Identification of organizational principle corresponding to experimental data of neuronal network activity

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Introduction

An interesting study of focus in neuroscience is how neurons communicate. What is known is that these elements are dynamic, and they arrange themselves in a complicated but functional structural network. Research in this field has been motivated because these networks are thought to provide the physiological basis for information processing and mental representations. Previous research has proposed hypothetical models as to how the neurons connect through synapses and organize in a complex network. Following previous work, the main objective of this project was to test different models against experimental data, which was obtained from microelectrode arrays. The models included a random model, scale-free model, and weighted network model. According to the random model, neurons form connections at random (i.e., there exists no basis as to how the neurons coordinate). On the other hand, the scale-free model incorporates the concept of preferential attachment in which the more connections a neuron has, the more likely it is to receive new links. Across all neurons, the distribution of links exhibits a power law. Finally, the weighted network model is similar to the scale-free model; however, connections between neurons have a specific value of strength associated with them. It may or may not exhibit the power law.

Weighted Network Dynamics:

The model begins from an initial seed network of N_0 neurons connected by links with an assigned weight w_0. At each time step, a new, randomly introduced neuron forms a connection of w_0 with a pre-existing neuron from the network. The network grows to a final size of N neurons. This model exhibits a strength driven attachment since incoming neurons are more likely to connect to neurons handling larger weights. The concept is signified by the probability distribution,

$$\Pi_{n\to i} = \frac{s_i}{\sum_j s_j}.$$

The presence of new connections introduces variations on the existing weights across the network, thereby allowing for a local rearrangement of weights. The introduction of new neurons is able to alter the total weight of the connections handled by a specific neuron. The neuron's overall strength s_i is defined as,

$$s_i = \sum_{j\in V(i)} w_{ij},$$

When a new connection enters the network, it induces a total increase of traffic (δ). In the simplest model, δ is constant. The traffic is proportionally distributed among the connections departing from a neuron according to their weights, yielding the equation $s_i \rightarrow s_i + \delta + w_0$. The purpose of assigning weights to connections has to do with the fact that not all connections have the same strength. The weights are a function of the connections. The function is the capacity of synapses and gap junctions in neural networks. However, this model only considers the case of symmetric weights (Barrat et al., 2004).

Methods

<u>Experimental approach</u>. Cultured cortical and hippocampal cells prepared from 40 day prenatal Sprague Dawley rats were placed on microelectrode arrays (MEAs). A MEA is an electrical device that records the activity of neurons. We measured information transfer between neurons through transfer entropy (TE), which quantifies the information in a neuron found in the past history of another neuron (Vincent et al., 2012).

<u>Theoretical approach</u>. A code corresponding to each model was generated using the programming language of Matlab (computer software). The code depicted the construction rule and model dynamics. We manipulated variables of the models and generated figures in order to match the experimental data to a specific model.

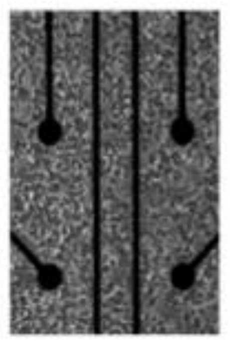

Figure 1. Culture of cortical neurons plated on a MEA (only a subset of the array is shown). Electrodes are spaced 200 µm apart.

Results

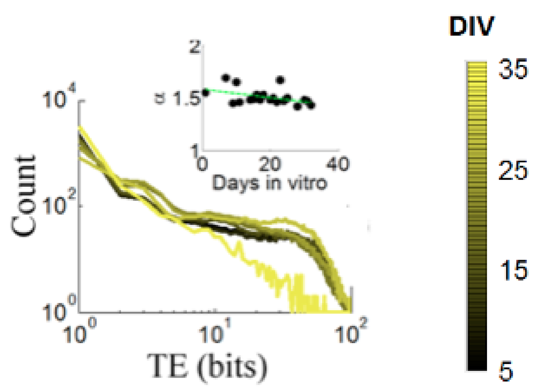

Figure 2. The distribution of transfer entropy (TE), measured in bits, over development. The inset graph plots the slopes for the individual days in vitro shown on the main graph. The green line depicts the slope of the decrease in distribution. The slope becomes more shallow as days in vitro increase. The main graph shows that as the cells develop more (i.e., days in vitro increase), the relationship between count and TE reaches a power-law distribution. The network changes, which signifies dynamic evolution. The DIV bar signifies the color scheme representing days in vitro.

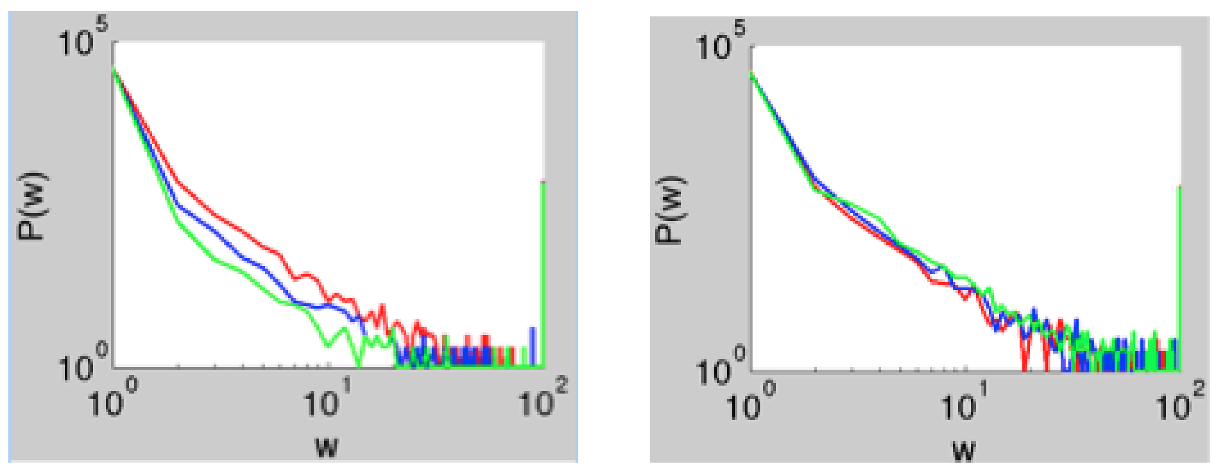

Figure 3. Manipulation of the traffic (δ) variable. As the traffic increases, the probability of finding a neuron with a strong connection weight decreases. To contrast, as the traffic decreases, the probability of finding a neuron with a strong connection weight increases.

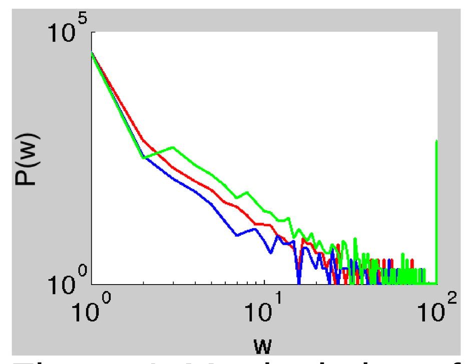

Figure 4. Manipulation of the initial weight ($w_{initial}$). As the $w_{initial}$ increases, the probability of finding a neuron with a strong connection weight increases. To contrast, as the $w_{initial}$ decreases, the probability of finding a neuron with a strong connection weight decreases.

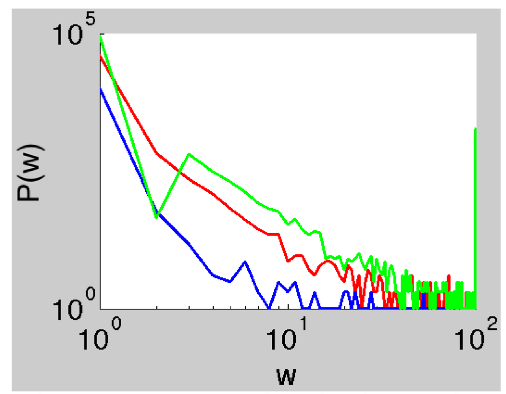

Figure 5. Manipulation of N_0 and N. As N_0 and N increase, the probability of a neuron occurring with a strong connection weight increases. To contrast, as the values decrease, the probability of a neuron occurring with a strong connection weight decreases. This manipulation ensures the model is working correctly.

Conclusion

Recordings from the MEAs showed that as neurons communicated, only a small portion of neurons had formed a large quantity of connections. Majority had fewer connections. This organizational principle eliminated the random model. The figures generated by the weighted network model were consistent with the experimental data. Therefore, the experimental data corresponds to a weighted network. The figures showed that the probability of finding neurons with strong connection weights is less than the probability of finding neurons with milder connection weights. Also, the total weight distribution followed a power-law. The match between the experimental data and model appeared to be practical because a neuron with fewer, but stronger individual connections could have a greater overall strength compared to a neuron with many, but weaker individual connections, resulting in a lower overall strength. The impact of these results will allow for enhanced understanding of the architecture of brain networks.

References

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