

AN ANALYSIS OF THE ELECTRICAL PROPERTIES OF A SKELETAL MUSCLE FIBER CONTAINING A HELICOIDAL T SYSTEM

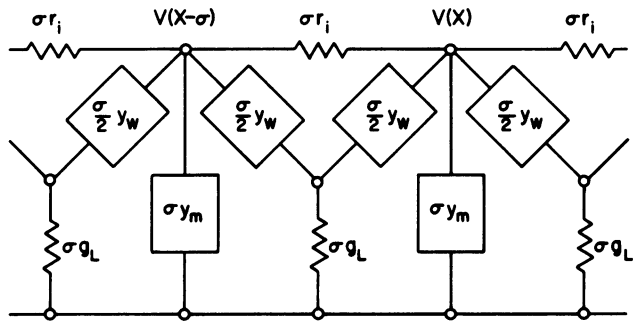
RICHARD T. MATHIAS, *Department of Physiology, Rush University, Chicago,
Illinois 60612 U.S.A.*

ABSTRACT The linear electrical properties of skeletal muscle fibers have been analyzed using lumped circuit analogues of a helicoidal T system. The geometry of a helicoid is assumed to produce two electrical effects, modeled separately. One model is motivated by the pitch or tilt of the T system, which forces the current flowing in the lumen of the tubules to have a longitudinal projection. The second model is motivated by the longitudinal continuity of a helicoid, which forms a structure similar to a cable within the fiber. The pitch or tilting of the T system plane modified the longitudinal resistance of the fiber, making it slightly frequency dependent; however, the magnitude of the change was $<0.1\%$. The longitudinal connections between T system networks had a more complicated effect; the magnitude of the correction was again $<0.1\%$. The conclusion from this analysis is that a helicoidal T system, whose pitch is constrained by the sarcomere spacing, will not affect electrical signals recorded intracellularly in intact fibers.

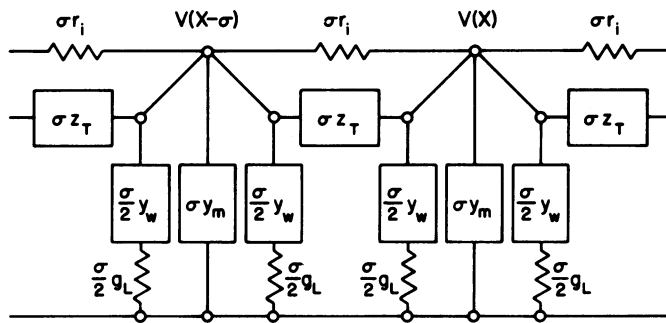
INTRODUCTION

The "transverse" tubular system has been shown to have a helicoidal—nontransverse—superstructure (Peachey and Eisenberg, 1978). Models used to describe the flow of current in the T system (Falk and Fatt, 1964; Adrian et al., 1969; Schneider, 1970; Mathias et al., 1977) have all assumed that the geometry constrained the current to flow in a transverse plane. Much of the electrical data from skeletal muscle have been gathered using the three-electrode voltage clamp of Adrian et al. (1970). This technique assumes that all paths for longitudinal current flow within a fiber are resistive and linear, an assumption that may be false if the T system carries longitudinal current. An analysis of the electrical effects owing to a nontransverse T system is therefore important.

A helicoidal T system has two geometrical properties distinct from those of a transverse T system: first, the plane of the network must be at some angle with respect to a transverse plane, and second, there will be longitudinal continuity between "networks." The tilt of the T system plane might cause a component of the radial current to be projected onto the longitudinal axis; radial voltage gradients in the T system would then drive part of the longitudinal current in the fiber. The longitudinal continuity of the T system could set up a cablelike network within the fiber, so that longi-



(a)



(b)

FIGURE 1 A lumped equivalent circuit for a muscle fiber with a tilted (nontransverse) T system. (a) The intuitive form of the equivalent circuit where one-half of one T system's membranes are connected to a different longitudinal location than the other half. (b) The Π equivalent form of the same circuit shown in a. See the text and glossary for the definitions of symbols.

tudinal voltage gradients in the sarcoplasm might drive current in the T system. Both possibilities are more likely significant for signals whose frequency content is in the low range, under 1,000 Hz, because high frequencies only excite a small outer annulus of T system causing very little current flow in most of the network where the helicoids occur.

Fig. 1 a is one possible analogue of a muscle fiber in which voltage gradients, which are primarily radial, could drive a longitudinal current. This model ignores the effect of series connections between neighboring networks and emphasizes the effect of tilting. The access resistance due to the lumen of one T system in one sarcomere of length σ is represented by σg_L . The walls of the tubules in this network connect the lumen of the tubules to the sarcoplasm through the admittance $(\sigma/2) y_w$, where, by virtue of the tilt, one-half of the walls are lumped together connecting to a different longitudinal

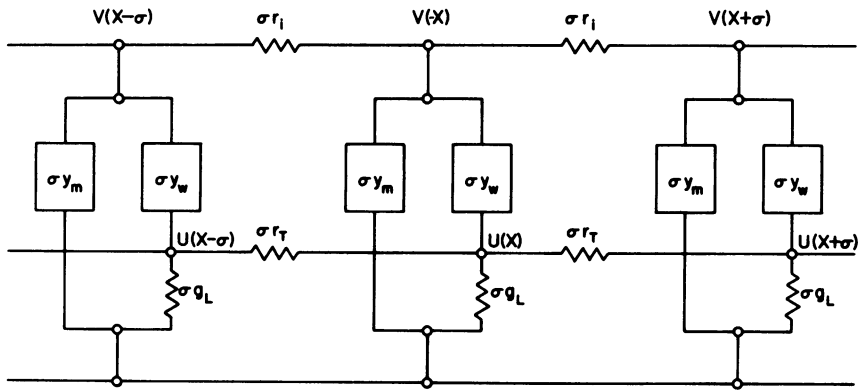


FIGURE 2 A lumped equivalent circuit for a muscle fiber whose T systems are connected to each other by a set of tubules. The resistance σr_T represents the resistance due to the lumen of all the tubules connecting neighboring T systems. See the text and glossary for definitions of symbols.

location than the other half. Thus the sarcoplasmic resistance, σr_i , separates the walls of the tubules in one-half of the network's plane from the walls of the other half. The admittances of the tubular membranes, σy_w , and of the surface membrane, σy_m , are both represented by a parallel resistor and capacitor.

The second possibility is that the longitudinal continuity of the T system produces a cablelike structure within a fiber. Fig. 2 is one possible analogue of this geometry; in this figure, the effect of tilting is ignored and the connections between neighboring networks are emphasized. The circuit elements are the same as described in the previous paragraph with the exception of the new symbol, σr_T , the resistance of the lumen of the tubules connecting T systems in neighboring sarcomeres.

GLOSSARY

- a Fiber radius (41×10^{-4} cm).¹
- c_m Capacitance per unit length of fiber due to the sarcolemma (2.8×10^{-8} F/cm).¹
- c_w Capacitance per unit length of fiber due to the walls of the T system (1.4×10^{-7} F/cm).^{1,2}
- g_L Conductance per unit length of fiber in series with the T system membranes (1.8×10^{-4} Ω^{-1} /cm).^{1,2}
- g_m Conductance per unit length of fiber due to the sarcolemma (3.6×10^{-6} Ω^{-1} /cm).¹

¹ These parameter values were used to estimate the effect of a helical T system. The values are either the averages in Table II of Mathias et al. (1977), or their values for curve fitting.

² The lumped T-system parameters are defined in Fig. 5 of Mathias et al. (1977). There is an error in the definition of g_L in this figure; the correct definition is:

$$g_L = \frac{V_T}{V_F} \frac{8\pi\tau}{R_L}$$

- g_w Conductance per unit length of fiber due to the walls of the T system ($2.2 \times 10^{-6} \Omega^{-1}/\text{cm}$).^{1,2}
- $i(x, j\omega)$ The frequency domain representation of the longitudinal current (amperes).
- $I_l(j\omega)$ The frequency domain representation of the current entering a fiber at a particular longitudinal location (amperes).
- $j\omega$ The Fourier transform parameter where $j = \sqrt{-1}$ and ω is angular frequency (s^{-1}).
- K The fraction of the T-system volume that is effectively carrying longitudinally oriented current (0.1).¹
- r_i Resistance of the sarcoplasm per unit length of fiber ($3.2 \times 10^6 \Omega/\text{cm}$).¹
- R_L Resistivity of the solution in the lumen of the T system ($136 \Omega\text{-cm}$).¹
- r_T Longitudinal resistance of the T-system lumen per unit length of fiber ($8.0 \times 10^9 \Omega/\text{cm}$).¹
- $U(x, j\omega)$ The frequency domain representation of the average voltage in the lumen of the T system (volts).
- $V(x, j\omega)$ The frequency domain representation of the voltage in the sarcoplasm (volts).
- V_T/V_F The volume of T system per unit volume of fiber (3.2×10^{-3}).¹
- x Longitudinal coordinate (cm).
- $y_m = g_m + j\omega c_m$, the admittance of the sarcolemma per unit length of fiber (Ω^{-1}/cm).
- $y_w = g_w + j\omega c_w$, the admittance of the T-system walls per unit length of fiber (Ω^{-1}/cm).
- $z_i = r_i z_T / (r_i + z_T)$ The longitudinal impedance per unit length of fiber (Ω/cm).
- $z_T = (g_L + y_w) / \frac{1}{4} \sigma^2 y_w^2$ The longitudinal impedance per unit length of fiber due to current flowing in a tilted T system (Ω/cm).
- $\gamma = \sqrt{r_i \left(y_m + \frac{g_L y_w}{g_L + y_w} \right)}$ The propagation coefficient for a fiber with a lumped, transverse T system (cm^{-1}).
- $\gamma_0 = \sqrt{r_i (y_m + y_w)}$ The propagation coefficient for a fiber with no resistance in series with the T-system walls (cm^{-1}).
- $\gamma_T = \sqrt{r_T (y_w + g_L)}$ The propagation coefficient for the longitudinal T system (cm^{-1}).
- $\epsilon_1 = \frac{1}{4} \sigma^2 r_i y_w^2 / (g_L + y_w)$ A dimensionless, small parameter.
- $\epsilon_2 = \gamma_0^2 / \gamma_T^2$ A dimensionless, small parameter.
- σ Sarcomere spacing ($2.5 \times 10^{-4} \text{ cm}$).¹

Analysis of Fig. 1

The Y network representing the T system in Fig. 1 *a* can be transformed into the π equivalent circuit shown in Fig. 1 *b*. Equations defining this transformation can be found in Weinberg (1962). In the circuit shown in Fig. 1 *b*, an element of the T-system admittance appears in parallel with the longitudinal resistance, and an element is in parallel with the surface admittance. The part in parallel with the surface admittance has the form of a lumped T system which appears as the low frequency limit in the disk model (Adrian et al., 1969) or the mesh model (Mathias et al., 1977). The new impedance, σz_T , which is in parallel with the sarcoplasmic resistance, does not have a representation in terms of standard circuit elements. It is, however, frequency dependent and also dependent upon the possibly nonlinear conductance of the wall of the tubules.

The parallel combination of r_i and z_T is the longitudinal impedance per length of fiber, z_i .

$$z_i = \frac{r_i}{1 + \epsilon_1}, \quad (1)$$

where

$$\epsilon_1 = \frac{\frac{1}{4} \sigma^2 r_i y_w^2}{g_L + y_w}. \quad (2)$$

If one considers σ to be a small increment in x , then the circuit shown in Fig. 1 *b* is the basis for the differential equations that describe a one-dimensional transmission line:

$$\frac{dV(x)}{dx} = - \frac{r_i}{1 + \epsilon_1} i(x), \quad (3)$$

$$\frac{di(x)}{dx} = - (y_m + y_w) V(x). \quad (4)$$

These equations describe the voltage or current flow in either of the circuits shown in Fig. 1. The solution of these equations requires that appropriate boundary conditions be specified for the preparation and experiment (see Jack et al., 1975, for examples).

We see, either in these equations or in Fig. 1 *b*, that the longitudinal resistance is multiplied by the frequency-dependent correction factor $(1 + \epsilon_1)^{-1}$. If we replace ϵ_1 with actual numbers from frog sartorius (Mathias et al., 1977), we find that, in the range of frequencies in which the lumped approximation of the T system is valid, $|\epsilon_1| < 10^{-4}$ frequency $< 1,000$ Hz. Thus the tilt will have no measurable effect at low frequencies.

If one can imagine a situation where the length constant for a fiber is very short and yet a lumped model of the T system is still valid, then this analysis indicates that tilting only becomes important when the length constant is comparable to the sarcomere length. In a healthy muscle fiber, a length constant this short would correspond to frequencies outside of the range of physiological interest.

Analysis of Fig. 2

In Fig. 2 the parameter σr_T is the resistance due to the lumen of the tubules connecting adjacent T systems. We know this resistance should be inversely proportional to V_T/V_F and directly proportional to R_L , but we do not know the fraction of the T system volume effectively conducting longitudinal current. One estimate of this fraction is $\sin \alpha$, where α is the pitch of the helicoid. Inasmuch as $\sin \alpha$ is approximately the sarcomere spacing divided by the fiber diameter, one finds that $< 5\%$ of the volume can be considered longitudinally oriented. In addition to this 5%, Eisenberg (1972) found that about 3% of the tubules run parallel to the myofibrils and directly connect adjacent T system networks. Thus we can estimate r_T by

$$r_T = R_L/K \frac{V_T}{V_F} \pi a^2, \quad (5)$$

where K is the factor that corrects for branching, bending, and the fraction of the T system longitudinally oriented. From a physical standpoint we know $0 \leq K \leq 1$. From the preceding discussion K would be estimated at 0.08; however, this estimate should be reduced to account for tortuosity. In any case, the conclusions of the following analysis are not changed for any allowable value of K .

If one assumes σ to be a small increment in x , the circuit in Fig. 2 may be described with differential equations; now, however, we need two coupled second-order equations.

$$\frac{d^2V}{dx^2} = r_i(y_w + y_m)V - r_i y_w U, \quad (6)$$

$$\frac{d^2U}{dx^2} = r_T(y_w + g_L)U - r_T y_w V, \quad (7)$$

where V is the intracellular potential and U is the potential within the lumen of the tubules.

Some of the nomenclature may be simplified by defining γ_0 , the propagation coefficient for a fiber that has zero access resistance in series with T system membranes,

$$\gamma_0^2 = r_i(y_w + y_m), \quad (8)$$

and also defining γ_T the propagation coefficient for the T system in the longitudinal direction:

$$\gamma_T^2 = r_T(y_w + g_L). \quad (9)$$

Eqs. 6 and 7 may be combined into a single fourth-order equation describing the intracellular voltage, V .

$$\frac{d^4V}{dx^4} - (\gamma_0^2 + \gamma_T^2) \frac{d^2V}{dx^2} - \gamma^2 \gamma_T^2 V = 0. \quad (10)$$

This equation has four roots or eigenvalues

$$r = \pm \sqrt{\frac{1}{2}(\gamma_0^2 + \gamma_T^2) \pm \sqrt{(\gamma_0^2 + \gamma_T^2)^2 - 4\gamma^2 \gamma_T^2}}. \quad (11)$$

If we define the small parameter ϵ_2 by

$$\epsilon_2 = \gamma_0^2 / \gamma_T^2, \quad (12)$$

then, neglecting terms of order ϵ_2^2 , we can approximate the roots by

$$r_{1,2} \simeq \pm \gamma / \sqrt{1 + \epsilon_2} \quad (13)$$

$$r_{3,4} \simeq \pm \gamma_T \sqrt{1 + \epsilon_2}. \quad (14)$$

The roots r_1 and r_2 contain the usual propagation coefficient, γ , divided by the frequency-dependent correction factor, $\sqrt{1 + \epsilon_2}$. Because ϵ_2 is the ratio of two parameters that have similar frequency behavior, it does not depend strongly on frequency. For typical parameter values from Mobley and Eisenberg (1975) and Mathias et al.

(1977) and using Eq. 5 (with $K \simeq 0.1$) to determine r_T , we see $|\epsilon_2| < 10^{-3}$. The parameter ϵ_2 is therefore negligible.

If there is a current source I_1 located at $x = x_1$, then the solution to Eq. 10 can be written as two terms

$$V(x) = V_1(x - x_1) + v(x), \quad (15)$$

where

$$V_1(x - x_1) = I_1(A e^{-\gamma|x-x_1|} + B e^{-\gamma_T|x-x_1|}), \quad (16)$$

and

$$v(x) = a e^{-\gamma x} + b e^{-\gamma_T x} + c e^{\gamma x} + d e^{\gamma_T x}. \quad (17)$$

The phasor V_1 represents traveling harmonic waves, originating at the current source I_1 and propagating away from x_1 with diminishing amplitude. The phasor v may represent reflections of V_1 from a termination of the cable, or waves propagating away from a different and as yet unspecified current source, or both. Reflections may be treated as if they are waves originating at another, imaginary, current source (Jack et al., 1975). The problem therefore reduces to determining $V_1(x - x_1)$, because other solutions can always be considered a sum of responses to independent current sources.

The function $V_1(x - x_1)$ can have one of two possible forms, depending on whether the source of I_1 is located intracellularly (the region described by $V[x]$ in Fig. 2) or in the lumen of the tubules (the region described by $U[x]$ in Fig. 2). The only form of physiological interest is when the source of current is intracellular. The boundary conditions at x_1 for this form are:

$$\frac{dV_1}{dx} \Big|_{x=x_1} \rightarrow -r_i \frac{I_1}{2}, \quad (18)$$

$$\frac{dU}{dx} \Big|_{x=x_1} = 0. \quad (19)$$

Eq. 6 may be differentiated and solved for dU/dx , then invoking condition 19 gives enough conditions on V_1 to determine the relative sizes of A and B .

$$\frac{B}{A} = \sqrt{\epsilon_2^3} \frac{(1 - \gamma^2/\gamma_0^2)\gamma/\gamma_0}{1 - \epsilon_2}, \quad (20)$$

giving $|B/A| < 10^{-4}$. Thus at $x = x_1$, the second term in Eq. 16 is negligible when compared to the first term. Because $\gamma_T > \gamma$, the second term also goes exponentially to zero more rapidly than the first term, so that the second term can be neglected at all x . The solution to Eq. 10 for a single source of current is therefore well approximated by

$$V(x) = \frac{I_1}{2} \frac{r_i}{\gamma} e^{-\gamma|x-x_1|}, \quad (21)$$

the error being about one part in 10^4 . Eq. 21 also is the solution for a single source of current in an infinite muscle fiber without connections between neighboring T system networks. The effect of these connections therefore is unimportant when measuring intracellular signals and passing current intracellularly.

DISCUSSION

The preceding analysis has considered the linear electrical properties conferred on a fiber by a helicoidal T system. The nonlinear properties are much more difficult to deduce, and the heuristic techniques employed here may not be applicable. Because the linear effects are quite small, one would guess that at least under normal physiological conditions a helicoidal T system does not appreciably alter the pattern of current flow during an action potential.

The physiological importance of the nontransverse superstructure of the T system is not obvious. If there are no appreciable electrical differences between transverse, helicoidal or random arrangements of the tubules, then perhaps the geometry of the T system is governed by factors outside the scope of this discussion. The conclusion from this analysis is that a helicoidal T system, whose pitch is constrained by the sarcomere spacing, will not affect electrical signals recorded intracellularly in intact fibers.

I am grateful to my colleagues B. Eisenberg, R. Eisenberg, R. Levis, and A. Gilai for their critical reading of this manuscript. Discussions with A. Peskoff and R. Eisenberg were most helpful in developing the theory presented here.

This work was partially supported by National Institutes of Health grant HL20230.

Received for publication 3 February 1978.

REFERENCES

- ADRIAN, R. H., W. K. CHANDLER, and A. L. HODGKIN. 1969. The kinetics of mechanical activation in frog muscle. *J. Physiol. (Lond.)* **204**:207-230.
- EISENBERG, B. 1972. Three dimensional branching of the T-system in frog sartorius muscle. *J. Cell Biol.* **55**:68a. (Abstr.).
- FALK, G., and P. FATT. 1964. Linear electrical properties of striated muscle fibers observed with intracellular electrodes. *Proc. R. Soc. Lond. B. Biol. Sci.* **160**:69-123.
- JACK, J. J. B., D. NOBLE, and R. W. TSIEN. 1975. *Electric Current Flow in Excitable Cells*. Clarendon Press, Oxford. 25-82.
- MATHIAS, R. T., R. S. EISENBERG, and R. VALDIOSERA. 1977. Electrical properties of frog skeletal muscle fibers interpreted with a mesh model of the tubular system. *Biophys. J.* **117**:57-93.
- MOBLEY, B. A., and B. EISENBERG. 1975. Sizes of components in frog skeletal muscle measured by methods of stereology. *J. Gen. Physiol.* **66**:31-45.
- PEACHEY, L. D., and B. R. EISENBERG. 1978. Helicoids in the T system and striations of frog skeletal muscle fibers seen by high voltage electron microscopy. *Biophys. J.* **22**:145-154.
- WEINBERG, L. 1962. *Network Analysis and Synthesis*. McGraw-Hill Book Company, New York. 71-75.