation law
- The electrical conduction law (Ohm's law)
- The consequence to the electromagnetic induction law

The law of conservation of charge states that an outward flow of positive charges must be balanced by a decrease of positive charges within the close surface [7, 8]. Hence, this requires that:

$$I = \oint_S j \cdot ds = -\frac{dQ}{dt} \quad (1)$$

where

- I is the current in Ampere (A)
- J is the current density in Ampere per square meter (A/m²)
- Q is the charge in Coulomb (C)
- S is the surface area in square meter (m²)
- t is the time in seconds (s)

Application of divergence theorem, which relates surface integral to volume integral, to equation (1) gives equation (2) [7, 8]:

$$\oint_S j \cdot ds = \int_{vol} (\nabla \cdot j) dv \quad (2)$$

Representing the enclosed charge Q by the volume integral of the charge density, equations (1) and (2) can be modified as:

$$\int_{vol} (\nabla \cdot j) dv = - \int_{vol} \frac{d\rho}{dt} dv \quad (3)$$

where ρ is the volume charge density in coulomb per cubic meter (C/m^3). Keeping the surface constant, the derivatives in equations (1), (2) and (3) becomes partial derivative and may appear within the integral as:

$$\int_{vol} (\nabla \cdot j) dv = - \int_{vol} \frac{\partial \rho}{\partial t} dv \quad (4)$$

Since equation (4) is true for any volume no matter how small [7, 8], then:

$$\nabla \cdot j = - \frac{\partial \rho}{\partial t} \quad (5)$$

Equation (5) is generally called the continuity equation [7, 8].

For a good conductor, the volume charge density is zero, $\rho = 0$, since the amount of positive and negative charges are equal [9]. Hence, if thoracic volume is assumed to be volume of conductor, equation (5) can be modified as:

$$\nabla \cdot j = 0 \quad (6)$$

Equation (6) is called the electrical charge conservation law.

Relating the current density j with the electric field E in volt per metre (V/m), the electric field E with the electric potential ϕ in volt (V) and current density j with the electric potential ϕ , the following fundamental laws emerge [7, 8]: the electric conduction law (Ohm's law), consequence to electromagnetic induction law and modified Ohm's law represented by:

$$j = \sigma E \quad (7)$$

$$E = -\nabla \phi \quad (8)$$

$$j = -\sigma \nabla \phi \quad (9)$$

where σ is the conductivity in siemen per metre (S/m).

Hence, equations (6), (7), (8) and (9) form the basis for the derivation of the bidomain equations. To fully adapt equations (6) to (9) to cardiac electrical activity, the bidomain model assumes the cardiac tissue as a homogenized two-phase Ohmic conducting medium with one phase representing the intracellular space and the other, extracellular space. The phases are linked by a network of resistors and capacitors representing the ion channels and the capacitive current driven across the cell membrane due to a difference in potential respectively as shown in Figure 1 [10].

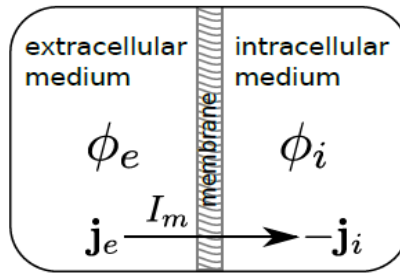


Figure 1: Schematic model of the bidomain space; the intracellular and extracellular domains are separated by cell membrane [10]

Considering a post homogenization process, the intracellular and extracellular domains can be assumed to be superimposed to occupy the whole heart volume Ω_H [3, 11, 12, 13] and this also applies to the cell membrane. Hence, the average intracellular and extracellular current densities, j_i and j_e , conductivity tensors σ_i and σ_e and electric potentials ϕ_i and ϕ_e are defined in Ω_H .

Hence, application of equation (6) to the heart volume gives equation (10) leading to equation (11):

$$-\nabla \cdot j_i = \nabla \cdot j_e = \chi_m I_m \quad (10)$$

where χ_m is the surface – to – volume ratio of the cell membrane per meter
(m^{-1})

I_m is the cell membrane current in ampere (A)

$$\nabla \cdot (j_i + j_\varepsilon) = 0 \quad (11)$$

Putting equation (9) in (10) yields:

$$-\nabla \cdot (\sigma_\varepsilon \nabla \phi_\varepsilon) = \nabla \cdot (\sigma_i \nabla \phi_i) \quad (12)$$

The transmembrane potential, V_m , defined as difference in potential between intracellular and extracellular spaces is represented by:

$$V_m \stackrel{\text{def}}{=} \phi_i - \phi_\varepsilon \quad (13)$$

where ϕ_i is the intracellular electric potential in volt (V)

ϕ_ε is the extracellular electric potential in volt (V)

Substitution of equation (13) in (12) yields equation (14):

$$-\nabla \cdot ((\sigma_i + \sigma_\varepsilon) \nabla \phi_\varepsilon) = \nabla \cdot (\sigma_i \nabla V_m) \quad \text{in } \Omega_H \quad (14)$$

Extending the cell model formulated by Hodgkin and Huxley in 1952 as reported in Matthias [10] with its electric circuit equivalence diagram as shown in figure 2 to the bidomain model gives:

$$I_m = C_m \frac{\partial V_m}{\partial t} + I_{ion}(V_m, w) - I_{app} \quad (15)$$

where C_m is the membrane capacitance in per area unit

I_m is the membrane current in ampere (A)

I_{app} is the excitation current in ampere (A)

I_{ion} is the ionic current in ampere (A)

The use of equations (13) and (15) in (10) yields:

$$\nabla \cdot (\sigma_i \nabla V_m) + \nabla \cdot (\sigma_i \nabla \phi_\varepsilon) = \chi_m (C_m \frac{\partial V_m}{\partial t} + I_{ion}(V_m, w) - I_{app}) \quad \text{in } \Omega_H \quad (16)$$

The ionic variable w satisfies a system of ODE of the type given by equation (17):

$$\frac{dw}{dt} = g(V_m, w) \quad \text{in } \Omega_H \quad (17)$$

where g is a vector-valued function.

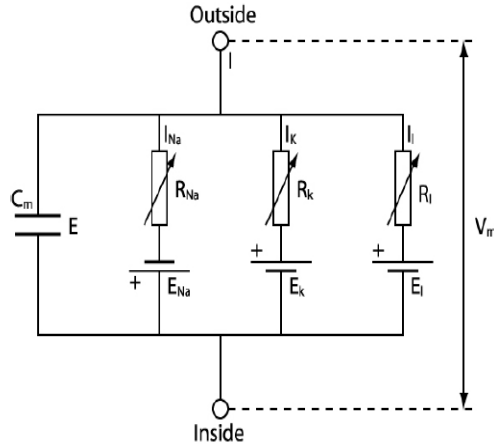


Figure 2: Cell model equivalent circuit diagram; ionic currents are parallel-connected to membrane capacitor [10]

The bidomain model described by equations (14), (16) and (17) depicts a non-linear elliptic equation for the extracellular potential ϕ_ε coupled with the parabolic differential equation for the transmembrane potential V_m as well as an ordinary differential equation representing the ionic current w .

Equations (14) and (16) give the description of the electrical propagation through the cardiac tissue while (17) describes the electrochemical reaction in the cell.

For complete description of cardiac electrical activity, the bidomain model described by the equations (14), (16) and (17) has to be coupled to an ionic model and complemented with appropriate initial and boundary conditions.

2.1 Ionic Model

Various cell models have been proposed to obtain expressions for I_{ion} and g . The cell model considered in this work is FitzHugh-Nagumo's (FHN) ionic model. It was considered basically because of its simplicity and wider theoretical and computational applications. It has just two variables and a cubic non-linearity. Different variants of FHN exist. However, the variant adopted in this work is represented by equations (18) and (19) [14].

$$I_{ion} = \frac{1}{\varepsilon_1} (V_m - \frac{V_m^3}{3} - w) \quad (18)$$

$$g = \varepsilon_2 (V_m - \gamma w + \beta) \quad (19)$$

where $\varepsilon_1, \varepsilon_2, \gamma, \beta$ are the basic parameters of the adopted FHN model. They are typical assumed to be positive constant.

2.2 Initial and Boundary Conditions

The bidomain equations described (14), (16), and (17) are subjected to the initial conditions given by equation (20):

$$V_m(x, 0) = V_m^0(x), \quad w(x, 0) = w^0(x), \quad \forall x \in \Omega_H \quad (20)$$

The boundary conditions imposed on this system of equations (14), (16) and (17) is that of a sealed boundary, where no current flows across the boundary between the intracellular and extracellular domains, that is:

$$\sigma_i \nabla \phi_i \cdot n = \sigma_\varepsilon \nabla \phi_\varepsilon \cdot n, \quad \text{on } \Sigma \quad (21)$$

where n is the normal vector to the domain boundary.

Hence, the complete system of differential equations describing the cardiac electrical activity with ionic model and initial and boundary conditions fully defined is summarised in equation (22).

$$\left\{ \begin{array}{l}
-\nabla \cdot ((\sigma_i + \sigma_\varepsilon) \nabla \phi_\varepsilon) = \nabla \cdot (\sigma_i \nabla V_m) \quad \text{in } \Omega_H \\
\nabla \cdot (\sigma_i \nabla V_m) + \nabla \cdot (\sigma_i \nabla \phi_\varepsilon) = \chi_m (C_m \frac{\partial V_m}{\partial t} + I_{ion}(V_m, w) - I_{app}) \quad \text{in } \Omega_H \\
\frac{dw}{dt} = g(V_m, w) \quad \text{in } \Omega_H \\
I_{ion} = \frac{1}{\varepsilon_1} (V_m - \frac{V_m^3}{3} - w) \\
g = \varepsilon_2 (V_m - \gamma w + \beta) \\
V_m(x, 0) = V_m^0(x), \quad \forall x \in \Omega_H \\
w(x, 0) = w^0(x), \quad \forall x \in \Omega_H \\
\sigma_i \nabla \phi_i \cdot n = \sigma_\varepsilon \nabla \phi_\varepsilon \cdot n \quad \text{on } \Sigma
\end{array} \right. \quad (22)$$

Bidomain equations (14), (16) and (17) are solved for ϕ_ε , V_m and w which are the variables of interest.

2.3 Discretization

Generally, the non-linear bidomain equations (14), (16) and (17) are both time and space dependent and the process of discretization (linearization) has to be dealt with separately. Various time discretization techniques have been explored for use in many modelling works involving differential equations but of interest in this work is the explicit forward Euler method given by equation (23) [15]:

$$U_{n+1} = U_n + hf_n \quad (23)$$

where U represents the discretized version of the function to be evaluated, h , the step size, and f , real-valued function. One major advantage of using equation (23) is that it is most straightforward and easy to solve numerically. However, h , must not be taken too large so that the solution to equation (23) does not become numerically unstable.

Modification and application of equation (23) to equations (16) and (17) which contain the time derivatives with I_{ion} and g replaced by their

FitzHugh-Nagumo's equivalent gives equations (24) and (25) respectively.

$$V_m^{n+1} = V_m^n + \Delta t \left[\frac{1}{\varepsilon_1} \left(V_m^n - \frac{(V_m^n)^3}{3} - w^n \right) - G_i (V_m^n + \phi_\varepsilon^n) + I_{app} \right] \quad (24)$$

with χ_m and C_m assumed unity; G_i , the intracellular admittance matrix equivalent to $-\nabla \cdot \sigma_i \nabla$, and Δt , time step size.

$$w^{n+1} = w^n + \varepsilon_2 \Delta t (V_m^n - \gamma w^n + \beta) \quad (25)$$

Also, owing to the fact the computation of equations (24) and (25) requires the value of ϕ_ε^n , hence, equation (14) becomes:

$$\phi_\varepsilon^n = (G_i + G_\varepsilon)^{-1} [-G_i \cdot V_m^n] \quad (26)$$

where G_ε , the intracellular admittance matrix equivalent to $-\nabla \cdot \sigma_\varepsilon \nabla$.

For the space discretization, 2-D network (discrete) modelling has been employed. Owing to this spatial specification, G_i and G_ε were constructed by considering node arrays N_x -by- N_y defined in the 2-D network domain to be linked by network of resistors arranged along x- and y-direction with η_{ex} , η_{ey} , η_{ix} , and η_{iy} representing the extracellular and intracellular resistance values along these directions. These resistors arrays were then transformed into matrices in the implementation code.

2.4 Application of Computer

Computer programming has become an important tool for the study and comprehension of many complex phenomena such as the cardiac electrophysiology involving the electrical wave propagation in the cardiac tissue (heart). Computer programming generally reduces the computational complexities and requirements of this type of problem using simple mathematical algorithms which take shorter time to implement by writing few lines of codes.

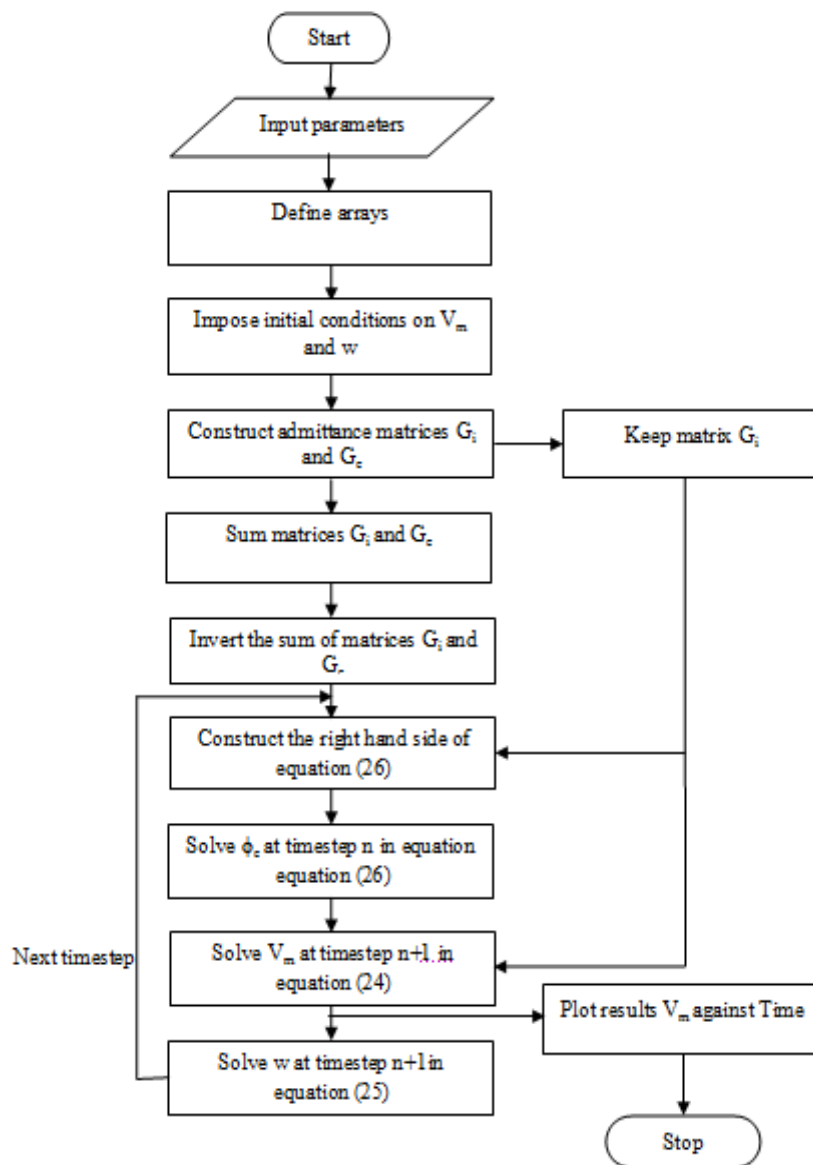


Figure 3: Flow chart for the bidomain implementation code

Java programming language, specifically Java 6.0 version was adopted for the development of the implementation code for the bidomain equations in this

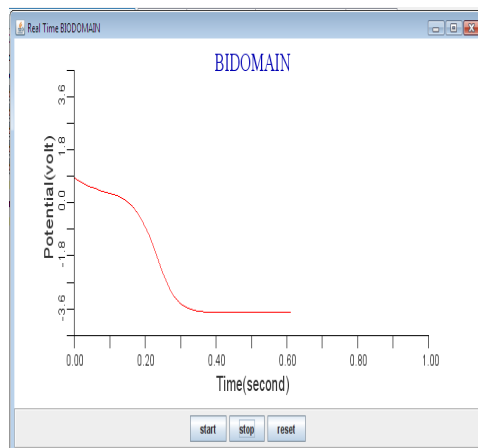
work. It is an object-oriented programming language. It is principally adopted because of its enriched mathematical library for easy implementation of mathematical algorithms and well-designed Graphical User Interface (GUI) to give graphical representation of results. Equally important is the fact it can run on most computer systems. Figure 3 is the flow chart for the developed bidomain implementation code.

3 Numerical Simulation and Results

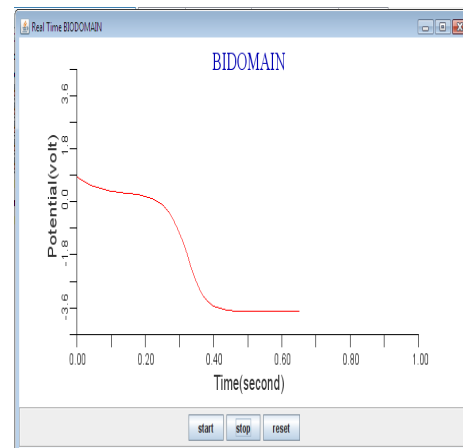
The developed 2-D Java implementation programming code was used simulate the non-linear bidomain equations (14), (16) and (17) based on the discretised equations (24), (25) and (26) with the considered parameters given in table 1. The selected cells 4, 6, 8, 10, 15, 17, 19 and 21 of the 50-by-50 nodes (cells) specified in 2-D network domain produced the propagated electrical waves in the normal cardiac tissue as shown in figure 4a to h respectively. The first stage witnessed a sharp depolarization from negative resting potential to a positive peak within a millisecond. This was followed by a very short period of partial repolarization of less than 100ms. The wave later propagated to a plateau where the potential remains almost positively constant. The signals presented here showed varying plateau periods with the longest around 400ms. Finally, the wave returns to its negative resting potential, indicating the cell has repolarized. These stages are represented in Figure 4(d) for clarity by values 0, 1, 2, 3, and 4 respectively. These processes summed-up to what is called the action potential, with the highest period observed in this work around 600ms. The variation in the plateau sizes in (a) to (h) was due to the fact that the considered cells were at different positions. Figure 4(a) to h are typically of the same wave pattern, consistent with the theoretical standard and the experimental findings from other researchers [3, 16, 17].

Table 1: Values of Basic Parameters [14]

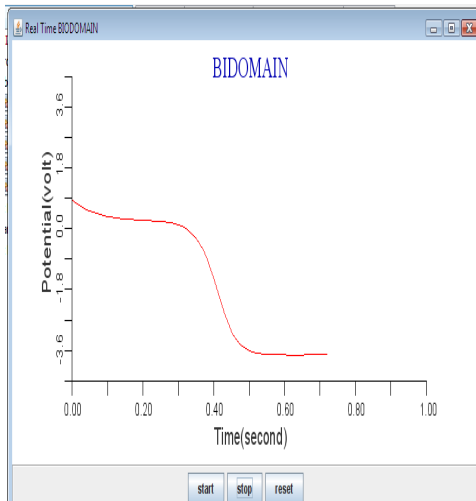
Parameter	Symbol	Value
Excitation rate constant	ε_1	0.2
Recovery rate constant	ε_2	0.2
Excitation decay constant	β	0.7
Recovery decay constant	γ	0.8
Time step size	Δt	0.01
Extracellular resistance in x-direction	η_{ex}	1.0
Extracellular resistance in y-direction	η_{ey}	3.0
Intracellular resistance in x-direction	η_{ix}	1.0
Intracellular resistance in y-direction	η_{iy}	3.0
Resting transmembrane potential	V_m^0	-1.2
Initial value of ionic variable	w^0	-0.62



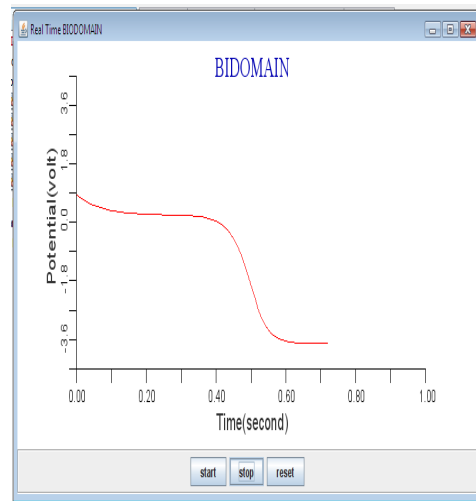
(a)



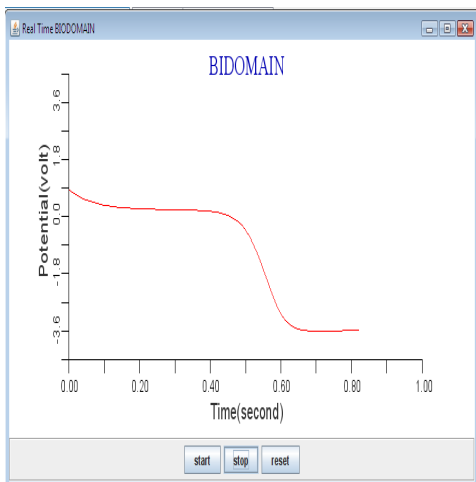
(b)



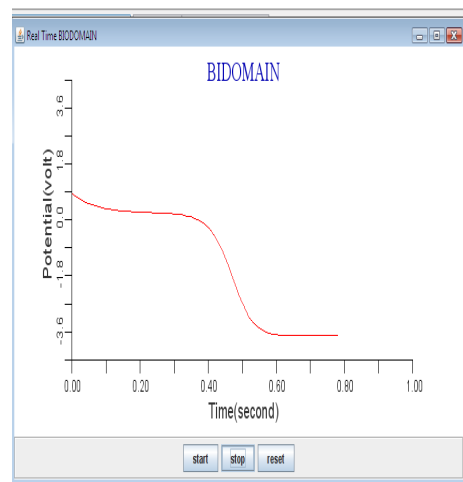
(c)



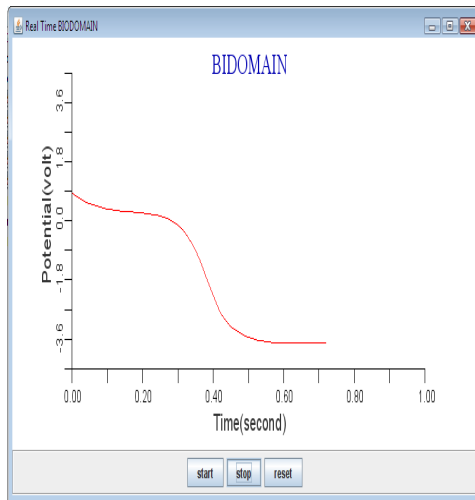
(d)



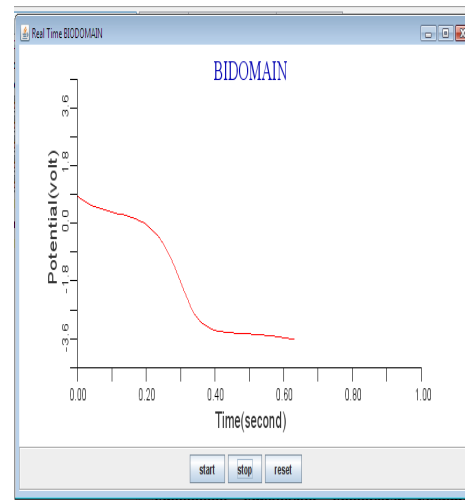
(e)



(f)



(g)



(h)

Figure 4: Electrical wave propagation in the normal cardiac tissue: (a) at cell 4, (b) at cell 6, (c) at cell 8, (d) at cell 10, (e) at cell 15, (f) at cell 17, (g) at cell 19 and (h) at cell 21

4 Conclusion

In this work, a bidomain approach based mathematical model of cardiac electrical activity was presented. This work has been able to create some insights about the electrical behaviour of human heart, revealing the nature of the electrical wave propagation pattern in the normal cardiac tissue. The electrical activity of the cardiac tissue presented in this work was based on coupling the bidomain model with the FitzHugh–Nagumo's ionic model with consideration of sealed boundary conditions between the intracellular and extracellular domains to give a complete description of the cardiac electrical wave propagation. The simulation results showed the excitation pattern in 2-D. The simulation from selected cells 4, 6, 8, 10, 15, 17, 19 and 21 as presented in this work produced wave patterns which were consistent with the theoretical standard and experimental findings of other

researchers. The obtained results in this work are very useful in studying the characteristic properties of action potential as it propagates through the cardiac tissue and in effect detect any electrical wave abnormalities in the cardiac tissue. However, the 2-D network (discrete) modelling approach adopted for spatial discretization still leaves this work for further research based on continuum modelling with particular interest on finite element analysis.

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