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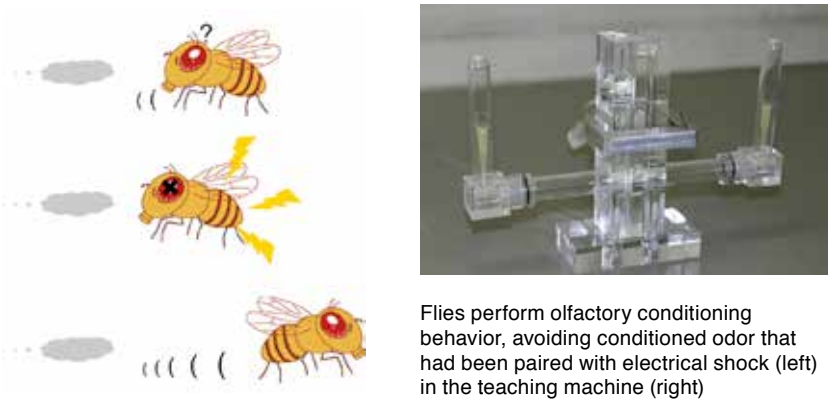
Project Leader **Minoru Saitoe** Learning and Memory Project

Investigating the Molecular Mechanisms that Generate Memory-encoding Neural Networks

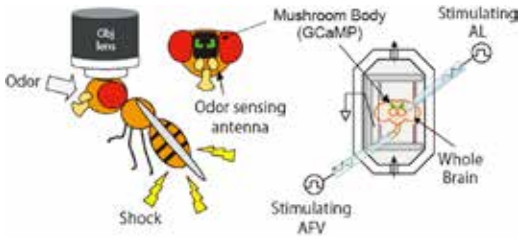
Memories mold our personalities to make us who we are. Using powerful genetic tools, numbers of genes and neural substrates underlying memory-associated behaviors have been identified in Drosophila. Given these scientific backgrounds, we have investigated when, where and how identified memory-associated gene products function to produce memory-based behavior, and how the underlying mechanism is changed in response to changes in physical condition such as aging.

In addition to behavioral genetic approach, we employ in vivo and ex vivo imaging techniques to characterize physiological properties of memory-associated neural networks, and understand how memory-associated genes and neuromodulatory systems regulate function of these networks; how sensory information is associated and how memory information is stored in neural substrates and recalled upon receiving test stimuli.

"Combining behavioral genetics and state-of-arts imaging techniques, we aim to understanding how our brains form, store and retrieve memory."



Flies perform olfactory conditioning behavior, avoiding conditioned odor that had been paired with electrical shock (left) in the teaching machine (right)

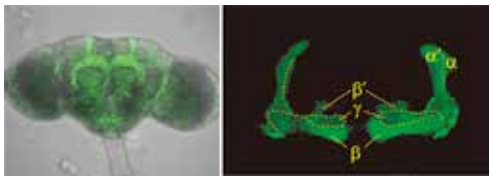


Left, in vivo imaging of fixed fly under microscope is used to investigate activity of identified neurons and network during sensory association (odor and shock), reinforcement, storage and retrieval. Right, using ex vivo imaging we attempt to make artificial memory in cultured brain, thereby elucidate the whole picture of the memory-associated networks.

Learning and Memory

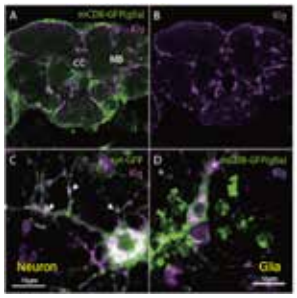
Current Research Topics

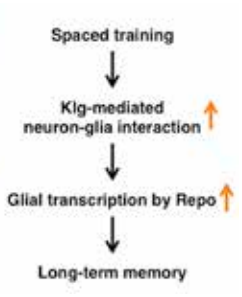
Encoding and decoding of memory: In Drosophila, the mushroom body (MB) is a neural center for olfactory memory. As described by Hermann Ebbinghaus (1885), repetitive olfactory conditioning with rest intervals, namely spaced training, stabilizes labile short-term memory (STM) into robust long-term memory (LTM), which requires transcriptional activity of CREB. Interestingly, STM and LTM are encoded in different subset of MB neurons. While aversive STM is encoded in gamma neurons, aversive LTM is encoded in alpha/beta neurons. We are interested in how such anatomical shifting is occurred during stabilization of STM to LTM, functional relationship between STM and LTM.



Structure of MBs and their lobe
Left: MBs in the fly brain expressing GFP.
Right: Subdivision of MB lobes derived from each type of MB neurons.

Neuron-glia interactions: Recent research demonstrates that neuron-glia communication is also important for memory formation. We have identified a cell adhesion molecule Klingon (Klg) that mediates neuron-glia communication required for LTM-based behavior. Currently, we are studying how Klg-mediated neuron-glia interaction regulates memory acquisition, stabilization and retrieval. Also, we are interested in how this mechanism is altered upon aging.



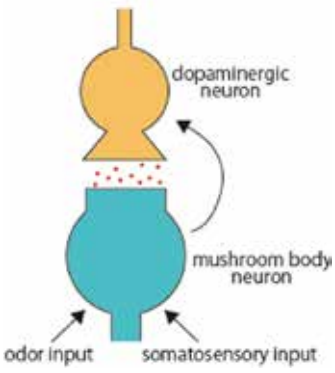


Klingon mediates neuron-glia interaction for LTM formation. A, B) Expression of Klingon (Klg) in the fly brain. C) Expression of Klg in neurons. D) Expression of Klg in glial cells.
Spaced training increases Klg-mediated neuron-glia interaction, thereby induces Repo-dependent glial transcription required for LTM.

Senior Research Scientist Kohei Ueno

Exploring Physiological Systems Underlying Learning and Memory

Neural plasticity in the MBs is believed to be a cellular basis of olfactory memory. To understand how odor and shock information are associated to produce plastic changes in the MB neurons, we developed ex vivo brain imaging system. Using this system, we found that simultaneous stimulation of odor and shock input pathways to the MBs produces long-term enhancement (LTE) in MB neurons in a manner dependent on activity of D1 receptor in the MBs. We further discovered a novel mode of dopamine release locally evoked by postsynaptic MB neurons which have been coincidentally activated by odor and shock input pathways. We have investigated how coincidentally activated MB neurons direct dopamine release and whether such on-demand release mode also takes place for other neuromodulators and other animals.



If mushroom body neurons are activated by two inputs, namely odor and somatosensory inputs, the activated mushroom body requires dopamine release from dopaminergic neurons.

Learning and Memory