Nerve conduction models in myelinated and unmyelinated nerves based on three-dimensional electrostatic interaction

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Abstract

Until now, nerve conduction has been described on the basis of equivalent circuit model and cable theory, both of which supposed closed electric circuits spreading inside and outside the axoplasm. With these conventional models, we can simulate the propagating pattern of action potential along the axonal membrane based on Ohm’s law and Kirchhoff’s law. However, we could not fully explain the different conductive patterns in unmyelinated and myelinated nerves with these theories. Also, whether we can really suppose closed electrical circuits in the actual site of the nerves or not has not been fully discussed yet. In this report, a recently introduced new theoretical model of nerve conduction based on electrostatic molecular interactions within the axoplasm will be reviewed. With this new approach, we can explain the different conductive patterns in unmyelinated and myelinated nerves. This new mathematical conductive model based on electrostatic compressional wave in the intracellular fluid may also be able to explain the signal integration in the neuronal cell body and the back-propagation mechanism from the axons to the dendrites. With this new mathematical nerve conduction model based on electrostatic molecular interactions within the intracellular fluid, we may be able to achieve an integrated explanation for the physiological phenomena taking place in the nervous system.

Key Words: nerve conduction; ion channels; electrostatic interactions; electrostatic compressional wave; saltatory conduction; myelinated nerves; unmyelinated nerves; saltatory equations

Introduction

In the nervous system, conduction of the signals has been described as a form of electrical current with membrane potential change. To explain the propagation of membrane action potential in the axon, the conventional cable theory assumed closed electric circuits that fulfill Ohm’s law and Kirchhoff’s law, spreading inside and outside the axoplasm (Hodgkin and Huxley, 1952; Koch, 1984).

These conventional theories can theoretically explain the physiological phenomena of the nerve conduction and can also predict some potential-related properties like the anodal break (Guttman and Hachmeister, 1972; Daly et al., 2015). The following equation is the famous “cable equation”, with which we can describe and simulate the membrane potential at the location of “x” at a specific time of “t” (V_m(x,t)) by using the space constant of “λ” and the time constant of “τ_m”:

$$\lambda^2 \frac{\partial^2 V_m(x,t)}{\partial x^2} - \tau_m \frac{\partial V_m(x,t)}{\partial t} - V_m(x,t) = 0 \quad (1)$$

Though these conventional theories are certainly sophisticated, there are some issues in their premises that have not been fully addressed yet. First, whether we can really suppose closed electric circuits in the actual site of the nervous system or not from the viewpoint of electrostatic molecular interactions has not been fully discussed yet. Another issue is that we cannot explain the different relationships between axonal diameter and conduction velocity in unmyelinated and myelinated nerves. The cable theory explains the two-dimensional propagation of membrane action potential across the axonal membrane, but whether we can also apply the model to saltatory conduction in myelinated nerves or not is not clear. The conduction velocity is proportional to the axonal diameter in myelinated nerves, but it is proportional to the square root of diameter in unmyelinated nerves. However, until now, there is no mathematical model that can explain the saltatory conduction.

From before, the membrane action potential has known to be accompanied by some mechanical changes in axonal parameters like radius, length, pressure, and heat (El Hady and Machta, 2015). Based on this fact, some axonal structures like neurofilament, lipid bilayer, or axoplasm have been supposed to play some roles in nerve conduction (Shrivastava and Schneider, 2014). Though the exact mechanism of saltatory conduction is still unknown, these recent findings imply that we are better to consider not only the two-dimensional signal propagation along the axonal membrane but also three-dimensional mechanical signal conduction as the nature of nerve conduction.

In this report, a new model of nerve conduction from a viewpoint of molecular interaction between electrically-charged particles in the axoplasm will be presented. Different from the conventional theories that focused to the two-dimensional propagation of membrane potential, the new conduction model focuses to the three-dimensional ionic/molecular interaction within electrolytes like axoplasm. With this new conductive model, we do not need to assume closed electric circuits in the intracellular or extracellular fluid and we can just focus on the density and distribution of voltage-gated sodium (NaV) channels in the membrane.
Actual Scale of the Structures in Nervous System

The illustrations of neuronal structures with approximate measures in unmyelinated nerves and in myelinated nerves are shown in Figure 1. To be noted, the absolute scale of the figures in unmyelinated nerves (Figure 1A) and in myelinated nerves (Figure 1B) are totally different. As can be seen, the distance between two adjacent NaV channels in unmyelinated nerves is less than one-thousandth of that between two adjacent Ranvier’s nodes in myelinated nerves. This simple scale-related issue would result in different conductive pattern in unmyelinated and myelinated nerves; the forefront of the signal in unmyelinated nerves would proceed along the internal surface of the axonal membrane but the forefront of saltatory conduction in myelinated nerves would proceed across the whole cross-section of the axoplasm. Previously, this scale-related issue between unmyelinated nerves and myelinated nerves has not been fully considered and all of the nerve conduction has been explained from the viewpoint of two-dimensional propagation of membrane action potential across the axonal membrane.

In this report, for the nerve conduction in unmyelinated nerves, we consider a micro-scale three-dimensional propagation of an electrostatic compressional wave with hemispheric surface along the internal surface of axonal membrane. For the saltatory conduction in myelinated nerves, we consider a macro-scale one-directional internodal propagation of an electrostatic compressional wave with plane surface across the whole cross-section of the axoplasm.

Electrostatic Mechanism of NaV Channel Activation

When a NaV channel is activated, a specific rate of sodium ions influx will be triggered and a mass of positive electric charges will appear in the intracellular fluid. The extracellular space where the transferred cations originally located will be instantly supplied by other numerous cations existing in the extracellular fluid. As a result, we can assume a situation that a mass of positive electric charges has gradually appeared on the internal surface of the NaV channel. This newly appeared positively-charged mass would exert electrostatic force for both intracellular and extracellular electric charges. Here, NaV channel is known to be negatively-charged and attracting cations on its surface (Hille et al., 1975; Dani, 1986; Yin et al., 2013). Then, we can estimate that the distribution of electric charges are different between the internal and external surfaces of the axonal membrane in unmyelinated nerves (Figure 1A) and in Ranvier’s nodes in myelinated nerves (Figure 1B).

From before, voltage-gated ion channels have been regarded to open by responding to the decrease in potential difference between the internal and external sides of the membrane. To produce such difference in the potential gradient across the membrane, actual drift of some electrically-charged substances (i.e., intracellular ions, membrane protein, or membrane itself) as a chain reaction is required. To create such changes in the potential gradient across the membrane at the next NaV channel, the conducted signal needs to alter the horizontal (i.e., parallel to the membrane) potential gradient across the internal surface of the next.
channel. The separation of cations on the internal surface of the NaV channel depends on the horizontal component of the transmitted electrostatic force, which would be transmitted directly or as an electrostatic compressional wave within the axoplasm. Because the transmitted electrostatic force originally results from the sodium ion influx at the preceded depolarized NaV channels in unmyelinated nerves and from the influx at the preceded depolarized Ranvier’s nodes in myelinated nerves, the distance between NaV channels and the amount of NaV channels in each Ranvier’s node would be important. However, both of these variables have not been fully taken into considerations in the conventional theories. In the new conduction model, these variables will be incorporated as the essential components of the nerve conduction. The list of the abbreviations of the variables used in this mathematical conduction model and their theoretical roles are listed in Table 1 in the alphabetical order.

### Distribution of the Product of Two Variables with Normal Distribution

Before starting to build up a mathematical conduction model, we need to consider about the distribution of the product of two variables each of which shows normal distribution. Here, we prepare two independent random variables of “A” and “B”, which independently follows normal distributions of \( N(\mu_A, \sigma_A) \) and \( N(\mu_B, \sigma_B) \), respectively. Here, we describe their probability densities with \( f_A(a) \) and \( f_B(b) \).

The distribution of the product \( AB \) is known not to follow the normal distribution; thus, its mode is not equal to \( AB \). On the other hand, the expected value of \( AB \) (i.e., \( \mathbb{E}(AB) \)) fulfills the following equations, because \( f_{AB}(a,b) \) is equal to the product of \( f_A(a) \) and \( f_B(b) \).

\[
\mathbb{E}(A \cdot B) = \int \int AB \, f_{AB}(a,b) \, da \, db
= \int A \, f_A(a) \, da \cdot \int B \, f_B(b) \, db
= \mathbb{E}(A) \cdot \mathbb{E}(B)
\]

Thus, if the sample sizes of “A” and “B” are enough large, the mean of the product \( AB \) can be expected to match the value of the product \( \mu_A \cdot \mu_B \).

\[
A \cdot B = \mathbb{E}(A \cdot B) = \mathbb{E}(A) \cdot \mathbb{E}(B) = \mu_A \cdot \mu_B
\]

Based on similar considerations, the relationships below also holds.

\[
\overline{A \cdot B} = \mathbb{E}(A) \cdot \overline{B} - \overline{A} \cdot \mathbb{E}(B) - \mu_A \cdot \mu_B
\]

These facts will be applied to the following proportional expressions as their rationales.

### Mathematical Model for Three-Dimensional Electrostatic Interaction within Electrolyte Solution

The strength of electrostatic force between two spots with electrical charges can be described below.

\[
\text{Electrostatic force} = \frac{1}{4 \pi \varepsilon} \frac{Q_1 Q_2}{r^2}
\]

In this equation, \( Q_1 \) and \( Q_2 \) are the strength of electrical charges [C], “r” is the distance between the two spots [m], and “\( \varepsilon \)” is the permittivity of the medium [N·m/C²]. Next, we apply the above-mentioned equation to the electrostatic force working in electrolyte solution like intracellular fluid or axoplasm. If we suppose that a mass of electrical charges appeared in an electrically-charged medium, the charged mass would exert electrostatic force to the surrounding charges. The strength of electrostatic force that the ion particles at the distance of “x” [m] from the center of the mass would receive from the inner solution can be described as below (Akaishi, 2018).

\[
F_{(x,t)} = \lim_{m \to \infty} \sum_{m} \left( \frac{1}{4 \pi \varepsilon} \frac{Q_{m}}{r_{m}^2} \right) /
\left( (1 - \frac{2}{3}) r \times 10^{-6} \right)'^{2}
\]

In this equation, \( F_{(x,t)} \) stands for the strength of the electrostatic force [N] that the electrical charges with the distance of “x” [m] from the charged mass at the time of “t” receive from the inner solution and \( Q_{x,t} \) stands for the amount of positive electric charges [C] at the location of “x” [m] from the mass at the time of “t”. Because this equation holds in all the infinitesimal time, the following equation would also hold.

\[
\frac{\text{d}S_{x,t}}{\text{d}t} = \lim_{m \to \infty} \sum_{m} \frac{1}{4 \pi \varepsilon} \frac{Q_{m}}{r_{m}^2} /
\left( (1 - \frac{2}{3}) r \times 10^{-6} \right)'^{2}
\]

These concepts hold no matter of the dimension of the electrostatic force propagation (e.g., one-dimensional propagation with plane surface or three-dimensional propagation with hemispheric surface) as shown in Figure 2. No matter of unmyelinated nerves or myelinated nerves, the most important regulators for nerve conduction would be the distance from the depolarized NaV channels to those in resting state and the Na⁺ inflowing rate in the depolarized segments.

More detailed figure explaining the mathematical basis of three-dimensional electrostatic interaction in myelinated nerves is shown in Figure 3. This figure shows that the strength of the electric field in the axoplasm at the longitudinal distance of “X” created by the change of electrical charges in the k-th previous portion (\( E_{(k-th \ proximal-x)} \) [N/C]) would be proportional to the total amount of NaV channels...
in the adjacent depolarized Ranvier’s node. Thus, in a myelinated axon with a specific $D$ and $L_{internode}$, we can say that the strength of the electric field in the axoplasm at a specific distance of “X” from the previous node would be proportional to the amount of NaV channel in one Ranvier’s node.

**Conduction Model in Unmyelinated Nerves**

Propagation of electrostatic compressional wave along the internal surface of axonal membrane in unmyelinated axons

In unmyelinated nerves, we can ideally assume that the NaV channels in the axonal membrane would be almost homogeneously dispersed across the membrane. Certainly, the transmitted depolarized “excitation” segment on the axonal membrane would have variable ranges depending on the channel density ($C_d$) and conduction velocity ($V_c$) in unmyelinated nerves. As shown below, the estimated longitudinal (i.e., direction from the proximal to distal of the axon) width would be more than 100 times larger than the average distance between each adjacent NaV channels in the membrane, because the proceeding of the depolarized segment to the distal side is resulted from the electrostatic interaction between the depolarized segment and the adjacent next NaV channel on the minimally distal side (Figure 1A). Here, we define the electrostatic force from the depolarized “excitation” segment of axonal membrane to the closest adjacent NaV channel on the distal side as $f_{(depolarized→next NaV)}$, which can be described as below.

$$f_{(depolarized→next NaV)} = \lim_{n→∞} \sum_{k=1}^{n} \left( \frac{Q(x,t)}{(1-2)x \times 10^{-3}} \right)$$

$$= \lim_{n→∞} \sum_{k=1}^{n} \frac{Q(x,t)}{(1-2)x \times 10^{-3}}$$

Figure 2 Overview of the saltatory conduction model based on electrostatic interaction.

If we separate the internodal segment with the length of “x” into equal “n” segments, each partial segment possess the width of $x/n$. The transmitted strength of an electrostatic compressional wave at a specific location in the axoplasm can be described as the total sum of the electrostatic forces between the focused location and all of the separated proximal “n” segments. $C_d$: Channel density in the membrane; $D$: axonal diameter; $F_{(x,t)}$: The sum of transmitted electrostatic forces to the ions on the whole cross-section of axoplasm at the location of “x” at the time of “t” from the proximal axoplasm; NaV: voltage-gated sodium ion channel; $Q_{(x,t)}$: Amount of positive electric charges on the whole cross-section of the axoplasm at the location of “x” at the time of “t”.

Figure 3 Mathematical basis of the electrostatic compressional wave in myelinated nerves.

Strength of electric field at a specific location of axoplasm can be described as the summation of electric field created by each of the n-portions of the proximal axoplasm. With this mathematical basis, we can estimate that the strength of electric field at a specific longitudinal location in the axoplasm of a myelinated axon with a specific size would be proportional to the amount of NaV channels at the adjacent depolarized Ranvier’s node, $E_{(x,t)}$: Strength of electric field at the longitudinal location of “x” and the time of “t”; created by the inflowing sodium ions at the adjacent depolarized Ranvier’s node; X: specific longitudinal location in the internodal segment of myelinated nerves.

Duration of sodium conductance ($t_{Na}$) in each NaV $≈ 10^{-2}$ ms

Conductive time lapse in each NaV $≈ 10^{-4}$ ms

$\therefore$ Width of depolarized segment $≥ 10^{-2}d_{channel}$

Though the depolarized axonal segment in one signal conduction has a variable width with multiple NaV channels in the longitudinal direction, the most important factor that regulates the conduction velocity would be the average distance between each adjacent NaV channels in the membrane, because the proceeding of the depolarized segment to the distal side is resulted from the electrostatic interaction between the depolarized segment and the adjacent next NaV channel on the minimally distal side (Figure 1A). Here, we define the electrostatic force from the depolarized “excitation” segment of axonal membrane to the closest adjacent NaV channel on the distal side as $f_{(depolarized→next NaV)}$, which can be described as below.

$$\frac{d(f_{(depolarized→next NaV)})}{dt} = \lim_{n→∞} \sum_{k=1}^{n} \left( \frac{Q(x,t)}{(1-2)x \times 10^{-3}} \right)$$

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Here, based on (5), \( \partial f_{(k-1)\text{-th preceded NaV} \rightarrow \text{next NaV}}/\partial t \) can be described as below by using the NaV channel density of "\( C_d \)" and the amount of positive charges at the longitudinal location of "\( X \)" as "\( q_{(X)} \)."

\[
\frac{\partial f_{(k-1)\text{-th preceded NaV} \rightarrow \text{next NaV}}}{\partial t} = \frac{1}{\text{d} \text{t}} \left( \frac{\partial q_{(k-1)\text{-th preceded NaV}}}{\partial t} \right) \left( q_{(\text{next NaV})} \right)
\] (10)

Here, the section of \( \partial q_{(k-1)\text{-th preceded NaV}}/\partial t \) would be almost constant in the depolarized segment, especially in NaV channels with smaller values of "\( k \)" (i.e., closer to the next NaV). Thus, based on (9) and (10), the following relation would hold.

\[
\frac{\partial f_{\text{depolarized} \rightarrow \text{next NaV}}}{\partial t} \approx C_d \sum_{k=1}^{\infty} \left( \frac{1}{k^2} \right) \approx \frac{\pi^2 C_d}{6}
\] (11)

Strictly speaking, \( \partial q_{(k-1)\text{-th preceded NaV}}/\partial t \) cannot be regarded as constant in the later phase of depolarization state and other electrical states; thus, the upper limit range of "\( k \)" in the above relationship would not \( \infty \), but around 100–1000. However, the section of \( 1/k^2 \) can be negligible with enough large values of "\( k \)" and the segment of \( \sum_{k=1}^{\infty} (1/k^2) \) can still be regarded as constant. Thus, the following relationship would be derived.

\[
\frac{\partial f_{\text{depolarized} \rightarrow \text{next NaV}}}{\partial t} \approx C_d
\] (12)

Then, the time lapse of the depolarized “excitation” segment in the axonal membrane to activate the closest adjacent NaV channel on the distal side (\( T_{\text{depolarized} \rightarrow \text{next NaV}} \)) can fulfill the following relationship.

\[
T_{\text{depolarized} \rightarrow \text{next NaV}} \approx \frac{1}{C_d}
\] (13)

Because the longitudinal numbers of NaV channels on a specific length of axon is proportional to \( \sqrt{C_d} \), the conduction velocity of unmyelinated nerves (\( V_u \)) would fulfill the following relationship, which is compatible with the established fact.

\[
V_u \propto \sqrt{C_d}
\] (14)

Derived simultaneous equations in unmyelinated nerves

Based on the theories described above, the nerve conduction in unmyelinated nerves can be described with the following simultaneous equations.

\[
\frac{\partial q_{(X)}}{\partial t} = \sum_{k=1}^{\infty} \left( \frac{1}{k^2} \right) \left( \frac{\partial q_{(k-1)\text{-th preceded NaV}}}{\partial t} \right) \left( \frac{q_{(\text{next NaV})}}{C_d} \right)
\] (15)

\[
\int_{T_{\text{inter-NaV}}}^{T_{\text{inter-NaV} + \text{threshold}}} \frac{\partial q_{(X)}}{\partial t} \, dt = 1
\] (16)

\[
V_u = 10^\text{m/s} \int_{T_{\text{inter-NaV}}}^{T_{\text{inter-NaV} + \text{threshold}}} \sqrt{C_d} \, dt
\] (17)

In the equation (16), \( f_{\text{threshold}} \) stands for the minimum strength of received electrostatic force for each NaV channel to be activated. Here, though not described in detail in this report, the theoretical relationship between \( C_d \) and axonal diameter (\( D \)) can be theoretically supposed to be linear as shown in the previous reports (Akaishi, 2017, 2018). This is based on the previous reports describing that the amount of axonal transport to be proportional to the cross-sectional area (\( S \)) of the axon (Wujek et al., 1986). If we can suppose this assumption, combined with the relation (14), the following relationship can be deduced, which is compatible with the already known fact.

\[
V_u \propto \sqrt{C_d} \propto \sqrt{D}
\] (18)

Conduction Model in Myelinated Nerves

Propagation of electrostatic compressional wave on the whole cross-section of internodal axoplasm

Different from the propagation of nerve signal in unmyelinated nerves, signal conduction based on electrostatic interactions would proceed evenly on the whole cross-section of the internodal axoplasm in myelinated nerves. This is mostly because the internodal length between adjacent Ranvier’s nodes (300–2000 μm) is much larger than the axonal diameter (1–20 μm) in myelinated nerves (Akaishi, 2018).

In this section, for convenience, we focus to one internodal segment between two adjacent Ranvier’s nodes and regard the focused axoplasmic segment as a closed physical system, in which the total of mechanical energy is ideally preserved.

Significance of internodal length in the salutary conduction

When we consider about the salutary conduction in myelinated nerves, we need to define how to treat the internodal length (\( L_{\text{interode}} \)). We need to decide whether to treat \( L_{\text{interode}} \) as constant irrespective of \( D \) or as a covariate related to \( D \). To prove that we should not regard \( L_{\text{interode}} \) to be constant and that the correlation between \( L_{\text{interode}} \) and \( D \) is important, we will tentatively assume \( L_{\text{interode}} \) to be constant irrespective of \( D \) and will show the deduced conclusion is in conflict with the observed facts.

Here, we define \( F_{(x,t)} \) as the electrostatic force working from the whole proximal axoplasm to the ions on the whole axonal cross section at the longitudinal location of “\( X \)” (i.e., distance from the proximally adjacent depolarized node) at the time of “\( t \).” If we tentatively regard \( L_{\text{interode}} \) to be constant at “\( X \),” the following relationship would hold based on (7).

\[
\frac{\partial q_{(x,t)}}{\partial t} = \lim_{\text{m} \rightarrow \infty} \sum_{n=1}^{\infty} \left( \frac{1}{4\pi \varepsilon_0} \right) \left( \frac{\partial q_{(x,t)}}{\partial t} \right) \left( \frac{\partial q_{(x,t)}}{\partial t} \right) / \left( \left( 1 - \frac{1}{10} \right) X \cdot 10^{-6} \right)^3
\] (19)

From the viewpoint of ionic drift based on electrostatic interactions and ionic diffusion based on concentration gradient, the partial derivative of \( \partial q_{(x,t)} \) would be proportional to the change rate of ionic amount at the infinitesimally proximal location at the preceding infinitesimal time (\( \Delta t \)). If we can ignore the longitudinal (i.e., from proximal to distal) mechanical energy loss from friction with the internal surface of axonal membrane, the following equations hold by using the proportionality constant of “\( C \)” (0 < \( C < 1 \)), which is specific to the width of \( x/n \) and the type of the medium.

\[
\frac{\partial q_{(x,t)}}{\partial t} = C \cdot \frac{\partial q_{(x-n x, t-\Delta t)}}{\partial t}
\] (20)

Because we are now regarding \( L_{\text{interode}} \) as being constant at “\( X \),” these relations would hold irrelevant of the axonal diameter and the infinitesimal time of “\( \Delta t \)” can be regarded as a medium-specific constant. Combining (19) with (20), the following relationships can be derived.
Simultaneous Equations for the Salutory Conduction in Myelinated Nerves

Based on the theories described above, we need to incorporate the variable of $L_{\text{internode}}$ into the simultaneous equations. By using $A_{\text{internode}}$ as the attenuation ratio of the electrostatic force per each internodal length, the conduction model for the salutory conduction in myelinated nerves can be described with the following simultaneous equations.

\[
F_{\text{next node, } t} = F_{\text{previous node, } t} \cdot A_{\text{internode}} \\
F_{\text{internode}} \frac{\Delta F}{\Delta S} = \left( \frac{\frac{\partial F_{\text{next node, } t}}{\partial t}}{\Delta S} \right) dt = f_{\text{threshold}} \\
V_M = \frac{L_{\text{internode}}}{T_{\text{internode}}} 
\]  

In the equation (26), $F_{\text{previous node, } t}$ would be proportional to the total amount of NaV channel in the previous Ranvier’s node. In the equation (27), $\Delta S$ stands for infinitesimally small cross-sectional area of an axon at Ranvier’s nodes.

Relationship between Internodal Length and Conduction Velocity in Myelinated Nerves

Based on the results of the previous section that the internodal length, rather than axonal diameter, would be essential for the accelerated salutory conduction, in this section, we consider how the observed linear relationship between $L_{\text{internode}}$ and $D$ may affect the transmitted electrostatic compressional wave in the axoplasm.

First, based on the two below-mentioned linear relations, the required conductive time lapse in each internode between two Ranvier’s nodes ($T_{\text{internode}}$) is always constant irrespective of axonal diameter (Akaishi, 2018).

\[
T_{\text{internode}} = \frac{L_{\text{internode}}}{V_M} = \text{constant (irrespective of } D) 
\]  

Also, based on this fact, if we consider about one Ranvier’s node which has just turned to depolarization state, the electrostatic forces of the proximal and distal Ranvier’s nodes in each signal conduction are to be automatically determined irrespective of the axonal diameter.

Because $T_{\text{internode}}$ is always constant irrespective of $D$, $f_{\text{previous node→next node, } t}$ would be also constant irrespective of $D$. Now, $f_{\text{previous node→next node, } t}$ can be described as below.

\[
f_{\text{previous node→next node, } t} = \frac{DF_{\text{next node, } t}}{ds} \\
\alpha = \frac{pD}{s} = \text{constant (irrespective of } D) 
\]  

On the premise of $L_{\text{internode}} \propto D^3$, the total amount of NaV channels in each Ranvier’s node would fulfill the following relation.

\[
\text{Total amount of NaV channels in each Ranvier’s node} \propto \frac{1}{D^3} 
\]  

As conclusions of this section, based on the already established knowledge, the time lapse per each internode ($T_{\text{internode}}$) would be always constant, irrespective of the axonal diameter. Combined with the theoretical premise of $C_J \propto D^3$, the attenuation ratio of the electrostatic force per each internode ($A_{\text{internode}}$) was suggested to be proportional to the internodal length ($L_{\text{internode}}$).

Supposed Electrostatic Compressional Wave in Signal Integration and Neural Backpropagation

In the previous sections, we considered electrostatic compressional wave within the axoplasm in myelinated nerves.
Based on this model, in unmyelinated nerves, the channel on intracellular electrostatic interactions was described. In this review, the newly introduced conductive model based

Conclusions

The biggest problem of this new model at present is that the theoretical relationship of “ has not been experimentally confirmed yet. This will be evaluated by applying the immunofluorescent staining for the ion channels and measuring the luminescence and the axonal diameter. Another limitation is that we do not fully consider about the possible factors that can affect the conduction velocity in this model. Some of such factors are the full length of axon, extracellular electrolytic concentrations, and temperature. The last limitation is that, though we only considered intracellular factors to be the carrier of electric charges in this model, there are some other possible carriers like membrane protein, cell surface sugar chain, and the membrane itself. Whether we can really ignore these factors as electric carriers in nerve conduction or not is still to be verified.

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Conclusions

In this review, the newly introduced conductive model based on intracellular electrostatic interactions was described. Based on this model, in unmyelinated nerves, the channel density in the membrane (C_d) was suggested to be important to realize the faster conduction. In myelinated nerves, the inter

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Limitations

The biggest problem of this new model at present is that the theoretical relationship of “ has not been experimentally confirmed yet. This will be evaluated by applying the immunofluorescent staining for the ion channels and measuring the luminescence and the axonal diameter. Another limitation is that we do not fully consider about the possible factors that can affect the conduction velocity in this model. Some of such factors are the full length of axon, extracellular electrolytic concentrations, and temperature. The last limitation is that, though we only considered intracellular factors to be the carrier of electric charges in this model, there are some other possible carriers like membrane protein, cell surface sugar chain, and the membrane itself. Whether we can really ignore these factors as electric carriers in nerve conduction or not is still to be verified.

Conclusions

In this review, the newly introduced conductive model based on intracellular electrostatic interactions was described. Based on this model, in unmyelinated nerves, the channel density in the membrane (C_d) was suggested to be important to realize the faster conduction. In myelinated nerves, the inter

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Though we did not suppose such conductive mechanism in unmyelinated nerves because the forefront of the signal conduction would proceed along the internal surface of axonal membrane, the total number of NaV channels in a specific length of axon is estimated to be larger in unmyelinated nerves than in myelinated nerves. More specifically, though the length of Ranvier’s node is about one-thousandth of that in the internodal segment (L_internod), the channel density (C_d) in Ranvier’s nodes of myelinated nerves is no more than 100 times higher than that in unmyelinated nerves (Aranzibia-Carcamo et al., 2017). Thus, we can estimate that, though the forefront of conducted signals would proceed along the internal surface of axon, electrostatic compressional wave itself seems to exist even in unmyelinated axons and dendrites. The dendrites are known to be normally unmyelinated and widely express voltage-gated potassium channels (Kv channel) on them, not NaV channels as seen in the axons (Johnston et al., 2000, 2003). Though the type of the voltage-gated ion channels are different between dendrites and axons, the basic theoretical mechanism of signal conduction can be regarded as almost similar between them. Thus, in this section, we also apply the above-described conductive model in unmyelinated nerves to the dendritic signal conduction and assume a delayed electrostatic compressional wave on the cross-section of the dendrites. The density of NaV channels and Kv channels in the membrane of neural cell body has known to be significantly low (≈ 1.0 channel/μm²), and a previous study reported that an attempt to produce action potential in the soma failed even with a normal proper stimulating procedure (Safronov et al., 1997; Wolff et al., 1998). This fact suggests that we are better to think about the signal conduction, integration, and back-propagation in the neuronal cell body to spread not on the two-dimensional internal surface of the membrane of cell body but across the cytoplasm with three-dimensional extent.

We do not have much information about the signal conduction, integration, and back-propagation in the neural cell body yet. Three-dimensional propagation of electrostatic compressional wave not only in the axon but also in the neuronal cell body may be a promising candidate of the element realizing the above-mentioned neural physiological functions.