# POTASSIUM ION CURRENT IN THE SQUID GIANT AXON: DYNAMIC CHARACTERISTIC

KENNETH S. COLE *and* JOHN W. MOORE

*From the National Institutes of Health, Bethesda, Maryland, and the Marine Biological Laboratory, Woods Hole, Massachusetts*

ABSTRACT Measurements of the potassium current in the squid axon membrane have been made, after changes of the membrane potential to the sodium potential of Hodgkin and Huxley (HH), from near the resting potential, from depolarizations of various durations and amplitudes, and from hyperpolarizations of up to 150 mv. The potassium currents $I$ given by

$$I = I_\infty\{1 - \exp[-(t + t_0)/\tau]\}^{25},$$

where $t_0$ is determined by the initial conditions, represent the new data and approximate the HH functions in the regions for which they are adequate. A corresponding modification for the sodium current does not appear necessary. The results support the HH assumptions of the independence of the potassium and sodium currents, the dependence of the potassium current upon a single parameter determined by the membrane potential, and the expression of this parameter by a first order differential equation, and, although the results drastically modify the analytical expressions, they very considerably extend the range of apparent validity of these assumptions. The delay in the potassium current after severe hyperpolarization is used to estimate a potassium ion mobility in the membrane as $10^{-5}$ of its value in aqueous solutions.

Hodgkin and Huxley, (HH I)[1] have separated the current flow across the squid axon membrane, after a change of the membrane potential, into two principal components, a sodium ion current, $I_{Na}$, and a potassium ion current, $I_K$. Each of these currents was expressed (HH II) in terms of the respective conductances $g_{Na}$ and $g_K$, and the membrane potentials at which the respective currents were zero, the sodium and potassium potential $E_{Na}$ and $E_K$. The total current is

$$I = I_{Na} + I_K = g_{Na}(V - E_{Na}) + g_K(V - E_K),$$

where $V$ is the membrane potential difference and the leakage current $I_L$ is ignored for the present.

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[1] Hodgkin and Huxley will be referred to by HH and their four papers 1952*a, b, c, d* by I, II, III, IV.

As a part of our program to make a critical survey and evaluation of the HH formulations of the properties of the squid giant axon membrane, we have investigated the time course of the potassium ion current $I_K$. Instead of following the extensive HH experimental and analytical procedures based on choline substitution for external sodium, we have restricted ourselves to measurements made at or near the sodium potential. At $V = E_{Na}$, $I_{Na} = 0$, and $I = I_K = g_K (V - E_K)$ no matter what the value of $g_{Na}$.

Hodgkin and Huxley (HH IV) expressed their potassium conductance data by $g_K = \bar{g}_K n^4$ where $\bar{g}_K$ is a constant and $n$ is a parameter, something like a probability, varying from zero to unity and given by the differential equation

$$dn/dt = (n_\infty - n)/\tau \tag{1}$$

$n_\infty$ and $\tau$ are defined empirically as functions of the membrane potential with $n_\infty$ as the steady state value and $\tau$ as a time constant of the approach to that value.

If at $t = 0$, $n = n_0$ and for $t > 0$, $V = E_{Na}$ then $n = n_\infty - (n_\infty - n_0) \exp(-t/\tau)$ is the appropriate solution of equation (1) with $n_\infty$ as the steady state value. When $n_0 = 0$

$$\begin{aligned} I &= \bar{g}_K n_\infty^4 [1 - \exp(-t/\tau)]^4 (V - E_K) \\ &= I_\infty [1 - \exp(-t/\tau)]^4 \end{aligned} \tag{2}.$$

For $0 < n_0 < 1$,

$$\begin{aligned} n &= n_\infty \left[ 1 - \frac{n_\infty - n_0}{n_\infty} \exp(-t/\tau) \right] \\ &= n_\infty [1 - \exp(-t_0/\tau) \exp(-t/\tau)] \\ &= n_\infty \{1 - \exp[-(t + t_0)/\tau]\} \end{aligned} \tag{3},$$

where $t_0 = \tau \ln[n_\infty/(n_\infty - n_0)]$

is the time in which $n$ would have risen from zero to the initial value of $n_0$ at $t = 0$. The initial condition, $n_0$, is usually unimportant for an equivalent delay of $t_0 < 0.1\ \tau$ and certainly so for $t_0 < 0.01\ \tau$. The corresponding values of $n_0$, which the HH axon reaches for hyperpolarizations of less than 20 and 50 mv, are then $n_0 < 0.1\ n_\infty$ and $n_0 < 0.01\ n_\infty$ respectively.

The experimental work has been done in three phases. In the first $I$ has been measured after a step change of the membrane potential from near the resting potential to the sodium potential and compared with equation (2) for several environmental conditions. In the second phase, the step to $E_{Na}$ was made after initial depolarizations of various amplitudes and durations. $I$ was compared with equation (3), as suggested by Dr. Richard FitzHugh, to test the assumption that it was the function of the single parameter, $n$, described by a first order differential equation. The third phase was an extension of the second, in which continuous or comparatively long hyperpolarization was applied to the membrane before the test steps to $E_{Na}$. Some observations on the effect of initial hyperpolarization on the ion cur-

rents during potential steps to other than the sodium potential are included as a fourth phase.

The results of the first two phases are much as had been anticipated. Those of the third phase require such a considerable modification and extension of the HH formulation that it becomes essentially a new expression for the potassium current. The need of a similar alteration for the sodium current is not apparent.

## EXPERIMENTAL

The giant axon in the hindmost stellar nerve of the squid, *Loligo pealii,* has been used throughout as shown schematically in Fig. 1 and discussed and described in detail by Cole and Moore (1960) and Moore and Cole (1961). The membrane potential is measured

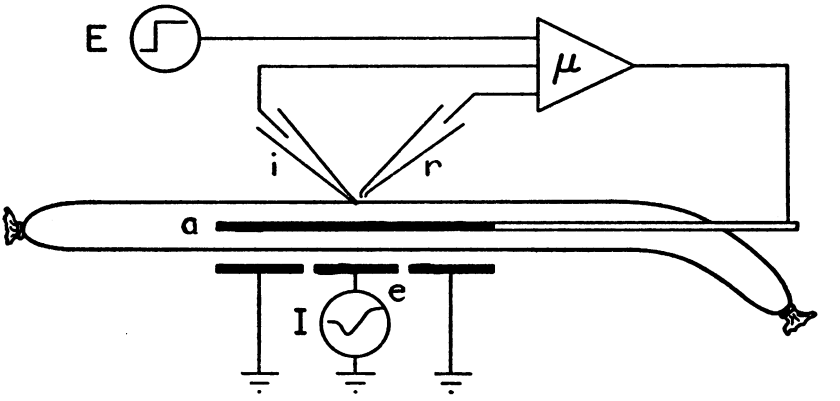


FIGURE 1 Diagram of method for control of the membrane potential. The potential is measured between the micropipette, internal, and capillary, external, electrodes, *i* and *r*. The electronic control system, $\mu$, provides the current between the internal axial and external electrodes, *a* and *e*, needed for the membrane potential to follow the command potential, *E*. The membrane current, *I*, is measured for a length of axon corresponding to the guarded central electrode, *e*. (Reproduced from Moore, 1959*b*, with permission.)

between the micropipette internal and capillary external potential electrodes, *i* and *r*, and controlled by the electronic system $\mu$. This system applies such a potential to the internal axial wire, *a*, as is necessary to force the membrane potential to follow the command potential, *E*, within tens of microseconds and a few millivolts. The membrane potential is usually held at a constant value somewhat more negative than the resting potential and the experimental steps are applied from this holding potential $E_H$. The membrane current, *I*, is measured over the length of axon determined by the central, guarded, external electrode, *e*.

## RESULTS

1. *Initial Resting Potential.* The records of this first phase were made in 1956 with the assistance of Professor Ulrich Franck and subsequently mostly measured and analyzed by him. The four axons were held hyperpolarized by several

millivolts from the resting potentials and steps were applied to bring the potential to that value, $E_{Na}$, at which no initial sodium current was seen. Twenty-seven current records were made at sodium potentials which were varied from 0 to +50 mv, at temperatures from 5°C to 20°C, and with a few changes of external Ca and K concentrations. The initial current was subtracted and the steady state current, $I_\infty$, was extrapolated to approximately correct for any slow "droop" after the maximum. These data, $I$, from individual records were plotted as log $I$ *versus* log $t$ and superposed as shown in Fig. 2.

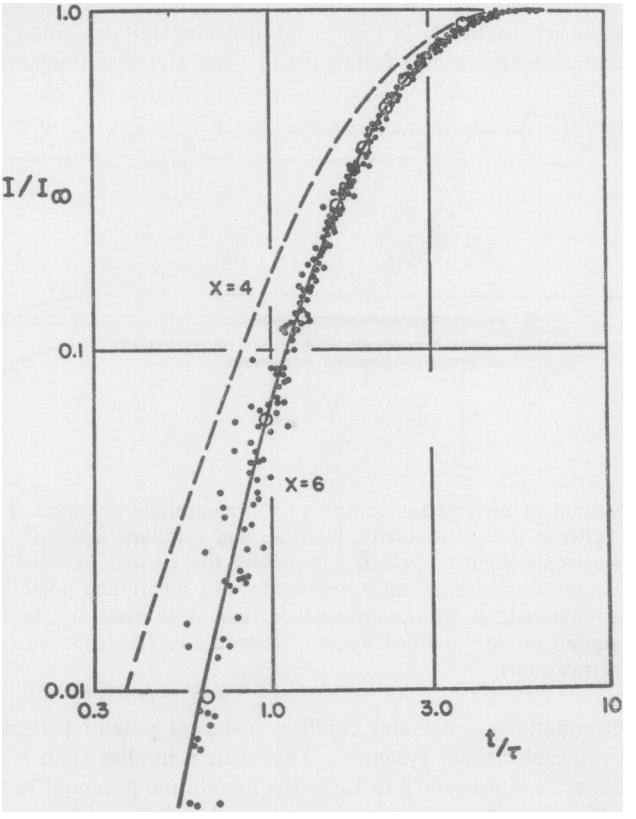


FIGURE 2 Potassium current, $I$, as a function of time, $t$, after changes from near resting to the sodium potential, with $I_\infty$ as the steady state current and $\tau$ the time constant of the process. The points are from four 1956 axons and the circles are from HH IV, Fig. 3. The solid line is given by equation (4) and the broken line by equation (2).

The data of Fig. 2 are rather well represented by the solid curve

$$I = I_\infty[1 - \exp(-t/\tau)]^6 \quad (4)$$

but it was often necessary to take the origin for time to be somewhat different from that at which the potential was actually changed. Thus these data have been fitted

by an equation, such as equation (3), involving $t_0$, and so depending upon the initial condition, $n_0$. The variations of $n_0$ are attributed to differences between the axons and the holding potentials, $E_H$, used for them.

As HH suggested might be the case and is illustrated by points from their data on Fig. 2, this higher power of the time function is clearly more satisfactory than the broken line which is the fourth power they found more convenient to use. We see no basis to disagree with the HH conclusion that the difference between the exponents of 6 and 4 is not particularly important, so this phase is essentially a confirmation of their analysis.

2. *Initial Depolarization.* Potential steps to $E_{Na}$ were made in this second phase either at successive times after the start of preliminary depolarizing steps or at fixed times after the start of preliminary steps having various amplitudes. Examples of the membrane current patterns for both procedures are shown in Figs. 3*a* and 4*a* and the corresponding superpositions of the currents at $E_{Na}$ by translations on the time axis are given as Figs. 3*b* and 4*b*. These superpositions are quite good except for the capacity transients and the early excess outward currents. The latter were often smaller than those in Figs. 3*b* and 4*b* but were also sometimes larger.

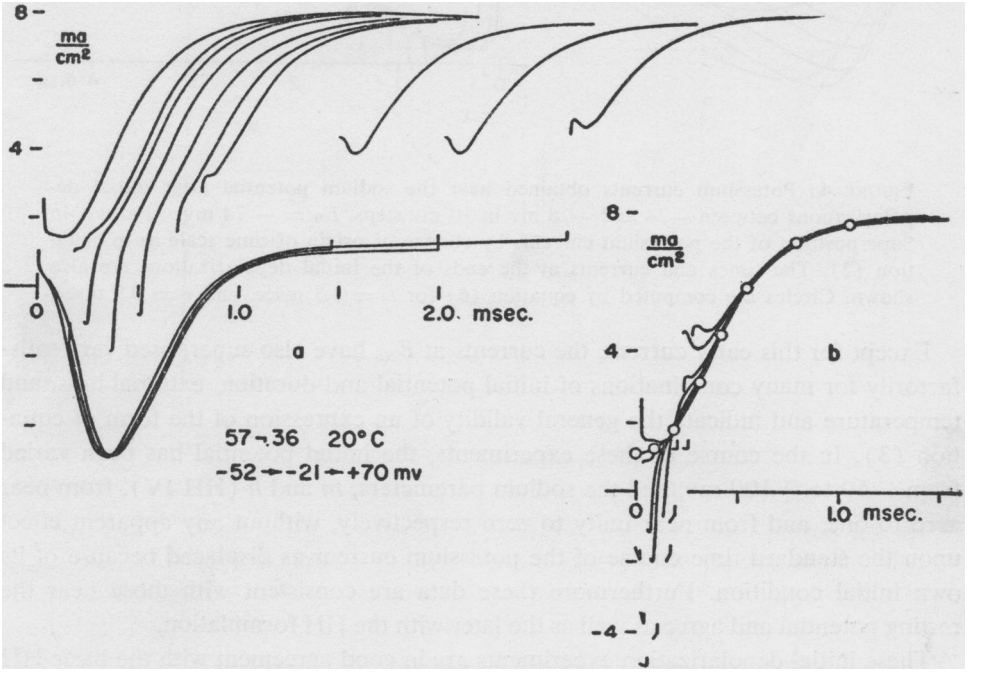


FIGURE 3*a* Potassium currents obtained at 70 mv, after various durations of an initial depolarization to −21 mv from a holding potential of −52 mv. FIGURE 3*b* Superposition of the potassium currents by changes of origin of time scale as in equation (3). The times and currents at the ends of the initial depolarizations are also shown. Circles are computed by equation (6) for $t_0 = 0.29$ msec. and $\tau = 0.2$ msec.

A small hyperpolarization was routinely used for $E_H$ in these experiments and the end of the capacity transient, a small sodium current, and the beginning of the potassium current often overlapped. This led to the choice of a value for the sodium potential which was afterwards found to be somewhat too high. These sodium currents are quite clear and constant at the beginning of the three slowest test step responses of Fig. 4*a*. Their increase and decrease with increasing initial depolarizations, as seen in Fig. 4*b*, is much as is to be expected from the corresponding changes of the sodium conductance $g_{Na}$.

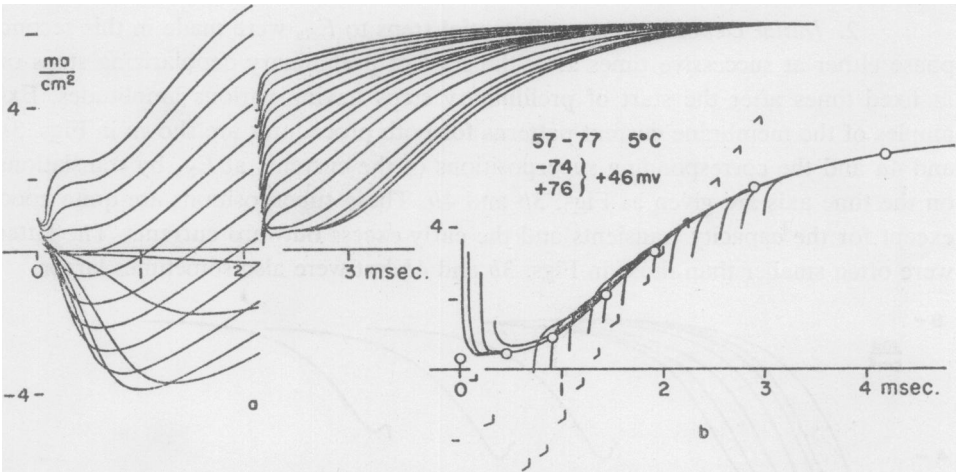


FIGURE 4*a* Potassium currents obtained near the sodium potential after initial depolarizations between —74 and +76 mv in 10 mv steps. $E_H = -74$ mv. FIGURE 4*b* Superposition of the potassium currents by change of origin of time scale as in equation (3). The times and currents at the ends of the initial depolarizations are also shown. Circles are computed by equation (6) for $t_0 = 1.3$ msec. and $\tau = 0.9$ msec.

Except for this early current, the currents at $E_{Na}$ have also superposed very satisfactorily for many combinations of initial potential and duration, external ions, and temperature and indicate the general validity of an expression of the form of equation (3). In the course of these experiments, the initial potential has been varied from —50 to +100 mv, and the sodium parameters, $m$ and $h$ (HH IV), from near zero to one, and from near unity to zero respectively, without any apparent effect upon the standard time course of the potassium current as displaced because of its own initial condition. Furthermore these data are consistent with those near the resting potential and agree as well as the later with the HH formulation.

These initial depolarization experiments are in good agreement with the basic HH assumption that the potassium current is a function of a single variable, such as $n$. Although the evidence is not clean cut, the explanation of the anomalies seems both reasonable and probable.

3. *Initial Hyperpolarization.* The initial hyperpolarizations were first ap-

plied continuously between the test steps to $E_{Na}$ and later as prepulses of a few milliseconds duration. They were varied up to —210 or —150 mv relative to the resting potentials in the neighborhood of —60 mv. Occasionally the current necessary to maintain the highest hyperpolarization would increase until a membrane breakdown or the removal of the potential.

A typical series of membrane current records is shown in Fig. 5*a* for 3 msec. prepulse potentials up to —212 mv. The initial capacity transients increase regularly but merge into a slower component, after the hyperpolarizations at —162 and

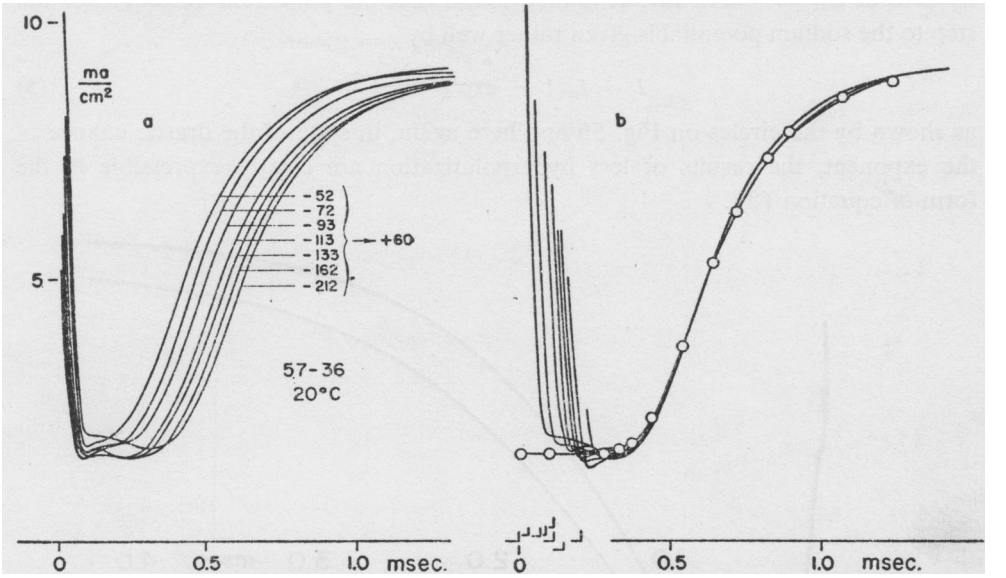


FIGURE 5*a* Potassium currents obtained near the sodium potential after 3 msec. hyperpolarizations at the indicated potentials. FIGURE 5*b* Superposition of the potassium currents by change of origin of time scale as in equation (3). The ends of the initial hyperpolarizations are also shown. Circles are computed by equation (5) for $\tau = 0.18$ msec.

—212 mv, that may be an indication of an incipient membrane breakdown. The initial sodium currents here appear even more clearly than in Figs. 3*a* and 4*a* because of the delayed onset of $I$. It is to be noticed that the delay, shape, and amplitude of this sodium current are not obviously and consistently affected by the amplitude of the hyperpolarization preceding the pulse.

As was done for the initial depolarizations, the current curves of Fig. 5*a* have been superposed by translations along the time axis as shown in Fig. 5*b*. Here the coincidence is better than in the previous examples probably because the interference of the sodium transient is not so confusing. Consequently these currents also can be expressed as a function of $t_0 + t$ where $t_0$ is again some function of the initial hyperpolarization. The currents are, however, delayed far too much to allow

the use of the HH fourth power function or even the sixth power as found above. To the extent that equation (4) is considered an adequate expression of the potassium current after a step change from near the resting potential to the sodium potential, the assumption that $n_0 = 0$ might be justified. But if this is true there should be no further change of $n_0$ or the current curve on hyperpolarization—quite contrary to these experimental findings. Even though the assumption of $n_0 = 0$ near the resting potential is not justified, we may, however, try again and assume that there is no potassium current flow at the maximum hyperpolarization used, so $n_0 = 0$ at $E_H = -212$ mv. It is then found that the potassium current after the step to the sodium potential is given rather well by

$$I = I_\infty[1 - \exp(-t/\tau)]^{25} \tag{5}$$

as shown by the circles on Fig. 5*b* and here again, in spite of the drastic change of the exponent, the results of less hyperpolarization are clearly expressible in the form of equation (3).

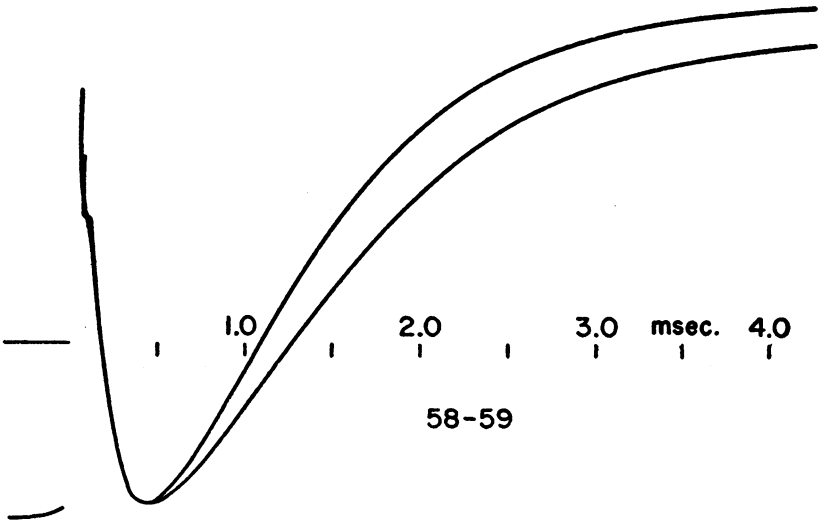


FIGURE 6 Superposition of two ionic currents records at $V = +5$ mv after initial 10 msec. hyperpolarizatons at −75 and −175 mv.

4. The principal phases above have the limitation that they depend upon measurements at rather few values of the sodium potential. It is therefore possible that such observations and conclusions are only valid with little or no sodium current. They can furthermore give but slight indication of the characteristics of the sodium current—particularly as influenced by hyperpolarization.

For other purposes, records have been made of the ionic current at potentials below $E_{Na}$ after various initial hyperpolarizations. The peak inward current attains a maximum, saturation, value, corresponding to $h = 1$ in the HH formulation, for

initial hyperpolarizations at −80 mv or more. Fig. 6 is typical of many other records in showing the superposition after two different initial hyperpolarizations that are both more than the value for inward peak current saturation. The identity of currents up to the time of the inward maximum strongly suggests that the HH sodium "on" process, described by $m$, is not affected by such initial hyperpolarization and is also indicative of a similar lack of effect on the sodium "off," given by $h$. However, the delay in current between the inward maximum and the outward steady state after increased initial hyperpolarization is most simply and consistently —if not uniquely—explained as an effect on only the potassium component, just as found at the sodium potential. The fact that such a "shift" does not appear before the maximum is consistent with other indications that, beyond saturation hyperpolarization, the potassium current is not appreciable until after the sodium maximum. It is also observed, in such records as those of Fig. 5*a*, that the small early sodium currents are very similar for all initial hyperpolarizations and are certainly not altered by an amount at all comparable to that found in the later potassium currents. The same appears to be true as seen after the small initial depolarizations of Fig. 4*a*. Both of these types of experiments support at least a tentative conclusion that, above saturation, the sodium currents do not depend upon initial hyperpolarization. Then, with consistent reservations, the delay of potassium current during the sodium "off" process is evidence that this delay can take place in the presence of a sodium current—although the quantitative details have not been investigated.

## DISCUSSION

It now becomes quite evident that the regularity of the early results, given in the first phase, is probably most significant as an indication of a consistency of experimental technique combined with the ability of small delays to compensate for the differences. Thus the approximation to a sixth power function is not particularly important. Fig. 5*b* shows that an equation of the form of equation (3) will allow quite an adequate expression of the data of Fig. 5*a* by a variation of the delay time, $t_0$. It is also found that the same equation is applicable to the experimental conditions of Figs. 3 and 4 as shown by the agreement of the calculated circles with the data in Figs. 3*b* and 4*b*.

In view of its wide application, the extension of equation (5) has been investigated, mostly numerically, as a substitute for the HH counterpart, equation (2) and the expression for our earlier data, equation (4). In Fig. 7*a*, the equation

$$I = I_\infty\{1 - \exp[-(t + t_0)/\tau]\}^{25} \tag{6}$$

as shown by the curves, with appropriate values of $t_0$, has been compared with

$$I = I_\infty[1 - \exp(-t/\tau_z)]^z \tag{7}$$

for $x = 4, 6, 10, 15$ as given by the circles. The values of $t_0/\tau$, $n_0/n_\infty$, and $\tau/\tau_x$, given in Table I, were chosen to give the same values of $t$ and $dI/dt$ at $I = 0.5\ I_\infty$.

The maximum differences of a few per cent of $I_\infty$ between equations (6) and (7) should be detectable but usually not obvious in experimental records. The qualitative difference between the time courses of the potassium current during the return to the resting potential after a depolarization seems likely to have been an important consideration in the choice of the original HH analytical formulation for this current. So for repolarization,

$$I = I_\infty \left[ \frac{n_0}{n_\infty} + \left(1 - \frac{n_0}{n_\infty}\right) \exp\left(-t/\tau\right) \right]^{25} \tag{8}$$

has been compared with

$$I = I_\infty \exp\left(-xt/\tau\right) \tag{9}$$

for $x = 4$ and 6 where now $n = n_\infty$ and $I = I_\infty$ at $t = 0$, are the initial conditions for equation (8) at the start of the repolarization to $n_0$. The currents given by equation (9) initially decrease somewhat more rapidly and finally more slowly than those from equation (8) for $\tau/\tau_x$ from Table I. But the two expressions agree throughout, as indicated in Fig. 7*b*, to within 5 per cent of the initial value and the depolarizations and repolarizations for $x = 4$ and 6 are to be compared with Fig. 2

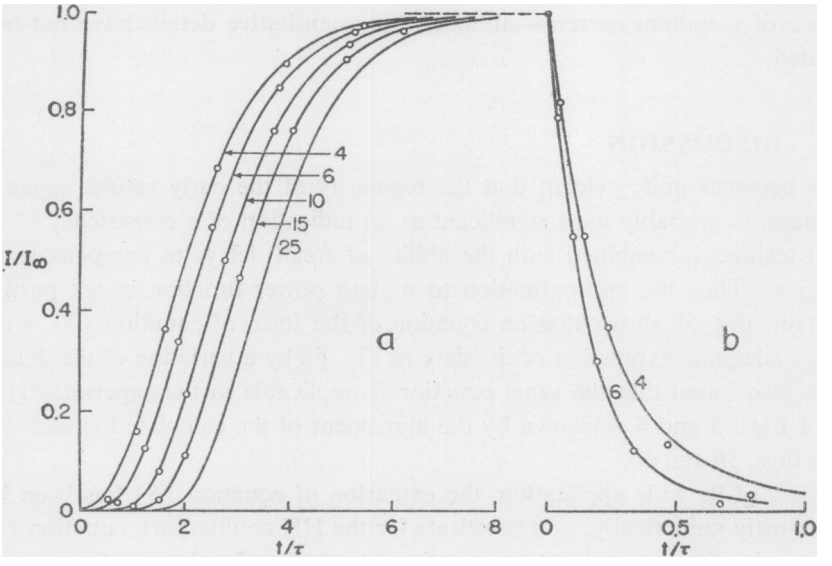


FIGURE 7a Potassium currents after depolarization computed by equation (6), solid lines where $t_0$ and $\tau$ have been adjusted to approximate equation (7). Circles are computed values of equation (7) for the exponents 4, 6, 10, and 15. FIGURE 7*b* Potassium currents after repolarization to initial conditions of Fig. 7*a* for exponents 4 and 6. The solid lines are computed by equation (8) and the circles by equation (9). Note change of scale for $t/\tau$ between Figs. 7*a* and 7*b*.

of HH IV. It seems unlikely that such experiments would produce decisive evidence against the use of equations (6) or (8).

The range of experimental conditions in the present work is somewhat limited but the ability of the new formulation to approximate the HH functions in their range of experimental success leaves little doubt that equation (6) will be equally valid in the ranges not here tested. It is true however that for general use, new values of $n_\infty$ as a function of $V$ will be required while from Table I the values of $\tau$

TABLE I

| $x$ | 4 | 6 | 10 | 15 | 25 |
|---|---|---|---|---|---|
| $t_0/\tau$ | 1.63 | 1.28 | 0.85 | 0.47 | 0 |
| $n_0/n_\infty$ | 0.804 | 0.722 | 0.572 | 0.375 | 0 |
| $\tau/\tau_x$ | 0.928 | 0.955 | 0.977 | 0.988 | 1 |

will apparently need but little change. Some other modifications of the HH axon functions are anticipated in order to adapt them to the average of more recent data and this partial revision has not been undertaken.

The prospect of having to use a high power, such as 25 or above, for hand, analog, or digital computation makes such computations seem even more forbidding than with the original fourth power (HH IV; Cole, Antosiewicz, and Rabinowitz, 1955; FitzHugh and Antosiewicz, 1959). However, the approximate validity of the latter for depolarizations from the resting potential seems to justify this simplification as long as excessive hyperpolarizations are not encountered.

There is no reason to expect that the steady state conductance will ever become actually zero for any finite hyperpolarization so that this assumption should not be made for the —212 mv prepulse. Instead an exponent somewhat higher than 25 should be used with an appropriate delay at the highest hyperpolarization available and would probably be as satisfactory otherwise.

Since the number of other and equally satisfactory empirical equations is probably limited only by the ingenuity and patience and by the number of their inventors, this particular formulation cannot now be expected to have a unique significance, except perhaps that it is singularly pliable. Some years ago, for example, we found expressions of the form

$$\frac{1}{1 + (t/\tau_x)^{-y}}$$

and their hyperbolic tangent equivalents to be quite useful. With $y = 4$ these forms represent the early data of Fig. 2 a little better than does equation (4) and with $y = 5$ they are practically indistinguishable from Fig. 5*b* and equation (5). Thus a theory of ion permeability will probably be successful in explaining a vast amount of data to the extent that it approximates one of these equivalent forms.

Although the HH suggestion that $n$ is the probability for one of four sites to be available is conceptually intriguing and the present modification to 25 may be more

indicative of a statistical distribution, there is no basis for such a comparison without a more detailed mechanism for either.

The ability of the equations

$$dn/dt = (n_\infty - n)/\tau; \qquad I = \bar{g}_K n^{25}(V - E_K)$$

to represent the data over almost the entire attainable ranges of $V$, $n$, $m$, $h$ is very impressive. The extension of the dependence of $n_\infty$ and $\tau$ upon $V$—and $V$ alone—adds further weight to this already highly significant HH contribution. The unique $I/I_\infty$ *versus* $t/\tau$ curve, where $I_\infty$ and $\tau$ are completely determined by the membrane potential, becomes the more attractive as it is found that any and all initial conditions (except from a positive prepotential to one less positive) are shown as a displacement of this one curve along the time axis. As has been emphasized to us by Dr. FitzHugh, these results are highly indicative of a single variable of state and will follow if this variable is given by a first order differential equation. Less simple differential equations are not, however, excluded.

The time displacement approach may be of considerable theoretical significance but leads even now to some interesting qualitative speculations about physical mechanisms.

One may like to think that the membrane contains fewer and fewer potassium ions as it is increasingly hyperpolarized until it is nearly empty at perhaps a few hundred millivolts negative inside. Then on depolarization to 50 mv, positive inside, a front of ions advances across the membrane to appear as the beginning of a current after the time needed for the transit. If indeed the front was very sharp as it left the inner boundary of the membrane it would soon broaden by the diffusion superposed on the translation outward to give the gradual, delayed rise much as seen in Fig. 5*a*. For a lesser hyperpolarization the initial concentration would be higher at each point in the membrane and the gradient less steep. As a consequence the front would reach the outside sooner but might have much the same form because the lower initial gradient would also be spread less by diffusion in the shorter transit time. Intuitively satisfactory as this picture may seem, it cannot be confidently advanced to explain the observed near identity of current from extreme hyperpolarization to near $E_{Na}$ until a supporting analysis is available.

It may, however, be assumed that the membrane is swept rather clear of ions at the highest hyperpolarization and that the time to half maximum current at the sodium potential approaches the transit time across the membrane. For a nominal membrane thickness of 100A, the average velocity is then $10^{-6}/0.6 \cdot 10^{-3}$ or $1.7 \cdot 10^{-3}$ cm/sec. The effective potential is $E_{Na} - E_K$ and the corresponding field is $0.12/10^{-6} = 1.2 \cdot 10^5$ v/cm. The mobility of $1.4 \cdot 10^{-8}$ cm/sec. per v/cm is thus about $2 \cdot 10^{-5}$ times the normal potassium ion mobility in water, $8 \cdot 10^{-4}$ in the same units. This is to be compared with an earlier estimate of $10^{-5}$ obtained by a somewhat different approach (Cole, 1947; 1949). However, the rate of rise observed is about a tenth that expected by diffusion on this basis.

Another possibility may be that the electric and concentration gradients combine in the membrane in such a way as to quickly form a characteristic concentration profile near the inner boundary. This might then be transmitted without change of form across the membrane, much as a boundary may move unchanged over long distances in a transference number determination. Appropriate analyses for such a steady state should be reasonably possible.

Apparent difficulties with these two suggestions arise from the fact that they are based on the Planck liquid junction model (1890). Even with the improvements of Goldman (1943), Teorell (1951), and Schlögl (1954) the steady state *V versus I* characteristic of the membrane should show a low ion rectification ratio equal to the ion concentration ratio across the membrane. Early measurements (Cole and Curtis, 1941) of the squid axon rectification were somewhat larger than the ion ratio and more recent ones (Cole and Moore, 1960) are considerably larger while there is no limiting value for the rectification ratio in the HH formulation. But the decisive evidence is from the squid axon in isoosmotic KCl. In this a negative resistance limb was found in the quasi steady state *V versus I* characteristic which does not appear in liquid junction theory but is as predicted by the HH empirical potassium conductance expression (Moore, 1959*a*). The possibility that such an effect may be produced by the electroosmosis factor, proposed by Teorell (1959), has not been investigated. But without some such modification, the liquid junction model should only be used with rather considerable reservations.

The constancy of current wave form also suggests a determining mechanism that is quite localized, perhaps at the inner face of the membrane, so that spatial variations along the ion path are relatively unimportant. In this case it may be somewhat more involved to have the mechanism controlled directly by the potential difference across the entire membrane. This difficulty is avoided in the pore distortion mechanism developed by Mullins (1959). Here the pores of a somewhat hyperpolarized membrane are closed enough by an electrostatic compression to block potassium ions. Upon depolarization the potassium permeability increases as the membrane relaxes to open the pores and allow these ions to pass. In his Fig. 11, Mullins gives a calculated potassium conductance curve that is quite similar to the experimental results. However, the delay is so much longer than the time of rise as to require an exponent of about 700 in place of the 25 appearing in equation (5). This difference can certainly be resolved by modification of already rather arbitrary assumptions.

Whatever may be the nature of the permeability controls, the apparent dependence of the potassium current characteristics upon potential alone—in spite of considerably varied sodium phenomena—gives additional support to the HH assumption that the potassium and sodium controls are quite independent of each other. It is of more than passing interest that evidence has not appeared to indicate a corresponding behavior of the sodium current in the range of considerable hyperpolarization.

In addition to the specific mention made of Professor Franck and Dr. FitzHugh, we wish to express our appreciation to them and to Drs. R. E. Taylor, W. J. Adelman, Jr., J. J. Chang, and Mr. J. H. Gebhart for their experimental, theoretical, and editorial assistance.

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