The 13th Annual
WPI-IIIS Symposium
~Science of Behaving and Sleeping Brains~

Date : Monday, November 25, 2024, 10:00-18:00
(Reception: 18:15 ~ 20:15)

Venue : Tokyo Conference Center Shinagawa, 5F Hall

IIIS INTERNATIONAL INSTITUTE FOR INTEGRATIVE SLEEP MEDICINE
University of Tsukuba
wpi World Premier International Research Center Initiative
MOONSHOT RESEARCH & DEVELOPMENT PROGRAM
眠気学 Drowsology
HIROSAKI COI-NEXT
HIROSAKI UNIVERSITY

Time Table

Opening				
10:00 - 10:15	Welcome	**Masashi Yanagisawa**	Director, WPI-IIIS, University of Tsukuba	
	Opening address	**Akira Ukawa**	WPI Academy Director	
Session 1 | Chair: Masashi Yanagisawa (WPI-IIIS, University of Tsukuba)				
10:15 - 11:00	Neural control of adenosine dynamics & implications to sleep-wake regulation	**Min Xu**	Chinese Academy of Sciences, Shanghai	Page 4
11:00 - 11:45	Sleep dynamics for consolidation and homeostasis in the amygdala	**Gabrielle Girardeau**	INSERM/Sorbonne Université	Page 5
11:45 - 12:05	Lunch preparation			
Session 2 | Chair: Sakiko Honjoh (WPI-IIIS, University of Tsukuba)				
12:05 - 12:50	Elucidating mechanisms and functions of default brain states	**Vladyslav Vyazovskiy**	University of Oxford	Page 6
12:50 - 13:35	Decoding the role of phase separation in fine-tuning circadian rhythms	**Yi Lin**	Tsinghua University	Page 7
13:35 - 14:00	Tea break			
Poster Session | Chair: Michael Lazarus (WPI-IIIS, University of Tsukuba)				
14:00 - 16:00	Data Blitz & Poster Presentation			
16:00 - 16:25	Photo / Break			
Session 3 | Chair: Takeshi Sakurai (WPI-IIIS, University of Tsukuba)				
16:25 - 17:10	Divergent spatiotemporal integration of whole-field motion in teleost species	**Yasuko Isoe**	Harvard University	Page 8
17:10 - 17:55	Fluorescent biosensors for probing neuronal activity and biochemical signaling *in vivo*	**Masayuki Sakamoto**	Kyoto University	Page 9
17:55 - 18:00	Closing remarks	**Takeshi Sakurai**	Vice-Director, WPI-IIIS, University of Tsukuba	
18:00	Closing			
18:15 - 20:15	Reception (3F Restaurant “Something Delicious”)			

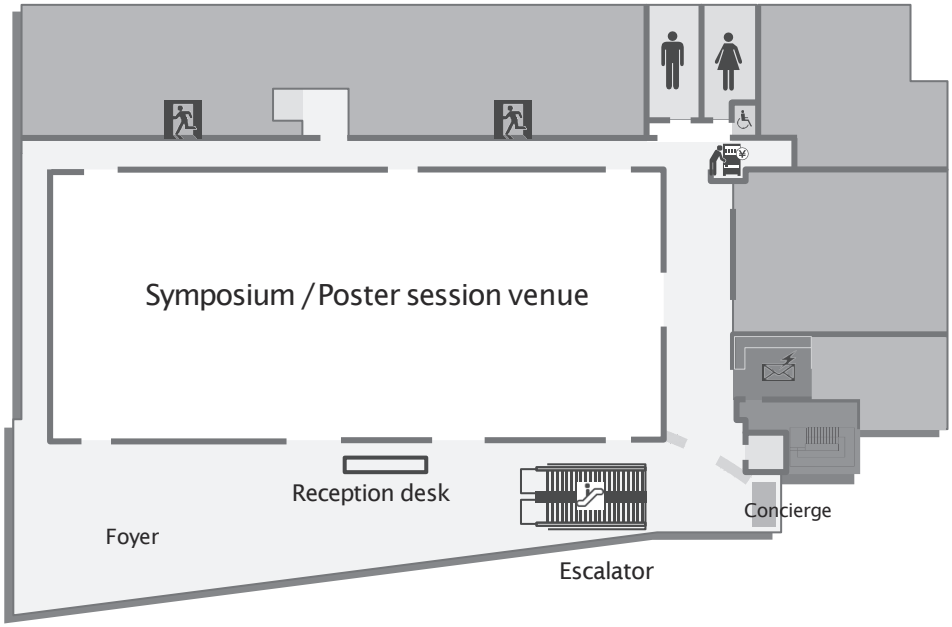
Information

Precautions
No outlets are available nearby audience seats
No smoking in the building
Wifi is available in the foyer

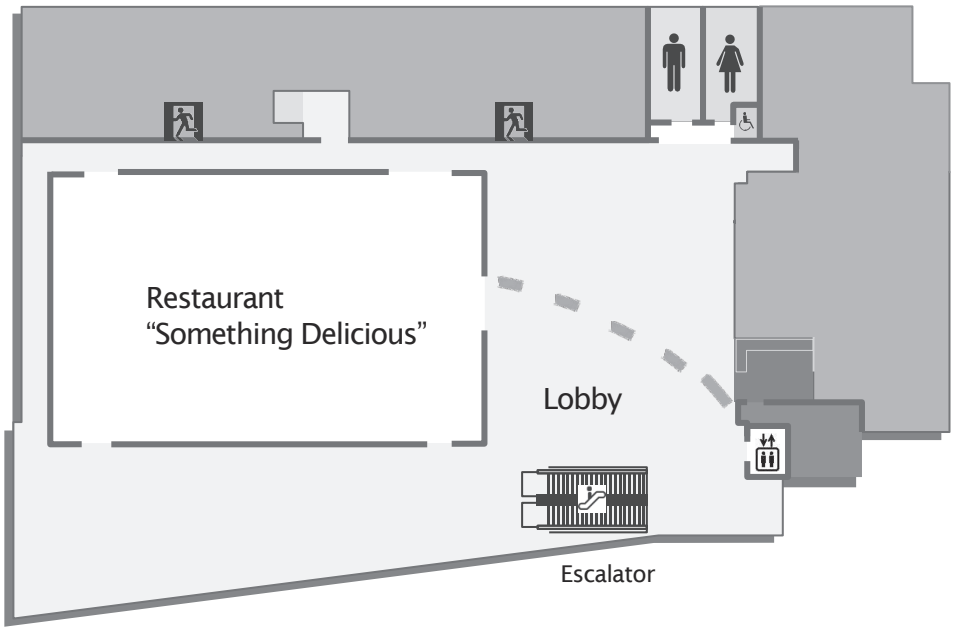
Lunch
Free lunch will be provided for pre-registered participants

Reception
18:15 - 20:15 at the restaurant on 3rd floor

Floor Map (5th floor) I Tokyo Conference Center Shinagawa



Floor Map (3rd floor) I Tokyo Conference Center Shinagawa



Neural control of adenosine dynamics & implications to sleep-wake regulation

Min Xu

Chinese Academy of Sciences, Shanghai, CHINA

ABSTRACT

Adenosine, a ubiquitous neuromodulator derived from cellular energy metabolism, has long been believed to play a crucial role in regulating the sleep-wake cycles. Using a genetically encoded adenosine sensor, we have now dissected the neural mechanisms underlying the control of extracellular adenosine accumulation in multiple brain regions. While extracellular adenosine levels are closely coupled with neural activity across all the brain regions studied, in the basal forebrain, the glutamatergic neurons, rather than the cholinergic neurons or astrocytes, serve as the primary drivers of adenosine increase during wakefulness. This suggests that wake-promoting neurons may underlie the buildup of sleep pressure during prolonged wakefulness by stimulating adenosine release. Furthermore, single-cell transcriptome analysis has uncovered a non-uniform expression of various adenosine receptors, related enzymes and transporters in different types of brain cells, further supporting the critical role of adenosine as a feedback regulator of increased neural activity. Together, our findings provide new insights into the complex neural mechanisms underlying the essential role of adenosine in maintaining homeostasis.

Sleep dynamics for consolidation and homeostasis in the amygdala

Gabrielle Girardeau

INSERM/Sorbonne Université, FRANCE

ABSTRACT

Sleep consists of two main stages, REM and Non-REM sleep. The neuronal dynamics of REM and Non-REM sleep have been extensively studied in the hippocampus and neocortex in link with homeostasis and memory consolidation. Notably, in the hippocampus, the replay of place-cell activity during Non-REM sleep sharp-wave ripples support the consolidation of spatial memories. The sleep dynamics of the baso-lateral amygdala (BLA), a core structure for emotional processing, are comparatively understudied, despite a hypothesized role for both REM and Non-REM sleep in emotional memory consolidation and emotional regulation involving the BLA. BLA neurons reactivate conjointly with dorsal hippocampus neurons during Non-REM sleep after a spatial aversive task (Girardeau et al. 2017), potentially sustaining the sleep dependent consolidation of space-threat associative memory. In parallel, there is a homeostatic regulation of firing rates in the BLA during NREM sleep affecting differentially principal neurons as a function of their basal firing rates. During REM sleep, the BLA transitions into a distinctive network state characterized by consistently elevated firing rates and low synchrony (Fernandes de Almeida, Khouader et al., in prep). Altogether, these findings contribute to better understanding the role of sleep in emotional processing.

Elucidating mechanisms and functions of default brain states

Vladyslav Vyazovskiy

University of Oxford, UK

ABSTRACT

Spontaneous, "default" brain states, typically characterised by regularly occurring bursts of neural activity at a slow frequency, is the first type of activity observed in early ontogeny, and also the state to which the adult brain gravitates during sleep, anaesthesia, brain injury or hypometabolic states, such as torpor. The dynamics and characteristics of default brain states are not well understood, and their occurrence is often considered a hallmark of pathology, or an indication that this state has no biological function. Contrary to this view, oscillatory activity during default brain states is often precisely regulated, and is characterised by structured, non-random dynamics both in space and in time. I will discuss examples of the occurrence of global and local default brain states, occurring spontaneously and induced using pharmacological and non-pharmacological means. This includes deep surgical anesthesia, sedation associated with a hypothermia, torpor induced by fasting or optogenetic stimulation of inhibitory neurons in the lateral preoptic area of the hypothalamus in laboratory mice and by shortening of the photoperiod in a seasonal rodent *Phodopus sungorus*, mouse models of deficient synaptic neurotransmission or mixed, hybrid states induced by activation of 5-HT_{1A} receptors. There are surprising commonalities among these widely distinct states, such as the general pattern of neural activity or elevated responsiveness to sensory stimulation, but also important differences, including spectral signatures and effects on behaviour and subsequent sleep. We posit that investigating the origin and mechanisms of the occurrence of default brain states in general represents an important opportunity for elucidating the biological meaning of conventional states, such as sleep.

Decoding the role of phase separation in fine-tuning circadian rhythms

Yi Lin

Tsinghua University, CHINA

ABSTRACT

Terrestrial organisms developed circadian rhythms for adaptation to Earth's quasi-24-h rotation. Achieving precise rhythms requires diurnal oscillation of fundamental biological processes, such as rhythmic shifts in the cellular translational landscape; however, regulatory mechanisms underlying rhythmic translation remain elusive. Here, we identified mammalian ATXN2 and ATXN2L as cooperating master regulators of rhythmic translation, through oscillating phase separation in the suprachiasmatic nucleus along circadian cycles. The spatiotemporal oscillating condensates facilitate sequential initiation of multiple cycling processes, from mRNA processing to protein translation, for selective genes including core clock genes. Depleting ATXN2 or 2L induces opposite alterations to the circadian period, whereas the absence of both disrupts translational activation cycles and weakens circadian rhythmicity in mice. Such cellular defect can be rescued by wild type, but not phase-separation-defective ATXN2. Together, we revealed that oscillating translation is regulated by spatiotemporal condensation of two master regulators to achieve precise circadian rhythm in mammals.

Divergent spatiotemporal integration of whole-field motion in teleost species

Yasuko Isoe

Harvard University, USA

ABSTRACT

Animals in different ecological niches have evolved to be receptive to specific, behaviorally relevant, sensory signals. Specialized sensory organs have been studied extensively in this context, but few studies have examined how behavioral algorithms and the underlying neural networks have been shaped by such processes. Here we used two fish model species, zebrafish (*Danio rerio*) and medaka fish (*Oryzias latipes*), both at comparable larval stages, and we map their spatio-temporal visual response profile with whole field coherent dot motion stimuli. We find that the effective visual field for motion processing is twice as large in medaka than in zebrafish, and that, accordingly, medaka are distinctly more sensitive to distractions in the periphery. Second, we systematically vary the lifetime of individual dots and show that zebrafish will respond robustly and with fast time constants to whole field coherent dot motion stimuli, even when the lifetime of dots is reduced to ~100ms. Medaka, on the other hand, fail to respond reliably to dots whose lifetime is less than a second, and they hold motion stimuli in memory for several seconds. The requirement for long object lifetime, combined with a fast rise time of the response and a long decay, are compatible with a specialized object classification circuit in medaka, that displays distinct aspects of object permanence. Zebrafish on the other hand seem to specialize in the quick processing of noisy, whole field motion that can extract fast directional changes of the background or substrate. We suggest that zebrafish, at this early stage, prioritize the fast processing of noisy whole field stimuli that facilitates position holding and navigation in moving currents, whereas medaka delegate computational real estate to the classification and short term storage of information related to conspecifics or other small moving objects swimming in their vicinity. This study sheds light on behavioral diversity in diverse ecological contexts and illustrates how animal brains implement neural circuits for adaptive behavior.

Fluorescent biosensors for probing neuronal activity and biochemical signaling *in vivo*

Masayuki Sakamoto

Kyoto University, JAPAN

ABSTRACT

To understand how neurons communicate to generate cognition, emotions, and memory, it is crucial to monitor neuronal activity and the associated biochemical signaling in the brain. Our research focuses on the design and development of fluorescent protein-based biosensors that can visualize these signals with a high signal-to-noise ratio *in vivo*. In this presentation, I will introduce our recent advancements in engineering genetically encoded indicators. First, we developed an improved red calcium indicator, RCaMP3, which features a larger dynamic range and higher fluorescence than its predecessors. This improvement allows for more precise monitoring of calcium dynamics *in vivo*, leading to a better understanding of neuronal activity and neural networks. Next, we engineered an ultrasensitive green cyclic adenosine monophosphate (cAMP) indicator, cAMPinG1, which surpasses previous indicators in both dynamic range and cAMP affinity. Using *in vivo* two-photon imaging, cAMPinG1 detected cAMP transients in the somata and dendritic spines of neurons in the mouse cortex over tens of seconds. Furthermore, dual-color two-photon imaging of RCaMP3 and cAMPinG1 enabled simultaneous measurement of population patterns in Ca^{2+} and cAMP from hundreds of neurons with single-cell resolution *in vivo*. This approach revealed dynamic interaction and information flow between Ca^{2+}, cAMP, and G-protein-coupled receptors. Overall, our multicolor suite enables detailed investigations of neuronal activity and biochemical signaling *in vivo*, facilitating the dissection of functional relationships within neural networks.