Spike timing-dependent plasticity induces complexity in the brain

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To study neuroplasticity, the capacity of neurons and neural networks to change temporarily or permanently their connections and behavior, we investigate the effects of spike timing-dependent plasticity (STDP) on synchronization in Hodgkin-Huxley neural networks. We consider spike timing-dependent plasticity of excitatory and inhibitory synapses according to the known Hebbian rules for synaptic plasticity. With regard to network architecture, initially the network presents an all-to-all topology, and due to the STDP the connectivity suffers alteration. With this procedure, we verify that the STDP induces complexity in the brain. In particular, we show that the synchronous behavior has a dependence on the initial conditions in the plastic brain and, in addition, when a perturbation is included, we show that the plastic brain is able to present bistability: synchronous and non synchronous behaviors.

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Neuroplasticity, also known as brain plasticity or brain malleability, is a composition of the words neuron\textsuperscript{[1, 2]} and plasticity and refers to the ability of the brain to reorganize neural pathways in response to new information, environment, development, sensory stimulation, or damage\textsuperscript{[3]}. In 1890, psychologist W. James mentioned, in his book entitled “Principle of Psychology”\textsuperscript{[4]}, the importance of brain reorganization in its development. Psychologist K. S. Lashley performed in 1923 experiments demonstrating changes in neural pathways\textsuperscript{[5]}. The term neuroplasticity was firstly introduced in 1948 by neuroscientist J. Kornoski\textsuperscript{[6]}, where he showed the associative learning as a result of neuroplasticity. In 1949, D. O. Hebb, in his book entitled “The Organization of Behavior”\textsuperscript{[7]}, proposed statements about mechanisms for synaptic plasticity, called Hebb’s rule.

There have been experimental investigations aiming to understanding neuroplasticity. Scientific advances in neuroimaging and in noninvasive brain stimulation have provided insights for neuroplasticity. Consequently, learning-induced structural alterations in gray and white matter have been documented in human brain\textsuperscript{[8]}. Draganski and collaborators\textsuperscript{[9]} used whole-brain magnetic-resonance imaging to observe learning-induced neuroplasticity. They verified structural changes in areas of the brain associated with the processing and storage of complex visual motion. Lu and collaborators\textsuperscript{[10]} demonstrated that neuroplasticity is affected by environmental stimuli. In addition, neuroimaging studies have showed alterations of neuroplasticity in depression, namely depressive disorder may be associated with impairment of neuroplasticity\textsuperscript{[10]}.Popovych and collaborators studied self-organized noise resistance of globally-coupled spiking Hodgkin-Huxley neurons with STDP of excitatory synapses\textsuperscript{[11]}. They showed that external perturbations cannot be an effective method for suppression of synchronized firing neurons in networks with STDP. In this work, we consider not only spike timing-dependent plasticity of excitatory synapses (eSTDP) but also inhibitory synapses (iSTDP) in a Hodgkin-Huxley neural network. We build a network with an architecture that initially presents global connectivity.

Neural spike synchronization is responsible for information transfer\textsuperscript{[19]}, and can be associated with forms of dysfunction. For instance, abnormally synchronized oscillatory activity has been observed in researches about Parkinson’s disease\textsuperscript{[12]}, Alzheimer’s disease\textsuperscript{[13]}, and epilepsy\textsuperscript{[14]}. Our main goal is to show that spike timing-dependent plasticity of excitatory and inhibitory synapses induces complexity in the plastic brain. We show that STDP is relevant to neural synchronous behavior.

In this letter, we address the influence of the perturbing eSTDP and iSTDP on the neuroplasticity dependence on the associated neural activity synchronization induction. We focus on the spike timing-dependent plasticity (STDP) based on Hebbian theory proposed in his already mentioned book\textsuperscript{[7]}. This plasticity mechanism consists of synapses that become stronger or weaker depending on the pre and postsynaptic neurons’ activity. To do that, we have considered an initial network with an all-to-all coupling, with chemical synapses where the connections are unidirectional, and the local dynamics is described by the Hodgkin-Huxley model\textsuperscript{[15, 16]}. The system is given by

\[C\dot{V}_i = I_i - g_K n^4 (V_i - E_K) - g_N a m^3 h (V_i - E_N) - \]
the neurons are excitatorily coupled (the postsynaptic neuron is the excitatory one from the presynaptic neuron) and inhibitory connectivity, them are inhibitorily coupled (the postsynaptic neuron is randomly distributed in the interval \([9, 10, 0.0]\), \(x_{\text{Exc}}\) (excitatory) and \(x_{\text{Inhib}}\) (inhibitory) are the average degree connectivity, \(\varepsilon_{ij}\) and \(\sigma_{ij}\) are the coupling strengths excitatory and inhibitorily from the presynaptic neuron \(j\) to the postsynaptic neuron \(i\). We consider that 80% of the neurons are excitatorily coupled \((N_{\text{Exc}})\) and 20% of them are inhibitorily coupled \((N_{\text{Inhib}})\). We also consider an external perturbation \(\Gamma_{i}\), so that each neuron receives an input with a constant intensity \(\gamma\) during 1ms. This input is applied with an average time interval of about 14ms. This time is approximately the inter-spike interval of a single neuron. Functions \(m(V_i)\) and \(n(V_i)\) represent the activation for sodium and potassium, respectively, and \(h(V_i)\) is the function for the inactivation of sodium. Functions \(\alpha_n, \beta_n, \alpha_m, \beta_m, \alpha_h, \beta_h\) are given by

\[
\alpha_n(V) = \frac{0.01V + 0.55}{1 - \exp(-0.01V - 5.5)},
\]

\[
\beta_n(V) = 0.125 \exp\left(-\frac{V - 65}{80}\right),
\]

\[
\alpha_m(V) = \frac{0.1V + 4}{1 - \exp(-0.1V - 4)},
\]

\[
\beta_m(V) = 4 \exp\left(-\frac{V - 65}{18}\right),
\]

\[
\alpha_h(V) = 0.07 \exp\left(-\frac{V - 65}{20}\right),
\]

\[
\beta_h(V) = \frac{1}{1 + \exp(-0.1V - 3.5)}.
\]

Parameter \(g\) is the conductance and \(E\) the reversal potentials for each ion. Depending on the value of external current density \(I_i\) (measured in \(\mu A/cm^2\)), the neuron can present single spike activity or periodic spikes. In the case of periodic spikes, if the constant \(I_i\) increases, the spike frequency also increases. In this Letter, we consider that the resting potential is equal to \(-65mV\), \(C = 1\) \(\mu F/cm^2\), \(E_{\text{Na}} = 50\) mV, \(E_K = -77\) mV, \(E_L = -54.4\) mV, \(g_{\text{Na}} = 120\) mS/cm\(^2\), \(g_K = 36\) mS/cm\(^2\), \(g_L = 0.3\) mS/cm\(^2\). The neurons are excitatorily coupled with a reversal potential \(V_{r_{\text{Exc}}} = 20\) mV, and inhibitorily coupled with a reversal potential \(V_{r_{\text{Inhib}}} = -75\) mV \cite{18}. The postsynaptic potential \(s_i\) is given by \(\frac{ds_i}{dt} = \frac{5(1 - s_i)}{1 + \exp\left(-\frac{V - \varepsilon_{ij}}{8}\right)} - s_i\).

One of the key principles of behavioral neuroscience is that experience can modify the brain structure, what is known as neuroplasticity \cite{22}. Although the idea that experience may modify the brain structure can probably be traced back to the 1890s \cite{23,24}, it was Hebb who made this a central feature in his neuropsychological theory \cite{25}. With this in mind, we consider excitatory and inhibitory spike timing-dependent plasticity according to the Hebbian rule. The coupling strengths \(\varepsilon_{ij}\) and \(\sigma_{ij}\) are adjusted based on the relative timing between the spikes of presynaptic and postsynaptic neurons \cite{26,27}.

\[
\Delta \varepsilon_{ij} = \begin{cases} 
A_1 \exp(-\Delta t_{ij}/\tau_1), & \Delta t_{ij} \geq 0 \\
-A_2 \exp(\Delta t_{ij}/\tau_2), & \Delta t_{ij} < 0
\end{cases},
\]

(12)

where \(\Delta t_{ij} = t_i - t_j = t_{\text{pos}} - t_{\text{pre}}, t_{\text{pre}}\) is the spike time of the presynaptic and \(t_{\text{pos}}\) the spike time of the postsynaptic neuron. Figure 1(a) exhibits the result obtained from Eq. (12) for \(A_1 = 1.0, A_2 = 0.5, \tau_1 = 1.8\) ms, and \(\tau_2 = 6.0\) ms. The initial synaptic weights \(\varepsilon_{ij}\) are normally distributed with mean and standard deviation equal to \(\varepsilon_M = 0.25\) and \(0.02\), respectively \((0 \leq \varepsilon_{ij} \leq 2\varepsilon_M)\). Then, they are updated according to Eq. (12), where \(\varepsilon_{ij} \rightarrow \varepsilon_{ij} + 10^{-3}\Delta \varepsilon_{ij}\).

For the inhibitory iSTDP synapses, the coupling strength \(\sigma_{ij}\) is adjusted based on the equation

\[
\Delta \sigma_{ij} = \frac{g_0}{g_{\text{norm}}\alpha^\beta} |\Delta t_{ij}| g_{\text{norm}}^{\beta-1} \exp(-\alpha |\Delta t_{ij}|),
\]

(13)

where \(g_0\) is the scaling factor accounting for the amount of change in inhibitory conductance induced by the synaptic plasticity rule, and \(g_{\text{norm}} = \beta^\beta \exp(-\beta)\) is the normalizing constant. Figure 1(b) exhibits the result obtained from Eq. (13) for \(g_0 = 0.02, \beta = 10.0, \alpha = 0.94\) if \(\Delta t_{ij} > 0\), and for \(\alpha = 1.1\) if \(\Delta t_{ij} < 0\) \cite{28}. The
initial inhibitory synaptic weights $\sigma_{ij}$ are normally distributed with mean and standard deviation equal to $\sigma_M$ and 0.02, respectively ($0 \leq \sigma_{ij} \leq 2\sigma_M$). Then, the coupling strengths are updated according to Eq. (13), where $\Delta \sigma_{ij} = \sigma_{ij} + 10^{-3}\Delta \sigma_{ij}$.

To study the effect of plasticity on the neural network, we have calculated the coupling strengths, and used the time-average order-parameter as a probe of spikes synchronization, that is given by

$$R = \frac{1}{t_{\text{final}} - t_{\text{initial}}} \sum_{t_{\text{initial}}}^{t_{\text{final}}} \left| \frac{1}{N} \sum_{j=1}^{N} \exp(i\psi_j) \right|,$$

(14)

where $t_{\text{final}} - t_{\text{initial}}$ is the time window for measuring,

$$\psi_j(t) = 2\pi m + 2\pi \frac{t - t_{j,m}}{t_{j,m+1} - t_{j,m}},$$

(15)

where $t_{j,m}$ represents the time when a spike $m$ ($m = 0, 1, 2, \ldots$) of a neuron $j$ happens ($t_{j,m} < t < t_{j,m+1}$), with the beginning of each spike being when $V_{j} > 0$.

In synchronous behavior, the order-parameter magnitude approaches unity. In addition, if the spike times are uncorrelated, the order-parameter magnitude is typically small and vanishes for $N \to \infty$. When identical neurons are coupled, the neural network may exhibit complete synchronization among spiking neurons, in other words, all neurons may present identical time evolution of their action potentials. In this Letter, we are not considering identical neurons, and as result it is not possible to observe complete synchronization. Nevertheless, an almost-complete synchronization may be observed.

**FIG. 2.** (Color online) (a) Mean order-parameter $\bar{R}$ versus $\sigma_M$ for $\gamma = 0.0$ and $\varepsilon_M = 0.25$, a result without STDP (black circles) and the other one with STDP (red triangles). The bar is the standard deviation for 30 different initial conditions. In the inset we consider $\sigma_M = 0.675$. Figures (b) and (c) exhibit the time evolution of the average time-difference for excitatory and inhibitory connections, respectively, where $\sigma_M$ is equal to 0.675. The black and red lines correspond to $\bar{R} \approx 0.1$ and $\bar{R} \approx 1$, respectively. The green dash represents the separation between potentiation and depression.

**FIG. 3.** (Color online) Coupling matrix for $\gamma = 0.0$, $\varepsilon_M = 0.25$, and $\sigma_M = 0.675$, where we choose the cases for (a) $\bar{R} \approx 0.1$ showing many uncoupled neurons, and (b) $\bar{R} \approx 1$ exhibiting many directed couplings, according to the inset in Fig. 2(a).

Figure 2(a) shows the mean order-parameter ($\bar{R}$), that is calculated for different initial conditions, as a function of the inhibitory coupling strength $\sigma_M$ for a neural network with excitatory and inhibitory synapses, where we consider one case without STDP (black circles) and another with STDP (red triangles). For $\varepsilon_M$ equal to 0.25 and varying $\sigma_M$, we do not observe a significant alteration of the $\bar{R}$ value without STDP, due to the fact that initially the network has an all-to-all topology. Nevertheless, considering STDP we verify that the $\bar{R}$ values decrease with the increase of $\sigma_M$ and present a large standard deviation. This standard deviation occurs due
to the existence of different synchronization states. In the inset (Fig. 2(a)), we consider \( \sigma_M = 0.675 \) and calculate the order-parameter for different initial conditions. As a result, we can see a distribution presenting different synchronization states, including desynchronization and synchronization. In Figs. 2(b) and 2(c) we consider \( \sigma_M = 0.675 \) according to the inset, and calculate the time evolution of the average time-difference for excitatory and inhibitory connections, respectively. The black line shows the case in which the network goes to a desynchronized state \( \bar{R} \approx 0.1 \), whereas the red line exhibits the case of a network that presents synchronous behavior \( \bar{R} \approx 1 \).

In Fig. 2 the synaptic weights \( \varepsilon_{ij} \) and \( \sigma_{ij} \) are encoded in color for \( \gamma = 0.0, \varepsilon_M = 0.25, \) and \( \sigma_M = 0.675 \), where we choose the cases for (a) \( \bar{R} \approx 0.1 \) and (b) \( \bar{R} \approx 1 \) according to the inset in Fig. 2(a). The synaptic weights are suppressed in the desynchronized regime (Fig. 2(a)), and consequently the coupling matrix presents a small number of connectivities. This behavior can be verified by means of the black lines in Figs. 2(b) and 2(c). In addition, the synaptic weights are potentiated (red lines in Figs. 2(b) and 2(c)) in the synchronized regime (Fig. 2(b)), and the coupling matrix exhibits a triangular shape. We have verified that, in this case, the synchronous behavior has a dependence on the direction of synapses.

Considering an external perturbation, we also study the cases without and with plasticity. In the case without STDP, we verify that the mean order-parameter has a small decay when the inhibitory coupling strength increases, as shown in Fig. 4(a) with black circles. The red triangles represent the case with STDP, and unlike the case without perturbation (Fig. 4(a)), there is an abrupt transition (blue triangles). Based on the results in the inset (Fig. 4(a)), we verify that this transition is due to a bistability, in other words, the network can be in either one of the states: (i) high \( \bar{R} \) with potentiation of the average-time difference for excitatory and inhibitory connections (red lines in Figs. 4(a) and 4(b)), or (ii) low \( \bar{R} \) with excitatory average time-difference in the depression region and inhibitory in the potentiation region (black lines).

**FIG. 4.** (Color online) (a) Mean order-parameter versus \( \sigma_M \) for \( \gamma = 10.0 \mu A/cm^2, \varepsilon_M = 0.25 \), a result without STDP (black circles) and another one with STDP (red triangles). Inset plot for \( \sigma_M = 0.575 \) (blue triangles). Figures (b) and (c) exhibit the time evolution of the average time-difference for excitatory and inhibitory connections, respectively, where \( \sigma_M \) is equal to 0.575. The black and red lines correspond to \( \bar{R} \approx 0.1 \) and \( \bar{R} \approx 0.8 \), respectively. The green dash represents the separation between potentiation and depression.

**FIG. 5.** (Color online) Coupling matrix for \( \gamma = 10.0 \mu A/cm^2, \varepsilon_M = 0.25 \). (a) \( \sigma_M = 0.55 \) (\( \bar{R} \approx 1 \)) showing a large quantity of coupled neurons, and (b) \( \sigma_M = 0.6 \) (\( \bar{R} \approx 0.1 \)) exhibiting connections from inhibitory to excitatory neurons.

Figure 5 illustrates the coupling matrix for the two states of the first-order transition. First-order transition
is a term that comes from Thermodynamics and here represents a discontinuity in the first derivative of the mean order-parameter with respect to the inhibitory coupling strength. In Fig. 5(a), we can see the coupling configuration that corresponds to high $\bar{R}$. The network presents high connectivity, and for this reason it is possible to observe the synchronous behavior. For the case of low $\bar{R}$, we verify that the coupling matrix has only connections from inhibitory to excitatory neurons, as shown in Fig. 5(b).

In conclusion, we have studied the effects of spike timing-dependent plasticity on the synchronous behavior in a neural network of Hodgkin-Huxley neurons. Without perturbations, we verify that the mean order-parameter not only decreases when the inhibitory coupling strength increases, but also depends on the initial conditions. With the inclusion of an external perturbation and without STDP, the mean order-parameter has a small decay. However, with STDP, the neural network presents a first-order transition, as well as a bistability. Therefore, STDP produces complexity in a neural network.

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