ADMITTANCE CHANGE OF SQUID AXON DURING ACTION POTENTIALS

CHANGE IN CAPACITIVE COMPONENT DUE TO SODIUM CURRENTS

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ABSTRACT   Since the discovery of Cole and Curtis (1938. *Nature (Lond.).* 142:209 and 1939. *J. Gen. Physiol.* 22:649) that the imaginary components, i.e., capacitive and inductive components, of the admittance of squid axon membrane remained unchanged during the action potential, there have been numerous studies on impedance and admittance characteristics of nerves. First of all, it is now known that the dielectric capacitance of the membrane is frequency dependent. Second, the recent observation of gating currents indicates that dipolar molecules may be involved in the onset of ionic currents. Under these circumstances, the author felt it necessary to reinvestigate the membrane admittance characteristics of nerve axons. The measurements by Cole and Curtis were performed mainly at 20 kHz, indicating that their observation was limited only to the passive membrane capacitance. To detect the change in the capacitive component during the action potential, we performed transient admittance measurements at lower frequencies. However, the frequency range of the measurements was restricted because of the short duration of the normal action potential. In addition, a change in the inductive component obscured the low frequency behavior of the capacitance. To use a wider frequency range and simplify the system by eliminating the inductive component, the potassium current was blocked by tetraethyl ammonium, and the increase in the capacitive component was reinvestigated during the long action potential. The admittance change under this condition was found to be mostly capacitive, and conductance change was very small. The increase in the capacitive component was from 1.0 to 1.23 μF/cm^2.

INTRODUCTION

Invariance of the capacitive component of nerve membrane admittance during activities has been one of the basic doctrines in axonology since the experiments by Cole and Curtis were published some years ago (1938, 1939). Since then, there have been more studies on the electrical properties of nerve membranes (Taylor, 1965; Matsumoto et al., 1970; Takashima and Schwan, 1974). It is now known that there are additional capacitive components which may arise from time-dependent ionic currents (Chandler et al., 1964; Mauro et al., 1961; Cole, 1968; Fishman, 1975) and also from dipole orientation of gating particles (Armstrong and Bezanilla, 1973, 1974; Bezanilla and Armstrong, 1974; Keynes and Rojas, 1974; Meves, 1974; Nonner et al., 1975). These components give rise to frequency-dependent capacitances with relatively long time constants and can be detected only at low frequencies. Recent time-domain (Adrian and Almers, 1976) and frequency-domain measurements (Takashima, 1976; Takashima and Yantorno, 1977; Takashima et al., 1977) with skeletal muscle membranes and squid axons confirm the presence of frequency and voltage-dependent capacitances under voltage clamp or current clamp conditions.

In view of these new developments, the capacitive components of membrane admittance of nerve axons have two elements, i.e., dynamic as well as passive capacitances. Under these circumstances, it is important to reinvestigate the behavior of the capacitive component of nerve membranes during activities and interpret the results in terms of the new membrane concept. The measurements by Cole and Curtis (1938) were performed mainly at 20 kHz and the measured capacitance perhaps included only the passive capacitance as a result of lipid molecules. In view of the facts that ionic currents and gating currents are slow processes, the measurements must be performed at low frequencies that are comparable to or lower than those of ionic and gating currents. Since the action potential lasts for only 1.5–2 ms under normal conditions, transient measurements become progressively difficult as the frequency decreases. To circumvent this difficulty, we elicited long action potentials by blocking the potassium current. The change in the capacitive and conductive components was investigated during these long action potentials with reasonable accuracies even below 1 kHz. As discussed below, we found that the increase in the conductivity during the long action potential is minimal whereas an enormous conductance increase was observed during the normal action potential. Above all, we found that the capacitive component increased from 1.0 to 1.23 μF/cm^2 in contrast to the early observation by Cole and Curtis (1939) at higher frequencies.

EXPERIMENTS

All experiments were carried out at the Marine Biological Laboratory, Woods Hole, Mass. using squid *Loligo pealei*. All measurements were performed at 6–10°C with running natural seawater. Measurements of capacitance and conductance were carried out with a Wayne-Kerr B-221 admittance bridge (Wayne-Kerr Lab Ltd., Chessington, Surrey, England) with a PAR (Princeton Applied Research, Princeton, N.J.) TM 124 lock-in amplifier as an oscillator and detector. Use of an amplifier with a low Q is the key to the successful measurement of transient states. The variable Q of the lock-in amplifier was adjusted to 5–10. Stimulating pulses to trigger the action potential were applied through the neutral lead of the isolation transformer of the bridge across a large blocking condensor (10 μF). The AC voltage used for the bridge measurement was limited below 2 mV peak-to-peak. The transient AC current resulting from the bridge unbalance caused by the action potential was monitored on an oscilloscope, and the bridge knobs were manually adjusted to rebalance the bridge at the peak of the action potential while the action potential was repeatedly triggered. The time constants of measuring instruments, i.e., lock-in amplifier and admittance bridge, are of the order of 2–5 μs. Because the duration of the peak region of the impulse is $\simeq 0.2$–0.3 ms for the normal action potential and 1–2 ms for the long action potential, these time spans can be considered as pseudo stationary states that allow transient measurements. The internal electrode was a Pt-Ir wire with a diameter of 75 μm. Ground electrodes consisted of two interconnected Pt plates located on both sides of the axon.

Determination of Series Resistance

Table I contains the conductances and capacitances measured at a few frequencies during resting state and at the peak of the action potential. This table seems to indicate the invariance of the capacitive component during the action potential as concluded by Cole and Curtis at higher frequencies. However, the presence of electrolyte solutions between electrodes and the membrane constitutes a series resistance (Moore and Cole, 1963) and, therefore, as previously noted by Takashima et al. (1977) the measured capacitance is given by Eq. 1 at low frequencies,

$$C_p = \frac{C_m}{(1 + R_s/R_m)^2},\tag{1}$$

TABLE I

MEASURED CAPACITANCE AND CONDUCTANCE FOR RESTING AND ACTIVE
MEMBRANES WITHOUT THE CORRECTION FOR SERIES RESISTANCE

Frequency, kHz	2	3	5
Capacitance, $\mu F/cm^2$			
Resting	0.855	0.754	0.658
Active	0.860	0.710	0.587
Conductance, $mmho/cm^2$			
Resting	3.79	5.81	9.83
Active	17.53	18.63	26.77

where C_p and R_s are measured capacitance and series resistance; R_m includes passive membrane resistance and active ionic resistances. C_m likewise includes passive membrane capacitance and reactance components of time varying ionic currents. According to Eq. 1, the magnitude of measured capacitances can be considerably smaller than the true capacitance (C_m) if R_s and R_m are comparable, a condition that might exist during the action potential. To obtain the true capacitance, therefore, measured capacitances must be corrected for series resistance. The series resistance has been determined to be ohmic and frequency independent (Cole, 1975; 1976). Therefore, the membrane in an electrolyte solution can be approximated by parallel capacitance (C_m) and resistance (R_m) and a series resistance (R_s). Analysis of this circuit readily shows that the plot of measured reactance against resistance will be an arc, and the intersection of the locus with the resistance axis will be the value of the desired series resistance (Cole, 1968). Experimental data shows that R_s stays constant during the action potential, indicating that the admittance changes during activities arise only from the membrane and (or) ion transports across it.

Effects of Fringe Capacitance

The importance of the correction for fringe effects at the tip of the internal electrodes has been discussed by several investigators (Takashima and Yantorno, 1977; Tasaki;[1] Schwan;[2] Fishman and Cole[3]). In the present work, a long internal electrode with a length of 27 mm was used to minimize the relative contribution of the fringe capacitance. Further correction was made by repeating the measurement at the resting state as well as during the action potential using another electrode having a length of 1 mm. The values of capacitance and conductance obtained with the short electrode were subtracted point by point from those obtained with the longer electrode. It was found that the fringe capacitance did not increase during the action potential.

Electrode Polarization

Internal and ground electrodes were carefully plated with platinum black to minimize the effect of electrode polarization. In general, capacitance of an electrolyte solution, if measured using metal electrodes, is given by the following equation (Schwan, 1963):

$$C = C_s + 1/R^2 C_p \omega^2, \qquad (2)$$

where C is measured capacitance, C_s is the capacitance of the solution, C_p is electrode polarization capacitance, R is resistance of the solution, and ω is radian frequency. Our electrodes usually have a C_p of 5–6 μF. R is typically 0.6 kΩ at 3 kHz at rest and 0.17 kΩ at the peak of the action potential. By using these values in Eq. 2, we obtain values of the second term (contribution of electrode polarization) to be

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[1] Tasaki, I. Personal communication.
[2] Schwan, H. P. Personal communication.
[3] Fishman, H. M., and K. S. Cole. Personal communication.

0.0034 µF for the resting state and 0.018 µF at the peak of impulses. Because the total capacitance at rest is ≃0.271 µF, electrode polarization causes an error of ≃1.5%. The total capacitance at the peak of impulses is ≃0.33 µF. The error as a result of electrode polarization reduces this value to 0.312 µF, which is still substantially larger than the value at rest. In the absence of K^+ current, the conductance increase is only slight (Fig. 5) and the error as a result of electrode polarization remains ≃2% or even less. Thus, the effect of electrode polarization is negligible.

RESULTS

Change in Capacitive Component during Normal Action Potential

Capacitances and conductances of squid axons at rest and during the normal action potential are shown in Fig. 1 a (150 Hz to 30 kHz for the resting state and 3–30 kHz at the peak of the action potential) after corrections for series resistance and fringe effect. In spite of the limited frequency range, it is clear from this figure that capacitance undergoes an increase at the peak of the action potential. However, because of the short duration of the normal action potential, measurements below 3 kHz are difficult, and we were unable to establish the low frequency–limiting value. (Although the lowest frequency we used was 2 kHz, the experimental error was large and the points at 2 and 2.5 kHz are not shown in Fig. 1.)

In view of this, it was necessary to prolong the action potential by blocking K^+ current
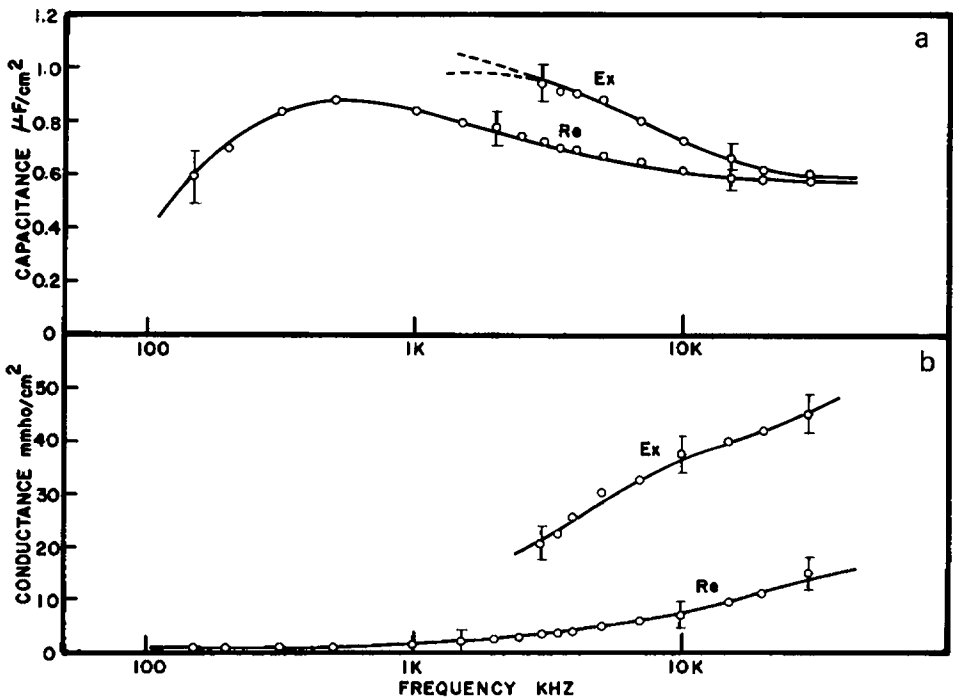

FIGURE 1 (a) Changes in the capacitive component of squid axon during the normal action potential. Curves Re and Ex are at rest and at the peak of the action potential, respectively. Curves are corrected for series resistance and fringe capacitance. Dotted lines indicate the possible behavior of the capacitive component at low frequencies. (b) Changes in conductance of squid axon during the normal action potential. Curves Re and Ex indicate the resting state and the peak of the action potential, respectively.

using internal tetraethyl ammonium. Moreover, under normal conditions, changes in the admittance during the action potential can be a result of changes in the values of m, n, and h parameters. It has been discussed by Chandler et al. (1964) and recently by Fishman (1975) and Fishman et al. (1977b) that the potassium activation and sodium inactivation give rise to an inductive reactance and cause an apparent negative capacitance at low frequencies (Cole and Curtis, 1938). Takashima and Schwan (1974) demonstrated that blocking of the potassium current eliminated the inductive reactance and proved that the inductive reactance indeed arises from the potassium channel. Moreover, Guttman and Feldman (1975), Fishman et al. (1977b) and Fishman et al. (1978) reported a considerable change in the magnitude and shifts in the frequency of the anti-resonance of the admittance of squid axon when K^+ current is suppressed. In view of these observations, change in the inductive component, in addition to changes in capacitive and conductive components, must be expected during the normal action potential. Thus, it became apparent that the normal action potential, by limiting the frequency range and by making the interpretation of the result unnecessarily ambiguous, is unsuitable for the intended experiment. Therefore, we decided to simplify the system by blocking K^+ current. In so doing, we eliminate the inductive component and also make the transient measurements much easier because of the prolonged action potential.

Change in Capacitive Component during Long Action Potential

For these experiments, nerve axons were internally perfused with a solution (KF 200 mM, glycerol or glucose, 200 mM, K-phos/dibasic 100 mM, K-phos, monobasic 25 mM and pH 7.3) containing 15 mM tetraethylammonium (TEA). The action potential elicited in the absence of the potassium current is $\simeq 70$–100 ms. The admittance change during these long action potentials is shown in Fig. 2 a. Inasmuch as the K^+ current is eliminated by TEA, the change in the admittance at the early stage of the action potential is clearly a result of sodium activation. (The sharp spike at the beginning of the signal is a result of stimulus artifacts.) The decay that follows is apparently because of fast and slow inactivations of sodium currents. The bridge is rebalanced at the initial stage of the action potential (disregarding stimulus artifacts) as shown in Fig. 2 b. The capacitance and conductance obtained from these measurements at various frequencies are illustrated in Fig. 3 a and b.

As shown in Fig. 3 b, the conductance change during the long action potential is much smaller than that for the normal impulse. This implies that a considerable portion of the conductance change observed by Cole and Curtis (also see Fig. 1 b) may be a result of K^+
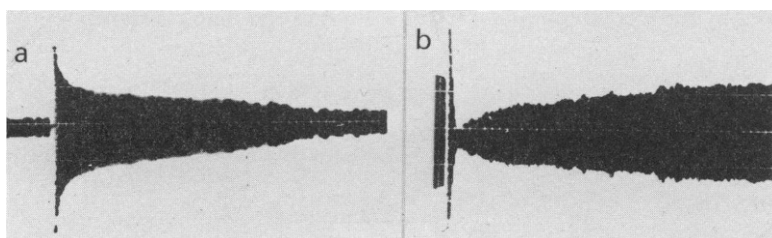

FIGURE 2   (a) Admittance change of squid axon during the long action potential without K^+ current. Time is 10 ms/division and frequency of measurement is 2 kHz. (b) Rebalancing of the bridge at the early stage of the long action potential (disregarding the stimulus artifact).
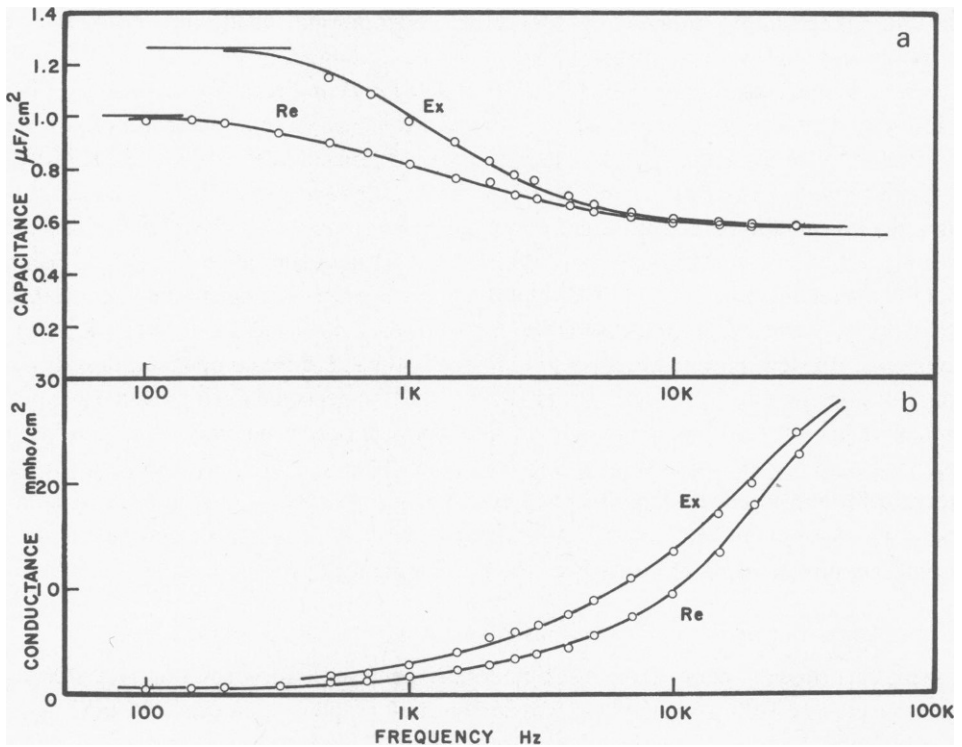
FIGURE 3   (a) Change in the capacitance component during the long action potential in the absence of K$^+$ current. Curves Re and Ex are at rest and at the peak of the action potential, respectively. Horizontal bars are obtained from the Cole-Cole plot (see Fig. 4). Solid curves were calculated using Eq. 7 assuming values 0.21 for the resting state and 0.03 for the action potential. (b) Changes in the conductance component during the long action potential. Note that elimination of K$^+$ current decreases the conductance change. Solid curves are empirical.

current. Inspection of the curves in Fig. 3 *a* readily reveals that blocking of the potassium current indeed eliminates the inductive component at rest as well as during the action potential. Also, the capacitive component increases during the action potential from 1.0 to 1.23 μF/cm^2. The horizontal bars were obtained from the Cole-Cole plot (C' vs. C'' plot; Cole and Cole, 1941) as described below.

The permittivity of a membrane is a complex quantity and its real and imaginary parts are generally given by the Debye equation (1929) assuming one time constant:

$$\epsilon' = \epsilon_\infty + \frac{\epsilon_0 - \epsilon_\infty}{1 + (\omega\tau)^2} \tag{3}$$

$$\epsilon'' = (\epsilon_0 - \epsilon_\infty)\frac{\omega\tau}{1 + (\omega\tau)^2}, \tag{4}$$

where ϵ_0 and ϵ_∞ are low and high frequency dielectric constants, ω is radian frequency, and τ is relaxation time. If one eliminates ($\omega\tau$) from Eqs. 3 and 4, the equation of circles is obtained

(Cole and Cole, 1941), i.e.,

$$\left(\epsilon' - \frac{\epsilon_0 + \epsilon_\infty}{2}\right)^2 + \epsilon''^2 = \left(\frac{\epsilon_0 - \epsilon_\infty}{2}\right)^2 \tag{5}$$

It is well known that the plot of ϵ' vs. ϵ'' is a circle with its center either on or below the real axis. In this experiment, C' and C'' are used instead of complex permittivities.

$$C' = \epsilon' \epsilon_r / d \tag{6}$$

$$C = \epsilon'' \epsilon_r / d, \tag{7}$$

where d is membrane thickness in cm and ϵ_r is the permittivity of free space (8.84×10^{-14} F/cm). The C' and C'' plots for the resting state and at the peak of the action potential are shown in Fig. 4. The intersections between arcs and the abscissa give the limiting values of C' at low frequencies at the peak of impulses is obtained from this plot, i.e., 1.23 μF/cm². The angle α indicates the distribution of time constants. If α is zero, C' is given by Eq. 3. However, if α is finite, C' must be calculated by the following equation (Cole and Cole, 1941).

$$C - C_\infty = (C_0 - C_\infty) \frac{1 + (f/f_c)^n \cos n(\pi/2)}{1 + (f/f_c)^n \cos n(\pi/2) + (f/f_c)^{2n}}, \tag{8}$$

where f_c is relaxation frequency and $n = 1 - \alpha$. Solid curves in Fig. 3 a calculated using Eq. 8 assuming $\alpha = 0.21$ and 0.03 for the resting state and during the action potential. It must be noted that the value of α decreases considerably at the peak of the action potential, although the relaxation time itself does not change (0.122 ms for the resting state and 0.10 ms at peak of action potential). This indicates that there are more than one dipolar species contributing capacitances at rest and that there is only one type of dipolar process operating in the channel at the peak of the action potential.
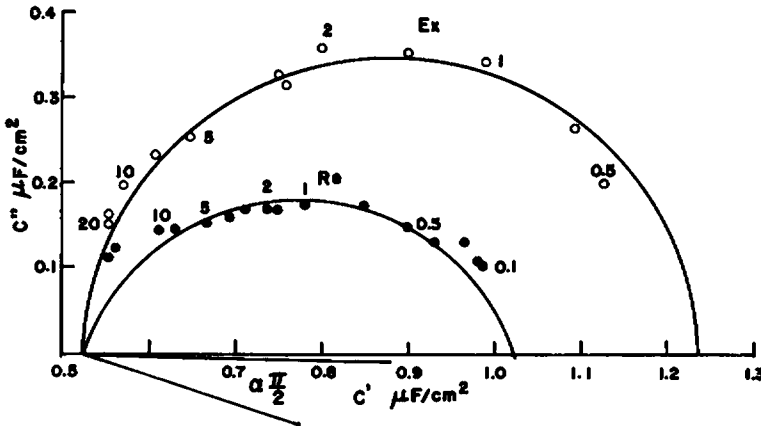

FIGURE 4   Cole-Cole plots for resting (Re) and excited (Ex) states. Horizontal bars shown in Fig. 3 a are obtained from intersections between the circles and the real axis.

DISCUSSION

The historic experiments by Cole and Curtis (1939) established the concept of membrane capacitance as a static and passive quantity which has no bearing on the physiology of nerve axons. However, more recent results, particularly those of Taylor (1965) indicate that membrane capacitance may be a frequency-dependent quantity. The work by Takashima and Schwan (1974) confirmed the presence of an anomalous dispersion of capacitance between 500 Hz and 10 kHz. These observations suggest that the overall capacitance of the nerve axon represents dynamic properties of the membrane rather than a static passive bulk. In addition, recent observations of the gating current added a new dimension to the study of the impedance characteristics of nerve membranes. Although the magnitude of gating currents is small, it nevertheless gives rise to a capacitance of 0.4 $\mu F/cm^2$ with a depolarization of 80 mV if it is transformed to the frequency domain assuming linearity (Bezanilla and Armstrong, 1975). These new results pose a question as to how to reconcile the discrepancy between the concept of gating current and the early observation of the invariance of the capacitive component (Cole and Curtis, 1939). First of all, the measurements by Cole and Curtis were mostly carried out at 20 kHz, a frequency which is too high for the observation of the increase in the capacitance due to the gating current. In addition to the limited frequency used by Cole and Curtis, their data processing was handicapped because of the lack of fast computing facilities at that time. Because of this difficulty, their capacitance data were uncorrected for the series resistance. As far as data are presented as an impedance, the reactance component does not require the correction for series resistance. However, if the data are presented as capacitance and conductance, they must be corrected for series resistance. Without this correction, the error in the value of capacitance can be serious, particularly during the action potential as discussed before.

Observations of the gating current and realization of the limitations of the experiments by Cole and Curtis prompted the author to repeat the measurement of the capacitive component of nerve axons during the action potentials at frequencies which are comparable to the time constants of sodium and (or) gating currents. As discussed in the foregoing, I found that the capacitive component of nerve axon admittance increases by $\simeq 25\%$ of the total capacitance. This result is contrary to the conclusion reached by Cole and Curtis (1939). The origin of the dynamic capacitance is still unknown. Although the additional capacitance component may be the frequency domain equivalence of the gating current, there are still unanswered questions concerning the relationship between the gating current and voltage dependent capacitance (Fishman et al. 1977; Takashima, 1978). On the other hand, the observed results may be due to the time-dependent sodium current. The magnitude of this capacitance can be calculated using the linearized Hodgkin-Huxley equation (Chandler et al. 1964). However, thorough analyses of the data using this theory, when one considers the frequency-dependent capacitance and also the term owing to the gating current, are beyond the scope of this work.

Usually, nonlinear dielectric behavior arises from the orientational saturation of polarization (Debye, 1929). Inasmuch as the field strength in the membrane is near 100 kV/cm, the dielectric properties of nerve axons can be considered nonlinear because of this effect. However, there is another cause for the nonlinearity of dielectric behavior. If the applied field causes chemical reactions, such as dimerization or dissociation of subunits, and if the reaction

produces excess dipole moments, this will produce a field dependent dielectric relaxation (Bergman et al., 1963; DeMaeyer et al., 1968; Schwarz, 1967).

The following equation shows the magnitude of dipole moment changes accompanying field-dependent rate processes:

$$\left(\frac{\partial \ln K}{\partial E}\right)_{p,T} = \frac{\Delta M}{RT},\tag{9}$$

where K is the equilibrium constant, T and p are temperature and pressure, and E is field strength. In the case of sodium channels, the equilibrium constant K can be calculated from the Hodgkin-Huxley parameters α_m and β_m at each depolarization. The plot of $\ln K$ vs. E was obtained by Levitan and Palti (1975) and also by Takashima et al. (1977). With depolarizations below 60 mV, the dipole moment change was found to be $\simeq 1000$ Debye Units (D.U.) and with large depolarizations, the change was about 700 D.U. If we take the average value of the dipole moment changes, we obtain a value of 850 D.U. This is the overall change in dipole moment associated with the gating mechanism of sodium channels and is related to the change in capacitance mentioned earlier. Thus, the dipole moment change calculated by using the voltage clamp data in time domain does not contradict with the observation of a capacitance change measured in frequency domain.

REFERENCES

ADRIAN, R. H., and W. ALMERS. 1976. The voltage dependence of membrane capacity. *J. Physiol. (Lond.).* **254:**317.

ARMSTRONG, C. M., and F. BEZANILLA. 1973. Current related to movement of the gating particles of the sodium channels. *Nature (Lond.).* **242:**459.

ARMSTRONG, C. M., and F. BEZANILLA. 1974. Charge movement associated with the opening and closing of the activation gates of the Na channels. *J. Gen. Physiol.* **63:**533.

BERGMANN, K., M. EIGEN, and L. DE MAEYER. 1963. *Ber. Bunsenges. Phys. Chem.* **67:**819.

BEZANILLA, F., and C. M. ARMSTRONG. 1974. Gating currents of the sodium channels. Three ways to block them. *Science (Wash. D.C.).* **183:**753.

BEZANILLA, F., and C. M. ARMSTRONG. 1975. Currents associated with the ionic gating structures in nerve membranes. *Ann. N. Y. Acad. Sci.* **264:**265.

CHANDLER, W. K., R. FITZHUGH, and K. S. COLE. 1962. Theoretical stability properties of a space-clamped axon. *Biophys. J.* **2:**105.

COLE, K. S. 1968. Membranes, Ions and Impulses. Part II. University of California Press, Berkeley, Calif. 134.

COLE, K. S. 1975. Resistivity of axoplasm. I. Resistivity of extruded squid axoplasm. *J. Gen. Physiol.* **66:**133.

COLE, K. S. 1976. Electrical properties of the squid axon sheath. *Biophys. J.* **16:**137.

COLE, K. S., and R. H. COLE. 1941. Dispersion and absorption in dielectrics. I. Alternating current characteristics. *J. Chem. Phys.* **9:**341.

COLE, K. S., and H. J. CURTIS. 1938. Electrical impedance of nerve during activity. *Nature (Lond.).* **142:**209.

COLE, K. S., and H. J. CURTIS. 1939. Electric impedance of the squid giant axon during activity. *J. Gen. Physiol.* **22:**649.

DEBYE, P. 1929. Polar Molecules. Dover Publishng Co., New York.

DE MAEYER, L., M. EIGEN, and J. SUAREZ. 1968. Dielectric dispersion and chemical relaxation. *J. Am. Chem. Soc.* **90:**3157.

FISHMAN, H. M. 1975. Rapid complex impedance measurements of squid axon membrane via input-output crosscorrelation function. Proceedings of the First Symposium on Testing and Identification of Nonlinear System. G. D. McCann and P. Marmarelis, editors. Cal. Inst. Tech., Pasadena, Calif. 257.

FISHMAN, H. M., L. E. MOORE, and D. POUSSART. 1977*a*. Asymmetry currents and admittance in squid axons. *Biophys. J.* **19:**177.

FISHMAN, H. M., D. POUSSART, and L. E. MOORE. 1978. Admittance of the Na conductance system in squid axons. *Biophys. Soc. Annu. Meet. Abstr.* **21:**163*a*.

FISHMAN, H. M., D. J. M. POUSSART, L. E. MOORE, and E. SIEBENGA. 1977*b*. K^+ Conduction description from the low frequency impedance and admittance of squid axon. *J. Membr. Biol.* **32:**255.

GUTTMAN, R., and L. FELDMAN. 1975. White noise measurement of squid axon membrane impedance. *Biochem. Biophys. Res. Commun.* **67:**427.

HODGKIN, A. L., and A. F. HUXLEY. 1952. A quantitative description of membrane current and its application to conduction and excitation in nerve. *J. Physiol. (London.).* **117:**500.

KEYNES, R. D., and E. ROJAS. 1974. Kinetics and steady state propertis of the charged system controlling sodium conductance in the squid giant axons. J. Physiol. *(Lond.).* **233:**393.

LEVITAN, E., and Y. PALTI. 1975. Dipole moment, enthalpy and entropy changes of Hodgkin-Huxley type kinetic units. *Biophys. J.* **15:**239.

MATSUMOTO, N., I. INOUE, and U. KISHIMOTO. 1970. The electrical impedance of the squid axon membrane measured between internal and external electrodes. *Jpn. J. Physiol.* **20:**516.

MAURO, A. 1961. Anomalous impedance, a phenomenological property of time-variant resistance. An analytical review. *Biophys. J.* **1:**353.

MEVES, H. 1974. The effect of holding potential on the asymmetry currents in squid giant axons. *J. Physiol. (Lond.).* **243:**847–867.

MOORE, J. W., and K. S. COLE. 1963. Voltage clamp technique. *In* Physical Techniques in Biological Research, Vol. 6. W. L. Nastuk, editor. Academic Press, Inc., New York. 263.

NONNER, W., E. ROJAS, and R. STAMPFLI. 1975. Displacement currents in the node of Ranvier. Voltage and time dependence. Pfluegers Arch. *Eur. J. Physiol.* **354:**1.

SCHWAN, H. P. 1963. Determination of biological impedances. *In* Physical Techniques in Biological Research. Vol. 6. W. L. Nastuk, editor. Academic Press, Inc., New York. 323.

SCHWARZ, G. 1967. On dielectric relaxation due to chemical rate processes. *J. Phys. Chem.* **71:**4021.

TAKASHIMA, S. 1976. Membrane capacity of squid giant axon during hyper- and depolarizations. *J. Membr. Biol.* **27:**21.

TAKASHIMA, S. 1978. Frequency domain analysis of asymmetry current in squid axon membrane. *Biophys. J.* **22:**115.

TAKASHIMA, S., and H. P. SCHWAN. 1974. Passive electrical properties of squid axon membrane. *J. Membr. Biol.* **17:**51.

TAKASHIMA, S., and R. YANTORNO. 1977. Investigation of voltage dependent membrane capacity of squid giant axons. *Ann. N.Y. Acad. Sci.* **303:** 306.

TAKASHIMA, S., R. YANTORNO, and R. NOVACK. 1977. Changes in dipole moment and membrane capacitance of squid axons during excitation. *Biochim. Biophys. Acta.* **469:**74.

TAYLOR, R. E. 1965. Impedance of the squid axon membrane. *J. Cell. Comp. Physiol.* **66:**21.