EFFECT OF PROPAGATION PARAMETERS ON THE REPOLARIZATION PHASES OF THE ACTION POTENTIAL OF A CARDIAC PURKINJE FIBER

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ABSTRACT

During the propagation of the action potential through a Purkinje fiber, a membrane current component (J_{mp}) is produced due to the propagation mechanism. This component is a function of the fiber electrical and geometrical parameters. It interacts with the capacitive and ionic current components of the membrane and therefore it affects the action potential (AP). The purpose of this paper is to study the effect of J_{mp} on the AP with special emphases on the repolarization phases for different electrical and geometrical parameters of a Purkinje fiber. The results obtained showed that J_{mp} affects the action potential duration (APD) and its effect is highly dependent on the fiber parameters. Also a mathematical matching condition at the fiber was proposed by this study.

Keywords: Repolarization, Depolarization, Purkinje fiber, Membrane action Potential.

1. INTRODUCTION

Several models were used to reconstruct the membrane of a cardiac cell [1-4]. Propagation of cardiac AP was considered in one dimension [5-7] and in two dimensions [8,9]. Spach M.S. et al [10] studied the role of the structural complexity of the fiber in the propagation of the depolarization phase of AP. The effect of the propagation boundaries was considered by Spach M.S and Kootsey T.M. [7]. The AP collision in a heart tissue was studied by Steinhouse B.M. et al [6]. The Collision was proved to affect the AP during the depolarization phase by increasing both the over shoot potential and the maximum rate of potential rise, but decreasing the sodium current. The local disturbance of J_{mp} produced at the collision site was proved to shorten the AP duration.

2. THEORETICAL CONSIDERATIONS

The present work is a study on the effect of the propagation current J_{mp} on the AP pattern specially on the repolarization phases. Two cases have been considered, namely i) a cylindrical fiber with a constant diameter, and (ii) a conical fiber with a linearly changing diameter.

2.i. Case of a uniform cylindrical fiber (Figure (1)):

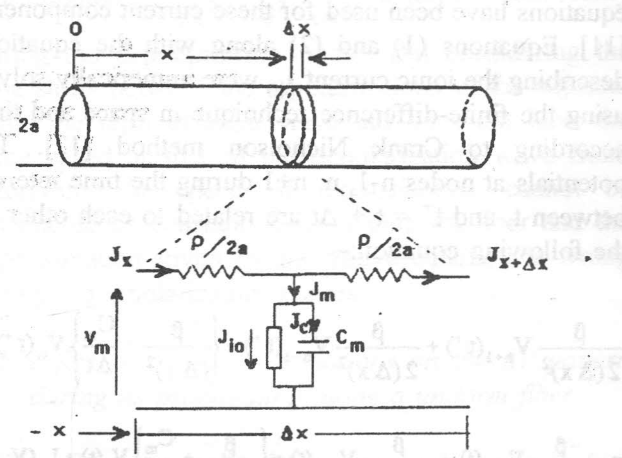

Figure 1. A simple representation of a segment of a uniform fiber. The membrane current density is the sum of the capacitive and the ionic current density components.

The equation controlling the propagation of the AP through a uniform cylindrical fiber is [5]:

$$J_{mp} = C_m \frac{\partial V_m}{\partial t} + J_{io}(V_m,t) \quad (1)$$

where J_{mp} is given by:

$$J_{mp} = \beta \frac{\partial^2 V_m}{\partial X^2} \quad (2)$$

Where;

β = $a/2\rho$ (μS)
a = Fiber radius (cm)
ρ = Specific resistivity of the intracellular fluid (MΩ.cm)
V_m = Membrane potential (V)
C_m = Membrane specific capacitance ($\mu F/cm^2$)
J_{io} = Ionic membrane current density ($\mu A/cm^2$)
J_{mp} = Total membrane current density ($\mu A/cm^2$)

The ionic current J_{io} is a multi-component current. It includes sodium, potassium, and chlorine components. These components are controlled by voltage and time dependent gating mechanisms. McAllister-Nobel-Tesin (M.N.T) model gives the details of these current components [1]. In the present work, simplified equations have been used for these current components [11]. Equations (1) and (2) along with the equations describing the ionic current J_{io} were numerically solved using the finite-difference technique in space and time according to Crank Nicholson method [12]. The potentials at nodes n-1, n, n+1 during the time interval between t, and $t^+ = t + \Delta t$ are related to each other by the following equation:-

$$\frac{\beta}{2(\Delta x)^2} V_{n+1}(t^+) + \frac{\beta}{2(\Delta x)^2} V_{n-1}(t^+) - \left\{\frac{\beta}{(\Delta x)^2} + \frac{C_m}{\Delta t}\right\} V_n(t^+)$$

$$= \frac{-\beta}{2(\Delta x)^2} V_{n+1}(t) - \frac{\beta}{2(\Delta x)^2} V_{n-1}(t) + \left\{\frac{\beta}{(\Delta x)^2} - \frac{C_m}{\Delta t}\right\} V_n(t) + J_{io}(V_n,t) \quad (3)$$

Where; ΔX is the length of the fiber segment and Δt is the time interval.

The solution of the above equations was obtained for different values of β ranging from 3.2 to 320 μS. The boundary condition at the fiber end would be treated as a short circuit or on open circuit

In the present work we introduced a new technique to match the fiber at its end. This was implemented by setting the potential of a hypothetical node V_{N+1} equals to the potential of the last node N with a time delay Δt, i.e., $V_{N+1}(t) = V_N(t-\Delta t)$. The time delay Δt was calculated from the time difference between the two rising phases of nodes N, N-1. This proposal included an acceptable approximation $\frac{\partial^2 V}{\partial x^2} = \frac{1}{\theta^2}\frac{\partial^2 V}{\partial t^2}$ to be applied only for the last segment. In this case the fiber would appear to be infinite.

2. ii Case of conical fiber with a linear change of its diameter

The fiber diameter may change at a sight where two different fiber tissues are connected together. Therefore we studied in this part the effect of a hypothetical linear change of fiber diameter along its length on the action potential pattern (AP).

Considering a conical fiber with a radius (a_x) as a function of x, (Figure (2)), equations (1) and (2) reduce to:

$$\frac{a_x}{2\rho}\frac{\partial^2 V_m}{\partial x^2} + \frac{K}{\rho}\frac{\partial V_m}{\partial x} = C_m \frac{\partial V_m}{\partial t} + J_{io}(V_m,t) \quad (4)$$

Where;

$$K = \frac{\partial a_x}{\partial x}$$

This equation may be written in the finite difference form as follows:

$$A\ V_{n+1}(t^+) + D\ V_{n-1}(t^+) - E\ V_n(t^+)$$

$$= -A\ V_{n+1}(t) - D\ V_{n-1}(t) - F\ V_n(t) + J_{io}(V_n,t) \quad (5)$$

Where;

$$A = \left[\frac{a_x}{4\rho(\Delta x)^2} + \frac{K}{4\rho\Delta x}\right] \quad (6\text{-a})$$

$$D = \left[\frac{a_x}{4\rho(\Delta x)^2} - \frac{K}{4\rho\Delta x}\right] \quad (6\text{-b})$$

$$E = \left[\frac{a_x}{2\rho(\Delta x)^2} + \frac{C_m}{\Delta t}\right] \quad (6\text{-c})$$

$$F = \left[\frac{a_x}{2\rho(\Delta x)^2} - \frac{C_m}{\Delta t}\right] \quad (6\text{-d})$$

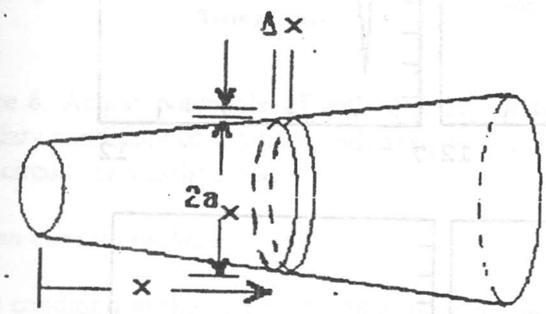

Figure 2. A conical fiber with linear change of its diameter.

3. RESULTS

3.1 *Effect of J_{mp} on the AP pattern of a uniform fiber*

3.1.i) *Depolarization phase*

Figure (3) shows the ionic and membrane currents during the depolarization phase of AP's for different fibers with β = 16,32, and 64 μS. It is obvious that the membrane current slightly affects the rate of rise $\frac{dV_m}{dt}$ of the (AP) during the depolarization phase. Due to the biphasic pattern of J_{mp}, the positive part helps the ionic current to increase the rate of rise of the depolarization phase while the negative part decreases the rate of the late depolarization phase. However, we may consider the effect of β on the membrane current, to be very limited. This means that the change of $\partial^2 V_m/\partial x^2$ is inversely proportional to the change of β, keeping the membrane current unchanged.

3.1. ii) *Repolarization phases*

The action potential duration (APD) decreases as J_{mp} increases. This is produced by the interaction between J_{mp} and J_{io} during the end of phase 1 and at the beginning of phase 2. Considering that J_{io} is generally very small during this period to produce the plateau of the AP the APD is highly sensitive to any change of J_{io} during this period. Therefore the interaction between J_{mp} and J_{io} during this sensitive period affects the APD. (Figure (4 & 5)). The negative value of J_{mp} tends to reduce the positive slope of the AP and may even turn it into negative reducing the APD with the increase of β.

3.1.iii) *Conduction velocity of the action potential*

In Biophysics, it is widely accepted that the conduction velocity θ is almost proportional to $\sqrt{\beta}$. This result has been verified by our calculations as shown in Figure (6). Also it shows that the approximation $\frac{\partial^2 V_m}{\partial x^2} = \frac{1}{\theta^2}\frac{\partial^2 V_m}{\partial t^2}$ is not far from reality during the depolarization phase. But considering the time shifts between the repolarizations of the adjacent cells, the repolarization wave tail does not have the same speed as that of the depolarization wave front. Therefore, the speed of repolarization cannot be considered as constant along a uniform fiber and the approximation given by the above equation is wrong during the repolarization phases.

3.2. *Effect of boundary conditions on the AP pattern during its propagating along a uniform fiber*

The AP were calculated for some mid-fiber cells (no. 20 - to -30) among the 50 cells of the fiber. Three boundary conditions were tested; open circuit, short circuit and matched end. The results obtained are shown in Figure (7).

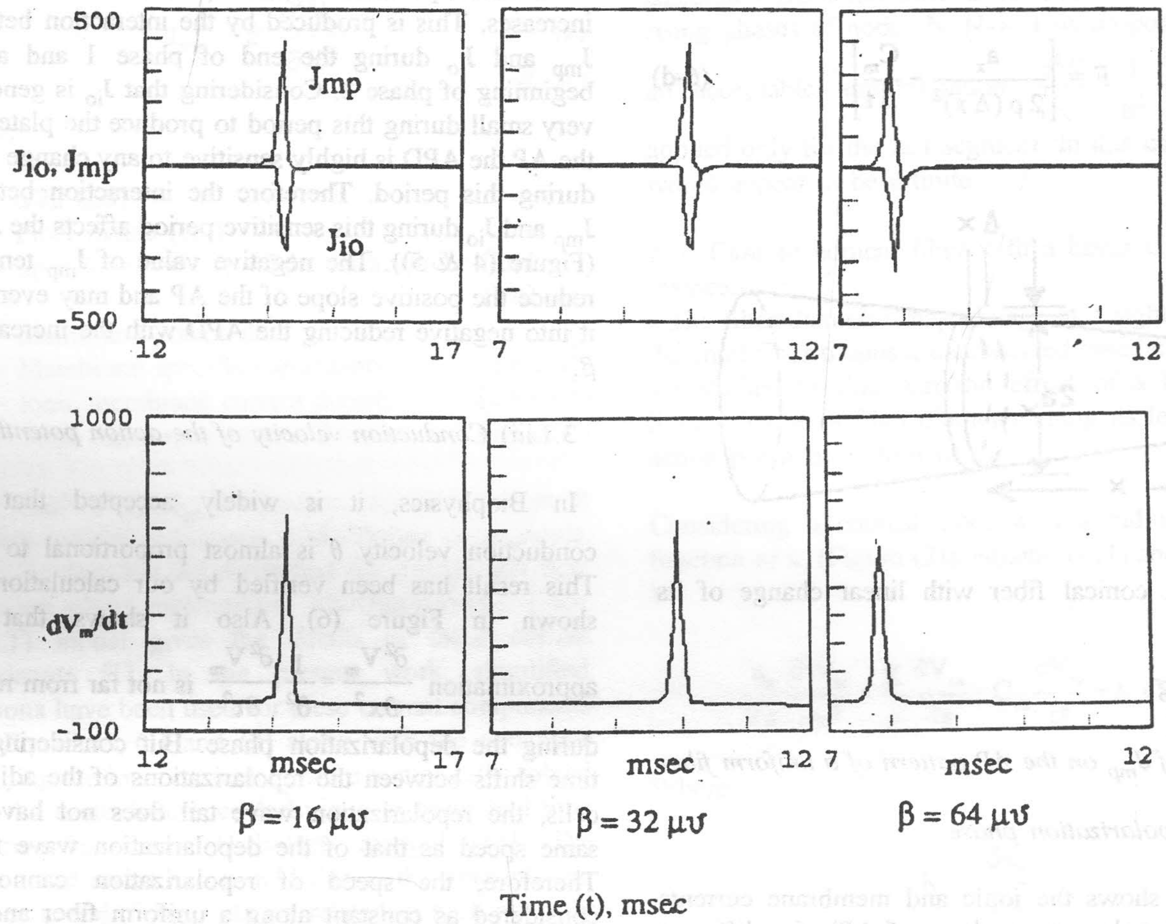

Figure 3. The membrane and ionic current densities J_{mp} & J_{io} (top) and the membranae voltage rate of rise dV_m/dt (bottom) as functions of time t for different values of β.

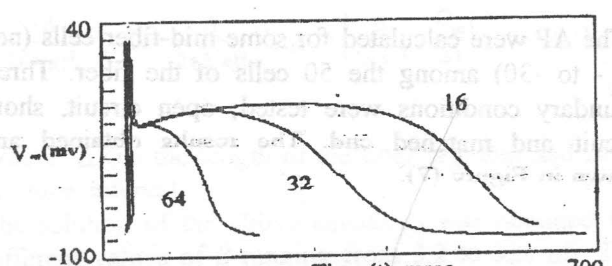

Figure 4. The membrane action potential for different values of β = 16, 32, and 64 μv. It is obvious that the APD decreases as β increases.

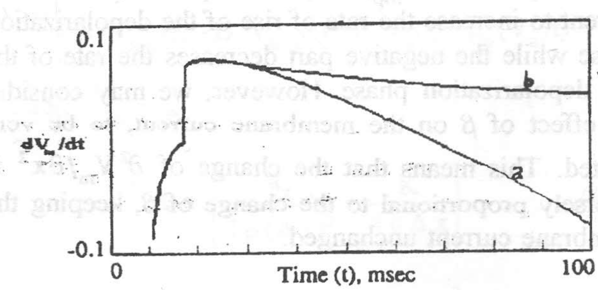

Figure 5. The slope of the action potential vD_m/dt during the plateau phase (2) of repolarization with (a) and without (b) the effect of J_{mp}.

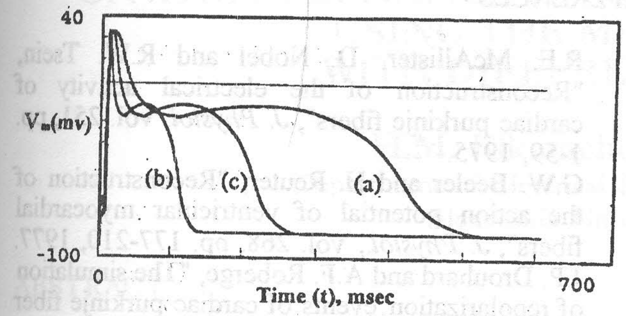

Figure 6. Action potentials of cells No. 25 for three boundary conditions at the fiber end; a) open circuit, b) short circuit, c) matched end.

i) *Open circuit condition*

This condition at the end of the fiber does not affect either the depolarization phase or the speed of conduction in the middle region of the fiber. But, the repolarization is generally prolonged due to the diminishing effect of J_{mp} on the repolarization phases, specially when we approach the open circuit end.

3.2. ii) *Short circuit condition*

Short circuiting the final cell produces a stimulating current at the end of the fiber. Therefore a depolarization wave starts backward from the end at the same time with the forward wave. This appears from the reversed depolarization sequence of cells no. 25 to 28. This result shows that a short circuit cannot be used as a condition to study the propagation of an action potential wave. However, we may conclude that short circuit condition is a source of stimulation which may explain the liable arrhythmias with myocardial infraction or ischemia where the cell potential at the defected site may reach a value of zero.

Considering the effect of the short circuit condition on the repolarization phases, Figure (7) shows that the APD is greatly reduced by the short circuit condition at the fiber end. This could be explained by the cumulative effect of J_{mp} produced by the forward and the backward propagated waves.

3.2. iii) *Matching condition*

Using the matching condition, which we proposed in this paper, a uniform speed of conduction along the fiber was obtained. Also the APD was almost the same along the fiber. and the differences in AP patterns were minimal. Figure (8) shows that J_{mp} under matching condition is, almost the same along the fiber during the repolarization phases which insures identical patterns of AP even near the fiber end. In the case of open circuit condition, J_{mp} in the middle of the fiber significantly differs from that near the end (Fig. 8), which leads to unequal APD along the fiber. Therefore we believe that the matching condition is the optimum way to represent an infinitely long fiber.

3.3. *Case of a non-uniform fiber:*

Considering that the fiber diameter changes at the intermediate region between two types of fibers, therefore, two cases were considered; i) the fiber diameter varies from a large size (35 μm) to a smaller size (10 μm) with a linear negative slope and, ii) the opposite case.

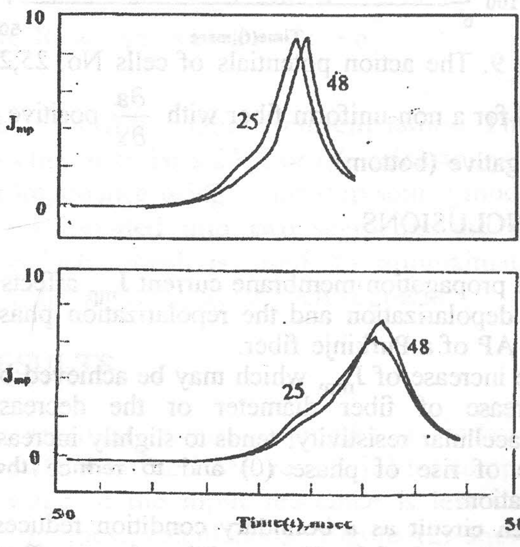

Figure 7. The membrane current density for cell No. 25 and No. 48 under open circuit condition at the fiber end (bottom) and the matching condition (top).

As shown in Figure (9), it is obvious that the APD is greatly reduced when an AP wave propagates in a fiber with a negative slope diameter (i) compared with the case of the positive slope diameter (ii). It seems that the negative slope of a fiber diameter creates progressive increase of membrane current J_{mp} which tends to reduce the APD. Also, from the calculated values, the speed of conduction in the middle region of the fiber (cells 25-28), is almost unaffected by changing the sign of the slope of the fiber diameter.

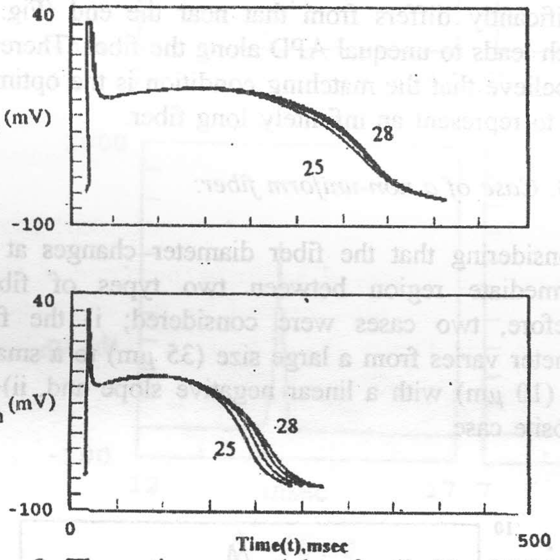

Figure 9. The action potentials of cells No. 25,26,27, and 28 for a non-uniform fiber with $\frac{\partial a}{\partial x}$ positive (top) and negative (bottom).

4. CONCLUSIONS

1- The propagation membrane current J_{mp} affects both the depolarization and the repolarization phases of the AP of a Purkinje fiber.
2- The increase of J_{mp}, which may be achieved by the increase of fiber diameter or the decrease of intracellular resistivity, tends to slightly increase the rate of rise of phase (0) and to reduce the AP duration.
3- Open circuit as a boundary condition reduces J_{mp} near the end of the fiber, and therefore it affects the AP in a similar way as the case of a reduced J_{mp}.
4- The matching condition at the end of the fiber, proposed by this paper, is a good approximation to represent an infinitely long fiber.
5- For a non-uniform fiber, the negative slope of fiber diameter shortens the APD and has no effect on the speed of conduction.

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