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Numerical treatment of nonlinear mixed delay differential equations

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Abstract

The mathematical modeling of many problems in biology (the model for myelinated axons) has been formulated as nonlinear delay differential equations. Some basic properties of the myelinated axons are discussed. The numerical scheme for solving this model is described. The convergence and stability of numerical treatments that are discussed analytically are tested. The dependence of both the solution and the internodal delay τ on the various physical parameters are investigated and its numerical results are presented and interpreted.

Keywords: Myelinated axons; Membrane; Nonlinear delay differential equations; Convergence; Stability; Pure saltatory conduction

1. Introduction

The manner in which a signal is propagated along a nerve axon is a basic problem in biology. Myelination of an axon allows it to conduct neuroelectric signals by exciting only a small part of membrane. This permits transmission at a greatly reduced energy expenditure and higher speed compared with unmyelinated axon [4,13,15].

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We are going to discuss some basic properties of the myelinated axons and derive the following mathematical model:

$$\begin{aligned} &RC\,\mathrm{d}y(t)/\mathrm{d}t = F(y(t)) + y(t-\tau) + y(t+\tau), \quad -\infty < t < \infty, \\ &y(-\infty) = 0, \quad y(+\infty) = 1, \end{aligned} \tag{1.1}$$

where $y(t)$ represents the transmembrane potential at a node in our simplified model for a myelinated axon. This internodal delay τ, represents the reciprocal of the speed of the potential wave as it propagates down the axon. This constant τ must be found simultaneously with the solution $y(t)$ since it is not known a priori. The constants R and C represent axoplasmic resistivity and nodal capacity, respectively.

We will describe numerical schemes for solving (1.1). The problem is solved on a finite interval with asymptotic approximations used outside the interval. The system is discretized by using a five-point formula for the time derivative terms, and cubic interpolation for the delayed and advanced terms. We present the numerical results of the method and test the convergence and stability of the method on a class of test problems, which are analytically solvable. Then we apply the methods to the model for myelinated axon, and investigate the dependence of both the solution and τ on the various physical parameters, and interpret the numerical results.

2. Formulation of the problem (model)

We first survey the physical background of myelinated axons, in particular myelin properties and show how they affect signal conduction. A travelling wave formulation of (the pure saltatory conduction model) in nondimensional form, gives rise to the advance-delay differential equation (1.1).

White matter forms about 40% of the human brain. This white matter is formed of myelinated nerve fibers. Therefore most of its fibers are covered by myelin which is a fatty substance formed by Schwann cells lying in a row parallel to the axon at intervals forming gaps called nodes of Ranvier.

The myelin sheath is characterized by a high resistivity and a low capacity. Therefore it allows the nervous conduction to occur at greatly reduced energy expenditure and higher speed compared with unmyelinated nerve fibers since the signal speed in a myelinated axon increases with approximately the square root of the axon's diameter. The axon is able to carry electric impulses away from the cell body because it maintains a voltage difference of approximately 10 mV across its membrane.

When an axon is stimulated by an electrical current of sufficient strength to depolarize the membrane, a dramatic potential charge, called the action potential, occurs [18]. Because myelin has so much higher a resistance and lower capacity than the membrane, when the membrane is depolarized at a node, it cannot depolarize the adjacent region of membrane, but instead, the signal appears to jump to the next node to excite the membrane there. This method of signal conduction is called saltatory conduction [16].

Many mathematical methods of myelinated axons have been formulated from an electrical circuit model which assumes what we call the pure saltatory conduction hypothesis. The myelin has such high resistance, and low capacitance that it completely insulates the membrane which does not allow the spread of depolarization from a depolarized node to the adjacent region of the membrane. Instead, the signal tends to jump to the next node. This type of conduction is called saltatory conduction.

3. Pure saltatory conduction model

In this model all excitable behavior is at the nodes and no transmembrane current is allowed through the internode. Consider the electrical circuit model given by Fig. 1. The r^i,r^0,v^i_k,v^0k, j^i_k,j^0_k represent, respectively, the membrane resistance, longitudinal potential and currents across the kth node [14]. The superscript "i" and "0" refer to axoplasmic and extracellular quantities, respectively, and j^m_k represents membrane current at the kth node. Applying Kirchhoff's laws to the circuit model. We get:

$$j^m_k = j^i_k - j^i_{k+1}, \quad j^m_k = j^0_{k+1} - j^0_k.$$

Applying Ohm's laws to the circuit model, we obtain:

$$r^i j^i_k = V^i_{k-1} - V^i_k, \quad r^0 j^0_k = V^0_{k-1} - V^0_k.$$

So we have:

$$r^i j^m_k = V^i_{k-1} - 2V^i_k + V^i_{k+1}, \tag{3.1a}$$

$$-r^0 j^m_k = V^0_{k-1} - 2V^0_k + V^0_{k+1}. \tag{3.1b}$$

Now let $R = r^i + r^0$, $V_k = V^i_k - V^0_k$. Then by subtracting (3.1b) from (3.1a), we get:

$$R j^m_k = V_{k-1} - 2V_k + V_{k+1}. \tag{3.2}$$

Now, as in [14], we suppose that the membrane current for the node is the sum of parallel capacity and ionic currents, thus giving

$$j^m_k = C\,\mathrm{d}V_k/\mathrm{d}T + I(V_k) \tag{3.3}$$

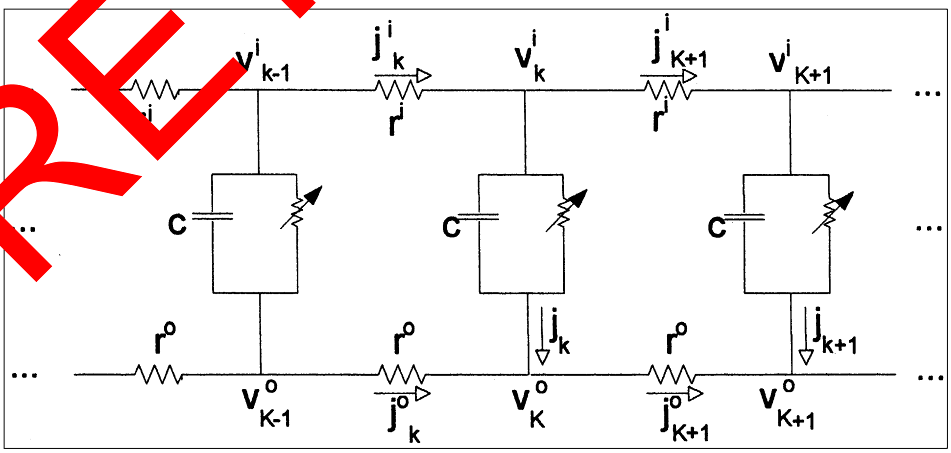

Fig. 1. Circuit for pure saltatory conduction model.

By combining Eqs. (3.2) and (3.3), we obtain the following difference-differential equation model of transmembrane potential V_k at the kth node:

$$(V_{k-1} - 2V_k + V_{k+1})/R = C\,\mathrm{d}V_k/\mathrm{d}T + I(V_k). \tag{3.4}$$

Here R and C are constants representing, respectively, axoplasmic resistance and nodal membrane capacity. The circuit model assumes that axon to be infinite in extent, those axons cross-section variations are negligible in potential and those nodes are point sources of excitation, electrically identical and uniformly spaced.

We choose the well known Fitzhugh–Nagumo model [11] at each node since it has been used in studies of unmyelinated axons and has proven to be quite useful in exploring threshold behavior, action potential and activity. With Fitzhugh–Nagumo dynamics for the nodal membrane, (3.4) becomes:

$$\begin{aligned}&(V_{k-1} - 2V_k + V_{k+1})/R = C\,\mathrm{d}V_k/\mathrm{d}T - F(V_k) + \varpi_k, \quad k \in Z,\\ &\sigma V_k - \gamma\varpi_k = \mathrm{d}\varpi_k/\mathrm{d}T.\end{aligned} \tag{3.5}$$

Here ϖ_k represents a "recovery variable" at node k, σ and γ are nonnegative rate constants, and $F(V)$ is a current–voltage relation that has the following nonlinear cubic behavior

$$\begin{aligned}&F \in C^1[0,Q] : F(0) = F(Q) = 0; \quad F(x) < 0 \quad \text{for } 0 < x < P, \quad F'(0) < 0;\\ &F(x) > 0 \quad \text{for } P < x < Q, \quad F'(Q) < 0.\end{aligned} \tag{3.6}$$

$V = 0$ represents the rest potential whereas the threshold potential is represented by $V \equiv P$ and $V \equiv Q$ represents the fully-activated potential level of the node. Some analytical results for this model are given in [3]. To simplify matters, we set $\varpi_k = 0$, $k \in Z$. Thus, we consider:

$$(V_{k-1} - 2V_k + V_{k+1})/R = C\,\mathrm{d}V_k/\mathrm{d}T - F(V_k), \tag{3.7}$$

where $F(V_k)$ satisfies the properties given by (3.6); for numerical simulation we take a specific function, namely $F(V) = B*V*(V-P)*(Q-V)$, where $0 < P < Q$ and $B > 0$.

Now if we assume that a suprathreshold stimulus initiates a propagated action potential, which then travels from node to node down the axon. Longitudinal circulating currents are set up and successive nodes are excited. Because of the uniformity hypothesis, each succeeding node responds exactly as its predecessor except for an internal time delay $\phi > 0$, that is

$$V_{j+1}(T + \phi) = V_j(T) \quad \text{for all } j \in Z, \quad \text{all } T. \tag{3.8}$$

If L is the internal length, the speed is given by $v = L/\phi$. One object here is to gain an understanding of how ϕ (and therefore v) depends on other model parameters. Because of (3.8) we can consider the behavior at a single node, since the behavior at any other node is just a time translation. Letting $V(T) = V_k(T)$, then V satisfies:

$$C\,\mathrm{d}V(T)/\mathrm{d}T = F(V(T)) + ((V(T-\phi) - 2V(T) + V(T+\phi))/R \tag{3.9}$$

with

$$V(-\infty) = 0, \quad V(+\infty) = Q.$$

This problem is a nonlinear, mixed-delay, boundary value problem defined on the real line in which ϕ is unknown a priori. Before proceeding, we want to reduce parameters by nondimensionalizing (3.9). To nondimensionalize the model, let

$$t = T/RC, \quad \tau = \phi/RC, \quad y(t) = V(T)/Q. \tag{3.10}$$

With these substitutions, the model becomes

$$\mathrm{d}y(t)/\mathrm{d}t = f(y(t)) + y(t-\tau) - 2y(t) + y(t+\tau) \tag{3.11}$$

with

$$y(-\infty) = 0, \quad y(+\infty) = 1,$$

where we obtain;

$$f(y) = by(y-a)(1-y), \quad a = P/Q, \quad 0 < a < 1, \quad \text{and} \quad b = R.B.Q, \quad b > 0. \tag{3.12}$$

In the nondimensional model, a, is the threshold potential, τ is the nondimensional time delay, and b is related to the strength of ionic current density.

Now we are going to solve numerically the problem (3.11) and (3.12).

4. Numerical scheme for a mixed delay differential equation

We are going to discuss a numerical approach for solving a class of delay differential equations of mixed type, with constant delay, see [6,8,10,20]. Let us consider the following class

$$y'(t) = \mathrm{d}y(t)/\mathrm{d}t = f(y(t)) + y(t-\tau) - 2y(t) + y(t+\tau), \tag{4.1}$$
$$-\infty < t < +\infty \quad \text{with } y(-\infty) = 0, \quad y(+\infty) = 1.$$

Here f is $C^1[0,1]$ and satisfies $f(0) = 0$, $f'(0) < 0$, $f(1) = 0$ and $f'(1) < 0$. The constant delay must be found simultaneously with the solution. We are looking for a monotone increasing solution $y(t)$ such that $0 < y(t) < 1$, for all t.

We choose $L > 0$ and use a difference method to approximate a solution of (4.1) in the interval $[-L, L]$.

4.1. Approximate solution outside the fixed interval

We first consider $t \leqslant -L$ with $y(t) \to 0$, $f(y(t)) \to 0$ as $t \to -\infty$. Using the Taylor expansion of f for x near 0, namely, $f(x) = a_1x + a_2x^2 + a_3x^3 + \mathrm{O}(x^4)$. The Eq. (4.1) becomes;

$$y'(t) = \mathrm{d}y(t)/\mathrm{d}t = a_1y(t) + a_2y(t)^2 + a_3y(t)^3 + y(t-\tau) - 2y(t) + y(t+\tau) + \mathrm{O}(y^4). \tag{4.2}$$

Since $y(-L) \to 0$ as $L \to +\infty$, let $\varepsilon = y(-L)$ and consider the formal expansion:

$$y(t) = \varepsilon u_1(t) + \varepsilon^2 u_2(t) + \varepsilon^3 u_3(t) + \mathrm{O}(\varepsilon^4), \tag{4.3}$$

where we impose the condition

$$u_1(-L) = 1, \quad u_2(-L) = 0, \quad u_3(-L) = 0. \tag{4.4}$$

Substituting (4.3) into (4.2) and defining the operator L_- by

$$L_-u(t) = u(t-\tau) + (a_1 - 2)u(t) + u(t+\tau).$$

We have the following equations

$$u_1'(t) - L_-u_1(t) = 0, \tag{4.5}$$

$$u_2'(t) - L_-u_2(t) = a_2u_1(t)^2, \tag{4.6}$$

$$u_3'(t) - L_-u_3(t) = a_3u_1(t)^3 + 2a_2u_1(t)u_2(t). \tag{4.7}$$

Since the Eq. (4.5) is linear and homogenous, we substitute $u_1(t) = Ce^{\lambda t}$ into the equation. This gives an equation for λ, namely

$$\lambda + 2 - a_1 - 2\cosh(\lambda\tau) = 0. \tag{4.8}$$

Now since $a_1 = f'(0) < 0$, then (4.8) has exactly two real roots, one positive and the other negative. We will consider only the real roots of (4.8), for monotone solution, let λ_+ be the positive root of (4.8). Thus a solution to (4.5) which satisfies $u_1(-L) = 1$ and vanishes as $t \to -\infty$ is

$$u_1(t) = \mathrm{e}^{\lambda_+(t+L)}. \tag{4.9}$$

A particular solution of the nonhomogeneous equation (4.6) is

$$u_2^p(t) = b_1\mathrm{e}^{2\lambda_+(t+L)} \quad \text{where } b_1 = a_2/(2\lambda_+ - a_1 + 2 - 2\cosh(2\lambda_+\tau)).$$

A particular solution of (4.6) which satisfies $u_2(-L) = 0$, is then

$$u_2(t) = b_1(\mathrm{e}^{2\lambda_+(t+L)} - \mathrm{e}^{\lambda_+(t+L)}). \tag{4.10}$$

A particular solution of (4.7) is

$$u_3^p(t) = b_2\mathrm{e}^{2\lambda_+(t+L)} + b_3\mathrm{e}^{3\lambda_+(t+L)},$$

where

$$b_2 = -2a_2b_1/(2\lambda_+ - a_1 + 2 - 2\cosh(2\lambda_+\tau)) = -2b_1^2 \tag{4.11}$$

and

$$b_3 = (2a_2b_1 + a_3)/(3\lambda_+ - a_1 + 2 - 2\cosh(3\lambda_+\tau)). \tag{4.12}$$

A particular solution of (4.7) which satisfies $u_3(-L) = 0$ is then

$$u_3(t) = b_2\mathrm{e}^{2\lambda_+(t+L)} + b_3\mathrm{e}^{3\lambda_+(t+L)} - (b_2 + b_3)\mathrm{e}^{\lambda_+(t+L)}. \tag{4.13}$$

Thus, for $t < -L$,

$$y(t) = \varepsilon\mathrm{e}^{\lambda_+(t+L)} + \varepsilon^2b_1(\mathrm{e}^{2\lambda_+(t+L)} - \mathrm{e}^{\lambda_+(t+L)}) + \varepsilon^3(b_2\mathrm{e}^{2\lambda_+(t+L)} + b_3\mathrm{e}^{3\lambda_+(t+L)} - (b_2 + b_3)\mathrm{e}^{\lambda_+(t+L)}) + \mathrm{O}(\varepsilon^4). \tag{4.14}$$

For $t > L$, $y(t) \to 1$ and $f(y(t)) \to 0$ as $t \to \infty$, with Taylor's expansion we get

$$f(x) = A_1(1-x) + A_2(1-x)^2 + A_3(1-x)^3 + O((1-x)^4).$$

Eq. (4.1) becomes

$$\begin{aligned} y'(t) &= dy(t)/dt \\ &= A_1(1-y(t)) + A_2(1-y(t))^2 + A_3(1-y(t))^3 + y(t-\tau) - 2y(t) + y(t+\tau) \\ &\quad + O((1-y(t))^4). \end{aligned} \tag{4.15}$$

Since $y(L) \to 1$ as $L \to +\infty$, let $y(L) = 1 - \varepsilon_+$, $0 < \varepsilon_+ \ll 1$ and consider the formal expansion

$$y(t) = 1 + \varepsilon_+ w_1(t) + \varepsilon_+^2 w_2(t) + \varepsilon_+^3 w_3(t) + O(\varepsilon_+^4), \tag{4.16}$$

where we impose the condition

$$w_1(L) = 1, \quad w_2(L) = 0, \quad \text{and} \quad w_3(L) = 0. \tag{4.17}$$

Substituting (4.16) into (4.15) and defining the operator K_+ by

$$K_+u(t) = u(t-\tau) + (A_1 + 2)u(t) + u(t+\tau).$$

We have the following relations

$$w_1'(t) - K_+w_1(t) = 0, \tag{4.18}$$

$$w_2'(t) - K_+w_2(t) = -A_2w_1(t)^2, \tag{4.19}$$

$$w_3'(t) - K_+w_3(t) = -A_3w_1(t)^3 - 2A_2w_1(t)w_2(t). \tag{4.20}$$

Since (4.18) is linear and homogeneous, let $w_1(t) = Ce^{\lambda t}$ in (4.18), so we get

$$\lambda + 2 + A_1 - 2\cosh(\lambda\tau) = 0. \tag{4.21}$$

Since $A_1 = -f'(1) > 0$, (4.21) has exactly two real roots, one negative and one positive. Let λ_- be the negative root of (4.21). Thus a solution of (4.18) which vanishes as $t \to \infty$, and satisfies $w_1(L) = 1$ is

$$w_1(t) = e^{\lambda_-(t-L)}. \tag{4.22}$$

Similarly, we find a particular solution of (4.19) which satisfies $w_2(+L) = 0$ is

$$w_2(t) = B_1(e^{2\lambda_-(t-L)} - e^{\lambda_-(t-L)}), \tag{4.23}$$

where the constant $B_1 = -A_2/(2\lambda_- + A_1 + 2 - 2\cosh(2\lambda_-\tau))$, and a particular solution of (4.20) which satisfies $w_3(L) = 0$ is then

$$w_3(t) = B_2e^{2\lambda_-(t-L)} + B_3e^{3\lambda_-(t-L)} - (B_2 + B_3)e^{\lambda_-(t-L)}, \tag{4.24}$$

where the value of these constants are

$$B_2 = 2A_2B_1/(2\lambda_- + A_1 + 2 - 2\cosh(2\lambda_-\tau)) = -2B_1^2,$$

$$B_3 = (-2A_2B_1 - A_3)/(3\lambda_- + A_1 + 2 - 2\cosh(3\lambda_-\tau)).$$

Therefore for $t > L$ with $\varepsilon_+ = 1 - y(L)$,

$$y(t) = 1 - \varepsilon_+ e^{\lambda_-(t-L)} - \varepsilon_+^2 B_1(e^{2\lambda_-(t-L)} - e^{\lambda_-(t-L)}) - \varepsilon_+^3(B_2 e^{2\lambda_-(t-L)} + B_3 e^{3\lambda_-(t-L)} - (B_2 + B_3)e^{\lambda_-(t-L)}) + O(\varepsilon_+^4). \tag{4.25}$$

4.2. Finite difference and interpolation schemes

Consider the following nonlinear mixed-delay problem

$$dy(t)/dt = f(y(t)) + y(t-\tau) - 2y(t) + y(t+\tau), \quad -L \leqslant t \leqslant L \tag{4.26}$$

with the condition:

$$y(0) = 0.5. \tag{4.27}$$

This equation is defined in a fixed interval, where f is nonlinear and $f(0) = f(1) = 0$. We divide $[-L, L]$ into N equal size subintervals, with $t_j = -L + jh$, $j = 0(1)N$, where $N = 2L/h$ and approximate $y(t_j)$ by y_j. We use a fourth order scheme to approximate the derivative term, from [5,9], we get

$$y'(t) = (y(t-2h) - 8y(t-h) + 8y(t+h) - y(t+2h))/12h + h^4 f^{(5)}(\xi)/30$$

for some ξ, $\xi \in (t-2h, t+2h)$. Then we have

$$y'(t_j) \approx (y_{j-2} - 8y_{j-1} + 8y_{j+1} - y_{j+2})/12h. \tag{4.28}$$

We use the approximate formula (4.14) for $t = +L - 2h$ and $t = +L - h$ to approximate y_{-2} and y_{-1} with $j = 0$ and $j = 1$ in Eq. (4.28). Similarly we use the formula (4.25) for $t = +L + h$ and $t = +L + 2h$ to approximate y_{N+1} and y_{N+2} with $j = N - 1$ and $j = N$ in Eq. (4.28).

To approximate the delayed and advanced term in (4.26) we use cubic interpolation. Let $M = [\tau/h]$, where $[x]$ means the integer part of x, and let $r = \tau - Mh$, $r \geqslant 0$. Then $t - \tau$ lies between $t - Mh - h$ and $t - Mh$, we use the cubic formula:

$$y(t-\tau) = C_4 y(t - Mh - 2h) + C_3 y(t - Mh - h) + C_2 y(t - Mh) + C_1 y(t - Mh + h) + 9h^4 f^{(4)}(\xi)/324, \quad \text{for some } \xi, \xi \in (t - Mh - 2h, t - Mh + h),$$

where the C_i's are constants given by

$$C_1 = -(2h - r)(h - r)r/6h^3, \quad C_2 = (2h - r)(h - r)(h + r)/2h^3,$$

$$C_3 = r(2h - r)(h + r)/2h^3, \quad C_4 = -r(h + r)(h - r)/6h^3. \tag{4.29}$$

Thus, we have for the delayed term:

$$y(t_j - \tau) \approx C_4 y_{j-M-2} + C_3 y_{j-M-1} + C_2 y_{j-M} + C_1 y_{j-M+1}. \tag{4.30}$$

The formula (4.14) is used to approximate the terms which have negative indices in Eq. (4.30). Similarly, we have for the advanced term:

$$y(t_j + \tau) \approx C_4 y_{j+M+2} + C_3 y_{j+M+1} + C_2 y_{j+M} + C_1 y_{j+M-1}, \tag{4.31}$$

where the formula (4.25) is used to approximate the terms which have indices exceeding N in Eq. (4.31).

By using (4.28) to (4.31) to replace the derivative, delayed and advanced terms in the equation(4.26), the approximation scheme has a local truncation error of order 4, then

$$\begin{aligned}(y_{j-2} - 8y_{j-1} + 8y_{j+1} - y_{j+2})/12h - f(y_j) + 2y_j - C_1 y_{j+M-1} - C_2 y_{j+M} - C_3 y_{j+M+1} \\ - C_4 y_{j+M+2} - C_4 y_{j-M-2} - C_3 y_{j-M-1} - C_2 y_{j-M} - C_1 y_{j-M+1} = 0, \quad \text{for } j = 0(1)N.\end{aligned} \tag{4.32}$$

In the system (4.32), the y_j's for $j < 0$ are functions of y_0, and are evaluated by (4.14) with $\varepsilon = y_0$ and neglecting the terms $O(\varepsilon^4)$. Also y_j's for $j > N$ are functions of y_N, and are evaluated by using (4.25) with $\varepsilon_+ = 1 - y_N$, and neglecting the terms $O(\varepsilon_+^4)$. In addition to the $N-1$ equations in (4.32), there is the following condition:

$$y_{N'} - 0.5 = 0, \quad \text{where } N' = [N/2] \tag{4.33}$$

which replaces (4.27), and in addition to the $N+1$ unknowns $y_0, y_1, \ldots, y_N$ and the unknown delay τ.

4.3. Solution of the system

We are going to discuss the scheme used to solve the discretized system and to determine the approximate delay τ. If we use the Newton Raphson scheme for solving the system (4.32) and (4.33), the approximate t would vary in each iteration step, and the coefficient matrix might vary in bandwidth, see [[illegible],9]. The integer M and the coefficients C_k, $k = 1(1)4$ depend upon τ. For discontinuous change in M and the C_k's during the iteration we construct a nested iteration scheme in which τ, will be fixed during the inner loop, see [17]. The outer loop is the solution of an equation $g(t) = 0$ by the secant method, where the function $g(t)$ is defined as follows:

For fixed τ we solve the system of $N+1$ equations:

$$\begin{aligned}&\text{Eq. (4.32)} \quad \text{for } j = 0(1)N' - 1, \\ &y_{N'} - 0.5 = 0, \\ &\text{and Eq. (4.32)} \quad \text{for } j = N'+1, \ldots, N\end{aligned} \tag{4.34}$$

for $y_0, y_1, \ldots, y_N$. Then, we define $g(\tau) =$ left hand side of (4.32) for $j = N'$.

To approximate a solution to this nonlinear system (4.34) we use Newton Raphson scheme. A sequence of iterates $Y^k = \{y_i^k\}, i = 0(1)N$, $k = 0, 1, \ldots,$ is generated that converges to the solution, provided that the initial approximation Y^0 is sufficiently close to the solution and Jacobian matrix, J, is nonsingular at the solution, see [5].

The Jacobian matrix for the system (4.34) is a banded matrix with both upper bandwidth and lower bandwidth equal to $M+2$. In the numerical scheme, one-sided numerical differencing approximated the Jacobian matrix. The known band structure of the matrix was used to minimize the number of function evaluations required.

4.4. The continuation method

We have a test problem as Eq. (4.1), which can be solved exactly with the following function f:

$$f(y) = f_v(y)\{1 + 2v(2y-1) - (1+v)(2y-1)^2 - v(3-2y)(2y-1)^3\}/\{2(1 + v(2y-1)^2)\}. \tag{4.35}$$

The solution of (4.1) and (4.35) is $y(t) = (1 + \tanh(t))/2$, $t \in R$ and $\tau = \tanh^{-1}(\sqrt{v})$. Now the difficulties of the determination for the initial guess of the Newton Raphson method inclosing to the solution are due to a large system of nonlinear equations which are obtained. Thus we take the advantage provided by the test problem and continuation methods to overcome this difficulties see [1,7,19,20].

Let the problem (4.1) with the nonlinearly $f_d(y)$ be the target system, we embed this problem in one parameter family of problems:

$$\begin{aligned} &\mathrm{d}y(t)/\mathrm{d}t = f_\alpha(y(t)) + y(t-\tau) - 2y(t) + y(t+\tau),\\ &y(-\infty) = 0, \quad y(\infty) = 1 \end{aligned} \tag{4.36}$$

$f_\alpha(y) = \alpha f_v(y) + (1-\alpha) f_d(y)$, $0 \leqslant \alpha \leqslant 1$ with $f_v(y)$ given by (4.35). We compute solutions for α varying from $\alpha = 1$ to $\alpha = 0$. For $\alpha = 1$, we are solving the test problem for which the exact solution $y(t)$ and τ are known. The exact solution is used as the initial guesses to solve the discrete correspond system (4.32). Once the problem for $\alpha > 0$ is solved, we decrease α incrementally by $\Delta\alpha$ and use the solution of the previous problem as the initial approximation for the solution of the current problem, until $\alpha = 0$.

5. Numerical results

Now we present the numerical solutions to some problem of the form (4.1) obtained by the previous discussion, determine how τ depends on various parameters.

5.1. One test problem with known solution

We discuss results for solving a test problem (4.1) with f given by (4.35) which has a known solution.

Consider the following problem:

$$\mathrm{d}y(t)/\mathrm{d}t = f_v(y(t)) + y(t-\tau) - 2y(t) + y(t+\tau) \tag{5.1}$$

$-\infty < t < +\infty$, with $y(-\infty) = 0$, $y(+\infty) = 1$, where f_v is given by (4.35). We use the previous scheme.

We replace the coefficients in item (4.1) by the following actual values:

$$a_1 = (2 - 6v)/(1 - v),$$

$$a_2 = (-2 + 16v + 2v^2)/(1 - v)^2,$$

$$a_3 = (-8v - 48v^2 - 8v^3)/(1 - v)^3,$$

$$A_1 = (2 + 2v)/(1 - v),$$

$$A_2 = (-2 - 8v - 6v^2)/(1 - v)^2,$$

$$A_3 = (8v + 48v^2 + 8v^3)/(1 - v)^3.$$

Since $a_1 < 0$ and $A_1 > 0$ then v lies in $(1/3, 1)$. To start the technique, we choose our test problem with $v = 0.35$. The exact solution is $y(t) = (1 + \tanh(t))/2$ with delay $\tau = \tanh^{-1}(\sqrt{v}) = 0.6801362709$, $h = 0.1$, $N = 41$ and $L = 2.0$.

As a result, we obtain the solution presented in Table 1, of the delay equation and $\tau = 0.6801398$, $h = 0.1$, with error between computed and exact delay being 3.543×10^{-6}.

In order to check the accuracy of our scheme, let $h = 0.05$, $N = 81$ and $L = 2.0$ then the τ will be 0.68013643 with the error being 1.653×10^{-7}. So, we can determine how the choice of step size

Table 1
Comparison between the numerical and the exact solutions for $a = 0.05$ and $b = 15.0$

τ	Numerical solution		Exact solution
	$H = 0.05$, $N = 81$	$H = 0.1$, $N = 41$	
−2.00	0.017986[illegible]	0.01798640	0.01798621
−1.80	0.0265[illegible]	0.02659710	0.02659699
−1.60	0.03916615	0.03916556	0.03916572
−1.40	0.05732449	0.05732348	0.05732418
−1.20	0.08317289	0.08317106	0.08317269
−1.00	0.11[illegible]20293	0.11919986	0.11920292
−0.80	0.[illegible]798139	0.16797676	0.16789162
−0.60	0.2314747[illegible]	0.23146886	0.23147522
−0.40	0.[illegible]100[illegible]03	0.31001916	0.31002552
−0.20	0.40[illegible]31199	0.40130841	0.40131234
0.00	0.50000000	0.50000000	0.50000000
0.20	0.59868791	0.59869026	0.59868766
0.40	0.68997476	0.68997652	0.68997448
0.60	0.76852496	0.76852432	0.76852478
0.80	0.83201848	0.83201591	0.83201838
1.00	0.88079715	0.88079408	0.88079708
1.20	0.91682738	0.91682473	0.91682730
1.40	0.94267590	0.94267389	0.94267582
1.60	0.96083436	0.96083294	0.96083428
1.80	0.97340309	0.97340216	0.97340301
2.00	0.83201848	0.98201329	0.98201379

affects the accuracy. This comparison is included in Table 1, where a and b are the threshold potential in the target problem and strength of ionic density, respectively.

5.2. Numerical results due to the continuation method

Now we apply the numerical scheme in conjunction with the continuation method to (5.1) and (4.35) with $v = 0.35$ for the initial test problem and $v = 0.45$ for the problem to be solved. First, we set $\alpha = 1$ and we use the exact solution as an initial guess for the problem. Also we choose a pair of numbers which are close to the exact τ (as the initial guesses of τ). Let $N = 51$, $h = 0.2$ and

Table 2
τ as a function of α with $N = 51$, $H = 0.2$ in the test problem (5.1) as $v = 0.45$

α	$v = 0.35$	$v = 0.4$
1.00	0.6801833932	0.74[illegible]009
0.98	0.6830484733	0.7469273518
0.95	0.6873217476	0.7489951971
0.90	0.6943819718	0.7524306741
0.80	0.7082885743	0.7592620436
0.70	0.7219392996	0.7660430915
0.60	0.7353637053	0.7727765621
0.50	0.7485863969	0.7794649836
0.40	0.7616281482	0.7861107006
0.30	0.7745067270	0.7927158866
0.20	0.7872375064	0.7992825658
0.10	0.79[illegible]8339[illegible]1	0.8058071754
0.00	0.8122964720	0.8122964720

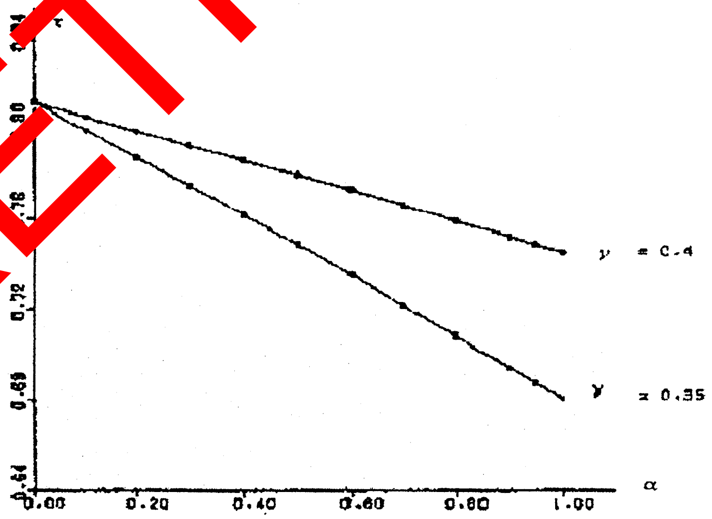

Fig. 2. Relation between α and τ with $v = 0.45$ for test problem, with $v = 0.35$ and $v = 0.4$ during the continuation method.

Table 3
Comparison of numerical solution with the exact solution

Time	Exact solution	Numerical solution	Error
−4.6	0.000101029	0.000101220	0.1900×10^{-6}
−4.4	0.000150710	0.000150904	0.1940×10^{-6}
−4.2	0.000224817	0.000225152	0.3330×10^{-6}
−4.0	0.000335350	0.000335718	0.3680×10^{-6}
−3.8	0.000500201	0.000500796	[illegible]
−3.6	0.000746029	0.000746685	[illegible]
−3.4	0.001112536	0.001113542	[illegible]
−3.2	0.001658801	0.001659933	1.1320×10^{-6}
−3.0	0.002472623	0.002474247	1.6240×10^{-6}
−2.8	0.003684240	0.003686012	[illegible]
−2.6	0.005486299	0.005488604	0.2305×10^{-6}
−2.4	0.008162571	0.008164775	[illegible]
−2.2	0.012128435	0.012130711	[illegible]
−2.0	0.017986210	0.017987145	0.0935×10^{-6}
−1.8	0.026596994	0.026595790	0.1203×10^{-6}
−1.6	0.039165723	[illegible]	0.6643×10^{-6}
−1.4	0.057324176	[illegible]	1.5272×10^{-6}
−1.2	0.083172696	[illegible]	3.0531×10^{-6}
−1.0	0.119202922	[illegible]	5.1115×10^{-6}
−0.8	0.167981615	0.167905662	7.5953×10^{-6}
−0.6	0.231475217	[illegible]	9.4923×10^{-6}
−0.4	0.310025519	[illegible]	9.4274×10^{-6}
−0.2	0.401312340	[illegible]	5.8468×10^{-6}
0.0	0.500000000	[illegible]	0.0000×10^{-6}
0.2	0.598687660	[illegible]	3.9636×10^{-6}
0.4	0.689974481	0.690003820	2.9339×10^{-6}
0.6	[illegible]	0.768512936	1.1847×10^{-6}
0.8	[illegible]	0.831975754	4.2631×10^{-6}
1.0	[illegible]	0.880751365	4.5713×10^{-6}
1.2	0.916827304	0.916793546	3.3757×10^{-6}
1.4	[illegible]	0.94265190	2.2634×10^{-6}
1.6	0.860834277	0.960818021	1.6257×10^{-6}
1.8	[illegible]	0.973391242	1.1764×10^{-6}
2.0	[illegible]	0.982006238	0.7552×10^{-6}
2.2	[illegible]	0.98787366	0.4199×10^{-6}
2.4	[illegible]	0.991835224	0.2205×10^{-6}
2.6	0.994513701	0.994512496	0.1205×10^{-6}
2.8	[illegible]	0.996315122	0.0638×10^{-6}
3.0	0.997527377	0.99727122	0.0254×10^{-6}
3.2	0.99834199	0.998341174	0.0025×10^{-6}
3.4	0.998887464	0.998887537	0.0073×10^{-6}
3.6	0.999253971	0.999254069	0.0098×10^{-6}
3.8	0.999499799	0.99499897	0.0098×10^{-6}
4.0	0.999664650	0.999664742	0.0092×10^{-6}

$L = 5.0$, then we get both the solution and τ of the delay equation. We will decrease $a$and repeat the iteration process again until $\alpha = 0$. Table 2 gives the solution and τ for various values of α,

Fig. 2 gives the relation between α and τ. The comparison between the exact and the computed solution are tabulated in Table 3. It is clear, from Table 3, which the continuation method is accurate since the largest error is 0.94×10^{-5}.

5.3. Results from pure saltatory conduction model

Now after we applied our numerical scheme to the problem (3.11) with $f(y) = by(y - a)(1 - y)$. Our test problem is (4.35) with $v = 0.35$. The coefficients, in item 4.1, will be $a_1 = -ab$, $a_2 = (1 + a)b$, $a_3 = -b$, $A_1 = b(1 - a)$, $A_2 = -(2 - a)b$ and $A_3 = b$.

We choose the values $a = 0.05$, $b = 15$, $h = 0.05$, $N = 41$ and $L = 1$, then we get $\alpha = 0.4351126$ and the solution of (3.11) described in Table 4. To check the accuracy of our results, we set $v = 0.4$

Table 4
Numerical solution of test problem for some $v = 0.35$, 0.4 and 0.425 with $a = 0.05$, $b = 15$

T-value	$v = 0.35$	$v = 0.4$	$v = 0.425$
−1.00	0.0071150078	0.0071150078	0.0071150078
−0.95	0.0089041614	0.0089041614	0.0089041614
−0.90	0.0111449632	0.0111449632	0.0111449632
−0.85	0.0139402392	0.0139402392	0.0139402392
−0.80	0.0174487830	0.0174487830	0.0174487830
−0.75	0.0218363269	0.0218363269	0.0218363269
−0.70	0.0273315939	0.0273315939	0.0273315939
−0.65	0.0341638783	0.0341638783	0.0341638783
−0.60	0.0426457062	0.0426457062	0.0426457062
−0.55	0.0531288513	0.0531288513	0.0531288513
−0.50	0.0661223457	0.0661223457	0.0661223457
−0.45	0.0822358647	0.0822358647	0.0822358647
−0.40	0.1022625067	0.1022625067	0.1022625067
−0.35	0.1270151100	0.1270151100	0.1270151100
−0.30	0.1572956680	0.1572956680	0.1572956680
−0.25	0.1937257888	0.1937257888	0.1937257888
−0.20	0.2369861873	0.2369861873	0.2369861873
−0.15	0.2879963810	0.2879963810	0.2879963810
−0.10	0.3480925348	0.3480925348	0.3480925348
−0.05	0.4186108238	0.4186108238	0.4186108238
0.00	0.5000000000	0.5000000000	0.5000000000
0.05	0.5900573033	0.5900573033	0.5900573033
0.10	0.6822976813	0.6822976813	0.6822976813
0.15	0.7665294699	0.7665294699	0.7665294699
0.20	0.8338294908	0.8338294908	0.8338294908
0.25	0.8815973635	0.8815973635	0.8815973635
0.30	0.9129542672	0.9129542672	0.9129542672
0.35	0.9330603668	0.9330603668	0.9330603668
0.40	0.9464838302	0.9464838302	0.9464838302

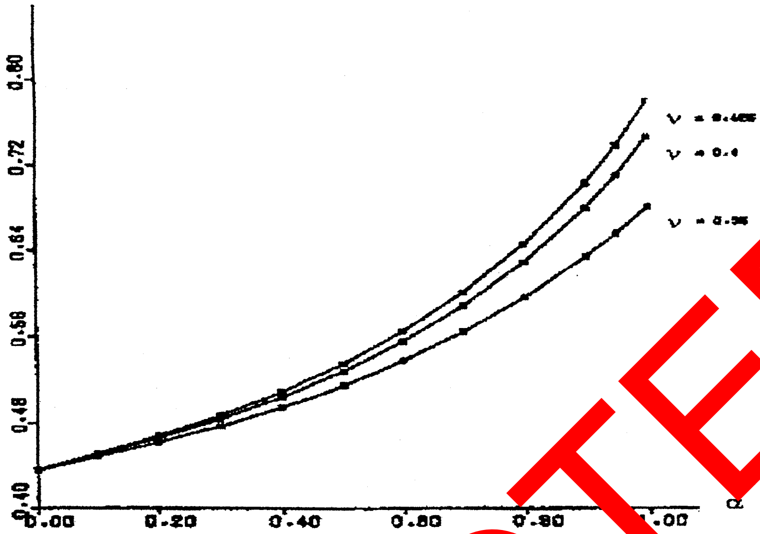

Fig. 3. Relation between α, τ for $v = 0.35$, 0.4, 0.425.

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Table 5
τ as a function of α with $a = 0.05$, $b = 15.0$, $N = 41$ an[illegible] $H =$ [illegible] solving the target problem (3.11)

α	$v = 0.35$	$v = 0.4$	$v = 0.425$
1.0	0.6801833932	[illegible]7455257632	0.7786585973
0.9	0.6329849848	0.6785881728	0.7020352711
0.8	0.594635[illegible]	0.6276371574	0.6447397934
0.7	0.56307[illegible]059	0.5871948416	0.5997731492
0.6	0.53[illegible]	0.5544462490	0.5639172767
0.5	0.51370604[illegible]	0.5269258205	0.5339375387
0.4	[illegible].4939542178	0.5034437521	0.5084824558
0.3	0.4766196022	0.4830681409	0.4865147547
0.2	0.4[illegible]2473139	0.4651822460	0.4672905699
0.1	[illegible]4475028[illegible]	0.4493192383	0.4502939511
0.0	[illegible]43511[illegible]922	0.4351126922	0.4351126922

and $v =$ [illegible] in (4.35), we get the same τ. The relation between α, τ, is shown as Fig. 3 for different [illegible] and the data which given in Table 5.

5.4. Changing the parameters

Because of the changing of the behavior of the delay τ and the solution of (3.11) due to parameter changes, we will do this for the parameters a, b, R and C.

Let $h = 0.05$, $N = 41$, $b = 15$ and $L = 1$ and varied the variable a from 0.01 to 0.12 with increments of 0.01. The solution $y(t)$ becomes steeper in the middle and flatter on the end that is shown

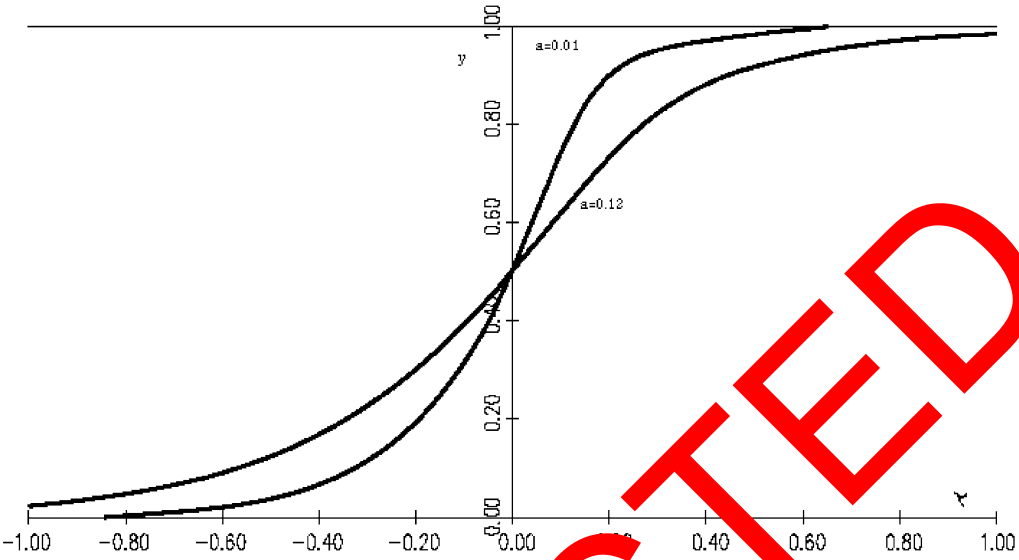

Fig. 4.

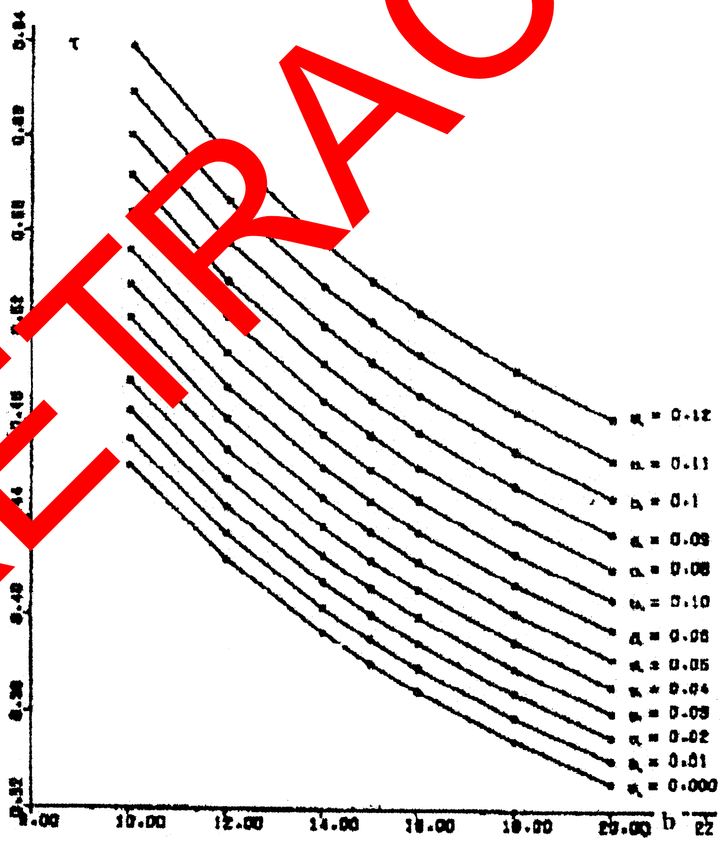

Fig. 5. Relation between b, τ for some as with $h = 0.05$, $N = 41$, $L = 1$.

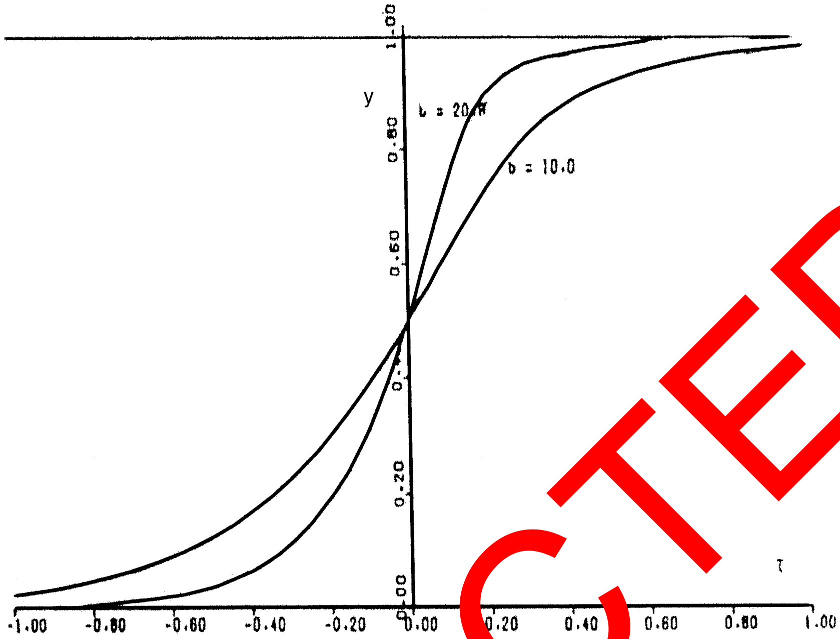

Fig. 6. Solution of the target problem for $b = 20.0$ and $b = 10.0$.

in Fig. 4. This means that the rise time of the membrane potential is faster for lower threshold potential. Fig. 5 described the graph of h and τ. Hence, axons with higher threshold potential have lower conduction speeds and slower rise times. This is consistent with the results that has been shown in [12,17].

Next, we shall discuss the relationship between the strength of ionic current density b, to the conduction speed and rise time of the membrane potential. Let $h = 0.05$, $N = 41$, $a = 0.05$ and $L = 1.0$, and let b vary from 10 to 20 with unit as increments as in Fig. 6. Hence the conduction speed becomes larger when the strength of ionic current density is larger as in Fig. 7.

Now we shall study the behavior of the delay τ and the solution to (3.9) under the control of nodal resistance R and nodal capacitance C. Consider the equation

$$Cy' = f(y(t)) + (y(t+\tau) - 2y(t) + y(t-\tau))/R,$$

where C is the nodal capacitance, R is the nodal resistance $f(y) = by(1-y)(y-a)$, $b > 0$ and $0 < a < 1$. We fixed $a = 0.05$, $b = 12.0$, $N = 41$, $h = 0.05$ and $L = 1.0$.

To determine the relation between the nodal capacitance C and the conduction speed and rise time of the membrane potential. We had to fix the nodal resistance $R = 1$ and let C vary from 0.7 to 1.3 with increment 0.1. As in Fig. 8, shows the rise time of the membrane potential is faster for lower nodal capacitance. Table 6 and Fig. 9 describe how C increases with τ this result has also been verified by [2,19].

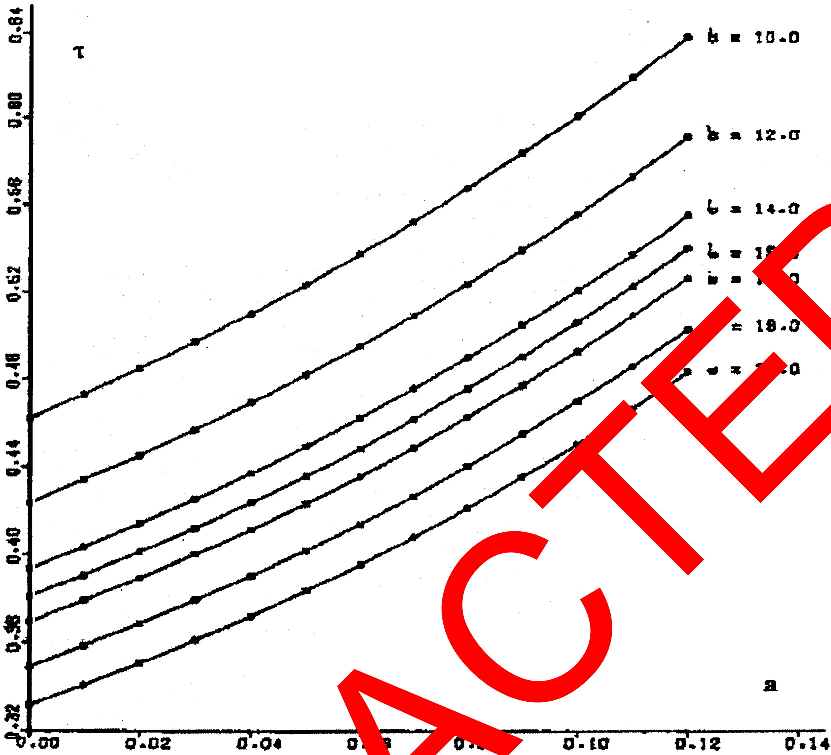

Fig. 7. Relation between a and τ for some b's with $h = 0.05$, $N = 41$, $L = 1$.

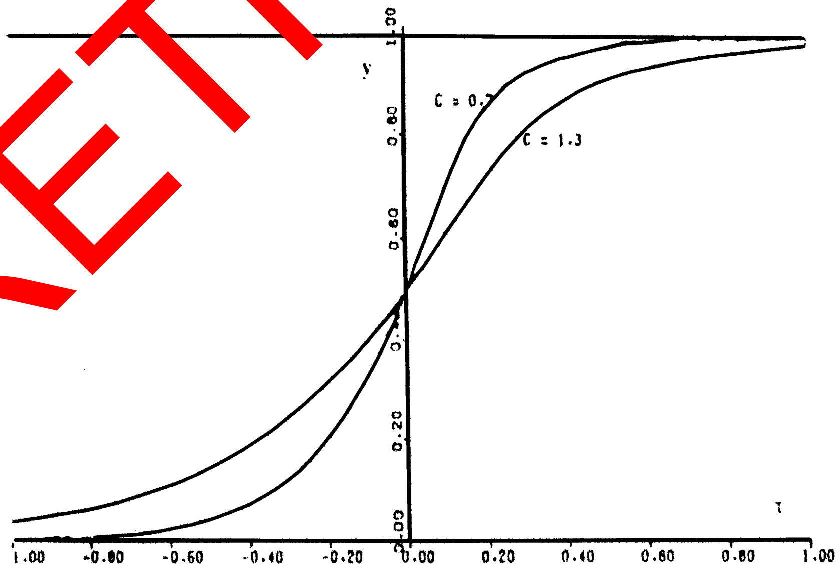

Fig. 8. Solution of the target problem for $c = 0.7$, $c = 1.3$ with $a = 0.05$, $b = 12$, $R = 1$, $h = 0.05$.

Table 6
τ as a function of R and C with $a = 0.05$, $b = 12$, $N = 41$, $h = 0.05$

R	C						
	0.7	0.8	0.9	1.0	1.1	1.2	1.3
0.50	0.232322	0.265792	0.299520	0.333515	0.367767	0.402093	0.436378
0.70	0.278036	0.318056	0.358196	0.398405	0.438538	0.478317	0.517602
0.90	0.318439	0.364144	0.409807	0.455201	0.500103	0.544044	[illegible]
1.00	0.337213	0.385495	0.433638	0.481345	0.528202	[illegible]	[illegible]
1.10	0.355187	0.405923	0.456403	0.506202	0.554854	[illegible]	[illegible]
1.30	0.389011	0.444480	0.499231	0.552634	0.604308	[illegible]	[illegible]
1.50	0.420796	0.480439	0.538795	0.595164	0.649747	0.700887	[illegible]
1.80	0.465205	0.530342	0.593325	0.653988	0.711529	[illegible]	[illegible]
2.00	0.492422	0.561355	0.627210	0.689966	0.749872	[illegible]	0.855154
2.50	0.556866	0.632690	0.705463	0.834156	[illegible]	[illegible]	0.934432

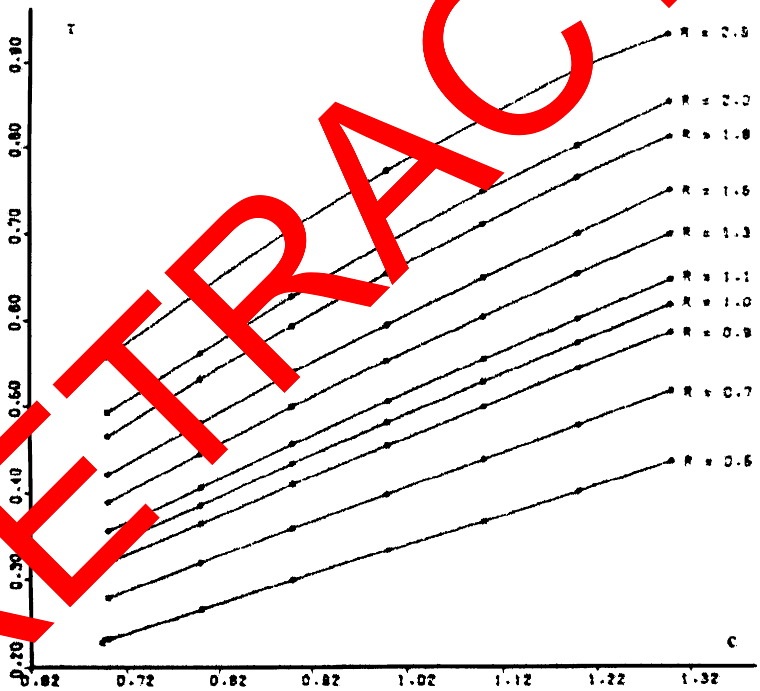

Fig. 9. Relation between c and τ with different R's.

Here, if we consider the same model with $C = 1$, fixed, and resistively R allowed to vary from 0.5 and 2.5. Fig. 10 shows that R decreases where the rise time of the solution increases. Again this is consistent with the numerical results in [2,19].

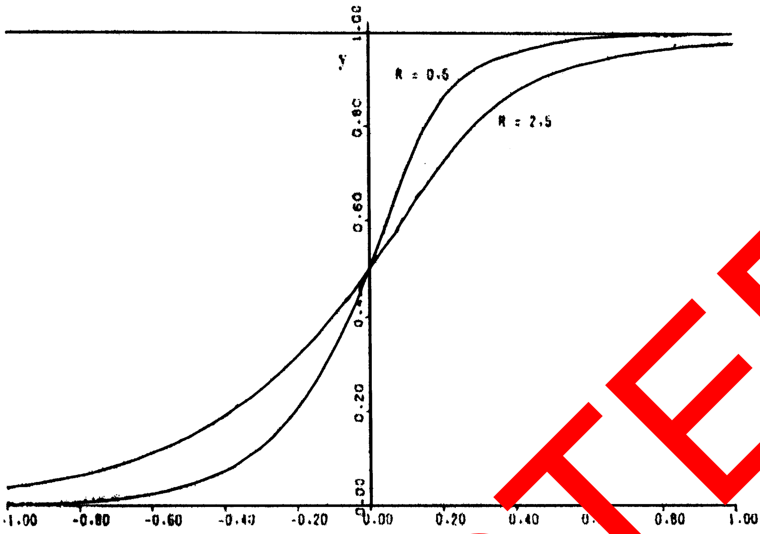

Fig. 10. Solution of target problem with some R's.

6. Conclusions

In this paper we are studying the conduction of impulses down myelinated axons and the nonlinear mixed delay differential equation which arises hence forth. Our overall goal of this research is to understand various mechanisms for modeling myelin simply. So far, we have studied one of the models for myelinated axon numerically. In our model all excitable behavior is at the nodes and no transmembrane current is allowed through the internode.

Myelin acts as a shield that insulates most of the axonal membrane. Myelin is characterized by a high resistance and a low capacity. Therefore, myelination allows the axon to conduct neuroelectric signals by exciting only a small percentage of the membrane, thus providing transmission at greatly reduced energy expenditure and higher speeds if compared to unmyelinated axons.

In this paper we discuss some basic properties of the myelinated axons and use our model problem (1.1) where $y(t)$ represents the transmembrane potential at a node in our simplified model for myelinated axon. This internodl delay τ, represents the reciprocal speed of the potential wave as it propagates down the axon. This constant t must be found simultaneously with the solution $y(t)$ since it is not known a priori. The constants R and C represent axoplasmic resistivity and model capacity, respectively.

The axon is able to carry electrical impulses (signals) away from the cell body because it maintains a voltage difference of approximately 70 mV across its cell membrane. This potential difference exists because of the difference in the sodium and potassium ion concentrates on either side of the membrane.

Our system consists of a single first order equation with boundary value given at $t = \pm\infty$. The problem is approximated via a difference scheme which solves the problem on a finite interval by utilizing an asymptotic representation at the end points, cubic interpolation and iterative techniques to approximate the delays, and a continuation method to start the procedure we have presented. We discuss results of solving a test problem with nonstiff function which has a known solution. We assess the accuracy of the method and determine how the choice of step size affects the accuracy. We test the continuation method. Both the initial problem and the target problem in this test have known solutions. To further test the continuation method, the experiment was repeated for another pair of initial and target problems. We find that the local error is of order 4. We believe that this was from errors in cubic interpolation. If we desire more accurate result, what we should do is to modify the scheme by using a more accurate interpolation scheme and end point expansions this might make the local truncation error of order 6 or higher. For stiff problems, the nonlinear equation cannot be solved by fixed point iteration and one is obliged to use some kind of simplifying Newtons iterations.

When an axon is stimulated by an electrical current of sufficient strength to depolarize the membrane, a potential charge called the action potential occurs. But due to the presence of myelin with its high resistance and low capacity, if the membrane is depolarized at a node, the adjacent region of the membrane cannot be depolarized. Instead the signal appears to jump to the next mode to excite the membrane there. This signal conduction is called saltatory conduction.

This change in parameters (i.e. threshold potential, strength of the ionic current density, nodal resistance and nodal capacitance) affect the behavior of the delay (t) as well as the solving of the delay equation (3.11), the rise time and the conduction speed. Therefore the action potentials (in myelinated fibers of cats) with slower conduction speeds have slower rise times.

As for the relationship between the strength of ionic current density to the conduction speed and rise time of the membrane potential. If the strength of the ionic current density is weak the rise time of the membrane potential is slower and also t is larger. Hence the conduction speed is larger when the strength of ionic current density is larger, i.e. increasing the membrane conductance increases the conduction speed.

Concerning the relationship between the nodal capacitance C, to the conduction speed and rise time of the membrane potential. The smaller "C" is the factor the solution rises.

Hence the premise we started with discussing some basic properties of the myelinated axons. Our model problem presents the transmembrane at a node in our simplified model for myelinated axon. The conclusion reached is that the rise time of the membrane potential is faster for smaller nodal resistance.

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