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A MODIFIED CABLE FUNCTION FOR REPRESENT THE EXCITATION OF PERIPHERAL NERVES BY TRANSVERSE FIELD INDUCED BY PULSED MAGNETIC FIELD

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Abstract-**The classical cable equation has been used to represent the excitation of peripheral nerves by longitudinal field. But it can not predict the excitation of peripheral nerves by transverse field. A modified cable equation is presented to represent the excitation of peripheral nerves in transverse field. It is in close agreement with Struijk's empirical data of the magnetic stimulation myelinated nerve in vitro. The modified cable equation can be used to represent the response of peripheral nerves in arbitrary electric field.**

Key words-**transverse field, excitation, peripheral nerves, cables equation, magnetic stimulation**

I. INTRODUCTION

The classic cable equation has been used to represent the excitation of long and straight peripheral nerves in electric field. It predicates that excitation occurs near the maximum of the negative first spatial gradient $E'_{\|} = -E_x / x$ in the direction of a x-axial fiber. Here, the electric field parallel to fiber is referred as longitudinal field $E_{\|}$ and the electric field perpendicular to fiber as transverse field $E_{\perp}$. The excitation of peripheral nerves by transverse fields has been found for a long time, but it has been attributed to tissue unhomogeneities or bends in the nerve. In 1999, Struijk found that the myelinated nerve could be excited by transverse field induced by pulsed magnetic stimulation without the affect of tissue unhomogeneities and bends in the nerve [1]. It sufficiently proves that the classical cable function does not completely explain the excitation of peripheral nerves and additional mechanisms must be involved. In the paper, a modified cable equation for mammalian myelinated fibers is presented, which contains both the effect of longitudinal field and the effect of transverse field.

II. MODELS

The research on the response of cell to external field demonstrates that the response is a two-stage process, which consists of the initial polarization (first stage) and the actual change of physiology state (second stage) [2]. Here, the response of peripheral nerves to transverse electric field is also considered as two-stage process so as to establish the model. The steady-state solution of initial polarization serves as the initial condition of the second stage that governs the subsequent evolution of membrane potential.

A. Initial polarization:

In the McNeal model [3], a myelinated axon is segmented into cylinders. Since the myelin is assumed to be a perfect insulator, axons have active membrane parts only at the nodes of Ranvier (NR). Therefore, the ionic currents enter into the axon just at NR and only the NR should be taken into account during initial polarization.

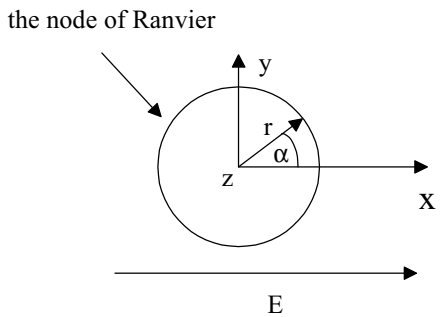

Fig.1 Idealized representation of a NR with radius R in a transverse steady uniform electric field.

Consider an idealized cylinder model of NR with radius R in a transverse steady uniform electric field shown in Fig.1. The field E is parallel to x-axis, the α represents the polar angle, and the axis of the NR is along z-axis. The x-axis and y-axis are in the radial direction of the NR. Intra- and extra-cellular regions are assumed purely resistive, with conductivities δ_i and δ_e. Hence, intra- and extra-cellular potentials satisfy Laplace's equations.

$$\nabla^2 V_i = 0 \qquad r < R \tag{1}$$

$$\nabla^2 V_e = 0 \qquad r > R \tag{2}$$

at $r = R$ the normal current is continuous, therefore

$$c_m \frac{dV_m}{dt} + i_{ion} = \hat{n} \bullet \{-\delta_e \nabla V_e\} = \hat{n} \bullet \{-\delta_i \nabla V_i\} \qquad r = R \tag{3}$$

where i_{ion} is the ionic current density determined by a complex dynamics of the excitable membrane, $\hat{n}$ is the unit normal outward from the NR, c_m is the membrane capacitance per area, V_m is the transmembrane potential.

$$V_m = V_i - V_e - V_r \qquad r = R \tag{4}$$

where V_r is the resting potential. It is assumed that the membrane is polarized uniformly along z-axis. Then the solutions of (1) and (2) are independent of z-axis, and in cylindrical coordinate they are as the following:

$$V_e = -Er\cos\alpha + \frac{B}{r}\cos\alpha \qquad r > R \tag{5}$$

$$V_i = Ar\cos\alpha \qquad r < R \tag{6}$$

where A and B are the coefficient determined by (3) and (4). In the CRRSS model [6] (active model), the ionic current i_{ion} is determined by (7)–(9):

$$i_{ion} = g_{Na} m^2 h (V_m - V_{Na}) + g_l (V_m - V_l) \tag{7}$$

$$\frac{dm}{dt} = \alpha_m (1 - m) - \beta_m m \tag{8}$$

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$$\frac{dh}{dt} = \alpha_h(1-h) - \beta_h h \tag{9}$$

where all the parameters can be found in [4].

The initial polarization is governed by (1)–(9). Since the analytic solution is not available, a numerical solution is given. The steady value of V_m is shown in Fig. 2. Since the polarization is symmetrical to the x-axis, the V_m as a function of α are shown with α varying from 0 to π. The "o" and "+" represent the V_m with the field intensity E equaling $500V/m$ and $200V/m$, respectively. Fig.2 demonstrates that the transmembrane potential V_m varies from positive (depolarization) at the end facing the cathode to negative (hyperpolarization) at the end facing the anode, V_m is zero where α equaling $\pi/2$.

B. Modified cable function

In fact, the whole membrane of NR is divided into several membrane patches in the initial polarization stage, i.e. the above equations just represent the polarization of membrane patches to external field, simultaneously the current entering the NR drove by the external field is ignored. Based on (3), there is normal current through the membrane while the external field is turn on. The current density is,

$$i = -\delta_e \nabla V_e \tag{10}$$

where the positive direction of current is referred to be outward from the NR. In the second stage, the net current entering the NR drove by the external field must not be ignored. There is outward current at the depolarized area while inward current at the hyperpolarized area. The net inward current flowing through the membrane is computed by integrating over the surface of the membrane.

$$i_{net} = \frac{1}{S}\int \delta_e \nabla V_e ds \tag{11}$$

where S is the surface area of NR. As to the numerical solution of active model, (16) is modified as the following:

$$i_{net} = \frac{1}{n}\sum_{k=1}^{n} i_e^k \tag{12}$$

where i_e^k is the current density with α equaling $2\pi k/n$. If the n =64, it will take quite a few minutes to work out the i_{net}

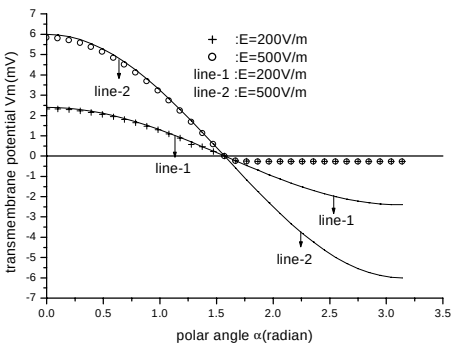

Fig.2 Transmembrane potential V_m of steady state during initial polarization as a function of α

Table 1 Fitting coefficients

Coefficient	Value
A	11.0712
B_1	-6.9939
B_2	0.3783
B_3	3.4018E-3
B_4	1.7612E-5
B_5	-5.4459E-8
B_6	9.9395E-11
B_7	-9.8828E-14
B_8	4.1292E-17

using a computer. So a fitting expression is applied here with the standard deviation of $15.84\mu A/cm^2$.

$$\begin{aligned} i_{net} &= A + B_1E + B_2E^2 + B_3E^3 + B_4E^4 \\ &\quad + B_5E^5 + B_6E^6 + B_7E^7 + B_8E^8 \end{aligned} \tag{13}$$

where A and $B_1 - B_8$ are the fitting coefficients shown in table 1.

Now, the modified cable function is obtained by adding the net inward current into the classical cable function,

$$\begin{aligned} & c_m \frac{dV_m(n,t)}{dt} S + i_{ion}(n,t)S - G_a[V_m(n-1,t) - 2V_m(n,t) + V_m(n+1,t)] \\ & = i_{net}(n)S + G_a[V_e(n-1,t) - 2V_e(n,t) + V_e(n+1,t)] \end{aligned} \tag{14}$$

where $i_{net}(n)$ is the net inward current density at the n th node, G_a is the inter-nodal conductance, S is the area of the surface of NR, $S = 2\pi Rl$, l is the length of NR, R is the axon radius. The term of $i_{net}(n,t)$ represents the effect of transverse field component and the term of $g_a[V_e(n-1,t) - 2V_e(n,t) + V_e(n+1,t)]$ represents the effect of longitudinal field component. Equation (14) suggests that the sufficient condition to excite the axon is an enough spatial gradient or an enough transverse field or an enough sum of both.

III. VERIFYING FOR THE MODEL

Krassowska [2] has obtained the change of the transmembrane potential $\Delta V_m = 2E_\perp R\cos\alpha$ of cylinder cell by transverse field during initial polarization, without taking account of the ionic current. Here, R is the radius of the cylinder cell. And based on Krassowska's results, Ruohonen [5][6] has introduced an additional term $\Delta V_m = 2E_\perp R\cos\alpha$ to the classical cable equation to represent the response of peripheral nerves to transverse field.

$$\lambda^2 \frac{\partial^2 V_m}{\partial z^2} - V_m = \tau \frac{\partial V_m}{\partial t} + 2R(\eta \frac{\partial E_\parallel}{\partial z} - E_\perp) \tag{15}$$

where, $-2E_\perp R$ is the transmembrane potential where α equaling π. In (15), Ruohonen assumed that the polarization result of the whole membrane is $-2E_\perp R$. The simulation result of CRRSS active model in Fig.2 demonstrates that the transmembrane potential in hyperpolarization area ($3/2\pi \ge \alpha \ge \pi/2$) does not equal $2E_\perp R\cos\alpha$. In Fig.2, the

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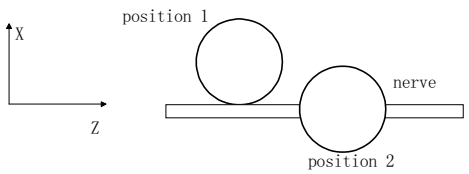

Fig 3 The top view of the position of coils and nerve.

transmembrane potential ($V_m = 2RE_\perp \cos\alpha$) as a function of α is shown as the line-1 with $E_\perp$ equaling $500V/m$ and line-2 with $E_\perp$ equaling $200V/m$, respectively. It demonstrates that the depolarization results of both models are in close agreement, but the hyperpolarization results have great difference. So it is not appropriate to ignore the ionic current to compute the initial polarization of NR in transverse field.

In 1999, Struijk found that the myelinated nerve could be excited in transverse field induced by pulsed magnetic field [4]. The top view of the positions of the coil and the nerve are shown in Fig 3. The nerve is excited by longitudinal nerve when the coil at the position 1 while the nerve is excited by transverse field when the coil at the position 2. The excitation thresholds were measured at the different stretch of the nerve. Here, the Ruohonen' cable function and the new cable function presented above will be verified by the Struijk's empirical data. Equation (14) shows that $i_{net}(n)S$ should equals $G_a[V_e(n-1,t)-2V_e(n,t)+V_e(n+1,t)]$ if the nerves generate the same response by the two kinds of stimulation at the same stretch of the nerve, as well as, in the (15) $\eta\partial E_\parallel/\partial z$ should equal $E_\perp$. The above four terms are referred to as: $F_1 = G_a[V_e(n-1,t)-2V_e(n,t)+V_e(n+1,t)]$, $F_2 = i_{net}(n)S$, $F_3 = \eta\partial E_\parallel/\partial z$, $F_4 = E_\perp$, respectively. The unbound model based on reciprocity theory is used to calculate the distribution of the induced field at the nerve [6]. The results are shown in table 2, it demonstrate that the new cable function is in agreement with the empirical data with the relative error 9.9% while 53% of Ruohonen's cable function.

IV. Discussion

The effect of transverse to the excitation of peripheral nerve has been ignored because the classical cable equation can represent the excitation of peripheral nerve and the transverse component is weaker than the longitudinal component in electric stimulation. More attention has been paid to the effect with the development of magnetic nerve stimulation. Ruohonen has used the modified continuous cable function to represent the effect of transverse field in the experiment of magnetic stimulation median nerve [5][6]. The above discussion shows that the Ruohonen's model is imperfect for myelinated nerve. Firstly, the Ruohonen's model is a continuous cable function but the myelinated nerve should be represented with a discrete cable function. Secondly, he ignored the ionic current when computing the polarization of NR. The modified cable function of mine is a discrete cable function and is obtained using the active CRRSS model. Above all things, the function is in close agreement with the empirical results in vitro.

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Table 2 The comparison of the results of the two models

Stretch (%)	New cable function			Ruohonen's cable function		
	F_1 (μA)	F_2 (μA)	relative error (%)	F_3 (V/m)	F_4 (V/m)	relative error(%)
0	1.21E-3	1.06E-3	12.4	1.4725E2	2.23E2	51.4
5	1.46E-3	1.36E-3	6.8	1.78E2	2.74E2	53.9
15	1.39E-3	1.47E-3	5.7	1.6875E2	2.95E2	74.8
20	1.87E-3	1.57E-3	16	2.275E2	3.12E2	37.1
25	1.91E-3	1.75E-3	8.4	2.325E2	3.43E2	47.5