【Grant-in-Aid for Scientific Research (S)】

Broad Section G

Title of Project： Dissecting the mechanism underlying behavioral regulation through real-time spatiotemporal manipulation of neural circuits

MORI, Ikue
(Nagoya University, Graduate School of Science, Professor)

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【Purpose and Background of the Research】

In contrast to computers, brain computation seems far more variable and complex. Intriguingly, the brain enables to generate variable yet distinct behavioral outputs even when the same sensory stimuli are presented to the animal. Such probabilistic feature of animal behaviors is thought to be important for the survival and reproduction of the animal in ever-changing environments. Despite how brain generates variable behavioral outputs is a fundamental question in neuroscience, the logics behind such variable feature are still elusive. The compact nervous system of *C. elegans* provides an excellent opportunity to dissect the neural mechanisms underlying variability in brain function.

We recently observed that optogenetic activation of a single *C. elegans* sensory neuron evoked multiple behavioral responses. A brain-wide single neuron ablation coupled with high-throughput behavioral analysis revealed that distinct behavioral responses induced by this single neuron activation required recruiting different neural circuits, each of which is composed of unique combination of neurons. Further, some neurons among the components of these neural circuits showed apparent spontaneous activities even when the sensory neurons were silent.

These observations suggested the possible basis of variability in brain function, where the changes in the activity of the sensory neuron can be interpreted differently depending on the internal state of the nervous system, and hence generate distinct behavioral outputs. In this study, we aim to investigate this possibility and identify the neural principle of variability in brain function.

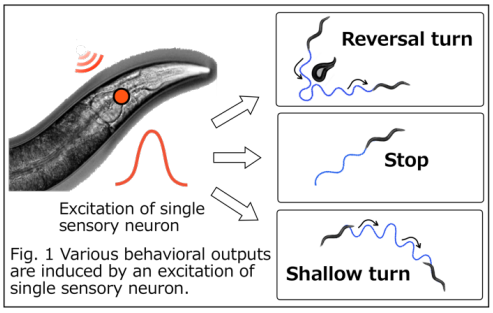

Fig. 1 Various behavioral outputs are induced by an excitation of single sensory neuron.

【Research Methods】

We will develop a new custom microscope system with real-time feedback system, in which timing of optogenetic manipulation of the sensory neuron can be determined by real-time monitoring of neural states of freely-moving animals. With this system, we plan to perform real-time analysis of the following components: 1) tracking the animal movement; 2) identifying neurons in the moving animals; 3) detecting the calcium signals from the neurons; and 4) analyzing the neural activity and determine the timing of optogenetic manipulation of the sensory neuron.

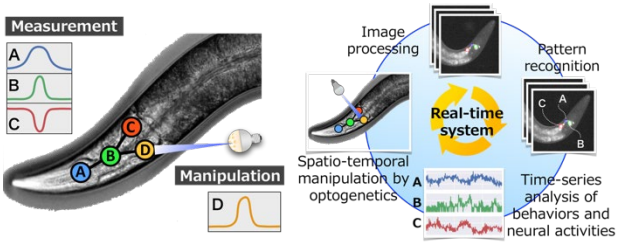

Fig. 2 Real-time optogenetic system to be established

【Expected Research Achievements and Scientific Significance】

Variability in behaviors is a unique feature of living organisms that distinguish them from computers. This study aims to understand the neural logics of information processing that confers variability in brain function. Understanding the principle of variability will be a milestone of neuroscience and also provide a platform for the development of new algorithms for soft computing.

【Publications Relevant to the Project】

Ikeda M., Nakano S., Giles A.C., Costa W.S., Gottschalk A., and Mori I.
Circuit Degeneracy Facilitates Robustness and Flexibility of Navigation Behavior in *C. elegans.* bioRxiv (2018)
https://doi.org/10.1101/385468

【Term of Project】

FY2019-2023

【Budget Allocation】

121,700 Thousand Yen

【Homepage Address and Other Contact Information】

https://nsi.bio.nagoya-u.ac.jp/en/
http://elegans.bio.nagoya-u.ac.jp/~lab/index.html