論文題目：A Study on Effects of Direct Inter-pyramidal Inhibition on Neural Network Dynamics

(錐体ニューロン間の直接抑制がニューラルネットワークダイナミクスに与える影響に関する研究)

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The collective dynamics of random neural networks was extensively studied in the past decade assuming that each neuron is models as constituting dynamical units. These models are in common in the point that they all assume random network topologies and networks are embedded into an unspecific external population, supplying excitatory drive to the local network. These networks are basic models for cortical networks and display activity states observed in vivo. In these previous works, it was assumed that all synapses of inhibitory neurons cause hyperpolarizing effect, while excitatory synapses have depolarizing effect on their postsynaptic neurons. This constraint is called as "Dale's principle". However, recent experimental results by Ren et al suggest the existence of an inhibitory neocortical pathway that involves inter-pyramidal inhibitory postsynaptic currents (IPSCs), though pyramidal neuron was thought to have excitatory synapses only. They observed that about 28% of pyramidal neuron in a single layer II/III (mouse visual cortex) evoked reliable, large, and constant-latency IPSCs in the other pyramidal neuron. Though the exact nature of this pathway is still under debate, Ren et al. hypothesize axo-axonic glutamate receptor. Effectively, this yields an inhibitory projection between two pyramidal cells and hence, a violation of Dale's principle. However, the effect of these inter-pyramidal direct inhibitions (neglecting of Dale's principle) is not clear. So in this article, we study the effects of a general regard or neglect of Dale's principle on the dynamics in random networks using Izhikevich's neuron model and current based synaptic model.

In chapter 3, we show some basic result. Our simulations showed that the population activity of spiking neural networks are dramatically changed, if we admit violating of Dale's principle and allow neurons to form both excitatory and inhibitory synaptic terminals on their axons (existence of direct inter-pyramidal inhibitions). As demonstrated by our numerical simulations in which all settings are identical otherwise than network structure, non-Dale connectivity randomization procedure leads to a state of asynchronous population activity in which individual neuron spikes irregularly and global fluctuations are strongly attenuated if the number of synaptic connection per one neuron is adequate. The distribution of population spike counts is comparably narrow and symmetric for the non-Dale wired network whereas it is broad and highly skewed in networks respecting Dale's principle.

To be precise, there have been works which refer to asynchronous-irregular activity of spiking neural network before. For example, in the work by Brunel (2000), the dynamical behavior of local networks consisting of leaky integrate-and-fire (LIF) neurons with current-based synapses of Dale-respecting network and a state of asynchronous population activity was referred. Theoretical stability analysis of the stationary states by a Fokker-Planck equation suggested that a state of asynchronous population activity can be achieved for network with recurrent inhibition and sufficiently strong external drive. Numerical simulations of that state, however, displayed residual globally synchronous activity that arises due to the finite size of the network and even for highly diluted networks of size 100000 neurons with synapse numbers of about 1000 to 10000, the predicted asynchronous irregular state is not asynchronous, as reflected in a high variance of the population activity. Hence, it seems that in Dale-respecting network dilution of the synaptic connection density far from biologically plausible values is needed to obtain local cortical networks with asynchronous-irregular activity.

However, our simulations suggest that by introducing direct inter-pyramidal inhibition and violating Dale's principle, asynchronous-irregular activity can be achieved even in the case that synaptic connection density of network is high (> 0.5).

This result can be understood as follow; In Dale's principle respecting network, correlation of synaptic recurrent input from pre-synaptic source shared by multiple neurons are usually positive. On the other hand, in non Dale-network, recurrent input correlation can be negative because of the breaking of Dale's principle. So total recurrent input correlation is decreased and after all, spiking activity of network shows asynchronous-irregular activity.

In chapter 4 and 5, we examine the effect of changing the strength of synaptic connections. In chapter 4, we studied the network dynamics at various synaptic weight values and balances of excitatory and inhibitory recurrent input. In chapter 5, on the other hand, we introduce Short-Term synaptic Depression (STD), depression of synaptic weight depending on spiking activity of each neuron, and observed the network dynamics. In both chapters, we observed large differences of dynamics between Dale-respecting and Dale-neglecting network.

In chapter 6, we added time-varying external input according to the sine function of various frequency (1~100Hz), and observed network dynamics. In Dale-neglecting network, temporal population activity strongly synchronized to external input, which similar in appearance to the external sine input and correlation between temporal population activity and input sine function is high, while in Dale-respecting network, appearance of temporal population activity is far from sine curve and correlation to input is near 0. Our result suggest the possibility that non-Dale-network impressive qualities as population encoder that represent the fluctuation of external input in population dynamics.

Direct inter-pyramidal inhibition is new knowledge of late, so our study is only the first stage. However, as general conclusion from this study, we can say that Breaking the Dale's principle by direct inter-pyramidal inhibition bring significant differences to neural network, achieve asynchronous irregular state and the network with direct inter-pyramidal inhibition may be more effective as temporal decoder than Dale-respecting network. It is a future problem to sophisticate our work and seek the way to more effectively utilize the direct inter-pyramidal inhibition.