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# Modeling and Analysis of Sinoatrial Cell using SIMULINK - A Computational Approach

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## ABSTRACT

**Cardiac action potential has proven to be a powerful tool for illuminating various aspects of cardiac function, including cardiac arrhythmias. Action Potential models containing detailed formulations of biological ionic currents like sodium, potassium, calcium and background currents. In this work, mathematical model of single channel sinoatrial node is modeled using Matlab/Simulink . The action potential output seems to be comparable with the experimental results of rabbit sinoatrial action potential. The action potential duration and height goes with the literature. The currents involving the action potential are blocked and outputs are observed it seems to produce satisfactory outcomes.**

*Keywords*- Action potential, cardiac cell, Iionic currents, Simulink model, Sinoatrial node cell

## I. INTRODUCTION

An action potential is a short-lasting event in which the electrical membrane potential of a cell rapidly rises and falls, following a consistent trajectory. Action potentials occur in several types of animal cells, called excitable cells, which include neurons, muscle cells, and endocrine cells, as well as in some plant cells. In neurons, they play a central role in cell-to-cell communication. There are various origins of action potential in our body; they are muscle action potential (muscle), nerve action potential (nerves) and cardiac action potential (heart). The cardiac action potential is a specialized action potential in the heart, with exclusive properties essential for function of the electrical conduction system of the heart. Heart has five nodes namely sinoatrial, atrial, ventricular, purkinge fiber, and atrioventricular node. Cardiac action potential varies from node to node. This differentiation of the action potentials allows the different electrical characteristics of the different portions of the heart. The action potential initiates at the sinoatrial node. It then travels through the pathways across atria until it reaches the atrioventicular node. Sum of all action potentials is called Electro cardiograph. The action potentials are formed by various ion channels. The major chemicals that involve action potential are sodium and potassium.

The Hodgkin-Huxley (H-H) theory of the action potential, formulated around 60 years ago, stays one of the great achievement stories in biology, and positions among the most important conceptual breakthroughs in neuroscience. From experiments using voltage-clamp protocols, they concluded that these two currents result from independent permeability mechanisms for $Na^+$ and $K^+$ with conductance changing as a function of time and membrane potential. This
was an astonishing conceptual breakthrough, later termed the 'ionic hypothesis,' a merging structure for the field. H-H model [1] describes how action potentials are initiated and propagated. Sinoatrial node is the pacemaker of the heart. Action potential is initiates from sinoatrial node.

The Hodgkin-Huxley modeled the action potential; the semi permeable cell membrane separates the interior of the cell from the extracellular liquid and acts as a capacitor [2-6]. If an input current I(t) is injected into the cell, it may add further charge on the capacitor, or leak through the channels in the cell membrane. Because of active ion transport through the cell membrane, the ion concentration inside the cell is different from that in the extracellular liquid. The Nernst potential generated by the difference in ion concentration is represented by a battery. The base of the modeling of action potential was taken the previous works [7]-[13].

The paper is organized as follows: in section 2, review of action potential is presented. Mathematical modeling of action potential is detailed in section 3. The modeling of the action potential is done using Matlab/Simulink software and results are presented in section 4.

## II. ACTION POTENTIAL

A typical action potential has four prominent stages, Depolarization phase, Re-polarization phase, Hyper-polarization phase and resting potential phase shown in figure1.

Depolarization phase is referred to be the starting stage of the action potential [14]. This phase is characterized with opening of voltage-gated sodium channels, wherein the entry of sodium ions stimulates more voltage-gated sodium channels to open, thereby acting like a feedback loop causing a great deal of sodium ions to enter. Inward-rushing Na+ ions would carry the inward current of the active membrane, depolarizing it from rest to near $E_{Na}$ and eventually bringing the next patch of membrane to threshold as well in close agreement with the theory, the action potential rose less steeply, propagated less rapidly, and overshot less in low-Na external solutions. Voltage-gated sodium channels remain open, voltage-gated potassium channels remain closed.

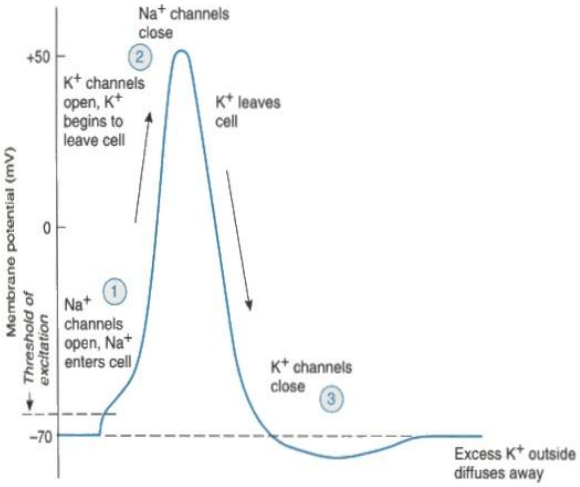


Fig.1. phases of Action potential

With the increase in sodium ions concentration, the potential raises higher and higher until the sodium ion concentration gets saturated. This was the point when the voltage-gated potassium channel starts to open, so that efflux of potassium ions happens from inside to outside, thereby the increased positive potential starts to reduce which reflects the re-polarization phase.

Re-polarization phase is voltage-gated sodium channels were closed and voltage-gated potassium channels start to open to counterbalance the accumulated positive potential developed inside with the entry of sodium ions. Movement of potassium ions continues until the potential reaches the resting level and drives the potential further below the resting level.

Hyper-polarization phase is the phase extends from the point when it goes below resting level and reaches again back to resting level. The dynamics of voltage-gated potassium channels were slower compared to voltage-gated sodium channels. Due to their slower recovery, more number of potassium ions was driven out taking the potential to below the resting potential. This period is also referred as refractory period. Two types of refractory periods exist: absolute refractory period and relative refractory period. Absolute refractory period refers to the period in which neuron cannot fire an action potential however strong the input is. On the other hand, relative refractory period refers to the definition close to absolute refractory period, only that firing of an action potential could be possible if it receives stronger input.Resting potential phase is the phase refers to the equilibrium state of the neuron. After the refractory period, the potential again returns back to the resting potential. The resting potential or equilibrium potential is determined by Nernst Equation.

## III. MATHEMATICAL MODEL OF ACTION POTENTIAL

The currents involving the action potential are sodium current $i_{Na}$, L type calcium current $i_{Ca,L}$, T-type calcium current $i_{Ca,T}$, $i_{to}$, 4-AP-sensitive sustained outward current $i_{sus}$, rapid potassium current $i_{K,r}$, slow potassium current $i_{K,s}$, and if. The models also include formulations for background currents $i_{b,Na}$, $i_{b,Ca}$, $i_{b,K}$, $i_p$, and $i_{NaCa}$.

The $i_{Na}$ was considered to be not present in sinoatrial node cells, and most previous models of the sinoatrial node action potential do not include $i_{Na}$. On the other hand, experimental results show that $i_{Na}$ is present and physiologically important [16]. Demir et al. [17] established $i_{Na}$ in their model of the rabbit sinoatrial node action potential. Sodium has two gates ‘m’and ‘h’ activation and inactivation gates respectively. The inactivation variable h is the weighted sum of $h_1$ and $h_2$. $F_{Na}$ is the fraction of inactivation that occurs slowly and is dependent on the membrane potential.

Calcium current also contributes to the action potential. There are two types of calcium current L-type and T-type [18] & [19]. The intracellular calcium uptake and release processes are essential features action potential. $i_{Ca,L}$are described with an activation gating variable $d_L$ and an inactivation gating variable $f_L$. The kinetics of $i_{CaT}$ is described with an activation gating variable $d_T$ and an inactivation gating variable $f_T$. The steady-state activation and inactivation are described by their equations Earlier models of the sinoatrial node action potential did not include $i_{to}$. On the other hand, $i_{to}$ is now identified to be present in the sinoatrial node as well as to play a key role [20]. The $i_{to}$ is known to be obstructed by 4-AP. In sinoatrial node cells, 4-AP blocks a transient outward current as well as a sustained outward current. It is vague whether the transient and sustained currents represent two stages of one

current or two separate currents. Therefore in this model we used the same variable for activation r for $i_{to}$ and $i_{sus}$. Obviously, the inactivation variable q only rules $i_{to}$.

Recent studies have shown that potassium current in sinoatrial node cells [21] & [22] can be divided into two different components rapid delayed rectifier current $i_{K,r}$and slow delayed rectifier current $i_{K,s}$. Two activation variables a fast activation variable ($p_{a,f}$) and a slow activation variable ($p_{a,s}$). The general activation variable ($p_a$) is the sum of the both activation variables. The time constants of the fast and slow activation variables ($t_{pa,f}$and $t_{pa,s}$) are bell-shaped functions of membrane potentials. The slow sigmoid activation of $i_{K,s}$is modeled by squaring a gating variable ($x_s$). The $i_{K,s}$has been examined to overturn at voltages positive to $E_K$, which advocates that the $i_{K,s}$channel is leaky to an ion in addition to potassium.

The current $i_f$ is a mixed current and carried by $Na_1$ and $K_1$ [11]. The current $i_f$ has two components, $i_{f,K}$and $i_{f,Na}$. The $i_f$ channel are permeable to both sodium and potassium ions. The experimentally observed $i_f$ current voltage relation is approximately linear and the reversal potential lies somewhere between the potassium equilibrium potential and the sodium equilibrium potential.

Background calcium current is needed to keep the diastolic level of the intracellular free calcium concentration in the generally accepted range. Potassium channels account for a small outward background current $i_{bK}$ adopted from Noble-Noble equations [23], scaled down by a factor of 100, to describe this current. The inward background sodium current [10] is described by the Noble-Noble are also taken into the account for action potential. The equations corresponding to all the above said currents are taken from [24]. Equations 1 and 2 represents, the total current which is the sum of all gate currents and the action potential voltage is denoted by ohm's law i.e. total current divided by membrane capacitance respectively.

$$i_{tot} = i_{Na} + i_{Ca,L} + i_{Ca,T} + i_{to} + i_{sus} + i_{K,r} + i_{K,s} + i_f + i_{b,Na} + i_{b,Ca} + i_{b,K} + i_{NaCa} + i_p \quad (1)$$

$$\frac{dv}{dt} = -\frac{1}{c_m} i_{tot} \quad (2)$$

## IV. Results and discussions

The mathematical model of the action potential is modeled in simulink is shown in figure 2.

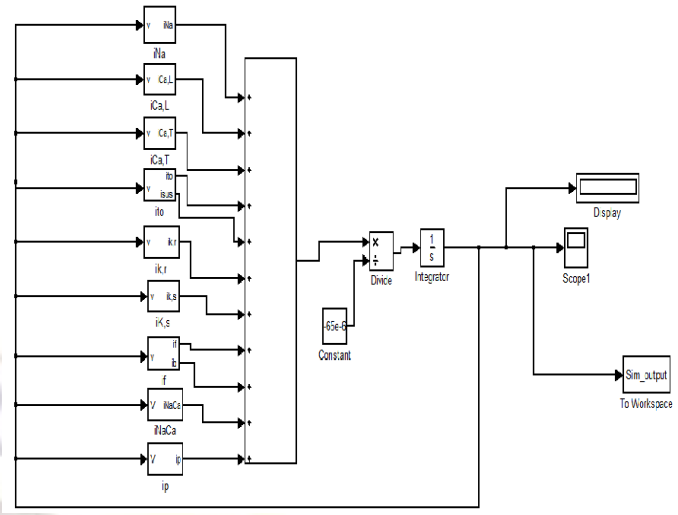


Fig.2. Schematic of model built to simulate action potential

The action potential output is shown in figure 3, the action potential duration is measured as 750ms and the action potential peak amplitude is measured as 74mV. These values are going with the literature.

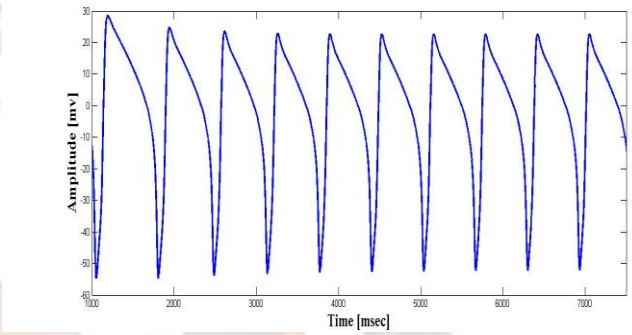


Fig.3. Sino atrial node the action potential.

From the simulation it is found that heart rate of the SAN node cell of rabbit is 200beats per minute, i.e. the pacemaker cells beat in the frequency range of 180 – 225 bpm.At the same time, the normal heart rate of the rabbit varies from 130 to 325 beats per minute. So it is clear that the heart rate of the pacemaker cells of the rabbit from the simulation coincides well with the normal heart rate of rabbit.

To show the importance of various currents in action potential, each current was blocked and their respective output are shown in figure 4 to figure 10.

Figure 4 shows the blockage of sodium current and its effects, the takeoff potential is transferred to a further positive value and the maximum upstroke velocity is reduced. The effect of block of $i_{Na}$ on spontaneous activity is less in the action potential.

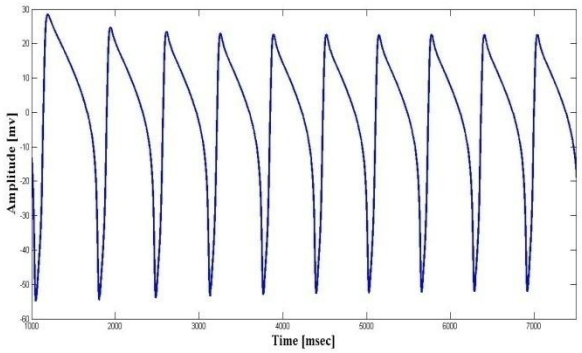


Fig.4. The blockage of sodium current in action potential.

Figure 5 shows the block of T-type calcium current, due to the blocking action potential is abolished.

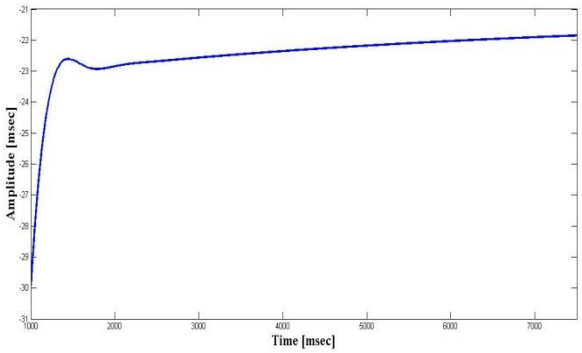


Fig.5. The blockage of $I_{caT}$ current in action potential.

Figure 6 shows the block of L-type calcium current, causes a small raise in cycle duration of action potential.

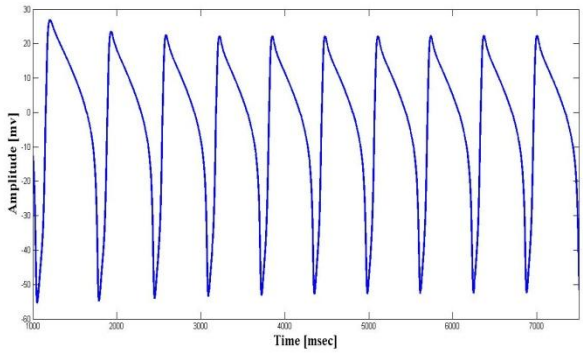


Fig.6. The blockage of $I_{caL}$ current in action potential.

Figure 7 shows the block of 4-AP-sensitive current leads to an increase in the peak value of the action potential and an increase in cycle length in action potential.

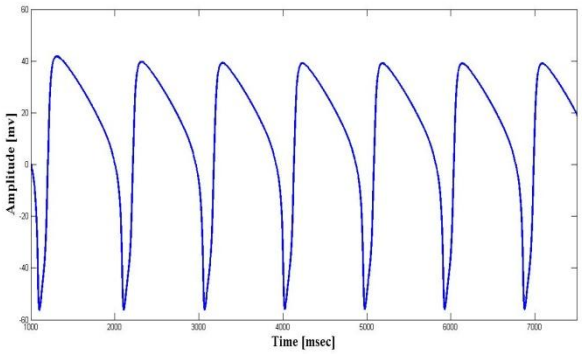


Fig.7.Tthe blockage of 4-AP sensitive current in action potential.

Figure 8 shows the block of $i_{kr}$ , results in abolishment of action potential. $i_{K,r}$is important for peacemaking, thus when $i_{K,r}$is blocked, the spontaneous activity ceases.

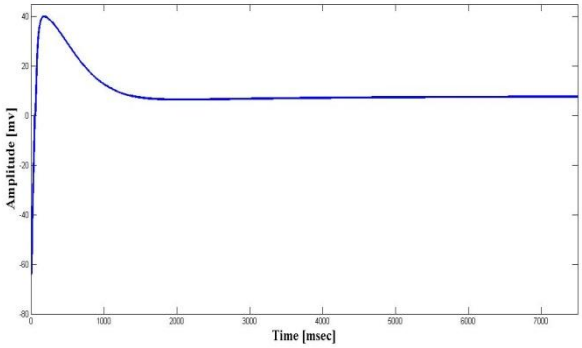


Fig.8.The blockage of iKr current in action potential.

Figure 9 shows the obstruction of $i_{ks}$, has little effect on the pacemaker activity. The cycle length of the action potential changes by 0.3 and 1%.

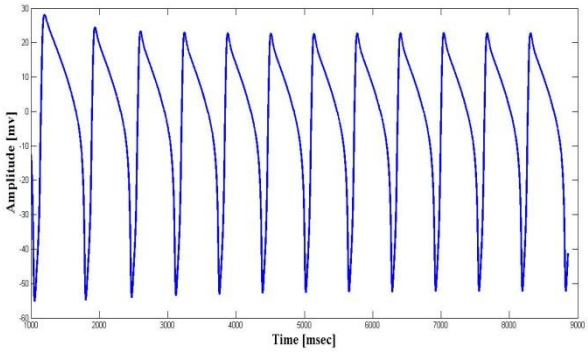


Fig.9. Theblockage of $i_{Ks}$current in action potential.

Blocking of $i_f$ is shown in figure 10, which results in slowing the spontaneous activity of action potential to greater extent.

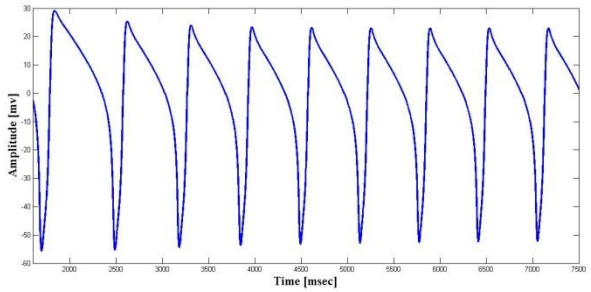


Fig.10.Tthe blockage of $i_{Ks}$ current in action potential

## V. CONCLUSION

From the modeling, it is concluded that in action potential of SA node, takeoff potential is more negative and the maximum upstroke velocity is higher, effect of elevated density of sodium current, the action potential has notch as a consequence of a higher density of $i_{to}$, the action potential is small as a result of higher densities of $i_{K,r}$and 4-AP-sensitive current, the utmost diastolic potential is more negative chiefly as a result of a higher density of $i_{K,r}$, and the impulsive activity is rapider as a effect of higher densities of $i_{Na}$ and *if* as well as the shorter action potential. The action potentials of the SA node cell models are comparable to action potentials recorded from peripheral tissue of the rabbit SA node. The effects of block of these currents are qualitatively similar to those seen experimentally.

In future work, it is proposed to develop the action potential for other nodes of the heart such as, atrial, ventricular, atrioventricular and Purkinje fiber. And also the modeling is extended to two and three-dimensional model of the intact sinoatrial node, which then can be used in the development of a whole heart model.

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