

A Theoretical Analysis of the Capacitance of Muscle Fibers Using a Distributed Model of the Tubular System

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ABSTRACT A model is developed to predict the changes in total capacitance (i.e. total charge stored divided by surface membrane potential) of the tubular system of muscle fibers. The tubular system is represented as a punctated disc and the area of membrane across which current flows is represented as a punctated annulus, the capacitance of the muscle fiber being proportional to this area. The area can be determined from a distributed model of the tubular system, in which the only resistance to radial current flow is presumed to be in the lumen of the tubules. Calculations are made of the variation of capacitance expected as the conductivity of the bathing solution is varied. These calculations include the effects of fixed charge in the tubular lumen and the effects of changes in the shape and volume of the tubular system in solutions of low conductivity. The calculated results fail to fit comparable experimental data, although they do qualitatively account for the known variation of the radial spread of contraction with conductivity of the bathing medium. It is pointed out that the existence of a significant "access resistance" at the mouth of the tubules might explain the discrepancy between theory and experiment.

The transverse tubular system of skeletal muscle is a dense network of tiny branching tubules which has been represented electrically as two discs of membrane enclosing a resistive solution (Fatt, 1964; Falk and Fatt, 1964; Falk, 1968; Adrian et al., 1969; Schneider, 1970). The electrical model used by these authors allows radial variation in the potential across the tubular membranes, *all* the variation being caused by potential drops within the resistive material filling the lumen of the tubules, so that the resistance

in series with any piece of membrane depends entirely on the radial location of the membrane. Thus, the tubular membrane is represented as an electrical circuit consisting of a parallel combination of resistance and capacitance distributed along the resistance of the tubular lumen.

Although the distributed model is appealing, especially because it so naturally fits the anatomical data, there is little evidence which supports it, at least in detail. Impedance measurements have been considered to oppose the distributed model (Falk and Fatt, 1964; Freygang et al., 1967) and to support it (Schneider, 1970); measurements of total capacitance seem difficult to reconcile with the model (Eisenberg, 1971) and quantitative measurements of the radial spread of contraction (Adrian, Costantin, and Peachey, 1969) do not agree with the predictions of the model. However, experiments do show that there is some kind of radial spread of contraction (see also Gonzalez-Serratos, 1971, and Costantin, 1970) and this spread is most easily interpreted if one postulates a radial variation of potential within the tubular system.

The purpose of this paper is to show how measurements of the total capacitance of muscle fibers (measured with step functions of current applied at a point: Fatt and Katz, 1951; for more recent references see Gage and Eisenberg, 1969) can be used to test the distributed theory of the tubular system. The analysis shows that the capacitance of the tubular system is simply related to the electrical properties of the distributed model, and therefore that relatively straightforward measurements, practical under a variety of conditions, can be used to test the theory. Finally, we conclude that the theory cannot account for the results of Vaughan et al. (1972).

THEORY

The Disc Model of the Tubular System

We will initially interpret the properties of the tubular system in terms of the simple geometrical model shown in Fig. 1. We approximate the tubular system as a punctated disc of membrane, the area and volume of which correspond to the parameters of the T system. The branching of the tubules is considered sufficiently dense that the equations for a disc can be used (the justification for this approach is discussed in Adrian et al., 1969 and Schneider, 1970). The area of membrane across which current flows is called F (the variable F is dimensionless and is taken as the ratio of this area to the total area of tubular membrane), the radial dimension of the annular region being called L . These variables are related by

$$F = \frac{\rho\pi a^2 - \rho\pi d^2}{\rho\pi a^2} = 2 \frac{L}{a} \left(1 - \frac{1}{2} \frac{L}{a} \right) \quad (1)$$

where a is the radius of the fiber, d is the inner diameter of the annulus, and ρ

is the fraction of the disc occupied by the tubular system. This approximate form of the distributed model assumes in effect that the potential in the tubular lumen is constant over some distance L and then drops to zero. Such an approach is justified below by an analysis based on the model of Adrian et al. (1969) and can be derived from any distributed model using the mean value theorems of the calculus. The approximate form has the advantage of clarity, the physical basis of the model being immediately apparent, and of generality, the results not depending on assumptions concerning the particular geometry of the tubular system.

Most electrical properties, and certainly the capacitance, are related to the area of membrane across which current flows. Thus, we write (this equation

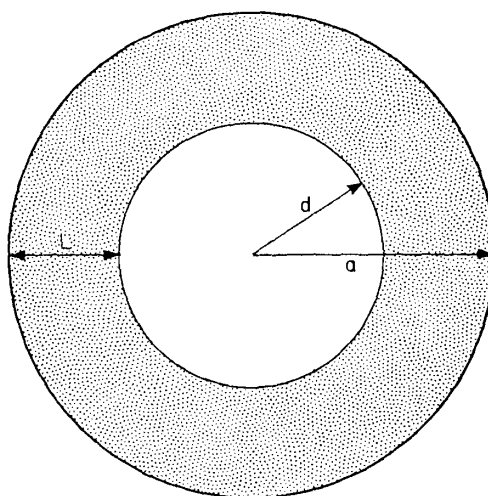


FIGURE 1. A disc model of current flow in the tubular system. The stippled area represents the mean area of tubular membrane across which current flows.

is also derived below from the model of Adrian et al. [1969])

$$C_e = AC_w F \quad (2)$$

where

C_e is the capacitance (in microfarads per square centimeter) of the tubular system associated with 1 cm^2 of surface membrane and is identical to the variable of the same name measured by Falk and Fatt (1964) and Gage and Eisenberg (1969).

A is the area of tubular membrane per square centimeter of surface membrane. This variable, measured by Peachey (1965, Table I), can be expressed in terms of the variables used by Adrian et al. (1969) by the formula $(a/2) (\rho/\zeta)$ where ζ is the volume-to-surface ratio of the tubules, and ρ is the fraction of fiber volume occupied by the tubular system.

C_w is the capacitance (in microfarads per square centimeter) of 1 cm^2 of tubular membrane.

F , qualitatively defined above, is a function which depends on the properties of the tubular membrane and lumen, the radius of the fiber, and the time or frequency at which the measurement of C_e is made.

Equation 2 can be rewritten in terms of the characteristic length L

$$C_e = 2A(L/a)(1 - 0.5L/a) C_w. \quad (3)$$

The usefulness of the equation will depend on finding an expression for L/a in terms of electrical parameters of the distributed model.

It is useful to write equation 3 in a dimensionless form. We denote the properties of the tubular system in the test condition by an asterisk (*) and the properties in the standard condition by variables with no superscript. Then, if the specific capacitance C_w does not vary with the test condition,

$$\frac{C_e^*}{C_e} = \frac{1 - \frac{1}{2} \frac{L^*}{L} \frac{L}{a} \frac{A^* L^*}{AL}}{1 - \frac{1}{2} \frac{L}{a} \frac{AL}{AL}}. \quad (4)$$

This equation is our key result, enabling us to predict changes in tubular capacitance. Note that the change in tubular capacitance will depend on the characteristic length in the standard solution (L/a), the change in characteristic length in the test solution (L^*/L), and the change in the total area of the tubular membranes (A^*/A). In the next section we derive a relation for L and L^* in terms of membrane parameters; later on we develop an equation which describes A^*/A in some conditions. Little is known about L/a , unfortunately, and therefore our calculations are all done for several values of the parameter. Finally, it must be realized that this analysis is not useful if the characteristic length exceeds the radius of the cell; in that case the potential in the tubular system does not vary significantly with radial position and no distributed model is applicable.

The Effective Capacitance and the Charge Stored in the Tubular System

In order to use equation 4 to make predictions about the variation in tubular capacitance C_e , we must be able to relate the various parameters of the equation to physical parameters of the tubular system. The parameter which causes particular difficulty is the characteristic length L , whose relationship to the properties of the tubular membrane and lumen is not clear. We will now develop an equation for the charge stored in the tubular system when sinusoidal currents are applied, and show that it is similar to equation 4 above. We then can relate the characteristic length, L , to the parameters which describe the physical properties of the tubular membrane and lumen.

Our analysis is based on the general expression for the voltage across the tubular membrane $u(r)$ at a distance r from the center of the fiber, derived by

Adrian et al. (1969). Different forms of the same relation have been derived by several authors; we choose this formulation because of the ease of interpreting the physical meaning and physiological significance of the parameters used. Except where otherwise noted, our nomenclature is identical with that of Adrian et al. (1969). We describe the membrane by an admittance \bar{Y}_w defined as a complex number in the usual manner of circuit theory (see van Valkenburg [1964] for the engineering treatment, and Eisenberg and Engel, [1970, Appendix 2] for a derivation in a physiological case): the phase angle of the complex number represents the phase angle between the voltage across and the current crossing the tubular membrane; the amplitude of the complex number represents the relative magnitude of the current and voltage. The expression for the voltage across the tubular membrane is then (see the analogous DC expression: equation 10 of Adrian et al. [1969]):

$$\frac{u(r)}{u(a)} = \frac{I_0(r\Gamma)}{I_0(a\Gamma)} = \frac{I_0[r(\bar{Y}_w/\bar{G}_L)^{1/2}]}{I_0[a(\bar{Y}_w/\bar{G}_L)^{1/2}]} \quad (5)$$

where

$u(a)$ is the potential across the surface membrane of the fiber (in volts),

a is the radius of the fiber (in centimeters),

I_0 is a modified Bessel function of the first kind (Tranter, 1969; Abramowitz and Stegun, 1964),

\bar{G}_L is the *effective* radial conductivity of the lumen of the tubule (in mho per centimeter) (Note that this variable is proportional to, but not identical to, the conductivity G_L of the solution filling the lumen of the tubules.),

Γ the propagation constant¹ is defined as $[\bar{Y}_w/\bar{G}_L]^{1/2}$ (in centimeters⁻¹), and \bar{Y}_w is the admittance of the tubular membrane per unit volume of the fiber (in mho per centimeters) = $\bar{G}_w + j\omega\bar{C}_w$ where \bar{G}_w and \bar{C}_w are conductance and capacitance of the tubular membrane per unit volume and $j = \sqrt{-1}$.

We can now compute the charge stored in the tubular system. We call the charge stored in 1 cm² of tubular membrane Q_w and the charge stored in the tubular membrane arising from 1 cm² of surface membrane Q_e . Then, $Q_e = AQ_w$. Note that Q_e and Q_w are both complex numbers if sinusoidal excitation is used.

In order to determine Q_w and thus Q_e , we need simple expressions for the total charge stored in the capacitance of the tubular system. This is given by

¹ This definition of the propagation constant as a complex number is precisely analogous to the definition used in the engineering formulation of one-dimensional cable theory (see Falk and Fatt, 1964; Eisenberg and Johnson, 1970, p. 61; LePage and Seely, 1952, Section 9-4). It is not simply related, however, to the variable of the same name defined by Adrian et al. (1969).

the sum (actually the surface integral) of the charge stored in each element of area ρdS of the tubular system:

$$\rho\pi a^2 Q_w = \oint u(r) \cdot C_w \cdot \rho dS = \int_0^a u(r) \cdot C_w \cdot \rho \cdot 2\pi r dr. \quad (6)$$

Now we substitute for $u(r)$ from equation 5.

$$\rho\pi a^2 Q_w = \frac{2\pi C_w \rho u(a)}{I_0(\Gamma a)} \int_0^a I_0(r\Gamma) r dr. \quad (7)$$

This integral is known (Dwight, 1961, No. 835.3) and thus we have an expression for Q_e

$$\frac{Q_e}{u(a)} = \frac{\rho a}{2\zeta} \frac{2 I_1(\Gamma a)}{\Gamma a I_0(\Gamma a)} \cdot C_w. \quad (8)$$

In order to complete this phase of our analysis we must now find a way to determine the effective capacitance C_e (which ought to be a real number) from the charge stored in the tubular system (described by Q_e , a complex number). Equation 8, which describes Q_e , gives both the amplitude and phase angle of the charge in the tubular system. It seems likely, however, that the amplitude of the stored charge will be of the greater importance in determining the effective capacitance of the tubular system. (If it is assumed that the real part of Q_e is the important variable, or that C_e ought to be a complex number, an equation similar to equation 10 is still the result.) Defining C_e in this way (vertical lines denote the amplitude of a complex number),

$$C_e \equiv \frac{|Q_e|}{|u(a)|} \frac{\rho a}{2\zeta} \frac{1}{|\Gamma a|} \frac{I_1(\Gamma a)}{I_0(\Gamma a)}. \quad (9)$$

Comparison of this equation with equation 3 can give the general relation between L and the membrane parameters. Since the equations defining and using L in the geometric model are useful only when L/a is less than one, we are justified in approximating the Bessel functions in equation 11 by their asymptotic expansions (Abramowitz and Stegun, 1964, equation 9.7.1). This gives an equation for L :

$$L = \frac{1}{|\Gamma|}. \quad (10)$$

Thus, there is a simple relation between the characteristic length of the geometric model and the membrane and luminal properties of the T system.

Consideration of the actual properties of the tubular membrane allow this expression to be further simplified. It is known that the tubular membrane has a very high resistance, at least under resting conditions (Eisenberg and Gage, 1969). Thus, under many conditions of interest almost all the current which crosses the membrane is capacitive current. This approximation is accurate to the extent that the frequency of the sinusoidal current is much greater than the natural frequency of the tubular membrane $\bar{G}_w/2\pi\bar{C}_w$.

The time constant of the tubular membrane (\bar{C}_w/\bar{G}_w) can be estimated from the data of Gage and Eisenberg (1969) as about 60 msec; thus, the following approximation is useful for frequencies much higher than 2 cycle/sec. The resulting expression for the magnitude of the propagation constant, that is to say the characteristic length L , is

$$L \simeq \left[\frac{\bar{G}_L}{\omega\bar{C}_w} \right]^{1/2}; \omega = 2\pi f \geq 20\pi. \quad (11)$$

Note that in this case the effective capacitance decreases inversely with the square root of frequency, and depends on the luminal resistance and the tubular membrane capacitance. At any frequency, L lies between its steady state value \bar{G}_L/\bar{G}_w (called λ_i by Adrian et al. [1969]) and the value given above by equation 11.

COMPUTATIONS OF TUBULAR CAPACITANCE

The theoretical analysis presented above can be used to predict the change in tubular capacitance C_e expected when the ionic strength of the external solution is lowered. The effects of lowering ionic strength are conceivably multiple: any of the variables in equation 4 might be affected.

We will consider different possibilities one at a time. First, we consider the effect of changes in ionic strength on a hypothetical tubular system, which changes neither size nor shape as the ionic strength of the bathing solution is changed. The change in tubular capacitance then reflects the change in the characteristic length produced by changes in the conductivity of the solution filling the tubular lumen. The calculations are made for different concentrations of fixed charge in the lumen of the tubules and for different values of the characteristic length in normal Ringer solution, since neither of these parameters is well known.

Our second set of calculations will include the variation of shape, area, and volume of the tubular system with changes in ionic strength reported by Rapoport et al. (1969). Again, calculations are made for several concentrations of fixed charge and several values of the normal characteristic length.

The Effect of Ionic Strength on Tubular Capacitance, Assuming no Changes in Tubular Shape, Volume, or Area

A phenomenon important in determining the capacitance C_e under all conditions is illustrated by the special case in which the shape, volume, and area of the tubular system are imagined to be independent of ionic strength. In this case the changes in capacitance reflect changes in the depth L (that is the area F in Fig. 1) to which radial currents can flow into the tubular system. The characteristic length L varies because the conductivity of the solution filling the lumen of the tubules presumably varies with ionic strength. If the tubules contain no fixed charge, then we have from equation 10 above

$$\frac{L^*}{L} = \left[\frac{\zeta^* G_L^*}{\zeta \bar{G}_L} \right]^{1/2} \quad (12)$$

where we have assumed that all measurements of capacitance can be characterized by the same value of \bar{Y}_w and where we have used the equations of Adrian et al. (1969, p. 224) to write the expression in terms of the conductivity G_L (as opposed to the effective conductivity \bar{G}_L). Note that $\zeta^*/\zeta = 1$ if there are no changes in the shape or volume of the tubules.

It is now a simple matter to calculate the expected tubular capacitance from equation 4. If there is no fixed charge in the tubular lumen, the conductivity of the luminal solution G_L^*/G_L is almost proportional to the ionic strength of the bathing solution, and the variation of C_e with ionic strength is as shown in Fig. 2 A for various values of the resting length constant. Comparison of this curve with the data of Vaughan et al. (1972) for the variation of tubular capacitance with ionic strength shows that the theoretical curve declines less slowly with ionic strength than the experimental points. This will be a general finding of this paper; indeed, all the features added onto the model tend to increase the figure predicted for the tubular capacitance in solutions of low ionic strength and thus aggravate the discrepancy with the experimental data. For example, Fig. 2 B was calculated allowing for the effects of fixed charge in the tubular lumen (called ψ ; here $\psi = 0.1$ m) according to equation 13 of Rapoport (1969). Since the presence of fixed charges requires the presence of an equal amount of counterions under all conditions there will be less effect on G_L^*/G_L in this case. If the fixed charge concentration is set to 0.4 m, calculations show that ionic strength has almost no effect. Thus, tubular capacitance decreases less with ionic strength if there is fixed charge in the tubules, and, further, the capacitance does not decrease to zero but to some limiting value.

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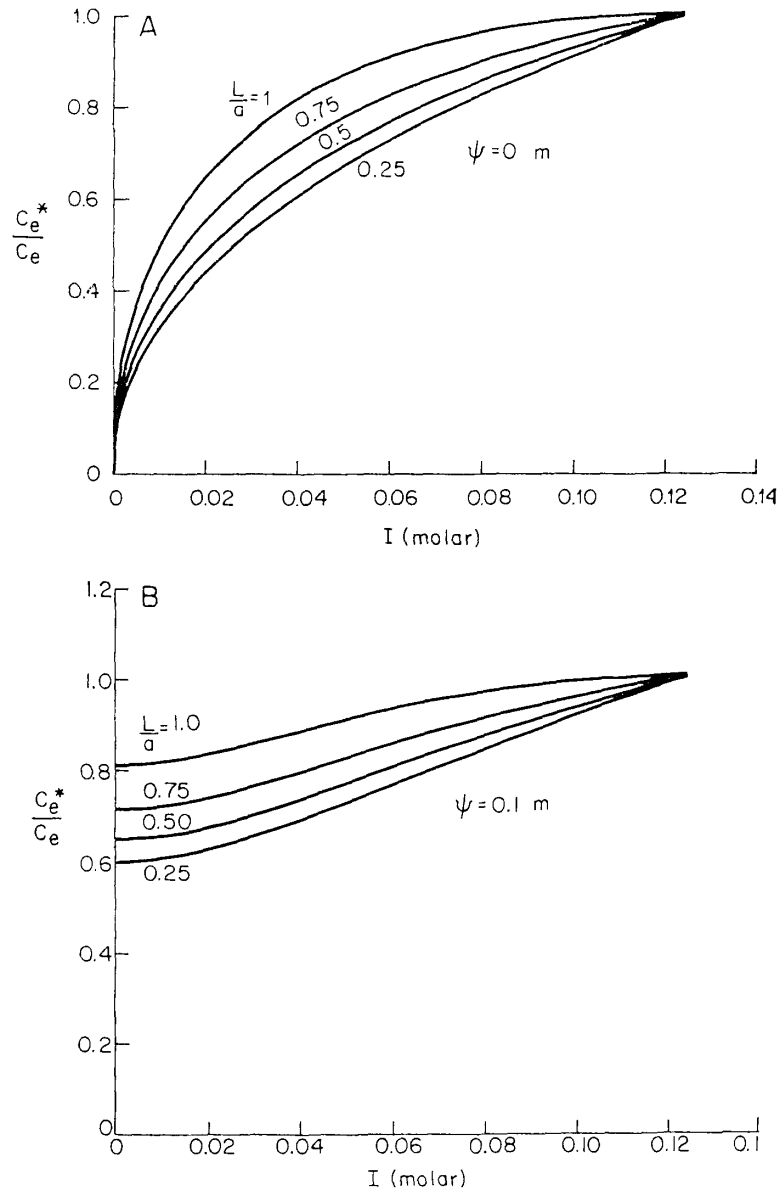


FIGURE 2. The variation of capacitance with ionic strength assuming no changes in tubular shape or area. Each curve is calculated assuming a different value of the characteristic length L in normal Ringer's. The upper curves (A) were calculated assuming no fixed charge in the tubules while the lower curves (B) were calculated assuming a fixed charge density of 0.1 m.

The Effect of Ionic Strength on Tubular Capacitance, Including Changes of Tubular Shape, Volume, and Area

In order to allow for changes of tubular shape in these calculations we must have a quantitative description of the effect of solutions of low ionic strength

on the geometry of the tubules. It is fortunate that such a description is available (Rapoport, et al., 1969; Rapoport, 1969). We have put their results into algebraic form by fitting to their data a geometric model of the tubules in which the tubule is considered to be rectangular in cross-section with sides of length w and b , and volume-to-surface ratio $wb/2(w + b)$. The data of Rapoport et al. (1969) suggest that the major effect of ionic strength is on the longitudinal dimension of the tubular system, b , the transverse dimension w being some 800 Å and relatively independent of ionic strength. The following

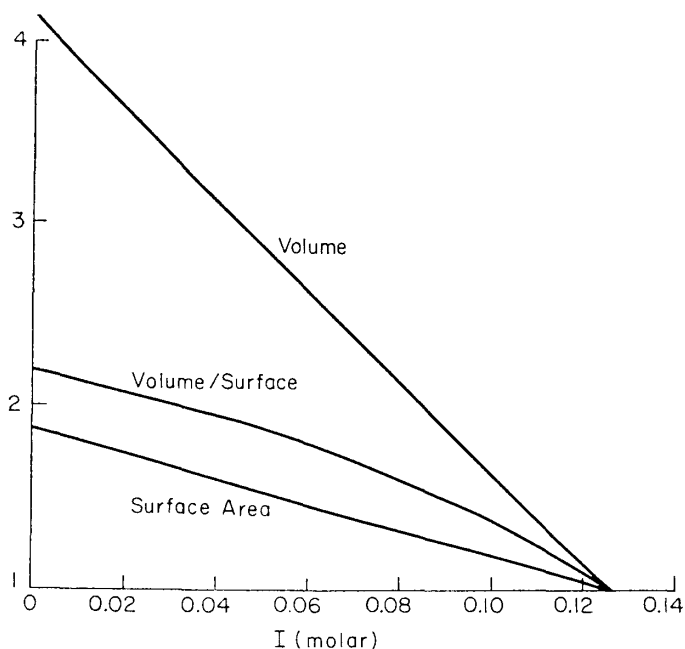


FIGURE 3. The change in size and shape of the tubules with changes in ionic strength. The curves were computed from a simple model fitted to the data summarized by Rapoport et al. (1969).

equation was fitted to the straight line in Fig. 1 of Rapoport (1969) and describes the variation of the longitudinal dimension with ionic strength.

$$b = 1290 - 7830 I \quad (13)$$

where the units of b are Ångstroms and the units of I , the ionic strength, are moles per liter. The area, volume, and volume-to-surface ratios have been calculated from the rectangular model described above (Fig. 3).

Further computations (using equations 4, 12, and 13) were carried out to determine the effects of ionic strength allowing changes in shape (i.e. volume-to-surface ratio) but considering the total area of membrane in the tubular system as a constant; these calculations gave curves qualitatively similar to those shown in Fig. 3. Finally, calculations were made including the effects of

fixed charge, change of shape, and change in the total membrane area of the T system (Fig. 4).

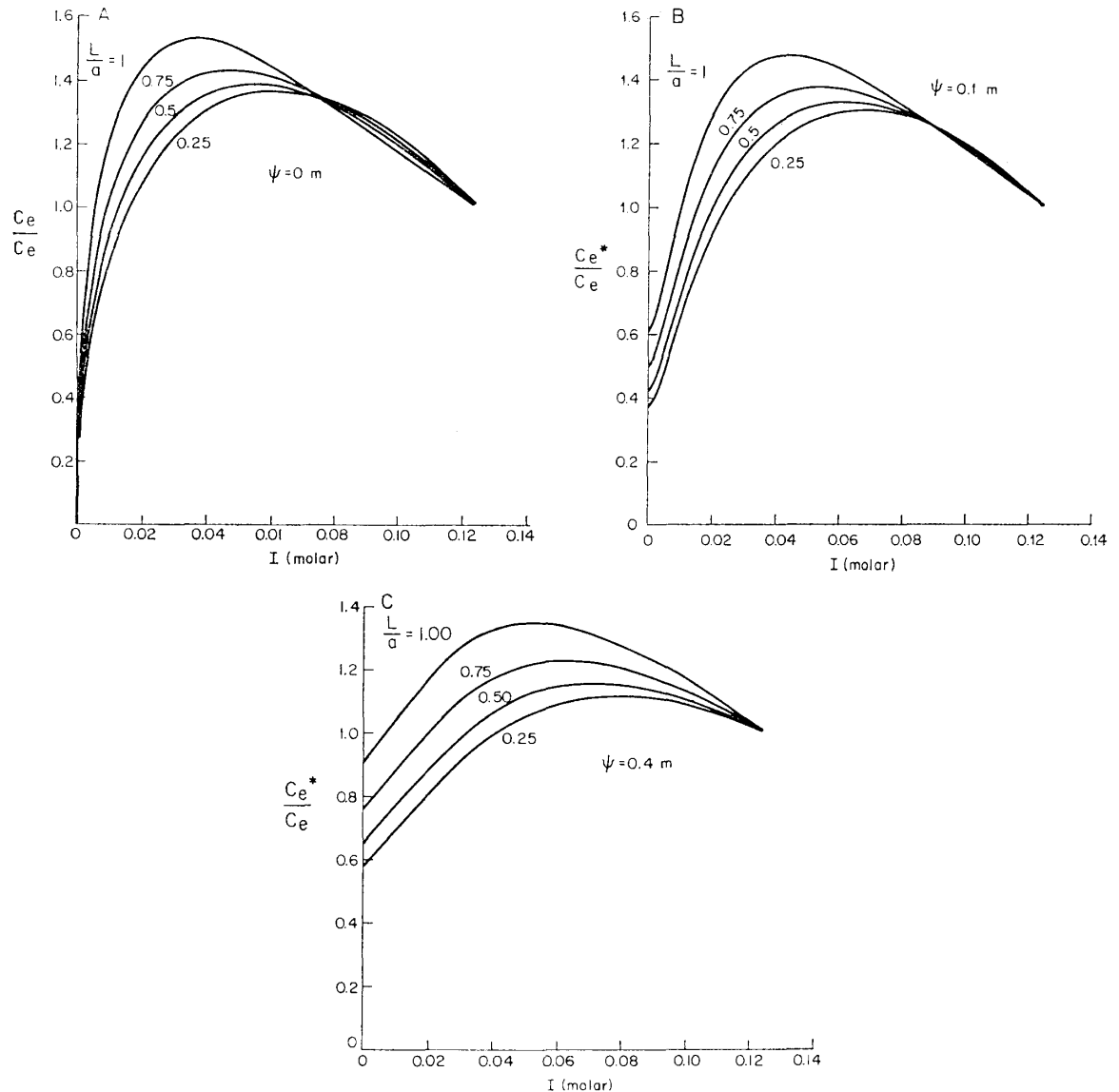


FIGURE 4. The variation of capacitance with ionic strength assuming changes in tubular shape, volume, and area. Each curve is calculated from a value of the characteristic length L in normal Ringer's. The curves in (A) were calculated assuming no fixed charge in the tubular lumen; the curves in (B) and (C) were calculated for the fixed charge concentration indicated.

It is clear that all the calculated curves show a slower decline in capacitance with declining ionic strength than the data of Vaughan et al. (1972). Indeed, the curves computed using the full available experimental information (Fig.

4), and thus allowing an increase in the total area of tubular membranes, show a substantial *increase* in capacitance as ionic strength is reduced.

DISCUSSION

Approximate Nature of Theory

The analysis presented here is based on physical reasoning applied to a geometrical and mathematical model. A full-scale rigorous analysis is not practical because the expressions resulting would most likely be quite unwieldy and not too useful in making predictions. For instance, the precise formula derived by Adrian et al. (1969) for a simpler case is an infinite series involving the roots of Bessel functions. The errors in our theory are hard to evaluate in a quantitative way, but it seems most unlikely that the errors could account for the gross qualitative discrepancy between the theory and experiments described below.

Comparison with Experimental Results

The analysis performed here was done for two purposes. One, to show how relatively simple measurements of capacitance can be used to test the distributed model of the tubular system, and two, to compare the predictions of the theory with measurements made in solutions of low ionic strength. The predictions in the latter case are complicated by the change in area, shape, and volume of the T system known to occur in these solutions. The measurements of these parameters have of necessity been done with the electron microscope after the muscle has been fixed, dehydrated, and imbedded in plastic. The uncertainties involved in this preparation of the tissue are serious and in the absence of an independent method of determining tubular size the results must be treated with caution. We are particularly puzzled by the apparent large increase in total membrane area in solutions of low ionic strength, not knowing whether this area increase represents the formation of new membrane or simply rearrangement of previously existing membrane. For these reasons we have performed our computations using various possible values for the tubular area, volume and shape in solutions of low ionic strength. Further, the possible existence of fixed charge in the tubular lumen, and the uncertain value of the characteristic length in normal Ringer have been included in the calculations.

Even with these uncertainties, however, it is clear that *none* of the theoretical curves is in qualitative agreement with the experimental data of Vaughan et al. (1972), and that the curves including the information available from structural studies are in striking disagreement with the experimental data. It is then necessary to discuss revisions in the theory which might remedy this situation. It is tempting to conclude simply that the distributed model of the

tubular system is incorrect, and that the source of resistance to current flow in the radial direction is located in some structure other than the lumen of the tubules, perhaps in the mouth of the tubules. There is, however, clear evidence (Adrian, Costantin, and Peachey, 1969; Costantin, 1970; Gonzalez-Serratos, 1971) which shows an inward spread of contraction as depolarization of the surface membrane is increased. Such an inward spread is easy to explain if there are radial potential drops in the lumen of the tubules, and cannot be simply explained if all the radial resistance is located in the mouths of the tubules. Thus, we are left with a paradox: the electrical measurements seem to contradict predictions made from the distributed model but experiments on inward spread of contraction seem to require a distributed model.

One set of experiments by Adrian, Costantin, and Peachey (1969) suggest a way out of this quandary. They studied the inward spread of contraction in low ionic strength solutions and concluded that "the large decrease in conductivity of the bathing medium was not effective in altering the inward spread of activation. . ." This result is what would be expected from our analysis of the distributed model, namely that the lowering of the conductivity of the bathing solution should not substantially change the radial spread of potential. Thus, it seems that one phenomenon reflecting the radial spread of potential does depend on ionic strength as predicted by the distributed model.

It is clear, however, from the results of Vaughan et al. (1972) that little current can enter the tubular system in these low ionic strength solutions since little of the capacitance of the tubular system can be charged in these solutions. Perhaps the resistance which limits the flow of current into the tubular system is not the resistance in the lumen of the tubules but is an "access resistance" (Peachey and Adrian, 1972) at the mouth of the tubules. Then, an increase in this resistance in solutions of low ionic strength could account for the results of Vaughan et al. (1972) while the effects studied in this paper could account for the results of Adrian, Costantin, and Peachey (1969). Furthermore, the existence of two resistances in the path for radial current flow would explain many other results concerning the electrical behavior (Peachey and Adrian, 1972) and equivalent circuit (Eisenberg, 1971) of muscle fibers.

It is not clear why the access resistance should be sensitive to ionic strength, but the complicated transverse impedance of muscle (Fatt, 1964), the difficulty of visualizing the mouth of the tubules in the electron microscope, and the lability of the structure to osmotic shock in the glycerol treatment all suggest that the mouth of the tubules has complicated properties.

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BIBLIOGRAPHY

- ABRAMOWITZ, M., and I. A. STEGUN. 1964. Handbook of Mathematical Functions. National Bureau of Standards, Washington, D. C. 6th printing.
- ADRIAN, R. H., W. K. CHANDLER, and A. L. HODGKIN. 1969. The kinetics of mechanical activation in frog muscle. *J. Physiol. (London)*. **204**:207.
- ADRIAN, R. H., L. L. COSTANTIN, and L. D. PEACHEY. 1969. Radial spread of contraction in frog muscle fibers. *J. Physiol. (London)*. **204**:231.
- COSTANTIN, L. L. 1970. The role of sodium current in the radial spread of contraction in frog muscle fibers. *J. Gen. Physiol.* **55**:703.
- DWIGHT, H. B. 1961. Tables of Integrals and Other Mathematical Data. The Macmillan Company, New York. 4th edition.
- EISENBERG, R. S. 1971. The equivalent circuit of frog skeletal muscle *In* Contractility of Muscle Cells. R. Podolsky, editor. Prentice-Hall Inc., Englewood Cliffs, N.J.
- EISENBERG, R. S., and E. ENGEL. 1970. The spatial variation of membrane potential near a small source of current in a spherical cell. *J. Gen. Physiol.* **55**:736.
- EISENBERG, R. S., and P. W. GAGE. 1969. Ionic conductances of the surface and transverse tubular membranes of frog sartorius fibers. *J. Gen. Physiol.* **53**:279.
- EISENBERG, R. S., and E. A. JOHNSON. 1970. Three-dimensional electrical field problems in physiology. *Progr. Biophys. Mol. Biol.* **20**:1.
- FALK, G. 1968. Predicted delays in the activation of the contractile system. *Biophys. J.* **8**:608.
- FALK, G., and P. FATT. 1964. Linear electrical properties of striated muscle fibers observed with intracellular electrodes. *Proc. Roy. Soc. Ser. B Biol. Sci.* **160**:69.
- FATT, P. 1964. An analysis of the transverse electrical impedance of striated muscle. *Proc. Roy. Soc. Ser. B Biol. Sci.* **159**:606.
- FATT, P., and B. KATZ. 1951. An analysis of the end plate potential recorded with an intracellular electrode. *J. Physiol. (London)*. **115**:320.
- FREYGANG, W. H., S. I. RAPOPORT, and L. D. PEACHEY. 1967. Some relations between changes in the linear electrical properties of striated muscle fibers and changes in ultrastructure. *J. Gen. Physiol.* **50**:2437.
- GAGE, P. W., and R. S. EISENBERG. 1969. Action potentials, afterpotentials, and excitation-contraction coupling in frog sartorius fibers without transverse tubules. *J. Gen. Physiol.* **53**:298.
- GONZALEZ-SERRATOS, H. 1971. Inward spread of activation in vertebrate muscle fibers. *J. Physiol. (London)*. **212**:777.
- LEPAGE, W. R., and SEELY, S. 1952. General Network Analysis. McGraw Hill Book Company, New York.
- PEACHEY, L. D. 1965. The sarcoplasmic reticulum and transverse tubules of the frog's sartorius. *J. Cell Biol.* **25**(3, Pt. 2): 209.
- PEACHEY, R. D., and R. H. ADRIAN. 1972. Electrical properties of the transverse tubular system. *In* Structure and Function of Muscle. G. H. Bourne, editor. Academic Press, Inc., New York. 2nd edition. In press.
- RAPOPORT, S. I. 1969. A fixed charge model of the transverse tubular system of frog sartorius. *J. Gen. Physiol.* **54**:178.
- RAPOPORT, S. I., L. D. PEACHEY, and D. A. GOLDSTEIN. 1969. Swelling of the transverse tubular system in frog sartorius. *J. Gen. Physiol.* **54**:166.
- SCHNEIDER, M. F. 1970. Linear electrical properties of the transverse tubules and surface membrane of skeletal muscle fibers. *J. Gen. Physiol.* **56**:640.
- TRANter, C. J. 1969. Bessel Functions. Hart Publishing Co. Inc., New York.
- VAN VALKENBURG, M. E. 1964. Network Analysis. Prentice-Hall Inc., Englewood Cliffs, N. J. 2nd edition.
- VAUGHAN, P. C., J. N. HOWELL, and R. S. EISENBERG. 1972. The capacitance of skeletal muscle fibers in solutions of low ionic strength. *J. Gen. Physiol.* **59**:347.