Synaptic plasticity caused by interaction of inputs on hippocampal CA1

Yukihiro Ito (PY)* and Toshiya Iwai**

1 Graduate School of Engineering, Nihon University
2 College of Engineering, Nihon University
E-mail: g2361@cc.ce.nihon-u.ac.jp

Abstract—Synaptic plasticity of some dendritic spine is induced by the pairing stimuli of back propagating action potential (BPAP) and excitatory post-synaptic potential (EPSP). Physiological experiments show that, in addition to these stimuli, generating EPSP on another dendritic spine causes further synaptic plasticity. We examined these synaptic plasticity by numerical simulation.

Keywords—Dendrite, Spike Timing Dependent Plasticity, GABA, Multi-Compartmental Model

1. Introduction

Synaptic plasticity is induced by repetitive stimulation with the relative timing (τ) between the onset of EPSP and the peak of BPAP in physiological experiments [1], known as spike timing dependent plasticity (STDP). Hippocampal CA1 area is suppressed by the GABAergic inhibitory interneurons via feed-forward (FF-GABA) and feed-back (FB-GABA) circuits[2]. Especially, the GABAergic interneurons project predominantly onto the proximal dendrite (PD), while the interneurons project little onto the distal dendrite (DD). Recently, it is found in physiological experiments [3] that synaptic plasticity at the DD is influenced by the relative timing of BPAP and EPSP from synapse at the PD. BPAP is amplified by EPSP at the PD around τ = 5ms, while BPAP is attenuated by EPSP and EPSP at the DD induce synaptic plasticity. To investigate such spatio-temporal interactions among various inputs, BPAP, EPSP and IPSP, in the dendrite is important to understand the meaning of synaptic learning rules at phenomenological level.

In this study, we numerically experimented to examine influences of both GABA A inhibition and the relative timing of BPAP and EPSP from synapse at the PD upon synaptic plasticity at DD, using a multi-compartmental model of a neuron with spines on the PD and DD.

2. Methods

2.1. Model Neuron

We constructed a multi-compartmental model of hippocampal CA1 neuron with two spines (Fig. 1). One is located at the PD, another is at the DD. The model consists of eight compartments, a soma (s), five dendrites (d1-d5), and two spines (rp, rd). The s is suppressed by both FF-GABA and FB-GABA, while the d1 is suppressed by FF-GABA. BPAP is inputted to the compartment s and EPSPs are generated on both compartments rp and rd through AMPA-R and NMDA-R. Time course of membrane potentials of compartments is represented by equations (1)-(8), where Vx, Cx and Rx are membrane potential, membrane capacitance and membrane resistance for each compartment, respectively (x = s, d1, d2, d3, d4, d5, rp, rd). gGABA is a conductance between two compartments y and z. G(t) is a conductance of a ligand-gated receptor L whose time dependence is represented by the alpha function.

![Fig. 1 multi-compartment model](image-url)

2.2. Calcium Ion Dependent Plasticity

Depending on calcium ion concentration in the spine, phosphorylation and dephosphorylation of AMPA-R cause conductance of AMPA-R to increase and decrease, respectively. That is, synaptic plasticity depends on calcium ion concentration in the spine. We considered this calcium dependent plasticity phenomenologically by BCM model [4].

The calcium ion concentrations in spines are described by equation (9), where [Ca], I_{SCC} and I_{MDA} are the equilibrium calcium ion concentration, the calcium ion current via voltage sensitive calcium ion channel and the calcium ion current via NMDA-R, respectively. Figure 2
represents the relation between the calcium ion concentration and the degree of phosphorylation/dephosphorylation of AMPA-R. The functional form of this relation is followed by Kitajima et al. [5].

\[
\frac{d[Ca_+]}{dt} = -k_0 [C_{A_1} - [Ca_{A_1}]) - \frac{1}{2F \cdot Vol} (I_{VSCC} + I_{NMDA}).
\]

2.3. Numerical Simulation

The relative timing of the onset of BPAP and the onset of EPSP at the PD/DD spine is defined by \( \tau_{pd}^{dd} \). When the onset of EPSP is followed by that of BPAP, the timing \( \tau \) is positive. For fixed \( \tau_{pd} \) and \( \tau_{dd} \), BPAP and two EPSPs are applied at 5Hz during repeated 80 times and synaptic plasticity at the DD spine is numerically measured with and without GABA inhibition. For various values of \( \tau_{pd} \) and \( \tau_{dd} \), numerical simulation are performed. Onsets of FF-GABA and FB-GABA are synchronized with that of EPSP at the PD and that of BPAP, respectively. In our study, delays in FF-GABA and FB-GABA are ignored.

3. Result

Figure 3 shows synaptic plasticity at \( \tau_{dd} = 5 \) and 20ms for various values of \( \tau_{pd} \). Upper two figures (Fig. 3(A) and (B)) are obtained from numerical simulation and lower two (Fig. 3(C) and (D)) are obtained from physiological experiments [3] corresponding to our study. Effects of GABA are not considered in Fig. 3(4), (5), (9) and (10), while the effects are considered in otherwise.

The control simulation (EPSP at the PD is absent) for \( \tau_{dd} = 5 \) ms results in LTP as shown in Fig. 3(1). This qualitatively corresponds to the control experiment in Fig. 3(11). Synaptic plasticity for \( \tau_{pd} = 5 \) ms in Fig. 3(2) is smaller that in Fig. 3(1). On the other hand, that in Fig. 3(12) is larger than that in Fig. 3(11). These results are contradictory to each other. However, synaptic plasticity from the simulation without GABA shown in Fig. 3(4) is larger than that in Fig. 3(1). Thus, GABAergic effects is too strong for \( \tau_{pd} = 5 \) ms in our simulation. Delay for GABA inhibition is probably important to reproduce physiological experiment for \( \tau_{pd} = 5 \) ms. Synaptic plasticity in Fig. 3(3) decreases compared with that in Fig. 3(1). This tendency is roughly the same as that seen in Fig. 3(11) and (13). On the other hand, unlike physiological experiment, numerical simulation shows that synaptic plasticity without GABA shown in Fig. 3(5) is larger than that in Fig. 3(1). Thus, GABA inhibition is necessary to reproduce physiological experiment.

The control simulation for \( \tau_{pd} = 20 \) ms results in LTD as in Fig. 3(6), while corresponding control experiment in Fig. 3(14) doesn’t show LTD. We think that the LTD is due to a question in BCM model under discussion, that is, LTD window appears in positive timing \( \tau \) by BCM model. If we focus relative change of synaptic plasticity, we can discuss about Fig. 3(B) and (D) in a similar way in above discussion for Fig. 3(A) and (C).

In conclusion, we confirmed the importance of GABAergic inhibition for synaptic plasticity at the DD of CA1 neuron from numerical simulation. We also confirmed the importance of interaction among BPAP, EPSP and IPSP for synaptic plasticity at the DD, where the interaction means nonlinear superposition of various inputs. For example, effects of BPAP upon the DD increase by EPSP at the PD around \( \tau_{pd} = 5 \) ms, while those decrease by GABA inhibition at the PD around \( \tau_{pd} = 20 \) ms. These interactions influence synaptic plasticity at the DD. The conclusions support physiological experiments [3].

References


