Long-Term Spine Volume Dynamics Corresponds Partially With Multiplicative STDP

Takashi Matsubara† and Hiroyuki Torikai‡

†the Graduate School of Engineering Science, Osaka University,
1–3Machikaneyama-cho, Toyonaka, Osaka 560–8531, Japan
‡Faculty of Computer Science and Engineering, Kyoto Sangyo University,
Kamigamo-Motoyama, Kita-ku, Kyoto, Kyoto 603–8555, Japan
Email: matubara@hopf.sys.es.osaka-u.ac.jp, torikai@cse.kyoto-su.ac.jp

Abstract—The spike-timing dependent plasticity (STDP) is a synaptic weight plasticity rule, and is observed mainly by electrophysiological measurements on the minute time scale. On the other hand, a morphological imaging shows the spine volume plasticity on the day time scale. They have been investigated independently but it is natural that the former can derive the latter since the weights of the synaptic connections correlate highly with the volumes of the spine. This paper shows that the spine volume plasticity corresponds partially with the STDP.

1. Introduction

Neurons are connected via spines and synapses. Connecting the neurons is considered to imply building the memory and disconnecting is considered to imply forgetting. Also, the connection has a amplitude called synaptic weight. The synaptic weight is plastic and is assumed to be mediated by some kind of plasticity rule.

The short-term electrophysiological measurements have found that the synaptic weights represented by the excitatory postsynaptic current (EPSC) injected to the soma change mainly depending on the difference between the spike timing of the pre-synaptic neuron and that of the postsynaptic neuron and also on the current synaptic weight. This plasticity rule is called *spike-timing dependent plasticity* (STDP) rule [1–7]. Many formulations of the STDP have been presented according to the experimental result curves, the biological limitation, and the information theory.

Another plasticity rule is measured by long-term morphological dendritic imaging of the expressed enhanced green fluorescent protein (eGFP) [8, 9]. The imaging can measure the volumes of the spines represented by the fluorescence intensity, and has found that the spine volume change depends on the current spine volume and the neuronal activity. This rule is called *spine volume plasticity* in this paper. Since the synaptic weight is proportional to the volume of the corresponding spine [10–14], it can be said that the synaptic weight changes depending on the current synaptic weight.

The above two plasticity rules should not occur independently but should come from the same phenomenon. This paper shows that the spine volume plasticity corresponds with one of the STDP formulations, called multiplicative STDP [4].

2. Results

Spike-Timing Dependent Plasticity

The synaptic weight is the amplitude of the connection of the two neurons and it is often represented by the excitatory postsynaptic current (EPSC) injected to the soma. The electrophysiological measurements have found that the EPSC changes mainly depending on the difference $\Delta t = t_{\mathrm{pre}} - t_{\mathrm{post}}$ between the spike timing t_{pre} of the presynaptic neuron and that t_{post} of the postsynaptic neuron. This plasticity rule is called *spike-timing dependent plasticity* (STDP) rule [1–7, 15]. For example, a presynaptic action potential which precedes a postsynaptic action potential (i.e., $\Delta t < 0$) depresses the EPSC, and vice versa. The detailed description is as follows;

$$\Delta W(W, \Delta t) = \begin{cases} W_+(W) \exp\left(-\dfrac{|\Delta t|}{\tau_+}\right) & \text{if } \Delta t < 0 \\ -W_-(W) \exp\left(-\dfrac{|\Delta t|}{\tau_-}\right) & \text{if } \Delta t > 0, \end{cases}$$

where W denotes the EPSC, $W_+(W)$ and $W_-(W)$ are the functions which determine the magnitude of the EPSC changes ΔW in the positive and negative directions, and τ_+ and τ_- are their time constant, respectively. As described above, the magnitude of the EPSC changes ΔW is assumed to depend on the current EPSC W, and many types of formulation have been presented. This paper focuses on the multiplicative STDP presented by van Rossum *et al.* [4], which is described as

$$\begin{aligned} W_+(W) &= \quad c_+ + \nu W \sim \mathcal{N}(\ \ c_+,\ (\sigma_n W)^2), \\ W_-(W) &= c_- W + \nu W \sim \mathcal{N}(c_- W,\ (\sigma_n W)^2), \end{aligned}$$

where $\nu \sim \mathcal{N}(0, \sigma_n^2)$ is a noise term. The parameters c_+, c_-, τ_+, and τ_- are determined by the electrophysiological measurements of the pyramidal neurons in the rat hippocampus

subregion CA1 [2, 4] as follows;

$$c_+ = 7\ [\mathrm{pS}], \quad c_- = 0.003,$$
$$\tau_+ = 17\ [\mathrm{msec}], \tau_- = 34\ [\mathrm{msec}],$$
$$\sigma_n = 0.0015.$$

Since the resting potential of a neuron and the reverse potential of an AMPA receptor are assumed to be −60 mV and 0 mV, c_+ is denoted as 0.42 [pA] alternatively.

The expectation value $\mu_{\mathrm{unit}}(W)$ of the EPSC changes ΔW per unit time is

$$\mu_{\mathrm{unit}}(W) = f_{\mathrm{post}} f_{\mathrm{pre}}(c_+\tau_+ - c_- W\tau_-),$$

where f_{pre} Hz (f_{post} Hz) is the probability of the evocation of the presynaptic (postsynaptic) action potential.

Spine Volume Plasticity

Dendritic spines are located on the dendrites of a neuron. They receive neurotransmitters the corresponding synapses release. When the neurotransmitters bind to the receptors on the spine, the corresponding ion channels are activated, and the miniature excitatory postsynaptic current (mEPSC) is injected to the spine. Since a large spine expresses a large number of AMPA glutamate receptors, the volume V of a spine is proportional to the amplitude of the mEPSC [10–14] The volume V of the spine can be measured morphologically by the dendritic imaging of the expressed enhanced green fluorescent protein (eGFP) [8, 9, 14]. The LTP enlarges the spine and vice versa [11, 12, 14, 16, 17]. Thus, measurements of the spine volumes contribute to understand the long-term plasticity of the synapse since this is a measurement of the spines on the day time scale in contrast to the electrophysiological measurements on the minute time scale.

In the case of the the pyramidal neurons in the rat hippocampus subregion CA1, the expectation value $\mu_C(V)$ of the spine volume changes ΔV per day by the spine volume plasticity [8, 9] is

$$\mu_C(V) = -\gamma V + \delta,$$

where the parameter values are

$$\gamma = 0.16\ \delta = 0.01\ [\mu\mathrm{m}^3].$$

Figure 1 shows the expectation value $\mu_C(V)$.

STDP and Spine Volume Plasticity

The presence of D-AP-5, which is an antagonist of the NMDA glutamate receptors, blocks any synaptic potentiation and depression induced by the STDP [2, 15]. This indicates that the STDP requires the activation of the NMDA glutamate receptors. Similarly, in the case of the presence of D-AP-5 [8], the expectation value $\mu_I(V)$ of the spine volume plasticity is zero. Hence, the spine volume plasticity is assumed to be induced mainly by the STDP. The EPSC W is assumed to be converted to the spine volume V as

$$V = WF_{V,W}^{-1},$$

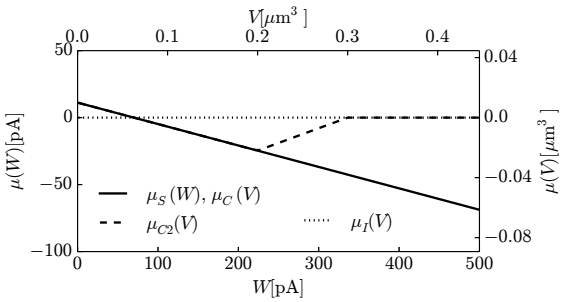

Figure 1: The expectation values μ of the plasticity. That $\mu_S(W)$ of the STDP, that $\mu_C(V)$ of the spine volume plasticity, and that $\mu_{C2}(V)$ of the spine volume plasticity for large spines, and that $\mu_I(V)$ of the intrinsic spine volume plasticity.

where F_{VW} is a coefficient. The probabilities f_{post} and f_{pre} are also undetermined but are assumed to be equal because of symmetry, i.e.,

$$\mu_{\mathrm{unit}}(W) = f_{\mathrm{AP}}^2(c_+\tau_+ - c_- W\tau_-),$$

where $f_{\mathrm{AP}} = f_{\mathrm{post}} = f_{\mathrm{pre}}$ is the probability of the evocation of the neuronal action potential. For simplicity, the expectation value $\mu(W)$ of the EPSC changes per day induced by the STDP is assumed as

$$\mu_S(W) = T_{\mathrm{day}} f_{\mathrm{AP}}^2(c_+\tau_+ - c_- W\tau_-),$$

where T_{day} is a number of unit time per day. The detailed discussion of this simplification is omitted due to the page length limitation. Therefore, the following relations are derived:

$$\gamma = T_{\mathrm{day}} f_{\mathrm{AP}}^2 c_-\tau_-,$$
$$\delta = \frac{\gamma}{F_{V,W}} \frac{c_+\tau_+}{c_-\tau_-},$$

and

$$f_{\mathrm{AP}} \approx 0.134\ [\mathrm{Hz}],$$
$$F_{V,W} = 1120\ [\mathrm{pA}/\mu\mathrm{m}^3].$$

Future works should validate of the values of the parameters $F_{V,W}$ and f_{AP}. At least, $f_{\mathrm{AP}} \approx 0.134$ [Hz] is not an inconceivable value for a rat hippocampus culture without any activations. Note that the relationships F_{V,W_m} of the spine volume V to the mEPSC (the EPSC for the spine) are measured [10–14] and it is around $F_{V,W_m} = 200$ [pA/μm^3], but that $F_{V,W}$ to the EPSC for the soma is unknown. Since the dendrites and the soma have voltage-gated ion channels, the injected current to the soma can be larger than the injected current to the spine. Thus, $F_{V,W} = 1120$ [pA/μm^3] is also not an inconceivable value.

Figure 1 shows $\mu_S(W)$, which is equal to $\mu_C(V)$ when converted with these parameter values.

Variance of Changes

The variance $\sigma_S^2(W)$ of the STDP per day is

$$\sigma_S^2(W) = T_{\mathrm{day}} f_{\mathrm{AP}}^2 \frac{1}{2}(\tau_+ + \tau_-)(\sigma_n W)^2,$$

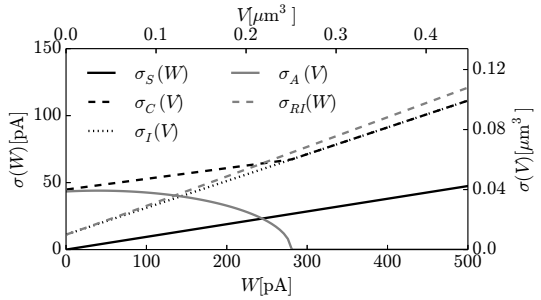

Figure 2: The standard derivation σ (the square-root of the variance $\sqrt{\sigma^2}$) of the plasticity. That $\sigma_S(W)$ of the STDP, that $\sigma_C(V)$ of the spine volume plasticity, that $\sigma_I(V)$ of the intrinsic spine volume plasticity, that $\sigma_A(V)$ of the activity-dependent spine volume plasticity, and that $\sigma_{RI}(V)$ of the combination of the STDP and the intrinsic spine volume plasticity.

where the detailed derivation is omitted due to the page length limitation. That $\sigma_C^2(V)$ of the spine volume plasticity [8, 9] is

$$\sigma_C^2(V) = \begin{cases} (0.08V + 0.04)^2 & \text{if } V \le 0.25, \\ (0.20V + 0.01)^2 & \text{if } V > 0.25. \end{cases}$$

Recall that in the case of the presence of D-AP-5, the STDP is blocked and the expectation value $\mu_I(V)$ of the spine volume plasticity is zero. However, the spine volume V fluctuates is spite of the presence of D-AP-5 [8,9]. This indicates that the synaptic weight is mediated not only by the STDP but also by the intrinsic spine volume plasticity. The variance $\sigma_I^2(V)$ of the intrinsic spine volume plasticity [8, 9] is

$$\sigma_I^2(V) = (0.20V + 0.01)^2.$$

Thus, the difference between $\sigma_C^2(V)$ and $\sigma_I^2(V)$ is the variance $\sigma_A^2(V) = \sigma_C^2(V) - \sigma_I^2(V)$ of the activity-dependent spine volume plasticity.

The intrinsic spine volume plasticity may be ignored in the existing STDP experiments since they induce the LTPs and LTDs repeatedly in a short time to measure the effect of the STDP. Since the activity-dependent spine volume plasticity is assumed to be induced by the STDP, their variances $\sigma_A^2(V)$ and $\sigma_S^2(W)$ are expected to be equal. Also, the variances $\sigma_C^2(V) = \sigma_A^2(V) + \sigma_I^2(V)$ and $\sigma_{RI}^2(W) = \sigma_I^2(V) + \sigma_R^2(W)$ combined with the intrinsic spine volume plasticity are expected to be equal. They are summarized in Figure 2. Unfortunately, the variances $\sigma_A^2(V)$ and $\sigma_S^2(W)$, and the variances $\sigma_C^2(V$ and $\sigma_{RI}^2(W)$ are different.

3. Discussion

Multiplicative and Other Types of STDP

Generally, the multiplicative STDP is the STDP whose expectation value $\mu(W)$ of the synaptic weight change is linear with respect to the current synaptic weight [4, 5]. We can consider other formulations. For example, the expectation value $E[W_+(W)]$ of the changes induced by the LTP is not constant but linear with respect to the current synaptic weight [5]. The other STDPs, such as power-law [6] or log [7], can be accepted. Their expectation value $E[W_+(W)]$ of the changes are nonlinear but are not so much different from the multiplicative STDP.

However, the principal problem is that the standard derivation $\sigma_A(V)$ of the activity-dependent spine volume plasticity shown in Figure 2 decrease with an increase in the spine volume, i.e., the synaptic weight. This phenomenon does not correspond with the electrophysiological measurements [2, 4].

Synaptic Weight Distribution

The synaptic weight has a unimodal distribution with long-tail and its mode is not zero [1, 8, 9, 13, 18–23]. The synaptic weight distribution induced by the plasticity after sufficiently long time can be calculated by Fokker-Planck equation [4–9] as

$$P(W) = \frac{C}{\sigma^2(W)} \exp\left(\int_{-\infty}^{W} \frac{2\mu(W')}{\sigma^2(W')} dW' \right),$$

where $P(W)$ is the probability density function and C is a constant parameter. The synaptic weight distribution which comes only from the STDP is

$$P(W) = \frac{C'}{(\tau_+ + \tau_-)(\sigma_n W)^2} \exp\left(\int_{-\infty}^{W} \frac{4(c_+\tau_+ - c_- W'\tau_-)}{(\tau_+ + \tau_-)(\sigma_n W')^2} dW' \right).$$

The multiplicative STDP shows a unimodal distribution with long-tail [4]. The power-law STDP [6] and the log STDP [7] also do that.

This equation indicates that the synaptic weight distribution is independent of the probability f_{AP} of the evocation of the neuronal action potential, since the ratio between $\mu(W')$ and $\sigma^2(W')$ are independent of the neuronal activity f_{AP}.

In combined with the intrinsic spine volume plasticity whose the variance $\sigma_I^2(V)$ are independent of the neuronal activity f_{AP}, the synaptic weight distribution depends on the neuronal activity f_{AP} as follows:

$$P(W) = \frac{C}{\sigma_S^2(W) + \sigma_I^2(W)} \exp\left(\int_{-\infty}^{W} \frac{2\mu_S(W')}{\sigma_S^2(W') + \sigma_I^2(W')} dW' \right),$$

Roughly speaking, larger neuronal activity f_{AP} decreases the probability of larger synaptic weights, since the large synaptic weights tend to be decreased by the multiplicative STDP and the activity-dependent spine volume plasticity. This is a remarkable result. The STDP or the activity-dependent spine volume plasticity can be said not only to develop the connections but to prune the connections appropriately. Of course, the correlated postsynaptic action potentials can provide another story; the large synaptic weight have more potential to increase since the correlation gives the presynaptic action potential with the large synaptic weight more potential to elicit the presynaptic action potential.

4. Conclusion

This paper has shown that the spine volume plasticity corresponds partially with the multiplicative STDP. Future work includes: (a) validating of the values of the parameters, (b) clarifying the effect of the correlated postsynaptic action potential, and (c) integrating the variances of the STDP and the spine volume plasticity.

The authors would like to thank Professor Toshimitsu Ushio of Osaka University for helpful discussions. This work was partially supported by Grant-in-Aid for JSPS Fellows.

References

[1] B. Barbour *et al.*, "What can we learn from synaptic weight distributions?" *Trends in neurosciences*, vol. 30, no. 12, pp. 622–629, 2007.

[2] G.-Q. Bi and M.-M. Poo, "Synaptic modifications in cultured hippocampal neurons: dependence on spike timing, synaptic strength, and postsynaptic cell type," *The Journal of Neuroscience*, vol. 18, no. 24, pp. 10 464–10 472, 1998.

[3] S. Song, K. D. Miller, and L. F. Abbott, "Competitive Hebbian learning through spike-timing-dependent synaptic plasticity." *Nature neuroscience*, vol. 3, no. 9, pp. 919–926, 2000.

[4] M. C. W. van Rossum, G.-Q. Bi, and G. G. Turrigiano, "Stable Hebbian learning from spike timing-dependent plasticity." *The Journal of Neuroscience*, vol. 20, no. 23, pp. 8812–8821, 2000.

[5] J. Rubin, D. Lee, and H. Sompolinsky, "Equilibrium Properties of Temporally Asymmetric Hebbian Plasticity," *Physical Review Letters*, vol. 86, no. 2, pp. 364–367, 2001.

[6] A. Morrison, A. Aertsen, and M. Diesmann, "Spike-timing-dependent plasticity in balanced random networks." *Neural computation*, vol. 19, no. 6, pp. 1437–1467, 2007.

[7] M. Gilson and T. Fukai, "Stability versus neuronal specialization for STDP: long-tail weight distributions solve the dilemma." *PLOS ONE*, vol. 6, no. 10, p. e25339, 2011.

[8] N. Yasumatsu *et al.*, "Principles of long-term dynamics of dendritic spines." *The Journal of Neuroscience*, vol. 28, no. 50, pp. 13 592–608, 2008.

[9] H. Kasai *et al.*, "Structural dynamics of dendritic spines in memory and cognition." *Trends in neurosciences*, vol. 33, no. 3, pp. 121–9, 2010.

[10] Z. Nusser *et al.*, "Cell type and pathway dependence of synaptic AMPA receptor number and variability in the hippocampus." *Neuron*, vol. 21, no. 3, pp. 545–59, 1998.

[11] M. Matsuzaki *et al.*, "Dendritic spine geometry is critical for AMPA receptor expression in hippocampal CA1 pyramidal neurons." *Nature neuroscience*, vol. 4, no. 11, pp. 1086–1092, 2001.

[12] H. Kasai *et al.*, "Structure-stability-function relationships of dendritic spines." *Trends in neurosciences*, vol. 26, no. 7, pp. 360–8, 2003.

[13] R. Yuste, *Dendritic Spines*. The MIT Press, 2010.

[14] H. Kasai *et al.*, "Learning rules and persistence of dendritic spines." *The European journal of neuroscience*, vol. 32, no. 2, pp. 241–9, 2010.

[15] D. E. Feldman, "Timing-based LTP and LTD at vertical inputs to layer II/III pyramidal cells in rat barrel cortex." *Neuron*, vol. 27, no. 1, pp. 45–56, 2000.

[16] M. Matsuzaki *et al.*, "Structural basis of long-term potentiation in single dendritic spines," *Nature*, vol. 429, no. June, 2004.

[17] C. D. Kopec *et al.*, "Glutamate receptor exocytosis and spine enlargement during chemically induced long-term potentiation." *The Journal of Neuroscience*, vol. 26, no. 7, pp. 2000–9, 2006.

[18] P. J. Sjöström, G. G. Turrigiano, and S. B. Nelson, "Rate, timing, and cooperativity jointly determine cortical synaptic plasticity." *Neuron*, vol. 32, no. 6, pp. 1149–64, 2001.

[19] P. Isope and B. Barbour, "Properties of unitary granule cell–¿Purkinje cell synapses in adult rat cerebellar slices." *The Journal of Neuroscience*, vol. 22, no. 22, pp. 9668–9678, 2002.

[20] C. Holmgren *et al.*, "Pyramidal cell communication within local networks in layer 2/3 of rat neocortex." *The Journal of Physiology*, vol. 551, no. Pt 1, pp. 139–53, 2003.

[21] S. Song *et al.*, "Highly nonrandom features of synaptic connectivity in local cortical circuits." *PLoS Biology*, vol. 3, no. 3, p. e68, 2005.

[22] A. Frick *et al.*, "Monosynaptic connections between pairs of L5A pyramidal neurons in columns of juvenile rat somatosensory cortex." *Cerebral cortex*, vol. 18, no. 2, pp. 397–406, 2008.

[23] S. Rieubland, A. Roth, and M. Häusser, "Structured Connectivity in Cerebellar Inhibitory Networks," *Neuron*, vol. 81, no. 4, pp. 913–929, 2014.