

Title**Electrochemical Interpretation of Propagation of the Change in the Membrane Potential
Using the Goldman-Hodgkin-Katz Equation**

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Abstract

Nerve conduction has been frequently explained by the Hodgkin-Huxley equation based on the flow of K^+ and Na^+ across the cell membrane. By considering the relation between the membrane potential and the membrane current based on the Goldman-Hodgkin-Katz equation, it becomes clear that the conventional analysis using the voltage-clamp method is not correct and that the hyperpolarization condition is artificially made. Taking into account the channel functions and the electronic properties, we suggested a new propagation mechanism. When the nerve cell is excited by an external stimulus, the ligand-gated channels at the synapse serve as an electric power source to propagate the change in the membrane potential to the synapse terminal along the axon and the voltage-gated channels at the axon locally assist the directional propagation along the axon.

1. Introduction

Until the 1930s, the detail mechanism for the conduction of the action potential had not been solved though it was thought that the change in the membrane potential was partially generated during the nerve conduction [1-5]. Several research groups suggested cable theory models based on the assumption that a nerve axon served as a cylindrical conducting core [6-9]. In order to precisely analyze the relation between the local membrane potential and the local membrane current on the surface of the nerve cell, Cole and Marmont developed the voltage-clamp method [10,11]. Hodgkin and his coworkers investigated the propagation of the action potential in the squid giant axon using the voltage-clamp method [12,13]. Hodgkin and Huxley then improved the cable theory and proposed the Hodgkin-Huxley model [14]. They elucidated that the conduction of the action potential is caused by the change in the membrane potential due to the selective transports of the K^+ and Na^+ across the cell membrane, and the conventional model for the nerve conduction was established, as described below [14-16]. The membrane potential of the nerve cells is usually determined by the ratio of the concentration of K^+ inside to that outside the cell and is called the resting potential. When channel-type receptors (ligand-gated Na^+ channels) at the synapse combine with neurotransmitters, Na^+ mainly moves from the outside to the inside of the cell in the neighborhood around the channel-type receptors. The transport of Na^+ evokes a change in the membrane potential from the resting potential to the action potential which is determined by the ratio of the concentration of Na^+ inside to that outside of the cell. Subsequently, the action potential is propagated along the axon toward the synaptic terminal by opening the voltage-gated Na^+ channels that have short open-lives (about 1 ms). Since the delayed K^+ channels present in the axon open one after another, the membrane potential immediately goes back to the resting potential via the hyperpolarization state. Thus, the propagation of the change in the membrane potential is directionally conducted along the axon toward the synaptic terminal, and transmitters are released with the fusion of the synaptic vesicles containing transmitters. Some

unexplained phenomena, such as the existence of the threshold of the membrane potential to change over from the normal condition to the exciting condition, the direction of the nerve conduction, the interpretation on the membrane potential at the microscopic domain, and the appearance of the hyperpolarization, still exist during the nerve conduction.

When the surface of the nerve cell is divided into multiple domains, it is difficult to accurately evaluate the membrane potential and membrane current of each domain. Therefore, the authors' group has conducted the interpretation of the propagation of the change in the membrane potential using an electrochemical cell system composed of several liquid-membrane cells which are connected in parallel [17-20]. It has been clarified that the change in the membrane potential is propagated by the generation of the circulating current through two liquid membrane sites (the potential-sending and potential-receiving sites) and that the magnitude of the circulating current determines the threshold to produce the change in the membrane potential by considering the electroneutrality and the mass-balance of every phase [17,21]. In addition, it was found that the ohmic drop generated by the resistor in the electric circuit decreased and slowed the propagation of the change in the membrane potential and that the charging current generated by the capacitor in the electric circuit delays the propagation analogous to the nerve transmission. The connection of the liquid membrane cell mimicking the function of the voltage-gated Na^+ channels using relay switches with the model electric circuit caused a directional propagation like the nerve conduction [22]. As for the hyperpolarization, the authors' group pointed out the contradiction in the conventional concept taking into account the electrochemical properties of the relation between the membrane potential and the membrane current [20,22]. Considering the relation between the direction of the local current and the i - E curves for the delayed K^+ channels and the voltage-gated Na^+ channels based on the Goldman-Hodgkin-Katz equation, it is clear that the membrane potential at any domains always changes within the potential range between the initial resting potential and the action potential.

In this study, a novel model for the nerve conduction is proposed based on the knowledge about the propagation of the change in the membrane potential using the liquid-membrane cell system. Since it has been found that there is a serious problem with the equivalent circuit in the conventional cable theory, we also propose a new equivalent circuit and the relation between the membrane potential and the membrane current in a certain domain of an axon.

2. Results and Discussion

2.1 Nerve conduction based on the Hodgkin-Huxley model

Figure 1 shows the equivalent circuit of the conventional cable theory based on the Hodgkin-Huxley model [14,15]. The nerve cell membrane (M) seems to be divided into many microscopic domains (N_A domains), and the extracellular and intracellular fluids are expressed as W_o and W_i , respectively. The domain N at the axon is usually composed of a lipid bilayer, delayed K^+ channels and voltage-gated Na^+ channels. In higher animals, the domain corresponds to a node of Ranvier. If the membrane potential ($E_{W_i-W_o, N}$) changes from the resting potential to the action potential, the membrane current ($I_{W_i-W_o, N}$) flows due to the charging around the membrane surface, the transport of Na^+ from W_o to the inside W_i and that of K^+ from W_i to W_o . These are juxtaposed to each other. When the cell outside is defined as the standard phase, the total current ($I_{W_i-W_o}$) and the current flowing to the domain N ($I_{W_i-W_o, N}$) can be expressed by eqns. (1) and (2).

$$I_{W_i-W_o} = I_{W_i-W_o,1} + I_{W_i-W_o,2} + \cdots + I_{W_i-W_o,N} + \cdots + I_{W_i-W_o,N_A} = 0 \quad (1)$$

$$I_{W_i-W_o, N} = I_{W_i-W_o, N(C)} + I_{W_i-W_o, N(K)} + I_{W_i-W_o, N(Na)} + I_{W_i-W_o, N(L)} \quad (2)$$

where $I_{W_i-W_o, N(C)}$, $I_{W_i-W_o, N(K)}$, $I_{W_i-W_o, N(Na)}$, and $I_{W_i-W_o, N(L)}$ express the charging current, the current due to the transport of K^+ , that due to the transport of Na^+ , and that due to the transport of other anions (L^-), respectively. Taking into account the electric properties of the equivalent circuit of domain N , eqn. (2) has to be corrected as eqn. (2').

$$I_{W_i-W_o, N} = C_{W_i-W_o, N(M)} \frac{dE}{dt} + I_{W_i-W_o, N(K)} + I_{W_i-W_o, N(Na)} + I_{W_i-W_o, N(L)} \quad (2')$$

The Hodgkin-Huxley equation is represented by eqn. (3) based on the electrochemical properties of ion fluxes.

$$I_{W_i-W_o, N} = C_{W_i-W_o, N(M)} \frac{dE}{dt} + g_K n^4 (E - E_K) + g_{Na} m^3 h (E - E_{Na}) + g_L (E - E_L) \quad (3)$$

where $C_{W_i-W_o, N(M)}$, g_K , g_{Na} , and g_L are the capacitance of the domain N , the conductance of the K^+ -flow system due to the delayed K^+ channels, the conductance of the Na^+ -flow system due to the voltage-gated Na^+ channels, and the conductance of the flow of the other ions due to the leak by other anion channels and direct transport across the lipid bilayer, respectively. On the other hand, h , m , and n indicate the probabilities depending on the time, and n^4 and m^3h imitate the membrane permeability changes measured in the voltage clamp experiments [14,15]. The real membrane potential, E , is evaluated using the resting potential, E_r , and the potential difference, ΔE , converted from the current flow by considering the change in the conductance. E_K , E_{Na} , and E_L are then equilibrium potentials for K^+ , Na^+ , and L^- , respectively, as described below.

$$E_K = \frac{RT}{F} \ln \frac{c_K^i}{c_K^o} \quad (4)$$

$$E_{Na} = \frac{RT}{F} \ln \frac{c_{Na}^i}{c_{Na}^o} \quad (5)$$

$$E_L = \frac{RT}{F} \ln \frac{c_L^o}{c_L^i} \quad (6)$$

where R , T , and F denote the gas constant, the absolute temperature, and the faradaic constant, respectively. In these equations, c_i indicates concentration of the electrolyte ion i (K^+ , Na^+ , L^-), and the superscript (i or o) expresses W_i or W_o .

2.2 Novel model on the nerve conduction using the liquid-membrane cell system

As shown in Fig. 1, solution resistances exist between two adjacent domains. The body fluids usually contain sufficient electrolyte ions, such as K^+ , Na^+ , Cl^- , etc. [16], and the total concentration of these electrolytes is greater than 0.1 mol dm^{-3} (M). For example, the electric conductivity of 0.1 M KCl at 308 K was reported to be $15.3160 \text{ mS cm}^{-1}$ [23]. Since the cross sectional area of the axon is very small ($10^{-8} - 5 \times 10^{-6} \text{ cm}^2$) [16], the solution resistance between two adjacent nodes of Ranvier (0.2–2 mm) seems to become higher than 1 M Ω . Assuming that 100 nA is flowing between two adjacent domains, much more than 10 mV is lost as an iR drop between two adjacent domains. Thus, the influence of the change in the membrane potential seems to spread out toward a distant domain. If the voltage-gated Na^+ channels do not simultaneously serve with the delayed K^+ channels at the same domain, it is not necessary to consider the circulating current within the same domain, as expressed in Fig. 2(a). The typical behaviors observed by the voltage-clamp method indicate that both transports temporarily occur in the same domain, as shown in Fig. 2(b) [15]. Since the solution resistance around the same domain is negligibly small, there is a high likelihood that a large circulating current occurs within the same domain. This phenomenon has not been confirmed until now.

As for the total charge transport concerning one living cell, several research groups have already reported the analysis based on the electrocoupling of plural ion transports and/or electron transport [24-26]. They succeeded in an explanation of action mechanism on the biological functions such as generation of action potentials, oscillations of membrane potentials, etc. by considering the electrocoupling of respective transport based on the Goldman-Hodgkin-Katz equation. In the case that we focus a certain domain like the node of Ranvier, the following relation also holds because they are connected in parallel.

$$E_{W_i-W_o, N} = E_{W_i-W_o, N(K)} = E_{W_i-W_o, N(Na)} = E_{W_i-W_o, N(L)} \quad (7)$$

where $E_{W_i-W_o, N(K)}$, $E_{W_i-W_o, N(Na)}$ and $E_{W_i-W_o, N(L)}$ indicate the membrane potential due to the transport

of K^+ , that due to the transport of Na^+ and that due to the transport of L^- , respectively, in the same domain N . Although the electric properties of the K^+ , Na^+ , and L^- channels (or the leakage) are usually expressed using variable electric resistors, it seems reasonable to assume that $E_{Wi-Wo, N(K)}$, $E_{Wi-Wo, N(Na)}$ and $E_{Wi-Wo, N(L)}$ are almost equivalent because the solution resistance of aqueous phases is negligibly small within the same domain. Consequently, the relation between $E_{Wi-Wo, N}$ and the membrane current due to the transport of Na^+ ($I_{Wi-Wo, N(Na)}$), that between $E_{Wi-Wo, N}$ and the membrane current due to the transport of K^+ ($I_{Wi-Wo, N(K)}$), and that between $E_{Wi-Wo, N}$ and the membrane current due to the transport of L^- ($I_{Wi-Wo, N(L)}$) should be expressed by the Goldman-Hodgkin-Katz equation [27-29], as represented by eqns. (8)-(10), respectively.

$$I_{Wi-Wo, N(Na)} = -\frac{P_{Na} F^2 E_{Wi-Wo, N} S}{RT} \left[\frac{c_{Na}^i \exp\left(\frac{FE_{Wi-Wo, N}}{RT}\right) - c_{Na}^o}{\exp\left(\frac{FE_{Wi-Wo, N}}{RT}\right) - 1} \right] \quad (8)$$

$$I_{Wi-Wo, N(K)} = -\frac{P_K F^2 E_{Wi-Wo, N} S}{RT} \left[\frac{c_K^i \exp\left(\frac{FE_{Wi-Wo, N}}{RT}\right) - c_K^o}{\exp\left(\frac{FE_{Wi-Wo, N}}{RT}\right) - 1} \right] \quad (9)$$

$$I_{Wi-Wo, N(L)} = -\frac{P_L F^2 E_{Wi-Wo, N} S}{RT} \left[\frac{c_L^i \exp\left(\frac{FE_{Wi-Wo, N}}{RT}\right) - c_L^o}{\exp\left(\frac{FE_{Wi-Wo, N}}{RT}\right) - 1} \right] \quad (10)$$

where P_{Na} , P_K , and P_L denote the permeability of Na^+ , that of K^+ , and that of L^- , respectively. S then indicates the area of the domain. By considering eqns. (8) - (10), eqn. (2') is rewritten as eqn. (11).

$$I_{Wi-Wo, N} = C_{Wi-Wo, N(M)} \frac{dE}{dt} - \frac{P_K F^2 E_{Wi-Wo, N} S}{RT} \left[\frac{c_K^i \exp\left(\frac{FE_{Wi-Wo, N}}{RT}\right) - c_K^o}{\exp\left(\frac{FE_{Wi-Wo, N}}{RT}\right) - 1} \right] - \frac{P_{Na} F^2 E_{Wi-Wo, N} S}{RT} \left[\frac{c_{Na}^i \exp\left(\frac{FE_{Wi-Wo, N}}{RT}\right) - c_{Na}^o}{\exp\left(\frac{FE_{Wi-Wo, N}}{RT}\right) - 1} \right] - \frac{P_L F^2 E_{Wi-Wo, N} S}{RT} \left[\frac{c_L^i \exp\left(\frac{FE_{Wi-Wo, N}}{RT}\right) - c_L^o}{\exp\left(\frac{FE_{Wi-Wo, N}}{RT}\right) - 1} \right] \quad (11)$$

In order to simplify the relation, only the transport of K^+ and that of Na^+ are treated hereafter. The typical $I_{Wi-Wo, N(Na)} - E_{Wi-Wo, N}$ and the typical $I_{Wi-Wo, N(K)} - E_{Wi-Wo, N}$ curves are displayed in Fig. 3

[15]. Since the K^+ and Na^+ channels mainly affect the fundamental electrophysiological properties of the nerve conduction, eqn. (11) can be simplified as eqn. (12).

$$I_{W_i-W_o,N} = -\frac{P_K F^2 E_{W_i-W_o,N} S}{RT} \left[\frac{c_K^i \exp\left(\frac{FE_{W_i-W_o,N}}{RT}\right) - c_K^o}{\exp\left(\frac{FE_{W_i-W_o,N}}{RT}\right) - 1} \right] - \frac{P_{Na} F^2 E_{W_i-W_o,N} S}{RT} \left[\frac{c_{Na}^i \exp\left(\frac{FE_{W_i-W_o,N}}{RT}\right) - c_{Na}^o}{\exp\left(\frac{FE_{W_i-W_o,N}}{RT}\right) - 1} \right] \quad (12)$$

In usual, the permeability (P) is expressed using the distribution coefficient (β), the diffusion coefficient (D) and the thickness of the membrane (d) as below [29].

$$P = \frac{\beta D}{d} \quad (13)$$

The values of P_K , P_{Na} and P_L , however, vary every moment during the nerve conduction [15]. Equation (12) cannot express the time-dependence and voltage-dependence of the K^+ and Na^+ channels, and the application of the functions, $f(t, E)$ and $g(t, E)$, like n^4 and $m^3 h$ is helpful to supply the properties. Therefore, eqn. (12) can be converted to eqn. (14).

$$I_{W_i-W_o,N} = -\frac{a_N f(t, E) \beta_K D_K F^2 E_{W_i-W_o,N} S}{RTd} \left[\frac{c_K^i \exp\left(\frac{FE_{W_i-W_o,N}}{RT}\right) - c_K^o}{\exp\left(\frac{FE_{W_i-W_o,N}}{RT}\right) - 1} \right] - \frac{b_N g(t, E) \beta_{Na} D_{Na} F^2 E_{W_i-W_o,N} S}{RTd} \left[\frac{c_{Na}^i \exp\left(\frac{FE_{W_i-W_o,N}}{RT}\right) - c_{Na}^o}{\exp\left(\frac{FE_{W_i-W_o,N}}{RT}\right) - 1} \right] \quad (14)$$

Here, D_{Na} and D_K are the diffusion coefficients of Na^+ and K^+ within the respective channel pores, and β_{Na} and β_K are the distribution coefficients of Na^+ and K^+ between the aqueous phase and the respective channel pores, respectively. Then a_N and b_N express the coefficients depending on the numbers of the respective channels within the domain N . Thus, it is clear that the membrane potential derived from the respective membrane current (the membrane current due to the voltage-gated Na^+ channels and that due to the delayed K^+ channels) is a mixed potential.

In the conventional analysis by the voltage-clamp method, the membrane potential is expressed as the potential of the inside against the outside [12-15]. The positive current is, however, defined as the flow of positive charged particle from the outside to the inside. This is an opposite direction by comparison with the electrochemical treatment. In addition, the resting potential (E_r) is used as the criterion to evaluate the real membrane potential (E : $E = E_{W_i-W_o, N}$), as

shown in Fig. S1. Based on the equation represented by eqn. (15), a lot of studies have been investigated up to now.

$$I = g_K n^4 (E - E_K) + g_{Na} m^3 h (E - E_{Na}) \quad (15)$$

Here, I indicates $I_{W_i-W_o, N}$ to simplify. Since the current consists of both the positive current (I_K) due to the transport of K^+ from W_i to W_o and the negative current (I_{Na}) due to the transport Na^+ from W_o to W_i , the potential difference (ΔE) converted from the current value using g_K tends to be overestimated, as illustrated in Fig. S2. The variation of I_K and I_{Na} should be individually analyzed, as indicated in Fig. S3. Besides E must be more positive than E_K because I is positive. Not only the membrane potential when the membrane current is caused by the transfer of Na^+ from W_o to W_i , but also the membrane potential when the membrane current is caused by the transfer of K^+ from W_i to W_o is more positive than the original resting potential ($\approx E_K$), as shown in Fig. 3. Since the definition of the electronic standard is the complete opposite direction, we can conclude that the conventional treatment is not correct. Although the hyperpolarization has been frequently reported in a number of studies [3,4,15], it can be concluded that, in truth, such a hyperpolarization does not occur in the liquid-membrane system [20, 22]. Since the local current is directly converted to the membrane potential using the change in the permeability, the hyperpolarization can be accidentally generated by the conventional analysis using the wrong standard, as noted in our previous study [20,22]. Figure 3 indicates the relation between the membrane potential and the membrane current by considering the transports of K^+ and Na^+ across the membrane. The black solid line shows the $I_{W_i-W_o, N(K)} - E$ curve caused by the delayed K^+ channels and the black dotted line indicates the $I_{W_i-W_o, N(Na)} - E$ curve caused by the voltage-gated Na^+ channels. Since the voltage-gated Na^+ channels have the threshold, the current due to the transport of Na^+ from the outside to the inside does not occur at the potential region more negative than the threshold. If the ordinary Na^+ channels (voltage-independent) exist in the domain N , the $I_{W_i-W_o, N(Na)} - E$ curve becomes the gray dotted line. These curves for the transports of K^+ and Na^+

across the membrane are derived from the Goldman-Hodgkin-Katz equation.

2.3 Nerve conduction mechanism based on the proposed model

By considering the relation based on eqn. (14), the mechanism of the nerve conduction can be reconsidered as follows. Figure 4(a) represents the scheme on the time-courses of $I_{W_i-W_o, N(K)}$, $I_{W_i-W_o, N(Na)}$ and $I_{W_i-W_o, N} (= I)$ in the domain N . The time-dependence of $E (= E_{W_i-W_o, N})$ is shown in Fig. 4(b). E usually remains at the resting potential before an external stimulus is received ($t = t_A$). Until the membrane potential at the domain N exceeds the threshold, a low membrane current ($I_{W_i-W_o, N(K)} \geq 0$ A) would be caused by the transport of K^+ from W_i to W_o at $t = t_B$. After opening the voltage-gated Na^+ channels at $t = t_C$ and t_D , a high membrane current ($I_{W_i-W_o, N(Na)}$) due to the transport of Na^+ from W_o to W_i flows and the total membrane current (I) is almost equivalent to $I_{W_i-W_o, N(Na)}$. While $I_{W_i-W_o, N(K)}$ gradually increases, $I_{W_i-W_o, N(Na)}$ suddenly decreases about 1 ms after opening the voltage-gated Na^+ channels ($t = t_E$ and t_F). After closing the voltage-gated Na^+ channels, the current flow ($I_{W_i-W_o, N(K)}$) due to the transport of K^+ from W_i to W_o lasts for a while ($t = t_G, t_H$ and t_I). The membrane potential in this domain then exists in the region between the resting potential and the action potential. Therefore, the voltage-gated Na^+ channels are immediately closed, but the membrane potential does not go back to the initial resting potential ($\approx E_K$) at once and remains at a more positive potential than the initial resting potential. Thus the membrane area indicating the action potential readily spreads to the synaptic terminal. Since multiple ligand-gated Na^+ channels at the synapse remain open for about 5 ms under the excited conditions [16], these Na^+ channels serve as the main electric source to propagate the change in the membrane potential to the synaptic terminal. The voltage-gated Na^+ channels existing at the axon work as the supplemental electric source to assist the propagation of the change in the membrane potential. Finally, the membrane potential goes back to the initial resting potential ($t = t_I$). The authors' research group reported the same mechanism of the directional propagation using

the nerve model composed of multiple liquid-membrane cells [20,22].

The conduction processes of the change in the membrane potential at any domains are explained from the viewpoint suggested by the authors, as follows. Typical current fluctuations are treated as an example [15]. Under the usual conditions, a few K^+ channels in all the domains of the nerve cell always open or K^+ directly permeates through the cell membrane [4,5]. The membrane potential of each domain is determined by the ratio of the K^+ concentration in W_i to that in W_o . Figure 5(a) shows the $I_{W_i-W_o, N(Na)} - E$ and $I_{W_i-W_o, N(K)} - E$ curves from t_A to t_D by comparison with Fig. 4. Points A to D correspond to the relations between $I_{W_i-W_o, N(K)}$ and E at $t = t_A$ to t_D , respectively. Similarly, points A' to D' correspond to the relations between $I_{W_i-W_o, N(Na)}$ and E at $t = t_A$ to t_D , respectively. Under the inactive condition, the membrane current does not flow in each domain ($I_{W_i-W_o, N} = 0, N = 1, 2, \dots, N_A$) ($t = t_A$ and t_B). When neurotransmitters are released from the adjacent nerve cell, a part of the neurotransmitters combines with the channel-type receptors which serve as Na^+ channels for about 5 ms at the synapse. Since a negative current flows at the synapse, the change in the membrane potential spreads from the synapse to a distant domain in the cell with a slight release of K^+ from W_i to W_o ($t = t_C$). Thus, the circulating current is generated around the ignition point. When the membrane potential at domain 1 (the node of Ranvier) exceeds the threshold, the membrane potential at domain 1 rapidly changes from the initial resting potential to the action potential ($t = t_D$). In a similar manner, the points E to J and those E' to J' correspond to the relations between $I_{W_i-W_o, N(K)}$ and E at $t = t_E$ to t_J and the relations between $I_{W_i-W_o, N(Na)}$ and E at $t = t_E$ to t_J , respectively, as presented in Fig. 5(b). Since the change in the membrane potential is promoted by the local change from the resting potential to the action potential within the axon, the domains showing the action potential are propagated to the synaptic terminal along the axon one after another. The voltage-gated Na^+ channels exist in the axon (nodes of Ranvier) and its life-time is very short (about 1 ms) [16]. It seems that the domain showing the action potential moves to the synaptic terminal. After the action potential is propagated to the

synaptic terminal, the neurotransmitters accumulated within the synaptic vesicles are released from the nerve cell to the cell outside by the membrane fusion of the synaptic vesicles with the cell membrane. Then, the adjacent nerve cell is excited, and the above process seems to repeat one after another in the nerve system. After the exciting condition maintains for a while, the membrane potential seems to go back to the resting potential. Since K^+ is pumped up from W_o to W_i against the potential energy, the hyperpolarization does not appear at that time.

3. Conclusion

The propagation of the change in the membrane potential can be reconsidered based on not only the coupling among several charge-transport systems by plural transporters and/or ion pumps but also the assumption that membrane potentials caused by all charge-transport systems are almost equivalent within a microscopic domain. It is easy to understand how the action of the channel-type receptors affects the nerve conduction in the postsynaptic terminal and why a hyperpolarization disappears just after closing the voltage-gated Na^+ channels.

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Figure captions

Fig. 1 Equivalent circuit of the cable theory

Fig. 2 The conceptional figure of the relation between the ion transport and the membrane current in domain N (a) and the time-courses of the membrane current in domain N , the conductivity of the Na^+ channels and that of the K^+ channels (b)

Solid line: the membrane potential, dashed line: conductivity of the Na^+ channels, one-dot chain line: conductivity of the K^+ channels.

Fig. 3 The relation between the membrane potential (E_{W1-W2}) and the membrane current (I_{W1-W2}) based on the Goldman-Hodgkin-Katz equation

Black solid line: The I_{W1-W2} - E_{W1-W2} curve for the transport of K^+ by the K^+ channels, black dotted line: the I_{W1-W2} - E_{W1-W2} curve for the transport of Na^+ by the voltage-gated Na^+ channels, gray dotted line: the I_{W1-W2} - E_{W1-W2} curve for the transport of Na^+ by ordinary Na^+ channels.

Fig. 4 Schemes on the time-courses of $I_{Wi-W0, N(K)}$, $I_{Wi-W0, N(Na)}$ and $I_{Wi-W0, N}$ in domain N (a) and the time-course of $E_{Wi-W0, N}$ (b)

a) Solid line: the membrane current, one-dot chain line: the current due to the transport of K^+ , dotted line: the current due to the transport of Na^+ .

b) Solid line: the membrane potential, dotted line: the membrane potential predicted by the conventional theory.

Fig. 5 The relation between the membrane potential (E_{W1-W2}) and the membrane current (I_{W1-W2}) based on the Goldman-Hodgkin-Katz equation from the beginning of the nerve excitement to the

period showing the action potential (a) and from the period showing the action potential to the end of the nerve excitement

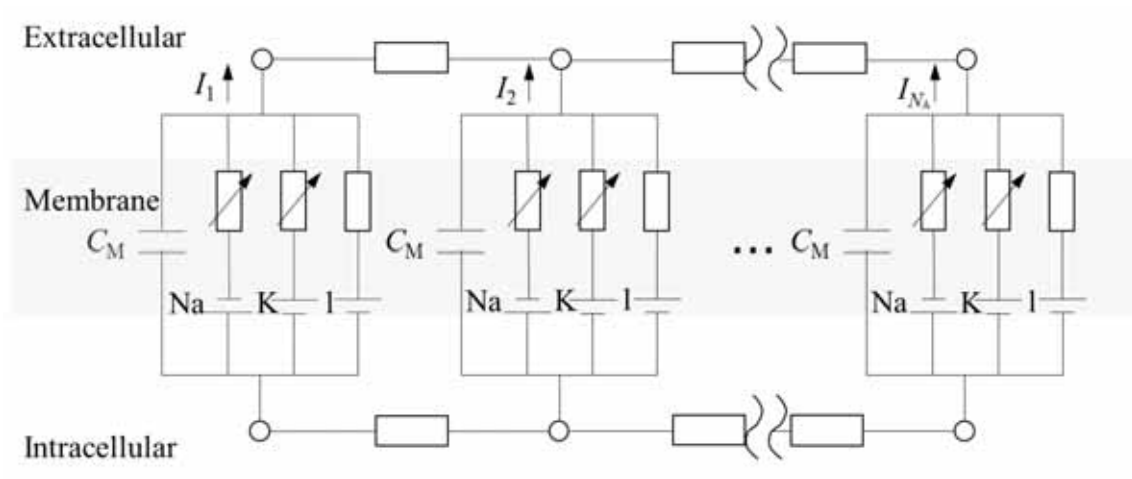


Fig. 1 O. Shirai, et al.

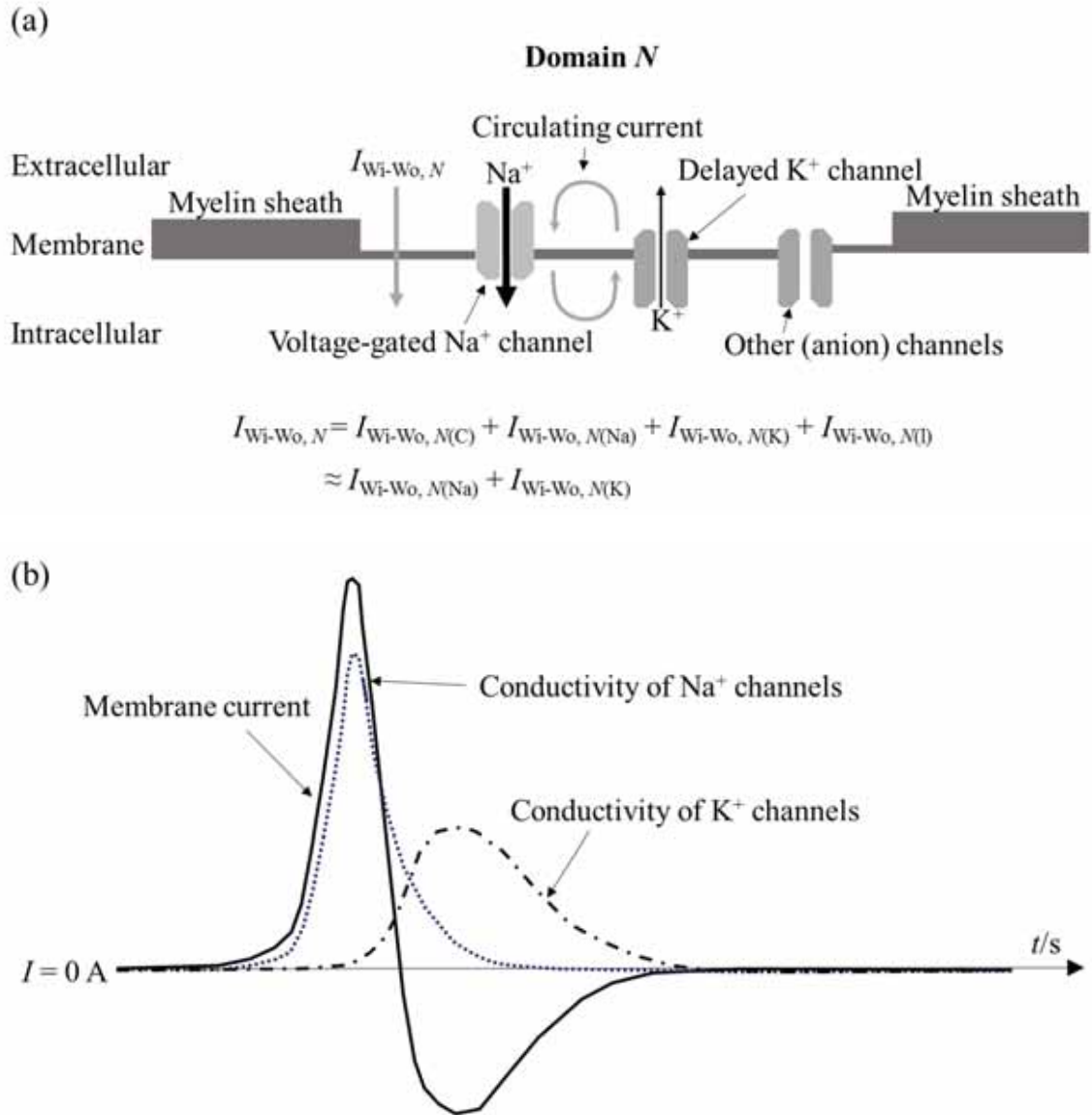


Fig. 2 O. Shirai, et al.

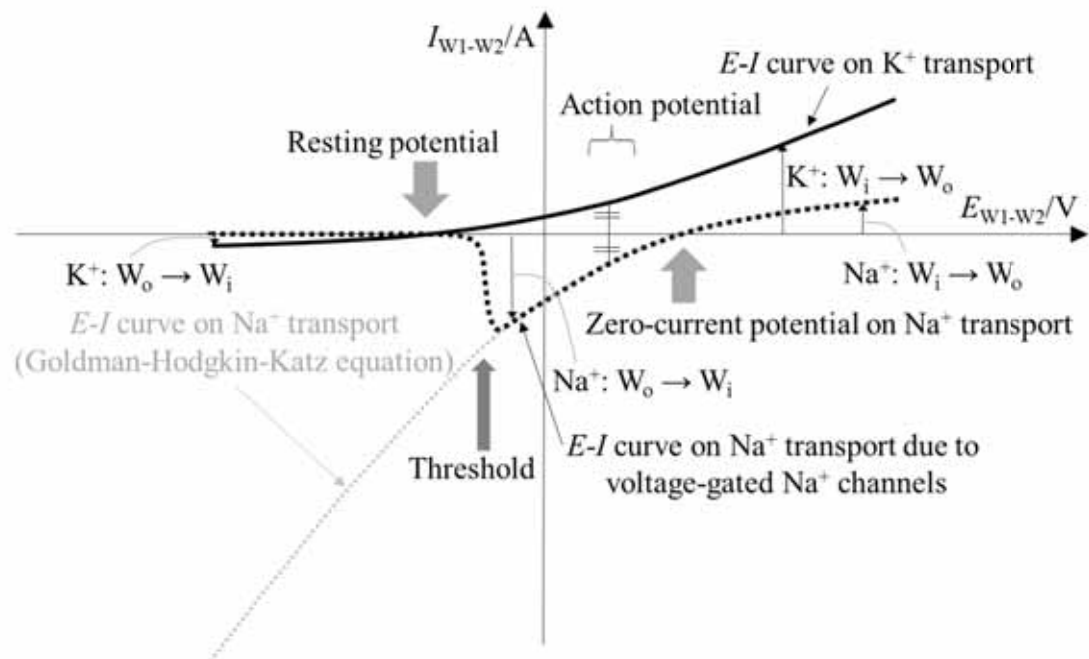


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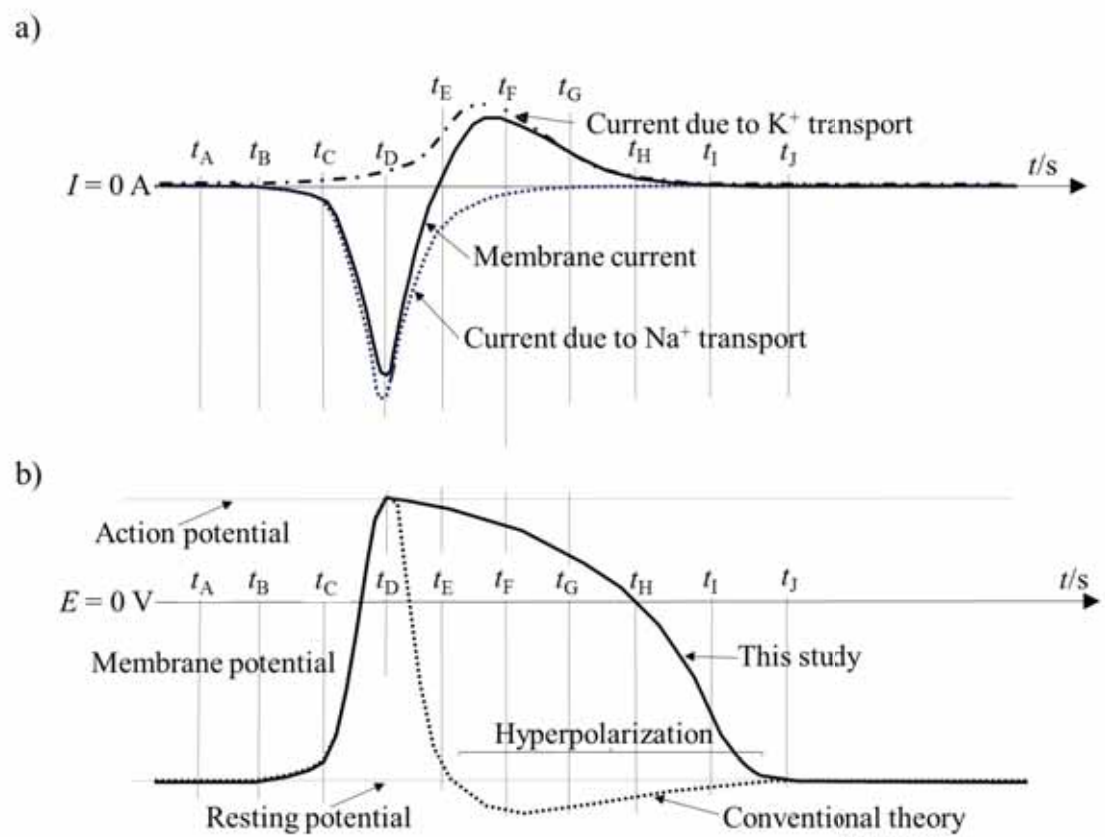


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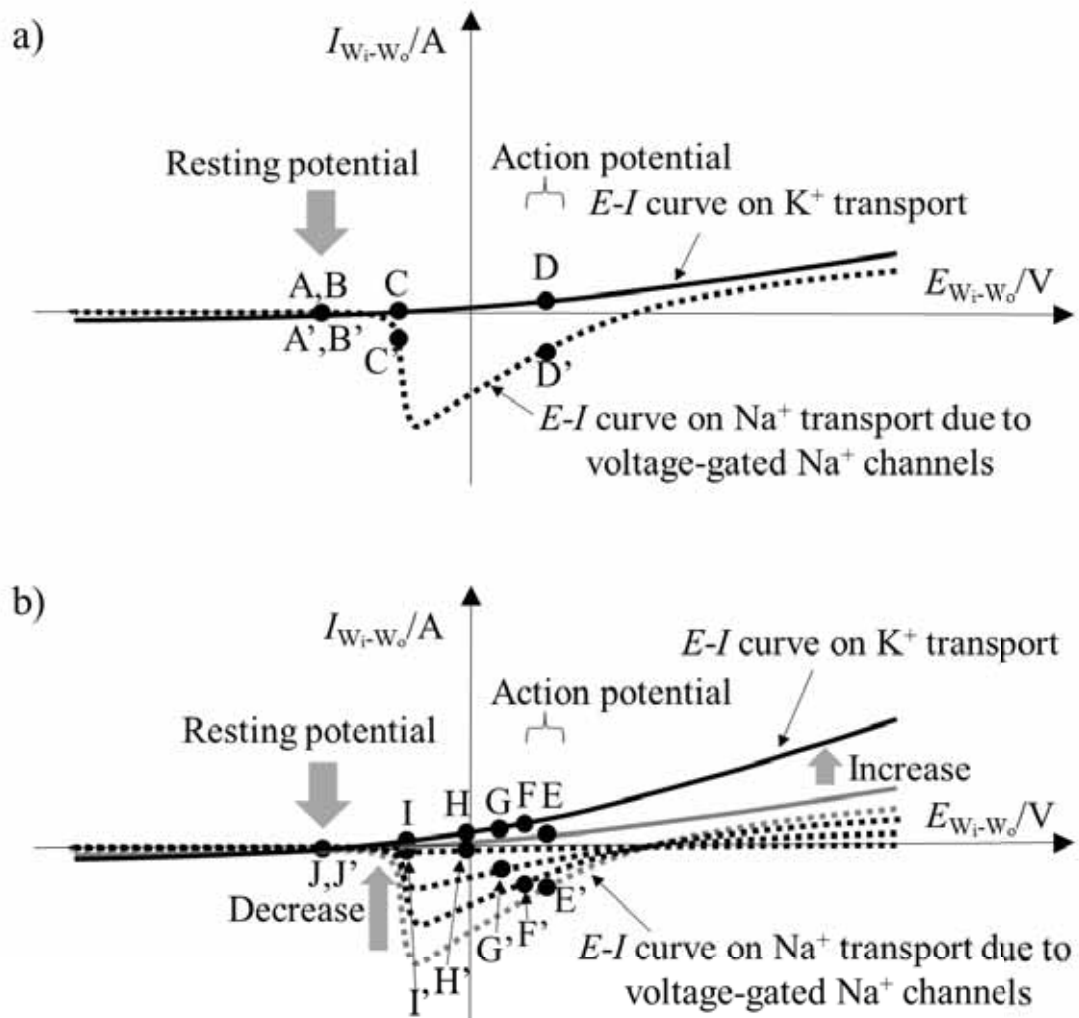


Fig. 5 O. Shirai, et al.

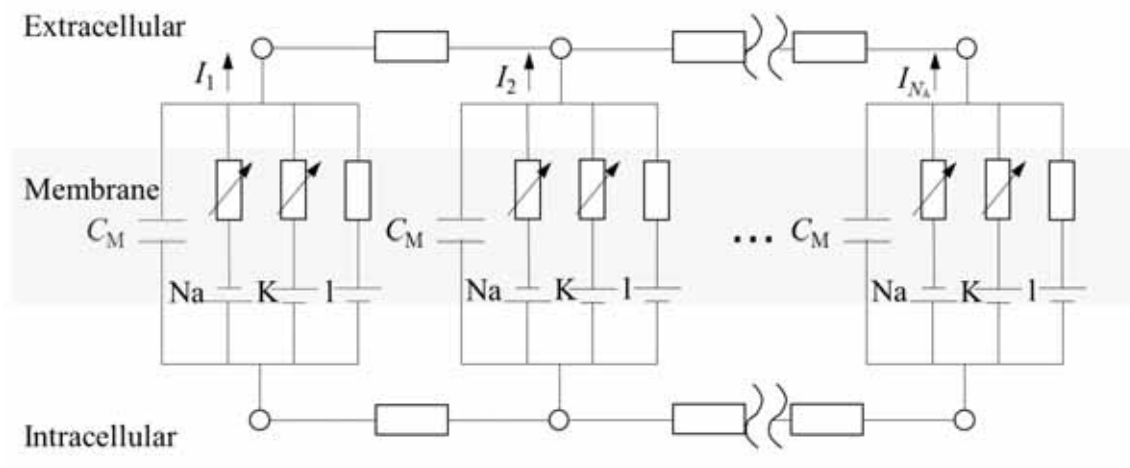


Fig. 1 O. Shirai, et al.

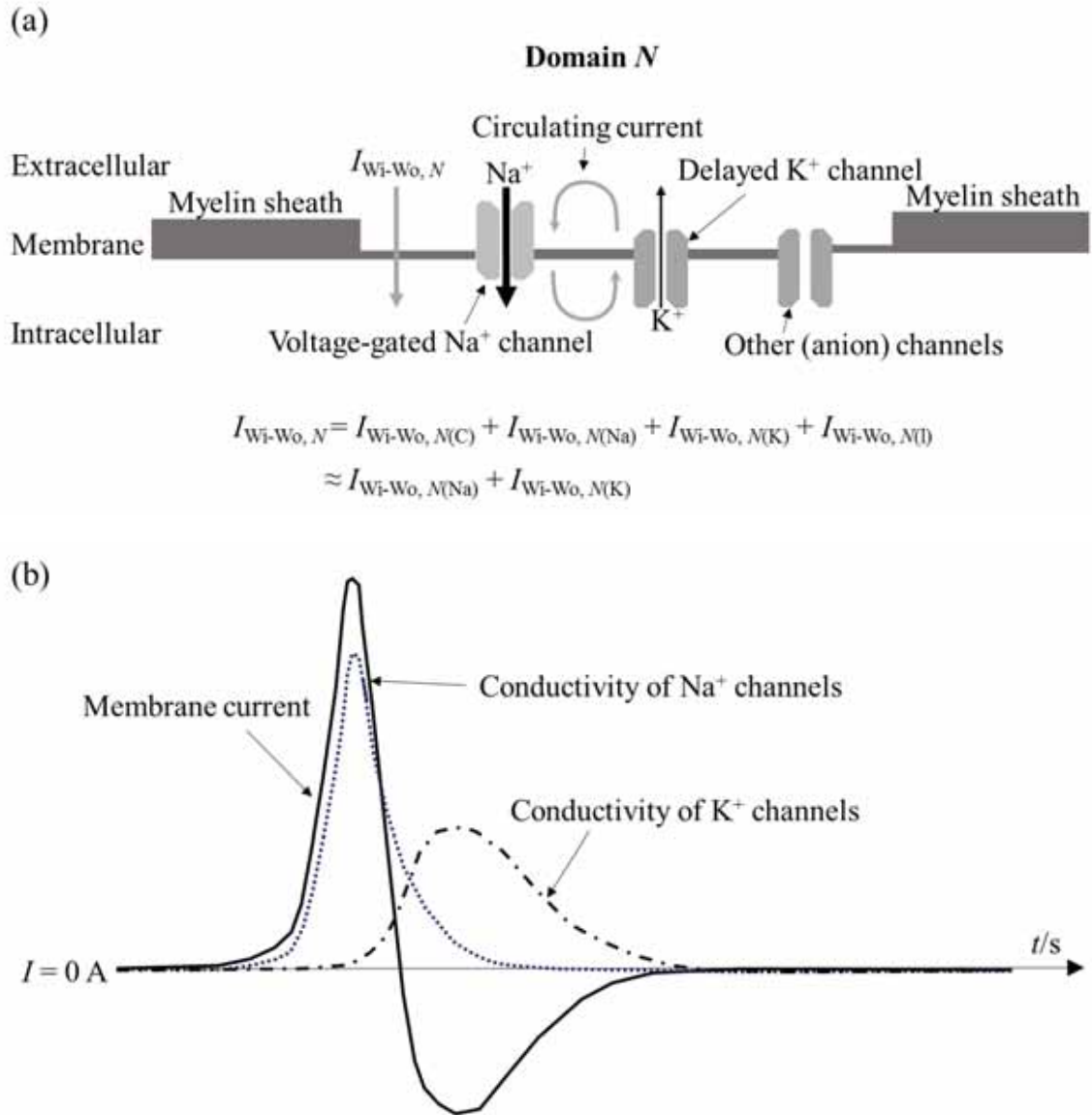


Fig. 2 O. Shirai, et al.

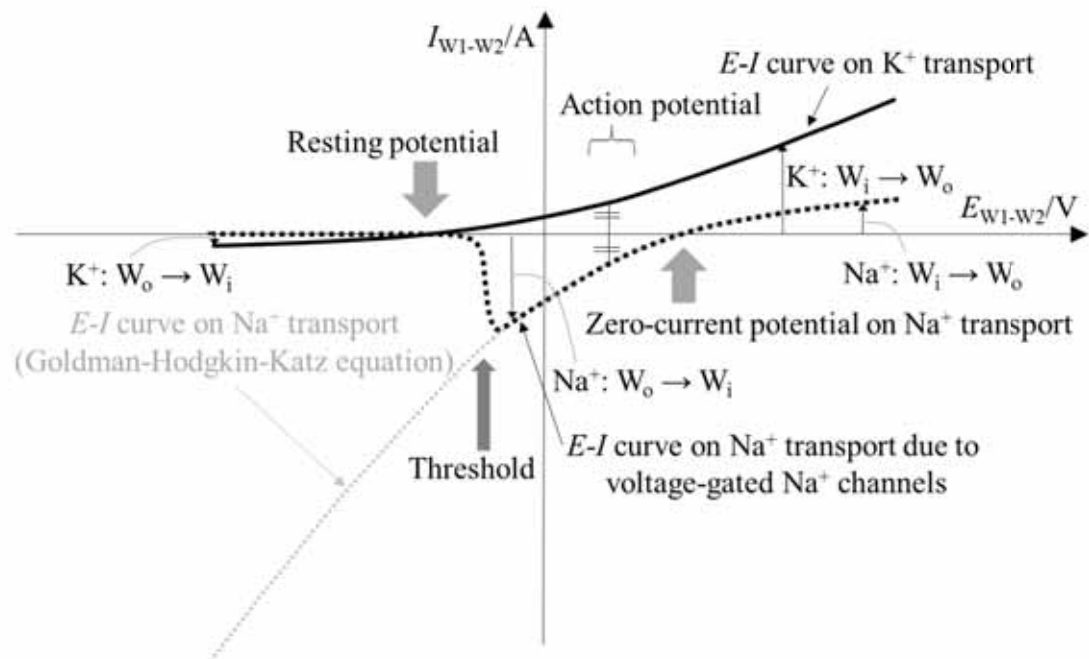


Fig. 3 O. Shirai, et al.

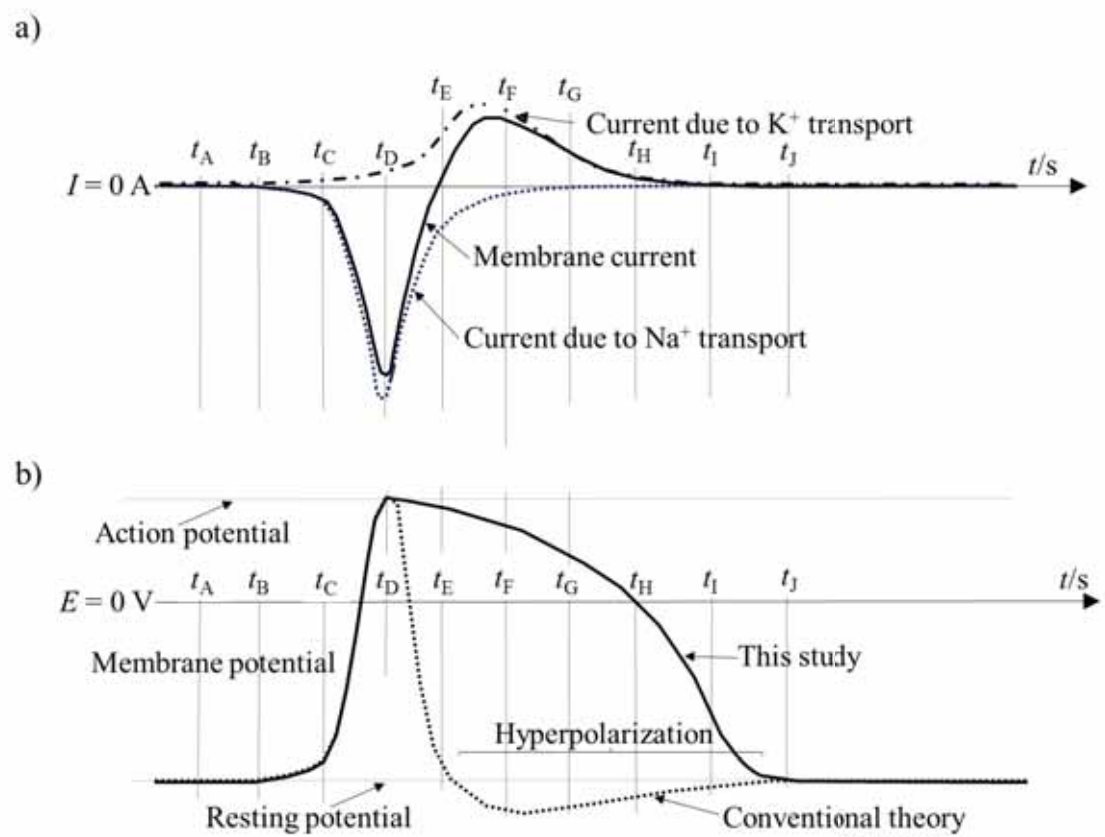


Fig. 4 O. Shirai, et al.

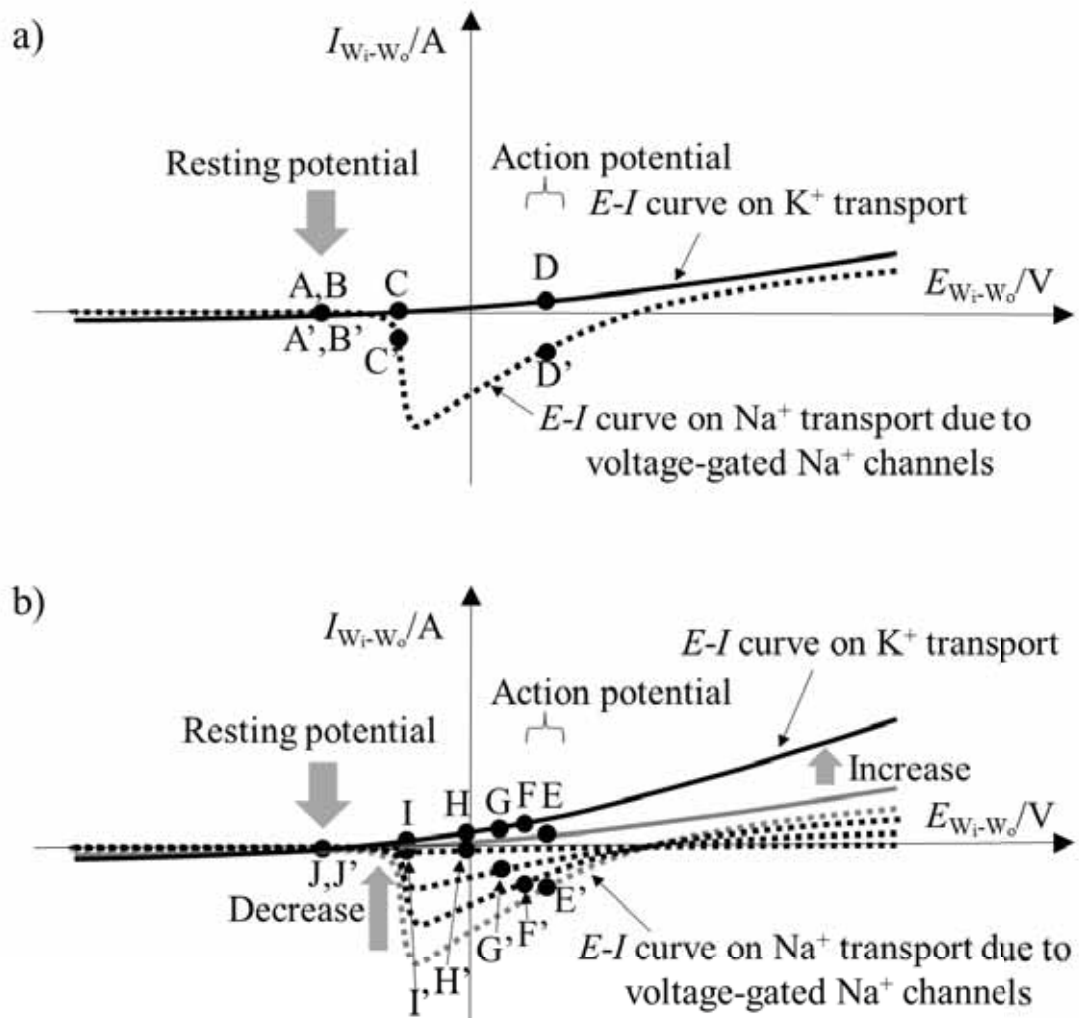
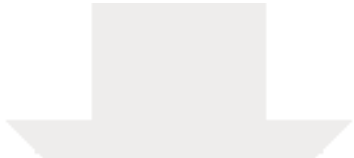


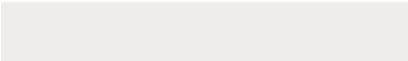
Fig. 5 O. Shirai, et al.



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