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# Keitaro Kiyosawa: Beyond the Hodgkin-Huxley phenomenological analysis for excitation in squid axons: From studies on excitation in characean internodal cells

Excitation phenomena observed in animal nerves have been studied mainly using squid axons. Phenomenological analysis and explanation of the excitation in squid axons was done by Hodgkin *et al.* (1952), and Hodgkin and Huxley (1952) by a voltage clamp method. However, they were able to explain only excitation of a short duration of ca. 1 ms. Thus, these analyses are not likely to be valid for explaining excitations of slow and long duration of 1s–3s, such as that in characean internodal cells. Presented here are some important findings on excitation in characean internodal cells that contradict Hodgkin-Huxley's phenomenological analysis and equation on excitation in squid axons.

*Key Index Words: Action potential—Charophyta—electroneutrality—excitation—Hodgkin-Huxley hypothesis.*

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The extended Hodgkin-Huxley hypothesis on excitation in nerves is composed of the following assumptions and explanations. The electrical membrane current I is composed of that carried by ions, $I_i$, and flowing to charge up the electrical membrane capacitance, $C_M$, i.e., $I=I_i+C_M$ (dV/dt). Thus, since (dV/dt)=0 under voltage clamp condition, $I=I_i$. $I_i$ is carried by an ion which creates a rapid inward current in the initial phase dut to the rapid increase in the electrical membrane conductance of the nerve cell membrane for the ion, followed by a late outward current carried by another ion due to the late, gradual increase in the electrical membrane conductance of the nerve cell membrane for the ion. However, in characean internodal cells which have much slower and longer action potential than that in nerves, the fundamental assumption that $I=I_i+C_M$ (dV/dt) does not hold. Ions which should carry the early rapid current and other ions which should carry the late, somewhat slow current in the Hodgkin-Huxley hypothesis, flow almost simultaneously across the characean cell membrane during a propagating excitation. In this review, I would like to point some important problems from the viewpoint of the electroneutrality rule in electrolyte solutions and transport phenomena of ions in and/or through synthetic membranes together with results obtained from experiments on excitation in characean internodal cells.

## I. Invalidity of the basic Hodgkin-Huxley assumption on electrical membrane current across the voltage-clamped axon plasma membrane against that across the characean cell membrane

The Hodgkin-Huxley analysis had its theoretical and experimental bases on the assumption that the total electrical current I across the cell membrane is composed of electrical current $I_i$ carried by ions (ionic current) and the electrical current which flows through a capacitance of the cell membrane $C_M$ due to the change in the electrical membrane potential dv/dt (capacity current, $C_M\frac{dV}{dt}$) (Hodgkin *et al.* 1952), that is,

$$I=I_i+C_M\frac{dV}{dt} \qquad (1)$$

Phenomenologically, this assumption is superficially reasonable because it has been shown that the cell membrane has an electrical membrane capacitance $C_M$ measured as 0.9 $\mu F\ cm^{-2}$ with the voltage clamp method (Hodgkin *et al.* 1952) and the transient electrical membrane current is observed much later (200 $\mu s$) when a short electrical pulse higher than the threshold is applied across the axonal

membrane under a voltage clamp. This electrical current should be carried by charged particles (ions), i.e., $I_i$ which is not affected by the initial electrical pulse inducing the current (Hodgkin *et al.* 1952). Since dv/dt=0 under a voltage clamp, Eq. (1) becomes

$$I = I_i \tag{2}$$

Although an externally applied electrical pulse can induce an electrical current amounting to I across the axonal membrane in the initial phase, no net electrical current should keep flowing, i.e., I=0 200 $\mu$s after the short electrical pulse in a non-propagating action potential without a voltage clamp. Therefore, with a non-propagating action potential without a voltage clamp, Eq. (1) becomes

$$I_i = -C_M \frac{dV}{dt} \tag{3}$$

Eq. (3) indicates that with a non-propagating action potential without a voltage clamp, the transient electrical current across the axonal membrane 200 $\mu$s after the short pulse flows as if it were charged with the electrical capacitance of the axonal membrane itself. This phenomenological relation derived from Eq (1) can explain the non-propagating action potential in squid axons without a voltage clamp (cf. Hodgkin *et al.* 1952).

In turn, Eq (2) indicates that all of the electrical current across the axonal cell membrane 200 $\mu$s after a short electrical pulse should be carried by only ions under a voltage clamp (Hodgkin *et al.* 1952). Based on this assumption, Hodgkin et al (1952) and Hodgkin and Huxley (1952a–d) developed their experiments and were able to successfully explain the action potential in squid axon in terms of an early rapid increase in $Na^+$ conductance, followed by a rapid decrease and later a somewhat slow increase in $K^+$ conductance, all of which are expressed with mathematically complicated formulae as functions of time and membrane potential.

However, my analysis of Kishimoto's experiments (1966) indicated that Eq. (1), the most fundamental and important assumption for Hodgkin *et al.* (1952) and Hodgkin and Huxley (1952a–d), was not valid for the action potential in *Nitella* internodal cells using a voltage clamp method. Kishimoto showed that a transient inward current across the cell membrane of the *Nitella* internode on excitation in artificial pond water (0.05 mM KCl, 0.05 mM $NaH_2PO_4$, 0.2 mM NaCl, 0.5 mM $Ca(NO_3)_2$, 0.1 mM $MgSO_4$) reached 3–9 $\mu A\ cm^{-2}$ at its peak under a voltage clamp. He calculated values of dV/dt during a non-propagating action potential and found the product of the electrical membrane capacitance $C_M$ of the *Nitella* internode and the (dV/dt) values assuming $C_M = 1\ \mu F\ cm^{-2}$ as a function of time, having transient inward $C_M$ (dV/dt) values peaking at 0.18–0.3 $\mu A\ cm^{-2}$. Namely, the transient inward current in characean internodal cells under a voltage clamp is much larger than $C_M$ (dV/dt) calculated from the (dv/dt) values in a non-propagating action potential. Kishimoto's results, if we assume the transient inward current in a *Nitella* internodal cell under a voltage clamp is $I_i$ in the Hodgkin *et al.* (1952) analysis of the transient inward current in a squid axon under a voltage clamp, indicate that the assumption of Hodgkin *et al.* (1952) and Hodgkin and Huxley (1952a–d) of

$$I = I_i + C_M\ (dV/dt) \tag{4}$$

would not be valid for the action potential in *Nitella* internodal cells which have a duration 1000–3000 times as long as that in squid axons because $I_i \neq C_M$ (dV/dt), in which $I_i$ is measured by the voltage clamp method while $C_M$ (dV/dt) is calculated from (dV/dt) values during a non-propagating action potential, in *Characeae* internodal cells.

In other words, Eq. (4) is phenomenologically valid for the action potential in squid axons having a very short duration and thus has large (dV/dt) values, but is invalid for the action potential in *Nitella* internodal cells which have much longer duration and thus small (dV/dt) values. These findings and analysis suggest the need to examine the physicochemical molecular bases of the phenomenological terms $I_i$ and $C_M$ (dV/dt) in excitation phenomena which are well-defined

in electrotechnology.

II. Alternative definitions of the electrical conductances for $Na^+$, $g_{Na}$, and $K^+$, $g_K$.

Hodgkin and Huxley (1952b) determined the electrical conductances of the axonal cell membrane for $Na^+$, $g_{Na}$, and for $K^+$, $g_K$, assuming that

$$I_{Na}(t)=g_{Na}(t)(V-E_{Na}) \quad (5)$$

$$I_K(t)=g_K(t)(V-E_K) \quad (6)$$

where V, $E_{Na}$, $E_K$, $I_{Na}(t)$ and $I_K(t)$ are the membrane potentials clamped by a voltage clamp method, the equilibrium potentials for $Na^+$ and $K^+$ being expressed by the equations (Hodgkin and Huxley 1952a)

$$E_{Na}=-\frac{RT}{F}\ln\frac{[Na^+]^i}{[Na^+]^o} \quad (7)$$

$$E_K=-\frac{RT}{F}\ln\frac{[K^+]^i}{[K^+]^o} \quad (8)$$

where R, T and F are the gas constant, absolute temperature and Faraday constant, respectively; superscripts i and o indicate the inside and outside of the cell, respectively, and $I_i(t)$ as functions of time measured in artificial sea water containing $Na^+$ and $I_i(t)$ measured in $Na^+$-lacking choline sea water, because V, $E_{Na}$ and $E_K$ are assumed to be constant in an intact squid axon under a voltage clamp.

From the Hodgkin and Huxley (1952a, b) assumption that $E_{Na}$ and $E_K$ should be determined by the $Na^+$ and $K^+$ concentrations in the external solution and the cytoplasm of the axon, and having V clamped at an arbitrarily constant value, we can obtain $g_{Na}(t)$ and $g_K(t)$ as a rapid transient increasing function and a slowly increasing function from Eqs. (5) and (6) in that $I_{Na}(t)$ and $I_K(t)$ change in such a manner in artificial sea water containing and not containing $Na^+$, respectively, and the electrical membrane potential difference across the cell membrane should be maintained at a constant value (V-E).

Kishimoto (1968) has tried to express the equivalent electrical circuit for the *Nitella* cell membrane on excitation as Fig. 1. This means that phenomenologically the equivalent circuit for the *Nitella* membrane can or only can be expressed as a membrane electromotive force, E, in series with a membrane resistance, r (reciprocal of a membrane conductance, g) which are functions of time, t, and membrane potential, V, during excitation; the membrane potential actually measured is the potential difference across such a series circuit as shown in Fig. 1. If Ohm's law is applicable even during excitation, the following equation should hold (cf. Tasaki and Spyropoulos 1958):

$$I_i(t)=g(t)(V\text{-}E(t)) \quad (9)$$

where V is the electrical membrane potential clamped by a voltage clamp method; E(t) is the putative electro-motive force of the characean cell membrane which may change with time t even under clamped electrical potential V, and g(t) is the electrical membrane conductance evaluated by the equation

$$g(t)=\frac{\Delta I(t)}{\Delta V} \quad (10)$$

where $\Delta V$ is a superimposed sinusoidal potential on the clamped potential V and $\Delta I(t)$ is a measured sinusoidal current in response to the externally applied V (Fig. 2). Kishimoto

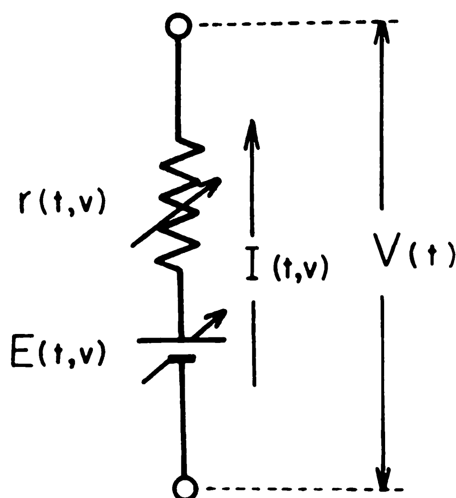


Fig. 1. Equivalent electrical circuit adopted by Kishimoto (1968) for the *Nitella* membrane.

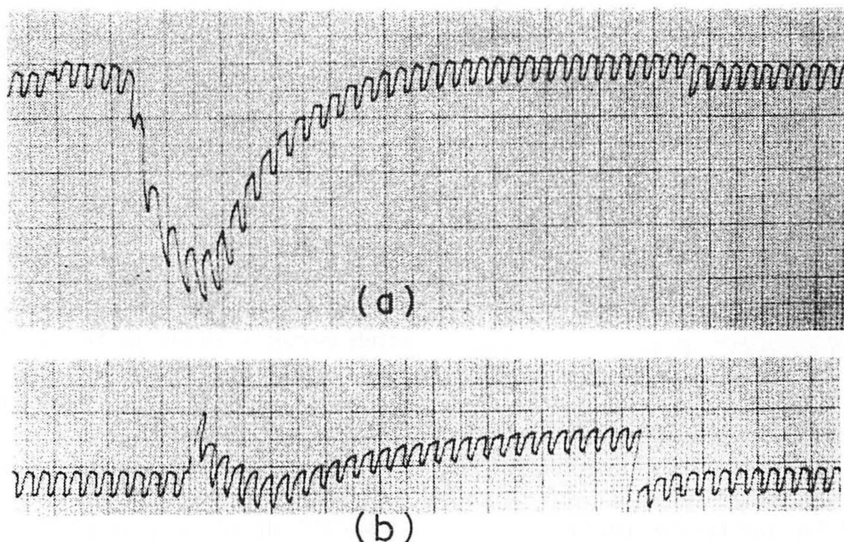


Fig. 2. Patterns of ionic current for depolarizations by 17 mV (a) and 78 mV (b), respectively. The superimposed small change in the current curve is caused by superposition of potential pulses of a small constant amplitude (Kishimoto 1968).

(1968) assumed that the electrical membrane potential difference could not alwasy be maintained at a constant value (V-E) in a voltage clamp method, but should change with time as (V-E(t)). He measured the electrical membrane conductance g(t) from a superimposed sinusoidal potential (Fig. 2) independently from the voltage clamped electrical membrane potential difference (V-E) used by Hodgkin and Huxley (1952b). Here we should note the difference in the difinition of the electrical membrane conductance g(t) between Hodgkin *et al.* (1952) and Hodgkin and Huxley (1952b) (cf. Eqs. (5), (6), (11) and (12)) and that of Tasaki and Spyropoulos (1958) and Kishimoto (1968) (cf. Eq. (10)).

The analysis by Kishimoto (1968) gave $I_i(t)$ as not being continuous for step potential change, but E(t) and g(t) as being continuous; E(t) has a transient characteristic, rising to a peak which is followed by a lower steady state level; the peak of E(t) coincides with the peak of the action potential, and the peak of g(t) is attained earlier than that of E(t) (Fig. 3).

In brief, the definition of Hodgkin *et al.* (1952) and Hodgekin and Huxley (1952b, d) of the electrical membrane conductance by Eqs. (5) and (6) is not the only possible one. Another possibility is that of Tasaki and Spyropoulos (1958) and Kishimoto (1968) using Eq. (10). Furthermore, the equivalent circuit for squid axonal membrane expressed in terms of capacity, C, inductance, L, and resistance, R, (Cole 1941, 1969; Fig. 4) is an alternative to that of Hodgkin and Huxley's (1952a-d) on the electrical properties of the axonal cell membrane (Fig. 5).

III. Argument against separate movement of $Na^+$ and $K^+$ across the axonal cell membrane inducing the ionic current $I_i$ as different functions of time without a voltage clamp using reversible electrodes.

Hodgkin *et al.* (1952) and Hodgkin and Huxley (1952a), after showing the inward transient electrical current followed by a late outward current across the axonal cell membrane in sea water under a voltage clamp (Hodgkin *et al.* 1952), presented the following findings: (1) the early inward current disappeared in sodium-free choline sea water (ca. 484 mM choline$^+$, ca. 10 mM $K^+$, ca. 11 mM $Ca^{2+}$, ca. 54 mM $Mg^{2+}$, ca. 621 mM $Cl^-$, ca. 3 mM $HCO_3^-$); (2) the late outward current was only slightly altered in the sodium-free solution; (3) the changes were reversed when

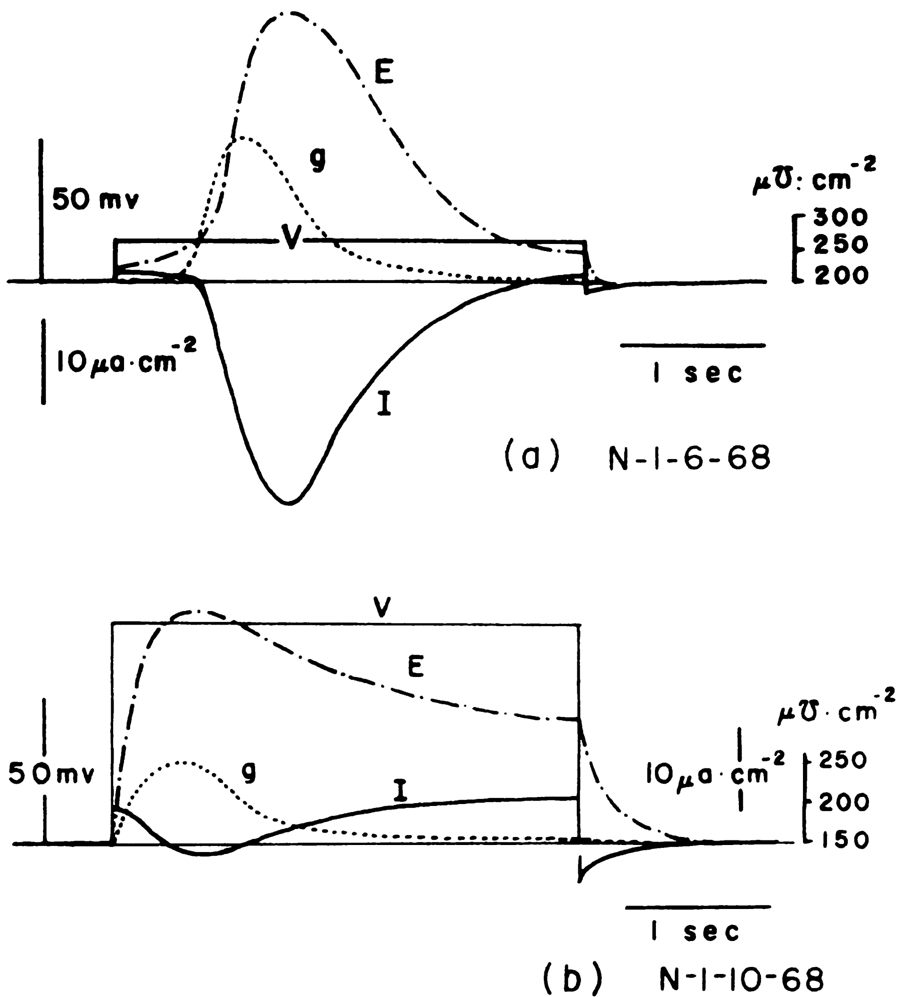


Fig. 3. Electromotive force, E, and conductance, g, defined by Eq. (9).

sea water was replaced; (4) the 'sodium potential' $E_{Na}$ could be expressed by Eq. (7).

Hodgkin and Huxley separated the ionic current $I_i$ into $I_{Na}$ ($I_i$ carried by $Na^+$) and $I_K$ ($I_i$ carried by $K^+$) by comparing the currents when the axon was in sea water with those in the low sodium solution under the assumptions that (1) the time course of $I_K$ was the same in both cases; (2) the time course of $I_{Na}$ was similar in the two cases with the amplitude and sometimes the direction being changed, but not the time scale or the form of the time course; (3) $dI_K/dt=0$ initially for a period about one-third of that taken by $I_{Na}$ to reach its maximum (Hodgkin and Huxley 1952a, b).

Thus, Hodgkin and Huxley (1952b) expressed $I_i$ in terms of eletrical conductances $g_{Na}(t)$ and $g_K(t)$ by the equations

$$g_{Na}(t)=I_{Na}(t)/(V-E_{Na}) \qquad (11)$$

$$g_K(t)=I_K(t)/(V-E_K) \qquad (12)$$

as functions of time. The origin of the propagating action potential is described as follows: (1) current from the neighbouring active region depolarizes the membrane by spreading along the cable structure of the fibre ('local circuit') (Fig. 6a). (2) As a result of this depolarization, sodium current $I_{Na}$

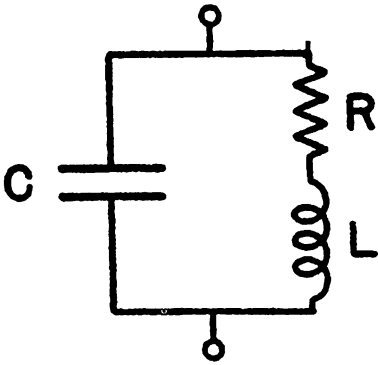


Fig. 4. Equivalent electrical curcuit for squid giant axons expressed by Cole (1941).

is allowed to flow. Since the external sodium concentration is several times greater than the internal one, this current is directed inward and depolarizes the membrane still further, until the membrane potential reverses its sign and approaches the value at which sodium ions are in equilibrium (Fig. 6b). (3) As a delayed result of the depolarization, the potassium current $I_K$ increases and the ability of the membrane to pass sodium current decreases. Since the internal potassium concentration is greater than the external one, the potassium current is directed outwards (Fig. 6c). When it exceeds the sodium current, it repolarizes the membrane, raising the membrane potential to the neighbourhood of the resting potential (Fig. 6d), at which time potassium ions inside and outside the fibre approach an equilibrium.

Their conclusions have two important problems from physicochemical viewpoints. One is whether or not the ionic currents, $I_{Na}(t)$ and $I_K(t)$, carried by $Na^+$ and $K^+$ can

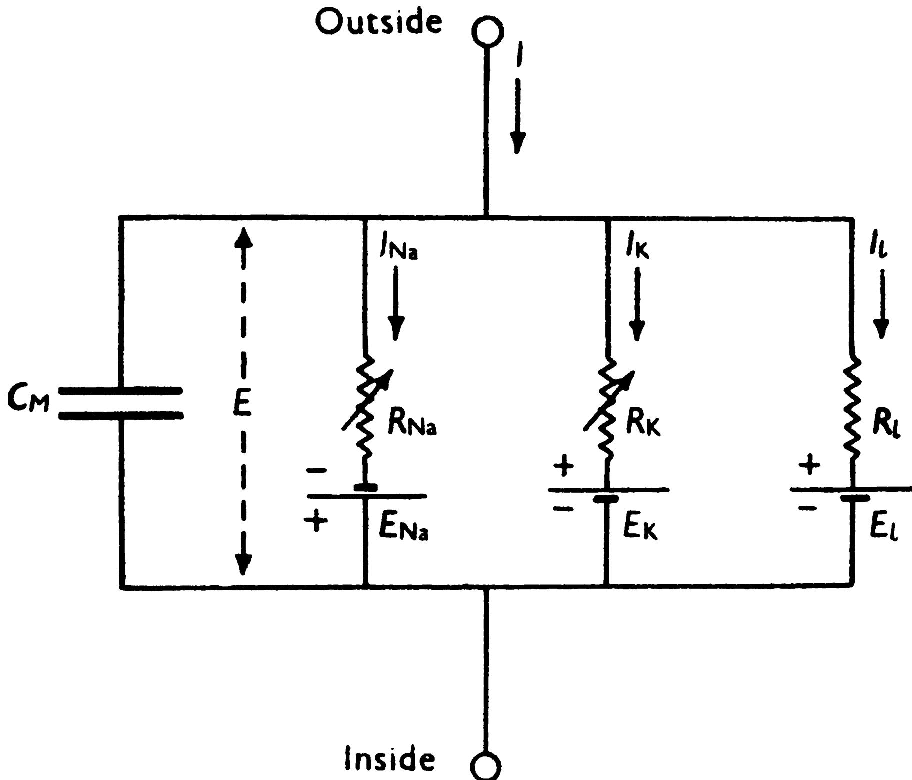


Fig. 5. Electrical circuit representing the axonal cell membrane expressed by Hodgkin and Huxley (1952). $R_{Ns}=1/g_{Na}$; $R_K=1/g_K$; $R_l=1/g_l$. $I_l$, $R_l$ and $E_l$ are the leakage current, electrical resistance to leakage current, and electrical membrane potential for generating leakage current, respectively. $E_K$, $E_{Na}$ and $C_M$ are 'potassium potential', 'sodium potential' and the membrane capacity, respectively. $R_{Na}$ and $R_K$ vary with time and membrane potential; the other components are constant.

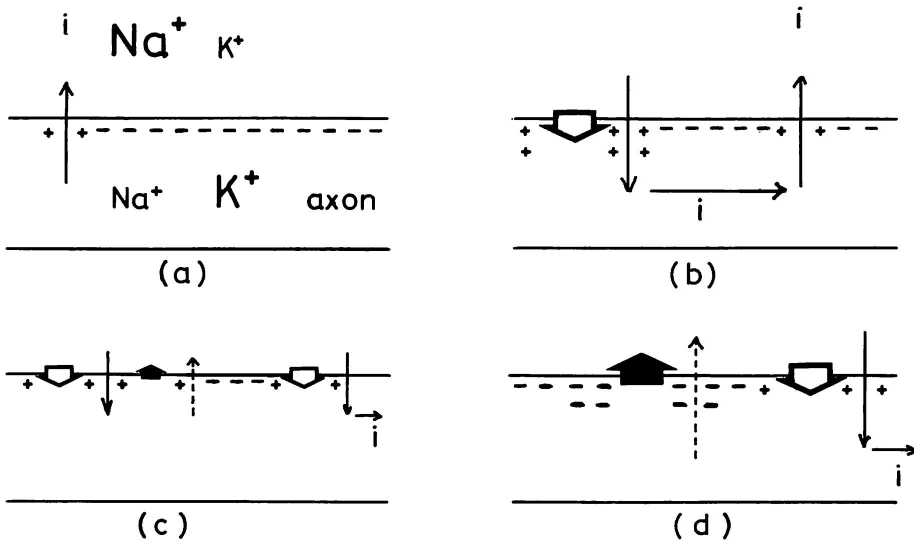


Fig. 6. Schematic illustration of Hodgkin-Huxley phenomenological explanation of propagating action potentials in squid giant axon. (a), (b), (c) and (d) indicate successive processes of $Na^+$ and $K^+$ flows, ionic currents and electrical currents across the axonal cell membrane as a function of time. ⇩ and ⬆ indicate $Na^+$ and $K^+$ flows across the axonal cell membrane, respectively, and their sizes indicate relative magnitudes of their flows. Thin solid and dashed arrows beside ⇩ and ⬆ without a letter i are $Na^+$ and $K^+$ ionic currents: their sizes indicate their relative magnitudes; thin arrows with a letter i are electrical currents in an axon and/or across the axonal cell membrane. Symbols + and − near the axonal cell membrane inside the axon indicate "depolarization" of the resting potential and its being a negative potential against the external solution, respectively. Large letters of $Na^+$ and $K^+$ and their small letters indicate $Na^+$ and $K^+$ of high and low concentrations, respectively.

actually flow across the cell membrane due to $Na^+$ and $K^+$ concentration differences or their electrochemical potential differences between the outside and inside of the axon during non-propagating action potentials, respectively. The other is whether or not the inward sodium current assumed to be carrieed by $Na^+$ flows into the axon first, then the potassium current assumed to be carried by $K^+$ flows out of it in the later phase of the non-propagating action potential.

1. Diffusional fluxes of ions across the cell membrane flow to maintain the electroneutrality rule, thus generating no ionic current.

The ionic current amounting to $I_i$ flows, when an electrical potential difference is externally applied across the axonal cell membrane, for a short period due to a supply of energy from outside the axon by voltage clamping equipment through reversible electrodes. If, however, only $Na^+$ or $K^+$ can permeate the membrane, the ionic current $I_i$ should produce just the corresponding unequal distribution of cations and anions across the cell membrane creating an electrical potential difference, polarization, against the externally applied potential across it, which would finally stop the electrical current flowing across the cell membrane.

In all recent theories on membrane transport across synthetic membranes under no externally applied electrical potential difference, the electroneutrality rule is assumed to be

$$0=\Sigma I_p = I_{Na^+}+I_{K^+}+I_{H^+}+I_{Ca^{2+}}+I_{Cl^-}+\ldots \quad (13)$$

where $I_p$ is the electrical current carried by the p-th ion transported across the membrane ($p=K^+, Na^+, H^+, Ca^{2+}, Mg^{2+}, Cl^-, NO_3^-$ and $H_2PO_4^-$ etc.; Kobatake *et al.* 1965, Lakshminarayanaiah 1969, 1984, Hanai 1988; cf. Kiyosawa and Okihara 1988, Kiyosawa 1993) and

$$I_p = -z_pFc_pu'_p\left(RT\frac{d\ln c_p}{dx} + z_pF\frac{dV}{dt}\right) \quad (14)$$

$$c_+ = c_- + X \quad (15)$$

where $z_p$, $u'_p$, $c_+$, $c_-$ and X are the valence of the p-th ion, the mobility of the p-th ion in the membrane, the concentrations of cations and anions in the membrane and fixed charge of the membrane, respectively. The x-axis is taken in the direction of the membrane thickness from the outside to the inside of the cell.

When there is no ATP consumption by ATPases in the cell membrane, the positive charge due to all cations to be transported should be equal to the negative charge due to all anions to be transported if the externally supplied electrical current is zero (cf. Kiyosawa and Okihara 1988, Kiyosawa 1993). In other words, when a cation flows from the inside of the cell to the external solution, an anion having the correspondengly equal negative charge must be transported together with the cation, or another cation having the correspondingly equal positive charge in the external solution must enter the cell across the cell membrane in exchange for the outgoing cation.

Since this electroneutrality rule, first applied to electrolyte solutions, is very strict, $Na^+$ or $K^+$ cannot move freely across the cell membrane independently of other anions or cations to create an electrical current when there is no ATP consumption or externally supplied electrical energy. This indicates that diffusional ion fluxes across the cell membrane cannot create an electrical current without active transport accompanied by ATP consumption or without energy supply from a voltage clamp equipment. Since total membrane current density I is negligible in non-propagating action potential at time periods greater than 200 $\mu$s after a short pulse to induce it (Hogkin *et al.* 1952), what occurs in or across the axonal membrane is diffusional processes of ions such as $Na^+$, $K^+$, $Cl^-$ etc. The diffusional processes themselves cannot create any electrical current amounting to $I_i$.

From this point of view, Kishimoto (1966) has found very interesting and important phenomena on a non-propagating action potential in *Nitella* internodal cells which

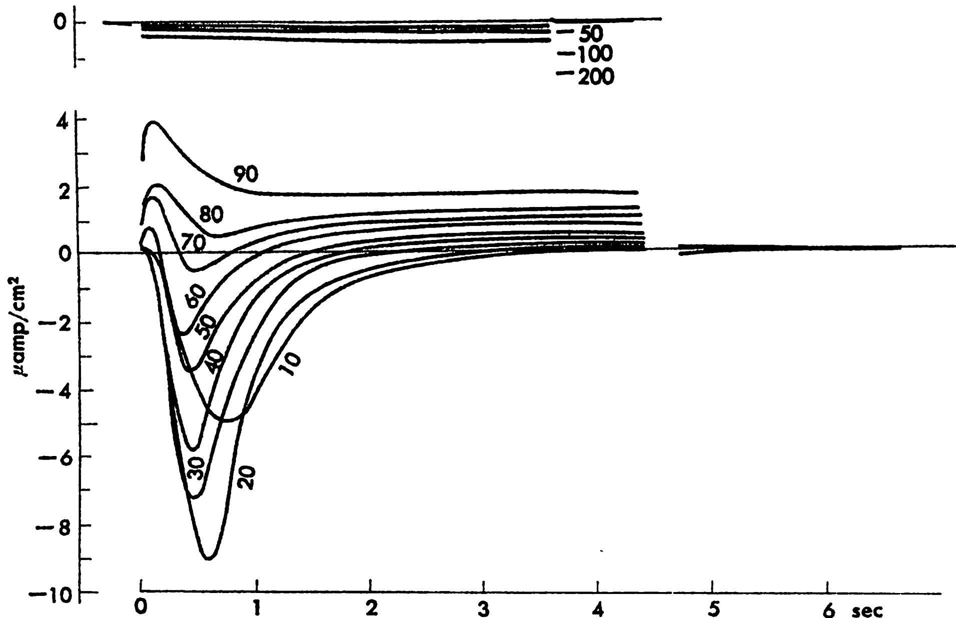


Fig. 7. Patterns of membrane currents at various levels of clamped membrane potential. The number attached to each curve indicates the amount of depolarization (lower curve) or hyperpolarization (upper figure) from the resting membrane potential (Kishimoto 1966).

generate much slower and longer action potential than that in squid axon. For moderate depolarization, the transient inward current was followed by a slowly rising outward current; for larger depolarization, a transient outward current preceded the transient inward current, and only monotonic inward currents were observed for hyperpolarizations (Fig. 7). When these curves were replotted against the potential level, the parameter being time in this case, the temporal variation of the current-voltage relation (I-V curve) was obtained (Fig. 8a). The transient inward current was the largest at about 0.5 s after the step change of the potential. The pattern, however, was not constant with time, but decayed and moved leftward along the voltage axis (V-axis) and finally converged into a steady delayed rectification curve. The potential at which the largest I-V curve crosses the V-axis corresponds almost exactly to the potential at the peak of the action potential, and the temporal locus of the potential at which a series of the I-V curves crosses the V-axis, i.e., I=0 coincided approximately with the potential change which actually occurred during the action potential (Fig. 8b). This finding indicates that the actual non-propagating action potential is a membrane phenomenon which occurs at I=0 in the temporal I-V curve obtained under voltage clamp method. In other words, the actual non-propagating action potential is phenomenon which occurs with electroneutrality being maintained.

2. Reports of experiments showing simultaneous outflows of $K^+$ and $Cl^-$ during excitation in characean internodal cells

Tsutsui *et al.* (1986) found that when the I-V curve of the *Chara* cell membrane was obtained by applying a slow ramp hyperpolarization to the internodal cell, the transient early inward current component disappeared almost completely under $La^{3+}$ treatment while no effect was observed on the late outward current. They interpreted these

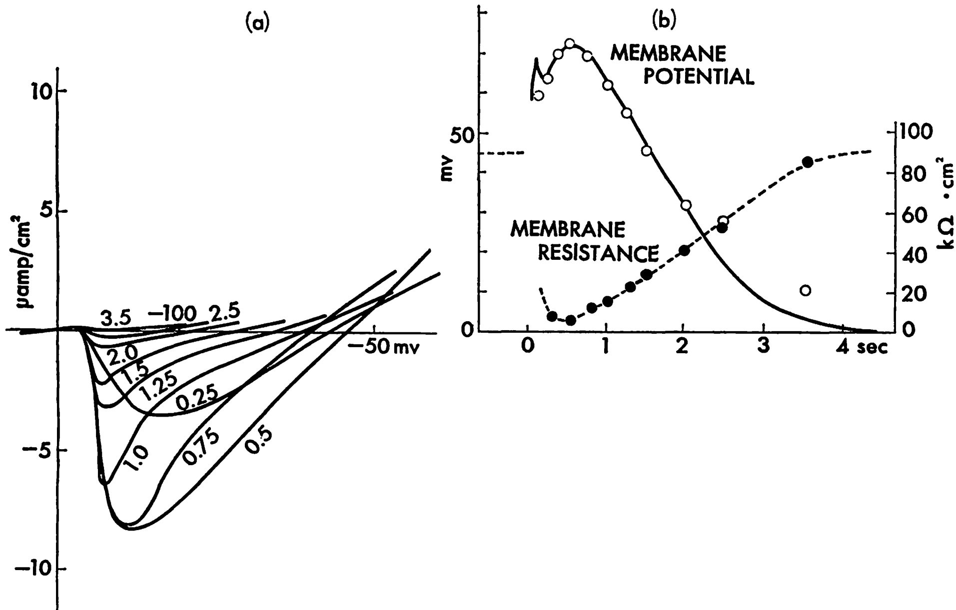


Fig. 8. a: Membrane currents during step potential changes in Fig. 7, replotted against the membrane potential level, the parameter being time here. The number attached to each curve is time in seconds after the step potential change. These curves show the temporal change of the I–V relation of the *Nitella* internode after stimulation. b: Temporal change of the potential at which a series of the I–V curves crosses the potential axis (open circles) coincides approximately with the action potential (full line). The temporal change of the membrane resistance (black circles) is obtained from the slope of the I–V curve at each intersection with the V-axis (Kishimoto 1966).

phenomena, as being similar to the Hodgkin-Huxley phenomenological analysis, that the transient early inward current is mainly carried by the efflux of $Cl^-$ and the late large outward current is mainly carried by the efflux of $K^+$; both ions exist predominantly in the internodal cell.

However, as stated in the Introduction and other sections, excitation in the *Characeae* internodal cell is of much slower and longer duration than that in the squid axon. Therefore, ion fluxes can be separately measured during excitation. If the Hodgkin and Huxley theory were also true for characean internodal cells, $Cl^-$ in the internodal cell should go out first, followed by a later $K^+$ outflow, as Tsutsui *et al.* (1986) suggest.

To examine this hypothesis, Oda (1975, 1976) constructed an apparatus having a groove in which a *Characeae* internodal cell could be placed and $K^+$-free artificial pond water could be kept flowing to a flame photometer to detect the $K^+$ leaving the internodal cell during excitation. In the groove, he placed two sets of two Ag-AgCl electrodes to measure the $Cl^-$ leaving the same internodal cell during excitation and the excitation itself. He detected simultaneous $K^+$ and $Cl^-$ effluxes of almost equal amount on excitation.

Later, Williamson and Ashley (1982) reported that *Chara* cells have a low free $Ca^{2+}$ concentration, comparable with those of animal cells, and that action potentials which inhibit cytoplasmic streaming substantially increase this $Ca^{2+}$ concentration. Kikuyama *et al.* (1984) showed that on excitation, *Chara* and *Nitellopsis* internodal cells produced a large amount of $K^+$ efflux but some cells showed action potentials without a detectable increase in $Cl^-$ efflux; they assumed $Ca^{2+}$ influx to be a candidate for the exchange with the $K^+$ efflux during excitation in cases where no $Cl^-$ outflow was detectable. Recently, Hayama *et al.* (1979), Kikuyama and Tazawa (1983) and Kikuyama *et al.* (1993) have shown that $Ca^{2+}$ in the external solution transiently enter the *Characeae* internodal cell during excitation using $^{45}Ca^{2+}$ and aequorin, respectively.

These phenomena observed in characean internodal cells disagree with the Hodgkin-Huxley hypothesis which assumes separate $Na^+$ inflow and $K^+$ outflow as different functions of time. Thus, further study is needed to establish a universal theory with equations that can explain excitation phenomena in both squid axons and characean internodal cells, i.e., excitation phenomena of short and long duration.

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## 清沢桂太郎：神経の興奮に関する Hodgkin-Huxley 説を超えて 車軸藻節間細胞での研究から見た一私見

イカの巨大神経は，静止時には内部の電位は外部に対し −60 mV を示すが，刺激により，一過性に +40 mV に達した後，元の値に戻る。Hodgkin ら，Hodgkin and Haxleg（以下，H-H と記す）は，この現象は刺激により，まず $Na^+$ に対する透過性が，一過性に増大し，外部の $Na^+$ が一過性に流入，その後，$Na^+$ に対する透過性が減少，一方 $K^+$ に対する透過性が増大し，内部の $K^+$ が外部に出ていくためであると説明した。岸本は，H-H の仮説は，一つの現象論としては，全く異論をはさむ余地はないが，実際にその通りの事が起こっているのかどうかは別であるとし，車軸藻節間細胞に，H-H と同様の膜電位固定法を適用し，彼らとは異なった表現法を提出した。小田は車軸藻節間細胞での興奮現象を H-H 流に説明すると，まず，細胞内の $Cl^-$ が出て，遅れて $K^+$ が出て行くことになるが，実測すると，$Cl^-$ と $K^+$ はほとんど同時に出ることを示した。ここではこれらの実験の紹介を含め，H-H の仮説は，単なる一つの現象論であって，実際に起こっている現象とは別である可能性があることを膜に関する物理化学的法則を基に論証した。（560 豊中市待兼山町1-3　大阪大学基礎工学部生物工学科）