BRIEF COMMUNICATION

THE REPRESENTATION OF MEMBRANE ADMITTANCE

M. W. P. STRANDBERG, *Department of Physics, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139 U.S.A.*

ABSTRACT An integral representation for the membrane admittance in terms of its known current response to a voltage step function is presented. It is demonstrated that the frequency-dependent terms in the contribution to the membrane admittance by the ion-selective conductance of the nerve membrane are proportional to the static conductances. The additional information contained in the real and imaginary parts of the membrane admittance should allow the parameters of the ion conductance to be determined. Eventually, these measurements should also give information about the electric dipole displacement currents of the conductance systems themselves, and about the metabolically supported active ion transport currents that maintain the ion concentration gradients.

INTRODUCTION

The form for the tangential electrical admittance of the membrane of the squid axon, as first derived in detail by Chandler et al. (1962), has been used in a variety of researches since then (Mauro et al., 1970; Takashima and Schwan, 1974; Takashima, 1976; Fishman et al., 1977). Since the admittance of a system may be derived directly from the known current response to a step change in potential, the admittance is independent of the representation used to describe the step function current response. The work to date is based on what is called the linearized Hodgkin-Huxley equations. I would like to point out that there is available another representation of the Hodgkin-Huxley voltage-clamp data. With this representation it is a simple calculation to determine the parameters that appear in the expression for the admittance. This alternate representation is also useful since it reveals that the conductance-dependent parameters that appear in the frequency-dependent terms of the admittance are each proportional to the static ion conductance of that ion. It is well known that the major features seen on plots of the magnitude of the admittance, or impedance, arise from the terms in the admittance contributed by the potassium channels. On the other hand, I point out that separate measurement of the real and imaginary parts of the admittance provides sufficient additional information that the conductance channel parameters for the slow and fast sodium channels, the sodium conductance, and their time constants can also be readily determined.

The simplest method to derive the admittance of a system is probably by using Duhamel's convolution theorem and the known step function current response of the system. If the current response for a step change in the transmembrane potential from V_o to $V_o + \Delta V$ is $I(t)$, then the current response for any general time variation of the transmembrane potential, $V(t) = V_o + v(t)$ is the convolution.

$$i(V,t) = i(V_o) + \int_{-\infty}^{t} \frac{dV(t')}{dt'} \left. \frac{dI(V,t-t')}{dV} \right|_{V_o} dt'. \tag{1}$$

If $v(t)$ is taken as a sinusoidally varying potential of radian frequency ω, $v_o \exp(j\omega t)$, then by definition the tangential admittance is the time-varying part of Eq. 1 divided by v_o. If one uses the Hodgkin-Huxley step response for $I(t)$ in Eq. 1, integrates, and retains first-order terms, one obtains the Chandler et al. (1962) equation. I have discussed another representation (Strandberg, 1976) which has the advantage in these calculations that the factor $I(t)$ is analytically simple in form and convenient to use in this calculation.

To explain, I have shown that the experimental data for the selective sodium ion conductance in the squid giant axon yield a representation of the conductance of the form,

$$g(V) = \frac{g_o}{1 + e^{-(E'+F')/kT} + e^{-(E''+F'')/kT}}. \tag{2}$$

After a step change in the transmembrane potential v from the resting potential V_o, the conductance change is found to be represented by Eq. 2 with $F' = 2.58\,v[\exp(-t/\tau_2) - \exp(-t/\tau_1] - [0.58v - 70\tanh(v/20.5)]\,[1 - \exp(-t/\tau_2)]$ meV, $E' = -72.2$ meV, $E'' = -207$ meV, $F'' = 6.0\,v[\exp(-t/\tau_2) - \exp(-t/\tau_1)] - [1.22\,v - 160\tanh(v/20.5)[[1 - \exp(-t/\tau_2)]$ meV, with $\tau_1 = 0.25$ ms and $\tau_2/\tau_1 = 20\exp(-v/60)$ at 6°C. The factor kT is 25 meV, and g_o is 25 mmho/cm^2. The sign convention is such that $V_o < 0$.[1]

A similar analysis of the experimental data for the potassium conductance channels in the squid giant axon yields a conductance which varies in the same form as given by Eq. 2. After a step change in membrane potential v from the resting potential V_o, the potassium conductance varies in time such that $E' = -31$ meV, $F' = 0.69v[1 - \exp(-t/\tau_k)]$ meV, $E'' = -90$ meV, $F'' = 3.6v[1 - \exp(-t/\tau_k)]$, with $\tau_k = 3.5$ ms at 6°C, and $g_o = 24$ mmho/cm^2.[2]

---

[1] These parameter values correct typographical errors that occured in a previous paper (Strandberg, 1976), pp. 42, 43, after Eq. 13). I have also added a small term in the representation so that the equation represents the Hodgkin and Huxley $m_\infty^3 h_\infty$ precisely at large departure from the resting potential.

[2] These parameters differ from those given in a previous paper. (Strandberg, 1976). The function is numerically the same. The choice between the forms is made not on the basis of which of the two better represents the Hodgkin-Huxley data, since they are equal in that respect, but on the basis of their serving as a representation for the noise in the membrane. The form I use here can be shown to be preferable in that respect. A discussion of the noise in membranes will be published later.

Since $I(V,t) = g(V,t)[V(t) - V_i]$, where V_i is the ion electrochemical potential as determined by the ion concentration gradient, then dI/dV is $g(V) + [V - V_i]\,dg/dV$. From Eq. 2 the derivative is found to be $g(V) + g(V)[V - V_i](dF''/dV)/kT$ to good approximation since the term in F'' dominates for transmembrane potentials within 30 mV of the resting potential. The integrals are trivial, and one obtains for the tangential admittance,

$$Y(\omega) = \frac{1}{R_m} + j\omega C_m + g_k(V_o) + \frac{g_k(V_o)[3.6(V_o - V_k)]}{kT(1 + j\omega\tau_k)}$$
$$+ g_{na}(V_o) + \frac{g_{na}(V_o)[6(V_o - V_{na})]}{kT(1 + j\omega\tau_1)} - \frac{g_{na}(V_o)[0.6(V_o - V_{na})]}{kT(1 + j\omega\tau_2)}. \quad (3)$$

The representation also allows one to show clearly that the frequency-dependent terms for each ion channel in the admittance are proportional to $g_i(V_o)$, the static conductance for that same ion at the DC transmembrane potential. The same factors expressed in terms of the Hodgkin-Huxley parameters would have the same numerical relationship, but the proportionality is not readily evident from the algebraic expressions for the terms.

At the resting potential, with $V_k = V_r - 12$ mV and $V_{na} = V_r + 115$ mV, $g_k = 580$ μmho/cm^2, $g_{na} = 6.3$ μmho/cm^2, and a membrane time constant $R_m C_m = 7$ ms, the numerical expression for the admittance is

$$Y(f) = \left[\frac{1}{R_m}\left(1 + j\frac{f}{24}\right) + 590 + \frac{1{,}000}{1 + j\dfrac{f}{45}} - \frac{175}{1 + j\dfrac{f}{800}} + \frac{17}{1 + j\dfrac{f}{40}}\right] \mu\text{mho/cm}^2. \quad (4)$$

In the absence of the ion-specific conductance terms the admittance magnitude has the form shown in Fig. 1 *a*. The conductance is constant as *f* approaches zero. As *f* increases above 24 Hz the membrane-distributed capacitative susceptance increases, and so the magnitude of the admittance increases as shown. With the ion conductance terms added it is evident from Fig. 1 *c* how the admittance magnitude is modified by observing the difference between Fig. 1 *c* and Fig. 1 *a*. Since the fast sodium conductance does not begin to change until much above 800 Hz, only the potassium and the relatively much smaller slow sodium conductance term vary in the frequency region below 100 Hz. It is seen that the ion channels increase the admittance as the frequency approaches zero. As the frequency increases, the potassium term decreases sufficiently to cause the admittance visibly to decrease. As the frequency is further increased, the frequency variation of the magnitude of the admittance becomes that of the distributed passive capacitative susceptance and the curve $|Y|$ of Fig. 1 *c* becomes the same as $|Y|$ of Fig. 1 *a*. The structure thus formed by the decrease in the potassium conductance appears to be an antiresonance, or a resonance on the plot of the impedance magnitude. On the other hand, the contributions of the sodium channels to the real and imagined parts of the admittance can be used to determine the sodium

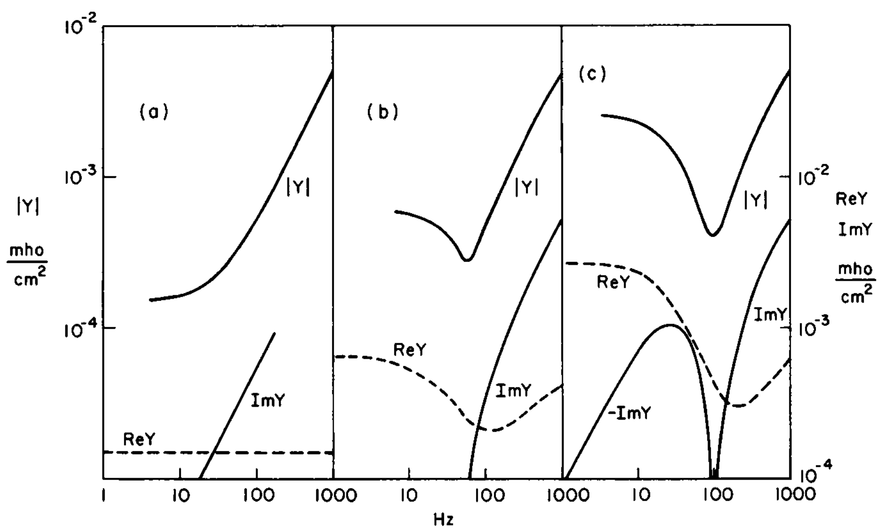

FIGURE 1 Plots of $| Y |$ using the experimental data of DeFelice et al. (1975) are shown at the top. The computed real part, *ReY*, and imaginary part, *ImY*, of the admittance are shown on the lower portion. In (*a*) the observed curve of $| Y |$ is duplicated with $C_m = 0.8\ \mu f/\text{cm}^2$ and $1/R_m = 150\ \mu\text{mho/cm}^2$. The calculation is one without ion conductance, the data being those for a transmembrane potential of −82 mV. In Fig. 1 *b* the observed $| Y |$ taken at −56 mV is indistinguishable from a calculation using Eq. 3 and the parameters suggested in the text for a membrane at 4°C, with a transmembrane potential −4 mV from resting, except that g_{na} must be increased by a factor of 5. This situation yields the curves of *ReY* and *ImY* as shown. The curve of $| Y |$ is also congruent with one calculated by using the standard parameters, with an offset of transmembrane potential of −6 mV, except that $V_k = -19$ mV from the resting potential. Only the behavior of *ReY* above 100 Hz will distinguish between these two conditions. In (*c*) the curve for the observed $| Y |$ taken at −49 mV is fit with Eq. 3 with the parameters given in the text for an offset of +4 mV, except that g_{na} must be increased by a factor of 2. This is the situation that yields the curves of *ReY* and *ImY* as shown. The curve of $| Y |$ is also congruent with that calculated with the standard parameters for an offset of +2 mV, except that $V_k = -19$ mV from the resting potential. Only the amount of rise in *ReY* above 100 Hz coming from the contribution of the sodium ion channels to the admittance will distinguish the two cases. Note that the relative offset potential between (*b*) and (*c*) used in the calculation—8 mV—agrees well with the experimental relative offset, 7 mV.

parameters. This is possible because the real and the imaginary parts of the admittance are simple sums of the contributions of each ion. This property is to be contrasted with that of the magnitude of the admittance or its phase angle, which are functions that intermingle and hence mask the contributions of the separate ion channels.

As I have pointed out elsewhere (Strandberg, 1975, 1976, 1977) when the accuracy of these measurements becomes sufficiently great, it will be necessary to consider contributions to the admittance from the displacement currents of the electric dipole moments of the conductance systems. Furthermore, if the admittance measurements are extended to very low frequencies, the order of 0.01 Hz or less, the contribution to the admittance from the metabolically supported active ion transport systems which maintain the net ion concentration gradients across the membrane will have to be considered.

This work was supported in part by a National Institutes of Health Biomedical Research Support Grant, and by a grant from The Eppley Foundation for Research, Inc.

Received for publication 19 April 1976 and in revised form 29 April 1977.

REFERENCES

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

DEFELICE, J. L., E. WANKE, and F. CONTI. 1975. Potassium and sodium current noise from squid axon membranes. *Fed. Proc.* **34**:1338.

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

MAURO, A., F. CONTI, F. DODGE, and R. SCHOR. 1970. Subthreshold behavior and phenomenological impedance of the squid giant axon. *J. Gen. Physiol.* **55**:497.

STRANDBERG, M. W. P. 1975. Contribution of active transport current to the effective membrane impedance. *J. Appl. Phys.* **46**:3654.

STRANDBERG, M. W. P. 1976. Action potential in the giant axon of *Loligo:* a physical model. *J. Theor. Biol.* **58**:33.

STRANDBERG, M. W. P. 1977. Transient polarization currents in the squid giant axon. *Biophys. J.* **19**:275.

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

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