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Correlation-based competition regulated by nonlinear interspike interaction in STDP

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Abstract: The development of visual cortical circuits is strongly influenced by the sensory experience during a restricted critical period, as demonstrated by the loss of neural responses to the eye that has been briefly deprived of vision. It has been suggested that to reflect the sensory experience into the pattern of synaptic weights, the competition between groups of correlated inputs to an identical postsynaptic cell is essential and that spike-timing-dependent plasticity (STDP) may provide the basis of this type of correlation-based competition. To predict the consequences of competition by STDP in natural physiological conditions, I here investigate the effects of nonlinear interspike interaction in STDP that is experimentally observed in the visual cortical cells. The simulations show that the interspike interaction can prevent the induction of competition and counteract the effect of activity-dependent feedback (ADFB) that facilitates competitive functions. However, once the competition occurs, the level of competition is not affected by the interspike interaction. These results may suggest that the interspike interaction in STDP acts to delay the induction of experience-dependent plasticity through suppressing synaptic competition, thereby leading to a delay in the onset of critical period plasticity in the visual cortex.

Keywords: Critical period, Visual cortex, STDP, Activity-dependent feedback.

1 INTRODUCTION

Neural circuits are developed through reflecting sensory experience during a critical period in postnatal development [1]. A representative example is an ocular dominance plasticity observed in visual cortical cells [1-3]: if either one eye is briefly deprived of vision within a critical period, the response of many visual cortical neurons is dominated by the non-deprived eye following deprivation; in contrast, the monocular deprivation before or after the critical period does not significantly affect the cell responses.

Both experimental and theoretical studies have suggested that the ocular dominance plasticity may involve the competition between different groups of inputs that originate from each eye and are correlated within each group [1, 4-6]. In the presence of correlation-based competition, the strengthening of the inputs from one eye leads to the weakening of those from the other eye. Therefore, the neural response can be dominated by one eye, as observed experimentally, and which group becomes dominant depends on the sensory experience, thereby inducing experience-dependent plasticity [4]. Furthermore, recent modeling studies have shown that spike-timing-dependent plasticity (STDP), wherein the magnitude and direction of plasticity depends on the precise timing of pre- and postsynaptic spikes, may provide a physiological mechanism that underlies correlation-based competition [4, 7].

To investigate the consequences of correlation-based competition by STDP in natural physiological conditions, I examine in this study the effects of interspike interaction in STDP [8], which is experimentally observed in the visual cortex, on the dynamics of synaptic population. The interspike interaction in STDP has been suggested to exert a suppressive effect on synaptic modifications such that the occurrence of a spike weakens the level of plasticity caused by a successive spike in the same neuron. The level of the suppressive effect of the preceding spike on the present spike follows an exponential function of the time interval between the two spikes, suggesting that the interspike interaction nonlinearly affects STDP [8]. In this study, I construct a conductance-based pyramidal neuron that receives many random inputs from synapses following STDP, as in *in vivo* conditions, and demonstrate that the interspike interaction in STDP tends to prevent the occurrence of competition between two groups of correlated inputs. This may suggest that the interspike interaction functions to suppress the ability of neurons to embed the correlation structure to synapses during early development and can contribute to delaying the onset of the critical period of ocular dominance plasticity in the visual cortex.

2 METHODS

2.1 Conductance-based neuron model

I constructed a two-compartment conductance-based pyramidal neuron, which comprises a soma and a dendrite, and is described by the following equation [4]:

$$C_m \frac{dV_s}{dt} = -I_{leak} - I_{Na} - I_K + \frac{g_c}{p}(V_d - V_s) + I_{inj}, \quad (1)$$

$$C_m \frac{dV_d}{dt} = -I_{leak} - I_{Na} - I_K - I_{Ca,V} - I_{AHP} + \frac{g_c}{1-p}(V_s - V_d) - I_{syn}. \quad (2)$$

Here, V_s and V_d are the membrane potentials of the somatic and dendritic compartments, respectively. Both the compartments contain leak (I_{leak}) and voltage-dependent Na^+/K^+ currents (I_{Na}/I_K). The voltage-dependent calcium currents ($I_{Ca,V}$) and calcium-dependent K^+ currents (I_{AHP}) are included in the dendrite to reproduce spike frequency adaptation observed in pyramidal cells [9]. g_c is a coupling conductance between the two compartments, and I_{inj} and I_{syn} are the injected and synaptic currents, respectively.

2.2 Synaptic inputs

The dendritic compartment receives random inputs, which are activated by Poisson processes, from 4000 excitatory (mediated by AMPA and NMDA receptors) and 800 inhibitory (GABAergic) inputs [10]. To explore the influences of input correlation, I divided excitatory inputs into two equally sized groups and introduced the same magnitude of correlation into each input group [11]. Any two inputs that belong to different groups are uncorrelated. All the inhibitory inputs are uncorrelated and activated by random homogeneous Poisson processes. Mean input frequencies are 3 Hz for all the synapses. Taking into account the low success rate (around 10 %) of synaptic transmission observed in central synapses [12], the input frequency of 3 Hz corresponds to the presynaptic firing rate of 30 Hz. This firing rate can be considered physiologically relevant as the sensory-evoked response of neocortical cells [9]. To quantify the level of the competition between the two groups of excitatory inputs, I introduced synaptic competition index (SCI) defined as $|\bar{w}_1 - \bar{w}_2| / (\bar{w}_1 + \bar{w}_2)$ with the average weight $\bar{w}_i$ for group i [4]. SCI of 0 means that the two groups have the same average weight, whereas SCI of 1 means that synaptic weighs of either one group converges to 0 and only one group contributes to the postsynaptic activity.

2.3 Biophysical STDP model

A previously proposed biophysical STDP model [13] was applied to all the excitatory synapses. In this model, plasticity induced by each pre- and postsynaptic spike pair is determined based on an STDP map $\Delta w(\Delta t, \tau_{NMDA}, g_{NMDA})$, which was constructed by using an *in vitro* pairing protocol simulation based on intracellular Ca^{2+}-dependent plasticity, and decides the magnitude of plasticity Δw as a function of an interspike interval between pre- and postsynaptic spikes Δt, NMDA receptor (NMDAR) peak conductance g_{NMDA}, and NMDAR decay time constant τ_{NMDA} [13]. Theoretical studies suggest that an approximate balance between LTP and LTD is required to activate competitive function of STDP [4, 7]. To attain the balanced state, I introduced activity-dependent feedback (ADFB) mechanism, in which the NMDAR peak conductance and decay time are dynamically regulated as a function of postsynaptic firing rate f_{post}:

$$\tau_{decay} = (1-\rho)\tau_1 + \rho\tau_2 - k_1 \rho f_{post}, \quad (3)$$

$$g_{NMDA} = g^0_{NMDA} - k_2 \rho f_{post}. \quad (4)$$

The parameter ρ represents the expression level of NR2A subunits in NMDARs, which considerably increases during early development [14-16]. In this model, the increase in ρ values functions to strength the ADFB modulation. ρ = 0 corresponds to a state where the ADFB function is absent because of very low level of NR2A subunits, whereas ρ = 1 corresponds to a state where the ADFB modulation is sufficiently strong due to a large number of NR2A-containing NMDARs. The first two terms in the right-hand side of Eq. 3 describes the alteration in the decay kinetics of single NMDAR currents by the increase in the NR2A-containing receptors [17, 18]. The ADFB model of STDP describes the activity- and subunit-dependent desensitization of NMDARs based on experimental observations and can contribute to facilitating the correlation-based competition [4, 19, 20].

2.4 Interspike interaction in STDP

I introduced the nonlinear interspike interaction observed in visual cortical STDP [8]. To incorporate the interspike interaction, each spike is assigned an efficacy, which is determined as a function of the time interval from a preceding spike in an identical neuron:

$$\varepsilon_K^f = 1 - \exp[-(t_K^f - t_K^{f-1})/\tau_K], \ (K = \text{pre or post}) \quad (5)$$

where the subscript K denotes the pre- or postsynaptic activity, ε_K^f is the efficacy assigned to the fth spike, t_K^f and t_K^{f-1} are the fth and (f−1)th spike timing of the K neuron, τ_{pre} = 28 ms and τ_{post} = 88 ms are the time constants by which the influence of a prior spike decays exponentially for the pre- and postsynaptic cells, respectively [8]. The change in the synaptic weights induced by the pair of the fth presynaptic spike and f'th postsynaptic spike is described as $\varepsilon_K^f \varepsilon_K^{f'} \Delta w(\Delta t, \tau_{NMDA}, g_{NMDA})$. The weight updating rule is assumed to be additive [21] and the effect of all the spike pair on STDP is taken into account.

3 RESULTS

To explore the influence of interspike interaction in STDP on its competitive property, I have examined

dynamics of synaptic population when a neuron receives correlated inputs from two groups of STDP synapses. As shown in the previous study [4], in the absence of interspike interaction, STDP elicited strong competition where one group dominates over the other in the equilibrium state (Fig. 1a). However, in the presence of the interspike interaction, competition disappeared and the two input groups were shown to converge to the same average weights (Fig. 1b). The interspike interaction did not significantly alter the average weight of all the synapses (Fig. 1a, gray).

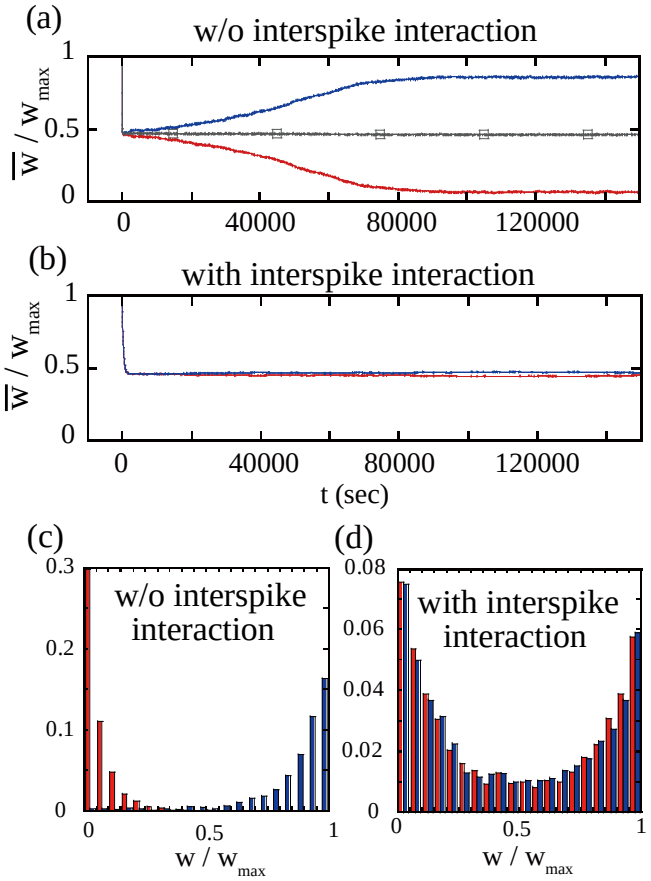

Fig. 1. The predicted effects of nonlinear interspike interaction in STDP on the correlation-based competition. (a and b) The time courses of weight averages for the two groups are shown by red and blue lines. The gray line in (a) denotes the average weight of all the inputs. (a) and (b) show the cases without and with the interspike interaction, respectively. (c and d) The final weight distributions of the two input groups are depicted by red and blue bars for the cases without (c) and with (d) interspike interaction.

These results have been clarified by examining the weight distribution at the equilibrium state (Fig. 1c and 1d). The figures show that without the interspike interaction, the weight distribution differs between the correlated groups such that the synaptic weights of one group accumulates near 0 whereas those of the other group tends to be pushed toward the maximum weight (Fig. 1c). However, without the nonlinear interaction, the weight distribution is nearly the same for the two groups, implying the lack of correlation-based competition.

To examine physiological significance of interspike interaction, I calculated the weight averages of the two groups with changing ρ, a parameter representing the level of NR2A subunit expression in NMDAR channels (Fig. 2a). The result shows that the interspike interaction significantly increases a threshold value of ρ required to induce the between-group competition. Accordingly, a threshold ρ value, above which SCI becomes positive, is significantly larger in the presence of interspike interaction (Fig. 2b). Interestingly, once the competition occurs for sufficiently larger ρ values, the level of competition is nearly the same independent of whether the interspike interaction is incorporated. These results suggest that the interspike interaction in STDP in the visual cortex can contribute to regulating the induction of competition and the resulting occurrence of critical period such that the nonlinear suppression delays the timing of the critical period, but does not affect the level of plasticity once it occurs.

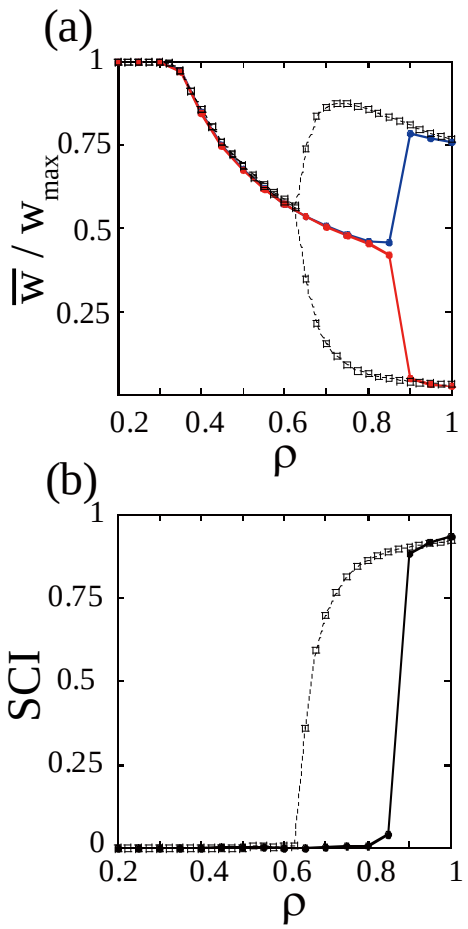

Fig. 2. The weight averages of the two groups (a) and synaptic competition index (SCI) (b) are plotted as a function of the strength of ADFB modulation ρ. Solid lines show the case of introducing nonlinear interspike interaction in STDP, whereas dashed lines show the case of not incorporating interspike interaction.

4 DISCUSSION

In this report, I have studied the effects of nonlinear interspike interaction in STDP on the competition between inputs based on their correlation structure, and have found that this interaction may function to prevent the occurrence of competition. This effect could be attributable to the net decrease in the correlation between the pre- and postsynaptic activity, because the nonlinear interaction would tend to weaken the actual influence of presynaptic inputs on the postsynaptic spike, particularly when the postsynaptic spikes occurs repetitively within a short time interval. The variance of the level of ocular dominance plasticity within the visual cortical cells might be partly explained by the variance in the level of the interspike interaction, although additional experiments would be clearly required to sort out how the effects of nonlinear interaction are physiologically regulated in individual neurons.

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