Effect of Dendritic Backpropagating Action Potential on Neural Interaction

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Abstract

We elucidate the effect of dendritic backpropagating action potentials on neural interactions. We propose a neural oscillator model that mimics the backpropagating potentials upon the dendrite. We show that backpropagating potentials change the stability structure of the system from monostable to bistable. Such bistability causes the multiple phase clustering of the neural population. The phase clustering is a cogent hypothesis to explain the information representation binding distributed codes in the brain.

Key words: dendrite, backpropagation, synaptic response, oscillator

It has been generally recognized that electrical signals within a nerve cell flow in a *feed-forward* direction: from the input sites (usually the dendrite) to the output sites (usually the soma). This hypothesis is referred to as the principle of dynamic polarization [1]. Almost all formal neuron models in theoretical studies are based upon this hypothesis. In such formal neuron models, the dendrite plays a role of just a cable transmitting synaptic input signals to the soma. However, the properties of the dendrite are more complicated than those of the formal neuron model. It has been reported that many kinds of voltage-activated ion channels are highly distributed over the dendrite, and that action

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potentials can be generated in the dendrites [2]. Under some conditions, action potentials are initiated at the dendrite by strong EPSP, and propagate to the soma (forward propagation). Under some conditions, action potentials are initialized at the soma even by strong EPSP, and propagate to the dendritic input sites (backpropagation). In this paper, we focus on the role of the backpropagation in the information processing of a single nerve cell. Backpropagation implies that output signals are fed back to the input sites. There is a possibility that in this case, a single nerve cell might be able to acquire a capacity of *active* information processing through the modification of synaptic responses by backpropagating action potentials. There are many reports on the relationship between backpropagating action potential and postsynaptic potential [3–6]. All these reports have focused on the amplification of backpropagating action potential and shunting inhibition of postsynaptic potential that are caused by interference between these two potentials. If the temporal coding hypothesis (that the information is coded in spike timing) is accepted, any discussion on neural information processing should focus on the timing modification of action potential initiation by the backpropagation rather than the amplification/inhibition of those potentials.

We analyze the impact of the spike-timing modification by backpropagation on neural interaction and neural cooperative behavior. We measure in regular oscillatory states the phase modification of action potential initiation as a function of relative timing between action potential initiation and postsynaptic potential generation. We propose a neural oscillator model that mimics backpropagating potentials upon the dendrite. This model enables us to extract the effect of the backpropagating potential only. Through the phase reduction, we demonstrate that at the synapse, a collision of synaptic inputs with backpropagating potentials induces bistable states consisting of in-phase locking and anti-phase locking. Models previously proposed [7,8] are similar to our model proposed here, but those authors did not clearly mention the role of the backpropagation. In previous studies, the phase description of whole systems has been numerically derived. The numerical calculation incorporated and renormalized the effects of the backpropagation into only a *phase-coupling function* to establish the phase equation, thus the effects of the backpropagation could not be dissociated from the phase equation. On the other hand, in our analysis, we clearly separate the effects of the backpropagation from the phase equation. In the phase equation obtained here, the dynamics of dendrite and synapse are represented only by the *transfer function* or *describing function* that describes their frequency response. Our theoretical result that a collision of synaptic inputs with backpropagating potentails causes such bistable states is a concrete example that validates physiological conjectures regarding the function of backpropagations. Through our analytical phase reduction we can elucidate the influence that the transmission lag caused by the dendrite and the synapse, which depends on the signal-transmission performance of the dendrite and synapse, has on the behavior of the whole system.

We consider symmetrically-connected pair of simple neurons. The dynamics of the membrane potentials of the soma in the jth neuron ($j = 1,\ 2$) is expressed by the Stuart-Landau (SL) oscillator[10]:

$$\frac{dv_j^{\rm s}}{dt} = i\Omega v_j^{\rm s} + v_j^{\rm s}\left(1 - \frac{|v_j^{\rm s}|^2}{R^2}\right) + I_j^{\rm sd}, \tag{1}$$

where $v_j^{\rm s}$ is the state variable (a complex number), and $I_j^{\rm sd}$ represents an input from the dendrite (a complex number). Ω is the natural frequency of two symmetric oscillators. It is well-known that the SL oscillators describe the essential structure of the Hopf bifurcation [10]. It is natural that the system is described to the complex state variable if this is in oscillatory states. When $I_j^{\rm sd} = 0$, the system has an unstable fixed point at $v_j^{\rm s} = 0$ and a stable limit-cycle orbit of R radius in the complex plane: $v_j^{\rm s}(t) = R\exp i\left(\Omega t + \phi_j\right),\ {}^\forall\phi_j \in \mathbf{R}/2\pi$. Here, the quantity ϕ_j, which depends only on the initial condition, is the phase of the jth oscillator.

Here, we treat two kinds of dendritic models, one with backpropagation and the other without. By comparing the backpropagation and non-backpropagation models, we elucidate the role of the dendritic backpropagation. In the back-propagation case, the dendrite, the synapse, and $I_j^{\rm sd}$ are expressed as

$$C_{\rm d}\frac{dv_j^{\rm d}}{dt} = -g_{\rm dl}v_j^{\rm d} - I_j^{\rm sd} + \epsilon s_k(E_{\rm s} - {\rm Re}\{v_j^{\rm d}\}), I_j^{\rm sd} = g_{\rm d}\left(v_j^{\rm d} - v_j^{\rm s}\right), \tag{2}$$

$$\tau_{\rm s}\frac{ds_k}{dt} = -s_k + G\Theta(v_k^{\rm s}),\ G = \frac{g_{\rm s}}{\theta_2 - \theta_1},\ \Theta(x) = \begin{cases} 1 & \theta_1 < \arg x < \theta_2 \\ 0 & \text{otherwise} \end{cases}. \tag{3}$$

Equation (2) represents the dynamics of the dendritic membrane potential approximated to a simple Capacitance-Resistance circuit (i.e., a first-order lag system). As Eq. (2) reveals, the dendrite has a strong input from the soma. Here, $v_j^{\rm d}$ is the membrane potential, $C_{\rm d}$ is the membrane capacitance, $g_{\rm d}$ is the conductance of the dendritic medium, $g_{\rm dl}$ is the leakage conductance of the dendritic membrane. The term containing coefficient ϵ is the synaptic current. s_k is the synaptic conductance, and E_s is the synaptic reversal potential. This term represents a perturbation, and the quantity ϵ controls the amplitude of the perturbation. Therefore, in this model, the dendrite is strongly driven by the soma and is weakly driven by the synapse. Equation (3) is the synaptic dynamics approximated to the first-order lag system and the threshold element with hysteresis. The action potential generated by our model is a sine wave, which is symmetrical and gentle. However, the action potential generated by realistic membrane oscillators is asymmetric and sharp. To mimic realistic wave form, we introduce the threshold function with hysteresis defined by Eq. (3). The effect of such realistic action potentials can be incorporated into this hysterical threshold element in our model.

In the non-backpropagation case, the dendrite, the synapse, and $I_j^{\rm sd}$ are expressed as

$$C_{\rm d}\frac{dv_j^{\rm d}}{dt} = -(g_{\rm d}+g_{\rm dl})v_j^{\rm d} + \epsilon s_k E_{\rm s},\ I_j^{\rm sd} = g_{\rm d}v_j^{\rm d},\quad \tau_{\rm s}\frac{ds_k}{dt} = -s_k + G\Theta(v_k^{\rm s}), \quad (4)$$

where all parameters are equal to their counterparts in the backpropagation model. As Eq. (4) reveals, the dendrite does not receive an input from the soma, thus the dendrite is only driven by the synapse. This model has *feed-forward* information flow, the same as in formal neuron models based on the principle of dynamic polarization.

In our model, there is an *adjoint* which can be explicitly obtained as $\Phi_j^*(t) = [iA\exp i(\tilde{\Omega}t+\phi_j-\psi),\ i\exp i(\tilde{\Omega}t+\phi_j)]^T$. Taking the inner product between $\Phi_j^*(t)$ and the perturbation, we obtain a pair of phase equations[10]. Then, using a new variable defined as $\phi = \phi_1 - \phi_2$, we can unite a pair of phase equations into one equation:

$$(1+C_{\rm d}A^2\cos 2\psi)\frac{d\phi}{d\tau} = \Gamma(\phi), \quad (5)$$

$$\Gamma(\phi) = A^2A^{(2)}\cos(\psi^{(2)})\cos(\phi)\sin(\phi) - \frac{E_s}{\tilde{R}}AA^{(1)}\cos(\psi+\psi^{(1)})\sin(\phi). \quad (6)$$

This equation describes the motion of a phase difference between two neurons. Here, $\Gamma(\phi)$ is referred to as a *phase coupling function*. In this case, the equilibrium states consist of in-phase locking, anti-phase locking, and two non-trivial solutions. The non-trivial solutions are caused by backpropagating action potentials.

Next, we show the result of the phase reduction from the non-backpropagation model. The phase difference equation is expressed as

$$\frac{d\phi}{d\tau} = \Gamma(\phi), \Gamma(\phi) = -\frac{E_s}{R}AA^{(1)}\cos(\psi+\psi^{(1)})\sin(\phi). \quad (7)$$

In this case, the equilibrium states consist of in-phase locking and anti-phase locking.

Here, A, ψ, $\tilde{R}$, and $\tilde{\Omega}$ are satisfied with respect to the equations: $A\exp i\psi = g_{\rm d}/(i\tilde{\Omega}C_{\rm d}+g_{\rm d}+g_{\rm dl})$, $\tilde{\Omega} = \Omega+\beta g_{\rm d}A\sin\psi$, and $\tilde{R} = R\sqrt{1-\beta g_{\rm d}+\beta g_{\rm d}A\cos\psi}$. A and ψ are self-consistently defined. This equation denotes the transfer function describing the frequency response of the dendrite. Such self-consistency means that the orbit of the SL oscillator driving the dendrite is modified by a reaction from the dendrite. $A^{(m)}$ and $\psi^{(m)}$ $(j=1,\ 2)$, which correspond to coefficients of the Fourier expansion for the synaptic conductance S_k, are defined by $A^{(m)} = |J^{(m)}|$, $\psi^{(m)} = \arg J^{(m)}$, where $J^{(m)} = \frac{e^{i\xi^{(m)}}\sqrt{2(1-\cos m(\theta_2-\theta_1))}}{m\pi(\theta_2-\theta_1)}\frac{g_{\rm s}}{1+im\tau_{\rm s}\tilde{\Omega}}$, $\xi^{(m)} = \arg\{i\exp(-im\theta_2) - i\exp(-im\theta_1)\}$. $\xi^{(m)}$ denotes the phase shift caused by

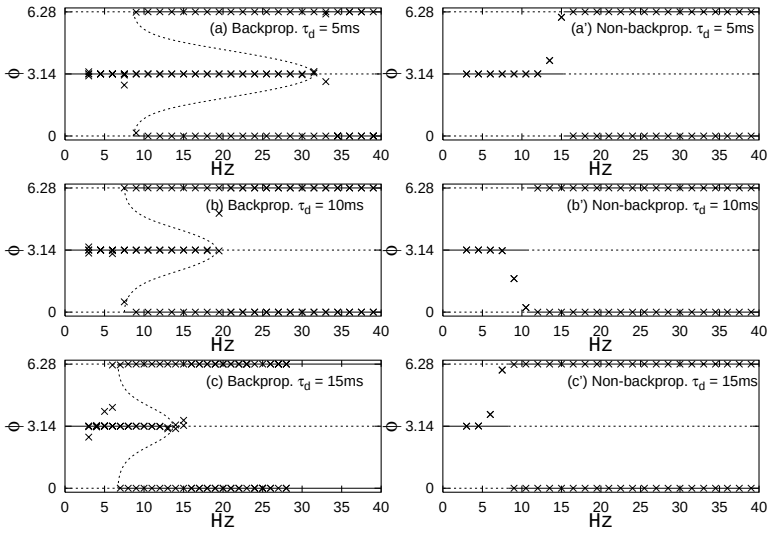

Fig. 1. Equilibrium states as a function of firing frequencies. Solid curves denote stable equilibrium states, and dashed curves represent unstable equilibrium states. The mark $\times$ denotes results obtained from simulations.

the hysteresis. At a fundamental frequency component, $J^{(1)}$ stands for the *describing function* in control engineering.

Finally, we compare Eqs. (6) and (7). The fundamental frequency component of Eq. (6) is equivalent to $\Gamma(\phi)$ in Eq. (7). This term represents a part of the neural interaction induced by the feed-forward signal. On the other hand, the higher harmonics of Eq. (6) are unique to the backpropagation model. This term, which induces the bistability, is due to the modification of synaptic responses by backpropagating action potentials. We succeeded in separating the two parts of the neural interaction induced by the forward signal and the backward signal, respectively.

In the following simulations, we set the parameters as $\tau_{\rm s} = 6$, $g_{\rm s} = 0.1$, $E_s = -30$, $\theta_1 = 0.6 - \pi/5$, $\theta_2 = 0.6 + \pi/5$, $g_{\rm d} = 0.2$, $g_{\rm dl} = 0$, and $R = 80$. In this case, the inhibitory synapse was used to verify the theoretical results. To estimate the influence of dendritic performance on the bistability, we used three kinds of dendrite with different capacitances: $C_{\rm d} = 1$, $C_{\rm d} = 2$, and $C_{\rm d} = 3$. In this case, the time constants of these dendrites became $\tau_{\rm d} = 5$, $\tau_{\rm d} = 10$, and $\tau_{\rm d} = 15$, respectively. As Fig. 1 reveals, the dendritic backpropagation induces bistable states that consist of in-phase locking and anti-phase locking. Comparing Figs. 1 (a), (b), and (c), we found that as the dendritic time constant τ_d decreased, the region of bistability widened.

It is well known that such bistability causes multiple phase clustering of the neural population [13]. This phase clustering is a cogent hypothesis that explains the information representation binding distributed codes in the brain [15]. Moreover, the bistability can selectively control the synaptic plasticity.

The in-phase locking facilitates the synaptic plasticity within the same cluster because the spike timing between presynapse and postsynapse is within a time window of the temporally asymmetric Hebb learning (TAH)[16]. On the other hand, the anti-phase locking blocks the synaptic plasticity, because the spike timing between pre-synapse and post-synapse is outside the TAH time window.

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