J. Membrane Biol. 25, 209–211 (1975)

On the Measurement of Series Resistance in Giant Axon Preparations

Received 15 May 1975

Laboratory of Biophysics, IRP, NINCDS
National Institutes of Health
Department of Health, Education and Welfare
Bethesda, Maryland 20014

Dear Sir:

In a recent publication on the measurement of the resistance in series with the giant axon membrane (L. Binstock, W. J. Adelman, Jr., J. P. Senft & H. Lecar, 1975. *J. Membrane Biol.* **21**:25), the series resistance and membrane capacitance were determined from analysis of the voltage transients observed in response to overdamped current steps. Although this method eliminates errors caused by the finite rise-time of the current step, it requires numerical curve-fitting to an explicit analytic form of the input current. We wish to discuss some general methods of measuring series resistance which do not require such an explicit approximation.

The first method involves the definition of an equivalent ideal step function to replace the actual input variable, $I(t)$. For a membrane preparation having a series resistance, R_s, much less than the membrane resistance, the voltage response to an applied current is approximately

$$V(t)=R_s I(t)+C^{-1}\int_0^t I(x)\,dx. \tag{1}$$

The response of the same circuit to an ideal step of current of amplitude, I_0, applied at a delayed time, t_0, would be

$$V'(t)=R_s I_0+C^{-1} I_0(t-t_0). \tag{2}$$

We shall show that there is a particular value of t_0 for which $V'(t_0)$ is just equal to $I_0 R_s$ regardless of the form of $I(t)$, provided only that $I(t)$ is asymptotically equal to I_0 for long times.

The value of t_0 for which this is true is the value which splits the difference between the actual and ideal step currents into equal areas as shown in Fig. 1*a*; that is, area *A* equal to area *B* in the figure.

Reproduction of this article will be permitted for purposes of the United States Government.

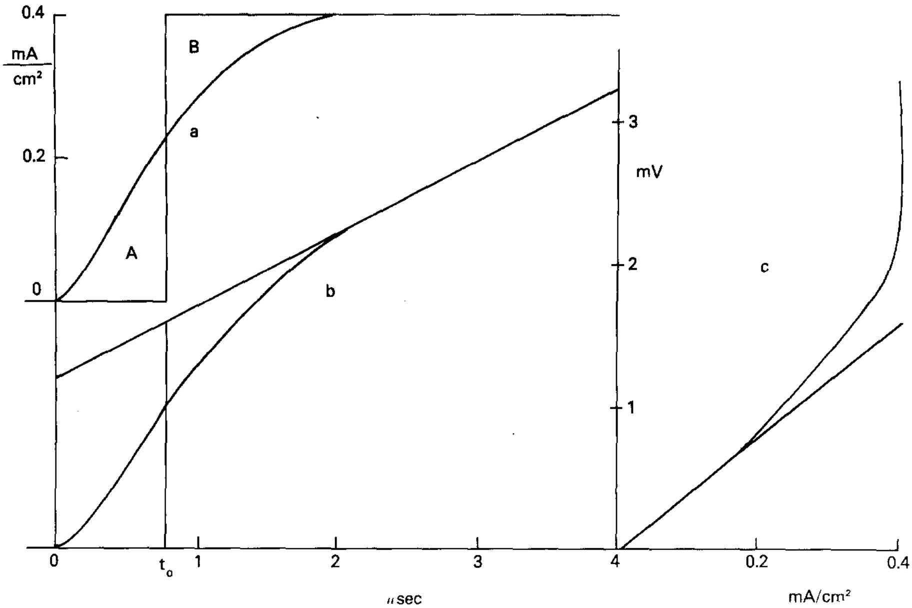

Fig. 1. Approximations from Fig. 5 of Binstock *et al.* (1975). (*a*) Input current *vs.* time showing time t_0 for equal charges A and B and an equivalent square step. (*b*) Calculated V *vs.* t showing the expected value of RI at t_0. (*c*) Parametric representation of $V(I)$ showing 10% error in R at half steady-state value of I in this particular case

The proof proceeds as follows:

$$\text{area } A = \int_0^{t_0} I(x)\, dx,$$

$$\text{area } B = \int_{t_0}^{\infty} [I_0 - I(x)]\, dx,$$

and t_0 is chosen so that $A = B$. Eq. (1) can be rewritten as:

$$V(t) = R_s I(t) + C^{-1}\left[\int_0^{t_0} I(x)\, dx + \int_{t_0}^{t} I(x)\, dx\right]. \tag{3}$$

But for $t \gg t_0$, $I(t)$ becomes asymptotically I_0 and Eq. (3) becomes

$$V_A(t) = R_s I_0 + C^{-1}\left[\int_0^{t_0} I(x)\, dx + \int_{t_0}^{t_1} I(x)\, dx + I_0(t - t_1)\right], \tag{4}$$

where $t > t_1 \gg t_0$. Eq. (4) can be rewritten as

$$V_A(t) = R_s I_0 + C^{-1}\int_0^{t_0} I(x)\, dx - C^{-1}\int_{t_0}^{t_1} [I_0 - I(x)]\, dx + C^{-1} I_0 (t - t_0). \tag{5}$$

In Eq. (5), the second term on the right is A and the third term is B. These two terms cancel for our choice of t_0, when $t_1 \to \infty$. Thus, for $t = t_0$, $V_A(t_0) = R_s I_0$ as desired. In practice, t_0 can sometimes be estimated with sufficient accuracy by judging equality of A and B by eye.

Another method for estimating R_s is to plot the current and voltage transients parametrically on an $X-Y$ oscilloscope. Plotting $I(t)$ *vs.* $V(t)$, as in Fig. 1*c*, produces a curve whose slope is I/R_s near the origin. Differentiating Eq. (1) and dividing by $\frac{dI}{dt}$, we obtain

$$\frac{dV}{dI} = R_s + C^{-1}\left(I \Big/ \frac{dI}{dt}\right), \tag{6}$$

which gives the desired relation in the limit as $I \to 0$. To estimate how close to the time origin one must measure the slope, we can consider the special case of an overdamped step as used by Binstock *et al.* (1975). For this case,

$$I(t) = I_0(1 - \exp(-t/\tau)), \tag{7}$$

and

$$\frac{dV}{dI} = R_s[1 + (\tau/R_s C)(\exp(t/\tau) - 1)]. \tag{8}$$

Typical values in a real experiment might be $\tau \sim 1$ μsec and $R_s C \sim 5$ μsec. For these values the slope would be in error by 34% after 1 μsec. Thus, the requirements for a practical $X-Y$ plot may be too stringent.

A more conventional stimulus for an $X-Y$ plot would be a current ramp which can be calculated by letting $t \ll \tau$ in Eq. (6) so that

$$I = I_0 t/\tau$$

and

$$\frac{dV}{dI} = R_s(1 + (\tau/R_s C)(I(t)/I_0)).$$

Here the error is seen to vary inversely with the ramp slope, I_0/τ.

In this note we have not considered the problems which arise when the series element is not a pure resistance or the membrane capacitance has dielectric loss. These situations are not amenable to rough and ready measurements.

K. S. Cole
H. Lecar
Laboratory of Biophysics
National Institutes of Health
Bethesda, Maryland 20014