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Significance of LTD Window in the Range of Positive Spike Timing of STDP Rule for Theta Phase Coding in a Network Having Background Noise

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Abstract– The hippocampus and the entorhinal cortex generate theta rhythm that is an underlying mechanism for sequence learning. Background noise also exists in those areas. Since synapses have features of spike-timing dependent plasticity (STDP), it is possible that background noise causes enhancement of irrelevant synaptic connections that obscure memory encoding. In the present study, we tested the significance of the LTD window for robust sequence learning amid background noise, using our previous model of the entorhinal cortex layer II. Our results indicate that a LTD window in the range of positive spike timing works well, with the progress of the sequence learning, to suppress the enhancement of irrelevant connections between neurons; one of which receives regular and random pulse trains both, and each of the other cells receives only a random pulse train.

1. Introduction

Principal neurons in the hippocampus and the entorhinal cortex fire successively within one cycle of the theta rhythm when a rat traverses a place field [1]. The theta rhythm is therefore an underlying mechanism for those neurons to fire keeping pace with each other. On the other hand, it has been found that synaptic change is subject to spike-timing dependent plasticity (STDP); if synaptic input is activated within about 10 ms before or after spiking of postsynaptic neuron, plastic change in synaptic conductance takes place.

STDP learning rules are roughly classified into two types: temporally asymmetric STDP rule that has one LTD window only in the range of negative spike-timing[1] (Fig. 4(i)) [2] and relatively symmetric STDP rule that has LTD windows on both sides of the LTP window (Fig. 4(h) and (j)) [3, 4]. It has been thought in general that the temporally asymmetric STDP rule may work for sequence learning of places, while the symmetric STDP rules may work for coincidence detection of spikes. However, significance of the LTD window in the range of positive spike-timing of the symmetric STDP rule for sequence learning and/or coincidence detection has not been well understood.

EPSPs caused by a low-rate random pulse train (a high-rate regular pulse train) are integrated slowly (rapidly) toward the spike threshold. Therefore, when neuronal firing keeps pace with theta rhythm, each neuron receiving a low-rate random pulse train that implies background noise tends to fire at later phases of the theta rhythm and each neuron receiving a relatively high-rate regular pulse train that implies a sensory signal tends to fire at earlier phases of the theta rhythm. If the instantaneous frequency of regular pulse train is quite high, the spike time difference between neurons, one of which receives the regular pulse train and another one receives a random pulse train, is large, and thus the synaptic connection weight is not influenced by any STDP rule. In contrast, if the frequency of regular pulse train is relatively low and the spike time difference is small, plastic change in synaptic connections take place through a STDP rule; this implies that irrelevant connections are enhanced due to the background noise.

In our previous work, we constructed a model of the entorhinal cortex layer II having entorhino-hippocampal loop connections and used a Mexican hat STDP learning rule in order to show that the theta phase coding was performed by selective enhancement of loop connections, guided by the order of frequencies of sensory signals [5]. In the present work, using the above model and three types of STDP rule (Mexican hat [3], temporally asymmetric [2], and Nishiyama [4] STDP rules), we tested the significance of the LTD window in the range of positive spike-timing of STDP rules for the robust, relevant sequence learning amid the background noise.

2. Brief Review of the ECII Model with Entorhino-Hippocampal Loop Connections

The entorhinal cortex layer II (ECII) receiving signals from the neocortex sends signals to the hippocampus and the hippocampus sends signals back to the entorhinal cortex layer V (ECV) sending signals to the neocortex. Moreover, since ECV→ECII projections exist, loop circuitry is formed in the entorhino-hippocampal system.

Our previous ECII network model consisted of 30 stellate cells and one inhibitory interneuron (Fig. 1). Those neurons are multi-compartmental. Stellate cells and the interneuron were connected to each other, whereas there was no excitatory connection between stellate cells

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[1] The positive spike-timing signifies that synaptic activation by the pre-synaptic neuron precedes spiking of the post-synaptic neuron. The negative spike-timing signifies neuronal activation in reverse order.

within ECII. The loop connections that mimicked the entorhino-hippocampal loop circuitry were modeled as simple delay lines. The stellate cells spontaneously generated individual subthreshold oscillations in a theta frequency range and received individual random pulse trains (mean interpulse interval = 1 s, standard deviation = 250 ms, Gaussian distribution) to synchronize the subthreshold oscillations. This resulted in an appearance of the theta rhythm. Each stellate cell fired at about 0.7 Hz by the random pulse train. Refer to our previous paper [5] for details of the model.
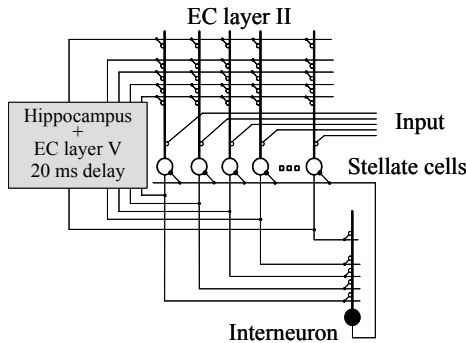

Fig. 1: ECII network model that consists of 30 stellate cells and one inhibitory interneuron. Individual random pulse trains were fed to the stellate cells to synchronize the subthreshold oscillations. Entorhino-hippocampal loop connections are simple delay lines.
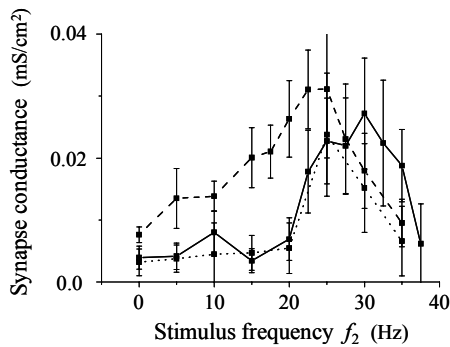

Fig. 2: Synaptic conductance of the loop connection from cell #1 to cell #2 30 s after the onset of stimulation. Stellate cell #1 was stimulated by a regular pulse train (f_1 = 40 Hz). Solid line: Mexican hat STDP rule; dashed line: asymmetric STDP rule; dotted line: Nishiyama STDP rule. Bars indicate standard deviation. Simulation was repeated 10 times using initial conditions randomly chosen.

As the signal transmission delay through the loop circuits was set equal to 20 ms, the 20 ms spike time difference resulted in coincidence of pre- and postsynaptic spike times. The ECII model in Fig. 1 therefore showed that, when one of the stellate cells received a 40 Hz regular pulse train and another cell received a regular

pulse train whose frequencies was less than 40 Hz, loop connections between stellate cells whose spike time difference was about 20 ms were enhanced. After loop connections were selectively enhanced, the stellate cells fired successively within a theta cycle when one of the stellate cells was stimulated by a regular pulse train. This successive firing replicates the theta phase coding.
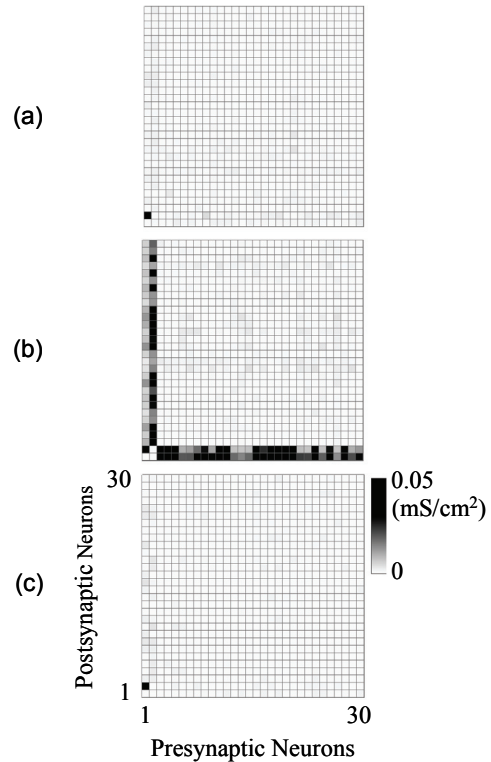

Fig. 3: Connection matrices of loop connections. Black squares represent enhanced connections. Stellate cells, #1 and #2, were stimulated by a pair of regular pulse trains for 280 s: (a) $\{f_1, f_2\}$ = {40, 30}, (b) $\{f_1, f_2\}$ = {40, 22.5}, (c) $\{f_1, f_2\}$ = {40, 25} Hz. Each of 30 stellate cells was stimulated by a random pulse train. Learning rules are Mexican hat (a), temporally asymmetric (b), and Nishiyama (c) STDP rules.

3. Results

Stellate cells, #1 and #2, were simultaneously stimulated by regular pulse trains (f_1 = 40 Hz and f_2 < 40 Hz) for 30 s, respectively. All of the stellate cells were stimulated by individual random pulse trains. The synaptic conductance for the loop connection from cell #1 to cell #2 was most enhanced by stimulation of cell #2 whose frequency was about 25 Hz, regardless of the types of STDP rule (Fig. 2). The dependence of the conductance enhancement on the frequency of stimulation of cell #2 is somewhat broader in the case of the asymmetric STDP rule. Probably, the cause is that the asymmetric STDP rule has no LTD window but a LTP window in the range of the positive spike-timing.

Two stellate cells, #1 and #2, were stimulated again for 280 s by a pair of regular pulse trains that most enhanced the loop connection from cell #1 to cell #2 in order to see changes in the strength of the other loop connections. All of the stellate cells were stimulated by individual random pulse train. The Mexican hat or the Nishiyama STDP rule being used, the loop connection from cell #1 to cell #2 was enhanced and the other loop connections were not (Fig. 3(a) and (c)), whereas, the asymmetric STDP rule being used, some other loop connections were also enhanced in addition to the loop connection from cell #1 to cell #2 (Fig. 3(b)). This indicates that the irrelevant connections may be enhanced due to background noise if an asymmetric STDP rule is used.
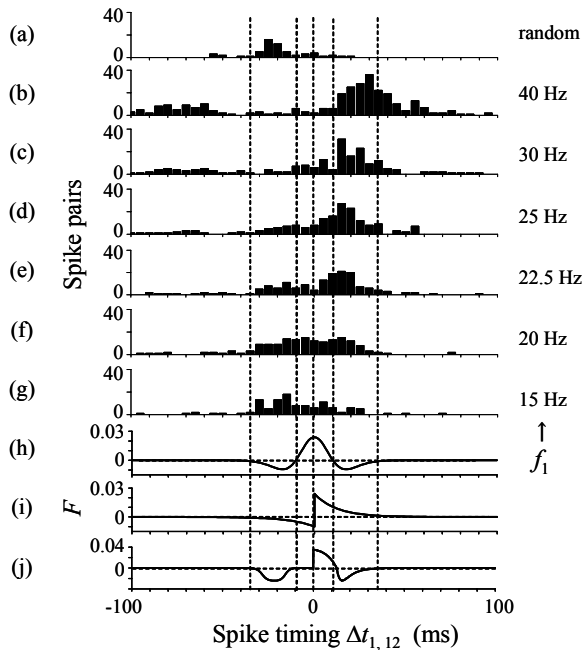

Fig. 4: Histograms of spike-timing $\Delta t_{1,\,12}$. (a) Each of 30 stellate cells was stimulated by a random pulse train and no regular pulse train was fed to the cells. (b-g) Each of 30 stellate cells was stimulated by a random pulse train and the cell #1 alone was simultaneously stimulated by a regular pulse train; the frequency is indicated on the right side of each panel. (h-j) Mexican hat, temporally asymmetric, and Nishiyama STDP rules, respectively.

The spike-timing $\Delta t_{i,\,j}$ is here defined as (spike time of cell #j) - (spike time of cell #i + 20 ms). When the spike time of cell #j is about 20 ms behind the spike time of cell #i, $\Delta t_{i,\,j} \sim 0$, i.e. the spike entering to cell #j from cell #i through the loop connection coincides with the spike of cell #j. Figure 4(a) shows the histogram of the spike timing $\Delta t_{1,\,12}$; each cell was stimulated by a random pulse train and no regular pulse train was fed to the cells. Each stellate cell fired at about 0.7 Hz by the stimulation. Since the distribution of spikes of the cells caused by each random pulse train is localized at a late phase of theta

rhythm, the spike-timing $\Delta t_{1,\,12}$ was distributed around -20 ms, i.e. in the LTD window of the STDP rules. The loop connection from cell #1 to cell #12 was, therefore, not enhanced regardless of three types of STDP rule. In Fig. 4(b)-(g), each cell was stimulated by a random pulse train and the cell #1 alone was simultaneously stimulated by a regular pulse train. The firing rate of cell #1 increased from 2.6 Hz to 4.7 Hz with increase in the instantaneous frequency of regular pulse train from 15 Hz to 40 Hz. When the frequency of regular pulse train was above 20 Hz, the spike-timing was mainly distributed in the range of positive $\Delta t_{1,\,12}$ (Fig. 4(b)-(e)). The connection from cell #1 to cell #12 was, therefore, enhanced through the asymmetric STDP rule, although the connection was not enhanced through the Mexican hat and the Nishiyama STDP rules that have a LTD window in the range of positive spike timing. In other words, irrelevant connections between cells receiving sensory signals and cells receiving background noise may be enhanced through a temporally asymmetric STDP rules.

When the frequency of regular pulse train was below 20 Hz, the major part of the distribution of spike-timing got into the LTP window even in the case of the Mexican hat and the Nishiyama STDP rules (Fig. 4(f)-(g)), resulting in enhancement of irrelevant connections. These irrelevant connections were however depressed with the progress of sequence learning. Four out of 30 stellate cells were simultaneously stimulated by individual regular pulse trains whose instantaneous frequencies were different. Regular pulse trains (40, 25, 15, and 5 Hz) were fed to the cells, #1 - #4, respectively during the first period of 40 s and those pulse trains were in turn fed to the cells, #2 - #5, during the next period of 40 s. After that, the other five groups of four cells, #3 - #6, #4 - #7, #5 - #8, #6 - #9, and #7 - #10, were successively stimulated by the above regular pulse trains every 40 s. All of the stellate cells were always stimulated by individual random pulse trains. When the Mexican hat STDP rule was used, loop connections (cell #1 → cell #2, cell #2 → cell #3, ---, cell #9 → cell #10) were successively enhanced every 40 s as shown in our previous paper. However, the asymmetric STDP rule being used, irrelevant loop connections were enhanced besides the above relevant loop connections and remained to the last. In the case of the Mexican hat and the Nishiyama STDP rules, irrelevant loop connections were enhanced temporarily and then depressed with the progress of learning; therefore, only relevant loop connections remained finally (data not shown).

4. Discussion

If the transmission delay between neurons is less than a few ms, the major part of the distribution of pre-post spike timing of the neurons receiving a random pulse train falls into the LTP window of the STDP rules. In other words, synaptic weights between the neurons are readily influenced by the background noise. For example, recurrent connection weights in the hippocampal CA3

change with time when CA3 neurons fire due to a random pulse train; this results in a bimodal distribution of synaptic conductances [6]. However, if the transmission delay is larger than 10 ms, the major part of the distribution of pre-post spike-timing is in the range of negative spike timing of STDP rules. This implies that the synaptic weights are hardly influenced by the background noise. Feedback loops such as the dentate gyrus-hippocampal CA3 and the hippocampal CA1-ECV/III in addition to the entorhino-hippocampal loops exist, and the transmission delay through those feedback loops is indeed larger than 10 ms [7, 8].

Given that a neural network generates theta rhythm and neurons receive a low-rate background noise, the neurons fire at later phases of the theta rhythm. Therefore, as some neurons receiving a sensory signal whose frequency is relatively high fire at earlier phases of theta rhythm, pre- and postsynaptic spike-timing at loop connection synapses distributes in the range of positive spike-timing of the STDP rules. Those positive spike timings enhance irrelevant connections if the learning rule is an asymmetric STDP rule that has no LTD window in the range of positive spike timing, but depress the irrelevant connections if the learning rule is a STDP rule that has a LTD window in the range of positive spike timing, such as the Mexican hat and Nishiyama STDP rules.

Place cells has important features for learning a sequence of places; the firing rate of place cells increases and the firing phase with respect to theta rhythm advances when the animal approaches the center of the place field [9]. Therefore, it is supposed that the frequency of the sensory signal conveying place information is low when the animal passes the edge of the place field and pre-post spike timing caused by the sensory signal and the background noise is small. This may result in enhancement of irrelevant synaptic connections because of the high probability that the spike timings fall into the LTP window regardless of the type of STDP rule. After that, as the animal approaches the center of the place field, the frequency of the sensory signal probably increases; this results in the larger positive spike timings. At this stage, if the synaptic weights change through the Mexican hat or the Nishiyama STDP rule, enhancement of irrelevant synaptic connections no longer takes place and previously enhanced irrelevant connections are depressed because those rules has a LTD window in the range of positive spike timing. In contrast, if the synaptic weights change through the temporally asymmetric STDP rule, enhancement of irrelevant synaptic connections still takes place and previously enhanced irrelevant connections remain because of no LTD window in the range of positive spike timing.

Background noise exists across the brain and, in general, it is possible that the noise causes enhancement of irrelevant synaptic connections that obscures memory encoding. In fact, the present results show that the asymmetric STDP rule causes enhancement of irrelevant loop connections and fails appropriate sequence learning at the presence of noise. In contrast, a LTD window in the range of positive spike timing of STDP rules, such as the Mexican hat and the Nishiyama STDP rules, works well to suppress enhancement of irrelevant connections between neurons due to spike timing caused by sensory signals and background noise. In other words, those STDP rules are suitable for robust sequence learning amid the background noise.

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