Non-Linear Current-Potential Relations in an Axon Membrane

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ABSTRACT The membrane current density, I_m, in the squid giant axon has been calculated from the measured external current applied to the axon, I_0, by the equation

$$I_m = \frac{r_1^2}{4(r_1 + r_2)} I_0 \frac{dI_0}{dV_m}$$

where V_m is the membrane potential under the current electrode and r_1 and r_2 are the external and internal longitudinal resistances. The original derivation of this equation included in one step an assumption of a linear relation between I_m and V_m. It is shown that the same equation can be obtained without this restricting assumption.

In an investigation of the membrane potential of the squid giant axon during current flow (1), the variation of the steady state membrane potential, V_m, under a short polarizing electrode was measured as a function of the total polarizing current, I_0. For small values of I_0, the resistance of a unit length of axon membrane, r_4, was computed by the usual equation for a uniform cable,

$$r_4 = \frac{4(r_1 + r_2)V_m^2}{r_1^2 I_0^2} \tag{1}$$

where r_1 and r_2 are the resistances for a unit length of the external medium and of the axoplasm, respectively. For larger values of I_0, V_m was no longer proportional to it and r_4 was replaced by a non-linear relation between V_m and the corresponding membrane current density calculated by

$$I_m = \frac{r_1^2}{4(r_1 + r_2)} \cdot I_0 \cdot \frac{dI_0}{dV_m} \tag{2}$$

With the subsequent advent and use of the Ling-Gerard (2) micropipette electrodes for both polarization currents and membrane potentials, such an analysis was not restricted to the squid axon. However, Professor A. L.

Hodgkin (3) and the author realized some years ago that the correctness of the above equation was quite undeserved because an assumption of linearity was made when Equation 3 was substituted in Equation 5 of the original derivation.[1] It seems appropriate to offer a less objectionable basis for this rather useful relation.

For any outside and inside longitudinal currents, I_1 and I_2

$$\frac{dV_m}{dx} = r_1 I_1 - r_2 I_2 \tag{3}$$

where x is distance along the axon. Then, since $I_m = dI_1/dx = -dI_2/dx$,

$$\frac{d^2V_m}{dx^2} = (r_1 + r_2)I_m \tag{4}$$

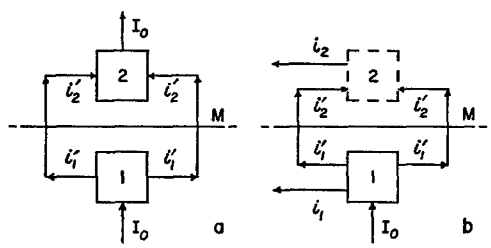

FIGURE 1. Schematic current flow across membrane M. (a) between external, 1, and internal, 2, electrodes and (b) between external electrode, 1, virtual electrode, 2, and remote external electrode.

which may be rewritten

$$\frac{d}{dx}\left(\frac{dV_m}{dx}\right) = \frac{dV_m}{dx} \cdot \frac{d}{dV_m}\left(\frac{dV_m}{dx}\right) = (r_1 + r_2)I_m \tag{5}$$ [2]

Consider first the case of a current flow between two short electrodes, 1 and 2 of Fig. 1 a, outside and inside an axon at $x = 0$. Here i'_1 and i'_2 are the integrated membrane currents on each side of the external and internal electrodes. At the electrode position $i'_1 + i'_2 = 0$ and $I_0 = 2i'_1$, so by equation (3)

$$\frac{dV_m}{dx} = (r_1 + r_2)i'_1 = \frac{r_1 + r_2}{2} I_0. \tag{6}$$

Then by equation (5)

$$I_m = \frac{r_1 + r_2}{4} I_0 \frac{dI_0}{dV_m}. \tag{7}$$

[1] "A correct result based on correct logic is commendable, an incorrect result based on incorrect logic is just, but a correct result based on incorrect logic is criminal," Wallie A. Hurwitz, *circa* 1924.
[2] Dr. Richard FitzHugh has shown that this expression is true but not obviously so.

Similarly for an axon in an extended volume of external conductor, in which r_1 and i_1 may be negligible,

$$I_m = \frac{r_2}{4} I_0 \frac{dI_0}{dV_m}. \tag{8}$$

In the original problem, the internal current electrode at $x = 0$ becomes a potential electrode and the current flow is to a remote external electrode. Since the longitudinal resistances are assumed linear, the interpolar currents may be separated into the components shown in Fig. 1 *b*. The components i'_1 flow from the external electrode, 1, to cross the membrane and become the components i'_2 at the virtual internal electrode, 2, as above. The components i_1 and i_2 are always external and internal, respectively, so that $r_1 i_1 = r_2 i_2$.

Then $I_0 = I_1 + I_2 = i_1 + i'_1 + i_2 + i'_2$

$$= i_1 + i_2 = \frac{r_1 + r_2}{r_2} i_1$$

since $i'_1 + i'_2 = 0$, and from equation (3), similarly,

$$\frac{dV_m}{dx} = r_1(i_1 + i'_1) - r_2(i_2 + i'_2)$$

$$= (r_1 + r_2)i'_1$$

But with $i_2 = 2i'_2 = 2i'_1$,

$$I_0 = \frac{r_2}{r_1 + r_2} I_0 + 2i'_1 ; i'_1 = \frac{r_1}{2(r_1 + r_2)} I_0$$

and

$$\frac{dV_m}{dx} = \frac{r_1}{2} I_0 .$$

Consequently by equation (5),

$$I_m = \frac{r_1^2}{4(r_1 + r_2)} I_0 \frac{dI_0}{dV_m} \tag{2}$$

which is the same as the expression obtained and used before.

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