SCALING LAWS FOR ELECTROMAGNETIC STIMULATION OF AN AXON

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ABSTRACT

A cable equation is presented that describes the subthreshold response of a nerve axon to electromagnetic stimulation. This equation is normalized to identify dimensionless parameters that determine whether the stimulus strength is sufficient to elicit an action potential. Scaling laws predict threshold stimulus strength is inversely proportional to current pulse duration for short pulses but is independent of duration for long pulses. Threshold stimulus strength is inversely proportional to fiber diameter in unmyelinated axons, and inversely proportional to the diameter squared in myelinated axons. These findings are consistent with numerical solutions of the dynamic equations that include membrane kinetics [2].

INTRODUCTION

Electromagnetic stimulation is a non-invasive and painless technique for exciting nerves [5]. It can be achieved by discharging a capacitor through a coil held in close proximity to a nerve axon (Fig. 1). If the spatial gradient of the induced electric field is sufficiently large, the axon will fire an action potential.

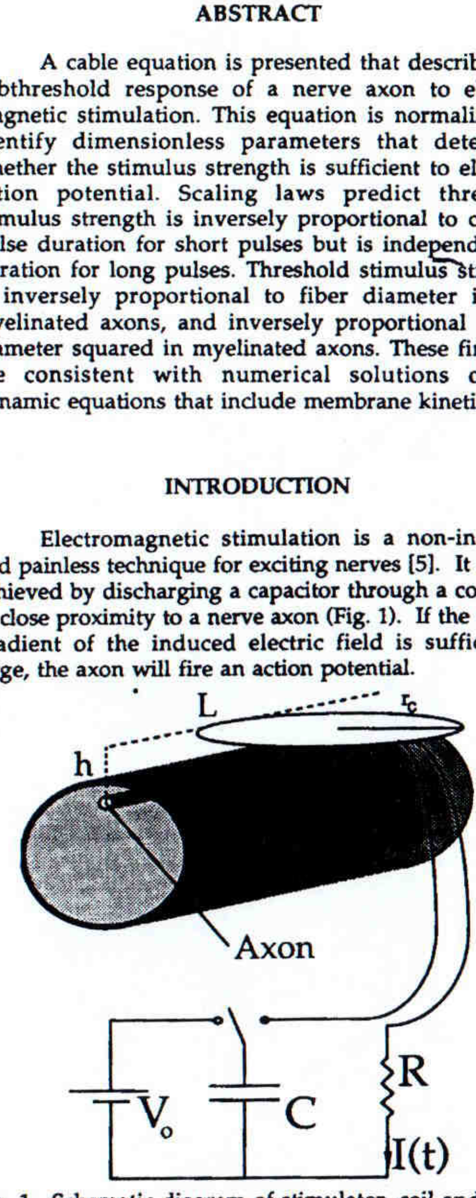

Fig. 1. Schematic diagram of stimulator, coil and axon.

METHODS

During electromagnetic stimulation, an axon's transmembrane potential (referenced to rest potential), V(x,t), a function of position x along the axon and time t, is related to the x-component of the induced electric field, $E_x(x,t)$, by the cable equation

$$\lambda^2 \frac{\partial^2 V}{\partial x^2} - \tau \frac{\partial V}{\partial t} - V = \lambda^2 \frac{\partial E_x(x,t)}{\partial x}, \quad (1)$$

where λ and τ are the axon length and time constants. The function $-\lambda^2 \partial E_x/\partial x$ is the source of the transmembrane potential. It determines the time and location of excitation [8] and is analogous to the activating function for stimulation with external electrodes [7].

By recasting the cable equation into a nondimensional form, we elucidate the behavior of the axon at threshold without having to solve the equation explicitly. We rescale all dependent and independent variables by their characteristic quantities. We normalize x by the radius of the stimulating coil, $\mathit{x} = x/r_c$, t by the rise time of the current pulse, $\mathit{t} = t/\tau_d$, and V by the threshold potential, $\mathit{V} = V/V_T$. Similarly, the axial electric field gradient is normalized by the maximum value it achieves with respect to both time and position along the nerve, $\partial E_x/\partial x_{max}$, $\partial \mathit{E_x}(\mathit{x,t})/\partial \mathit{x} = \partial E_x(x,t)/\partial x \; / \; \partial E_x/\partial x_{max}$. We then substitute these normalized variables into the cable equation, obtaining

$$\left(\frac{\lambda}{r_c}\right)^2 \frac{\partial^2 \mathit{V}}{\partial \mathit{x}^2} - \left(\frac{\tau}{\tau_d}\right)\frac{\partial \mathit{V}}{\partial \mathit{t}} - \mathit{V} = \left(\frac{\lambda^2}{V_T}\frac{\partial E_x}{\partial x}_{max}\right)\frac{\partial \mathit{E_x}(\mathit{x,t})}{\partial \mathit{x}}. \quad (2)$$

The behavior of this normalized cable equation is determined by the three dimensionless parameters enclosed in parentheses. Typically, the axon length constant is much smaller than the coil radius, so that the first term on the left hand side of Eq. (2) is negligible. Therefore, the transmembrane potential distribution is determined by the two remaining dimensionless parameters. The ratio τ/τ_d relates the membrane time constant to the rise time of the current pulse. The dimensionless constant on the right hand side of Eq. (2) is the ratio of the strength of the stimulus, $\lambda^2 \partial E_x/\partial x_{max}$, to the threshold potential, V_T.

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We call this parameter the *electromagnetic stimulation number* , S_{em}, where

$$S_{em} = \frac{\lambda^2}{V_T} \frac{\partial E_x}{\partial x}_{max} . \quad (3)$$

RESULTS

The stimulus duration, typically 150 μs [3], is often longer than the axon time constant, about 30 μs for mammalian nerves [11], ($\tau_d >> \tau$) so

$$V \approx S_{em} \frac{-\partial E_x(x,t)}{\partial x} , \quad (4)$$

Because $V = 1$ corresponds to threshold stimulation, and the electric field gradient is also normalized to unity, $S_{em} = 1$ is the condition for a rheobase threshold stimulus.

For a stimulus whose duration is short with respect to the axon time constant (i.e., $\tau >> \tau_d$), V is governed by

$$\frac{\partial V}{\partial t} \approx \frac{\tau_d}{\tau} S_{em} \frac{-\partial E_x(x,t)}{\partial x} . \quad (5)$$

Stimulation is achieved when

$$\frac{\tau_d}{\tau} S_{em} \approx 2 , \quad (6)$$

implying that threshold stimulus strength is inversely proportional to pulse duration in this regime.

To estimate the capacitor plate voltage, V_o, at threshold we must first approximate $\partial E_x/\partial x_{max}$. The induced electric field, E, from a coil is [4]

$$E(r) = -\frac{\mu_o N}{4\pi} \frac{dI(t)}{dt} \int \frac{dl'}{|r-r'|} , \quad (7)$$

where $\mu_o = 4\pi \times 10^{-7}$ V-s/A-m, N is the number of turns in the coil, dl' is an incremental length element and $|r-r'|$ is the distance between dl' and point r. We neglect the electric field from a charge distribution at the air/tissue interface [9] which can be of the same order of magnitude as the induced field. For a circular coil of radius r_c held a distance h from an axon (Fig. 1), we approximate E_x as

$$E_x \approx \frac{\mu_o N}{4\pi} \frac{dI}{dt} \frac{r_c}{h} . \quad (8)$$

The x-derivative of E_x is approximately E_x/r_c, so that

$$\frac{\partial E_x}{\partial x} \approx \frac{\mu_o N}{4\pi h} \frac{dI}{dt} \quad (9)$$

For a series RLC circuit, the maximum rate of rise of current in the coil, dI/dt_{max}, equals V_o/L where L is the coil inductance. Therefore,

$$\frac{\partial E_x}{\partial x}_{max} \approx \frac{\mu_o N V_o}{4\pi h L} . \quad (10)$$

Using $S_{em} = 1$, we estimate threshold plate voltage as

$$V_o \approx \frac{4\pi h L V_T}{\mu_o N \lambda^2} , \quad (11)$$

For a typical coil, $N \approx 10$, and $L \approx 20$ μH and $h \approx 1$ cm. For a 20 μm axon, $\lambda \approx 0.2$ cm and $V_T \approx 20$ mV. Thus, $V_o \approx 1$ kV. This estimate differs from the maximum plate voltages on commercial stimulators (2 to 3 kV) by only a factor of two or three.

We can also determine how the stimulus strength scales with the diameter of the axon. For an unmyelinated axon the length constant, λ, is proportional to the square root of the axon diameter, d. For a myelinated axon, we can use an averaging method [1] or the method of multiple scales [6], with Rushton's scaling relationships [10], to show that the effective length constant is proportional to the axon outer diameter. If we substitute these scaling laws into Eq. (11) we see that for unmyelinated nerves the threshold stimulus strength is inversely proportional to axon diameter, and for myelinated nerves the threshold stimulus strength is inversely proportional to the the axon diameter squared [2].

REFERENCES

[1] ANDRIETTI, F. & BERNARDINI, G. (1984) Segmented and "equivalent" representation of the cable equation. *Biophys. J.* **46**, 615-623.

[2] BASSER, P. J. & ROTH, B. J. (1990) Stimulation of a myelinated axon by electromagnetic induction. *Proceedings of the 16th Annual Northeast Bioengineering Conference*. ed. R. Gaumond, 129-130.

[3] BARKER, A. T., JALINOUS, R. & FREESTON, I. L. (1985) Non-invasive magnetic stimulation of human motor cortex. *Lancet*, **1**, 1106-1107.

[4] COHEN, L. G., ROTH, B. J., NILSSON, J., DANG, N., PANIZZA, M., BANDINELLI, S., FRIAUF, W. & HALLETT, M. (1990) Effect of coil design on delivery of focal magnetic stimulation. I. Technical considerations. *Electroenceph. clin. Neurophysiol.* (in press).

[5] HALLETT, M. & COHEN, L. G. (1989) Magnetism: A new method for stimulation of nerve and brain. *JAMA*, **262**, 538-541.

[6] KELLER, J. B. (1980) Darcy's law for flow in porous media and the two-space method, in: Nonlinear Partial Equations in Engineering and Applied Science, ed: R. L. Sternberg, A. J. Kalinowski, and J. S. Papadakis, Marcel Dekker, New York, pp. 429-443.

[7] RATTAY, F. (1986) Analysis of models for external stimulation of axons. *IEEE Trans. Biomed. Eng.*, **33**, 974-977.

[8] ROTH, B. J. & BASSER, P. J. (1990) A model of the stimulation of a nerve fiber by electromagnetic induction. *IEEE Trans. Biomed. Eng.*, (in press).

[9] ROTH, B. J., COHEN, L. G., HALLETT, M., FRIAUF, W. & BASSER, P. J. (1990) A theoretical calculation of the electric field induced by magnetic stimulation of a peripheral nerve. *Muscle & Nerve*, (in press).

[10] RUSHTON, W. A. H. (1951) A theory of the effects of fibre size in medullated nerve. *J. Physiol. (London)*, **115**, 101-122.

[11] SWEENEY, J. D., MORTIMER, J. T. & DURAND, D. (1987) Modeling of mammalian myelinated nerve for functional neuromuscular stimulation. In: *Proceedings of the 9th Annual Conf. EMBS*, 1577-1578.