Modeling on Heterosynaptic Plasticity Based on Postsynaptic Membrane Potential and Current Density

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Abstract. It is still elusive whether different regions in pyramidal neurons have the same heterosynaptic plasticity. To explain the heterosynaptic plasticity, we created a model of synaptic plasticity in which synaptic changes depend on the postsynaptic membrane potential and current density. We found that, in a simulated L5 pyramidal neuron, LTP (long-term potentiation) of synapses in each region of the neuron leads to LTD (long-term depression) of synapses in other regions, which is consistent with the experimental results of heterosynaptic plasticity. However, the effects of heterosynaptic plasticity in different regions are different. Compared with the basal and apical regions, LTP of synapses in the tuft region can not induce significant LTD in other regions. Our research provides a new way to solve the runaway growth of synaptic weights in a neural network.

Keywords: Heterosynaptic plasticity; homeostatic plasticity; runaway of weights.

1. Introduction
Hebbian learning rules often lead to unlimited growth of synaptic weights. To avoid this kind of weight out of control, we need to consider some restrictive mechanisms. One of the simplest ideas is to set the maximum and minimum hard boundary for synaptic weights. However, studies have shown that only depending on the setting of hard boundaries leads to the final clustering of synaptic weights to the maximum or minimum value, which greatly increases the energy consumption of neural networks and causes synapses to lose the necessary competitiveness for learning and memory[1,2]. The traditional method to solve this problem in a neural network model is to normalize the synaptic weights[3–7]. To overcome the runaway of synaptic weights caused by the Hebbian rule, the time scale of synaptic normalization must be similar to that of Hebbian plasticity. The known mechanism of synaptic normalization[5] may not be used to solve the problem of synaptic weight out of control because it needs a long time to adjust the weights. Recent studies have shown that heterosynaptic plasticity provides a feasible solution to the instability of Hebbian learning[9–12]. "Heterosynaptic" plasticity represents the change of synaptic weights in an unstimulated input pathway, while the corresponding is homosynaptic plasticity, which describes the change of synaptic weight in a stimulated input pathway. Long-term potentiation (LTP) of synapses in a stimulated pathway is usually accompanied by long-term depression (LTD) in surrounding unstimulated pathways. This indicates that heterosynaptic plasticity has typical homeostatic characteristics[13]. Experiments showed that in the CA1 (Cornu Ammon 1) region of the hippocampus, LTP at the Schaffer collateral input induced heterosynaptic LTD commissural inputs to basal dendrites[9]. However, it is still elusive whether different regions of pyramidal neurons have the same heterosynaptic plasticity.
The timing or frequency of presynaptic spikes is required for traditional models of homosynaptic plasticity\textsuperscript{[14–16]}. Synaptic weight without presynaptic spikes does not change, so these models cannot be directly used to express heterosynaptic plasticity. Since metabolic energy can be expressed by postsynaptic membrane potential and current density, we consider establishing a synaptic plasticity model using postsynaptic membrane potential and current density. In this way, this model without presynaptic variables can be used to study both homosynaptic and heterosynaptic plasticity.

In this paper, a synaptic plasticity model based on postsynaptic membrane potential and membrane current density was established. The model is a unified one of homo- and heterosynaptic plasticity because no information on the presynaptic spike is required. Using this model, the heterosynaptic plasticity in different regions of L5 pyramidal neurons was studied for the first time. The results provide a new way to solve the problem of weight out of control in Hebbian learning. The first section of this paper introduces the research background, the second section describes the synaptic plasticity model and its parameter settings, the third section gives the simulation results, and the last section discusses the conclusion of this paper.

2. Model and Parameters for Synaptic Plasticity

Maintaining a constant transmembrane ion gradient is essential for neurons to function normally and even survive. Neurons have potential energy similar to batteries due to the existence of a transmembrane ion gradient. We call the potential energy of neurons in the resting state the resting energy state. Activities, such as action potential, input integration, and synaptic transmission, will change the potential energy of the neuron, leading to a new energy state, which is referred to as the firing energy state. To maintain normal information processing ability, neurons can restore the firing energy state to the resting energy state through active transport by expending metabolic energy. We assumed that synaptic plasticity might function similarly to, or be a manifestation of, active transport and be closely related to changes in the energy state of neurons. To restore the resting energy state, when the firing energy state is larger than the resting energy state, the synaptic strength weakens, thus presenting as LTD. When the firing energy state is less than the resting energy state, the synaptic strength is enhanced, thus presenting as LTP. When the firing energy state is close to the resting energy state, the synaptic weight remains unchanged. The idea can be described by the following equation

\[ \Delta W_{ij} = A(E_{ij}^r - E_{ij}) \]

where \( W_{ij} \) is the weight of synapse \( j \), \( A \) is a scaling factor, \( E_{ij}^r \) and \( E_{ij} \) are the resting and firing energy states at the unit membrane of post-synapse \( j \), respectively. \( E_{ij}^r \) and \( E_{ij} \) are all dimensionless variables. \( E_{ij} \) represents the accumulated energy required when the membrane voltage is below the firing threshold voltage, while \( E_{ij}^r \) represents the accumulated energy when the membrane voltage is above the firing threshold voltage, so the two energy states cannot be changed at the same time. When the membrane voltage is lower than the firing threshold voltage, \( E_{ij} \) remains unchanged. Similarly, when the membrane voltage is above the firing threshold voltage, \( E_{ij}^r \) remains unchanged. The differential expression of equation 1 is

\[ \frac{dW_{ij}}{dt} = A \left( \frac{dE_{ij}^r}{dt} - \frac{dE_{ij}}{dt} \right) \]

When the membrane voltage is lower than the firing threshold voltage, \( \frac{dE_{ij}}{dt} = 0 \) because \( E_{ij} \) remains unchanged. Similarly, when the membrane voltage is above the firing threshold voltage, \( \frac{dE_{ij}^r}{dt} = 0 \) because \( E_{ij}^r \) remains unchanged. We defined a driving voltage \( f_j(v_m) \) to replace \( v_m \).

\[ f_j(v_m) = \text{sign}(v_m) |v_m - \theta| \]

where variable \( v_m \) is the postsynaptic voltage, \( \theta \) is a parameter called the resting threshold voltage, \( v_m \) and \( \theta \) are dimensionless with mV.
To make our model homeostatic, we constructed the following driving current

\[ g_j(I_m) = \begin{cases} 
I_m, & |I_m| < I_{max} \\
I_{max} \text{sign}(I_m) \exp[D(|I_{max}| - |I_m|)], & |I_m| \geq I_{max} 
\end{cases} \]  

(4)

where \( I_m \) is the current density at the postsynaptic membrane, \( I_{max} \) represents the maximum current density of the postsynaptic membrane, \( I_m \) and \( I_{max} \) are dimensionless with \( \text{pA}/\mu\text{m}^2 \). Parameter \( D \) denotes damping factor with \( 0 \leq D \leq 1 \). If \( |I_m| < I_{max} \), then the driving current \( g_j(I_m) \) is equal to \( I_m \); if \( |I_m| \geq I_{max} \), then the amplitude of \( g_j(I_m) \) decreases exponentially. Equation 2 representing the change in synaptic strength over time with the driving voltage and driving current described above is as follows

\[
\frac{dw_j}{dt} = A[\Theta(\theta - v_m)f_j(v_m)g_j(I_m) - \Theta(v_m - \theta)f_j(v_m)g_j(I_m)]
\]

(5)

combined with the hard bounds \( 0.0002 \leq W_j/W_{int} \leq 4 \). Here \( W_{int} \) is the initial weight. \( \Theta(x) \) represents \( \Theta(x) = 1 \) if \( x \geq 0 \) and \( \Theta(x) = 0 \) if \( x < 0 \). \( \theta \) is called the firing threshold voltage, which is a dimensionless parameter with the unit of \( \text{mV} \). \( \Theta(\theta - v_m)f_j(v_m)g_j(I_m) \) is the time derivative term of the resting energy state, namely \( \frac{dE_j}{dt} \); in equation 2. \( \Theta(v_m - \theta)f_j(v_m)g_j(I_m) \) denotes the derivative of the firing energy state, that is \( \frac{dE_{fj}}{dt} \).

In addition to the two variables of postsynaptic membrane voltage and postsynaptic membrane current density, our model includes five parameters: resting threshold voltage \( \theta \), maximum membrane current density \( I_{max} \), and damping factor \( D \), scaling factor \( A \) and firing threshold voltage \( \theta \). In the choice of model parameters, our goal is to make a set of parameters suitable for as many stimulation protocols as possible. The five model parameters are all determined by trial and error methods. The first is to estimate the range of parameters according to their physical meaning, such as \( \theta \) should be below \(-60\) \text{mV}, \( \theta \) should be between \(-60\) and \(-50\) \text{mV}, and so on. Then fine-tuning is done manually to make the simulation results match the experimental results as well as possible. Therefore, we simulated different parameters and determined four general model parameters by comparing the simulation results with the experimental data, that is, \( A = 0.0625 \), \( \theta = -68.5 \text{mV} \), \( \theta = -55 \text{mV} \), \( D = 0.05 \), and \( I_{max} = 3 \text{pA}/\mu\text{m}^2 \).

3. Simulations for Heterosynaptic Plasticity

In this paper, we implemented all simulations with the Brian2 neuron simulator\(^{[17]} \) and Python. The detailed biophysical model for L5 pyramidal neurons developed by Bono and Clopath\(^{[18]} \) based on the Brian2 was adopted for dendritic neurons and synapses. The L5 pyramidal neuron model consists of a spherical cell body, an axon, and several dendrite branches, with a total of 1181 compartments. The leakage potential \( E_L \) of each compartment is \(-60\) \text{mV}, and the resting potential is \(-69\) \text{mV}. Through the neuron and synaptic model of Bono and Clopath\(^{[18]} \), the \( v_m \) and \( I_m \) (in millivolts and ampere per meter squared, respectively) of each compartment can be obtained under any stimulation protocol. In the Brian2, the geometric size of neurons is usually expressed in micrometer, so the unit of \( I_m \) is pico-ampere per micrometer squared, which is equivalent to ampere per meter squared.

Our synaptic plasticity model can be described by pseudo-code in Python as follows:

\[
A = 0.0625 \\
\text{thetal} = -68.5 \\
\text{thetah} = -55 \\
D = 0.05 \\
I_{max} = 3 \\
\text{dwdt} = -A*\text{sign}(vm-\text{thetal}) \\
\quad * \text{abs}(vm-\text{thetal})*\text{sign}(vm) \\
\quad * \left( (\text{abs}(Im)<I_{max})*Im + (\text{abs}(Im)>=I_{max})*\text{sign}(Im)*I_{max}*\exp(D*(I_{max}-\text{abs}(Im))) \right) / \text{second} : 1
\]

3.1. Stimulation Protocol

The dendrite branches of L5 pyramidal neurons include basal, apical, and tuft regions (figure 1a). The
compartments shown in figure 1a are connected with 5 synapses each, all with an initial weight of 0.5. The 5 synapses are activated using a Poisson process with the same average rate of 40 Hz, lasting 50 milliseconds (ms). To facilitate data observation, the simulation time is set to 200 ms. In each simulation, only all synapses connected to one region are activated, and the average weights of synapses in each region are observed over time.

3.2. Computational Results
When the synapses in the basal region are activated and the synapses in other regions are not activated (figure 1b), the average synaptic weights in the basal region increase, while those in the other regions decrease. At this time, the average weight in the apical region closer to the basal region weakens greatly, while that of the tuft region far away from the basal region weakens slightly. When the synapses in the apical region are activated while those in the other regions are not activated (figure 1c), the average synaptic weights in the apical region increase, while those in the other regions decrease. At this time, although the basal and tuft regions are all close to the apical region, the decrease of synaptic weights in the basal region is more obvious. When the synapses in the apical cluster are activated and the synapses in other regions are not activated (figure 1d), the average synaptic weights in the apical cluster increase while those in other regions decreased. However, different from the activation in basal or apical regions, the decrease of synaptic weights in the inactive basal and apical regions is very small. The computational results above show that consistent with the experiments of heterosynaptic plasticity\textsuperscript{[1,9]}, LTP of synapses in one region of pyramidal neurons leads to LTD of synapses in other regions. However, the effect of LTD induced by LTP is different in different regions. The results show that the effect is obvious in the regions near the cell body (basal and apical), but weak in the region far away from the cell body (tuft).

![Figure 1](https://example.com/image1.png)

**Figure 1.** Simulations for heterosynaptic plasticity. (a) L5 pyramidal neurons and their different dendritic regions. (b) The average weights in each region during synaptic activation in the basal region. (c) The average weights in each region during synaptic activation in the apical region. (b) The average weights in each region during synaptic activation in the tuft region.

4. Conclusion
Based on the synaptic plasticity model of postsynaptic membrane potential and membrane current density, the heterosynaptic plasticity in L5 pyramidal neurons was calculated. The results show that
LTP of synapses in each region leads to LTD of synapses in other regions, which is consistent with the experimental results of heterosynaptic plasticity. On this basis, we found that the effects of heterosynaptic plasticity in different regions are different. Compared with the basal and apical regions, LTP of synapses in the tuft region can not induce significant LTD in other regions.

Our research provides a new way to solve the problem of weight out of control in Hebbian learning. Based on our model, with the increased weight of some activated synapses, the weights of the inactive synapses around them decrease. After a period of neural activity, all weights of activated synapses decrease through their inactive process. In this way, the neural network is not out of control due to the unlimited increase in all synaptic weights, and the neural network does not lose its learning and computing ability because the synaptic weight remains at the maximum value all the time.

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