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第 22 回 葉山セミナー / The 22nd Hayama Seminar

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Whole-brain imaging of small nervous systems: From leech ganglia to freely moving C. elegans

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Abstract:

Understanding how perception and behavior emerge from dynamic neuronal circuits remains one of the central challenges in neuroscience. While the immense complexity of the mammalian brain renders whole-brain recordings nearly impossible, small nervous systems in invertebrates provide a tractable platform for comprehensive neural imaging. The medicinal leech (*Hirudo verbena*), with approximately 400 neurons per segmental ganglion, and the nematode *Caenorhabditis elegans*, comprising just 302 neurons in total, offer unique opportunities to study the functional principles of neural circuits at cellular resolution.

In this seminar, I will introduce two imaging techniques developed for these model systems. First, we established a voltage-sensitive dye (VSD) imaging method at Caltech that enables the simultaneous recording of action potentials and synaptic potentials across entire leech ganglia This approach allowed us to generate functional maps of neuronal activity during sensory processing and motor output, and to uncover how individual neurons dynamically participate in different behaviors without altering their synaptic connections. Our work culminated in the creation of the world's first combined anatomical and physiological dataset of a leech ganglion using a CLEM (Correlated Light and Electron Microscopy) approach, linking structural connectivity to functional dynamics.

More recently, we at Hokkaido University applied an ultrafast light-sheet fluorescence microscope to perform whole-brain calcium imaging in freely moving *C. elegans*. By integrating a high-speed tracking stage with this microscope, we achieved volumetric imaging at 50 volumes per second without motion artifacts, enabling us to capture neural activity during various behaviors involving rapid movements. Leveraging deep neural network-based segmentation, we identified a large fraction of neurons and monitored their calcium dynamics. I will also introduce other application instances of the high-speed light-sheet microscopy for broader biological contexts.

Together, these advances illustrate the power of whole-brain imaging in small nervous systems to reveal the dynamic coordination of neural ensembles underlying behavior. I will discuss the implications of these approaches and how such large-scale physiological datasets may inform our understanding of circuit function across species.