MEMBRANE AND PROTOPLASM RESISTANCE IN THE SQUID GIANT AXON

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INTRODUCTION

The electrical structure of the squid giant axon has been investigated by measuring the alternating current impedance between electrodes placed on opposite sides of the axon. In these transverse measurements, the lines of current flow are primarily perpendicular to the axis of the fiber and the analysis of the results is relatively simple. It was found that the axoplasm is a good conductor and that it is bounded by a membrane with a relatively high resistance and a capacity of about 1μf./cm.^{2} (Curtis and Cole, 1938). Further experiments on active axons showed that the action potential was associated with a transient decrease in the electrical impedance (Cole and Curtis, 1938 *b*, 1939). The decrease was primarily due to a fall in the membrane resistance to about 25 ohm cm.^{2} at the height of activity while the membrane capacity was relatively little affected by excitation. These measurements gave no information about the resistance of the membrane in the resting state because the current flow through that resistance is always negligible. The resistance is so high and the electrodes are so close together that at low frequencies most of the current flows through the external medium. At high frequencies, the current penetrates the cell through the capacity of the membrane, and the resistance is again effectively short-circuited.

However, the resting membrane resistance may be determined from direct current measurements with a length of axon between two electrodes which surround the fiber. In such an axial or longitudinal arrangement, the lines of current flow are primarily parallel to the

axis of the fiber except where they cross the membrane. When the electrodes are close together nearly all of the current will flow in the connective tissue sheath,[1] but as the interpolar distance is increased, a larger proportion of it will cross the membrane in the neighborhood of one electrode, flow through the axoplasm, and leave in the neighborhood of the other electrode. In the squid axon, when the electrodes are a centimeter apart, about 80 per cent of the current crosses and recrosses the membrane. Since so much of the current flows through the membrane resistance, we may calculate it, as well as the resistances of the connective tissue sheath and the axoplasm, from the relation between the measured direct current resistance and the electrode separation.

It should be possible to calculate the unknown resistances from measurements made with any length of fiber in contact with the electrodes, but the analysis is involved unless the electrodes are very short or very long. When the electrodes are very short the calculation becomes simple, but the experiment is rather difficult. The interpretation of the data is somewhat more complicated when very long electrodes are used, but the experimental procedure is so much simpler that this method has been chosen.

EXPERIMENTAL METHOD

Fig. 1 shows the electrode system employed. One end of the fiber was drawn up through a narrow opening into the wide tube A which was joined to a calomel electrode and filled with sea water. The other end hung through a layer of oil into a large volume of sea water which connected with a second calomel electrode. The resistance of the two electrode systems was 800 ohms. The interpolar length was determined by the distance between the two sea water interfaces and could be varied by raising the upper electrode in an adjustable stand. Increments of distance could be measured to 50 μ by means of a micrometer scale which was attached to the screw control on the adjustable stand. The principal advantages of this electrode system were, first, that the interpolar distance could be altered very rapidly without changing the contact resistance of either electrode, and second that there was no opportunity for evaporation or condensation of water to alter the resistance of the preparation.

Giant axons were obtained from the hindmost stellar nerve of *Loligo pealii*. Great care was taken to remove as much connective tissue as possible because it

[1] This term is used to describe the layer of diffuse connective tissue and sea water which clings to a fiber in oil or air.

introduced irregularities in the resistance-length curve. About 35 mm. of axon were required, since the interpolar distance had to be increased to 10–15 mm. and 10 mm. were kept in each electrode. The reasons for using such long stretches in the electrodes are, first, that the theoretical analysis is based on the assumption of an infinite polar stretch; second, that the properties of the membrane might be altered by the injury currents which spread for several millimeters from the cut end. The diameter of the fibers was measured at intervals of 5 mm. with an

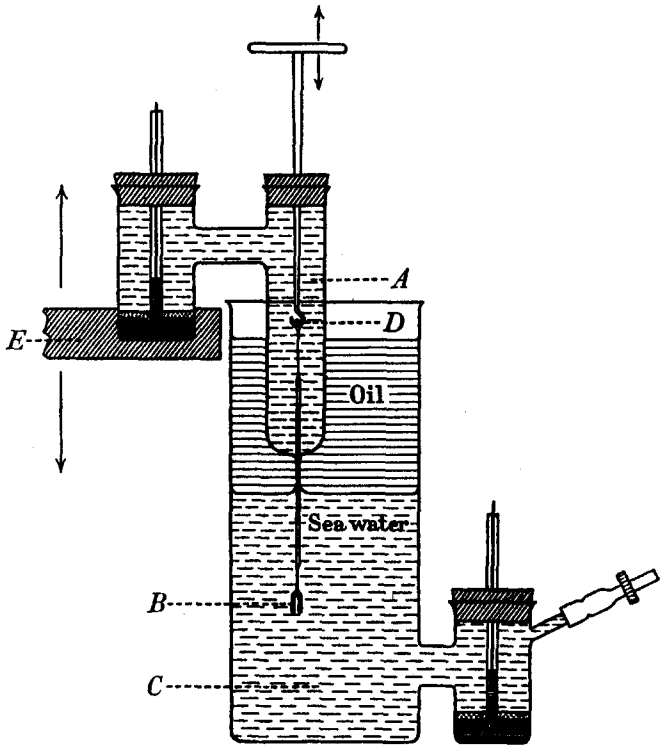

FIG. 1. Arrangement used for resistance-length determinations. E is an ebonite holder which is connected to an adjustable stand. For other letters, see text.

eyepiece micrometer which magnified 70 times. Although most axons tapered slightly, the diameter in the interpolar region was constant to within about 5 per cent, and this variation did not cause any large error.

The method of mounting the fiber in the electrode chamber was as follows. After the dissection was complete, a loop was tied in the silk ligature at one end of the fiber and a small platinum hook B attached to the other. The function of

this hook was to pull the fiber downwards and keep it in a vertical position when finally suspended in the electrode chamber. The upper electrode was raised out of the container C and lowered into a large dish of sea water. The fiber was placed in this dish and the silk loop at one end pushed through the 1.5 mm. pore at the bottom of the tube A. This loop was caught in the glass hook D which was then pulled up until about 10 mm. of fiber had been drawn into A. Finally the electrode and fiber were lifted out of the dish of sea water and lowered into position inside C.

At the beginning and end of each experiment the excitability of the whole axon was tested by recording the action potential with an amplifier and oscillograph. This was done inside the electrode chamber using the resistance electrodes as common stimulating and recording leads. The stimulus did not obscure the action potential, because it was applied through a balancing circuit. The resistance measurements were begun only if the axon was normally excitable. Some of the axons produced action potentials of 70 mv. and survived for 6 hours in the electrode chamber.

The electrical resistance of the nerve was determined by applying a known voltage and measuring the current with a galvanometer (Leeds and Northrup, Type R, $4.4 \cdot 10^{-10}$ amp./mm.). The voltages were adjusted to produce a current of about 0.4 μ amp. which was roughly one-tenth of that required to stimulate. The current was allowed to flow for about 15 seconds. Under these conditions the nerve seemed to behave as a simple resistance, since the current was proportional to the voltage and independent of its duration. An approximate value for the zero was first determined by noting the lowest resistance which could be obtained without permitting the two surfaces to coalesce. The resistance-length curve was usually started from a point which had a slightly greater resistance than this. Each observation was made with the current flowing first in one direction and then in the other. The two determinations usually agreed to within 3 per cent. The experiment was made as rapidly as possible in order to avoid progressive changes in the position of the zero and in the resistance of the nerve. When the curve was complete, one point was redetermined in order to make certain that there had been no serious drift in resistance. The experiments were usually made with increasing electrode separations, but occasional tests showed that similar curves could be obtained from measurements made in the reverse direction.

The experimental method was tested by measuring the relation between resistance and length in uniform rods of agar sea water. These were of the same dimensions as the nerve and could be mounted in the electrode chamber in a similar manner. The experimental points for the two rods, shown in Fig. 2, do not diverge from a straight line by more than 0.3 mm. As an additional test one experiment was made on a glass rod which had been coated with a thin layer of agar sea water. This also gave a linear relation between resistance and length.

Fig. 2D shows the resistance-length relation measured on a living axon with

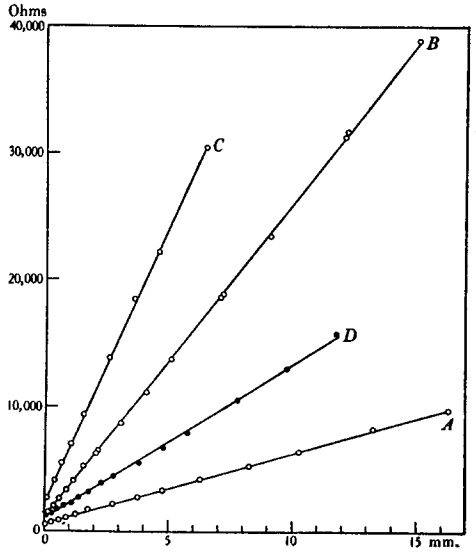

FIG. 2. Resistance-length measurements on

A. 720μ agar rod.

B. 340μ agar rod reinforced with 60μ hair.

C. 670μ glass rod coated with uniform layer of agar 28$\pm$ 5μ thick.

D. Living axon, resistance measured with 100 kc./sec. alternating current. This axon was the same as that in Fig. 3 and had a diameter of 540μ.

Temperature 22–25°C. Zero distance taken at point where two surfaces coalesce. Zero resistance as electrode resistance when two surfaces have coalesced.

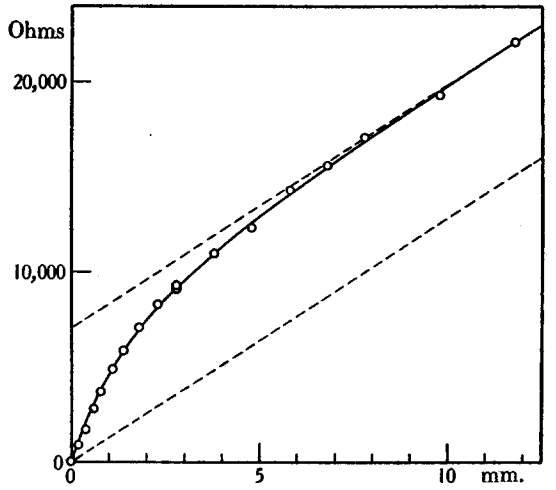

FIG. 3. Relation between resistance and length on a 540μ axon. The upper dotted line is drawn asymptotic to the curve for large lengths, the lower one through the origin and parallel to the upper line. Observations made with increasing electrode separations; upper point at 2.8 mm. determined at end of experiment.

100 kc. alternating current by the method described by Cole and Curtis (1937). Since the nerve membrane has a low impedance to high frequency current, it cannot prevent an even distribution of current throughout the fiber. Hence the high frequency resistance is directly proportional to the interpolar distance and is determined by the parallel resistance of core and external fluid.

Experimental Results

A typical resistance-length curve is shown in Fig. 3 where the circles are the experimental points. When the electrodes are close together very little current penetrates the fiber, because the resistance of the membrane is high compared to that of the external fluid. Therefore, the initial slope of the curve is steep and is determined by the external resistance. As the electrodes are separated and a greater area of membrane is exposed, more current penetrates the fiber. Hence the slope of the curve decreases, until at 8 to 10 mm. the relation becomes a straight line with a gradient equal to the parallel resistance of the core and the external fluid.

The form of the resistance-length relation is derived in the theoretical section from the equations of Kelvin (1856) which govern the spread of current in cable-like systems. There have been many applications of this type of analysis to nerve, and among the more recent are those of Labes and Lullies (1932), Rushton (1934), and Cole and Curtis (1936). With the type of electrode employed we obtain the equation

$$R = \frac{r_1 r_2}{r_1 + r_2} s + \frac{2 r_1^2 \lambda}{(r_1 + r_2)(\sqrt{(r_1 + r_2)/r_2} + \coth s/2\lambda)} \tag{1}$$

where R = total resistance of nerve, s = interpolar distance, r_1 = external resistance per unit length, r_2 = core resistance per unit length, $\lambda = \sqrt{r_4/(r_1 + r_2)}$, and r_4 is the resistance of a unit length of membrane.

Close agreement between the theoretical and experimental curves can be obtained as is shown in Fig. 3 where the smooth curve is drawn according to this equation.

For reasons which will be discussed, the interpolar distance s and the resistance R were both assumed to be zero when the upper and lower meniscuses just fail to touch. The constants in equation (1)

were determined by the method to be outlined later. For this particular fiber the following values were obtained:

$$r_1 = 61{,}800 \text{ ohm/cm.}$$
$$r_2 = 16{,}180 \text{ ohm/cm.}$$
$$r_4 = 4110 \text{ ohm cm.}$$

The membrane resistance per sq. cm. R_4 can be calculated from r_4 if the radius a of the fiber is known. Thus $R_4 = 2\pi a r_4$. The specific resistance of the protoplasm R_2 may be obtained from r_2 by the equation, $R_2 = \pi a_2 r^2$. The conducting material outside the fiber

TABLE I

Experiments made at 22–25°C. Zero taken at point of coalescence. Extreme values given in cases where data did not allow exact analysis. Brackets in first column indicate that successive measurements were made on one fiber.

Axon diameter	Membrane resistance (R_4)	Specific resistance of protoplasm (R_2)	Thickness of external fluid (b)
micra	*ohm cm².*	*ohm cm.*	*micra*
500	1100	34	14
480	500–800	25–23	23–20
—	500–600	27–26	18–17
360	900	28	8
—	1000	27	7
540	1000	38	28
—	700	37	20
—	600	37	16
480	400	24	21
460	600	22	13
—	400–700	27–22	15
—	600	26	12

consisted of a thin layer of connective tissue and sea water. The thickness b of this layer can be calculated approximately, if it is assumed to have the same conductivity as sea water, by $b = \sigma/2\pi a r_1$, where σ is the specific resistance of the material outside the fiber. This equation holds as long as b is small compared to a. In the present work σ has been taken as 20.5 ohm cm. which is the resistance of Woods Hole sea water at 25°. The fiber of Fig. 3 had a radius of 270μ, consequently

$$b = 19.6\ \mu;\ R_2 = 37.1 \text{ ohm cm.};\ R_4 = 697 \text{ ohm cm.}^2$$

Our results are summarized in Table I. The axons in these experiments were excitable and their thresholds remained constant while the measurements were in progress. Measurements were made on five more fibers, but the results were rejected. Two were found to be inexcitable at the end of the experiment. Two were excitable, but large differences in the resting potential and irregularities in the shape of the action potential showed that they were in poor condition. Inspection of the resistance-length curves obtained from these fibers showed that the membrane resistance must have been much lower than any in Table I. One experiment, made on an axon with a large amount of loose connective tissue, gave a very irregular resistance-length curve which could not be analyzed.

The External Resistance

Table I indicates that the thickness of the layer of sea water and connective tissue which adhered to a fiber in oil varied from 7–28μ. We did not try to check this result directly, but visual inspection left no doubt that the external layer was very thin compared to the axon diameter.

The Protoplasm Resistance

The average value for the specific resistance of the protoplasm is 29 ohm cm. which is about 1.4 times that of sea water. This result is smaller than those obtained from measurements with alternating current and transverse electrodes. Curtis and Cole (1938) obtained values ranging from 1.5 to 6.9 times that of sea water and gave 4 as an average.

The Membrane Resistance

The values of membrane resistance lie between 400 and 1100 ohm cm.^{2} with an average of about 700 ohm cm.^{2}

The Characteristic Lengths

The characteristic lengths in oil varied from 1.8 to 3.8 mm. with an average value of 2.3 mm. In sea water, the characteristic lengths were between 5.0 and 9.3 mm. The average value was 6.0 mm.

Theory

The Resistance-Length Relation.—The nerve fiber is assumed to behave like a uniform cable, with an external resistance, r_1, per unit length, due to adherent connective tissue and sea water, a core resistance, r_2 per unit length, due to the axoplasm, and a membrane, or insulation, resistance of r_4 per unit length. The corresponding sheath, core, and membrane currents, i_1, i_2, and i_4, are to be considered positive in the direction of current flow. The resting electromotive force of the membrane may be ignored when we assume that it is the same everywhere and is not affected by current flow. Since, by symmetry, there is then no potential difference across the membrane at the center of the interpolar region, distance and the potentials, V_1 of the sheath and V_2 of the core, will be measured from this point.

We shall define the interpolar region as the length of axon, s, in which r_1 is uniform, and the polar region as the length of axon where the outside potential, V_1, is constant, r_1 is negligible, and i_1 is zero.

By Ohm's law, we have

$$\frac{dV_1}{dx} = r_1 i_1 \ (2); \qquad \frac{dV_2}{dx} = r_2 i_2 \ (3); \qquad \text{and} \qquad V_1 - V_2 = r_4 i_4 \ (4),$$

and by continuity of current

$$\frac{di_1}{dx} = -\frac{di_2}{dx} = i_4 \ (5); \qquad \text{and} \qquad i_1 + i_2 = i_0 \ (6),$$

where i_0 is the total current flow. From (2), (3), and (6),

$$\frac{d(V_1 - V_2)}{dx} = r_1 i_1 - r_2 i_2 = (r_1 + r_2) i_1 - r_2 i_0 \tag{7}$$

By differentiation of (7) and substitution of (4) and (5),

$$\frac{d^2(V_1 - V_2)}{dx^2} = \frac{r_1 + r_2}{r_4} (V_1 - V_2) \tag{8}$$

The solution of this differential equation is

$$V_1 - V_2 = A \sinh x/\lambda + B \cosh x/\lambda \tag{9}$$

where $\lambda = \sqrt{r_4/(r_1 + r_2)}$ is the characteristic length. Since $V_1 - V_2$

$= 0$ when $x = 0$, we have $B = 0$. Differentiating (9) and substituting in (7) gives

$$\frac{d(V_1 - V_2)}{dx} = \frac{A}{\lambda} \cosh \frac{x}{\lambda} = r_1 i_1 - r_2 i_2 \tag{10}$$

with this value for A, (9) becomes

$$V_1 - V_2 = (r_1 i_1 - r_2 i_2)\lambda \tanh x/\lambda \tag{11}$$

Integration of (2) and substitution of (7) gives

$$V_1 = \int_0^x \frac{dV_1}{dx}\, dx = r_1 \int_0^x i_1\, dx = \frac{r_1 r_2}{r_1 + r_2}\, i_0 x + \frac{r_1}{r_1 + r_2}\, (V_1 - V_2) \tag{12}$$

Then from (6) and (11)

$$V_1 = \frac{r_1 r_2}{r_1 + r_2}\left(x + \frac{r_1}{r_2}\lambda \tanh \frac{x}{\lambda}\right) i_1 + \frac{r_1 r_2}{r_1 + r_2}\left(x - \lambda \tanh \frac{x}{\lambda}\right) i_2 \tag{13}$$

and similarly,

$$V_2 = \frac{r_1 r_2}{r_1 + r_2}\left(x - \lambda \tanh \frac{x}{\lambda}\right) i_1 + \frac{r_1 r_2}{r_1 + r_2}\left(x + \frac{r_2}{r_1}\lambda \tanh \frac{x}{\lambda}\right) i_2 \tag{14}$$

These equations completely describe the interpolar region, where r_1 is constant, and the coefficients of i_1 and i_2 are called resistance coefficients. The quantities V_1, V_2, i_1, and i_2 depend upon conditions at the end of this region and it is necessary to determine them before the measured resistance can be calculated.

If the electrode potential is V_0, then corresponding to (13) and (14) we have the equations

$$V_0 - V_1 = \beta_{11} i_1 + \beta_{12} i_2 \tag{15}$$

$$V_0 - V_2 = \beta_{12} i_1 + \beta_{22} i_2 \tag{16}$$

where the resistance coefficients β_{11}, β_{12}, and β_{22} are to be determined. In the electrode region proper, where the outside potential is constant, we may apply (13) and (14) by remembering that r_1 is negligible and i_1 is zero, and obtain

$$V_0 - V_1' = 0; \qquad V_0 - V_2' = \sqrt{r_2 r_4}\, i_2' \tanh x/\lambda_p \tag{17}$$

where V_1' and V_2' are the potentials of the sheath and core at the boundary of the electrode, $\lambda_p = \sqrt{r_4/r_2}$ is the polar characteristic length, and x is the distance from the boundary to the point where the

sheath and core are at the same potential. We may expect these potentials to be equal where the axon is ligated, but if $x = 2\lambda_p$ we have within 5 per cent

$$V_0 - V_2' = \sqrt{r_2 r_4}\, i_2' \tag{18}$$

The simplest and ideal condition is the one in which there is a sharp boundary between the polar and interpolar regions. Then $V_1 = V_1' = V_0$; $V_2 = V_2'$; $i_2 = i_2'$; and by eliminating V_2, i_1, and i_2 between equations (6), (13), (14), and (18) we obtain for the resistance

$$R = \frac{2V_0}{i_0} = \frac{r_1 r_2}{r_1 + r_2} s + \frac{2r_1^2 \lambda}{(r_1 + r_2)(\sqrt{(r_1 + r_2)/r_2} + \coth s/2\lambda)}. \tag{1}$$

Analysis of Resistance-Length Curves.—One way of finding the correct values for the three constants in equation (1) would be to try a number of values and select those which gave the best agreement between the theoretical and the experimental curves. This method would be possible if a single constant were involved, but it becomes exceedingly laborious when three have to be determined. The following method was finally adopted.

Equation (1) can be written

$$R = ms + y \tag{19}$$

where

$$m = \frac{r_1 r_2}{r_1 + r_2} \tag{20}$$

$$y = \frac{2r_1^2 \lambda}{(r_1 + r_2)(\sqrt{(r_1 + r_2)/r_2} + \coth s/2\lambda)} \tag{21}$$

When s is infinite we have

$$y_\infty = \frac{2r_1^2 \lambda}{(r_1 + r_2)(\sqrt{(r_1 + r_2)/r_2} + 1)} \tag{22}$$

Introduce a new constant h defined by the relation

$$(h + 1)^2 = \frac{r_1 + r_2}{r_2} \tag{23}$$

Then from (21) and (22) we have

$$\frac{y}{y_\infty} = \frac{2 + h}{1 + h + \coth s/2\lambda} \tag{24}$$

Equation (22) may be written

$$y_\infty = 2mh\lambda \tag{25}$$

where m and h are defined by (20) and (23).

Hence

$$\lambda = y_\infty/2mh \tag{26}$$

Substituting this value in (22) we obtain

$$\frac{y}{y_\infty} = \frac{2 + h}{1 + h + \coth h(ms/y_\infty)} \tag{27}$$

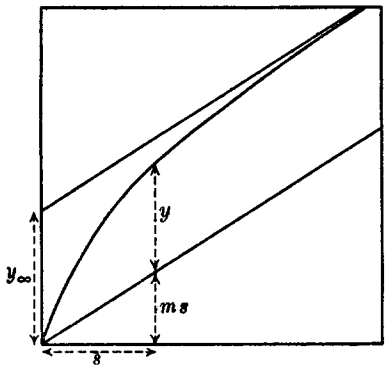

FIG. 4. Diagram illustrating measurement of y, y_∞, and m.

y, y_∞, and m can be measured directly from the resistance-length curve, as shown in Fig. 4. Hence we can plot y/y_∞ against ms/y_∞ and obtain a curve which depends only upon h. The best value for h may then be determined by comparing this curve with a standard family of the form $\dfrac{2 + h}{1 + h + \coth hx}$.

The values for r_1 and r_2 can be obtained by means of the following equations which may be derived from (20) and (23).

$$r_1 = m(h + 1)^2 \quad (28); \qquad r_2 = \frac{m(h + 1)^2}{h^2 + 2h} \tag{29}$$

λ can be determined from (26), and r_4 from the relation,

$$r_4 = \lambda^2(r_1 + r_2) \tag{30}$$

DISCUSSION

The Polar Region.—Equation (1) assumes an infinite length of axon in each electrode, but in practice there might be as little as 1 cm. between a ligature and the interface. It is found in equation (18) that the polar resistance for an infinite stretch is $\sqrt{r_2 r_4}$. For a short-circuited end we have $\sqrt{r_2 r_4}$ tanh x/λ_p (17), and for an insulated end,

$\sqrt{r_2 r_4}$ coth x/λ_p. In either case, when $x > 2\lambda_p$, the error will be less than 5 per cent of the polar resistance and a considerably smaller percentage of the total resistance. Since the average value of λ_p is 0.6 cm., the polar length should have been greater than 1.2 cm. on this basis, but 1.0 cm. was satisfactory. If the membrane is injured at the ligature in such a manner as to reduce the membrane resistance and approach the short-circuited end condition, the experimental points should fall below the theoretical curve as the end nears the interface. However, it was found in every case that the resistance was higher than predicted, indicating that the resistance at and near the ligature was high and that the membrane was not severely injured in this region.

The Meniscus Region.—The principal difficulty in the interpretation of the experimental data was caused by the capillary rise of the sea water on the axon at each oil-water interface. Because of it there is no simple way of determining either the electrode separation or resistance corresponding to a zero interpolar length, and these quantities should be determined accurately because the characteristic length in oil is quite small—2.3 mm.

In the theoretical section, the interpolar region was defined as the length of axon having a constant external resistance r_1 and the polar region as that in which the sheath potential is constant and the longitudinal current i_1 and resistance r_1 are negligible, and these two regions were assumed to have a common boundary. This condition would probably be met if it were possible to pull each end of the axon into a thin close-fitting metal tube which would serve as an electrode, but with liquid electrodes there is certainly a transitional region.

As an approximation, the transitional region may be ignored and the resistance-length curve extrapolated back to a zero determined by the resistance of the electrodes alone. When this is done for the data in Fig. 3, the point of coalescence corresponds to an interpolar distance of about 0.4 mm. and a resistance of 2100 ohms. From the analysis of the data on this basis, r_1 is 20 per cent larger, r_2 is 4 per cent less, and r_4 is 25 per cent larger than was obtained above. This method of analysis was not generally employed because it has slight theoretical foundation and because the experimental points agreed

more closely with equation (10) when the point of coalescence was taken as the zero interpolar distance.

If there were no meniscus and the sea-water oil interfaces were perfectly plane, there would be a crowding of the lines of current flow before they enter the sheath, which would result in a potential gradient in the sea water along the sheath and give rise to an external resistance. An approximate calculation of this resistance for the axon of Fig. 3 gives a value of 1000 ohms for the two interfaces. The actual resistance would be higher than this because the interfaces were curved and not plane as assumed in the calculation. The smallest resistance observed experimentally was only about 2000 ohms, and so must have been due primarily to the constriction of the lines of current flow in the two meniscuses. Hence there is some justification for taking the point of coalescence as zero distance.

To determine the effect of the meniscus on equation (1), the combined characteristics of the meniscus and polar region may be given in the form of equations (15) and (16). From these and equations (13) and (14) we find the resistance

$$R = \frac{r_1 r_2}{r_1 + r_2} s + \frac{2 r_1^2 \lambda p^2 q^2}{(r_1 + r_2)(q\sqrt{(r_1 + r_2)/r_2} + \coth s/2\lambda)} + R_0 \qquad (31)$$

where R_0 is the resistance for zero interpolar length, q is a function of β_{11}/β_{22} and β_{12}/β_{22} and p involves these ratios and r_2/r_1. This equation is too complicated to use for a direct evaluation of r_1, r_2, and r_4 and the method of analysis used with equation (1) is not valid but the errors can be estimated. For rough calculation we may take $\beta_{11} = 1000$ ohms, $\beta_{12} = 20$ ohms, and $\beta_{22} = 8000$ ohms from equation (18), and then for the data on p. 677, $p = 0.97$, $q = 0.88$. It is found that r_1 should be about 25 per cent greater, r_2 about 7 per cent less, and r_4 about 20 per cent less than the values previously calculated. The experimental points accidentally agree equally well with equations (1) and (31).

The Membrane Resistance.—The method of analysis is based upon a theory which neglects the transitional region between the polar and interpolar lengths of the axon. It is best applied by measuring the resistance and interpolar length from their values when the upper and lower meniscuses just remain separate. A less satisfactory

method is to ignore the meniscus resistance and extrapolate the resistance-length curve back to the resistance of the electrodes alone; this gives values for the membrane resistance which are 25 per cent larger than those obtained by the first method. A more complete theory including the transitional region is too involved for practical use, but approximations from it suggest a 20 per cent smaller membrane resistance.

The average value for the membrane resistance was 700 ohm cm.^{2}, but we propose to adopt a value of 1000 ohm cm.^{2} as a tentative estimate for the membrane resistance. Only a few of the axons had this membrane resistance, but they seemed to survive longer and so were probably more nearly normal. The membrane resistance may be high when the axons are in their natural state inside the body and may then fall to a relatively low value during the dissection. At present there is no way of deciding whether the value of 1000 ohm cm.^{2} is a normal one; all that can be said is that it was obtained on axons which behaved as if they were in good physiological condition.

Previous measurements of membrane resistance have been made on *Nitella* and *Valonia*. Blinks (1930 *b*) obtained an average value of 250,000 ohm cm.^{2} for the resistance of the thin protoplasmic layer which bounds the vacuolar sap in *Nitella*. However, *Nitella* is surrounded by fresh water, and for this reason its outer membrane may have a high resistance. Blinks (1930 *a*) found considerably lower resistances in the marine cell *Valonia*. Here the resistance varied from less than 1000 ohm cm.^{2} in freshly gathered cells to over 50,000 ohm cm.^{2} in cells which had been kept under constant conditions, and 10,000 ohm cm.^{2} was given as an approximate value for a normal cell. In *Valonia* the current must cross two protoplasmic membranes, and the resistance of each would therefore be about 5000 ohm cm.^{2} in a normal cell. The largest membrane resistance observed in our experiments was 1100 ohm cm^2. This suggests that the physiological condition of an isolated axon may be similar to that of freshly gathered *Valonia*.

The resistance-length curves described in this paper are qualitatively similar to those obtained on medullated nerve by Rosenberg and Schnauder (1923), Lullies (1930), and Rushton (1934). Their experiments were made with whole nerve trunks and the results

cannot be analyzed with any certainty. However, a rough value for the combined resistance of myelin sheath and membrane can be obtained by making a number of simplifying assumptions as to the structure of the nerve trunk. Analysis of Rosenberg and Schnauder's data gives a value of 4×10^4 ohm cm.^{2} for the resistance of sheath and membrane. Hill (1932) calculated a value of 2.2×10^5 ohm cm.^{2} on the basis of Rushton's (1927) measurements. Both these estimates are open to a number of objections, but there can be little doubt that the combined myelin sheath and membrane resistance is much larger in medullated than in non-medullated fibers. This difference could be explained if myelin were a material with a high specific resistance.

SUMMARY

The direct current longitudinal resistance of the squid giant axon was measured as a function of the electrode separation. Large sea water electrodes were used and the inter-electrode length was immersed in oil. The slope of the resistance *vs.* separation curve is large for a small electrode separation, but becomes smaller and finally constant as the separation is increased.

An analysis of the resistance *vs.* length curves gives the following results. The nerve membrane has a resistance of about 1000 ohm cm.^{2} The protoplasm has a specific resistance of about 1.4 times that of sea water. The resistance of the connective tissue sheath outside the fiber corresponds to a layer of sea water about 20μ in thickness. The characteristic length for the axon is about 2.3 mm. in oil and 6.0 mm. in sea water.

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