Research Proposal

Jizheng Dong

1 Introduction

It has been an important mission in neuroscience to probe the organization of neural networks at the cellular level, thus determine its function.

The topological structure of networks has been studied by many physicists, computer scientists and biologists [1] [2]. The research methods, including graph theory and statistical physics, have been adapted to the research of networks in the brain [3] [4]. The study of network topology in brain has steadily accumulated evidence in the particular function of a small population of highly active neurons between the networks, called hub cells [5] [6].

Yassin et al. have revealed the existence of hub cells from the perspective of the firing activity [7]. In addition, molecular neurobiology research suggests that γ-aminobutyric acid–releasing (GABAergic) interneurons satisfy the definition of hub cells, which play crucial roles in neural circuit activity, including circuit formation and synaptic plasticity [8] [9] [10]. Researches have been done to reveal the anatomical circuit about hub neurons. Jiang et al. have provided a comprehensive view of the connectivity between diverse types of neurons, particularly among GABAergic interneurons [11].

The anatomical structure has preliminarily investigated, however, few functions of hub cells in the process of information flow are known. Therefore, more attention should be poured into the combined research of electrical activity and anatomical structure to define the function of the neural network in the information flow [12].

Although many areas, like the hippocampus, provide an ideal circuit to investigate the existence of hub cells. Neurons in the hippocampal network are involved in many behaviors [12] [13] [14]. Thus we need an area performing simplicity function to test the relationship between the structure and function. Some researchers have found that the optic tectum in vertebrates, such as fish, reptiles and birds, particularly, barn owl optic tectum, is a good palace to combine the audio and visual information [15]. In the research, it is revealed that neurons sensitive to vision in a particular direction will only respond to the corresponding auditory information.

Besides, this connection does need a long time to accomplish. It doesn't like the retinal ganglion cells which can change their properties to encode light information within a few seconds [16], which means it hardly can be analyzed in the perspective of neural network. This finding gave us an appropriate area in the brain to probe the relation between structure and function.

2 Methodology

Our experiment is made up of three main parts.

In the first part, we let owls or other suitable vertebrates learn visual information and corresponding auditory information in specific directions. To ensure that they establish a connection between visual and auditory information, the prerequisite of finding optic tectum neurons that play a key role in information integration, the fine-scale electrode array is used to record their activities with surrounding neurons. According to the temporal analysis methods, we may obtain the relationship between information transmission. Some possible results according to the firing time sequence of neurons, as mentioned in [17], those cells will have some connectivity pattern at the micro-level. Firing activities of some cells can cause other adjacent cells to fire.

In the second part, we let the experimental animals wear prismatic spectacles to form another new connection between the auditory information and incorrect visual information. It can be expected that there exist differences between the new connection and the old one. For example, cells that were previously sensitive to both the visual information in front and the auditory information in front will be sensitive to the visual information in front and the anterolateral auditory information. These new connections may lead to different firing patterns of neurons. Here we will do the same analysis as in the first part.

In the third part, we will use the precise transmission electron microscopy, to reconstruct the specific information of optic tectum neurons connection in the computer, including the detailed anatomy, the actual synapses between different neurons. Therefore, we may integrate with the information obtained in the first two parts. After knowing the electrical activity and anatomical structure, we can make an overall analysis to speculate what changes have taken place in the topology of neural network in the process of connectivity dynamics, which will be very crucial to our research on the specific structure and related functions of neural network.

References

[1] Albertlaszlo Barabasi and Reka Albert. Emergence of scaling in random networks. *Science*, 286(5439):509–512, 1999.

[2] S Boccaletti, Vito Latora, Yamir Moreno, Mario Chavez, and Donguk Hwang. Complex networks: Structure and dynamics. *Physics Reports*, 424:175–308, 2006.

[3] Edward T Bullmore and Olaf Sporns. Complex brain networks: graph theoretical analysis of structural and functional systems. *Nature Reviews Neuroscience*, 10(3):186–198, 2009.

[4] Duncan J Watts and Steven H Strogatz. Collective dynamics of 'small-world' networks. *Nature*, 393(6684):440–442, 1998.

[5] Christopher J Honey and Olaf Sporns. Dynamical consequences of lesions in cortical networks. *Human Brain Mapping*, 29(7):802–809, 2008.

[6] Lina Yassin, Brett L Benedetti, Jeansebastien Jouhanneau, Jing A Wen, James F A Poulet, and Alison L Barth. An embedded subnetwork of highly active neurons in the neocortex. *Neuron*, 68(6):1043–1050, 2010.

[7] Lina Yassin, Brett L Benedetti, Jean-Sébastien Jouhanneau, Jing A Wen, James FA Poulet, and Alison L Barth. An embedded subnetwork of highly active neurons in the neocortex. *Neuron*, 68(6):1043–1050, 2010.

[8] Paul G Anastasiades, Andre Marquessmith, Daniel Lyngholm, Tom Lickiss, Sayda Raffiq, Dennis Katzel, Gero Miesenbock, and Simon J B Butt. Gabaergic interneurons form transient layer-specific circuits in early postnatal neocortex. *Nature Communications*, 7(1):10584–10584, 2016.

[9] Nathalie Dehorter, Nicolas Marichal, Oscar Marin, and Benedikt Berninger. Tuning neural circuits by turning the interneuron knob. *Current Opinion in Neurobiology*, 42:144–151, 2017.

[10] Paolo Bonifazi, Miri Goldin, Michel Aime Picardo, Isabel Jorquera, Adriano Cattani, Gregory Bianconi, Alfonso Represa, Yehezkel Benari, and Rosa Cossart. Gabaergic hub neurons orchestrate synchrony in developing hippocampal networks. *Science*, 326(5958):1419–1424, 2009.

[11] Xiaolong Jiang, Shan Shen, Cathryn R Cadwell, Philipp Berens, Fabian Sinz, Alexander S Ecker, Saumil S Patel, and Andreas S Tolias. Principles of connectivity among morphologically defined cell types in adult neocortex. *Science*, 350(6264):1055–1055, 2015.

[12] Kevin L Briggman and William B Kristan. Multifunctional pattern-generating circuits. *Annual Review of Neuroscience*, 31(1):271–294, 2008.

[13] James M Weimann and Eve Marder. Switching neurons are integral members of multiple oscillatory networks. *Current Biology*, 4(10):896–902, 1994.

[14] John G White, Eileen Southgate, J N Thomson, and Sydney Brenner. The structure of the nervous system of the nematode caenorhabditis elegans. *Philosophical Transactions of the Royal Society B*, 314(1165):1–340, 1986.

[15] Michael S Brainard and Eric I Knudsen. Sensitive periods for visual calibration of the auditory space map in the barn owl optic tectum. *The Journal of Neuroscience*, 18(10):3929–3942, 1998.

[16] Toshihiko Hosoya, Stephen A Baccus, and Markus Meister. Dynamic predictive coding by the retina. *Nature*, 436(7047):71–77, 2005.

[17] Gabrielle J Gutierrez, Timothy Oleary, and Eve Marder. Multiple mechanisms switch an electrically coupled, synaptically inhibited neuron between competing rhythmic oscillators. *Neuron*, 77(5):845–858, 2013.