

Cable equation for a myelinated axon derived from its microstructure

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Abstract—A simplified cable equation that describes the subthreshold behaviour of a myelinated axon is derived from its microstructure. Specifically, a microcontinuum cable model of a composite axon is homogenised, yielding a familiar macrocontinuum cable equation of electrotonus, for which the space and time constants depend on microstructural electrical parameters. Activating functions for magnetic and electrical stimulation can be incorporated into this homogenised cable equation as sources or sinks of transmembrane potential. An integral solution to the forced cable equation is also presented for the subthreshold regime. Errors are introduced when myelin membrane resistance is assumed to be infinite.

Keywords—Cable equation, Composite model, Homogenisation, Microcontinuum, Myelinated axon, Subthreshold response

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1 Introduction

THRESHOLD STIMULUS strength and its dependence on pulse duration in nerve axons are useful in determining their patency (HALLETT and COHEN, 1989). Nonlinear cable models have been developed to predict the transmembrane potential along myelinated axons following stimulation by surface electrodes (MCNEAL, 1976; RATTAY, 1986; 1987; 1988), by transmembrane current injection (FITZHUGH, 1962; FRANKENHAEUSER and HUXLEY, 1964; GOLDMAN and ALBUS, 1968), and, recently, by current-carrying coils (BASSER and ROTH, 1991).

An often-used assumption that simplifies the prediction of transmembrane potential distribution is that the myelinated membrane is perfectly insulating (MCNEAL, 1976). As we shall see, this approximation leads to an underestimate of the effective time constant and an overestimate of the space constant of the axon in the subthreshold regime. To overcome this problem, we should include the impedances of both the myelinated and nodal regions. However, doing so increases the complexity of the model, even in the subthreshold regime. (Instead of solving a system of nonlinear differential equations, now we must solve a system of nonlinear partial differential equations with matching boundary conditions at the myelin/nodal interfaces.) One goal of this paper is to propose a model of the myelinated nerve that can be used to describe subthreshold electrical and magnetic stimulation, incorporating both nodal and myelinated impedances, without significantly increasing its complexity. We derive a simplified macroscopic electrotonic model from a nonlinear

cable model of a composite axon, which includes active membrane currents.

ANDRIETTI and BERNARDINI (1984) attempted to derive such a macrocontinuum cable equation from the microstructure of a myelinated axon. They used a cable equation to describe each internode and node of a composite axon, and required that transmembrane potential and axial current be continuous at each interface (between adjacent nodes and internodes). This strategy, which has also been used to model heat transfer in composite media (CARSLAW and JAEGER, 1959), unfortunately leads to an intractable set of matrix equations as the length of the axon goes to infinity. Nevertheless, numerical solutions of transmembrane potential distribution for nodal current injection agreed well with analytical solutions to their proposed macrocontinuum equation (ANDRIETTI and BERNARDINI, 1984).

An equivalent subthreshold cable equation for a composite, myelinated axon can be derived from basic principles using a homogenisation technique. Similar methods have been used successfully to derive macroscopic dynamic equations of poro-elastic and thermally conductive composite media by space-averaging dynamic equations valid at a microscopic scale (BENSOUSSAN *et al.*, 1978; BURRIDGE and KELLER, 1981; KELLER, 1977; 1980; KUNIN, 1982; 1983; SANCHEZ-PALENCIA, 1980. KRASSOWSKA *et al.* (1987) used this approach to incorporate periodic discontinuities introduced by gap junctions in an infinite string of cardiac cells. In her model, the extracellular impedance was uniform, whereas the intracellular impedance was discontinuous. In the myelinated axon, the intracellular impedance is uniform, whereas the extracellular impedance is discontinuous. Homogenisation of a composite nonlinear cable equation of a myelinated axon yields a familiar macrocontinuum cable equation describing

electrotonus of an unmyelinated axon (HODGKIN and RUSHTON, 1946; DAVIS and DENÓ, 1947), the space and time constants of which depend on nodal and internodal electrical parameters.

Sources of transmembrane potential arising from either electrical or magnetic stimulation are naturally incorporated into this homogenised cable equation (BASSER and ROTH, 1990a; RATTAY, 1988; ROTH and BASSER, 1990). When the length scale of these applied fields is greater than the space constant of the equivalent axon, further simplification of the homogenised cable equation is achieved by scaling arguments and dimensional analysis (BASSER and ROTH, 1990b; 1991). In principle, this model can be used to predict the transmembrane potential distribution along the axon caused by electrostatic and quasimagnetostatic fields.

2 Composite cable equation of a myelinated axon

A diagram of a myelinated axon is given in Fig. 1. It contains segments with active membranes called nodes of Ranvier that are δ wide and spaced a distance L apart. The nodes are joined by membranes that are insulated by myelin sheaths.

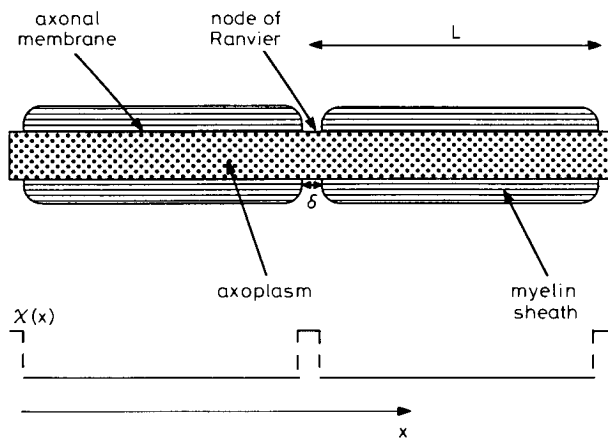


Fig. 1 Diagram of a myelinated axon. Below is the indicator function $\chi(x)$, which is 1 within a node of Ranvier and 0 within an internode.

The axon is modelled as a composite medium, following ANDRIETTI and BERNARDINI (1984), but the composite cable equation is written in a new form that makes it amenable to simplification by the two-space method:

$$\frac{\partial^2 V}{\partial x^2} = (1 - \chi(x)) \left(\frac{\tau_m}{\lambda_m^2} \frac{\partial V}{\partial t} + \frac{V}{\lambda_m^2} \right) \quad \text{myelin} \quad (1)$$

$$+ \chi(x) \left(\frac{\tau_n}{\lambda_n^2} \frac{\partial V}{\partial t} + \frac{V}{\lambda_n^2} + \phi_{ion}(V, t) \right) \quad \text{node of Ranvier}$$

Above, $V(x, t)$ is the distribution of transmembrane potential along the composite cable with respect to rest potential (which is assumed uniform), and τ_m , λ_m , τ_n and λ_n are the myelin and nodal time and space constants. The function $\chi(x)$ contains microscopic anatomical information about the axon. As shown in Fig. 1, $\chi(x)$ is a train of boxcar functions that are δ wide and spaced L apart. One way to represent $\chi(x)$ is by superposing unit Heaviside functions $H(x)$, i.e.:

$$\chi(x) = \sum_{n=-\infty}^{\infty} \left(H\left(x - nL + \frac{\delta}{2}\right) - H\left(x - nL - \frac{\delta}{2}\right) \right) \quad (2)$$

The function $\chi(x)$ selects the term on the right-hand side of eqn. 1 that is appropriate for each value of x . For example, when x is within a node of Ranvier, $\chi(x) = 1$; the transmembrane current is produced by the second term on the right-hand side of eqn. 1. When x lies within the internodal region, $\chi(x) = 0$; the transmembrane current arises from the first term on the right hand side of eqn. 1. BURRIDGE and KELLER (1981) call χ a characteristic or indicator function.

The contribution of the active transmembrane ionic current in eqn. 1 is contained in ϕ_{ion} . It will be shown that this term is significant only when close to threshold and can be ignored below it.

In eqn. 1, the space constant of the internodal region, $\lambda_m(\text{cm})$, is defined as:

$$\lambda_m = \sqrt{\frac{r_m}{r_a}} \quad (3)$$

and the time constant, τ_m , is defined by:

$$\tau_m = r_m c_m \quad (4)$$

where r_m is the resistance of myelin membrane ($\text{k}\Omega \text{cm}$), r_a is the resistance per unit length of axoplasm ($\text{k}\Omega \text{cm}^{-1}$), and c_m is the membrane capacitance ($\mu\text{F cm}^{-1}$). Analogously, the space constant of the node, $\lambda_n(\text{cm})$, is defined as:

$$\lambda_n = \sqrt{\frac{r_n}{r_a}} \quad (5)$$

where r_n is the resistance of the nodal membrane ($\text{k}\Omega \text{cm}$). The nodal time constant, τ_n , is given by:

$$\tau_n = r_n c_n \quad (6)$$

where c_n is the capacitance of the nodal membrane ($\mu\text{F cm}^{-1}$). Using the material parameters given in Table 1 for a myelinated axon, the following space and time constants can be calculated: $\lambda_m = 0.433 \text{ cm}$; $\tau_m = 500 \mu\text{s}$; $\lambda_n = 0.0061 \text{ cm}$; and $\tau_n = 100 \mu\text{s}$.

Because Kirchoff's laws were used to derive the cable equation within every nodal and internode domain, a solution to eqns. 1 and 2 should satisfy the continuity of axial current and transmembrane potential within each domain. However, requiring that admissible solutions to eqns. 1 and 2 be continuous and possess continuous first derivatives everywhere along the axon implies that Kirchoff's laws are automatically satisfied at the interfaces between adjacent domains. Therefore, implicit in eqns. 1 and 2 is the continuity of current and potential at all interfaces between nodes and internodes. This formulation differs from ANDRIETTI and BERNARDINI'S (1984) composite cable model, in which continuity of current and transmembrane potential must be explicitly satisfied at each boundary between adjacent segments. Although FITZHUGH (1962; 1969) models the node of Ranvier as a point source of current, he still has to impose continuity of current and potential between adjacent nodal and internodal segments.

Continuity of current at any boundary between a node and an internode in eqn. 1 is demonstrated below. Imagine there is a boundary $x = x_0$. Because of the assumed continuity of the first derivative of V , we can now employ the fundamental theorem of integral calculus to integrate the left and right sides of eqn. 1 with respect to x across the interface.

$$\int_{x_0-a}^{x_0+a} \frac{\partial^2 V}{\partial x^2} dx = \frac{\partial V(x_0+a)}{\partial x} - \frac{\partial V(x_0-a)}{\partial x} = \int_{x_0-a}^{x_0+a} h(u, t) du \quad (7)$$

Table 1 Material parameters for a myelinated axon

Physical variables		Unit
x	distance along the nerve-fiber axis	cm
t	time	s
$V(x, t)$	transmembrane potential	mV
$f(x, t)$	activating function	mV cm ⁻²
Nerve model		Unit
E_{Na}	sodium Nernst potential at 37°C	35.35 mV
E_L	leakage Nernst potential at 37°C	-80.01 mV
g_{Na}	sodium conductance	1.445 × 10 ³ mS cm ⁻²
g_L	leakage conductance	0.128 × 10 ³ mS cm ⁻²
δ (TASAKI, 1955)	width of node of Ranvier	1.0 × 10 ⁻⁴ cm
d_o	outer diameter of myelin sheath	1.5 × 10 ⁻³ cm
d_i (HURSH, 1939)	inner diameter of axonal membrane	0.7 d_o
C_n (TASAKI, 1955)	nodal capacitance per unit area	5.0 μF cm ²
C_m (TASAKI, 1955)	myelin capacitance per unit area	5.0 × 10 ⁻³ μF cm ⁻²
R_n (TASAKI, 1955)	nodal resistance area	0.02 kΩ cm ²
R_m	myelin resistance area	100 kΩ cm ²
R_a (SCHWARTZ, <i>et al.</i> , 1979)	axoplasm resistivity	0.14 kΩ cm
$c_n = C_n \pi d_i$	nodal capacitance per unit length	μF cm ⁻¹
$c_m = C_m \pi d_i$	myelin capacitance per unit length	μF cm ⁻¹
$r_n = \frac{R_n}{\pi d_i}$	nodal resistance length	kΩ cm
$r_m = \frac{R_m}{\pi d_i}$	myelin resistance length	kΩ cm
$r_a = \frac{4R_a}{\pi d_i^2}$	axoplasm resistance	kΩ cm ⁻¹

Above, α is a small positive number, $h(x, t)$ is the right-hand side of eqn. 1 and u is a dummy variable. It follows directly that the axial gradient of the transmembrane potential is continuous in the limit as α approaches zero, as long as $h(x, t)$ is bounded on the interval $(x_0 - \alpha < x < x_0 + \alpha)$, i.e.:

$$\lim_{\alpha \rightarrow 0} \left(\frac{\partial V(x_0 + \alpha)}{\partial x} - \frac{\partial V(x_0 - \alpha)}{\partial x} \right) = \lim_{\alpha \rightarrow 0} \int_{x_0 - \alpha}^{x_0 + \alpha} h(u, t) du = 0 \quad (8)$$

Because axoplasmic resistivity is assumed continuous between nodes and internodes (ANDRIETTI and BERNARDINI, 1984), eqn. 1 implies continuity of the axial current, i.e.:

$$r_a \frac{\partial V(x_0^+)}{\partial x} = r_a \frac{\partial V(x_0^-)}{\partial x} \quad (9)$$

It is also easy to show that continuity of transmembrane potential is implicit at the boundary between any internodal and nodal region. By integrating eqn. 1 with respect to x with an indefinite limit of integration, we obtain:

$$\frac{\partial V(x_0 + x)}{\partial x} = \frac{\partial V(x_0 - \alpha)}{\partial x} + \int_{x_0 - \alpha}^{x_0 + x} h(u, t) du \quad (10)$$

Integrating again between $-\beta$ and β (where β is another small positive number) with respect to x , we obtain:

$$V(x_0 + \beta) - V(x_0 - \beta) = \frac{\partial V(x_0 - \alpha)}{\partial x} (2\beta) + \int_{-\beta}^{\beta} \int_{x_0 - \alpha}^{x_0 + z} h(u, t) du dz \quad (11)$$

Taking the limit as α and β both approach zero:

$$\lim_{\beta \rightarrow 0} \lim_{\alpha \rightarrow 0} (V(x_0 + \beta) - V(x_0 - \beta)) = \lim_{\beta \rightarrow 0} \lim_{\alpha \rightarrow 0} \left(\frac{\partial V(x_0 - \alpha)}{\partial x} (2\beta) + \int_{-\beta}^{\beta} \int_{x_0 - \alpha}^{x_0 + z} h(u, t) du dz \right) \quad (12)$$

Both terms on the right-hand side of eqn. 12 vanish. Therefore we are left with:

$$V(x_0^+) = V(x_0^-) \quad (13)$$

verifying continuity of the transmembrane potential between adjacent segments.

3 Deriving an equivalent cable equation of a composite axon

In the two-space method, two spatial variables are identified: x' , which describes large-scale variations in transmembrane potential of the order of the internodal distance; and $y(x') = x'/\epsilon$, which describes small-scale variations of the order of the nodal width δ . Typically, $\epsilon \sim O(10^{-3})$ for a myelinated axon. The transmembrane potential is assumed to depend on both length scales, and so eqn. 1 can then be written in the following form:

$$\frac{\partial^2 V \left(x', \frac{x'}{\epsilon}, t \right)}{\partial x'^2} = h \left(x', \frac{x'}{\epsilon}, t \right) = h(x', y(x'), t) \quad (14)$$

where the right-hand side of eqn. 1 is written as $h(x', y(x'), t)$. As x' and $y(x')$ are treated as independent variables, the partial differentiation operator with respect

to x must be replaced by the following operator in x' and y by the chain rule:

$$\frac{\partial}{\partial x} \equiv \frac{\partial}{\partial x'} + \frac{1}{\varepsilon} \frac{\partial}{\partial y} \quad (15)$$

Therefore, eqn. 14 becomes:

$$\left(\frac{\partial^2}{\partial x'^2} + \frac{2}{\varepsilon} \frac{\partial}{\partial y} \frac{\partial}{\partial x'} + \frac{1}{\varepsilon^2} \frac{\partial^2}{\partial y^2} \right) V(x', y, t) = h(x', y, t) \quad (16)$$

The transmembrane potential is expanded as a power series in the perturbation parameter, ε :

$$V(x', y, t, \varepsilon) = v_0(x', y, t) + v_1(x', y, t)\varepsilon + v_2(x', y, t)\varepsilon^2 + O(\varepsilon^3) \dots \quad (17)$$

Each function $v_i(x', y, t)$ is assumed to be bounded. We also expand the right-hand side of eqn. 16 in the same way:

$$h(x', y, t, \varepsilon) = h_0(x', y, t) + h_1(x', y, t)\varepsilon + h_2(x', y, t)\varepsilon^2 + O(\varepsilon^3) \dots \quad (18)$$

Substituting eqns. 17 and 18 into eqn. 16 and grouping terms with like powers of ε , we obtain:

$$\varepsilon^{-2}: \frac{\partial^2 v_0(x', y, t)}{\partial y^2} = 0 \quad (19a)$$

$$\varepsilon^{-1}: \frac{\partial}{\partial y} \left(\frac{\partial v_0(x', y, t)}{\partial x'} + \frac{\partial v_1(x', y, t)}{\partial y} \right) = 0 \quad (19b)$$

$$\varepsilon^0: \frac{\partial^2 v_0(x', y, t)}{\partial x'^2} + 2 \frac{\partial}{\partial y} \frac{\partial v_1(x', y, t)}{\partial x'} + \frac{\partial^2 v_2(x', y, t)}{\partial y^2} = h_0(x', y, t) \quad (19c)$$

With no loss of generality, we can integrate the ε^{-2} equation, eqn. 19a, with respect to y in the interval $(0, y)$:

$$v_0(x', y, t) = v_0(x', t) + y \frac{\partial v_0(x', y, t)}{\partial y} \Big|_{y=0} \quad (20)$$

As v_0 is bounded for all values of y and t , the second term on the right-hand side of eqn. 20 must vanish in the following limit:

$$\lim_{y \rightarrow \infty} y \frac{\partial v_0(x', y, t)}{\partial y} \Big|_{y=0} \quad \text{so that} \quad \frac{\partial v_0(x', y, t)}{\partial y} \Big|_{y=0} = 0 \quad (21)$$

This implies that v_0 is independent of y , i.e.:

$$v_0(x', y, t) = v_0(x', t) \quad (22)$$

Integrating the ε^{-1} equation, eqn. 19b, with respect to y using eqn. 22 yields:

$$v_1(x', y, t) = v_1(x', t) + y \frac{\partial v_1(x', y, t)}{\partial y} \Big|_{y=0} \quad (23)$$

For $v_1(x', y, t)$ to be bounded, we again require that:

$$\frac{\partial v_1(x', y, t)}{\partial y} \Big|_{y=0} = 0 \quad (24)$$

or

$$v_1(x', y, t) = v_1(x', t) \quad (25)$$

Finally, using eqns. 22 and 25 in the integration of the ε^0 equation (eqn. 19c) with respect to y yields:

$$\frac{1}{y} \frac{\partial v_2(x', y, t)}{\partial y} \Big|_0^y = - \frac{\partial^2 v_0(x', t)}{\partial x'^2} + \frac{1}{y} \int_0^y h_0(x', u, t) du \quad (26)$$

where u is a dummy variable. In the limit as y approaches infinity, the term on the left-hand side of eqn. 26 vanishes by the assumption of the boundedness of $\partial v_2(x', y, t)/\partial y$. This quantity is bounded on physical grounds. If it were not, the electric field would be infinite, which is a physical impossibility. Therefore, the equation for the lowest-order term in the perturbation expansion is given by:

$$\frac{\partial^2 v_0(x', t)}{\partial x'^2} = \lim_{y \rightarrow \infty} \frac{1}{y} \int_0^y h_0(x', u, t) du \quad (27)$$

The expression on the right-hand side of eqn. 27 is the mean value of $h(x', y, t)$ with respect to the small variable y , which is denoted by $\langle h_0(x', t) \rangle$. As this quantity no longer explicitly depends upon y , small-scale variations in nodal impedance have been eliminated by integration, although their macroscopic effect has been preserved.

The function $h_0(x', y, t)$ can be rewritten in terms of x' and y :

$$h_0(x', y, t) = (1 - \chi(y)) \left(\frac{\tau_m}{\lambda_m^2} \frac{\partial v_0(x', t)}{\partial t} + \frac{v_0(x', t)}{\lambda_m^2} \right) + \chi(y) \left(\frac{\tau_n}{\lambda_n^2} \frac{\partial v_0(x', t)}{\partial t} + \frac{v_0(x', t)}{\lambda_n^2} + \phi_{ion}(v_0(x', t)) \right) \quad (28)$$

where the function χ is now expressed in terms of y :

$$\chi(y) = \sum_{n=-\infty}^{\infty} \left(H\left(y - \frac{nL}{\delta} + \frac{1}{2}\right) - H\left(y - \frac{nL}{\delta} - \frac{1}{2}\right) \right) \quad (29)$$

This form of χ guarantees that $h(x', y, t)$ is continuously differentiable with respect to x' (KELLER 1980). Because $\chi(y)$ has a period L/δ , $\langle h_0(x', t) \rangle$ in eqn. 27 reduces to:

$$\langle h_0(x', t) \rangle = \frac{\delta}{L} \int_{-(L/2\delta)}^{L/2\delta} h_0(x', t, u) du \quad (30)$$

Homogenisation has produced as equivalent cable equation of the following form:

$$\frac{\partial^2 v_0(x', t)}{\partial x'^2} = \frac{\tau}{\lambda^2} \frac{\partial v_0(x', t)}{\partial t} + \frac{v_0(x', t)}{\lambda^2} + \frac{\delta}{L} \phi_{ion}(v_0(x', t)) \quad (31)$$

in which the effective space and time constants λ and τ are functions of the space and time constants of the myelinated and nodal membrane; i.e.:

$$\lambda = \left(\left(1 - \frac{\delta}{L}\right) \frac{1}{\lambda_m^2} + \frac{\delta}{L} \frac{1}{\lambda_n^2} \right)^{-1/2} \quad (32)$$

$$\tau = \lambda^2 \left(\left(1 - \frac{\delta}{L}\right) \frac{\tau_m}{\lambda_m^2} + \frac{\delta}{L} \frac{\tau_n}{\lambda_n^2} \right)$$

These equivalent space and time constants in eqn. 32 are rewritten in terms of membrane resistances and capacitances of the node and internodes using eqns. 3–6:

$$\lambda = \left(\left(1 - \frac{\delta}{L}\right) \frac{r_a}{r_m} + \frac{\delta}{L} \frac{r_a}{r_n} \right)^{-1/2} \quad (33)$$

$$\tau = \lambda^2 \left(\left(1 - \frac{\delta}{L}\right) r_a c_m + \frac{\delta}{L} r_a c_n \right)$$

An axon with the properties given in Table 1 has the following equivalent space and time constants: $\lambda = 0.208$ cm and $\tau = 192$ μ s.

These expressions, eqns. 31 and 33, are similar but not identical to formulas for λ and τ suggested by ANDRIETTI and BERNARDINI (1984). Although these authors showed good agreement between analytical solutions to a simplified cable equation and numerical solutions to their segmented cable model for both nodal and transmembrane potential stimuli and a particular set of membrane parameters, they were unable to demonstrate the correspondence between eqns. 31 and 33 and derive the cable model for a composite myelinated axon. Above, it has been shown that the homogenised cable equation is the lowest-order approximation to a microcontinuum segmented cable model of a myelinated axon using the small-perturbation parameter ε . Additional advantages of the two-space method are that:

- it furnishes an estimate of the accuracy of the solutions for a particular geometry: $O(\varepsilon^3)$.
- it provides an iterative prescription for calculating higher-order terms in the perturbation expansion of $V(x, t)$, and
- it permits the treatment of nonlinear equations describing membrane kinetics.

In eqn. 31, the active nodal membrane ϕ_{ion} is assumed to be distributed uniformly over the entire axon, and the total active membrane current per unit internodal length is unchanged. Because $\phi_{ion}(v_0(x', t))$ is multiplied by δ/L in eqn. 31, and it is already small (except when v_0 is close to threshold potential), we can safely ignore $\phi_{ion}(v_0(x', t))\delta/L$ in most calculations of subthreshold response (BASSER and ROTH, 1991).

4 Applications to electrical and magnetic stimulation

It has not yet been established whether the full nonlinear equation, eqn. 31, coupled with the kinetic equations of the membrane, accurately predict the suprathreshold behaviour of the myelinated axon. However, there are many interesting phenomena that one can predict in the subthreshold regime, such as the response of a myelinated nerve stimulated by applied electric fields produced, for instance, by electromagnetic induction (during magnetic stimulation) or by electrodes (in electrical stimulation).

Typically, the characteristic length of applied electric fields is several centimetres. In electrical stimulation, for instance, it is often the separation between cathodic and anodic electrodes. In magnetic stimulation, the characteristic length is of the order of the diameter of the stimulating coil (BASSER and ROTH, 1990b) in the far field limit (BASSER, 1993). However, the dimensions of the anatomical structures which determine the response of the axon to stimulation are typically several orders of magnitude smaller. For instance, the space constant of the internode of a myelinated axon, its characteristic length, is typically no greater than 0.3 cm, whereas the space constant of the node of Ranvier is typically $O(10^{-3})$ cm (TASAKI (1955), and its width is only about 0.0001 cm (TASAKI, 1955). A detailed microcontinuum model using a microscopic length scale commensurate with the dimensions of a node of Ranvier would require millions of computational elements to predict the macroscopic transmembrane potential distribution along a myelinated axon. Therefore it is useful to have developed a macrocontinuum model of the response of the myelinated axon that correctly incorporates a microscopic level of anatomical detail.

An electric field applied externally to a nerve is represented in the cable equation as sources or sinks of transmembrane potential $f(x, t)$ added to the right-hand

side of eqn. 1. In electromagnetic stimulation, the activating function $f(x, t) = -\partial\varepsilon_x(x, t)/\partial x$, where $\varepsilon_x(x, t)$ is the net applied electric field in the direction of the nerve fibre axis (BASSER and ROTH, 1990a; ROTH and BASSER, 1990). In electrical stimulation, $f(x, t) = \partial^2 V_e(x, t)/\partial^2 x$, where $V_e(x, t)$ is the applied extracellular potential (RATTAY, 1986; 1988).

These source terms can also be expanded as a power series of the perturbation parameter ε , i.e.:

$$f(x', y, t, \varepsilon) = f_0(x', y, t) + f_1(x', y, t)\varepsilon + f_2(x', y, t)\varepsilon^2 + O(\varepsilon^3) \dots \quad (34)$$

If this forcing function is carried along as a term in $h(x', y(x'), t)$ in eqn. 14, it is easy to show that the resulting forced cable equation is:

$$\frac{\partial^2 v_0(x', t)}{\partial x'^2} = \frac{\tau}{\lambda^2} \frac{\partial v_0(x', t)}{\partial t} + \frac{v_0(x', t)}{\lambda^2} - f_0(x', t) \quad (35)$$

It is possible to express the transmembrane potential $v_0(x', t)$ as a convolution of the activating function (RATTAY, 1986; 1988) and a kernel appropriate for electrotonus in a myelinated nerve. This solution can be obtained by solving eqn. 35 for the transmembrane potential in the subthreshold regime for electrical or magnetic stimulation. If it is assumed that there is no stimulation prior to $t = 0$, i.e. $v_0(x, 0) = 0$, and that the stimulus is bounded, i.e. $v_0(\pm\infty, t) = 0$, then the transmembrane potential can be obtained by Fourier and Laplace transform techniques:

$$v_0(x, t) = \frac{\lambda}{2\sqrt{\pi\tau}} \int_0^t \frac{1}{\sqrt{t-\gamma}} \int_{-\infty}^{\infty} f_0(\xi, \gamma) \times \exp\left(-\frac{(t-\gamma)}{\tau} - \left(\frac{x-\xi}{2\lambda}\right)^2 \frac{\tau}{t-\gamma}\right) d\xi d\gamma \quad (36)$$

In eqn. 36, $f_0(x', t)$ is a single-pulse or a periodic-pulse train. This formula, proposed by DAVIS and DENÓ (1947) for an unmyelinated axon, also applies to magnetic and electrical stimulation of myelinated axons using the appropriate space and time constants; eqns. 32 or 33.

If the characteristic lengths of the spatial variations in the activating function (RATTAY, 1986; 1988) are substantially greater than the space constant of the homogenised axon, then it is possible to use dimensional analysis to further simplify the cable equation, eqn. 35 (BASSER and ROTH, 1990a; 1991). This simplification has led to the prediction of scaling relationships between threshold stimulus strength, pulse duration and axon diameter by requiring that the transmembrane potential equal the threshold potential of the membrane, i.e. $v_0(x, t) = V_T$ (BASSER and ROTH, 1990b; 1991).

Finally, using the homogenised model, we can assess the validity of the assumptions used by MCNEAL (1976) in modelling excitation of a myelinated nerve. He writes, 'The most serious error in the [his] model is introduced by the assumption that the myelin sheath is a perfect insulator, which it is not'. Surprisingly, ignoring leakage and capacitance of the myelinated membrane leads to a significant underestimate of the effective time constant of the axon and an overestimate of its effective space constant. We can see this from eqn. 31 or 32. Although the resistance of the myelin membrane is much greater than that of the node, so is its relative area. These effects nearly cancel each other out, producing an effective resistance of the membrane that has contributions from the myelin and node that are of the same order of magnitude. This is also the case for the membrane capacitance. The contributions from the nodal and myelinated regions are of the same order of

magnitude. As a result, the axon time constant is significantly underestimated and the effective space constant is significantly overestimated.

5 Concluding remarks

This simplified cable equation has applications beyond the scope of electrical and magnetic stimulation. It has recently been reported that sensory responses have been observed during echo-planar MRI (BOURLAND *et al.*, 1990; BUDINGER *et al.*, 1990). Another timely application is in calculating the response of axons to induced electrical fields caused by high-voltage power lines. This model may also be appropriate to describe the electrical behaviour of skeletal muscle fibres (ANDRIETTI and BERNARDINI, 1984).

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