DIVISION OF BRAIN CIRCUITS

Professor
MATSUZAKI, Masanori

Postdoctoral Fellow: *MASAMIZU, Yoshito*
Visiting Scientists: *HIRA, Riichiro*
OHKUBO, Fuki
Technical Assistant: *SUGIYAMA, Tomomi*

Various firing patterns of many neurons represent information in the brain. The microarchitecture of synaptic connections control information processing in cortical circuits. The structure and location of synapses determine and modify the strength of this information processing. The aim of our laboratory is to reveal how information is formed, maintained, selected, and decoded in the brain at the levels of single cells and of single synapses. To do so, we mainly use two-photon microscopy that has recently revolutionized the biological sciences. In particular, two of its features are proving to be very useful when compared with normal excitation modalities, namely imaging fluorescence signals from deep within living tissue and localized photochemical release of caged compounds.

I. Development of novel techniques to stimulate single inhibitory synapses

Recently, we developed two caged-GABA compounds. Two-photon excitation of the first caged GABA produced rapid activation of GABAergic currents in neurons in brain slices with an axial resolution of approximately 2 μm and enabled high-resolution functional mapping of GABA-A receptors. The second caged GABA, combined with an appropriate caged glutamate, allowed bimodal control of neuronal membrane potential with subcellular resolution using optically independent two-photon uncaging of each neurotransmitter. We used two-color, two-photon uncaging to fire and block action potentials from rat hippocampal CA1 neurons in brain slices with 720-nm and 830-nm light, respectively (Figure. 1). Thus, two-photon photolysis of caged GABA compounds should be a powerful tool for clarifying classical neurophysiological problems of synaptic function including dendritic integration, 'AND'-'OR' gate systems, diversity of GABA input points and others at the micrometer and even single-synaptic level.

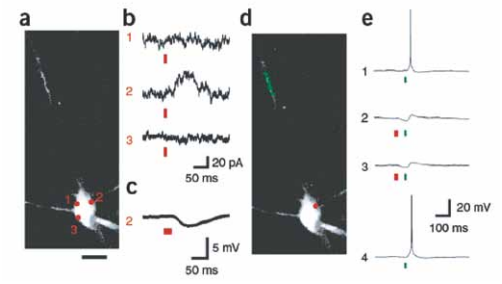

Figure 1. Two-photon excitation (at 830 nm) of GABA around the soma (red) inhibited the neural firing induced by two-photon excitation (at 720 nm) of glutamate at the dendritic locations (green, Kantevari et al., 2009)

II. Relationships between the synaptic connections and the geometry of dendritic spines

Dendritic spines of pyramidal neurons possess a variety of morphologies associated with synaptic strength and are distributed along the complicated structure of the dendritic branches. However, it has not been known whether the spine size and location (spine geometry) relate to the position of presynaptic cells innervating the spines. Here, we activated layer 2/3 pyramidal cells in the motor cortex by two-photon uncaging of glutamate and simultaneously performed two-photon calcium imaging of the dendritic spines of layer 5 pyramidal cells. We found that large spines were preferentially innervated by the cells on the ipsilateral side of the spines, whereas small spines were innervated by cells on both sides. The spines located distally from the parent soma were innervated exclusively by cells on the ipsilateral side of the spines. Our results indicate that synaptic connections are anisotropic and depend on spine geometry, which possibly increases the effectiveness of dendritic integration in information processing.

III. Spatio-temporal representation of motor information in the brain

The aim of this study is to reveal how voluntary movement is represented in cortical circuits. We are now combining a number of cutting-edge techniques to clarify the activity, distribution, and connections of the cortical neurons that are involved in sequential motor phases. The activities of the cortical neurons will be modulated by using 'optogenetic' tools to clarify the direction of flow of motor information. Our results will provide insights into the principles of circuit operation and the cellular basis for recovery from brain cortical damage.

Publication List

〔Original papers〕

- Kantevari, S., Matsuzaki, M., Kanemoto, Y., Kasai, H., and Ellis-Davies, G.C.R. (2010). Two-color, two-photon uncaging of glutamate and GABA. Nat. Methods *7*, 123-125.
- Matsuzaki, M., Hayama, T., Kasai, H., and Ellis-Davies, G.C.R. (2010). Two-photon uncaging of γ-aminobutyric acid in intact brain tissue. Nat. Chem. Biol. *6*, 255-257.
- Obi, N., Momotake, A., Kanemoto, Y., Matsuzaki, M., Kasai, H., and Arai, T. (2010). 1-Acyl-5-methoxy-8-nitro-1,2-dihydroquinoline: A biologically useful phtolabile precursor of carboxylic acids. Tetrahedron Lett. *51*, 1642-1647.