Synaptic modification and entrained phase are phase dependent in STDP

Gang Zhao
Institute of Complex Bio-dynamics, Jiangxi Blue Sky University, Nanchang, Jiangxi, 330098, People's Republic of China

Abstract

Synapse strength can be modified in an activity dependent manner, in which the temporal relationship between pre- and post-synaptic spikes plays a major role. This spike timing dependent plasticity (STDP) has profound implications in neural coding, computation and functionality, and this line of research is booming in recent years. Many functional roles of STDP have been put forward. Because the STDP learning curve is strongly nonlinear, initial state may have great impacts on the eventual state of the system. However, this feature has not been explored before. This paper proposes two possible functional roles of STDP by considering the influence of initial state in modeling studies. First, STDP could lead to phase-dependent synaptic modification that have been reported in experiments[1, 2]. Second, rather than leading to a fixed phase relation between pre- and post-synaptic neurons, STDP that includes suppression between the effects of spike pairs [3] lead to a distributed entrained phase which also depend on the initial relative phase. This simple mechanism is proposed here to have the ability to organize temporal firing pattern into dynamic cell assemblies in a

probabilistic manner and cause cell assemblies to update in a deterministic manner. It has been demonstrated that olfactory system in locust, and even other sensory systems, adopts the strategy of combining probabilistic cell assemblies with their deterministic update to encode information. These results suggest that STDP rule is a potentially powerful mechanism by which higher network functions emerge.

Since the discovery of spike-timing dependent plasticity (STDP) [4-6], in which a synapse is depressed or potentiated according to the time of pre- and post-synaptic spikes, the functional role of STDP has been an intensive field of research. Recent findings, both theoretical and experimental, on fundamental questions include facilitation of dual coding[7, 8], bringing about competition between different synapse[9, 10], converging a neural network to a stable state[11, 12], enhancing synchronization of neuron and neural networks[13-19], shaping the selectivity of neuron or neural circuits [20-24] and mediating sensory experience-dependent circuit refinement in the developing nervous system[25, 26]. Other results have also been reported, such as bridging the gap between time scales of behavioral tasks and neuron firing[27], generating great memory capacity[28], eliminating location dependence of synapses and enabling democratic plasticity[29], reducing variability of neural response[30], leading to reinforcement learning[31, 32], leading to slowness learning required for recognizing objects in variable context[33] and solving the distal reward problem[34].

Here I present two possible consequences of STDP : initial relative phase dependent probabilistic frequency synchronization (entrainment), which could result in phase-dependent LTP/LTD, and initial relative phase dependent entrained phase, which could lead to formation of probabilistic cell assemblies and cause deterministic updates between them.

Neural synchronization is believed to underlie many important functional aspects of neural systems, such as perception, learning, memory and attention [35, 36]. Mechanisms that lead to neural synchronization have been widely discussed in the literature. As demonstrated in [13] and [19], STDP facilitates frequency synchronization (entrainment) to a great extent if potentiation and depression is well balanced. However, since the modification of synapse conductance in STDP is bi-directional and the corresponding learning curve is strongly nonlinear, little difference in initial state may cause great difference in the ultimate fate of the system, e.g. success or failure of entrainment, just as initial value does in a deterministic chaotic system. Moreover, the interactions between the effects of spike pairs [3] further complicate the dynamics of the synapse by introducing suppressions between them, therefore allowing more possibilities for initial state to play.

To consider the effects of initial state in STDP and synchronization is not trivial, since it has been reported experimentally that phase sensitive synaptic modifications is present both in θ (7Hz)[1, 37-40] and β-γ (20-60Hz) [2]oscillation in vitro. And it has also been demonstrated that STDP is involved in olfactory information flow in locusts to ensure precise synchronization [15]. Furthermore, it has been demonstrated earlier that olfactory information in locust is encoded by both transient cell assembly, in which the firing of a specific neuron is probabilistic, and the precise temporal sequence in which cell assemblies are updated [41]. It is natural to conjecture that the update sequence of cell assemblies is determined by the initial state of neurons in consequent cell assemblies. Therefore, it is reasonable and meaningful to ask whether and, if yes, how, initial state of a STDP system would have great impacts on the eventual state of the system.

This paper presents an effort to study the influence of initial state in STDP, by numerically investigating a simple system which consists of an excitatory STDP synapse and two repetitive firing neurons with different autonomous period. Detailed numerical studies strongly support that initial state is a major determinant to the eventual state of the system. Specifically, the probability of successful entrainment is largely determined by the initial relative phase of the system. Moreover, the synaptic conductance evolves to a stable value if successful entrainment is established and, decreases to zero if not. Therefore, this mechanism may be able to account for the phase sensitivity of synaptic modification [1, 2, 37-40], a phenomenon that has been reported experimentally. Furthermore, if STDP with suppression[3] is considered, the stable entrained phase is no longer fixed to a unified value. In stead, the entrained phase is dependent on the initial relative phase and distributed in a wide range. Thus STDP with suppression provides a natural mechanism to organize post-synaptic neurons' temporal firing pattern according to their initial state and allow probabilistic cell assemblies to update in a determinant manner.

Results

The model is numerically integrated via a 4th order Runge-Kutta scheme. The two neurons fire periodically first, then at a predefined time, the synapse is activated. The pre-synaptic neuron keeps its firing period while the post-synaptic one is now driven by the synaptic current, which is regulated by the time difference between pre- and post-synaptic neurons through STDP rule. Two statistics are analyzed, one is inter-spike interval of the post-synaptic neuron (ISI_2), and the other is the relative phase ($\Delta\Phi$) of the pre-synaptic neuron's spike calculated according to spike time of the post-synaptic one (Fig.1, $\delta t/ISI_2$). The phase relation just before synapse activation is termed as initial relative phase. The initial relative phase may be positive or negative, indicating the order of pre- and post-synaptic spike just before synapse activation.

Put Figure 1 here

Synchronization of pre- and post-synaptic neurons occurs when $T_1/ISI_2 = 1$. This criterion has been employed in[14] and [13]. Since the relative phase of the two neurons is also constant if $T_1/ISI_2 = 1$, and phase relations are factors of major interests in this paper, therefore, an alternative criterion of synchronization based on relative phase is used. The spike time of the pre-synaptic neuron is converted into relative phase of spike time of the post-synaptic neuron. Typically, one simulation contains 300 runs, each from random initial conditions. Each run of simulation yields about 95 relative phases ($\Delta\Phi$) among which the last 40 are used to compute coefficient of variation:

$$\frac{\sqrt{\langle \Delta\Phi^2 \rangle - \langle \Delta\Phi \rangle^2}}{\langle \Delta\Phi \rangle}.$$

The coefficient of variation of relative phase (CVRP) indicates not only whether synchronization is achieved, but also precision and robustness of synchronization.

STDP rule modifies the synaptic conductance g(t) according to $\Delta t = t_1 - t_2$, a dynamic factor that in turn is controlled by g(t). The outcome of this interaction between Δt and g(t) may be dependent on the initial value of Δt. Fig. 2 gives an example. The left column shows inter-spike interval and the right column plots corresponding synapse conductance g(t). Fig.2 (a)~(d) correspond to STDP rule in which synaptic update is only based on a pair of nearest spikes (nearest STDP). Fig. 2(a) shows a case where the post-synaptic neuron is successfully entrained by the pre-synaptic one. The corresponding synaptic conductance (Fig. 2(b)) keeps hopping between two stable states, allowing a dynamical and flexible entrainment. Fig. 2(c) shows a case where the period of the post-synaptic neuron returns to its original state, indicating that the STDP synapse between two neurons goes to zero (Fig. 2(d)). Fig. 2 (e)~(h) are results from STDP with suppression[3]. Note that in this case if entrainment is successful, the synaptic conductance achieves one stable value instead of hopping between two states (Fig. 2(f)). If entrainment fails, the synaptic conductance will also achieves a non-zero level (Fig. 2(h)), different from the case shown in Fig. 2(d). All simulations employ the same set of parameters; however, they are started from different initial states.

Put Figure 2 here

With nearest STDP, eventual fates of the synapse have no third choice. It can either take the value according to the synchronization mechanism described in[13], corresponding to entrainment, or decrease to zero (Fig. 3(a)). This is in agreement with simulations in[9], where a bimodal distribution of synapse resulted from nearest STDP rule. However, in the case of STDP with suppression, the synaptic conductance will evolve to a nonzero level, regardless of whether entrainment is successful (Fig.3 (b)).

Put Figure 3 here.

To get a global view of entrainment, I carried out simulations to scan the autonomous period of post-synaptic neuron. The results of scanning T_2, with T_1 fixed at 143ms, are presented in Fig. 4. The left column plots times of synchronization in total 300 runs as a function of T_2. The criterion of synchronization has been set to across 2 orders of magnitude (inset in (c)) to gain more information about synchronization precision. The right column is the corresponding entrained phase, with the criterion of CVRP <= 0.001. Fig. 4(a) and (b) are results from nearest STDP, Fig. 4(c) and (d) are results from STDP with suppression. Note that the initial value of v_1, v_2, g_0 and S are random in each of 300 runs. Therefore it is reasonable to regard the ratio of times of synchronization to 300 (number of total runs) as synchronization probability.

Put Figure 4 here

Probabilistic synchronization exists in a wide range of T_2 both for nearest STDP and STDP with suppression and, the probability of synchronization varies nonlinearly with T_2. One could find local minimum and maximum on curves of Fig. 4 (a) and (c). Except for those T_2 whose probability of synchronization equals 1, there are four phases on the curves in Fig. 4(a) and (c), two monotonous increasing and two monotonous decreasing. Nearest STDP has wider range of entrained post-synaptic period than that of STDP with suppression. However, STDP with suppression lead to more precise entrainment. This is indicated by the overlapping of the three curves, each corresponding to different synchronization criterion, in Fig. 4(c). In contrast, curves in Fig. 4(a) only overlap in the middle part.

Nearest STDP yields phase-locked synchronization (Fig. 4(b)), which has been pointed out in [13] and has been demonstrated in [15] to facilitate olfactory information flow in locust. In contrast, STDP with suppression leads to entrainment with distributed phase relation (Fig. 4(d)). The distributed entrained phase and the probability of synchronization are further studied by investigating the influence of initial relative phase.

The idea of paying special attention to initial relative phase is based on the fact that regular repetitive firing neurons could be described as phase oscillators [42]. In the case of STDP in which synapse conductance is continuously modified, however, the fast intrinsic dynamics of the post-synaptic neuron do not play a major role. The dynamical behavior of the system depend more on the dynamics of the synapse conductance [13]. Therefore, a natural step to explore into probabilistic synchronization and distributed entrained phase (Fig. 4(d)) is to investigate the influence of initial relative phase. I carried out simulations for different T_2, with T_1 fixed at 143ms. One simulation consists of 15000 runs, each are from random v_1, v_2, S and g_0. Some typical results of these simulations are shown in Figure 5 and 6, in which synchronization probability and entrained phase (Fig. 6 red dot) are plotted as functions of initial relative phase. Each of the four subplots in Fig. 5 and 6 corresponds to one T_2 value in the four different phases in Fig. 4(a) and (c) respectively.

Put Figure 5 here

.

Put Figure 6 here

Synchronization probability is a function of both T_2 and initial relative phase. When T_2 is relatively near to T_1, appropriate positive and negative initial relative phase could lead to synchronization (Fig. 5(a) and (b), Fig. 6(a) and (b)). However, as T2 increased, only certain positive initial relative phase could lead to entrainment (Fig.

5(c) and (d), Fig. 6(c) and (d)).

In the case of nearest STDP, entrained phase is strictly fixed, regardless of initial relative phase and T_2. However, if STDP with suppression is considered, the entrained phase varies with respect to both initial relative phase and T_2. The largest lag between entrained phases in Fig.6 is about half of the period of T_1, i.e. 70ms.

Discussion

Timing is important in neural systems[43]. However, how does timing demonstrate its importance? Answers to this question are not complete now. This paper tried to shed some light on this question by considering the influence of initial relative phase in STDP. Numerical results strongly support that the initial relative phase influence the ultimate state of the model severely. The probability of synchronization, entrained phase and the stable synaptic conductance all show dependence on the initial relative phase.

Phase sensitive synaptic modification has been reported in experiments [1, 2, 37-40]. Fig. 3 and Fig. 5 demonstrate that synaptic modification is sensitive to initial relative phase in the case of nearest STDP. If the synapse conductance is at a mediate value before the stimulus incoming, whether LTP or LTD will be induced by the stimulus depends on initial relative phase. However, a decrease of synaptic conductance to zero (Fig. 2(d)) is not biologically plausible. This defection may not occur if other types of synaptic plasticity[44] are included.

The entrained phases are fixed in nearest STDP. This mechanism has been demonstrated both in locust olfactory system[15] and a StdpC experiment[13, 45]. However, results in this paper predicts that, if STDP with suppression[3] is working, entrained phase is no longer fixed. Instead, it is also dependent on the initial relative phase and the autonomous period of the post-synaptic neuron T_2. Here, I propose this result may have implication in the formation of cell assemblies and the dynamical update between them.

Neurons are grouped into transient subpopulations, also known as cell assemblies in which neurons are in strong synchrony, to perform specific tasks. It has been suggested in [46] and proved[47] that the phase relation between two cell assemblies determines the conductance of their mutual influence. In locusts[41],.odor information is represented not only by the active cell assembly, in which any neuron's firing is probabilistic, a situation that brings about some ambiguities if information is represented only by the active cell assembly, but also by the deterministic updated sequence between them.

Supposing a configuration in which synchronous synaptic inputs excite many spontaneous spiking post-synaptic neurons. These post-synaptic neurons may have same or different spontaneous periods. According the results in Fig. 6, the synchronous inputs could entrain the post-synaptic neuron probabilistically according to initial relative phase. Furthermore, those entrained post-synaptic neurons will fire at different phases in a deterministic manner. Thus, post-synaptic neurons are divided into different subpopulations and will fire in a temporal pattern that is determined by their spontaneous period and their initial relative phases. STDP with suppression seems to be an appropriate and a potentially powerful mechanism to support the encoding strategies in locust olfactory system and other sensory systems[41].

However, there are some questions with respect to the above proposal. Odor identification could be finished in a few hundred millisecond in insects and mammals[41]. Can the synchronous inputs entrain post-synaptic neurons with a fast enough speed if the proposed mechanism is working? And, does neural noise destroy these effects? I have observed in simulations that if STDP with suppression is considered, the model behaves more robust in the presence of neural noise and reaches its stable state faster than if nearest STDP is involved (data not shown). The most difficult question, if the proposed mechanism is working, may be how the update sequence of cell assemblies can be stimulus specific and how neurons' firing can be phase locked the oscillation of local field potential. Answers to these questions are not available within the simple model considered in this paper.

In conclusion, this paper investigates the influence of initial state in STDP. Initial relative phase dependent probabilistic synchronization is found to exist in a large parameter range. Phase sensitive synaptic modification is found to occur in nearest STDP. STDP with suppression could lead to distributed entrained phase, which may have implications in the probabilistic formation of cell assemblies and the deterministic update between them.

Methods

The model consists of two Hodgkin-Huxley type neurons coupled by an excitatory

STDP synapse. Each neuron is modeled with the standard formalism:

$$C\frac{dV_i(t)}{dt} = -g_{Na}m(t)^3h(t)(V_i(t)-E_{Na}) - g_Kn(t)^4(V_i(t)-E_K) - g_L(V_i(t)-E_L) - I_{syn}(t) - I_i$$

Here the suffix i=1 and 2, denotes pre- and post-synaptic neuron respectively, V denotes membrane potential. If V reaches a threshold value of -20 mV, the neuron is considered to fire a spike. I_i is a constant input current that drives each neuron to fire periodically. In other words, the autonomous periods of neurons, labeled as T_1 and T_2, are determined by I_i. I_{syn} denotes the synaptic current from the pre-synaptic neuron. Parameters are: $C=30\mu F$, $g_L=1\mu S$, $E_L=-64mV$, $g_{Na}=360\mu S$, $E_{Na}=50mV$, $g_K=70\mu S$, $E_K=-95mV$. The gating variables that govern activation and inactivation of ion channels $y_i(t)=\{m_i(t),h_i(t),n_i(t)\}$ satisfy first order kinetics:

$$\begin{aligned}
&\frac{dy_i(t)}{dt} = \alpha_y[V_i(t)][1-y_i(t)] - \beta_y[V_i(t)]y_i(t)\\
&y = m,h,n;\ \ i = 1,2\\
&\alpha_m = 0.32(-52-V)/(\exp((-52-V)/4)-1) \quad \beta_m = 0.28(25+V)/(\exp((25+V)/5)-1)\\
&\alpha_h = 0.128\exp((-48-V)/18) \qquad\qquad\qquad\quad \beta_h = 4/(\exp((-25-V)/5)+1)\\
&\alpha_n = 0.032(-50-V)/(\exp((-50-V)/5)-1) \quad \beta_n = 0.5\exp((-55-V)40)
\end{aligned}$$

The term I_{syn} in the model denotes the synaptic current from the pre-synaptic neuron. It is modeled as $I_{syn}=g(t)S(t)(V_2(t)-V_{rev})$. Here V_{rev} =20mV is the reversal potential of the post-synaptic neuron, S(t) is an activation variable which obeys

$$\frac{dS(t)}{dt} = \frac{S_\infty(V_1(t)) - S(t)}{t_{syn}(1-S_\infty(V_1(t))}$$

$$S_\infty(V) = \begin{cases} \tanh((V-V_{th})/V_{slope}) & for\ \ V > V_{th} \\ 0 & otherwise \end{cases}$$

Parameters are V_{th}=-20mV, V_{slope}=12mV and t_{syn}=40msec. The initial value of S is taken from a uniformly distributed random number between 0 and 1 to simulate the probabilistic nature of synaptic processes. $g(t)$ is the maximal conductance which undergoes modification continuously. The modification of *g(t)* is carried out through an intermediate variable g_{raw} which is updated in an additive STDP manner:

$$g(t) = \frac{g_{\max}}{2}(\tanh(\frac{g_{raw} - g_{mid}}{g_{slope}}) + 1)$$

$$g_{raw} = g_{raw} + \Delta g_{raw}$$

$$\Delta g_{raw} = \begin{cases} A_{+}\dfrac{\Delta t - \tau_0}{\tau_{+}} e^{\frac{\Delta t - \tau_0}{\tau_{+}}} & if \;\; \Delta t > 0 \\ A_{-}\dfrac{\Delta t - \tau_0}{\tau_{-}} e^{\frac{\Delta t - \tau_0}{\tau_{-}}} & if \;\; \Delta t < 0 \end{cases}$$

Here τ_0 reflects the finite time of information transport through the synapse. Parameters are g_{max}=25nS, g_{min}=g_{slope}= g_{max}/2=12.5nS, τ_0=30msec, τ_+=100msec, τ_-=200msec, A_+=9nS, A_-=6nS. The initial value of the intermediate variable g_{raw0} is set to be g_{max}/2=12.5nS. The initial value of the maximal conductance g is set to a random number distributed equally in the interval of [5, 20] nS.

If interactions between spike pairs[3] are considered, the corresponding update rule of synaptic conductance takes the form

$$\Delta g_{raw} = e_1 e_2 \begin{cases} A_{+}\dfrac{\Delta t - \tau_0}{\tau_{+}} e^{\frac{\Delta t - \tau_0}{\tau_{+}}} & if \;\; \Delta t > 0 \\ A_{-}\dfrac{\Delta t - \tau_0}{\tau_{-}} e^{\frac{\Delta t - \tau_0}{\tau_{-}}} & if \;\; \Delta t < 0 \end{cases}$$

$$e_i = \prod_{k=1}^{n} E_i(t_i^n - t_i^{n-k})$$

$$E_i(x) = 1 - \exp(-x/\tau_i) \quad i = 1, 2$$

Here *n* is the number of the most recent spike of neuron *i*. Parameters are τ_1=100msec and τ_2=200msec.

The same model, with similar set of parameters, has been used in[13] to approximate the Aplysia neuron in a “Spike timing-dependent plasticity Clamp” experiment. One could find more detailed description of this model in[13].

1. Holscher, C., R. Anwyl, and M.J. Rowan, *Stimulation on the Positive Phase of Hippocampal Theta Rhythm Induces Long-Term Potentiation That Can Be Depotentiated by Stimulation on the Negative Phase in Area CA1 In Vivo.* J. Neurosci. 17, 6470-6477 (1997)
2. Wespatat, V., F. Tennigkeit, and W. Singer, *Phase Sensitivity of Synaptic Modifications in Oscillating Cells of Rat Visual Cortex.* J. Neurosci. 24, 9067-9075 (2004)
3. Froemke, R.C. and Y. Dan, *Spike-timing-dependent synaptic modification induced by natural spike trains.* Nature 416, 433-8 (2002)
4. Magee, J.C. and D. Johnston, *A Synaptically Controlled, Associative Signal for Hebbian Plasticity in Hippocampal Neurons.* SCIENCE 275, 209 (1997)
5. Levy, W.B. and O. Steward, *Temporal contiguity requirements for long-term associative potentiation/depression in the hippocampus.* Neuroscience 8, 791-7 (1983)
6. Markram, H., et al., *Regulation of Synaptic Efficacy by Coincidence of Postsynaptic APs and EPSPs.* Science 275, 213-215 (1997)
7. Masuda, N. and K. Aihara, *Dual coding hypotheses for neural information representation.* Mathematical Biosciences 207, 312-321 (2007)
8. Masuda, N. and K. Aihara, *Self-Organizing Dual Coding Based on Spike-Time-Dependent Plasticity.* Neural Computation 16, 627-663 (2004)
9. Song, S., K.D. Miller, and L.F. Abbott, *Competitive Hebbian learning through spike-timing-dependent synaptic plasticity.* Nature Neuroscience 3, 919 (2000)
10. Appleby, P.A. and T. Elliott, *Stable competitive dynamics emerge from multispike interactions in a stochastic model of spike-timing-dependent plasticity.* Neural Comput 18, 2414-64 (2006)
11. Karbowski, J. and G.B. Ermentrout, *Synchrony arising from a balanced synaptic plasticity in a network of heterogeneous neural oscillators.* Physical Review E 65, 31902 (2002)
12. Tsukamoto-Yasui, M., et al., *Active Hippocampal Networks Undergo Spontaneous Synaptic Modification.* Plos One 2, (2007)
13. Nowotny, T., et al., *Enhancement of Synchronization in a Hybrid Neural Circuit by Spike-Timing Dependent Plasticity.* The Journal of Neuroscience 23, 9776 (2003)
14. Zhigulin, V.P., et al., *Robustness and enhancement of neural synchronization by activity-dependent coupling.* PHYSICAL REVIEW E 67, 021901 (2003)
15. Cassenaer, S. and G. Laurent, *Hebbian STDP in mushroom bodies facilitates the synchronous flow of olfactory information in locusts.* Nature 448, 709-13 (2007)
16. Zhigulin, V.P. and M.I. Rabinovich, *An important role of spike timing dependent synaptic plasticity in the formation of synchronized neural ensembles.* Neurocomputing 58, 373-378 (2004)
17. Hosaka, R., O. Araki, and T. Ikeguchi, *STDP provides the substrate for igniting synfire chains by spatiotemporal input patterns.* Neural Comput 20, 415-35 (2008)
18. Talathi, S.S., D.U. Hwang, and W.L. Ditto, *Spike timing dependent plasticity promotes synchrony of inhibitory networks in the presence of heterogeneity.* J Comput Neurosci (2008)
19. Masuda, N. and H. Kori, *Formation of feedforward networks and frequency synchrony by spike-timing-dependent plasticity.* Journal of Computational Neuroscience 22, 327-345 (2007)
20. Guyonneau, R., R. VanRullen, and S.J. Thorpe, *Neurons Tune to the Earliest Spikes Through*

STDP. Neural Computation 17, 859-879 (2005)

21. Masquelier, T. and S.J. Thorpe, *Unsupervised learning of visual features through spike timing dependent plasticity.* PLoS Comput Biol 3, e31 (2007)
22. Zou, Q. and A. Destexhe, *Kinetic models of spike-timing dependent plasticity and their functional consequences in detecting correlations.* Biological Cybernetics 97, 81 (2007)
23. Wenisch, O.G., J. Noll, and J.L. Hemmen, *Spontaneously emerging direction selectivity maps in visual cortex through STDP.* Biol Cybern 93, 239-47 (2005)
24. Yoshida, M. and H. Hayashi, *Emergence of sequence sensitivity in a hippocampal CA3-CA1 model.* Neural Netw 20, 653-67 (2007)
25. Mu, Y. and M.M. Poo, *Spike timing-dependent LTP/LTD mediates visual experience-dependent plasticity in a developing retinotectal system.* Neuron 50, 115-25 (2006)
26. Constantine-Paton, M., *Shining light on spike timing-dependent plasticity.* Neuron 50, 5-7 (2006)
27. Drew, P.J. and L.F. Abbott, *Extending the effects of spike-timing-dependent plasticity to behavioral timescales.* Proc Natl Acad Sci U S A 103, 8876-81 (2006)
28. Izhikevich, E., *Polychronization: Computation with Spikes.* Neural Computation 18, 245 (2006)
29. Rumsey, C.C. and L.F. Abbott, *Synaptic democracy in active dendrites.* J Neurophysiol 96, 2307-18 (2006)
30. Bohte, S.M. and M.C. Mozer, *Reducing the variability of neural responses: a computational theory of spike-timing-dependent plasticity.* Neural Comput 19, 371-403 (2007)
31. Florian, R.V., *Reinforcement learning through modulation of spike-timing-dependent synaptic plasticity.* Neural Comput 19, 1468-502 (2007)
32. Farries, M.A. and A.L. Fairhall, *Reinforcement learning with modulated spike timing dependent synaptic plasticity.* J Neurophysiol 98, 3648-65 (2007)
33. Sprekeler, H., C. Michaelis, and L. Wiskott, *Slowness: an objective for spike-timing-dependent plasticity?* PLoS Comput Biol 3, e112 (2007)
34. Izhikevich, E.M., *Solving the distal reward problem through linkage of STDP and dopamine signaling.* Cereb Cortex 17, 2443-52 (2007)
35. Sauseng, P., et al., *Cross-frequency phase synchronization: a brain mechanism of memory matching and attention.* Neuroimage 40, 308-17 (2008)
36. Bob, P., *Consciousness and co-consciousness, binding problem and schizophrenia.* Neuro Endocrinol Lett 28, 723-6 (2007)
37. Pavlides, C., et al., *Long-term potentiation in the dentate gyrus is induced preferentially on the positive phase of theta-rhythm.* Brain Res 439, 383-7 (1988)
38. Huerta, P.T. and J.E. Lisman, *Heightened synaptic plasticity of hippocampal CA1 neurons during a cholinergically induced rhythmic state.* NATURE 364, 723-725 (1993)
39. Huerta, P.T. and J.E. Lisman, *Bidirectional synaptic plasticity induced by a single burst during cholinergic theta oscillation in CA1 in vitro.* Neuron 15, 1053–1063 (1995)
40. Doyle, C.A., et al., *Low-frequency stimulation induces homosynaptic depotentiation but not long-term depression of synaptic transmission in the adult anaesthetized and awake rat hippocampus in vivo.* Neuroscience 77, 75-85 (1997)
41. Wehr, M. and G. Laurent, *Odour encoding by temporal sequences of firing in oscillating neural assemblies.* NATURE 384, 162-166 (1996)

42. Kopell, N., et al., *Multiple rhythms and switches in the nervous system*. Frontiers of Applied Mathematics, ed. D. Hsieh, M. Zhang, and W. Sun. 2007: World Scientific. 1-17.

43. Larimer, P. and B.W. Strowbridge, *Systems neuroscience: Timing is everything.* NATURE 448, 652-654 (2007)

44. Nelson, L.F.A.a.S.B., *Synaptic plasticity: taming the beast.* nature neuroscience supplement 3, 1178 (2000)

45. Nowotny, T., et al., *StdpC: A modern dynamic clamp.* Journal of Neuroscience Methods 158, 287-299 (2006)

46. Schoffelen, J.M., R. Oostenveld, and P. Fries, *Neuronal Coherence as a Mechanism of Effective Corticospinal Interaction.* SCIENCE 308, 111-113 (2005)

47. Womelsdorf, T., et al., *Modulation of Neuronal Interactions Through Neuronal Synchronization.* Science 316, 1609 (2007)

Figure Legends

Fig. 1. Relative phase, $\Delta\Phi=\delta t/ISI_2$, is illustrated. The relative phase just before the synapse activation is of particular importance and is termed as initial relative phase. The synapse is activated at a pre-defined time (solid arrow or dashed arrow) in simulation. The case represented by the solid arrow denotes a positive initial relative phase, while the dashed arrow indicates a negative initial relative phase. Blue solid line: trajectory of the membrane potential of the pre-synaptic neuron. Red dashed line: that of the post-synaptic neuron.

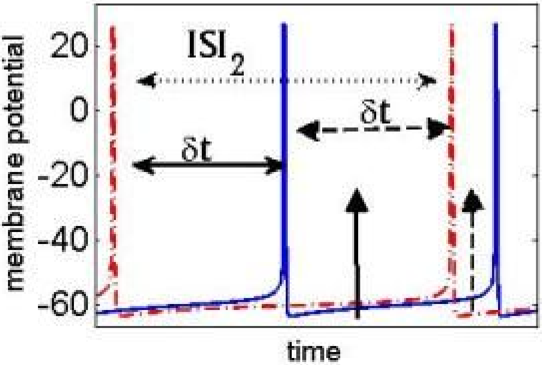
Fig. 2. Examples of initial state dependent synchronization are shown. Parameters are T_1=143ms, T_2=200ms, g(0)=12.5nS. Left column shows ISI_2, right column shows corresponding synaptic conductance. (a)~(d) are results from nearest STDP, (e)~(h) are results from STDP with suppression

Fig. 3. Histograms of stable synaptic conductance drawn from 300 runs are plotted. The last 40 conductance of each run is used in plotting. (a): nearest STDP. Two components located in the interval of (15, 20) nS correspond to hopping synaptic conductance in Fig. 2(b). The component located at zero corresponds to entrainment failure in Fig. 2(d). (b): STDP with suppression. In this case, whether entrained or not is not indicated by the distribution of stable synaptic conductance. Parameters are: T_1=143ms, T_2=206ms.

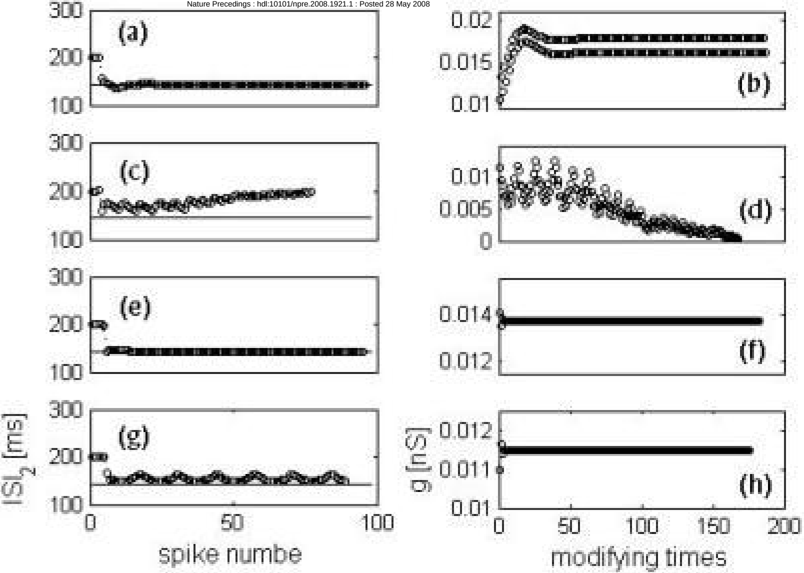
Fig. 4. Synchronization probability and entrained phase are plotted as functions of T_2. T_1 is set to 143ms. (a) and (b): nearest STDP; (c) and (d): STDP with suppression. Inset in (c) indicates the criterion of synchronization used in plotting. T_1 is fixed at 143ms.

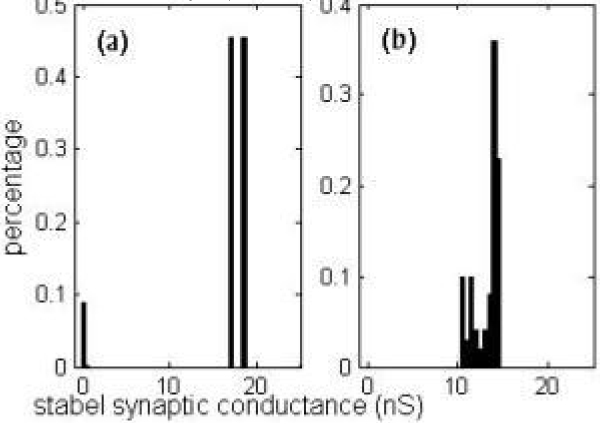
Fig. 5. Probability of synchronization is plotted as a function of initial relative phase in the case of nearest STDP. Parameters are: T_1=143ms, T_2=168ms (a), 222ms (b), 235ms (c), 252ms (d).

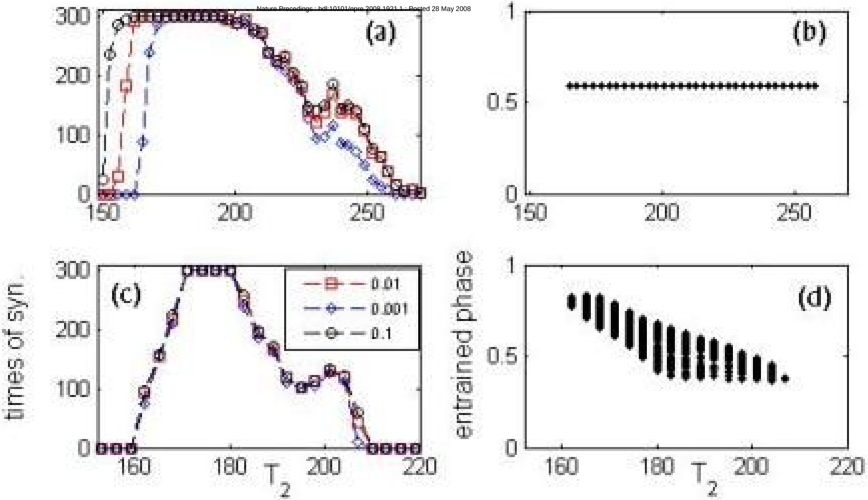
Fig. 6. Both probability of synchronization and entrained phase (red circle) are plotted as functions of initial relative phase in the case of STDP with suppression. Parameters are T_1=143ms, T_2=165ms (a), 188ms (b), 198ms (c), 206ms (d).

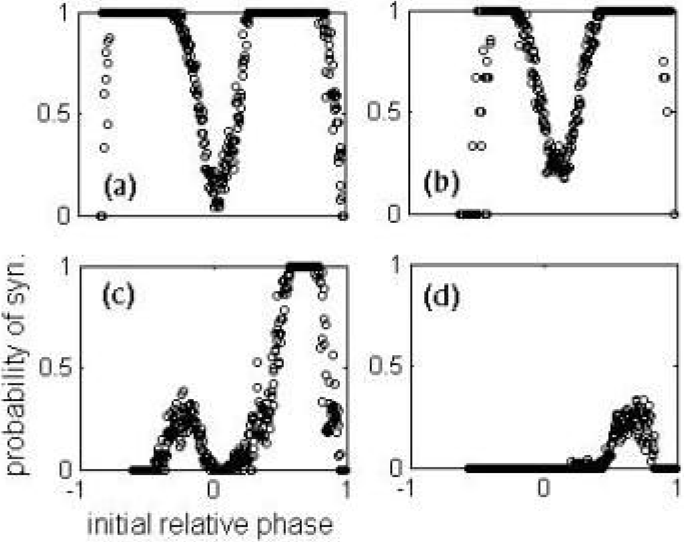


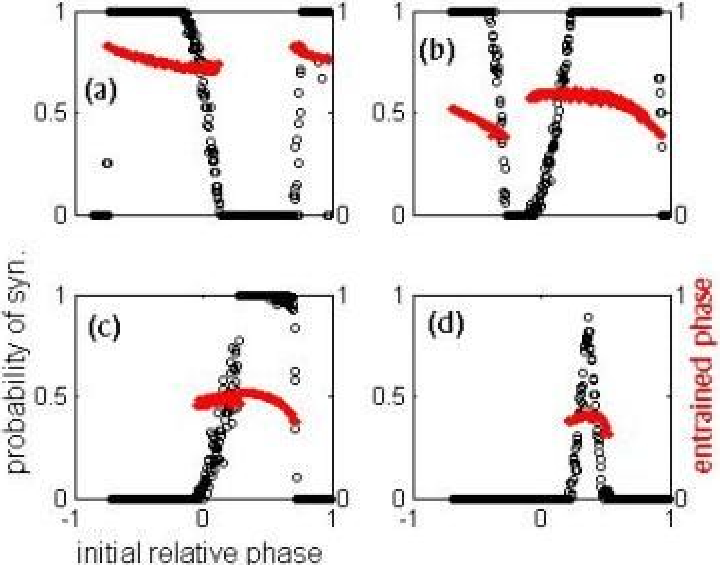
ISI$_2$
δt
δt
membrane potential
20
0
-20
-40
-60
time


(a)
(b)
(c)
(d)
(e)
(f)
(g)
(h)
300
200
100
0.02
0.015
0.01
0.005
0
0.014
0.012
0.011
ISI_2 [ms]
g [nS]
0
50
100
150
200
spike numbe
modifying times


(a)
(b)
percentage
0
0.1
0.2
0.3
0.4
0.5
0
0.1
0.2
0.3
0.4
0
10
20
0
10
20
stabel synaptic conductance (nS)


(a)
(b)
(c)
(d)
times of syn.
entrained phase
T_2
T_2
0.01
0.001
0.1
300
200
100
0
150
200
250
1
0.5
0
160
180
200
220


(a)
(b)
(c)
(d)
probability of syn.
initial relative phase
1
0.5
0
-1
0
1


(a)
(b)
(c)
(d)
probability of syn.
entrained phase
initial relative phase
0
0.5
1
-1
0
1