Inhibition Increases Modularity in Bursting Neuronal Networks

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Introduction

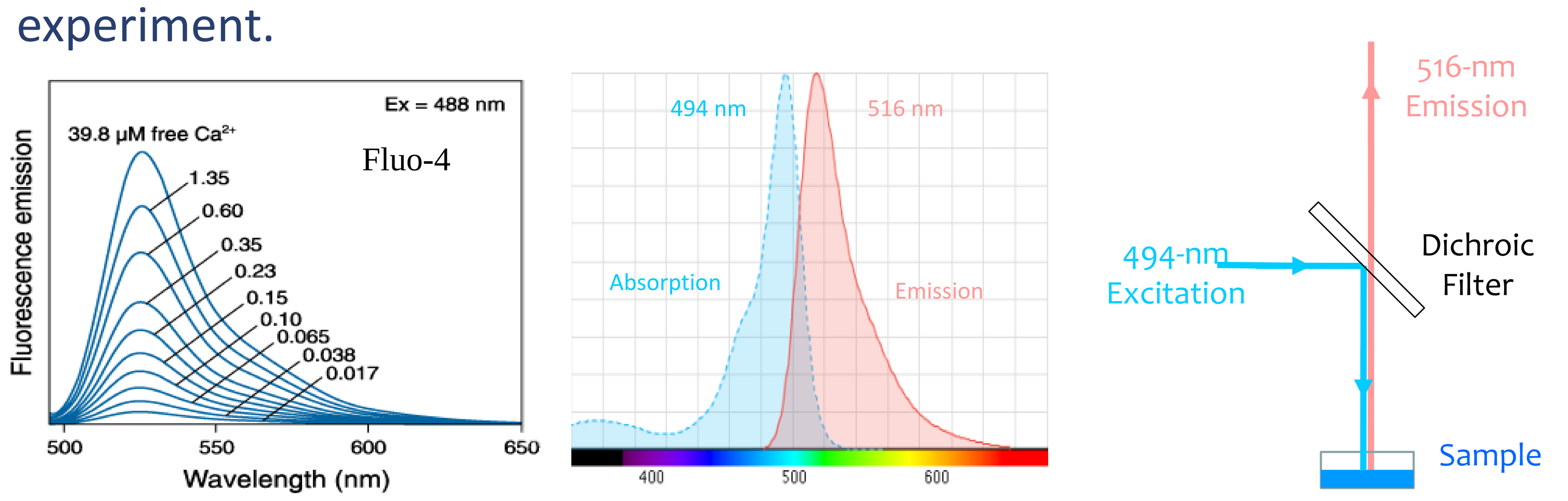
Neuronal networks in dissociated cultures spontaneously generate synchronous activity known as network bursting, which is characterized by the firing of nearly all neurons every 30–100 seconds. There has been much research directed toward understanding the initiation of bursts [1], as well as the role of underlying network topology [2]. Research has also focused on determining the role of excitatory and inhibitory connections in synchronous bursting behavior; however, it is still unclear how these connections determine network properties. Removing inhibitory connections with bicuculline, a $GABA_A$ receptor antagonist, decreases bursting frequency. Theoretical modelling [2] has shown that frequency changes are due to changes in network properties, such as modularity and clustering coefficient. This experiment had the following aims:

1) investigate the effects that inhibitory connections have on modularity and clustering coefficient
2) compare our experimental results with theoretical findings

Methods

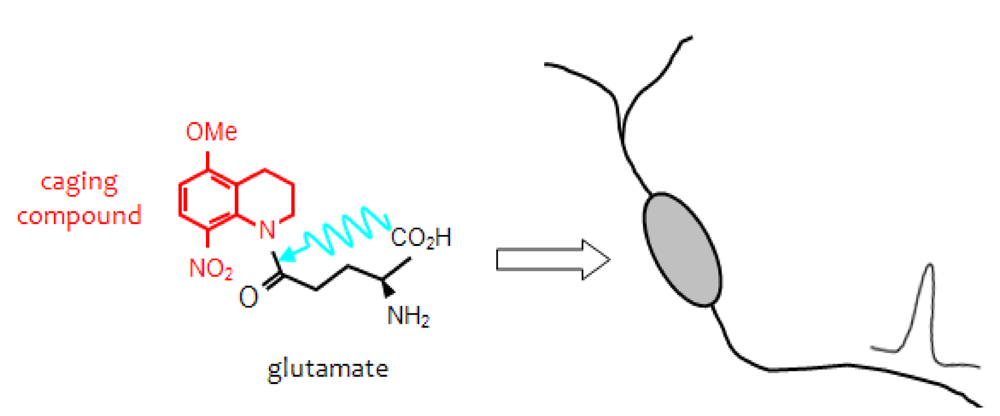
Calcium Imaging

Activity increases intracellular. A Ca^{2+} sensitive dye (Fluo-4) is loaded into neurons. Activity is monitored by detecting changes in dye fluorescence. During this, a 494 nm LED is active at 1 Hz for the entire duration of an experiment.



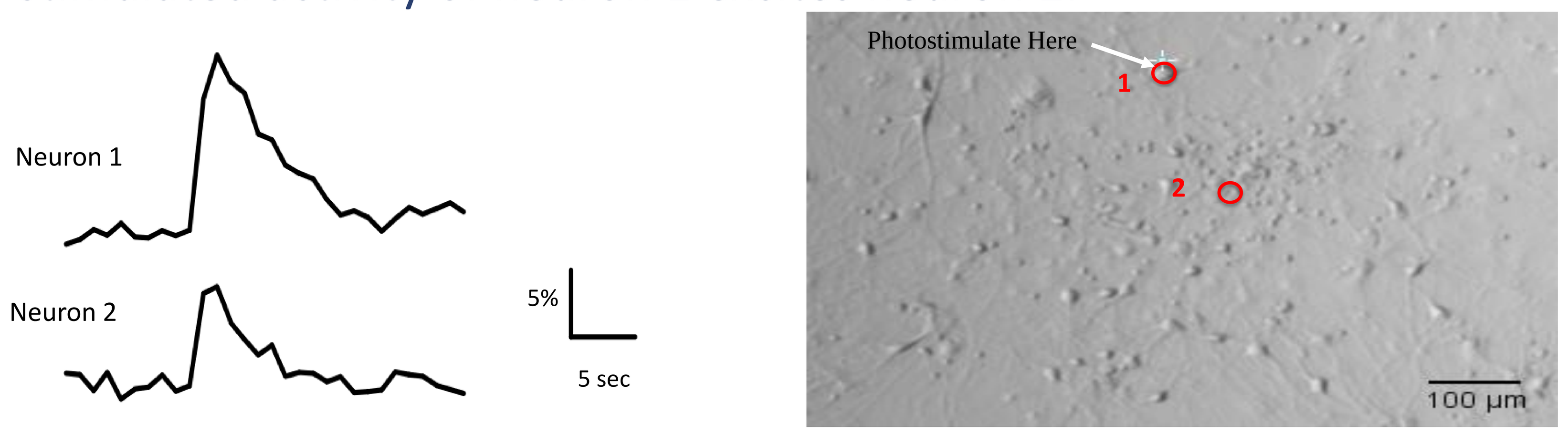
Laser Photostimulation

UV laser light releases glutamate from caging compound, causing neuron to fire action potentials (spikes). This allows us to study the network topology of individual neurons.



Ca Response to Laser Photostimulation

The stimulated activity of neuron 1 excites neuron 2.



Data & Results

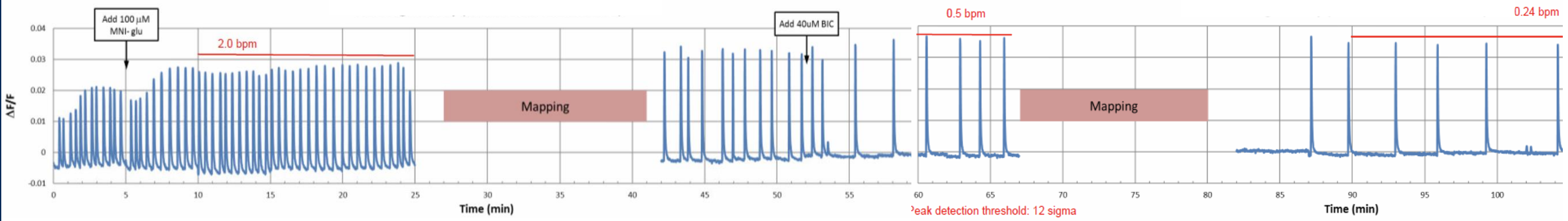


Figure 1: After the addition of bicuculline, fluorescence amplitudes increased and bursting frequency decreased.

Connectivity Maps

Map 1 - PreBIC
Nodes: 107 nodes
Links: 520 links
Avg. degree ($\bar{k}$): 4.9
Avg. clustering coef. ($\bar{C}$): 0.46
Modularity (Q_w): 0.72

Map 2: PostBIC
Nodes: 107 nodes
Links: 628 links
Avg. degree ($\bar{k}$): 5.9
Avg. clustering coef. ($\bar{C}$): 0.47
Modularity (Q_w): 0.67

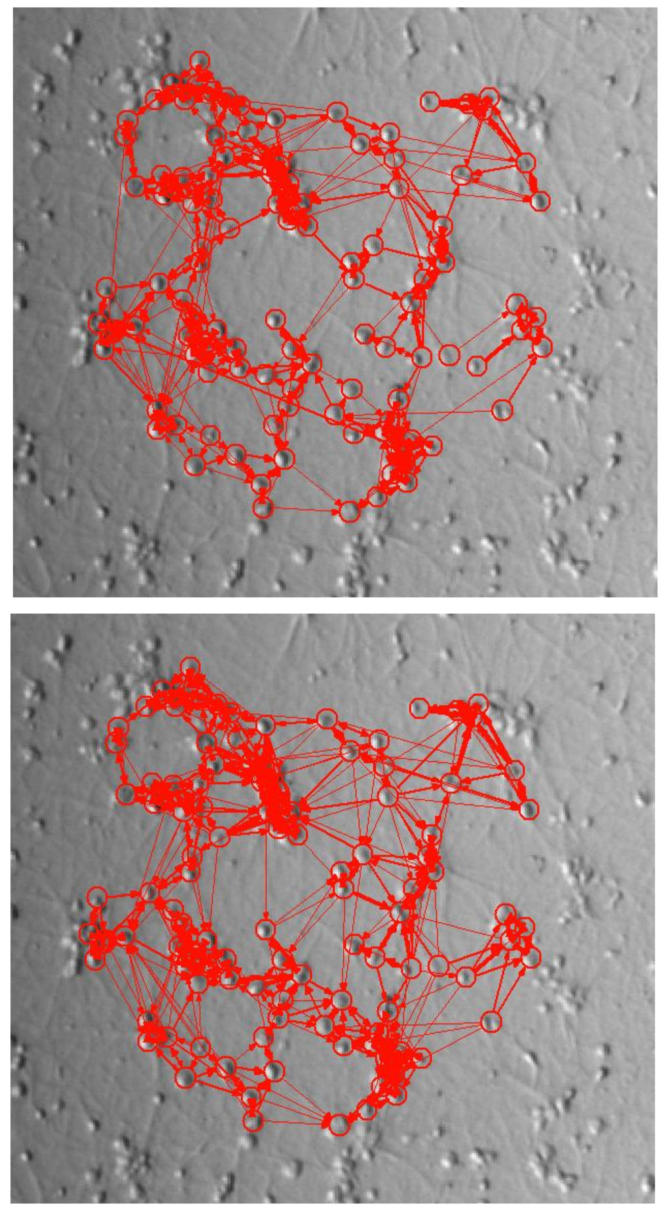


Figure 2: Connectivity maps before (top) and after (bottom) addition of bicuculline.

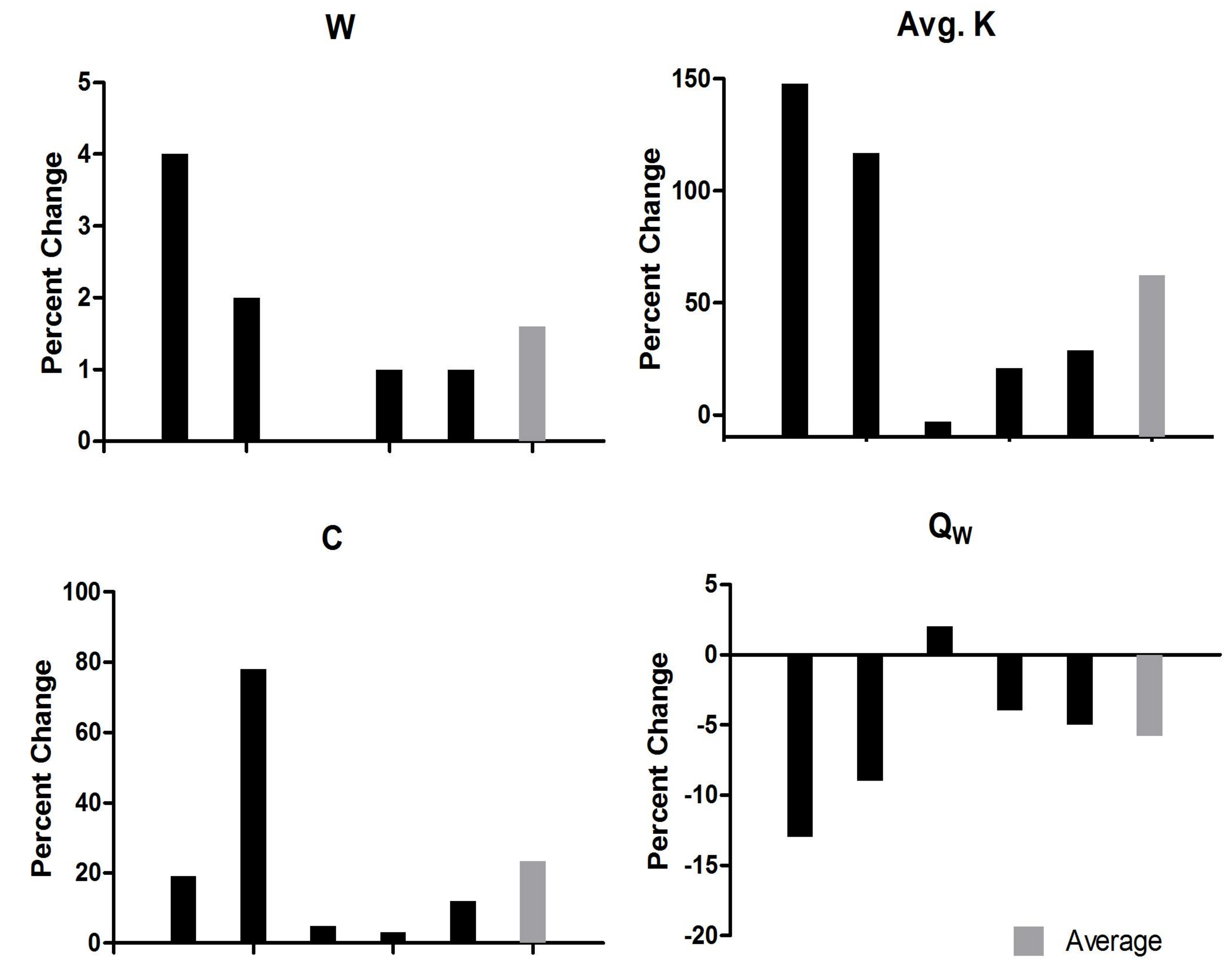
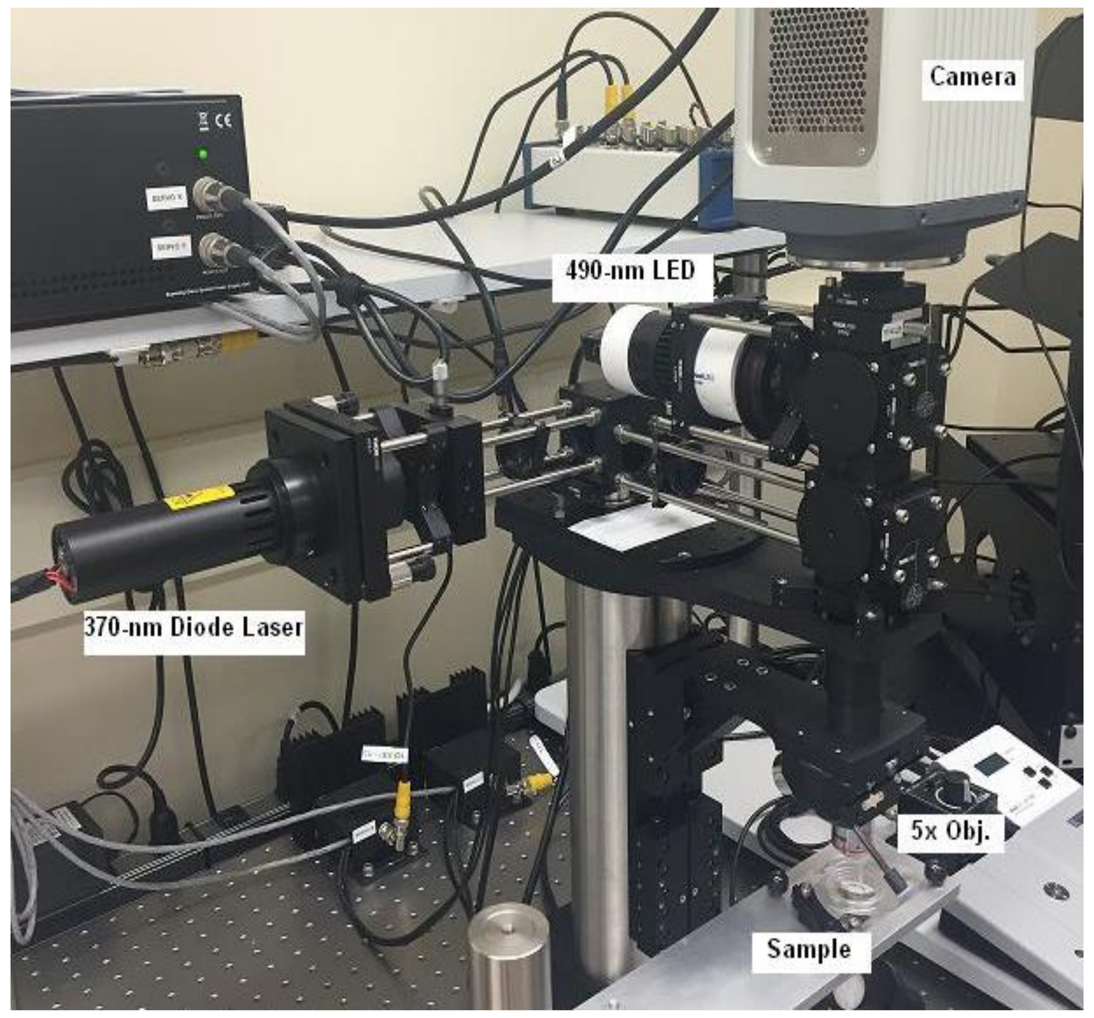


Figure 3: Percent change of a) link weight, b) average k-degree, c) clustering coefficient, and d) weighted modularity after the addition of bicuculline for 5 experiments (black bars).

Apparatus



Discussion

We observed that with the addition of bicuculline, fluorescence amplitudes increased while bursting frequency decreased (Fig.1). Analysis of connectivity maps (Fig. 2) revealed that the modularity coefficient decreased by 6% , and the clustering coefficient increased by 3%. Finally, we synthesized results from 5 experiments (Fig. 3) and concluded that addition of bicuculline increases the weight of the links, average k-degree and clustering coefficient and decreases network modularity.

Our experimental findings are consistent with the theoretical framework in the literature, suggesting that synchronous bursting behavior depends on the connectivity of the network.

References

[1] Orlandi J., Soriano J., Alvarez-Lacalle E., Teller S., Casademunt J.: Noise focusing and the emergence of coherent activity in neuronal cultures. Nature Physics 9(9), 582–590 (2013) . [2] Moriya S., Yamamoto H., Hisanao A., Hirano-Iwata A., Niwano, M., Kubota S., Sato S.: Modularity-dependent modulation of synchronized bursting activity in cultured neuronal network models. Proceedings of the International Joint Conference on Neural Networks (IJCNN) 1163–1168 (2017)