Membrane Potential and Input Resistance Are Ambiguous Measures of Sealing of Transected Cable-Like Structures

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ABSTRACT For many years, membrane potential (V_m) and input resistance have been used to characterize the electrophysiological nature of a seal (barrier) that forms at the cut end of a transected axon or other extended cytoplasmic structure. Data from a mathematical and an analog model of a transected axon and other theoretical considerations show that steady-state values of V_m and input resistance measured from any cable-like structure provide a very equivocal assessment of the electrical barrier (seal) at the cut end. Extracellular assessments of injury currents almost certainly provide a better electrophysiological measure of the status of plasma membrane sealing because measurements of these currents do not depend on the cable properties of extended cytoplasmic processes after transection.

INTRODUCTION

Neurons and other cell types are able to survive transection of cable-like structures because a high resistance barrier (seal) forms at the injury site. No previous study has provided an analysis of whether cable properties such as membrane potential (V_m) and input resistance can be used to assess the extent of the sealing of cable-like structures. Nevertheless, most previous studies have used V_m and/or input resistance to assess the extent of seal formation after transecting cable-like structures such as nerve axons (Meiri et al., 1981; Yawo and Kuno, 1983, 1985; Spira et al., 1993), nerve dendrites (Lucas et al., 1985), or muscle fibers (Deleze, 1970; De Mello, 1973). In this study, we have determined the steady-state electrical properties of a transected axon by mathematical computation and by direct experimental measurement from an equivalent circuit of a transected cable consisting of a ladder network of discrete elements (resistors). V_m and input resistance were calculated or measured at various distances from the cut end as the resistance of the cut end (R_s) was varied. Our mathematical computations and steady-state data from our analog model show that V_m and input resistance are *very* ambiguous measures of the extent of sealing even when V_m and input resistance are measured one-hundredth of a space constant (0.01λ) or closer to the cut end. That is, in the absence of an assessment of their suitability to measure seal formation, V_m and input resistance have been improperly applied as electrophysiological measures of an electrical barrier (seal) that is assumed to form at the cut end of a transected axon or other extended cytoplasmic structures with cable-like properties.

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MATERIALS AND METHODS

To formulate our steady-state model of a transected cable-like structure (e.g., a nerve axon), we made the following assumptions. 1) Only passive membrane electrical properties remain if all voltage-dependent ion channels are blocked. 2) λ does not change after axonal transection if all voltage-dependent ion channels are blocked. 3) A seal is complete if the specific resistance (area-independent resistance) of the seal equals or exceeds the specific resistance of the axolemma. 4) V_m is the same at all points along a completely sealed axon.

Mathematical formulation of our model of a transected cable-like structure

We mathematically analyzed a semi-infinite cable extending in one direction from an origin (R_s) to infinity (Fig. 1) in which the number (n) of repeating 0.1λ sections (or 0.01λ sections) could be any finite number. To allow measurements of input resistance to be simulated across any arbitrary R_m element in the model, we let the number of sections to the left of this arbitrary R_m element be l and to the right of it be r, such that $n = l + r$. Input resistance measured at the cut end of a single-sided cable extending to the left of R_s was defined to equal R_l, where $r = 0$. For all other values of r measured away from the cut end, input resistance for a double-sided cable was defined to be equal to $R_{l,r}$.

For a single-sided cable, the dependence of R_l on R_m, R_i (intracellular resistance), R_o (extracellular resistance), and R_s was calculated as a continued fraction (Khinchin, 1964)

$$R_l = \cfrac{1}{1/R_m + \cfrac{1}{R_o + R_i + \cfrac{1}{1/R_m + \cfrac{1}{R_o + R_i + \cfrac{1}{\ddots + \cfrac{1}{R_m} + \cfrac{1}{R_i + R_o + R_s}}}}}} \quad (1)$$

Generally, R_l is a function of l, except when

$$\frac{R_s}{R_o + R_i} = \left[-1 + \sqrt{1 + 4\frac{R_m^2}{(R_o + R_i)^2}}\right] \Big/ 2, \quad (2)$$

for which R_l is constant at all values of l. Furthermore, as $l \to \infty$ (a semi-

infinite cable), R_l converges to a limiting value (R_c) as follows

$$R_c = \lim_{l\to\infty} R_l = \frac{-(R_o + R_i + \sqrt{(R_o + R_i)^2 + 4R_m(R_o + R_i)})}{2}. \quad (3)$$

For a double-sided cable, if input resistance is measured across an arbitrary R_m element l sections to the left and r sections to the right in the model (Fig. 1), then $R_{l,r}$ can be expressed as

$$R_{l,r} = 1 \Big/ \left(\frac{1}{R_m} + \frac{1}{R_o + R_i + R_l} + \frac{1}{R_o + R_i + R_r}\right), \quad (4)$$

where R_r is defined as input resistance measured at the end of the semi-infinite cable when $l = 0$ and R_l is the input resistance measured at the end of a semi-infinite cable when $r = 0$ as defined in Eq. 1.

Construction of our analog model of a transected cable-like structure

To provide experimental data on how accurately steady-state measures of V_m and input resistance reflect the extent of an electrical barrier (seal) at the cut end of an extended cable, we assembled a finite number (n) of repeating sections made from discrete resistor elements (Fig. 1), which allowed us to simulate measurements made with driving and recording electrodes placed close together. The values chosen for the resistors used to construct this analog model were based on values previously published for the squid giant axon (GA). For a 500-μm-diameter GA with a λ of 6.5 mm, unit length resistances of the internal fluid (r_i) and surface membrane (r_m) are 15.3 kΩ and 6.4 k$\Omega \cdot$ cm, respectively (Cole, 1972). The unit length resistance of the external fluid (r_o) is negligible with respect to r_i because the large extracellular fluid volume has a very low resistance per unit length. From these standard cable parameters (r_i, r_m, and r_o), we calculated the resistances necessary to construct a 2-λ length of cable having 20 0.1λ identical (n = 20) repeating sections (*dotted lines* in Fig. 1) consisting of intracellular resistances (R_i), extracellular resistances (R_o), and axolemmal resistances (R_m) arranged in series and parallel. This analog model of a GA was terminated at one end by the characteristic resistance of a semi-infinite cable (R_c) and terminated at the other end by the resistance of the transected axonal end (R_s). R_s was varied from 0 to $\geq R_m$ to simulate changes in the resistance of an electrical barrier (seal) at the cut end. Using conventional cable equations ($R_i = r_i(\lambda/n)$, $R_o = r_o(\lambda/n)$, $R_m = r_m/(\lambda/n)$) and R_c as given by Eq. 3, and the published values for λ, r_i, and r_m, we calculated specific values for the resistances used to represent these cable electrical properties of a transected GA (R_i = 1 kΩ, R_o = 0 Ω, R_m = 100 kΩ and R_c = 9.51 kΩ). Although we chose to model the squid GA because its cable parameters have been extensively characterized, a similar model using appropriate values for R_i, R_o, R_m, R_c, and R_s could have been constructed to represent any other transected axon or long cellular process (dendrite, muscle fiber, etc.) with cable-like properties.

Steady-state changes in the passive electrical properties of our analog model of a transected axon were assessed as sealing progressed from a completely open end (R_s/R_m = 0) to a completely sealed end ($R_s/R_m \geq 1$). V_m and input resistance were measured across R_m while R_s was increased as a constant fraction (0, 0.25, 0.5, 0.75, 1, 2, etc.) of R_m. To simulate the effect of electrode placement upon values measured for V_m and input resistance, we measured steady-state input resistance with an ohmmeter placed across an R_m at a point corresponding to a specific electrotonic distance (0.1λ, 0.2λ, 0.3λ, and 0.4λ) from R_s. To determine V_m at several values of R_s, we applied a potential representing the resting membrane voltage (−60 mV in an intact axon) at an electrotonic distance of 2λ (Fig. 1; section #1) from R_s; DC potentials were measured with a voltmeter placed 0.1λ (Fig. 1; section #20), 0.2λ, 0.3λ, and 0.4λ from R_s. V_m was then calculated at each fraction of a λ from R_s as

$$V_m = -60\text{ mV} \cdot \frac{\text{potential measured}}{\text{potential measured when } R_s/R_m = 1}. \quad (5)$$

RESULTS

Mathematical assessments of our model of a transected cable-like structure

To determine how values for the various resistances affect input resistance in our mathematical model of a transected cable (see Materials and Methods and Fig. 1), we computed the dependence of $R_{l,r}$ on (R_o + R_i) and on R_m in a three-dimensional plot (Fig. 2 *A*) for the range of the variables over which the function has the greatest curvature. Fig. 2 *A* shows the region of $R_{l,r}$ that converges most slowly to its limiting value ($(R_o + R_i)/R_m \ll 1$, where $(R_o + R_i)/R_m$ is a dimensionless parameter proportional to λ). For most nerve, muscle, and other biological preparations, λ ranges from 1 to 3 mm (Berne and Levy, 1988) and $(R_o + R_i)/R_m$ ranges from 0.005 to 0.02. Because $(R_o + R_i)/R_m$ equals 0.01 for the squid GA, data using values for R_m, R_i, and R_o from the squid GA, therefore, apply to most nerve and muscle preparations.

To assess the convergence of the input resistance of our semi-infinite model to the characteristic resistance of an infinite cable (R_∞), we assumed a semi-infinite cable to the left of our measurement point and added up to 50 0.1λ sections to the right of the measurement point. Fig. 2 *B* illustrates how $R_{l,r}$ varies with r, assuming R_o = 0Ω, R_i = 1 kΩ, and R_m = 100 kΩ) so that $(R_o + R_i)/R_m$ = 0.01. The upper curve is calculated for R_s = 10 MΩ (a sealed end) and the lower curve for R_s = 0Ω (an open end). The middle curve is calculated for R_s = 9.51 kΩ, which is the precise value for R_c to which the 50 0.1λ sections converge. (In many textbooks, the value given for R_c in a discrete cable model of a squid GA is 10 kΩ, which is calculated by $R_c = ((R_o + R_i)R_m)^{1/2}$. We note that $R_\infty \approx R_c/2$ and that the relationships for R_c and R_∞ given in textbooks are approximations that hold for a continuous cable model only when $R_i \ll R_m$ in Eq. 3.) When $(R_o + R_i)/R_m$ is $\leq$ 0.01, input resistance rapidly converges to R_c within 20 0.1λ sections (Fig. 2 *B*) as previously reported (Deleze, 1970). Because input resistance closely (<3%) approximates R_c in 20 repeating 0.1 λ sections, our analog model accurately assesses the ability of V_m and input resistance to measure the extent of seal formation (R_s) in transected cable-like structures.

We also determined that a model of a transected cable of 200 0.01λ sections (Fig. 3 *B*) behaved very much like our model comprised of 20 0.1λ sections (Figs. 2, 3 A, and 4).

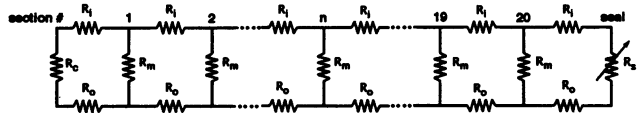

FIGURE 1 Schematic diagram of our electrical model of a transected axon. Lumped circuit model of the passive DC cable-like electrical properties of an axon with n identical repeating sections terminated by a section representing the transection site (seal). Each repeating section is comprised of three resistors: an intracellular resistance (R_i), an extracellular resistance (R_o), and an axolemmal resistance (R_m). The resistance of the uncut end is represented by the equivalent resistance of a semi-infinite cable (R_c); the resistance of a seal at the cut end is represented by a variable resistor (R_s).

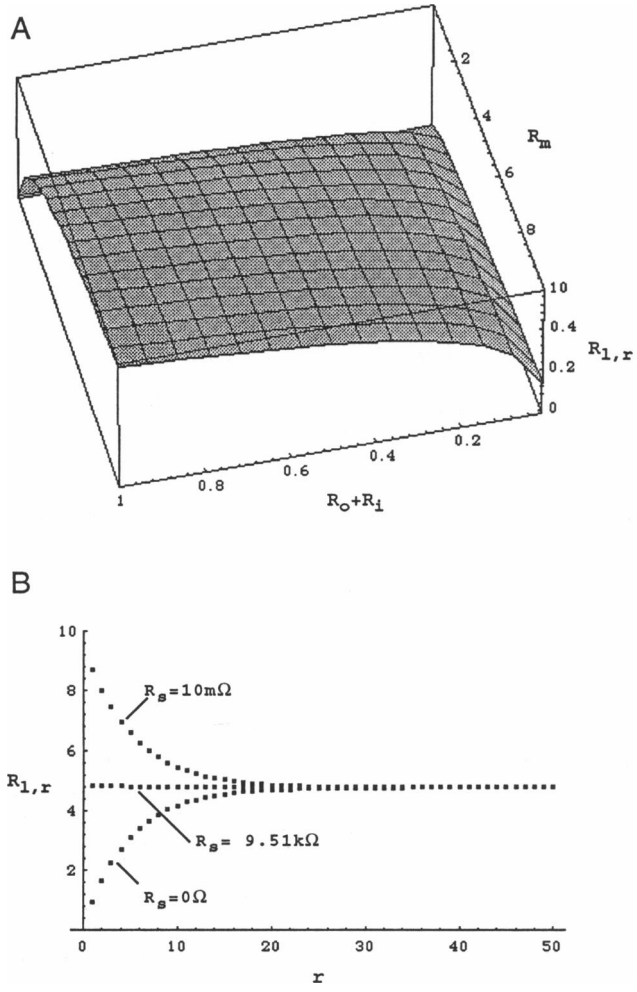

FIGURE 2 $R_{l,r}$ of a double-sided cable as a function of (R_o + R_i) and R_m (*A*) or on *r* and R_s (*B*). (*A*) $R_{l,r}$ as a function of R_m and (R_o + R_i) when the number of 0.1λ sections to the left and right of a point of measurement are sufficiently large (20) to allow $R_{l,r}$ to converge on its limiting value. (*B*) $R_{l,r}$ for a double-sided cable for which one side (left) of the point of measurement has an infinite number of 0.1λ sections and the other side (right) has a variable number (*r*) of 0.1λ sections that terminate in one of three values for R_s (R_s = 10 MΩ, 9.51 kΩ, or 0Ω). When R_s = 9.51 kΩ (the precise value given by Eq. 3 for R_c in our model of a transected squid axon), then $R_{l,r}$ converges to within 20 0.1λ sections of R_∞ (the characteristic resistance of an infinite cable whose membrane properties are that of a squid GA). That is, 20 0.1λ sections are sufficient for a semi-infinite cable model of a squid GA.

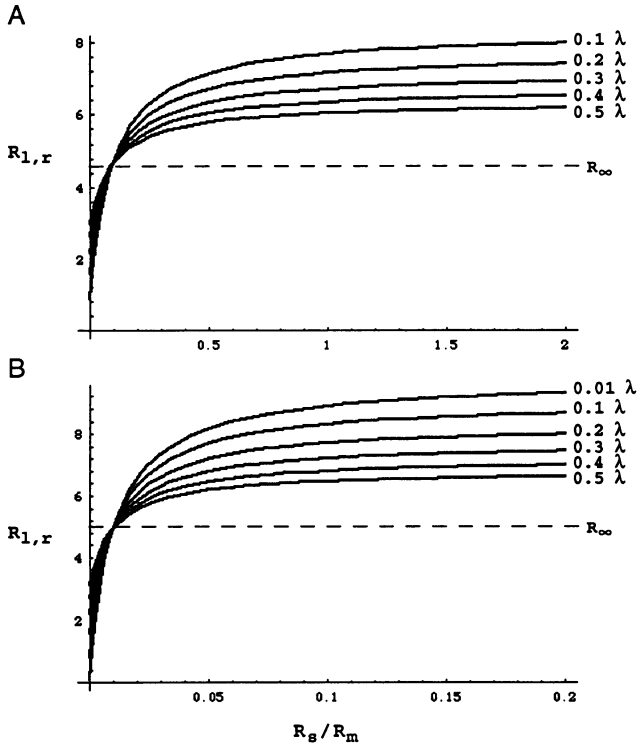

FIGURE 3 $R_{l,r}$ of a double-sided cable as a function of the ratio R_s/R_m for a 20 0.1λ section cable (*A*) or a 200 0.01λ cable (*B*). (*A*) $R_{l,r}$ measured at various electrotonic distances (0.1λ-0.5λ) from the cut end (R_s) when the total number of 0.1λ sections is 20, R_m = 100 kΩ, R_i = 1 kΩ and R_o = 0 Ω. (*B*) $R_{l,r}$ measured at various electrotonic distances (0.01λ-0.5λ) from the cut end (R_s) when the total number of 0.01λ sections is 200, R_m = 1 MΩ, R_i = 0.1 kΩ, and R_o = 0 Ω. Note several features of these plots in *A* and *B*. First, each curve approaches an asymptotic value as R_s/R_m increases. Second, measures of $R_{l,r}$ are *very* insensitive to increases in R_s/R_m as R_s approaches or exceeds R_m, i.e., as a seal is formed. Third, the intersection of all of the curves is precisely equal to R_∞ of each model of a double-sided cable shown in *A* or *B*. Finally, the value of R_∞ (~5 kΩ) for the 20 0.1λ section model in *A*) is very close to the value of R_∞ for the 200 0.01λ section model in *B*.

Furthermore, measurements of $R_{l,r}$ as close as 0.01λ from the cut end are very similar to measurements made 0.1λ from the cut end using this 200 0.01λ section model or the 20 0.1λ section model (Compare Figs. 3, *A* and *B*, and 4). That is, data obtained 0.1λ from the cut end of our 20 0.1λ section analog model are very similar (within 1%) to data that would have been obtained 0.01λ from the cut end had we constructed a 200 0.01λ section analog model.

Measurements from our analog model of a transected cable-like structure

A lumped-circuit cable model of a severed squid GA consisting of 20 0.1λ sections (Fig. 1) was used to assess the dependence of V_m and input resistance on changes in R_s at the cut end of an extended cable. This model was also used to assess the dependence of V_m and input resistance on changes in the electrotonic distance between the measurement site and the cut end (see Materials and Methods).

Data from our analog circuit model show that the sensitivity of V_m to changes in R_s (Fig. 4 *A*) is *very* poor, especially as R_s approaches R_m. Furthermore, the sensitivity of V_m to changes in R_s depends upon the electrotonic distance (λ) between the cut end and the site of measurement. For example, when V_m is measured 0.4λ from the seal site, then V_m increases only ~0.1% as R_s/R_m increases 33% from 0.75 to 1.0 (*open triangles* in Fig. 4 *A*). When V_m is measured 0.1λ from the cut end and the ratio of R_s to R_m (R_s/R_m) is increased ~33% from 0.75 to 1.0 (75% sealed to completely sealed), then V_m increases only 2% from −58.2 to −60 mV (*filled circles* in Fig. 4 *A*). That is, the sensitivity of V_m to changes in R_s is *very* poor when measured 0.1λ from the cut end, and is even less sensitive when measured at greater distances

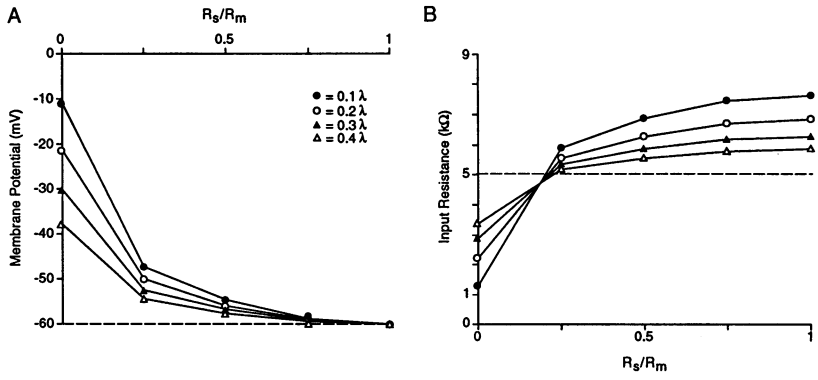

FIGURE 4 Dependence of V_m and input resistance on changes in R_s. V_m and input resistance were measured from an analog electrical model (Fig. 1) that simulated the cable-like electrical properties of a transected squid GA. V_m and input resistance were measured at various distances (0.1λ (●); 0.2λ (○); 0.3λ (▲); 0.4λ (△)) from a transected end whose seal resistance (R_s) was expressed as a fraction of axolemmal resistance (R_m); $R_s/R_m \geq 1$ for a completely sealed axon. Dashed lines show the value of V_m and input resistance in an infinitely long (intact) GA (Fig. 2 *A*). (*A*) V_m measured at various distances from the cut end of a severed GA as R_s is varied from zero to R_m. (*B*) Input resistance measured at various distances from the cut end of a severed GA as R_s is varied from zero to R_m. All curves have an asymptotic character as R_s/R_m goes from 0 to 1. The sensitivity of input resistance to changes in R_s greatly diminishes as R_s/R_m approaches 1. Input resistance increases very little as $R_s \gg R_m$ (data not shown).

from the cut end. At 0.1–0.4λ from the cut end, *very small* (≤2%) changes in V_m due to *rather large* (≥30%)changes in R_s would almost certainly be masked by other factors that influence V_m, such as drift in the potential of the measuring electrode, ion diffusion, etc. (see Discussion).

The sensitivity of input resistance to changes in R_s (Fig. 4 *B*) is also very poor, especially as R_s approaches R_m and/or as the electrotonic distance increases between the cut end and the site of measurement. For example, when R_s/R_m is increased ~33% from 0.75 to 1.0, then input resistance increases about 0.1% when measured at 0.4λ from the cut end (*open triangles* in Fig. 4 *B*). When input resistance is measured only 0.1λ from the cut end, then input resistance increases about 1% from 8.5 to 8.7 kΩ as R_s/R_m increases ~33% from 0.75 to 1.0 (*filled circles* in Fig. 4 *B*). Furthermore, the actual measured value of input resistance depends upon the electrotonic distance between the measuring site and the seal at the cut end. For example, when R_s/R_m is held constant at 1.0 (i.e., a complete seal), input resistance measured at 0.1λ from the cut end (8.7 kΩ) is ~22% greater than input resistance measured 0.4λ from the cut end (7.1 kΩ) *of the same axon* (compare *filled circles* and *open triangles* in Fig. 4 *B*). (Note that input resistance does *not* depend upon the site of measurement in an infinitely long intact axon as indicated by the dotted line in Fig. 4 *B*.) As R_s becomes much larger than R_m ($R_s/R_m \geq 1$), then input resistance changes very little. (This result follows from the asymptotic nature of all curves in Fig. 4 *B*.) Finally, if R_i and R_m do not change, then input resistance of a sealed axon *after* transection (asymptotic values of *solid lines* in Fig. 3 *B*) is greater than the input resistance of that same axon *before* transection (*dotted line* in Fig. 4 *B*), as would be predicted from previous analyses of values for input resistance measured at the end of a semi-infinite cable versus values for input resistance measured anywhere from an infinitely long cable (Weidman, 1952).

DISCUSSION

For many years, V_m and/or input resistance have frequently been used as the *only* electrophysiological measures to assess the extent of plasmalemmal repair of transected cytoplasmic structures with cable-like properties (Deleze, 1970; De Mello, 1973; Meiri et al., 1981; Yawo and Kuno, 1983, 1985; Lucas et al., 1985; Spira et al., 1993). However, the appropriateness of V_m and input resistance as measures to assess the extent of sealing has not been critically examined although published values for these measures during sealing have varied widely, even when data are taken from the *same* transected preparation (Meiri et al., 1981; Yawo and Kuno, 1983). As discussed below, our data from mathematical computations and from an analog circuit model of a transected squid GA show that measures of V_m and input resistance are *very* insensitive to changes that occur during formation of an axonal seal. Furthermore, V_m and/or input resistance also change in response to changes in various properties (e.g., R_m, axonal diameter, ionic composition, etc.) *other* than R_s.

V_m and input resistance are ambiguous or inadequate electrophysiological measures of the extent of sealing of axons and other cable-like structures for several reasons. Most importantly, our mathematical calculations and analog data show that V_m and input resistance measured as close as 0.1–0.01λ from the cut end are very insensitive to the extent of sealing. Even if it were possible to place electrodes within 0.01λ of the transection site in any axon, the λ *after* transection and the distance of the measurement site from the cut end *after* transection would all have to be determined to better then 0.01λ. However, in practice λ and the exact locations of the two electrodes have not been—and almost certainly could not be—determined with such accuracy after transection. As a further complication, λ would change in a spatially

complex manner after transection because voltage-sensitive ion channels would be activated to different (and unknown) extents by the spatial variation in V_m produced by injury currents at the cut end. (All voltage-sensitive ion channels have not been blocked in any previous study, and λ has been reported to decrease by as much as 50% after axonal transection (Yawo and Kuno, 1985).)

In addition to their dependence upon the λ between the site of measurement and the cut end, V_m and input resistance also depend upon other factors that are not directly related to the extent of axonal sealing (R_s/R_m). As one example, V_m can change because of changes in the internal ionic concentrations of K^+, Cl^-, etc., that enter at the cut end before it seals or that enter via voltage-sensitive channels far from the cut end before or after the cut end seals. As a second example, a reduction in axon radius caused by constriction of the cut axonal end (Gallant, 1988; Fishman et al., 1990; Krause et al., 1994) could dramatically increase axonal measures of input resistance independent of any high resistance seal that might form at the cut end (input resistance $= R_m R_i / 2\pi^2 r^3 l^{1/2}$, where r is the radius of the axon, l is the unit length, and R_m and R_i are the specific resistances in $\Omega \cdot cm^2$ of the membrane and axoplasm, respectively). As a third example, it has not been clear in some previous studies (Meiri et al., 1981; Spira et al., 1993) whether the authors realized that the value of input resistance measured at a point in the middle of a long intact axon should be half the value of input resistance measured an infinitesimally short electrotonic distance from the sealed end of that same axon (Weidmann, 1952; Jack et al., 1983). As a fourth example, some studies (Lucas et al., 1985; Spira et al., 1993) have measured V_m and/or input resistance from the cell body to assess the extent of sealing of a cut axonal or dendritic process. When the length of an axon or dendrite is reduced by transection, the ratio between the resistance of the cell body and the resistance of the axon decreases (Rall, 1969) and the input resistance measured in the cell body is dominated by the resistance of the cell body.

In conclusion, our calculations from our mathematical model and our data from our analog model of a transected cable show that recordings of V_m and input resistance made from an axon (Meiri et al., 1981; Yawo and Kuno, 1983; 1985)—much less from a cell body (Lucas et al., 1985; Spira et al., 1993)—cannot be used to assess the time course and extent of axonal or dendritic sealing after transection. Rather, an extracellular vibrating probe (Jaffe and Nuccitelli, 1974) that measures injury current at the cut end provides the best currently available electrophysiological assessment of axonal sealing (Krause et al., 1994). Data from injury current measures combined with morphological and ultrastructural observations suggest that transected earthworm medial giant axons seal by forming a tightly packed plug of vesicles at the cut end (Krause et al., 1994).

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REFERENCES

Berne, R. M., and M. N. Levy. 1988. Physiology. C. V. Mosby Co., St. Louis, MO.

Deleze, J. 1970. The recovery of resting potential and input resistance in sheep heart injured by knife or laser. *J. Physiol.* 208:547–562.

De Mello, W. 1973. Membrane sealing in frog skeletal muscle fibers. *Proc. Natl. Acad. Sci. USA.* 70:982–984.

Fishman, H. M., K. P. Tewari, and P. G. Stein. 1990. Injury-induced vesiculation and membrane redistribution in squid giant axon. *Biochim. Biophys. Acta.* 1023:421–435.

Gallant, P. E. 1988. Effects of the external ions and metabolic poisoning on the constriction of the squid giant axon after axotomy. *J. Neurosci.* 8:1479–1484.

Jack, J. J. B., D. Noble, and R. W. Tsien. 1983. Electrical Current Flow in Excitable Cells. Clarendon Press, Oxford.

Jaffe, L. F., and R. Nuccitelli. 1974. An ultrasensitive vibrating probe for measuring steady extracellular currents. *J. Cell Biol.* 63:614–628.

Khinchin, A. V. 1964. Continued Fractions. University of Chicago Press, Chicago.

Krause, T. L., H. M. Fishman, M. L. Ballinger, and G. D. Bittner. 1994. Extent and mechanism of sealing in transected giant axons of squid and earthworms. *J. Neurosci.* 14:6638–6651.

Lucas, J. H., G. W. Gross, D. G. Emery, and C. R. Gardner. 1985. Neuronal survival or death after dendrite transection close to the perikaryon: correlation with electrophysiologic, morphologic and ultrastructural changes. *Central Nervous System Trauma* 2:231–255.

Meiri, H., M. Spira, and I. Parnas. 1981. Membrane conductance and action potential of a regenerating axon tip. *Science.* 211:709–712.

Rall, W. 1969. Time constants and electrotonic length of membrane cylinders and neurons. *Biophys. J.* 9:1483–1508.

Spira, M. E., D. Banbassat, and A. Dormann. 1993. Resealing of the proximal and distal cut ends of transected axons: electrophysiological and structural analysis. *J. Neurobiol.* 24:300–316.

Weidmann, S. 1952. The electrical constants of Purkinje fibres. *J. Physiol.* 118:348–360.

Yawo, H., and M. Kuno. 1983. How a nerve fiber repairs its cut end: involvement of phospholipase A_2. *Science.* 222:1351–1353.

Yawo, H., and M. Kuno. 1985. Calcium dependence of membrane sealing at the cut end of the cockroach giant axon. *J. Neurosci.* 5:1626–1632.