Verification of dielectric-applied axon equivalent circuit for high-speed conduction of action potential in the myelinated fiber

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Comprehensive introduction

The ability of animals to capture prey—or to flee predators rapidly—requires the high-speed transmission of both sensory signals from sensory organs to the brain and motor control signals from the brain to the muscles. Such signals propagate as action potentials along the axons of neurons. High conduction velocities of up to 120 m/s have been reported for myelinated neurons, even those with axons just 20μm in diameter. The length of the axon may be about 1 m. Action potentials propagate fast and are relayed frequently. If the action potential is relayed every 1 cm, it will be relayed 12,000 times in 1 s. If a large amount of time is spent in relaying the action potential, the propagation time of the action potential is thought to shorten. Therefore, I investigated the mechanism of high conduction velocity of the action potential by clarifying the relationship among three elements: the relay interval, relay time, and velocity of the action potential.

In Part Ⅰ, using the circuit constant that Hodgkin compiled, I calculated the propagation speed of the action potential itself and the attenuation constant of the action potential using a conventional representative axon equivalent circuit. However, the thickness of the myelin sheath allows little leak current. The result of the calculation indicated high attenuation of the propagation and very slow speed of propagation of the action potential itself. Therefore, an axonal factor that accounts for longitudinal, rapid propagation of the action potential is necessary. In other words, the axon resistance must be smaller. Otherwise, the presence of a different carrier that rapidly conveys the action potential is needed. Therefore, I considered an effect of the electric field generated by the action potential from electromagnetic theory. That is, if an electric charge exists in a dielectric medium such as axon fluid, one of Maxwell's equations states that an electric field proportional to the dielectric constant of the dielectric medium forms and broadens around the electric charge. Furthermore, one of Maxwell's equations shows that the displacement current Id is generated in proportion to the rate of change of the electric field. The displacement current I increases the propagation velocity of the electric field. If the electric field reaches the threshold of a voltage-gated Na channel of a distant node of Ranvier and triggers generation of an action potential, the electric field and displacement current Id play a role as a new carrier in propagating the action potential. Therefore, I proposed the existence of a new axon equivalent circuit in which the dielectric characteristic of axon fluid is applied. I quantitatively investigated the effect of the axon fluid as a new carrier of the action potential. The attenuation constant became small in the new axon equivalent circuit in which the dielectric characteristic of the axon fluid is applied, and I could calculate the fast conduction velocity because the propagation speed of the action potential itself became fast. However, I began to doubt the reliability of this approach because the dielectric constant calculated from this new axon equivalent circuit was very high.

Therefore, in PartⅡ, I made a simple experimental device and measured the dielectric constant of KCl liquid, which is similar to axon fluid. I confirmed that the dielectric constant calculated from the new axon equivalent circuit was in near agreement with the dielectric constant measured by the experimental device. In addition, documents have reported that the result of measurement of NaCl ion liquid, which is almost the same as the concentration of KCl in axon fluid, and the result of measurement of the gray matter of the human brain demonstrated very high dielectric constants. In this way, I could demonstrate that axon fluid as the dielectric medium greatly contributed to the high-speed conduction velocity of the action potential.

In PartⅢ, I report two discoveries based on the results of research in PartⅠ and PartⅡ. One of the discoveries using the approach of the distributed element circuit for a new axon equivalent circuit is that conduction velocity is proportional to the square root of the membrane thickness of the myelin sheath. However, previous studies have reported that conduction velocity is proportional to the axon diameter. Another discovery is related to the dielectric constant of KCl liquid, which is similar to axon fluid. Usually, the value of the dielectric constant of capacitance of the electronic part does not depend on the frequency, but the dielectric constant of KCl liquid does depend on the frequency. The dielectric constant of KCl liquid is inversely proportional to the frequency. I discovered that a maximum point of the raw velocity of the action potential exists at a frequency of 2 kHz using the new axon equivalent circuit and the longitudinal capacity, which is applied to the dielectric constant of KCl liquid.

Part Ⅰ

Verification of the effect of the axon fluid as highly dielectric medium in the high-speed conduction of action potentials using a novel axon equivalent circuit

Abstract

Both sensory neurons and motor neurons transfer signals rapidly through long pathways. Such signals propagate as action potentials through neurons. In myelinated neurons, high conduction velocities of 120 m/s have been reported, even for axons of just 20 μm in diameter. Such a high conduction velocity is enabled by the characteristic morphology of a myelinated axon: repeated regions encased by long uniform myelin sheaths alternating with extremely short exposed regions of the axon called nodes of Ranvier, which generate extremely sharp action potentials. Although the need for the action potential to cross many nodes increases the relay time, it is still able to propagate rapidly. This phenomenon motivated us to derive a new mechanism of the action potential propagation. First, the dielectric effect of the axonal fluid was considered, and it was investigated whether the combination of the characteristic axonal morphology and the dielectric constant of the axonal fluid contributes significantly to the realization of high conduction velocities even with the inclusion of a large loss in the relay time. To this end, we propose a new axon equivalent circuit that incorporates the effect of the dielectric characteristics of the axonal fluid. It was confirmed that a realistically high conduction velocity could be calculated using the proposed circuit and that the dielectric constant calculated using the proposed circuit was in agreement with that of an ionic fluid similar to axonal fluid. Moreover, the contribution of the combination of the axonal morphology and axonal fluid to the conduction velocity was confirmed.

1. Introduction

Both sensory signals from sensory organs to the brain and motor control signals from the brain to the muscles are required to transmit rapidly. Such signals propagate as action potentials along neurons [1, 2]. High conduction velocities of up to 120 m/s have been reported for myelinated neurons, even those with axons just 20 μm in diameter [3-6]. High velocity is enabled by the characteristic morphology of the myelinated axon, shown in Figure 1-1a; this morphology consists of regions enveloped by long and multiple layered myelin sheaths alternating with extremely short gaps called nodes of Ranvier at which extremely sharp action potentials are generated as shown in Figure 1-1b [1]. As a consequence of this morphology, action potentials are relayed from node to node via mechanism called saltatory conduction [7-9], and this relay occurs extremely many times in long motor or sensory neurons because action potential is quickly attenuated in a short length and each relay operation takes time. Because of this, the conduction velocity of the action potential is influenced by the time loss of relay of action potential rather than the propagation speed of the action potential. Therefore, the actual propagation speed of an action potential itself (hereafter called the raw velocity) may be more than 10 times the conduction velocity which includes the large relay time loss. In our study, a significantly low raw velocity of 82 m/s which is less than 1/10 times the raw required velocity which is 1200m/s (120m/s x 10) ,was calculated in an axon of 20 μm in diameter using the distributed-element circuit approach for a conventional general axon equivalent circuit [10-13]. This large difference in raw velocity indicates that there is another carrier of action potentials apart from conventional charged particles which propagates through the axonal resistance. That new carrier is the propagation of electric field produced by polarization of dielectric medium of axon fluid generated by action potential. Therefore, in this study, we considered that propagation of the electric field by polarization of the axon fluid activates the voltage-gated Na channels [14] of distant nodes. This indicates that high-speed conduction may be achieved by a combination of the characteristic axonal morphology and the dielectric properties of the axon fluid, even if a large relay time is involved.

1.1 Three factors determining conduction velocity and the wave equation of the action potential

The conduction velocity v of an action potential is determined mainly by the numerous relays time as the action potential relay from node to node, as described above. Therefore, v is determined by three elements: the relay interval x, the travel time t to the relay point x at the raw velocity Vr, and the relay time τ which is the rise time of the action potential at point x. The equation $v = x/(t + \tau)$ was devised to express v in terms of these three elements. The first term t in the denominator corresponds to the travel time x/Vr. And to determine τ of the second term in the denominator, the attenuation of the action potential by a factor $1/e^{\alpha x}$ as a result of traveling the distance x must be considered. This means that the wave equation of the action potential must be defined such that it gives attenuation constant α and a phase constant β which determines the raw velocity Vr.

1.2 Role of the dielectric characteristics of the axon fluid

Because axon fluid is a solution in which ions are dissolved in water, which has a high dielectric constant with orientation polarization [16], it can be considered as a strong dielectric medium. The dielectric constant is proportional to the relative permittivity ε_r. The relative permittivity ε_r is the ratio of dielectric constant ε of the medium to the permittivity ε_0 of a vacuum. It is an index that indicates the ease with which a medium is polarized and makes an electric field. The dielectric constant and permittivity express the same characteristic. If an electric charge σ exists in a dielectric medium, electric flux density **D** proportional to the dielectric constant ε of the dielectric medium occures and broadens around the electric charge σ, as mentioned in Maxwell's equations ($\sigma = \varepsilon\nabla\cdot\mathbf{E} = \nabla\cdot\mathbf{D}$). **E** and **D** are the vector representations of the electric field and the electric flux density; however, in this paper, **D** is hereafter referred to simply as the electric field. A strong electric field **D** proportional to the axonal dielectric constant ε occurs when there is a large quantity of electric charge by Na^+ ions in a node of Ranvier, as shown in Figure 1-1a. Furthermore, the displacement current Id is generated in proportion to the rate of change of the electric field **D,** as mentioned in Maxwell's equations Id = $d\mathbf{D}/dt$. The displacement current Id increases the propagation velocity of the electric field. If the electric field **D** reaches the threshold of a voltage-gated Na channel of a distant node of Ranvier, and triggers to generate an action potential, it indicates that electric field **D** and displacement current Id play the role of propagating action potential as a new carrier.

1.3 Dielectric characteristics and longitudinal capacitance of axon fluid

To model the axon fluid in an equivalent circuit of the axon, it is necessary to quantitatively define the role of the dielectric characteristics of the axon fluid as capacitance. And a new capacitance that plays the role of a carrier by the dielectric medium must be attached in parallel with the axonal resistance of the pathway for charged particles. Therefore, the longitudinal capacitance was defined as follows for inclusion in the newly proposed equivalent circuit of the axon. The essence of the capacitance is a polarization of the dielectric medium. Generally, a capacitor consists of two electrodes, as shown in Figure1-2a. By applying a voltage across the two electrodes, the dielectric medium contained between them becomes polarized. Therefore, one electrode can be used if there was an alternative method of polarizing the dielectric medium. In an axon, the existence of a net positive electric charge produced by a large number of Na^+ ions flowing into the axon to produce an action potential at a node of Ranvier functions as an electrode and causes the dielectric medium of the axon fluid to become polarized. An electric field proportional to the dielectric constant of the axon fluid induced by the polarization is thus propagated in both directions longitudinally along the axon. The electric field generated by each action potential spreads out equally in both longitudinal directions if a new action potential is generated at the adjacent node of Ranvier. Therefore, as shown in Figure 1-2b the longitudinal capacitance C_1 is considered to be given by $C_1 = 2\varepsilon S/d$, where the factor of 2 indicates the contribution of the two directions, ε is the dielectric constant, S is the area of the node of Ranvier where the positive electric charge from the Na^+ ions is located, and d is the distance from the electrode of the node to measurement point.

1.4 Analysis of the axon equivalent circuit using the approach of a distributed element circuit

The myelin sheath region has long, uniform high impedance like a good transmission line. However, two kinds of leak currents are present. One is the leak current I_{mr}, which is generated in proportion to the potential difference *V* between the inner and outer axon through membrane resistance *R2*. The other leak current is the displacement current I_{mc}, which is proportional to the speed of the change in the potential difference *V* between the inner and outer axon through membrane capacity *C2*. The relationship is shown below.

$$I_m = I_{mr} + I_{mc} = V/R2 + C2\ dV/dt$$

In the above equation, *V* is the amplitude of the action potential. Amplitude *V* of the action potential decreases during propagation due to axon resistance *R1*. In addition, amplitude *V* of the action potential increases as a function of time until the peak value. In other words, the leak current through the membrane calculated from the above equation is the function of the axonal place and time. I considered that axon resistance *R1*, membrane resistance *R2*, and membrane capacity *C2* are uniform across the entire length of the myelin sheath region. Therefore, I used these variables in a differential equation that relates the amplitude change and electric current change to the action potential. This means the distributed element circuit approach in the differential equation for a transmission line. Furthermore, this equation is a partial differential equation that uses the two variables of time and location. Generally speaking, solving partial differential equations is difficult, but I could calculate the answer for that equation by considering the sine wave as equivalent to the action potential as shown in the next section.

2. Materials and Methods

This chapter describes the methods used in this study to demonstrate that the high conduction velocity of the action potential is achieved by a combination of the axon fluid acting as a carrier of the electric field and the characteristic morphology of the axon.

2.1 Calculation environment, calculation software, and unit system

In this study, a partial differential equation with respect to time and position was considered; however, the final equation derived from this is a simple expression using the circuit constants R_1, R_2, C_1, and C_2 and the angular frequency ω. Therefore, the calculation environment is a normal PC, and the calculation and drawing software is the standard office application Microsoft Excel (Microsoft Corporation). The circuit constants and solutions were assessed in the MKS unit system; that is, the unit length, weight, time, and speed were considered to be 1 m, 1 kg, 1 s, and 1 m/s, respectively.

2.2 Longitudinal capacitance applied to the axon equivalent circuit

As mentioned in section 1.3, the longitudinal capacitance C_1 is defined as

$$C_1 = 2\varepsilon S/d = 2\varepsilon_0\varepsilon_r\pi r^2/d \qquad (1\text{-}1)$$

where the factor of 2 corresponds to the contribution from the two directions longitudinally along the axon, ε is the dielectric constant of the axon fluid, ε_0 (= 8.854 $\times 10^{-12}$) is the permittivity of a vacuum, and the relative permittivity ε_r is the ratio of the dielectric constant ε of the axon fluid to permittivity of a vacuum ε_0. In addition, S is the axonal cross section; r is the axonal radius, where the radii of the axon and the node of Ranvier are equal [22, 23]; and d is the distance from the electrode. The capacitance C_1 is merely inversely proportional to the distance d. Because the relative permittivity ε_r of the axon fluid is much larger than that 5-10 of the axonal membrane (Table 1-1), the electric field propagates mostly in both directions along the longitudinal axis of the axon with negligible diffusion towards the axonal membrane. This is why the longitudinal capacitance C_1 is inversely proportional to the distance d

linearly, not the square of the distance *d*.

2.3 Membrane capacitance of the myelin sheath

The membrane capacitance C_2 of the cylindrical myelin sheath was calculated as

$$C_2 = C_m = 2\pi \varepsilon_m / ln\ (D_o/D_i) \qquad (1\text{-}2)$$

where ε_m is the dielectric constant of membrane of the myelin sheath, *ln* expresses a natural logarithm and D_o and D_i are respectively the outer and inner diameter of the axon [15], as shown in Figure 1-2c.

2.4 Relationship between the circuit constants and axon diameter

Longitudinal axonal resistance R_1 is inversely proportional to the square of the diameter, and capacitance C_1 is proportional to the square of the diameter of the axon. However, membrane resistance R_2 and membrane capacitance C_2 of the myelin sheath are independent of the diameter of the axon. Berthold et al.'s study [24] states that thickness of the myelin sheath is proportional to diameter of axon. In their study, increasing the diameter makes the membrane thick, which increases the membrane resistance and results in a wide area of inner wall of the axon that decreases the membrane resistance. Therefore, the effect of the change in diameter of the axon is cancelled. As for the membrane capacitance C_2, the above reference [24] states that the ratio of the outer and inner diameter remains constant, even if the diameter changes. Therefore, the membrane capacitance C_2 does not change, because the capacitance of a cylinder such as a myelin sheath is calculated using the dielectric constant and the ratio of the outer and inner diameters. Based on these relationships, the circuit constants were set as given in Table 1-1.

2.5 Conventional axon equivalent circuit and axon equivalent circuit with applied dielectrics

In the conventional representative axon equivalent circuit, circuits representing the node of Ranvier and the myelin sheath region alternate sequentially, as shown in Figure 1-3a [10,12]. In a myelinated nerve, the ratio of the length of the node of Ranvier to that of the myelin sheath is approximately 1/1000 [17,18]. For this case, the propagation speed and attenuation coefficient were calculated for the myelinated region, and the influence of these factors on the unmyelinated nodes of Ranvier were investigated using the calculation results. Therefore, the myelin sheath region was first considered in the development of the axon equivalent circuit. Figure 1-3b and c show a representative conventional axon equivalent circuit and the newly proposed axon equivalent circuit including the dielectric constant of the axon fluid, respectively. The only difference between the two equivalent circuits is the addition of the longitudinal capacitance C_1 considered as a new signal transmission carrier between *A* and *B* in the proposed circuit (Figure 1-3c). In addition, in both equivalent circuits, an action potential generated between *A* and *C* propagates along the axon from *A* to *B*. However, if a signal propagates from *B* to *C*, this indicates that the action potential has leaked out from the axon to the extracellular space through the membrane of the myelin sheath. Therefore, if the electric potential at *B* in the node of Ranvier reaches the threshold of the voltage-gated Na channels in the node of Ranvier, these channels activate and generate an action potential; this behavior of the node of Ranvier is not represented in the depicted axon equivalent circuit.

2.6 Influence of the axon equivalent circuit on input signals

Both axon equivalent circuits are characterized by the form of a ladder-type circuit with resistive and capacitive components. An input signal is able to pass through such a circuit without influence by reflection. Therefore, regardless of the overall shape of the action potential signal input into these axon equivalent circuits, the input signal can propagate without colliding with a reflection from the circuit. An action potential will thus activate a voltage-gated Na channel when the rising phase of the action potential reaches the threshold of the voltage-gated Na channel [14]. Therefore, the propagation of the rising phase from the start to peak of the action potential (1/4 period of sine wave in Figure1-1b) is the most important aspect and the waveform after the peak is inconsequential for the propagation of action potential.

2.7 Amplitude and rise time of action potential

When the electric potential of a propagating action potential exceeds the threshold of the voltage-gated Na channels at a node of Ranvier, an action potential begins to be generated at that node. These nodes are very narrow, with a capacitance of 0.6-1.5 pF (Table 1-1), a width of 2μm, and a diameter of 10μm. However, the density of voltage-gated Na channels is very high at 12,000 sites / μm^2 [25], and a total of 753,600 voltage-gated Na channels are present in the axonal membrane of the node. Na^+ ions with an electric charge of 1.6×10^{-19} Coulombs per particle rapidly flow into the axon fluid through these voltage-gated Na channels, and a net positive charge Q of 1.2048×10^{-13} Coulombs is charged to the capacitance of the node (C_n = 0.6-1.5 pF). Therefore, the peak voltage V of the action potential is approximately 80-200 mV [26-28], as given by the equation $V = Q/C_n$. It is thought that the rate of voltage increase of the action potential is very high because a large quantity of Na^+ ions suddenly enters the intracellular space at the node of Ranvier via the rapid activation of all of the voltage-gated Na channels at the node. In this study, the amplitude of the action potential was set to 100 mV as a general representative quantity, as shown in Figure 1b. The rise time was set to 125μs by modeling the rising phase of the action potential as the first quarter period of a sine wave with a frequency of 2 kHz; this rise time was selected based on previously reported values [29].

2.8 Definition of the waveform of the action potential

The waveform of the rising phase of the action potential is similar to the first quarter period of a sine wave, which also resembles a charge curve (Figure1-1b). Moreover, because the waveform after the peak does not affect the propagation of action potential as mentioned in the section 2.6, action potentials were modeled as an entire period of a sine wave. Because the circuits contain capacitors, the complex representation that is generally used to express the voltage in an electric circuit was employed here so that calculations including phase shifts are possible [15]. Thus, the action potential waveform considered here is given by

$$e^{j\omega t} = W \sin(\omega t)\, e^{j\omega t} = W \sin(\omega t)\,(\cos(\omega t) + j \sin(\omega t)) \quad (1\text{-}3)$$

where j is the imaginary part, ω is the angular frequency, and W is the max amplitude of the sine wave representing the action potential.

2.9 Equations for the axon equivalent circuits

The equivalent circuit for the myelin sheath region of the axon (Figure 1-3b and c) consists of uniform impedance in the *AB* and *BC* segments, whose length ranges from infinitesimal to long. Therefore, the raw velocity *Vr* and attenuation constant α can be accurately calculated using the distributed-element circuit approach. The main purpose of this study was to confirm the effect of the longitudinal capacitance of the axon fluid as a newly proposed carrier of propagating action potentials. For both axon equivalent circuits, an action potential was generated at point *A* in the form of the voltage function $V = V_1 e^{j\omega t}$; then, the voltage drop over the infinitesimal segment *AB* (in the longitudinal direction) and the current flowing between points *B* and *C* (through the axonal membrane to the extracellular space) are given by the following action potential conduction equations.

In the conventional axon equivalent circuit:

$$-\mathrm{d}V/\mathrm{d}x = R_1 I = ZI \qquad (1\text{-}4)$$

$$-\mathrm{d}I/\mathrm{d}x = V/R_2 + C_2(\mathrm{d}V/dt) = (1/R_2 + j\omega C_2)V = YV. \qquad (1\text{-}5)$$

In the axon equivalent circuit with applied dielectrics:

$$-\mathrm{d}V/\mathrm{d}x = I/(1/R_1 + j\omega C_1) = ZI \qquad (1\text{-}6)$$

$$-\mathrm{d}I/\mathrm{d}x = V/R_2 + C_2(\mathrm{d}V/\mathrm{d}t) = (1/R_2 + j\omega C_2)V = YV \qquad (1\text{-}7)$$

For these two circuits, Equations (1-4) and (1-6) were differentiated with respect to *x*, and d*I*/d*x* on the right-hand sides of the resulting equations was substituted by the left-hand side of Equations (1-5) and (1-7). This yielded

$$\mathrm{d}^2V/\mathrm{d}x^2 = ZYV. \qquad (1\text{-}8)$$

The quantity *Z* was defined differently for the two types of circuits but took the same general form, and the solution is given by

$$V = V_1 e^{-\sqrt{ZY}X} + V_1 e^{\sqrt{ZY}X} = V_1 e^{-\sqrt{P+jQ}X} + V_1 e^{\sqrt{P+jQ}X} = V_1 e^{-(\alpha+j\beta)X} + V1 e^{(\alpha+j\beta)X}. \qquad (1\text{-}9)$$

Because *ZY* includes complex numbers, it is convenient to separate the real and imaginary parts as

$$ZY = P + jQ = (\alpha + j\beta)^2 \qquad .(1\text{-}10)$$

Because the real part is needed to reach the threshold of the voltage-gated Na channels, the imaginary part was ignored. Additionally, V_1 was substituted by $W \sin(\omega t) e^{j\omega t}$, yielding

$$V = W \sin(\omega t)\, e^{-\alpha x} \cos(\omega t - \beta x) + W \sin(\omega t)\, e^{\alpha x} \cos(\omega t + \beta x). \quad (1\text{-}11)$$

Equation (1-11) represents the wave equation of the action potential. The first term of Equation (1-11) describes a cosine wave with an amplitude of $W \sin(\omega t)$ propagating in the positive x-direction with raw velocity Vr (= $dx/dt = \omega/\beta$) and attenuating by a factor of $e^{-\alpha x}$ (=$1/e^{\alpha x}$) after traversing a distance of x. The second term describes a wave propagating with the same velocity and attenuation in the negative x-direction. Thus, as illustrated in Figure 1-44, Equation (1-11) indicates that an action potential generated at a node of Ranvier (x = 0) propagates in both directions longitudinally along the axon with attenuation according to the attenuation constant α. Correspondence was then established between the circuit constants and the real and imaginary parts P and Q of ZY in Equation (1-10), as shown below.

In the conventional axon equivalent circuit, P and Q are given by

$$P = R_1/R_2 \quad (1\text{-}12)$$

$$Q = \omega R_1 C_2. \quad (1\text{-}13)$$

In the axon equivalent circuit with applied dielectrics, P and Q are given by

$$P = (1/(R_1R_2) + \omega^2(C_1C_2))/((1/R_1)^2 + (\omega C_1)^2) \quad (1\text{-}14)$$

$$Q = \omega(C_2/R_1 - C_1/R_2)/((1/R_1)^2 + (\omega C_1)^2). \quad (1\text{-}15)$$

Using Equation (1-10) to construct relationships between the real and imaginary parts P and Q and the attenuation and phase constants α and β yielded

$$\alpha = \sqrt{(P + \sqrt{P^2 + Q^2})/2} \quad (1\text{-}16)$$

$$\beta = \sqrt{(-P + \sqrt{P^2 + Q^2})/2} \quad (1\text{-}17)$$

The phase constant β, which determines the raw velocity V, and the attenuation constant α, which determines the attenuation, can be expressed simply as functions of the circuit constants R_1, R_2, C_1, and C_2 and the angular frequency ω. Therefore, these equations can be solved using a general PC with Microsoft Excel. From the attenuation constant α, the remaining fraction h of the action potential amplitude after traveling a distance x was calculated as

$$h = 1/e^{\alpha x}. \quad (1\text{-}18)$$

The raw velocity Vr was calculated from the angular frequency and phase constant β given by Equation (1-11), because raw velocity means phase velocity as

$$Vr = \mathrm{d}x/\mathrm{d}t = \omega/\beta = 2\pi f/\beta. \quad (1\text{-}19)$$

2.10 Maximum reachable distance

The maximum reachable distance L was defined as the distance at which the peak value of the action potential attenuated to the level of the threshold of the voltage-gated Na channels, as shown in Figure 4. Therefore, nodes of Ranvier within the maximum reachable distance L from an activated node of Ranvier can generate an action potential, but more distant nodes of Ranvier cannot. The maximum peak value of the action potential was considered to be 35 mV on the basis of the assumption that the amplitude of the action potential is W = 100 mV and the resting potential of the axon fluid is the conventionally accepted value of −65 mV [30, 31]. Additionally, the threshold of the voltage-gated Na channel was considered to be −40 mV [14]. Thus, L is given at the distance at which the reduced amplitude w becomes 25 mV. The remaining fraction h of the action potential at the maximum reachable distance L is then given by w/W, which is equal to 1/4 for W = 100 mV and w = 25 mV, as considered here. Substituting $x = L$ and $h=1/e^{\alpha L} = w/W$ into the equation for the remaining amplitude fraction (Equation (18)) yields

$$L = \ln (W/w)/\alpha. \quad (1\text{-}20)$$

2.11 Equation for conduction velocity

From the equation for the wave equation of the action potential (Equation (1-11)), the change in the amplitude of the action potential with propagation distance x and time t. Equation (1-11) indicates that the amplitude with respect to time is W and that this amplitude attenuates with increasing distance x; additionally, the wave propagates with a raw velocity of $Vr = \omega/\beta$. If the attenuated action potential exceeds the threshold

w of the voltage-gated Na channels at a node of Ranvier, the node of Ranvier will fire. Thus, the conduction velocity v is given by

$$v = x/(t + \tau) = x/\{(x/Vr) + A\sin(w/W/(1/e^{\alpha x}))/\omega\}. \qquad (1\text{-}21)$$

The second term in the denominator of this equation is the rise time τ (relay time τ) at a distance of x as shown in Figure 5a. Substituting the distance $x = L$ when the relay point is at the maximum reachable distance L yields the following result. From $1/e^{\alpha L} = w/W$, the term $A\sin(w/W/(1/e^{\alpha x}))/\omega$ becomes $A\sin((w/W)/(w/W))/\omega = \pi/2/\omega = \pi/2/2\pi f = 1/4f = \tau$; thus, the rise time is 1/4 of the period of the sine wave. In other words, the peak value of the sine wave at this point is equal to the threshold of the voltage-gated Na channel at the maximum reachable distance L, in accordance with the definition given previously. From this, the conduction velocity v_L at the maximum reachable distance is given by

$$v_L = L/(L/Vr + \tau) = L/(L/Vr + 1/4f) \qquad (1\text{-}22)$$

Equation (1-22) is calculated with the maximum reachable distance L, the frequency f and the raw velocity Vr. Equation (1-21) is used to calculate the maximum conduction velocity v against the relay interval x based on a given attenuation constant α and raw velocity Vr, as shown in Figure 5b. Therefore, we must calculate using Equation (1-22) the attenuation constant α and raw velocity Vr against the target conduction velocity v before using Equation (1-21). The maximum conduction velocity is calculated using the ratio of the results of Equations (1-21) and (1-22).

2.12 Preconditions and definitions in this study

In this study, the axon fluid was newly considered as a carrier conveying the action potential, and the mechanism underlying the high conduction velocity of action potentials was elucidated based on this assumption. To this end, the following preconditions and definitions were considered in this study. However, it should be noted that these preconditions and definitions can be considered correct, if it is demonstrated that the dielectric constant (relative permittivity) of the axon fluid required using the dielectric applied axon equivalent circuit to achieve the conduction velocity of 120 m/s in an axon of 20 μm in diameter is equal to the actual measured dielectric constant (relative permittivity) of the axon fluid and the ratio of conduction velocity v with the axon diameter is the same even if diameter of axon of the axon equivalent circuit with applied dielectrics is changed, as mentioned in the document [3, 4].

a. On the basis of its dielectric properties, the axon fluid was newly considered as a carrier conveying action potentials.
b. The longitudinal capacitance was defined in accordance with the dielectric constant and cross section of the axon fluid.
c. The rising phase of the action potential was considered to correspond to the charging of the capacitor C_n by Na^+ ions, and the waveform of this charge curve was modeled as the first quarter phase of a sine wave.
d. The action potential, which is a soliton, was considered to be representable by a periodic function because there is no reflection from the circuit, a ladder-type circuit with resistive and capacitive components.
e. A collision of action potentials is a collision of each wave equation. Each wave has its own generated timing and place. (See 4.4)

3. Results

From the equations described in the previous section, the effect of the dielectric constant of the axon fluid, newly considered here as a carrier of the action potential, was assessed, and the results are listed and shown graphically in this section. With the angular frequency as a variable, the calculation results of the conventional and proposed axon equivalent circuits are shown based on analysis in Microsoft Excel. Moreover, the relationship between the conduction velocity and the axon diameter in the proposed axon equivalent circuit with applied dielectrics was derived using axons of different diameters. The results are presented in the MKS unit system, as mentioned previously.

3.1 List of calculation results of two axon equivalent circuits

Table 1-2 lists the calculation results of the two axon equivalent circuits. The upper and lower halves of the table indicate the conventional axon equivalent circuit and the proposed axon equivalent circuit with applied dielectrics, respectively. The only difference between the two circuits is the inclusion of the longitudinal axonal capacitance C_1 in the proposed circuit. C_1 was set to yield a conduction velocity v of 120 m/s at 2000 Hz. The column labeled f indicates the frequency of the sine wave, ranging from 1 to 4000 Hz. The column labeled ω indicates the angular frequency, which is equal to $2\pi f$, and the column labeled τ indicates the rise time to a peak of 1/4f. R_1, R_2, and C_2 are circuit constants specified in the column corresponding to an axon diameter of 20μm in Table 1-1. The columns labeled P and Q indicate the real and imaginary parts of ZY. P and Q of conventional circuit are given by Equations (1-12) and (1-13), and P and Q of the proposed circuit are given by Equations (1-14) and (1-15). The columns labeled α and β indicate the attenuation and phase constants given by Equations (1-16) and (1-17), respectively. The column labeled *Vr* indicates the raw velocity given by Equation (1-19), and the column labeled *L* indicates the maximum reachable distance given by Equation (1-20). The column labeled *v* indicates the conduction velocity *v* given by Equation (1-22) *x 1.23* for the conventional circuit and Equation (1-22) *x 1.48* for the proposed circuit, as mentioned at the end of Section 2.11. The column labeled "Nodes/*L*" indicates the number of nodes of Ranvier within the maximum reachable distance *L*, and the column labeled "Wavelength" gives the wavelength computed as the ratio of the raw velocity to the frequency. At 2000 Hz, the conduction velocity *v* in the conventional axon equivalent circuit is 42.5 m/s, and the raw velocity *Vr* is 81.7 m/s. In contrast, the conduction velocity *v* in the proposed axon equivalent circuit with applied dielectrics is 120.0 m/s, and the raw velocity *Vr* is 1,769.4 m/s. In this case, the propagation time is 0.068 s (120 m/1769 m/s) and the relay time 0.932s, which indicates that time for relay is very long compared with the propagation time.

3.2 Plots of calculation results of two axon equivalent circuits

Table 1-2 gives the precise calculation results; however, it is difficult to understand the differences between the trends of the two axon equivalent circuits. Therefore, the trends of the two circuits are shown graphically in Figure 1-6a–e for the sake of clarity. In each of the plots in Figure 1-6a–e, the horizontal axis indicates the frequency, which is inversely proportional to the rise time. The thin red vertical line represents 2000 Hz, which corresponds to a rise time of 125μs. The black curves with triangles indicate the results of the conventional axon equivalent circuit, and the red curves with circles indicate the results of the axon equivalent circuit with applied dielectrics.

Raw velocity *Vr*: Figure 1-6a indicates the raw velocity *Vr* of the two circuits. The raw velocity *Vr* of the conventional axon equivalent circuit increased slightly with increasing frequency from approximately 1000 Hz, whereas the raw velocity *Vr* of the axon equivalent circuit with applied dielectrics increased exponentially with increasing frequency from approximately the same frequency. Therefore, the vertical axis is given in an exponential scale. The exponential trend strongly supports the effect of the axon fluid as a dielectric medium. However, the achieved velocity of 1,769 m/s at 2000 Hz was very slow in comparison with the velocity of the conventional electric circuit; additionally, this velocity is approximately 1/170,000 of the speed of light (3×10^8 m/s). This reveals an important theme about the signal transmission property of axons, as will be discussed below in the subsection Wavelength. These results of raw velocity *Vr* support the understanding that the polarization of the axon fluid, a heavy dielectric medium, acts as a carrier conveying the action potential.

Maximum reachable distance *L*: Figure 1-6b indicates the maximum reachable distance *L* of the two circuits. In the conventional axon equivalent circuit, the leakage current produced by the displacement current through the axonal membrane capacitance C_2, which increases with increasing frequency, yielded a maximum reachable distance of less than 7.46 mm from approximately 1000 Hz. In contrast, in the axon equivalent circuit with applied dielectrics, the longitudinal capacitance C_1 yielded a longitudinal displacement current that increased in proportion to the frequency. This compensated for the leakage current from the membrane capacitance C_2 and produced a maximum reachable distance of 10.62 mm, representing a lesser attenuation than in the conventional case.

Conduction velocity *v*: Figure 1-6c indicates the conduction velocity *v* of the two circuits. The conduction velocity *v* of 120 m/s of the proposed axon equivalent circuit is higher than that of 42.54 m/s of the conventional circuit because the inclusion of the axonal longitudinal capacitance C_1 resulted in a higher raw velocity *Vr* faster and a larger maximum reachable distance *L*.

Number of nodes of Ranvier within the maximum reachable distance *L*: Figure 1-6d indicates the number of nodes of Ranvier within the maximum reachable distance *L* for the two circuits. Even if defective nodes of Ranvier were present, the action potential could be propagated by the remaining nodes of Ranvier within the maximum reachable distance *L*. This number represents a safety factor [32].

Wavelength: Figure 1-6e indicates the wavelength of an action potential in the two circuits. The data in this plot are valuable, as they indicate the wavelength of an action potential as it propagates through an axon. The significance of this is that if the wavelength is on the same order of magnitude as the circuit length through which signals pass, the signal is strongly affected by the circuit. Because the length of motor and sensory neurons is approximately 1 m and the wavelength of an action potential is 0.885 m, the length of the axons of these neurons cannot be ignored. However, the length of a uniform myelin sheath is 2 mm, approximately 1,000 times the 2 μm length of a node of Ranvier. Therefore, 99.9% of the axon length is composed of uniform regions of reasonable impedance, yielding a suitable transmission pathway as mentioned in the Section 1.4. In other words, the myelin sheath may be considered as a structure to cope with the short wavelength of the action potential. In addition, the influence of the very low impedance of the node of Ranvier can be ignored because the ratio of the length of a node of Ranvier (2μm) to that of the wavelength (0.885 m) is less than 1/440000. It is generally said that values below 1/100 can be considered negligible.

3.3 Applying the axon equivalent circuit with applied dielectrics to axons of different diameters

The conduction velocity *v* grows in proportion to the axon diameter [3, 4]. Thus, from the value of the axon longitudinal capacitance C_1 determined by the procedure described above, Equation (1-1) was applied to scale this capacitance to axons of various diameters, and then the diameter-dependent values in Table 1 were applied as the circuit constants R_1, R_2, and C_2 in the axon equivalent circuit with applied dielectrics (see Section 2.4). The results are shown in Figure 1-7a–e. The raw velocity *Vr* (Figure 1-7a), the maximum reachable distance *L* (Figure 1-7b), conduction velocity *v* (Figure 1-7c), and the wavelength (Figure 1-7e) were all found to be proportional to the axon diameter. However, because the spacing between the nodes of Ranvier and the maximum reachable distance *L* are also proportional to the diameter [4, 17], the number of nodes of Ranvier contained within maximum reachable distance *L* (Figure 1-7d) remained constant. This shows that the safety factor [32] is a constant independent of the conduction velocity *v* and the diameter of the axon. As shown in Figure 6c, the conduction velocities *v* of axons with diameters of 13 and 6μm were 78 and 36 m/s, respectively. These are yield the same ratio of conduction velocity *v* to diameter as that for an axon diameter of 20μ m in diameter, i.e., the ratios of 120 m/s/20μm, 78 m/s/13μm and 36 m/s/6μm are all the same value. These calculation results show that the preconditions and definitions considered in this study (Section 2.12) are valid.

3.4 Comparison of relative permittivity of the longitudinal capacitance and the axon fluid

The aim of this study was to confirm the hypothesis that dielectric characteristics of axon fluid contributes to the conveyance of action potentials. To confirm this hypothesis, for an axon of 20μm in diameter, the longitudinal capacitance necessary to achieve conduction velocity v of 120 m/s was calculated using the proposed axon equivalent circuit with applied dielectrics. The relative permittivity of an ionic fluid like axon fluid was compared with the relative permittivity calculated from the longitudinal capacitance using Equation (1-1). On the basis of the circuit constants given in Table 1, the value of longitudinal capacitance *C1* was considered to be $C1 = 7.409 \times 10^{-14}$ F m. The relative permittivity ε_r corresponding to this *C1* value calculated using Equation (1-1) was 1.33×10^{7}. This result would be ideally compared with the relative permittivity ε_r of actual axon fluid; however, this data could not be obtained. Therefore, we used the measurement data from [33] reporting the relative permittivity of an ionic liquid containing NaCl at 0.09 M; this is similar to axon fluid which is composed primarily of KCl at a concentration of 0.1 M. According to this, the relative permittivity of 0.09 M NaCl is approximately 3×10^{7} at 200 Hz and 10^{6} at 2000 Hz. Therefore, the calculated value is in fair agreement with the previously reported value. This result further confirms that the high-speed conduction of the action potential is achieved by a combination of the axonal characteristic morphology and the dielectric effect of the axon fluid.

4. Discussion

4.1 Equation for the conduction velocity of the action potential and axonal factors

As mentioned in Sections 1.1 and 2.11, the conduction velocity v of the action potential depends on the relay interval x, the travel time t to reach the relay point x, and the relay time τ at the relay point x. The relay time τ is defined as the time from the start of an action potential until the voltage reaches the threshold of the voltage-gated Na channel.

$$v = x/(t + \tau) = x/\{(x/Vr) + A\sin(w/W/(1/e^{\alpha x}))/\omega\}. \quad (1\text{-}21)$$

Equation (1-21) indicates that the conduction velocity v is determined by the angular frequency ω (rising speed of the action potential), the raw velocity Vr (= ω/β), the attenuation constant α, the amplitude W of the action potential, and the attenuated amplitude w. The amplitude W is determined by capacitance C_n and voltage-gated Na channel density of node of Ranvier and the attenuated amplitude w is determined by the resting potential of the axon fluid and the threshold of the voltage-gated Na channel, and the attenuation constant α and phase constant β are determined from the wave equation of the action potential using the circuit constants R_1, R_2, C_1, and C_2. Therefore, it was demonstrated that conduction velocity v could be calculated quantitatively from the main electric factors representing the axonal morphology.

In squid, the giant axon is covered by a layer of Schwann cells but quite different from a typical multiple layered myelin sheath. Thus, the structure of myelinated nerve fiber consisting of axon, myelin sheath and node of Ranvier to produce salutatory conduction, a high conduction velocity system, was phylogenically obtained only in vertebrates. In demyelinating diseases in human, the significantly diminished conduction velocity, even if mild segmental loss of myelin sheath, was observed [34].

4.2 Characteristic axonal morphology and behavior as a dielectric carrier

From the standpoint of electric circuit theory, the axon appears to comport rather naturally with the paradigm of distributed-element circuit analysis. Of course, distributed-element circuit modeling is typically reserved for signal frequencies of several hundred megahertz or more, but this conventional wisdom is based on the idea that signals pass through the electric circuits at nearly the speed of light. However, the degree of influence of the transmission line on the signal being transmitted depends on the ratio of the length of the transmission line to the wavelength of the signal. As stated in Section 3.2, the wavelength of an action potential is 0.885 m at a frequency of 2000 Hz, and the action potential is affected by an axonal transmission characteristic to approach the same level of length of the motor and sensory nerve. However, the properties of the myelin sheath make it a good transmission line, as mentioned in Section 1.4. The morphology of the myelin sheath is a good complement to the extremely short wavelength of the action potential of the carrier of axon fluid. On the other hand, it becomes the domain where impedance is very low, where the membrane is very thin because the node of Ranvier does not have a sheath. However, the length of node of Ranvier region (2μm) is very short compared with the wavelength (0.885 m), and it is less than 1/440000. Therefore, we thought that the quantity of energy loss of one wavelength of action potential by node of Ranvier region is negligible. Rather, it is thought that this very short length is useful to ensure a low capacitance C_n of the node of Ranvier.

4.3 Steeply rising waveform of the action potential and voltage-gated Na channel density

A high raw velocity Vr and short relay time τ are necessary to achieve a high conduction velocity v. This means that the rise time from the start of the wave pattern of the action potential to its peak value is very important. As mentioned in Section 2.7, it was considered in this study that the phenomenon of Na^+ ions flowing into the small capacitance C_n of the node of Ranvier via a large number of Na channels produces a steeply rising waveform characteristic of an action potential. Therefore, this rising phase was modeled as the first quarter period of a sine wave, which is similar to a charge curve. In addition, according to a previous report [35, 36] the channel of the voltage-gated Na channel is very narrow; it has been suggested that the time for a Na^+ ion to enter into the channel of same voltage-gated Na channel through which another Na^+ had just passed is required a time because of the thermal motion and the repulsion among Na^+ ions near the channel. Therefore, on the basis of the density of voltage-gated Na channels (12,000 sites/μm²) in the sciatic nerve of the rabbit reported by Ritchie (1977) [25], it is thought that the structure of the node of Ranvier enables the generation of a large amplitude and a steeply rising waveform if each of the Na channels operates with the same timing as the capacitance C_n of the node of Ranvier. From the standpoint of high density technology, we were surprised at the extremely high density of voltage-gated Na channel that is 1.2 x10^{10}/mm², because this channel has complicate functions that recognizes Na ion and controls the path-way of Na ion depending on the voltage of action potential.

4.4 Collision between action potentials

The presence of multiple nodes of Ranvier within the maximum reachable distance L from a firing node senses the generated action potential and produces action potentials in response. Therefore, action potentials generate proximally in time and collide with one another. But in here, I talk about only the collisions of action potentials of nodes of Ranvier in the direction for axon terminal, because the nodes of Ranvier in the direction for axon hillock are in refractory period. Collision of action potentials is a collision of waves of the form given in Equation (1-11). This equation demonstrates that action potentials propagate in both directions longitudinally along the axon with a raw velocity Vr (= ω/β) and take on the temporal form of a sine wave of amplitude W that attenuates in space according to the attenuation constant α as mentioned in Section 2.9. When action potentials collide, a wave equation that specifies when and where the action potentials were generated is added at the place of collision. In addition, the directions toward the axon terminal and the axon hillock were defined as positive and negative directions. Therefore, in the case of the collision of action potentials traveling in the same direction, their waveforms are added, and in the case of the collision of action potentials traveling in different directions, their waveforms are subtracted. On this basis, when an action potential traveling in the positive direction from the (*N*-1) th node of Ranvier meets an action potential traveling in the negative direction from the *N*th node of Ranvier, it is eliminated if the amplitude of the positive traveling wave is smaller than that of the negative traveling wave. However, if the action potential from the (*N*-1) th node of Ranvier is not eliminated at the *N*th node of Ranvier, the positive traveling action potential from the *N*th node of Ranvier is added to it.

That is, the waveforms of (*N-1*) th node of Ranvier are subtracted in the region before the *N*th node of Ranvier and added in the region beyond this node. However, the phases of the added waves are different because each wave is generated independently.

4.5 Relative permittivity of ionic fluid similar to axon fluid

Using the axon equivalent circuit with applied dielectrics, the value of the capacitance C_1 that yields a conduction velocity v of 120 m/s in an axon of 20 μm in diameter was calculated to be 7.41×10^{-14} F m. The relative permittivity calculated using Equation (1-1) was very large (1.37×10^{7}) at this capacitance C_1. However, data on the frequency properties of the relative permittivity and electric current of axon fluid are not available. Thus, data on the frequency characteristics of relative permittivity and electric current were obtained for an ionic liquid composed of NaCl with a concentration of 0.09 M, which is similar to the KCl concentration of 0.1 M of axon fluid. Usually, it is less than 10^4 when the relative permittivity ε_r is high [38]; therefore, we were surprised at the value of the calculated relative permittivity ε_r of 1.37×10^{7} of axon fluid, but we relieved to find the relative permittivity data of Gabriel [33]. From the previous report on the NaCl data, the permittivity is inversely proportional to the frequency, the growth rate of the electric current decreases with increasing frequency from 1 kHz, and the current is nearly flat near 10 kHz [33]. This trend suggests a balance point between the frequency of the axon fluid and the structure of the node of Ranvier. In addition, these extremely large values have been reported about the biological tissue, brain and heart [37-40]. In future study, we will examine the influence of the extremely high relative permittivity ε_r of the ion solution inside and outside neurons.

Conclusions

In this study, it was demonstrated that a high conduction velocity *v* of 120 m/s could be achieved when modeling an axon of 20μm in diameter using a newly proposed axon equivalent circuit incorporating the dielectric behavior of the axon fluid as a longitudinal capacitance C_1. The raw velocity *Vr* for this conduction velocity *v* was 1769.4 m/s, and under the same conditions, the conventional axon equivalent circuit achieves a conduction velocity *v* of 42.5 m/s and a raw velocity *V* of 81.7 m/s. These results show that propagation of the electric field produced by the polarization of the dielectric axon fluid acts as a carrier conveying action potentials. It was also demonstrated that the conduction velocity *v* calculated for axons of different diameters is proportional to the diameter. This is evidence of the validity of the definition of the longitudinal capacitance *C1* and the proposed axon equivalent circuit with applied dielectrics. Furthermore, it was revealed that the long and uniform structure of the myelin sheath, which has a high impedance, is a good complement to the very short wavelength of the action potential and that the structure of the node of Ranvier enables the production of action potentials with a high amplitude and steep rise for the sake of fast raw velocity and short relay time. And we could indicate the equation (1-21) of conduction velocity v which includes all of main factors of axon. Finally, it was confirmed that the relative permittivity calculated from the longitudinal capacitance C_1 is very high (10^6–10^7) and nearly equal to the relative permittivity of an ionic fluid composed of NaCl with a concentration of 0.09 M, similar to the KCl concentration of 0.1 M in axon fluid. In this study, the circuit constants were used as listed in Table 1; these constants were derived by Hodgkin on the basis of data collected by Huxley, Stampfli, and Tasaki [20] in 1964[19].

Figures

Figure 1-1: Axon morphology and action potential

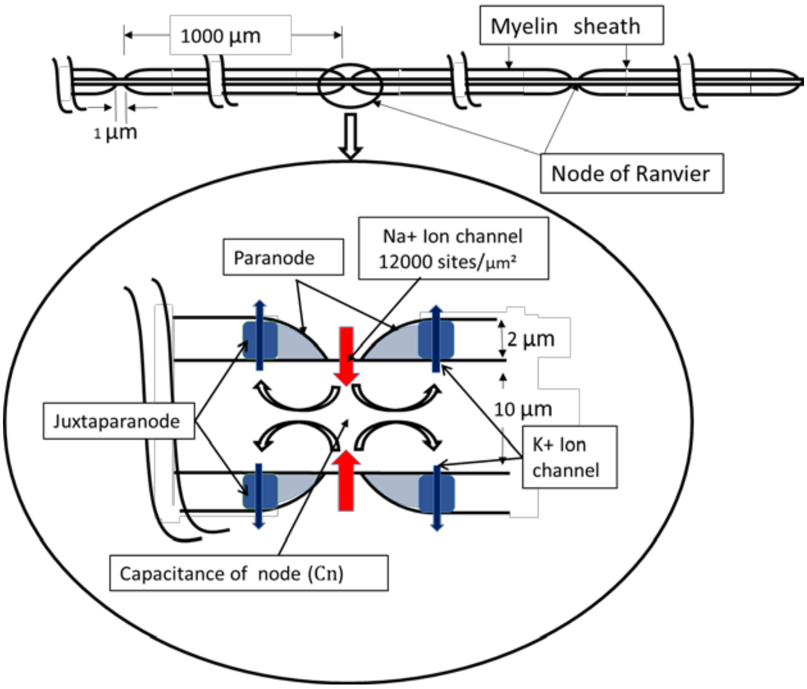
(a) Myelin sheath and node of Ranvier.

Top: the length of the myelin sheath is about 1000 times longer than that of a node of Ranvier. Bottom: positively charged Na^+ ions flow through Na ion channels into the disc-shaped area of capacitance C_n of the node of Ranvier, subsequently, an equivalent positive charge carried in is expelled through K^+ ion channels by K^+ ions. Two local ion current loops are formed by Na^+ ion channels in the node and K^+ ion channels in juxtaparanodes on both sides of the node.

(b) Action potential and sine wave.

An influx of positively charged Na+ ions into the disc-shaped area of capacitance C_n of the node of Ranvier results in an increase of positive charge Q, and that makes action potential high voltage as shown by the equation (V=Q/Cn). Between the initial point and the peak value, the action potential waveform (red curve) resembles a sine wave (black dashed curve) of 2 000 Hz. The rising time 125μs is equal to a quarter of period of 2000 Hz.

(a)


1000 µm
Myelin sheath
1 µm
Node of Ranvier
Paranode
Na+ Ion channel
12000 sites/µm²
2 µm
10 µm
Juxtaparanode
K+ Ion
channel
Capacitance of node (Cn)

(b)

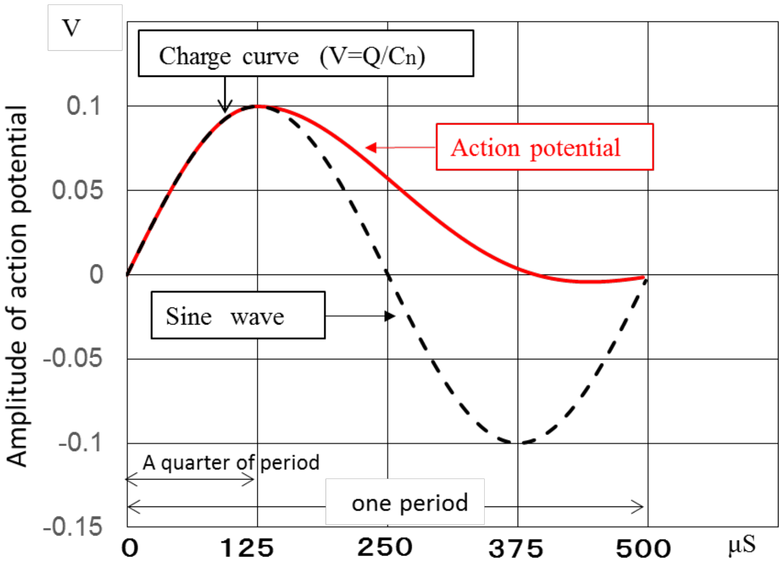


Figure 1-2: Three kinds of capacitance

(a) Capacitance by parallel plate electrodes

This equation is normally used to calculate the capacitance of a condenser.

The d means distance between two electrodes.

(b) Capacitance of a Na ion electrode

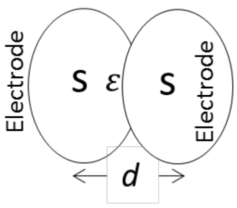
This equation was defined to calculate the axonal longitudinal capacitance in this study. The d means distance from Na ion electrode to measurement point.

Distance d (1m) may be omitted, because this document is described by MKS unit system.

(c) Capacitance by Do and Di electrode

This equation is used to calculate the capacitance of a cylinder-like myelin sheath. Width (1m) of electrode may be omitted, because this document is described by MKS unit system.

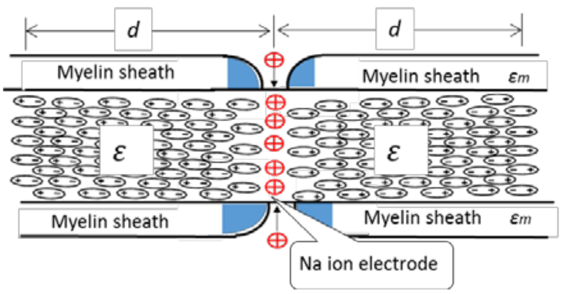
(a)



$C = \varepsilon S / d$

Capacitance is proportional to area of electrode and inversely proportional to distance.

(b)



$C = 2\varepsilon S / d = 2\varepsilon_0\varepsilon_r\pi r^2 / d$

Capacitance is formed in both directions and is proportional to area of Na ion electrode.

(c)

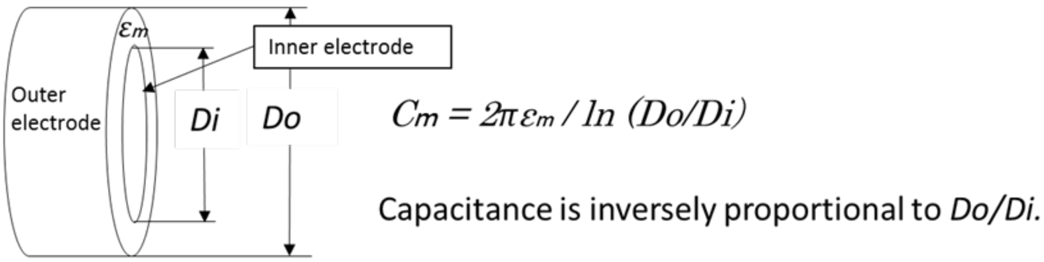


Figure 1-3: Axon equivalent circuit

(a) Sample conventional axon equivalent circuit

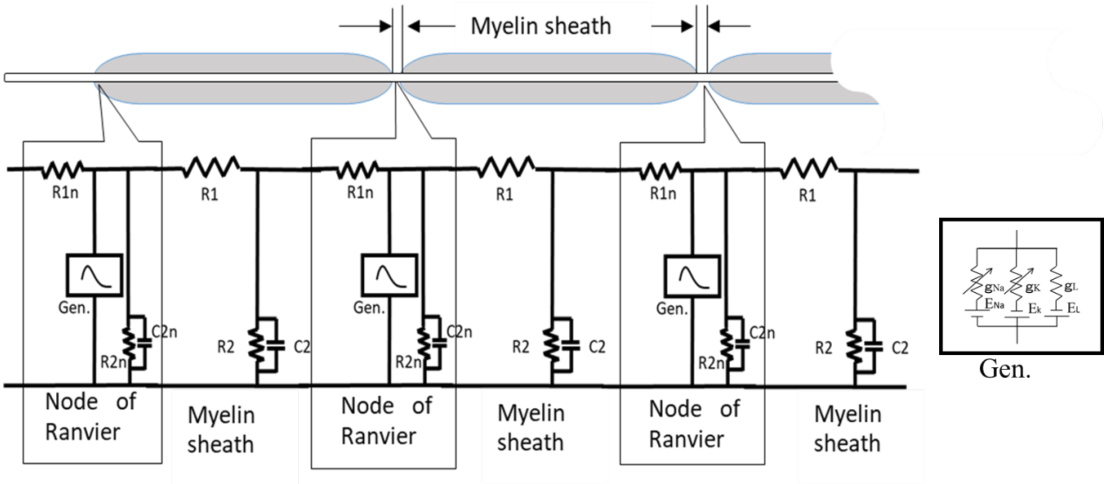
When *Gen.* provides high impedance, an axonal longitudinal resistor *R1*, membrane resistor *R2*, and membrane capacitance *C2* are present at the myelin sheath region, and an axonal longitudinal resistor *R1n*, membrane resistor *R2n*, and membrane capacitance *C2n* are present at the node of Ranvier region. Those resistors and capacitances constitute a ladder circuit that does not reflect back a signal regardless of the terminal condition. Gen. is the action potential generator. gL and EL produce voltage during the resting situation. gNa and ENa insert Na^+ ions into the axon, and gK and EK allow flow of the same quantity of K^+ ions as Na^+ ions that flow out of the axon.

(b) Conventional axon equivalent circuit

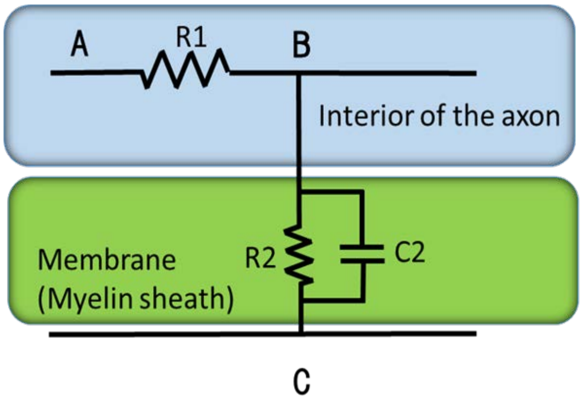
(c) Axon equivalent circuit with applied dielectrics.

The difference between the conventional axon equivalent circuit and the axon equivalent circuit with applied dielectrics is the existence of axonal longitudinal capacitance *C1*.

(a)



(b)



(c)

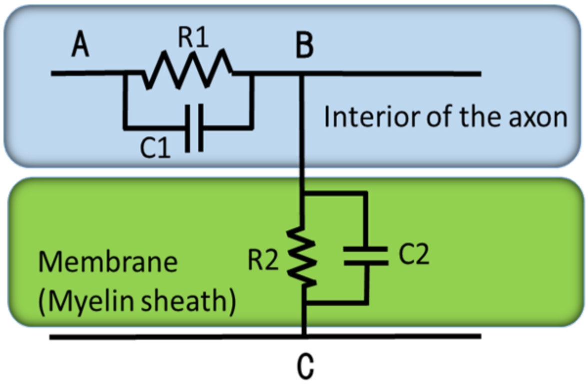


Figure 1-4: Propagation of the action potential

An action potential generated at a node of Ranvier propagates to the left and to the right with raw velocity *Vr* while decaying by a factor $1/e^{\alpha x}$ after traveling distance *x*. W is maximum amplitude of the action potential. And w is the smallest amplitude that could be the threshold of voltage gated Na channel. Nodes of Ranvier lying beyond the maximum reachable distance *L* do not fire, but nodes of Ranvier lying within that distance do fire. Needless to say, nodes of Ranvier to the left are in a refractory period and thus cannot fire. From this figure, conduction velocity v_L can be calculated by the equation $v_L = L/(L/Vr + \tau)$, in the case of a relay interval of maximum reachable distance *L*.

Figure 1-5: Optimum conduction velocity

(**a)** Relay time τ (rise time τ) and relay interval *x*.

Relay time τ increases exponentially near maximum reachable distance *L* as shown in (a). Fire timing is obtained by adding travel time *t* (*x/Vr*) and this relay time τ. And conduction velocity *v* is obtained by dividing distance ***x*** of the node of Ranvier (relay interval *x*) by fire timing *(t+τ)*.

(b) Conduction velocity *v* and relay interval *x*

The relation of relay interval *x* and conduction velocity *v*, in an axon of diameter 20µm with a rise time frequency of 2000 Hz is shown in (b). Curve A indicates conduction velocity *v* as computed using the conventional axon equivalent circuit with the Type I values of α and *Vr* from Table1- 2. Curve B indicates conduction velocity *v* as computed using the axon equivalent circuit with applied dielectrics with the Type II values of α and *Vr* from Table1-2.

Figure 1-4

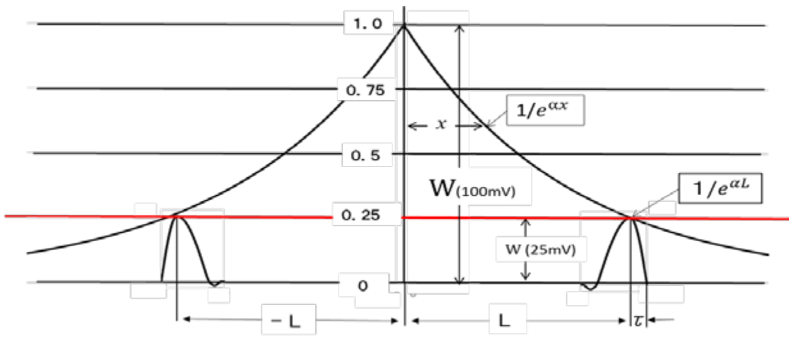
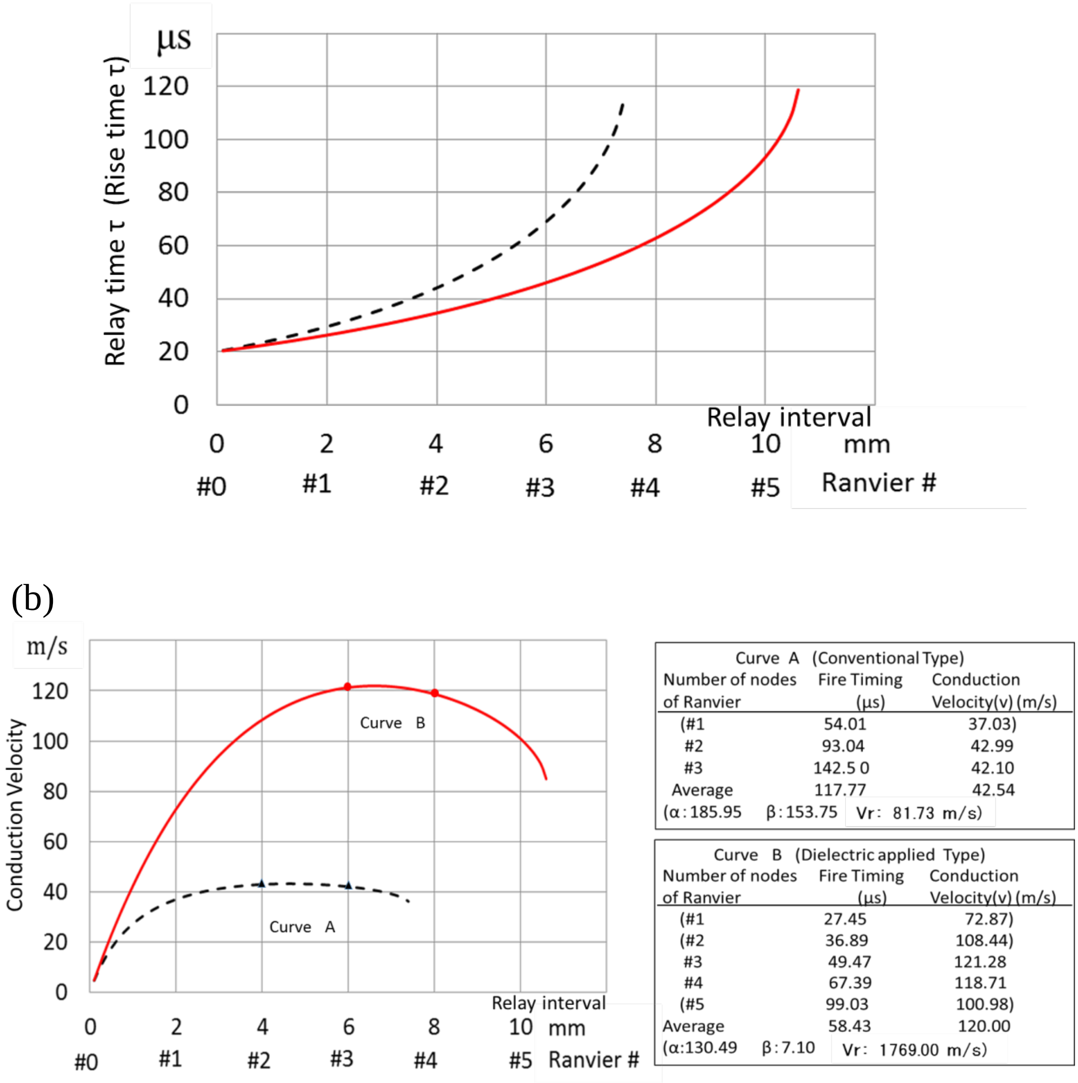


Figure 1-5

(a)



Curve A (Conventional Type) Number of nodes of Ranvier	Fire Timing (µs)	Conduction Velocity(v) (m/s)
(#1	54.01	37.03)
#2	93.04	42.99
#3	142.5 0	42.10
Average	117.77	42.54
(α:185.95	β:153.75	Vr: 81.73 m/s)

Curve B (Dielectric applied Type) Number of nodes of Ranvier	Fire Timing (µs)	Conduction Velocity(v) (m/s)
(#1	27.45	72.87)
(#2	36.89	108.44)
#3	49.47	121.28
#4	67.39	118.71
(#5	99.03	100.98)
Average	58.43	120.00
(α:130.49	β:7.10	Vr: 1769.00 m/s)

Figure 1-6: Computation results for both types of axon equivalent circuits for axons of diameter 20µm.

The longitudinal capacitance C_1 in the axon equivalent circuit was chosen with applied dielectrics to yield a conduction velocity of 120 m/s in 2000 Hz. Black curves indicate results for the conventional axon equivalent circuit, and red curves are for the axon equivalent circuit with applied dielectrics. Horizontal axis indicates the frequency. A quarter of period of the frequency is equal to rising time of the action potential.

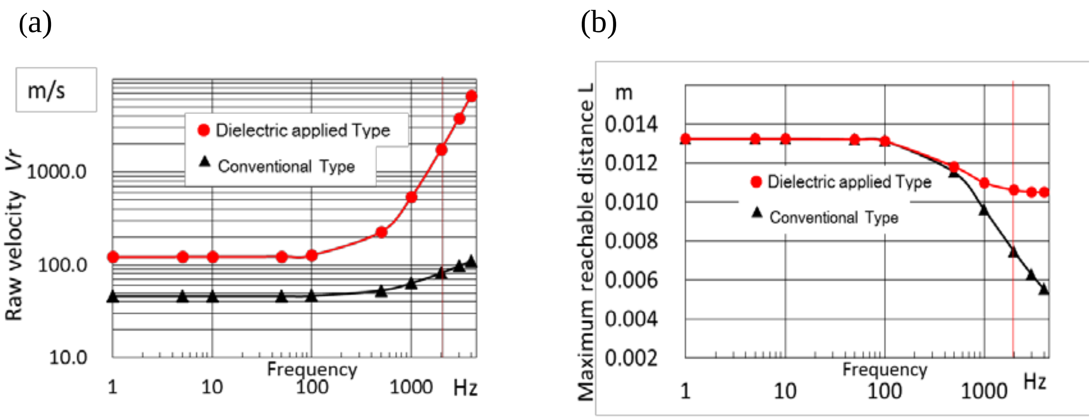
(a) Raw velocity *Vr* (that is phase velocity). Because the Raw velocity *Vr* increased greatly beyond around 1000 Hz for the axon equivalent circuit with applied dielectric, we used a logarithmic scale for the vertical axis as well as for the horizontal axis. Longitudinal capacitance C_1 contributed largely to increase the raw velocity *Vr*.

(b) Maximum reachable distance *L*. In the conventional axon equivalent circuit, the maximum reachable distance *L* rapidly decreased at frequencies beyond around 1000 Hz. Longitudinal capacitance C_1 prevented the maximum reachable distance *L* from becoming shorter.

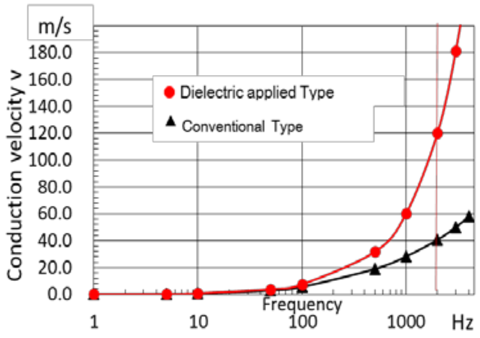
(c) Conduction velocity *v*. The slow values obtained for the conventional equivalent circuit at 2000 Hz agreed with previously reported values [10-13]. In the axon equivalent circuit with applied dielectrics, the conduction velocity *v* 120m/s is achieved.

(d) **N**umber of nodes of Ranvier /*L*. The safety factor is relative to the number of nodes of Ranvier within the maximum reachable distance. In the axon equivalent circuit with applied dielectrics, number of nodes was five, even above 2000 Hz, and for the conventional axon equivalent circuit, the number of nodes was three or below.

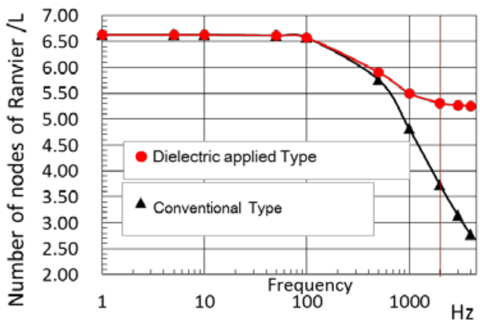
(e) Wavelength. In the dielectric applied axon equivalent circuit with applied dielectrics, the raw velocity *Vr* was rapid, but still far below the speed of light, yielding a wavelength of 0.885 m at 2000 Hz.



(c)



(d)



(e)

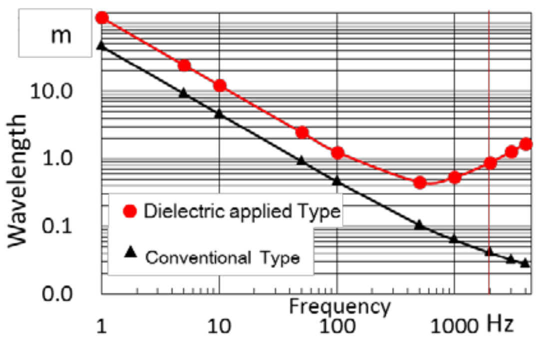


Figure 1-7: Data comparison of axons of different diameters

Figure 1-7 a-c and e indicate the value which is proportional to the diameter. These data demonstrated that definitions of longitudinal capacitance by axon fluid and of new equivalent axon circuit are correct.

(a) Raw velocity *Vr*.

(b) Maximum reachable distance *L*.

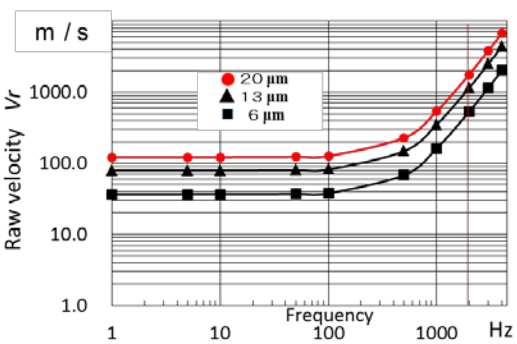
(c) Conduction velocity *v*.

(d) Number of nodes of Ranvier /*L*.

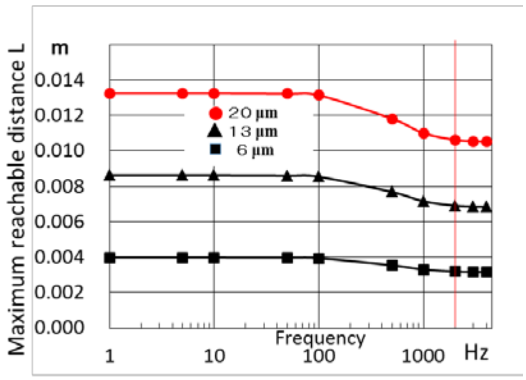
Number of nodes of Ranvier being included in maximum reachable distance *L* is independent of the diameter.

(e) Wavelength

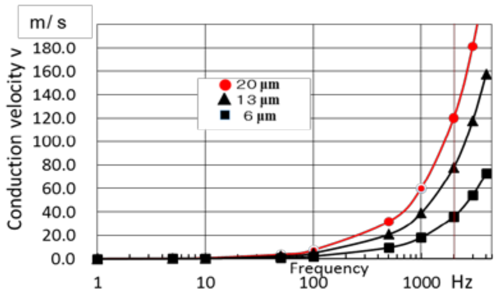
(a)



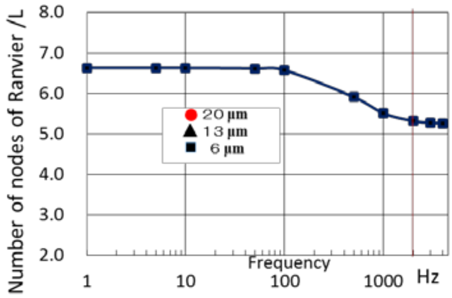
(b)



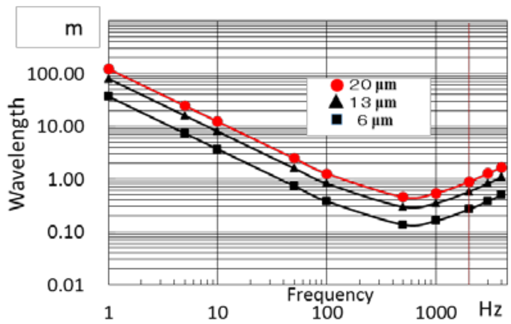
(c)


m/ s
Conduction velocity v
180.0
160.0
140.0
120.0
100.0
80.0
60.0
40.0
20.0
0.0
20 µm
13 µm
6 µm
Frequency
1
10
100
1000
Hz

(d)


Number of nodes of Ranvier /L
8.0
7.0
6.0
5.0
4.0
3.0
2.0
20 µm
13 µm
6 µm
Frequency
1
10
100
1000
Hz

(e)


m
Wavelength
100.00
10.00
1.00
0.10
0.01
20 µm
13 µm
6 µm
Frequency
1
10
100
1000
Hz

Tables

Table 1-1: Data about the axon

Circuit constants that are used to calculate the conduction velocity like R1, R2, C1 and C2 are shown in Table1-1.

[a] This column includes data of the frog myelinated nerve originally obtained by Huxley and Stampfli (1949) and by Tasaki (1955) and compiled by Hodgkin in (1964) [19].

[b] These data were obtained by applying the conversion formulas of Section 2.4 to axons of various diameters.

[C] These data were obtained from reference document [4].

Relative permittivity of myelin sheath which decides the membrane capacitance *C2* is very small value (5-10) as shown in table 1-1.

Table 1-1 Data about the Axon

Variable	Location	Data assembled by Hodgkin [a]	Myelinated axon [b]		
			20 µm	13 µm	6 µm
	Diameter (outer) of axon	14 µm	28 µm	18.2 µm	8.4 µm
	Diameter (inner) of axon	10 µm	20 µm	13 µm	6 µm
	Thickness of myelin	2 µm	4 µm	2.6 µm	1.2 µm
R1	Resistance per unit length of axis cylinder	14,000 MΩ/m	3,500 MΩ/m	8,284 MΩ/m	38,888 MΩ/m
R2	Resistance ×unit length of myelin sheath	0.25-0.4 MΩ m	0.32 MΩ m	0.32 MΩ m	0.32 MΩ m
C1	Capacity per unit length of axis cylinder	Not defined	7.409×10^{-14} Fm	3.130×10^{-14} Fm	6.668×10^{15} Fm
C2	Capacity per unit length of myelin sheath	1,000-1,600 pF/m	1300 pF/m	1300 pF/m	1300 pF/m
	Relative permittivity of myelin sheath	5-10	5-10	5-10	5-10
	Length of myelin sheath [c]		2 mm	1.3 mm	0.6 mm
	Length of the node of Ranvier		2 µm	1.3 µm	0.6 µm
Cn	Capacity of the node of Ranvier	0.6-1.5 pF			

Table 1-2: List of calculation results of two axon equivalent circuits

Values for the type Ⅰ (conventional axon equivalent circuit) and type Ⅱ (axon equivalent circuit with applied dielectrics) axon equivalent circuits computed in the framework of distributed-element circuit analysis. The vertical axis indicates the action potential rise velocity, expressed in form of a frequency. The horizontal axis indicates the major quantities of interest computed via the equations described in Section 2.9 and 2.10. The value of C1 in the type 2 circuit was chosen to yield a conduction velocity of v=120m/s utilizing the equation (1-21) and (1-22) for an axon of diameter 20μm at arise frequency of 2000 Hz.

Table 1-2 List of calculation results of two axon equivalent circuit

Type	*f*	*ω*	*τ*	*R1*	*R2*	*C1*	*C2*	*P*	*Q*	*α*	*β*	*V*	*L*	*v*	*Nodes/L*	*wave length*
Type I	1	6.28318	0.25	3.5E+09	320000	0	1.3E-09	10937.5	28.58847	104.58	0.14	45.970	0.01326	0.07	6.63	45.970
	5	31.4159	0.05	3.5E+09	320000	0	1.3E-09	10937.5	142.9423	104.58	0.68	45.971	0.01326	0.33	6.63	9.194
	10	62.8318	0.025	3.5E+09	320000	0	1.3E-09	10937.5	285.8847	104.59	1.37	45.974	0.01326	0.65	6.63	4.597
	50	314.159	0.005	3.5E+09	320000	0	1.3E-09	10937.5	1429.423	104.80	6.82	46.068	0.01323	3.09	6.61	0.921
	100	628.318	0.0025	3.5E+09	320000	0	1.3E-09	10937.5	2858.847	105.46	13.55	46.355	0.01315	5.83	6.57	0.464
	500	3141.59	0.0005	3.5E+09	320000	0	1.3E-09	10937.5	14294.23	120.28	59.42	52.872	0.01153	19.80	5.76	0.106
	1000	6283.18	0.00025	3.5E+09	320000	0	1.3E-09	10937.5	28588.47	144.13	99.18	63.354	0.00962	29.53	4.81	0.063
	2000	12566.36	0.000125	3.5E+09	320000	0	1.3E-09	10937.5	57176.94	185.95	153.75	81.734	0.00746	42.54	3.73	0.041
	3000	18849.54	8.333E-05	3.5E+09	320000	0	1.3E-09	10937.5	85765.41	220.68	194.32	97.001	0.00628	52.33	3.14	0.032
	4000	25132.72	0.0000625	3.5E+09	320000	0	1.3E-09	10937.5	114353.9	250.81	227.97	110.247	0.00553	60.53	2.76	0.028
Type II	1	6.28318	0.25	3.5E+09	320000	7.409E-14	1.3E-09	10937.518	10.76772	104.58	0.05	122.052	0.01326	0.08	6.63	122.052
	5	31.4159	0.05	3.5E+09	320000	7.409E-14	1.3E-09	10937.939	53.83518	104.58	0.26	122.063	0.01326	0.39	6.63	24.413
	10	62.8318	0.025	3.5E+09	320000	7.409E-14	1.3E-09	10939.254	107.6489	104.59	0.51	122.095	0.01326	0.78	6.63	12.210
	50	314.159	0.005	3.5E+09	320000	7.409E-14	1.3E-09	10981.071	534.838	104.82	2.55	123.143	0.01323	3.83	6.61	2.463
	100	628.318	0.0025	3.5E+09	320000	7.409E-14	1.3E-09	11108.404	1048.929	105.51	4.97	126.407	0.01314	7.47	6.57	1.264
	500	3141.59	0.0005	3.5E+09	320000	7.409E-14	1.3E-09	13573.856	3236.138	117.32	13.79	227.785	0.01182	31.68	5.91	0.456
	1000	6283.18	0.00025	3.5E+09	320000	7.409E-14	1.3E-09	15737.942	2946.281	125.99	11.69	537.39	0.01100	60.20	5.50	0.537
	2000	12566.36	0.000125	3.5E+09	320000	7.409E-14	1.3E-09	16977.43	1853.509	130.49	7.10	1769.40	0.01062	120.00	5.31	0.885
	3000	18849.54	8.333E-05	3.5E+09	320000	7.409E-14	1.3E-09	17280.734	1297.724	131.55	4.93	3821.51	0.01054	181.14	5.27	1.274
	4000	25132.72	0.0000625	3.5E+09	320000	7.409E-14	1.3E-09	17394.216	990.7054	131.94	3.75	6694.27	0.01051	242.68	5.25	1.674

Part Ⅱ

The measurement of the dielectric property of KCl liquid similar to axon fluid

Abstract

To verify the mechanism of high conduction velocity of an action potential, I

proposed a new axon equivalent circuit that incorporates the effect of the dielectric property of axon fluid. A high-speed conduction velocity could be calculated with the proposed equivalent circuit. Therefore, this hypothesis is correct if the dielectric constant that was calculated from the new axon equivalent circuit is the same as the dielectric constant of the real axon fluid. However, the calculated dielectric constant was a very large value. No documents that reported the dielectric characteristic of axon liquid that could confirm this value were found. Therefore, I designed an experimental device to measure the dielectric constant of 0.1 M KCl liquid, which is similar to axon fluid. And I confirmed that the value of the dielectric constant that I measured with the experimental device is almost the same as the dielectric constant calculated from the new axon equivalent circuit.

1. Introduction

For the axon equivalent circuit in which the dielectric characteristic of the axon

fluid was applied, the dielectric constant that was required to realize high-speed conduction velocity, namely the relative permittivity, was a very large value.
No documents that reported the dielectric characteristic of axon liquid that could confirm this value were found. Therefore, I designed an experimental device to measure the dielectric constant of KCl liquid that is similar to axon fluid, as shown in Figure 2-1a. However, generally measuring the direct current resistance and dielectric constant of fluid is very difficult. For example, even when I only insert an electrode into the liquid a potential difference occurs between the electrode and liquid interface. Air bubbles from the electrolysis attach to the electrode when I apply voltage to the electrode, and contact resistance may become higher. In addition, an electric field spreads around the electrodes and not only in the space sandwiched between two electrodes. Particularly, the back sides of the electrodes that face each other generate an electric field to the dielectric medium in contact. Regarding the output of the general signal generator, the output voltage fluctuates due to a change in the load and depends on the frequency. Consideration about the correction for this phenomenon is necessary. Therefore, I designed an experimental device that avoids these problems as much as possible and thereby measured dielectric property of KCl liquid.

1.1 Treatment of electrodes

I thought that the same contact potential difference would be canceled out by electrodes of the same metal in the same ion liquid. When using an electrode with air bubbles and applying DC voltage to the electrode, the contact resistance became higher, and therefore, I lowered the applied voltage as much as possible. If amplitude of the sine wave that was too low was selected, measurement errors increased, and therefore, I selected amplitude of about 2V. I avoided taking too much time to avoid air bubbles due to electrolysis when attaching an electrode when I applied direct current voltage to an electrode. In addition, I ensured that liquid of the dielectric medium was not present around the back side of the electrode plate to reduce the influence from the back side of the electrode plate, as shown in Figure 2-1a.

1.2 Treatment of the output voltage instability of the signal generator

For capacity *C*, which was made by pouring the ion liquid between two electrodes, I connected resistance *R* tandemly, as shown in Figure 1-1b and connected both ends to the Function Generator. I assumed *V*1 for the voltage of the connection point with the Function Generator and assumed *V2* for the voltage of both ends of capacity *C*.

I utilized differences between voltage *V1* and voltage *V2*, and between the ratio and the frequency of the sine wave, and calculated capacity *C* (including the internal resistance) and a circuit electric current. In this manner, I managed to separate the influence of the instability of the output voltage (*V1*) of the Function Generator.

I selected the value of resistance *R* that makes the value of V1 and V2 suitable for measurement.

1.3 Output signal of the Function Generator

The Function Generator outputs a sine wave of approximately 2.0 V from 1 Hz to 1,000,000 Hz, and accordingly, the frequency of the sine wave, *V1*, and *V2* are measured to calculate the capacitance. To calculate the internal resister r of capacity *C*, I measured *V1* and *V2* in the direct current mode in a short time, that is, at 0 Hz.

2. Materials and Methods

2.1 Experimental apparatus that measures the dielectric

characteristic of KCl liquid

To investigate the contribution of the dielectric constant of axon fluid to the action potential conduction velocity v, I conducted an experiment to measure the relative permittivity of concentration 0.1M of KCl liquid resembled to axon fluid. Therefore, the dielectric constant and conductivity of 0.1 M KCl liquid used in this experiment were considered to be higher than those of real axon fluid of which concentration of Cl- ion is 0.013M. For the experimental method, we established capacitance *C* with two electrodes of 2 cm^2 with a distance of 10 mm in an acrylic box (inside dimensions 30 mm, 40 mm, 10 mm), as shown in Figure 2-1a. Although the electrodes of the actual capacitor C_1 in a node of Ranvier are arranged in a left-right configuration, in this experiment, I formed a capacitor from the two facing electrodes alone. Therefore, we do not need to think about the influence of the back side of the electrodes. Figure 2-1b shows the equivalent circuit of our experimental apparatus. *V2* is the potential difference between the two terminals of the capacitor, whereas *V1* is the potential difference between one capacitor terminal and the opposite terminal of the series resistor *R*. Therefore, *V1* equals the output potential of the Function Generator (IWATSU SG-4104). *V1* and *V2* are monitored by Smart Digital Storage Oscilloscopes (OWON SDS5032E (V)). We used three concentrations of KCl (0.001 M, 0.01 M, and 0.1 M) to investigate the influence of the concentration of the ion solution.

2.2 The equation for calculating capacitance, relative permittivity, and circuit current

Generally, ion fluid consists of resistance and capacitance, and Figure 2-1b shows the resistance r in parallel with capacitance *C*. For a series connection, the current *I* flowing in the capacitor that includes resistance *r* must equal that flowing in the resistor *R*. The impedance *Z1* is a series connection of *R* and *Z2*, and the impedance *Z2* is a parallel connection of *C* and *r*. Thus, we have

$Z1=R+Z2$

$Z2=1/(1/r+j\omega C)=r/(1+j\omega Cr)=r(1-j\omega Cr)/(1+(\omega Cr)^2)$

$|Z2|=\sqrt{r^2+(\omega Cr^2)^2}\ /(1+(\omega Cr)^2)$

$|Z1|=\sqrt{(r+R+R(\omega Cr)^2)^2+(\omega Cr^2)^2}\ /(1+(\omega Cr)^2)$

$V1=|Z1|I$

$V2=|Z2|I$

$V1/V2=|Z1|/|Z2| =\sqrt{(r+R+R(\omega Cr)^2)^2+(\omega Cr^2)^2} \;/\sqrt{r^2+(\omega Cr^2)^2}$

$(V1/V2)^2=((r+R+R(\omega Cr)^2)^2+(\omega Cr^2)^2/(r^2+(\omega Cr^2)^2)$

$(V1/V2)^2=(r+R+RX)^2+Xr^2/(r^2+Xr^2) \quad \because \quad X=(\omega Cr)^2$

$\qquad =r^2+2rR+R^2+X(2rR+2R^2+r^2)+X^2(R^2)/(r^2+Xr^2)$

$X^2(RV2)^2 +X ((2rR+2R^2+r^2)V2^2-r^2V1^2)+V2^2(r^2+2rR+R^2)-V1^2r^2=0$

$X= ((r^2V1^2-(2rR+2R^2+r^2)V2^2+$

$\sqrt{((2rR+2R^2+r^2)V2^2-r^2V1^2)^2-4(RV2)^2(V2^2(r^2+2rR+R^2-V1^2r^2)} \;)/2(RV2)^2$

And then, we can calculate C as below,

$C=\sqrt{X}/\omega\, r \quad \because \quad X= (\omega Cr)^2$ (2-1)

When ω is 0 (direct current), C is ignored and so $V2/V1=r/(r+R)$

$r=R\, V2/(V1-V2)$ (2-2)

Therefore, we can obtain C using $V1$, $V2$, R, and ω from above equation.

On the other hand, the capacitance of parallel plate electrodes is defined as follows:

$C=\varepsilon S/d=\varepsilon_0\varepsilon_r S/d$ (2-3)

Therefore, we can obtain the relative permittivity ε_r of KCl liquid as:

$\varepsilon_r =Cd/\varepsilon_0 S$ (2-4)

Furthermore, we can obtain the circuit current I as:

$I= (V1-V2)/R$ (2-5)

And we can obtain the longitudinal capacitance $C1$ of an axon 20μm in diameter using the relative permittivity ε_r of KCl liquid by the Equation(1-1) mentioned in section 2.2 of Part Ⅰ.

$C1=2\varepsilon_0\varepsilon_r\pi r^2/d=2\varepsilon\pi r^2/d$ (1-1)

3. Results

I measured the characteristics of KCl liquid of concentrations of 0.001 M, 0.01 M, and 0.1 M to determine the influence of the concentration of KCl liquid that is similar to axon fluid.

3.1 Measurement results

Table 2-1 indicates the characteristic differences according to the concentration. The Frequency column shows the frequency from 1 Hz to 1000000 Hz. The KCl (0.2 V/DIV) column shows the readings from oscilloscopes, and the KCl (1 V/DIV) column shows the value that I converted into the voltage. The column *R* shows the value of tandemly connected resistance. The next column is the concentration. Column *r* indicates the value of the resistance of the ion liquid between two electrodes calculated with Equation (2-2). Column *C* indicates the value of the capacity calculated with Equation (2-1). Column ε_r indicates the relative permittivity calculated with Equation (2-4). Column *I* indicates the circuit electric current calculated with Equation (2-5). Column *C1* indicates the value of axonal longitudinal capacity *C1* of an axon 20μm in diameter calculated with Equation (1-1) from the relative permittivity of 0.1 M KCl liquid. Resistance *r* of the KCl liquid is inversely proportional to the concentration of ion liquid that is calculated from an electric current when direct current was applied to two electrodes. Resistance *r* is 8,715 Ω, 2,092 Ω, and 647 Ω for the concentration of 0.001 M, 0.01 M, and 0.1 M, respectively. Generally, capacity does not depend on the frequency. However, in the case of ion liquid, relative permittivity ε_r is calculated from capacity, and capacity is inversely proportional to frequency. In addition, the capacity of an electrode comprised of two pieces 1 cm apart and 2 cm^2 in size is very large: 0.418 μF, 1.01 μF, and 3.59 μF at 2,000 Hz for 0.001 M, 0.01 M, and 0.1 M, respectively. Therefore, the relative permittivity at 2000 Hz is very large for each concentration: 2.36×10^6, 5.73×10^6, and 2.03×10^7, respectively.

3.2 Graphed measurement results

Figure 2-2a-d indicates graphs to assist in understanding Table 2-1. The horizontal axis indicates the frequency of 1000,000 Hz from 1 Hz of the sine wave for two electrodes. The solid line indicates the result for 0.1 M, the dotted line indicates the result for 0.01 M, and the dashed line indicates the result for 0.001 M KCl liquid.

Figure 2-2a Capacity *C*. Capacity *C* is calculated from *V1, V2, r* and *R* using Equation (2-1). Capacity *C* is proportional to concentration and inversely proportional to frequency.

Figure 2-2b Relative permittivity ε_r. Because this is calculated from capacity *C* using equation (2-4), relative permittivity ε_r has the same tendency as capacity *C*.

Figure 2-2 Circuit current *I*. Circuit current *I* increases in proportion to frequency, but the current at each concentration gradually becomes flat when the frequency exceeds 2000 Hz. In other words, the displacement current is not affected when the frequency exceeds 2000 Hz.

Figure 2-2d Conductance. Conductance is the product of capacity *C* and angular frequency ω. This graph becomes flat at more than 2000 Hz, demonstrating that electric current depends on the conductance by capacitive impedance.

3.3 Comparison between capacity *C1* calculated from measured relative permittivity ε_r and *C1* calculated from an equivalent circuit

The relative permittivity ε_r of 0.1 M KCl liquid is calculated from C that is calculated from measurement data, V1, V2, r, R and ω, using Equation (2-1).

Using the relative permittivity ε_r of 0.1 M KCl liquid that is similar to axon fluid, I indicate the value that was calculated for longitudinal capacity *C1* for an axon 20μm in diameter with Equation (1-1) in column *C1* of Table 2-1. This capacity *C1* of 11.26×10^{-14} F at 2000 Hz is 1.52 times higher than the capacity *C1* of 7.409×10^{-14} F, which was calculated with the new axon equivalent circuit. However, these two capacity *C1* agree relatively well.

Furthermore, the concentration of Cl ions is 0.013 M in real axon fluid, but naturally the concentration is slightly higher, because the same concentration of K ions and Cl ions is present in 0.1 M KCl liquid used in this experiment.

4. Discussion

4.1 Effect of the high relative permittivity of the KCl liquid

The direct current resistance and the capacitive resistance ($1/\omega C$) are both influenced strongly by the concentration and are inversely proportional to the concentration of KCl liquid. I found a very high value for the relative permittivity of 0.1 M KCl liquid. Regarding the influence of such a high relative permittivity, not only the axon but also dendritic synapse integration provides a substantial contribution.

4.2 Frequency properties of KCl liquid and rising frequency of the action potential

Generally, for the capacity used as an electrical component, the value of the capacity is little affected by frequency. But in the case of KCl liquid, the capacity is inversely proportional to frequency at each concentration. The electric current through KCl liquid increases in proportion to frequency, but the current at each concentration gradually flattens when the frequency exceeds 2000 Hz. In other words, the displacement current does not so increase when the frequency exceeds 2000 Hz. This is caused by the fact that the capacitive impedance, which is calculated by the equation $1/(\omega C)$, becomes constant when the frequency exceeds 2000 Hz, as shown in Figure 2-2d. Therefore, the effects of a carrier conveying the action potential by the dielectric property of the axon liquid become small, after the frequency exceeds 2000 Hz. I think that there is the significant relation between the rise time of 125μs for the action potential reported in reference [29] and the impedance of the axon fluid at 2000 Hz.

Conclusions

The relationship between the axonal morphology and dielectric property of axon fluid is an important theme in this study. I found that the structure of the node of Ranvier, which has very small capacitance *Cn* but a vast number of voltage-gated Na channels to generate a large and steep action potential, is suitable for the relative permittivity of axon fluid.

Figures

Figure 2-1: Experimental apparatus to measure a dielectric property of the KCl liquid

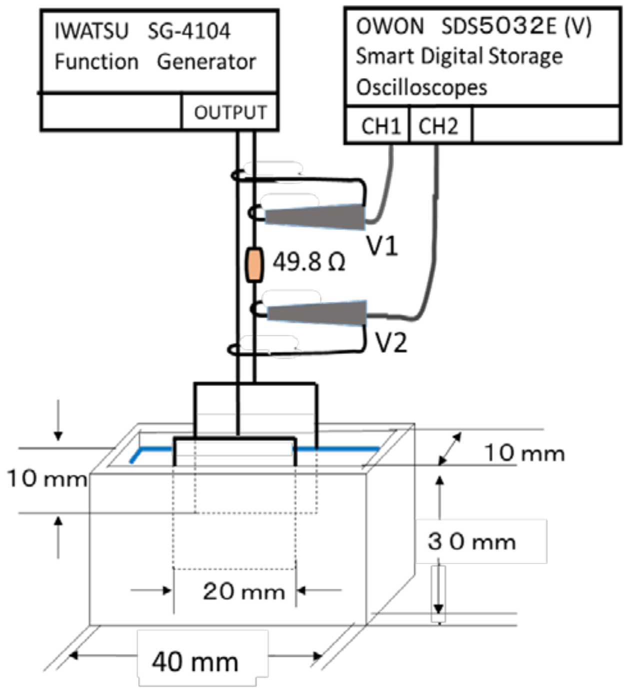
(a) Experimental apparatus

This apparatus Figure 2-1a is to measure a dielectric property of the KCl liquid. The electrodes are made from copper plates of two pieces of 2cmx2cm. Because half of the electrodes are inserted into the ion liquid, the area of the electrode becomes 2cmx1cm. And the distance of two electrodes is 1cm.

(b) Equivalent circuit of the experimental apparatus

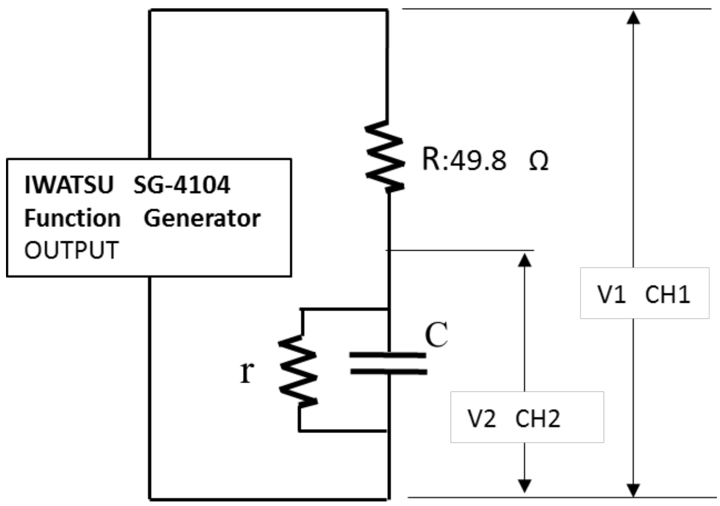
Equivalent circuit Figure 2-1b indicates the experimental apparatus Figure 2-1a that measures a dielectric property of the KCl liquid. *C* is capacitance which is made from KCl liquid and two electrodes and r is resistance of KCl liquid between two electrodes. Because C and r are connected in parallel, impedance $Z2$ is $1/(1/r + j\omega C)$. And because $Z2$ is connected to resistor R in series, impedance $Z1$ is $Z2 + R$. If circuit current is I, $Z2$ x I makes $V2$ and $Z1$ x I makes $V1$. And so, $V1/V2 = Z1/XZ2$, and $I = (V1-V2)/R$.

(a)



IWATSU SG-4104
Function Generator
OUTPUT
OWON SDS5032E (V)
Smart Digital Storage
Oscilloscopes
CH1
CH2
V1
49.8 Ω
V2
10 mm
10 mm
3 0 mm
20 mm
40 mm

(b)



R:49.8 Ω
IWATSU SG-4104
Function Generator
OUTPUT
V1 CH1
r
C
V2 CH2

Figure 2-2: The result of measurement and calculation

The solid line expresses 0.1M, and the dotted line expresses 0.01M, and the dash line expresses 0.001M.

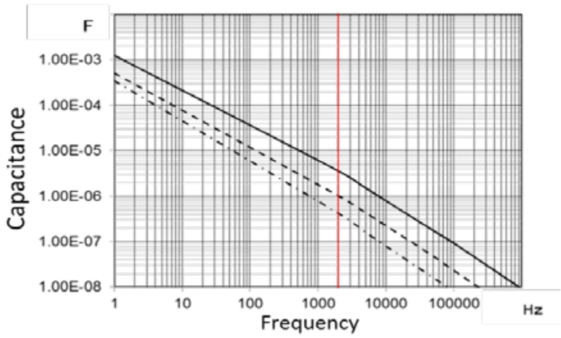
(a) Value of the capacitor *C* of the experimental apparatus. At 2000Hz, capacitor *C* of 0.1M, 0.01M and 0.001M is 3.59μF, 1.01μF and 0.42μF respectively.

(b) Relative permittivity ε_r of KCl liquid calculated from the capacitor *C* using the equation ($C = \varepsilon S/d = \varepsilon_0 \varepsilon_r S/d$). The ε_0 is permittivity of vacuum (8.854×10^{-12}) and *S* is 2 cm² and *d* is 1cm. At 2000Hz, relative permittivity of 0.1M, 0.01 and 0.001M is 2.03×10^7, 5.73×10^6 and 2.36×10^6 respectively.

(c) Circuit current *I* calculated by the equation ($I = (V1-V2)/R$). At 2000Hz, circuit current *I* of 0.1M, 0.01M and 0.001M is 13.45 mA, 5.22mA and 1.33mA respectively.

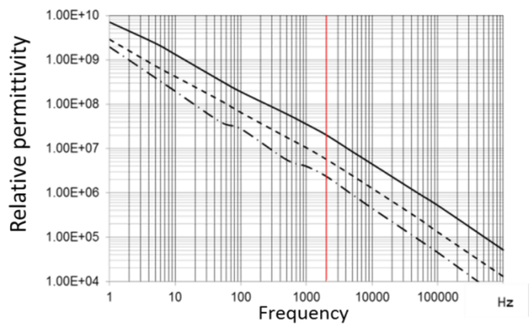
(d) Conductance *S*. Conductance *S* is the product of capacitance *C* and angular frequency ω. Each conductance curve is similar to circuit current curve, and the value of conductance becomes almost constant level when frequency exceeds 2000Hz.

(a)



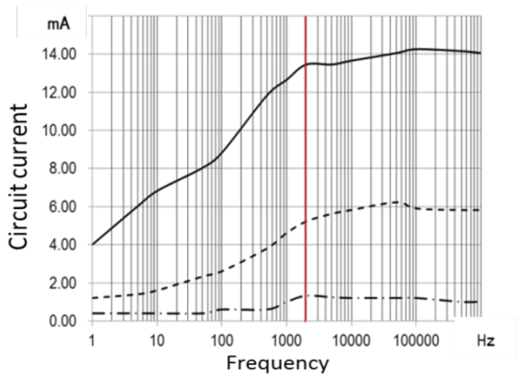
F
Capacitance
1.00E-03
1.00E-04
1.00E-05
1.00E-06
1.00E-07
1.00E-08
1
10
100
1000
10000
100000
Hz
Frequency

(b)



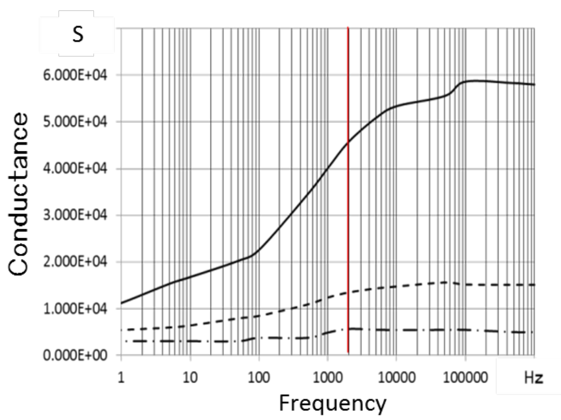
Relative permittivity
1.00E+10
1.00E+09
1.00E+08
1.00E+07
1.00E+06
1.00E+05
1.00E+04
1
10
100
1000
10000
100000
Hz
Frequency

(c)



mA
Circuit current
14.00
12.00
10.00
8.00
6.00
4.00
2.00
0.00
1
10
100
1000
10000
100000
Hz
Frequency

(d)



S
Conductance
6.000E+04
5.000E+04
4.000E+04
3.000E+04
2.000E+04
1.000E+04
0.000E+00
1
10
100
1000
10000
100000
Hz
Frequency

Table

Table 2-1: Characteristic of KCl liquid

Characteristic of KCl is indicated in Table 2-1 and explanation of column is below.

The column frequency indicates the frequency of sine wave supplied to the circuit from 1Hz to 1,000,000 Hz.

The column KCl (1V/Div) indicates the voltage of sine wave supplied to the circuit.

The column *R* indicates the resistance connected to capacitor C in series.

The column *r* of each concentration indicates resistance of KCl liquid between two electrodes.

The column *C* of each concentration indicates capacitance of KCl liquid between two electrodes.

The column ε_r of each concentration indicates relative permittivity of KCl liquid.

The column *I* of each concentration indicates the circuit current.

The column *C1* of concentration 0.1M indicated the longitudinal capacitance C1 of axon 20μm diameter which is calculated using the relative permittivity of 0.1M KCl liquid.

Table 2-1 Characteristic of KCl liquid

Frequency	KCl (0.2V/DIV.)						KCl(1V/DIV)						R	0.001M				0.01M				0.1M				
	0.001 M		0.01 M		0.1 M		0.001M		0.01M		0.1M			r	C	ε_r	I	r	C	ε_r	I	r	C	ε_r	I	C1
Hz	V1	V2	V1	V2	V1	V2	V1	V2	V1	V2	V1	V2	Ω	Ω	F		mA	Ω	F		mA	Ω	F		mA	F
1	8.8	8.7	8.6	8.3	7.85	6.85	1.76	1.74	1.72	1.66	1.57	1.37	49.8	8715	3.45E-04	1.95E+09	0.40	2092	5.09E-04	2.88E+09	1.20	647	1.25E-03	7.07E+09	4.02	3.934E-11
5	8.75	8.65	8.4	8.05	7.3	5.8	1.75	1.73	1.68	1.61	1.46	1.16	49.8	8715	6.94E-05	3.92E+08	0.40	2092	1.29E-04	7.28E+08	1.41	647	4.16E-04	2.35E+09	6.02	1.308E-11
10	8.75	8.65	8.4	8	7.3	5.6	1.75	1.73	1.68	1.6	1.46	1.12	49.8	8715	3.47E-05	1.96E+08	0.40	2092	7.45E-05	4.21E+08	1.61	647	2.35E-04	1.33E+09	6.83	7.375E-12
50	8.75	8.65	8.28	7.7	6.75	4.75	1.75	1.73	1.66	1.54	1.35	0.95	49.8	8715	6.94E-06	3.92E+07	0.40	2092	2.10E-05	1.19E+08	2.33	647	5.93E-05	3.35E+08	8.03	1.862E-12
100	8.75	8.6	8.25	7.6	6.55	4.35	1.75	1.72	1.65	1.52	1.31	0.87	49.8	8715	4.92E-06	2.78E+07	0.60	2092	1.15E-05	6.51E+07	2.61	647	3.36E-05	1.90E+08	8.84	1.057E-12
500	8.75	8.6	7.85	6.9	5.95	3	1.75	1.72	1.57	1.38	1.19	0.6	49.8	8715	9.84E-07	5.56E+06	0.60	2092	3.17E-06	1.79E+07	3.82	647	1.06E-05	6.01E+07	11.85	3.344E-13
1000	8.75	8.5	7.7	6.55	5.7	2.55	1.75	1.7	1.54	1.31	1.14	0.51	49.8	8715	7.02E-07	3.96E+06	1.00	2092	1.85E-06	1.04E+07	4.62	647	6.26E-06	3.54E+07	12.65	1.967E-13
2000	8.75	8.42	7.65	6.35	5.6	2.25	1.75	1.68	1.53	1.27	1.12	0.45	49.8	8715	4.18E-07	2.36E+06	1.33	2092	1.01E-06	5.73E+06	5.22	647	3.59E-06	2.03E+07	13.45	1.126E-13
5000	8.68	8.37	7.5	6.1	5.45	2.1	1.74	1.67	1.5	1.22	1.09	0.42	49.8	8715	1.62E-07	9.13E+05	1.24	2092	4.35E-07	2.46E+06	5.62	647	1.51E-06	8.53E+06	13.45	4.741E-14
10000	8.6	8.3	7.45	6	5.4	2	1.72	1.66	1.49	1.2	1.08	0.4	49.8	8715	7.97E-08	4.50E+05	1.20	2092	2.25E-07	1.27E+06	5.82	647	7.91E-07	4.47E+06	13.65	2.486E-14
50000	8.5	8.2	7.35	5.8	5.3	1.8	1.7	1.64	1.47	1.16	1.06	0.36	49.8	8715	1.60E-08	9.07E+04	1.20	2092	4.77E-08	2.70E+05	6.22	647	1.75E-07	9.90E+05	14.06	5.503E-15
100000	8.5	8.2	7.25	5.78	5.25	1.7	1.7	1.64	1.45	1.16	1.05	0.34	49.8	8715	8.02E-09	4.53E+04	1.20	2092	2.32E-08	1.31E+05	5.90	647	9.25E-08	5.23E+05	14.26	2.906E-15
500000	8.4	8.15	7.2	5.75	5.23	1.7	1.68	1.63	1.44	1.15	1.05	0.34	49.8	8715	1.44E-09	8.14E+03	1.00	2092	4.61E-09	2.60E+04	5.82	647	1.84E-08	1.04E+05	14.16	5.780E-16
1000000	8.4	8.15	7.2	5.75	5.2	1.7	1.68	1.63	1.44	1.15	1.04	0.34	49.8	8715	7.20E-10	4.07E+03	1.00	2092	2.30E-09	1.30E+04	5.82	647	9.15E-09	5.17E+04	14.06	2.874E-16

Part Ⅲ

New discovery based on the results of this study

Abstract

I was able to demonstrate that the dielectric property of the axon fluid and the characteristic axonal morphology increased the conduction velocity of the action potential. The region of a long uniform myelin sheath, which is one of the characteristic features of axonal morphology, works well as a signal transmission line. When voltage-gated Na channels at the node of Ranvier, which have a very short width, sensed a certain level of the action potential propagated, the channels begin to generate a new action potential with a steep rise wave form and high amplitude. Thus, the action potential is relayed along the long axon. I demonstrated that axon fluid with a high dielectric constant functions as transmission medium for a very effective signal. At first, based on these results, I indicated the effect generated by the thickness of the membrane of the myelin sheath for the conduction velocity by using a new axon equivalent circuit and the approach of the distributed element circuit. Then, by using a new axon equivalent circuit, I demonstrated the interesting relationship of the raw velocity *Vr*, maximum reachable distance *L* and conduction velocity *v* against the longitudinal capacity *C1* of the dielectric property of KCl liquid. Naturally, membrane thickness in the region of myelin sheath means sheath thickness.

1. Introduction

In Part I and Part II, I observed that the characteristic axonal morphology cooperated with the dielectric constant of the axon fluid to increase the conduction velocity v of the action potential. Regarding the characteristic axonal morphology, conduction velocity v of the action potential is proportional to the axon diameter. This relationship was confirmed also by the calculation using the new axon equivalent circuit. However, no report has described the relationship between the thickness of the membrane of the myelin sheath and the conduction velocity v. Therefore, using the new axon equivalent circuit and considering an axon 20μm in diameter as a base, I investigated the raw velocity *Vr*, maximum reachable distance *L* and conduction velocity *v* against the thickness of membrane of myelin sheath. Furthermore, I calculated the raw velocity *Vr*, maximum reachable distance *L* and conduction velocity *v*, using the new axon equivalent circuit against the longitudinal capacity *C1* which used a dielectric constant corresponding to the frequency of KCl liquid that is similar to axon fluid which was measured in Part Ⅱ. I assessed the relationships between the results of the above calculation and the frequency of the action potential.

Materials and Methods

2.1 Relationship between the membrane thickness of the myelin sheath and raw velocity *Vr*, maximum reachable distance *L*, and the conduction velocity *v*

As mentioned in Part I, the relationship between membrane thickness *d* and the capacity *Cm* of the myelin sheath is shown as:

$$Cm=2\pi\varepsilon / \ln(Do/Di)=2\pi\varepsilon_0\varepsilon_{mr} / \ln((Di+2d)/Di) \qquad (3\text{-}1)$$

In addition, *Do* and *Di* are the outer and inner diameters, respectively. ε is the dielectric constant of the myelin sheath, ε_0 is the permittivity of a vacuum, ε_{mr} is the relative permittivity of the myelin sheath, and *ln* is the natural logarithm. Similarly, resistance *Rm* of membrane thickness *d* is shown as:

$$Rm= \ln((Di+2d)/Di)\rho/ (2\pi) \qquad (3\text{-}2)$$

In addition, ρ is the electric specific resistance.

For a membrane thickness of 4μm and an axon of diameter (the inside diameter) of 20μm, the relationship between *ln(Do/Di)* and 1/4 and 1/16 of membrane thickness d is shown as:

ln(28/20) : ln(22/20) : ln(20.5/20) = 1.000 : 0.283 : 0.073

I converted resistance *R2* and longitudinal capacity *C1* for a diameter of 20μm for each membrane thickness using the above relationship. I calculated the raw velocity *Vr*, maximum reachable distance *L*, and the conduction velocity *v* using a new axon equivalent circuit.

2.2 Raw velocity *Vr*, maximum reachable distance *L*, and conduction velocity *v*, against longitudinal capacity *C1* used of relative permittivity of KCl liquid

I calculated raw velocity *Vr*, maximum reachable distance *L*, and conduction velocity *v* using the new axon equivalent circuit and longitudinal capacity *C1* in which I applied the relative permittivity (dielectric constant) that I measured with KCl liquid.

3. RESULTS

3.1 Raw velocity *Vr,* maximum reachable distance *L* and the conduction velocity *v* for different membrane thicknesses

As shown in Table 3-1, at 2000 Hz, against the membrane thickness of 4μm, and an axon of diameter (the inside diameter) of 20μm, I calculated the raw velocity *Vr* in the case of membrane thicknesses 1/4 and 1/16 and obtained 1769.4 m/s, 739.3 m/s, and 356.2 m/s, respectively (as shown in red vertical line in Figure 3-1a). For maximum reachable distance *L,* I obtained 10.62 mm, 5.33 mm, and 2.66 mm (as shown in red line in Figure 3-1b). Furthermore, for conduction velocity *v*, I obtained 120.0 m/s, 59.61 m/s, and 29.76 m/s (as shown in red line in Figure 3-1c). The calculation result for 4m, 1m and 1/4m of the membrane thickness of the myelin sheath shows in Figure 3-1a-c each in a solid line, a dotted line and a dash line. For an axon 20μm in diameter, maximum reachable distance *L* and conduction velocity *v* are proportional to the square root of the thickness of the myelin sheath. These results (as shown in Table 3-1) are a new discovery in the conduction velocity system of the axon. However, a previous study reported that the conduction velocity of the action potential is proportional to the axon diameter [4].

3.2 Raw velocity *Vr*, maximum reachable distance *L* and conduction velocity *v,* against longitudinal capacity *C1* used of relative permittivity of KCl liquid

Table 3-2 indicates the result of calculation of raw velocity *Vr*, maximum reachable distance *L* and conduction velocity *v* with the new axon equivalent circuit using longitudinal capacity *C1* in which I applied the relative permittivity that I measured with KCl liquid as mentioned in partⅡ. Figure 3-2a-c indicates the content shown in Table 3-2. All graphs show the result of calculations using the new axon equivalent circuit in which I applied the measured dielectric constant, indicated by the red solid line and red circles. The black solid line shows the calculated value from the new axon equivalent circuit shown in Part I, and the black dashed line is the result of calculations with the conventional axon equivalent circuit shown in Part I.

Furthermore, the red vertical line shows 2 kHz.

Raw velocity *Vr* is indicated in Figure 3-2a. This graph shows that the black solid line and black dotted line are faster than the red solid line with red circles in the area where the frequency is low. However, the red line with red circles becomes fast and gradually surpasses the black dotted line at 200 Hz in proportion to the frequency, and it suddenly exceeds the black solid line at 500 Hz. The velocity becomes approximately 23000 m/s, which is the maximal value at the frequency of 2000 Hz, and its red line becomes slow from over that frequency and becomes slower than the black solid line from approximately 4000 Hz.

Maximum reachable distance *L* is indicated in Figure 3-2b. The red solid line with red circles exceeds the black solid line and dotted line from 1 Hz. The distance increases in proportion to frequency, becomes maximum (23mm) at around 100 Hz, and becomes lower than the black solid line when the frequency exceeds 3000 Hz.

Conduction velocity *v* is indicated in Figure 3-2c. The red solid line with red circles exceeds the black solid line and dashed line from 100 Hz, and when the frequency exceeds 3000 Hz red line with red circle becomes slower than black lines.

From above data, I discovered that the structure of node of Ranvier is suitable for the relative permittivity of axon fluid at 2000Hz.

4 . DISCUSSION

4.1 Relationship between conduction velocity *v* and membrane thickness of the myelin sheath

The membrane thickness of the myelin sheath is proportional to the axon diameter [24]. Therefore, the membrane capacity *C2* does not depend on the axon diameter by the Equation (3-1), and also the membrane resistance *R2* does not depend on the axon diameter by the Equation (3-2). However, because the axon resistance *R1* and longitudinal capacitance *C1* depend on the diameter of the axon, it has been reported that the conduction velocity *v* of the action potential is proportional to the axon diameter [4]. In this study, I found that the conduction velocity *v* of the action potential is proportional to the square root of the membrane thickness as shown in Figure 3-1c. Because a thin layer of myelin is wrapped around the axon several hundred times to create the myelin sheath, conduction velocity v is thought to become fast as the number of layers of membranes increases during the growth process.

4.2 Raw velocity *Vr*, maximum reachable distance *L*, and conduction velocity *v*, by longitudinal capacity *C1* which used KCl liquid relative permittivity

Raw velocity *Vr* of the red solid line with red circles shown in Figure 3-2a is slower than the black solid and dotted lines in the low frequency area. The measured data indicated that the dielectric constant of the KCl liquid is higher at the lower frequency. Generally, the medium of higher dielectric constant seems to allow more high speed transmission of the action potential as an electric field. Therefore, the phenomenon shown in low frequency region of Figure 3-2a seems to be the reverse phenomenon.

I considered that this phenomenon occurs because the power of the electric field, which absorb the energy, becomes too large compared to the energy of the action potential. The energy of an electric field is defined as half of the product of the dielectric constant and the square of electric field. Therefore, the medium with a nigh dielectric constant can absorb a large amount of energy. In light of this, a bigger capacitance *C1* is not always better. I think there is a suitable value of *C1* that is related to axon morphology. According to Figure 3-2a, b, and c, the longitudinal capacitance *C1* applied with the dielectric constant of KCl liquid at 2000 Hz is suitable for the propagation of the action potential. From Equation (1-19) in Part Ⅰ, increasing the raw velocity *Vr* requires a decreases in the phase constant β. According to Equation (1-17) in Part Ⅰ, decreasing β decreases the imaginary part *Q*.

The Equation (1-15) in Part Ⅰ of imaginary part *Q* is shown as below.

$$Q = \omega\,(C_2/R_1 - C_1/R_2)/((1/R_1)^2 + (\omega C_1)^2) \qquad (1\text{-}15)$$

Therefore, if *C2/R1* equals *C1/R2*, *Q* becomes zero and consequently β becomes zero. This means raw velocity *Vr* becomes infinity. The longitudinal capacitance *C1* is calculated by the equation *C1=C2R2/R1*. I calculated the *C1* using the value of circuit constants (*R1*, *R2* and *C2*) of 20μm diameter axon shown in table 1-1 in Part I and obtained the value $1.1886\text{x}10^{-13}$ F of *C1*. This calculated value of *C1* is almost equal to the *C1* using the relative permittivity of 0.1M KCl liquid at 2000Hz. Therefore, the effect of the longitudinal capacitance *C1* agrees with the reported rising time of the action potential of 125 μs, namely a frequency of 2000 Hz, as mentioned in section 2.7 of Part Ⅰ. In other words, the structure of the node of Ranvier is thought to generate a 2000 Hz action potential in conjunction with the dielectric property of the axon fluid.

Conclusion

The relation between the axonal morphology and dielectric property of axon fluid is important theme in these studies. By the study of Part Ⅱ, I found that the structure of node of Ranvier which has very small capacitance *Cn* and has tremendous number of voltage-gated Na channels to generate big and steep action potential is suitable for the relative permittivity of axon fluid. By the study of Part Ⅲ, I found raw velocity *Vr* indicates maximal velocity such as 23000m/s at 2000Hz. This maximal velocity is produced by the value of longitudinal capacitance *C1* applied the relative permittivity of KCl liquid. The condition for achieving maximum raw velocity *Vr* is to satisfy the relation of *C2/R1=C1/R2*. Axonal resistance *R1* and longitudinal capacitance *C1* depend on the axonal property, and membrane resistance *R2* and membrane capacitance *C2* depend on the myelin sheath property. I found that axonal morphology and dielectric property cooperates with each other to achieve high conduction velocity of action potential through the logical view and experimental view.

Figures

Figure 3-1: Effect of the membrane thickness of the myelin sheath

The calculation result for 4μm, 1μm and 1/4μm of the membrane thickness of the myelin sheath shows in Figure 3-1a-c each in a solid line, a dotted line and a dash line. Furthermore, the red vertical line indicates 2 000Hz.

(a) Raw velocity *Vr*.

A solid line, a dotted line and a dash line indicate raw velocity of 1769.4 m/s, 739.3 m/s, and 356.2 m/s at 2000 Hz.

(b) Maximum reachable distance *L*.

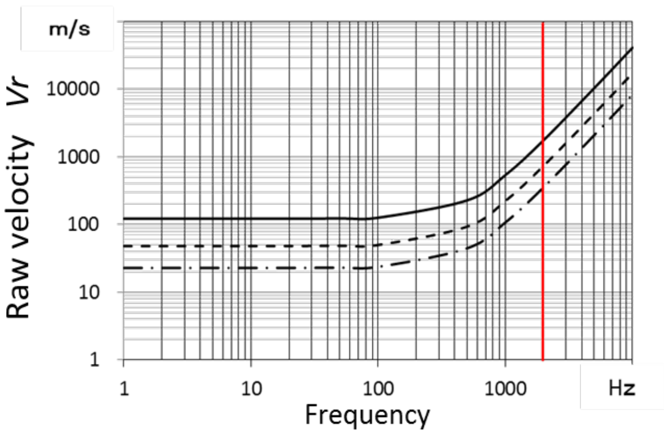
A solid line, a dotted line and a dash line indicate maximum reachable distance of 10.62 mm, 5.33 mm, and 2.66 mm at 2000 Hz.

(c) **C**onduction velocity *v*.

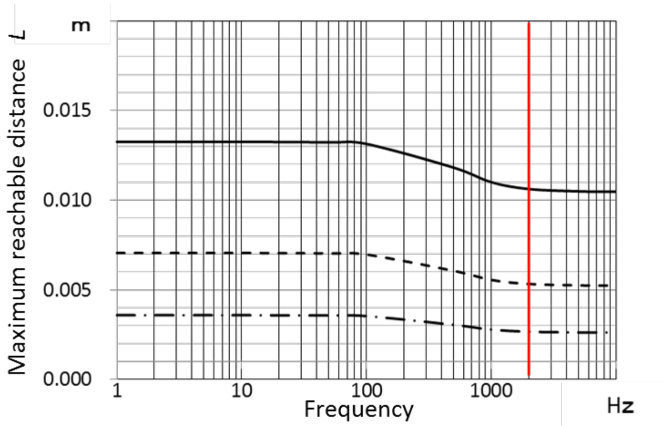
A solid line, a dotted line and a dash line indicate conduction velocity of 120.0 m/s, 59.61 m/s, and 29.76 m/s at 2000 Hz.

(b) and **(c)** indicate that the results of calculation are proportional to the square root of membrane thickness.

(a)


m/s
Raw velocity Vr
10000
1000
100
10
1
1
10
100
1000
Hz
Frequency

(b)


m
Maximum reachable distance L
0.015
0.010
0.005
0.000
1
10
100
1000
Frequency
Hz

(c)

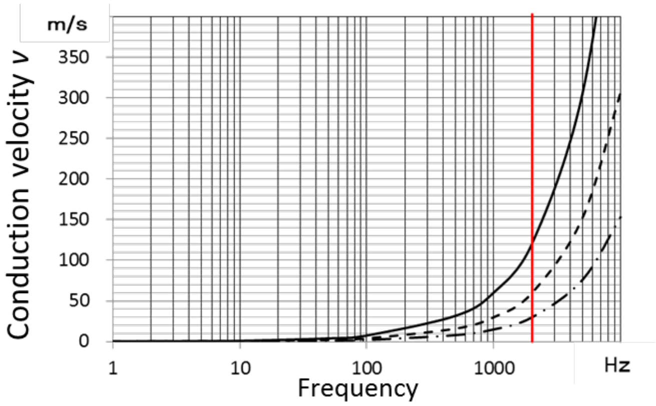

m/s
Conduction velocity v
350
300
250
200
150
100
50
0
1
10
100
1000
Hz
Frequency

Figure 3-2: Effect of the longitudinal capacity *C1* which used relative permittivity of 0.1M KCl liquid.

In each graph, the red solid line with red circles shows the result of calculations using the new axon equivalent circuit with *C1* which used relative permittivity of 0.1M KCl liquid. And the black solid line shows the calculated value from the new axon equivalent circuit with C1 which is decided by calculation and the black dashed line is the result of calculations with the conventional axon equivalent circuit. Furthermore, the red vertical line indicates 2000 Hz.

(a) Raw velocity *Vr*.

In the low frequency region red solid line indicates slower speed than 2 black curves. But its red line indicates very interesting curve which achieves the maximum speed 23044m/s at 2000Hz. This phenomenon means that phase constant β becomes the minimum value when frequency is 2000Hz, because *Vr* is equal to ω/β.

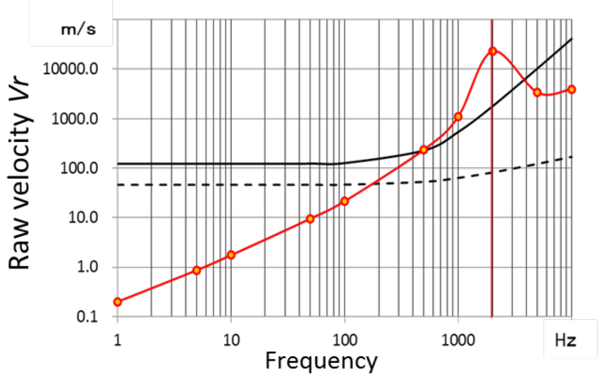
(b) Maximum reachable distance *L*.

Maximum reachable distance L of red solid line depends on the frequency greatly.

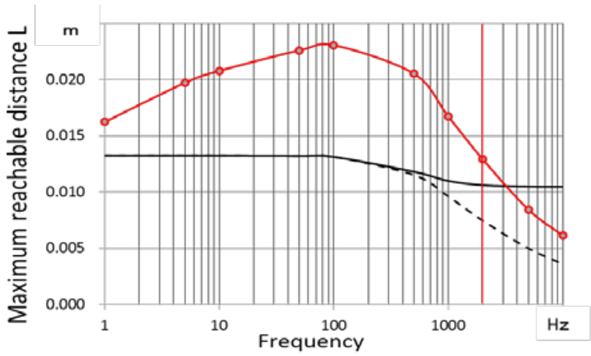
(c) Conduction velocity *v*.

Conduction velocity *v* of red solid line depends on the value of C1. Especially in the region from 500Hz to 2,000Hz red curve indicates higher speed than black curves.

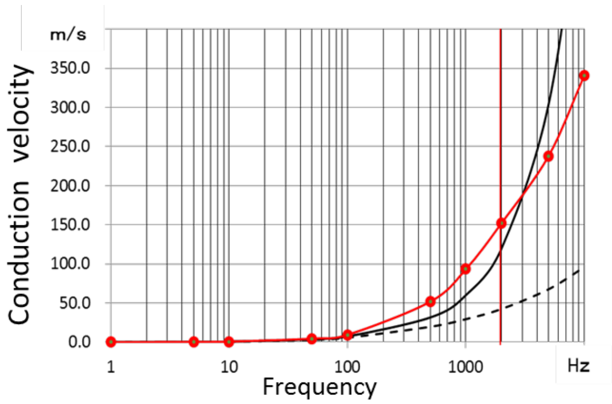
(a)


m/s
10000.0
1000.0
100.0
10.0
1.0
0.1
Raw velocity Vr
1
10
100
1000
Hz
Frequency

(b)


m
0.020
0.015
0.010
0.005
0.000
Maximum reachable distance L
1
10
100
1000
Hz
Frequency

(c)


m/s
350.0
300.0
250.0
200.0
150.0
100.0
50.0
0.0
Conduction velocity
1
10
100
1000
Hz
Frequency

Tables

Table 3-1: Effect of thickness of myelin sheath

Naturally, thickness of membrane in the region of myelin sheath means thickness of myelin sheath. Raw velocity *Vr,* maximum reachable distance *L*, and the conduction velocity *v* depend on the thicknesses of myelin sheath**.** Column thickness of sheath indicates the thickness of 4μm, 1μm and 1/4μm respectively. The circuit constants of membrane resistance *R2* and membrane capacitance *C2* are changed by the change of thickness of sheath. And raw velocity *Vr,* maximum reachable distance *L* and conduction velocity *v* are influenced by *R2* and *C2* as shown in column *Vr, L* and *v*.

Table 3-1 Effect of the thickness of myelin sheath

Thickness of sheath	f	ω	τ	$R1$	$R2$	$C2$	$C1$	V	L	v
(1/1) *4μm*	1	6.28318	0.25	3.50E+09	3.20E+05	1.3E-09	7.409E-14	122.052	0.01326	0.08
	5	31.4159	0.05	3.50E+09	3.20E+05	1.3E-09	7.409E-14	122.063	0.01326	0.39
	10	62.8318	0.025	3.50E+09	3.20E+05	1.3E-09	7.409E-14	122.095	0.01326	0.78
	50	314.159	0.005	3.50E+09	3.20E+05	1.3E-09	7.409E-14	123.143	0.01323	3.83
	100	628.318	0.0025	3.50E+09	3.20E+05	1.3E-09	7.409E-14	126.407	0.01314	7.47
	500	3141.59	0.0005	3.50E+09	3.20E+05	1.3E-09	7.409E-14	227.785	0.01182	31.68
	1000	6283.18	0.00025	3.50E+09	3.20E+05	1.3E-09	7.409E-14	537.387	0.01100	60.20
	2000	12566.36	0.000125	3.50E+09	3.20E+05	1.3E-09	7.409E-14	1769.395	0.01062	120.00
	5000	31415.9	0.00005	3.50E+09	3.20E+05	1.3E-09	7.409E-14	10387.762	0.01049	304.38
	10000	62831.8	0.000025	3.50E+09	3.20E+05	1.3E-09	7.409E-14	41166.625	0.01047	613.63
(1/4) *1μm*	1	6.28318	0.25	3.50E+09	9.06E+04	4.59E-09	7.409E-14	48.042	0.00705	0.04
	5	31.4159	0.05	3.50E+09	9.06E+04	4.59E-09	7.409E-14	48.047	0.00705	0.21
	10	62.8318	0.025	3.50E+09	9.06E+04	4.59E-09	7.409E-14	48.061	0.00705	0.42
	50	314.159	0.005	3.50E+09	9.06E+04	4.59E-09	7.409E-14	48.517	0.00703	2.02
	100	628.318	0.0025	3.50E+09	9.06E+04	4.59E-09	7.409E-14	49.936	0.00697	3.91
	500	3141.59	0.0005	3.50E+09	9.06E+04	4.59E-09	7.409E-14	93.050	0.00606	15.86
	1000	6283.18	0.00025	3.50E+09	9.06E+04	4.59E-09	7.409E-14	223.051	0.00555	29.89
	2000	12566.36	0.000125	3.50E+09	9.06E+04	4.59E-09	7.409E-14	739.256	0.00533	59.61
	5000	31415.9	0.00005	3.50E+09	9.06E+04	4.59E-09	7.409E-14	4349.442	0.00525	151.67
	10000	62831.8	0.000025	3.50E+09	9.06E+04	4.59E-09	7.409E-14	17242.389	0.00524	306.25
(1/16) *0.25μμm*	1	6.28318	0.25	3.50E+09	2.34E+04	1.78E-08	7.409E-14	22.805	0.00358	0.02
	5	31.4159	0.05	3.50E+09	2.34E+04	1.78E-08	7.409E-14	22.807	0.00358	0.11
	10	62.8318	0.025	3.50E+09	2.34E+04	1.78E-08	7.409E-14	22.814	0.00358	0.21
	50	314.159	0.005	3.50E+09	2.34E+04	1.78E-08	7.409E-14	23.036	0.00357	1.02
	100	628.318	0.0025	3.50E+09	2.34E+04	1.78E-08	7.409E-14	23.727	0.00353	1.97
	500	3141.59	0.0005	3.50E+09	2.34E+04	1.78E-08	7.409E-14	44.596	0.00305	7.93
	1000	6283.18	0.00025	3.50E+09	2.34E+04	1.78E-08	7.409E-14	107.302	0.00278	14.92
	2000	12566.36	0.000125	3.50E+09	2.34E+04	1.78E-08	7.409E-14	356.160	0.00266	29.76
	5000	31415.9	0.00005	3.50E+09	2.34E+04	1.78E-08	7.409E-14	2096.497	0.00262	75.78
	10000	62831.8	0.000025	3.50E+09	2.34E+04	1.78E-08	7.409E-14	8311.695	0.00262	153.06

Table 3-2: Influence of the value of *C1*

Raw velocity *Vr*, maximum reachable distance *L*, and the conduction velocity *v* depend on the value of longitudinal capacitance *C1*.

. The column type indicates the group of *C1*. Generally, the value of the capacitance of electric parts does not so change by frequency. Because the relative permittivity of the KCl liquid of 0.1M is inversely proportional to frequency, the value of *C1* is inversely proportional to frequency. Therefore, as for *C1* applied relative permittivity of KCl liquid, the results of calculation of raw velocity *Vr*, maximum reachable distance *L* and conduction velocity *v* are very interest.

Table 3-2 Influence of the value of C1

Type	*f*	ω	τ	*R1*	*R2*	*C2*	*C1*	*V*	*L*	*v*
Relative permittivity of KCl fluid applied to C1	1	6.28318	0.25	3.50E+09	3.20E+05	1.3E-09	3.934E-11	0.199	0.01626	0.07
	5	31.4159	0.05	3.50E+09	3.20E+05	1.3E-09	1.308E-11	0.869	0.01973	0.40
	10	62.8318	0.025	3.50E+09	3.20E+05	1.3E-09	7.375E-12	1.742	0.02080	0.83
	50	314.159	0.005	3.50E+09	3.20E+05	1.3E-09	1.862E-12	9.536	0.02262	4.54
	100	628.318	0.0025	3.50E+09	3.20E+05	1.3E-09	1.057E-12	21.415	0.02309	9.55
	500	3141.59	0.0005	3.50E+09	3.20E+05	1.3E-09	3.344E-13	237.352	0.02056	51.85
	1000	6283.18	0.00025	3.50E+09	3.20E+05	1.3E-09	1.967E-13	1095.848	0.01674	93.36
	2000	12566.36	0.000125	3.50E+09	3.20E+05	1.3E-09	1.126E-13	23044.848	0.01292	152.24
	5000	31415.9	0.00005	3.50E+09	3.20E+05	1.3E-09	4.741E-14	3380.490	0.00845	238.15
	10000	62831.8	0.000025	3.50E+09	3.20E+05	1.3E-09	2.486E-14	3885.261	0.00613	341.08
CI is not Applied.	1	6.28318	0.25	3.50E+09	3.20E+05	1.3E-09		45.970	0.01326	0.08
	5	31.4159	0.05	3.50E+09	3.20E+05	1.3E-09		45.971	0.01326	0.39
	10	62.8318	0.025	3.50E+09	3.20E+05	1.3E-09		45.974	0.01326	0.78
	50	314.159	0.005	3.50E+09	3.20E+05	1.3E-09		46.068	0.01323	3.70
	100	628.318	0.0025	3.50E+09	3.20E+05	1.3E-09		46.355	0.01315	6.99
	500	3141.59	0.0005	3.50E+09	3.20E+05	1.3E-09		52.872	0.01153	23.75
	1000	6283.18	0.00025	3.50E+09	3.20E+05	1.3E-09		63.354	0.00962	35.42
	2000	12566.36	0.000125	3.50E+09	3.20E+05	1.3E-09		81.734	0.00746	51.02
	5000	31415.9	0.00005	3.50E+09	3.20E+05	1.3E-09		122.091	0.00499	81.27
	10000	62831.8	0.000025	3.50E+09	3.20E+05	1.3E-09		169.397	0.00360	115.13
Calculated relative permittivity applied to C1	1	6.28318	0.25	3.50E+09	3.20E+05	1.3E-09	7.409E-14	122.052	0.01326	0.08
	5	31.4159	0.05	3.50E+09	3.20E+05	1.3E-09	7.409E-14	122.063	0.01326	0.39
	10	62.8318	0.025	3.50E+09	3.20E+05	1.3E-09	7.409E-14	122.095	0.01326	0.78
	50	314.159	0.005	3.50E+09	3.20E+05	1.3E-09	7.409E-14	123.143	0.01323	3.83
	100	628.318	0.0025	3.50E+09	3.20E+05	1.3E-09	7.409E-14	126.407	0.01314	7.47
	500	3141.59	0.0005	3.50E+09	3.20E+05	1.3E-09	7.409E-14	227.785	0.01182	31.68
	1000	6283.18	0.00025	3.50E+09	3.20E+05	1.3E-09	7.409E-14	537.387	0.01100	60.20
	2000	12566.36	0.000125	3.50E+09	3.20E+05	1.3E-09	7.409E-14	1769.395	0.01062	120.00
	5000	31415.9	0.00005	3.50E+09	3.20E+05	1.3E-09	7.409E-14	10387.762	0.01049	304.38
	10000	62831.8	0.000025	3.50E+09	3.20E+05	1.3E-09	7.409E-14	41166.625	0.01047	613.63

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Appendix

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