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Theory of Wave Propagation in Nervous System
—An Example of Dissipative Structure in an Open System—

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Propagation of an action potential in a nervous cell is studied theoretically on the basis of the notion that the excitation of nerve membrane is a transition between two non-equilibrium steady states. Basic phenomenological equations are derived for the excitation process taking consideration of the long-range dissipative interaction caused by the electric eddy current. Numerical calculations of these equations show the occurrence of a solitary wave of an action potential under appropriate initial and boundary conditions, where both the nonlinear effect of the eddy current and the non-markoffian effect of accumulation of ions at the membrane surface are shown to play a role in the appearance of a nervous soliton. Characteristics of the nervous soliton are studied numerically by the use of a simplified basic equation, and compared with the other types of solitary waves, e.g., the KdV soliton in a shallow water wave and the Toda soliton in a lattice vibration.

§ 1. Introduction

Recent physicochemical studies carried out with perfused squid giant axons revealed that the electric current caused by non-uniform distribution of electric potential along the membrane surface plays a decisive role in the process of excitation.\(^1\) In a previous paper concerned with an ensemble theory of dissipative process, we showed that the nerve excitation is plausibly interpreted in terms of a transition between steady states mediated by the electric eddy current across the membrane, and gave a set of basic equations describing the dynamic behavior of the transition.\(^2\) It was not studied, however, whether or not the transition is able to propagate as a solitary wave along the membrane surface. This paper will be devoted to an analysis of propagation of an action potential on the basis of the transition between two steady states.

On the basis of the theoretical model for the excitable membrane proposed in the previous paper,\(^3\) basic equations are derived, where the long-range interaction due to the electric current is taken into consideration. Numerical solutions to these basic equations show the occurrence of a solitary wave similar to that observed as an action potential in a nervous cell. A pulse-like wave propagation in the dispersive medium is widely known in many branches of physics, e.g., hydrodynamics, solid state physics, optics and elementary particle physics.\(^4\) It is shown that our nervous equation proposed in this article is not dispersive but...
dissipative. In other words, a solitary wave in the nervous cell is considered as an example of solitons in dissipative media.

§ 2. Basic equation of nervous excitation

As illustrated in Fig. 1, the electric current flowing in the membrane system is composed of two parts, i.e., the transmembrane current $I_t$ and the current which flows out of the membrane into the solution phase $I_{nt}$. The transmembrane current $I_t$ satisfies the following relation:

$$\int_{-\infty}^{\infty} I_t \, dr = 0$$

(1)

unless the membrane is subjected to an external electrical force such as voltage clamp. In Eq. (1), $r$ is coordinates along the membrane surface. The subsequent arguments are confined to the case where Eq. (1) is satisfied. $I_{nt}$ forms a long-range nonlocal current and depends on the membrane state in the neighbouring region. Since the total current is assumed to be zero, the nonlocal current $I_{nt}$ must be equal to the transmembrane current $I_t$ and the continuity equation of electric current is given by

$$I_t = I_{nt}.$$  

(2)

As illustrated in the previous article, the transmembrane current $I_t$ is represented by the equation

$$I_t = C \frac{\partial V}{\partial t} + g_a P (V - E_a) + g_r (1 - P)(V - E_r),$$

(3)

where $P$ is the mean fraction of the excited domain, $V$ is the transmembrane potential, $C$ is the membrane capacitance, $g_a$, $g_r$, $E_a$ and $E_r$ are the membrane conductance per unit area and the membrane potential of the exciting and resting domains of the membrane, respectively. On the other hand, the nonlocal current $I_{nt}$ is represented as follows:

$$I_{nt} = \int_{-\infty}^{\infty} d(\Delta r) \, W(r, \Delta r) \, [V(r + \Delta r) - V(r)],$$

(4)

where $W(r, \Delta r)$ is the electric conductance of solutions between two different points distant $\Delta r$ on the membrane. Since the electric conductance of solutions is assumed isotropic and uniform along the membrane surface, $W(r, \Delta r)$ is an even function of $\Delta r$. Therefore, $I_{nt}$ takes the form
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\[ I_{nt} = D_2 \frac{\partial^4 V}{\partial r^4} + D_1 \frac{\partial^4 V}{\partial r^4} + \cdots, \quad (5) \]

where \( D_n \) is the \( n \)-th moment of \( \Delta r \), i.e.,

\[ D_n = \int_{-\infty}^{\infty} d(\Delta r) (\Delta r)^n W(\Delta r). \quad (5') \]

Even in the case where the total current is zero, the transmembrane current \( I_t \) is not always zero at a given point on the membrane. Therefore, we can expect that the transmembrane current \( I_t \) acts as a generalized force for inducing a change in state of a part on the membrane. With the effect mediated by \( I_t \) taken into consideration, the time evolution of the exciting fraction is represented as follows:

\[ \frac{\partial P}{\partial t} = k_1 (V - V_c) P (1 - P) - k_2 P \Gamma_1 (t) + A(I_t), \quad (6) \]

where \( k_1 \) and \( k_2 \) are rate constants and \( V_c \) is the threshold level of the membrane potential. The first term on the right-hand side of Eq. (6) gives the effect of the local eddy current which is controlled by the membrane potential, and the second term gives the non-markovian effect stemmed from the irreversible accumulation of ions onto the membrane surface. The effects of the first and second terms were studied in the previous paper by assuming \( \Gamma_1 (t) \) as follows:

\[ \Gamma_1 (t) = \int_{0}^{t} [V(t') - E_r] e^{-(t-t')/\tau_1} dt', \quad (7) \]

where \( \tau_1 \) is the relaxation time of the ion accumulation. The last term of Eq. (6) represents the effect of the nonlocal current \( I_{nl} \), where the continuity of current given by Eq. (2) has been used. To proceed to further discussion, we assume a linear relation as follows:

\[ A(I_t) = A(I_{nl}) = k_3^* I_{nl}, \]

where \( k_3^* \) is a rate constant. On the assumptions introduced above, the basic equations (3) and (6) are rewritten as follows:

\[ \frac{\partial P}{\partial t} = k_1 (V - V_c) P (1 - P) - k_2 P \int_{0}^{t} [V(t') - E_r] e^{-(t-t')/\tau_1} dt' + k_3 \frac{\partial^2 V}{\partial r^2}, \]

\[ C \frac{\partial V}{\partial t} = -P g_a (V - E_a) - (1 - P) g_r (V - E_r) + D_2 \frac{\partial^2 V}{\partial r^2}, \quad (8) \]

where we have introduced the approximation \( I_{nt} = D_2 (\partial^2 V / \partial r^2) \) and put \( k_3 = D_3 k_3^* \).

When the system attains the quasi-steady state, \( V \) and \( P \) satisfy the following relations:

\[ k_1 (V - V_c) P (1 - P) - k_2 P \Gamma_1 (t) = 0, \]

\[ P g_a (V - E_a) + (1 - P) g_r (V - E_r) = 0. \quad (9) \]
Fig. 2. The propagation of an action potential $V$ and an exciting fraction $P$. The dotted line shows the quasi-steady state as mentioned in the text. Parameters are taken as follows:

- $g_m = 10^{-4}$ mho cm$^{-2}$, $g_s = 10^{-4}$ mho cm$^{-2}$,
- $E_a = 70$ mV, $E_r = -50$ mV, $V_x = -30$ mV,
- $C = 10^{-4}$ F cm$^{-2}$, $r_1 = 3.5$ sec,
- $k_1 = 2 \times 10^4$ V$^{-1}$ sec$^{-1}$, $k_2 = 1.5 \times 10^4$ V$^{-1}$ sec$^{-1}$,
- $k_3 = 10^{-4}$ V$^{-1}$ sec$^{-1}$ mm$^{-1}$,
- $D_s = 10^{-4}$ mho.

$t$ and $x$ are measured by second and millimeter, respectively, but the unit of $x$ depends on the unit of $k_s$.

It must be remembered that the relations given by Eqs. (9) are obtained by putting $\partial/\partial t = 0$ and $\partial^2/\partial r^2 = 0$ in Eqs. (8), and that they hold at an arbitrary point on the membrane surface. The reason why the state given by Eqs. (9) has been referred to as the quasi-steady state is that the state changes gradually by the time-dependent variable $I_1(t)$. As is mentioned in the previous paper, there are three solutions satisfying Eqs. (9) in general, but two quasi-steady state solutions corresponding to the exciting and threshold states disappear simultaneously with the increase of $I_1(t)$ and only one solution, i.e., $V = E_r$ and $P = 0$ corresponding to the resting state remains. Figure 2 shows an example of numerical solution of Eqs. (8) in the special case of one-dimensional propagation of an action potential. It shows the time courses of the membrane potential $V$ and the mean fraction $P$ as a function of distance at various times. In the calculations, the parameters in Eqs. (8) are taken as values listed in the figure caption and the free boundary condition is imposed. The wave front travels at an almost constant speed from the left to the right. The wave tail turns back to the resting level and a solitary wave appears. The soliton thus obtained travels along the membrane surface without changing its shape and velocity. The quasi-steady states given by Eqs. (9) are shown by the dotted lines. The upper dotted curve is the exciting level, and the lower one is the threshold level. When a stimulus exceeds the threshold level, the state of membrane jumps to the exciting level. Just behind the passage of a soliton, there is no threshold level. Hence the membrane cannot be excited by any strength of external stimulus. The period of duration in which no excitation is elicited by any strength of stimulus is generally called a refractory period in the field of physiology. After the refractory period, the exciting level again appears, and the membrane recovers the excitability. It is interesting to note that the soliton in the membrane system leaves a memory in the medium behind the wave, which
is different from the other types of solitons such as those in the KdV equation for the surface wave in shallow water and in the Toda equation for lattice vibration.\cite{5,6} The profile of a soliton at an instant is the same as the time course of an action potential (non-propagating) observed at a fixed point, because the speed of propagation of a soliton is constant. If appropriate values of parameters in Eqs. (8) are chosen, we are able to reproduce a theoretical action potential which well accords in shape with the observed action potential as shown in the previous paper.\cite{3} We do not discuss further details of a quantitative representation of the profile of an action potential, but confine our discussion to a general feature of nervous soliton in this article.

§ 3. Simplified model of nervous excitation

The basic equation given by Eqs. (8) is rather too complicated to see the general characteristics of the nervous soliton. Therefore, we will simplify Eqs. (8) under an appropriate approximation. Since the time courses of the mean exciting fraction $P$ and the membrane potential $V$ quite resemble each other as is seen in Fig. 2, we may boldly make an approximation that

$$P \propto (V - E_r).$$

(10)

Equations (8) are then simplified to give

$$\begin{align*}
\frac{\partial P}{\partial t} &= k_4 P(1 - P)(P - P_0) - k_6 P \int_0^t P(t') e^{-\alpha(t - t')} dt' + k_6 (\partial^2 P / \partial x^2), \\
\text{where the } k_i \text{'s are rate constants, } P_0 \text{ is the threshold level of the mean exciting fraction } P \text{ and } T_1 \text{ is the relaxation time of the irreversible accumulation of ions. Here we have introduced a set of parameters } k_i \text{ different from those used in Eqs. (8), because we use a non-dimensional differential equation in this section. The quasi-steady state is obtained by the following equation:}
\end{align*}$$

$$\begin{align*}
k_4 P(1 - P)(P - P_0) - k_6 P \Gamma_0(t) = 0, \\
\text{where}
\end{align*}$$

(12)

$$\begin{align*}
\Gamma_0(t) &= \int_0^t P(t') e^{-\alpha(t - t')} dt'.
\end{align*}$$

When we denote the steady state solutions of $P$ for exciting and threshold levels as $P_a^*(t)$ and $P_e^*(t)$, respectively, Eq. (11) becomes

$$\begin{align*}
\frac{\partial P}{\partial t} &= k_4 P_a^*(t) - P_a^*(t) (P - P_e^*(t)) + k_6 (\partial^2 P / \partial x^2), \\
\text{where } P_a^*(t) \text{ and } P_e^*(t) \text{ are given by the equations}
\end{align*}$$

$$\begin{align*}
P_a^*(t) &= \frac{1}{2} \left(1 + P_e + \sqrt{(1 - P_e)^2 - (4k_6/k_4) \Gamma_0(t)} \right), \\
P_e^*(t) &= \frac{1}{2} \left(1 + P_e - \sqrt{(1 - P_e)^2 - (4k_6/k_4) \Gamma_0(t)} \right).
\end{align*}$$

(14)
Fig. 3. The wave propagation in a simplified equation of the nervous system with various values of $T_s$ with $P_s=0.1$, $k_s=2.0$, $k_{S}=0.1$ and $k_a=1.562\times10^{-4}$.

(a) The wave propagation of $P$ in the case $T_s=4.0$.
(b) The wave propagation of $P$ in the case $T_s=8.0$.
(c) The wave propagation of $P$ in the case $T_s=13.0$.
(d) The wave propagation of $P$ in the case $T_s=30.0$. 

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The states given by Eqs. (14) are defined at an arbitrary point on the membrane surface in the same way as in Eqs. (9).

If we consider the limiting case where the time variation of $\Gamma_2(t)$ is either zero or extremely slow, i.e., $\Gamma_2(t) \approx \Gamma_2(0)$, we easily get a particular solution of Eq. (13) in the form

$$P = \frac{1}{2} P_a^*(0) \left[ 1 - \tanh \left\{ \sqrt{\frac{k_4}{8k_6}} P_a^*(0) (x - vt) \right\} \right],$$

where

$$v = P_a^*(0) \left( \frac{1}{2} \frac{P_c^*(0)}{P_a^*(0)} \right) \sqrt{2k_4 k_6}.$$  \hspace{1cm} (15)

This is not a solitary wave but a transition propagating stepwise along the $x$-axis. The wave front proceeds with a constant velocity given by Eq. (16), but the wave tail is prolonged indefinitely and remains at a fixed level of $P = P_a^*(0)$.

We can consider that the solution shown by Eqs. (15) and (16) denotes the non-linear wave which describe the dynamical feature of the transition from the resting level ($P=0$) to the excited level ($P=P_a^*(0)$).

Even if the time variation of $\Gamma_2(t)$ is very slow in comparison with that of the mean exciting fraction $P$, the accumulated effect caused by the non-marcovian term, $\Gamma_2(t)$, cannot be neglected. Therefore, the solution denoted by Eqs. (15) and (16) is considered to be a crude approximation of the real system represented by Eq. (13). Furthermore, $P_a^*(t)$ and $P_c^*(t)$ take complex values with the increase of $\Gamma_2(t)$, and the steady state solutions given by Eqs. (14) disappear even if we take the approximation introduced above. As soon as the

![Fig. 4. Disappearance of solitons by collision in the case $P_a=0.1$, $k_4=2.0$, $k_3=0.1$, $k_4=1.562 \times 10^{-4}$ and $T_2=20.0$.](http://ptp.oxfordjournals.org/)}
exciting level vanishes, the state of the membrane flips back to the resting level and the wave tail of the excitation is attenuated. Equation (11) is numerically solved in the case where the parameters $k_t$ and $P_e$ take fixed values as $k_t=2.0$, $k_5=0.1$, $k_6=1.562\times10^{-6}$ and $P_e=0.1$. When either $k_6$ or $T_2$ is small, the tail of the transition wave stays on the excited level for a long period of time and a catastrophic flip-back does not occur (see Fig. 3(a)). The dotted lines in Fig. 3 show quasi-steady states given by Eqs. (14).

When $T_2$ increases without changing values of other parameters $k_4$, $k_5$ and $k_6$, the membrane state gets back to the resting level at the wave tail, and a solitary wave is formed (see Fig. 3(c)). If $T_2$ is close to a critical value, the transition wave oscillates at the plateau of the exciting level (see Fig. 3(b)). When both $k_6$ and $T_2$ are large enough, the exciting level disappears monotonically and does not form a travelling wave (see Fig. 3(d)).

It is interesting to note that when two solitons travelling in opposite directions collide with each other, they are destroyed simultaneously at the instant of the collision because there remains a refractory period just behind a nervous soliton. Figure 4 shows the extinction of two colliding solitons.

The last part of this section is devoted to clarifying the character of a solitary wave given by Eq. (11). The velocity $v$ and the height $h$ characterize the nervous soliton. By changing the value of $T_2$ the relation between the velocity $v[-=10^8(dx/dt)]$ and the height $h$ of a soliton is obtained. An example of the numerical calculation is shown in Fig. 5. The height $h$ and the velocity $v$ are measured at the peak of a soliton. In region I shown by the dotted line in Fig. 5 a prolonged wave shown in Fig. 3(a) is formed. In region III where
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$T_z > 20$, the excited level decays monotonically as illustrated in Fig. 3(d). Hence no clear relation between $v$ and $h$ is observed in region III. Only in region II a linear relation between $v$ and $h$ of a soliton is obtained. In the critical region where branch I changes to branch II, fluctuation at the plateau of the membrane potential is observed as shown in Fig. 3(b), and hence the height and the velocity of a wave cannot be measured steadily.

§ 4. Discussion

Since the conductivity in the external and internal solution phases are pretty high in comparison with that in the membrane phase, the interaction caused by the current between active patches acts as a long-range one, and hence the transition in the membrane system becomes cooperative. In fact, as shown in the previous paper, the excitation phenomenon in the membrane system is a cooperative transition between two stable steady states. Furthermore, it is shown in this paper that the nonlocal long-range current plays an indispensable role in the propagation of an action potential in the nervous membrane.

The basic equation for the excitation process proposed in this paper have a simple form as compared with that derived by Hodgkin and Huxley; the present model is not based on any microscopic assumptions of the imaginary substance such as the so-called $h$- and $n$-particles. Our equation also permits the derivation of another model thus far proposed; e.g., the basic equation used by Nagumo et al. can be derived as a special case where $T_z$ tends to infinity in Eq. (11). Notwithstanding the limitation of our discussion to the most simple case given by approximation $A[I_n] = \frac{\partial^2 V}{\partial x^2}$, the wave propagation obtained from our model agrees with the experimental results relevant to the nerve excitation or the propagation of nervous impulse. That is, there is a refractory period just behind a passing of the impulse, and two action potentials travelling in the opposite directions disappear simultaneously by means of collision. Therefore, we believe that at least qualitatively all relevant factors are properly taken into account in our model, even though the dynamical equation describing the excitation process must be more complicated in the real system.

The membrane excitation is considered to be a thermodynamical phenomenon induced by the difference of the electro-chemical potential of some species of ions between the inside and the outside of the nervous cell membrane. Besides no action potential can be propagated without dissipating free energy by the ion transport. Due to this reason, an action potential or a nervous soliton is a typical example of dissipative structure with temporal and spacial order in the thermodynamical sense. The most serious difference between a nervous soliton and other types of solitons, e.g., the KdV soliton and the Toda soliton, is that a nervous soliton leaves a memory in the medium just behind the passage of a soliton. A nervous soliton has an inherent shape and velocity and besides it
consumes a constant energy per unit time. Therefore a nervous soliton is never a mass of energy such as the Toda soliton. Despite these differences between a nervous soliton and others (the KdV and the Toda solitons), the relation between the height and the velocity of a nervous soliton is almost linear in the same way as in the KdV soliton. Since our results are numerical ones, further analytical treatment of the conservation law, the stability and the $h$-$v$ relation is necessary.

References

7) P. Glansdorff and I. Prigogine, *Thermodynamic Theory of Structure, Stability and Fluc-