The 14th Annual
WPI-IIIS Symposium
~Science of Behaving and Sleeping Brains~

Date : Monday, December 1, 2025, 8:30 - 17:50
(Reception: 18:00 - 20:00)

Venue : 1F Hall, IIIS Building, University of Tsukuba

IIIS
INTERNATIONAL INSTITUTE FOR INTEGRATIVE SLEEP MEDICINE

筑波大学
高等研究院
Tsukuba Institute for Advanced Research

University of Tsukuba

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MOONSHOT
RESEARCH & DEVELOPMENT PROGRAM

Timetable

Opening				
8:30 - 8:45	Welcome Address	**Masashi Yanagisawa**	Director, WPI-IIIS, University of Tsukuba	
	Opening Address 1	**Akira Ukawa**	WPI Academy Director	
	Opening Address 2	**Noriko Osumi**	WPI Academiy Officer / Tohoku University	
Session 1 | Chair : Kaspar Vogt (WPI-IIIS, University of Tsukuba)				
8:45 - 9:30	Temporal dynamics of oligodendroglia in health and disease	**Erin Gibson**	Stanford University	Page 4
9:30 - 10:15	Monoaminergic regulation of mammalian sleep dynamics – recent insights and next-level questions	**Anita Lüthi**	University of Lausanne	Page 5
10:15 - 10:35	Break			
Session 2 : Keynote Lecture | Chair : Masashi Yanagisawa (WPI-IIIS, University of Tsukuba)				
10:35 - 11:35	Deconstructing the serotonin system in the mouse brain	**Liqun Luo**	Stanford University	Page 6
11:35 - 11:55	Lunch Preparation / Break			
Session 3 : Luncheon Lecture | Chair : Yu Hayashi (WPI-IIIS, University of Tsukuba / The University of Tokyo)				
11:55 - 12:40	Neurochemical and behavioral changes during NREM and REM sleep for learning in humans	**Masako Tamaki**	RIKEN CBS	Page 7
12:40 - 13:25	Sleep and the heart-brain axis	**Cameron McAlpine**	Icahn School of Medicine at Mount Sinai	Page 8
13:25 - 13:50	Photo / Break			
Poster Session | Chair : Michael Lazarus (WPI-IIIS, University of Tsukuba)				
13:50 - 14:30	Data Blitz			
14:30 - 15:30	Poster Presentation			
Session 4 | Chair : Shoi Shi (WPI-IIIS, University of Tsukuba)				
15:30 - 16:15	Sleep, Dragons, CPGs	**Lorenz Fenk**	Max Planck Institute for Biological Intelligence	Page 9
16:15 - 17:00	Genetic evidence for two independent sleep homeostats in zebrafish	**Jason Rihel**	University College London	Page 10
17:00 - 17:45	The evolution of social behaviors in nature and under domestication	**Andrés Bendesky**	Columbia University	Page 11
Closing				
17:45 - 17:50	Closing Remarks	**Takeshi Sakurai**	Vice Director, WPI-IIIS, University of Tsukuba	
Reception				
18:00 - 20:00	Reception Party			

Temporal dynamics of oligodendroglia in health and disease

Erin Gibson

Stanford University, USA

ABSTRACT

The age-related failure to generate myelinating oligodendrocytes from oligodendrocyte precursor cells (OPCs) contributes to the progressive nature of demyelinating brain disorders such as multiple sclerosis (MS) and is often associated with oligodendroglial metabolic dysfunction. The normal process of aging is associated with declining circadian (~24 hour) function, and we previously demonstrated the importance of the core circadian transcription factor BMAL1 in OPC dynamics. Circadian disruption has further been linked to metabolic dysfunction and neurodegenerative disorders like MS. However, how aging drives these deficits in OPC maturation and remyelination, and how this contributes to disease progression remain incompletely understood. Here, we posit that BMAL1 acts as an upstream homeostatic regulator of the cumulative metabolic phenotype observed in OPCs during aging and MS. We show that BMAL1 is essential for maintaining energy balance and sirtuin homeostasis in OPCs, and that its loss-of-function induces a metabolically senescent phenotype that closely mirrors the dysfunction seen in aging and MS oligodendroglia. This BMAL1-deficient state is marked by altered mitochondrial physiology, disrupted sirtuin signaling, elevated oxidative stress, and increased cellular senescence. Notably, we observe parallel disruptions in BMAL1 and sirtuins in both aged and lesion-associated MS oligodendroglia. Importantly, timed therapeutic targeting of sirtuin signaling restores OPC proliferation and differentiation with BMAL1 loss. Collectively, our work suggests that aberrant BMAL1 function with aging drives OPC metabolic dysfunction and accelerates senescence during aging and MS pathology, subsequently leading to myelination deficits. This work underscores the interplay between circadian disruption, metabolic decline, and neurodegenerative disease progression, and identifies new metabolic targets for the development of chronotherapeutic strategies aimed at promoting remyelination in aging and demyelinating disease like MS.

Monoaminergic regulation of mammalian sleep dynamics – recent insights and next-level questions

Anita Lüthi

University of Lausanne, SWITZERLAND

ABSTRACT

The monoamines noradrenaline, serotonin and dopamine are neuromodulators that enable the brain to sustain alertness, attention, and motivation by modulating cortical and subcortical substrates of waking brain states. New research, including from my lab, now shows that these monoamines are also released during states of sleep and key for sleep's dynamic progression at the spectral, architectural, autonomic and behavioral levels.

Our work has so far focused on noradrenaline, which is released during non-rapid-eye-movement (non-REM) sleep from the brainstem *locus coeruleus* on an infraslow (~50 s) interval throughout large portions of the forebrain. These infraslow noradrenergic fluctuations divide non-REM sleep into two alternating substates, with one showing high spontaneous and evoked arousability, low sleep spindle density and accelerated heart rate, while the other one is permissive for entries into REM sleep, showing high sleep spindle density and slower heart rate. Importantly, although *locus coeruleus* activity and noradrenaline release during non-REM sleep appear occasionally as high as in wakefulness, the associated brain states show spectral characteristics of incomplete arousals that are delimited to subcortical (thalamic) and autonomic arousals.

These observations break with the classical notion that monoaminergic signaling is primarily important for wakefulness and indicate a so far unanticipated fluidity of sleep states, with the brain states of non-REM sleep 'moving physiologically more closely' to wakefulness on repeated time scales. We propose that such fluidity is indispensable for sleep to reconcile two fundamental opposing needs, which is to maintain vigilance towards the environment on the one hand, while ensuring internal processing on the other hand. I will discuss the next steps in exploring the neuromodulatory conditions of mammalian sleep states. I will also propose that dysfunctional neuromodulatory regulation of sleep can cause an imbalanced response to external and internal stimuli - a possible common denominator for diverse sleep disorders.

Deconstructing the serotonin system in the mouse brain

Liqun Luo

Stanford University, USA

ABSTRACT

Serotonin powerfully modulate physiology and behavior in health and disease. In the mammalian brain, serotonin neurons are clustered in the raphe nuclei in the brainstem, but their axons innervate the entire brain. Our previous studies suggested that serotonin neurons likely comprise parallel subsystems with distinct transcriptomic features, projection patterns, input biases, physiological response properties, and behavioral functions (Ren et al., 2018; 2019). Building on these findings, I will describe three unpublished stories on (1) the architecture of serotonin projectome in the entire mouse brain; (2) modulation of female social behaviors by projection-specific serotonin neurons; (3) deconstructing the serotonin system via the receptor axis.

Neurochemical and behavioral changes during NREM and REM sleep for learning in humans

Masako Tamaki

RIKEN CBS, JAPAN

ABSTRACT

Sleep is essential for the continuity and development of life. Sleep-related problems can alter brain function and cause potentially severe psychological and behavioral consequences. However, the role of sleep in our mind and behavior is far from clear. We have previously demonstrated that non-rapid eye movement (NREM) and rapid eye movement (REM) sleep facilitates and stabilizes learning in humans. By measuring neurochemical changes during sleep, we show that the excitation-inhibition (E/I) balance increased during NREM sleep and decreased during REM sleep. Notably, the E/I balance during NREM sleep correlates with performance improvements, while the E/I balance during REM sleep correlates with stabilization of learning. Leveraging a novel method combining 7-Tesla magnetic resonance spectroscopy with polysomnography, we further show that these E/I balance shifts are closely associated with spontaneous brain oscillations and neural events during NREM and REM sleep. However, the first-night effect, a transient sleep disruption experienced in unfamiliar environments, significantly impairs learning and alters the E/I balance dynamics. These findings highlight the complementary roles of NREM and REM sleep in learning, mediated by distinct neurochemical dynamics mediated by sleep-specific brain activity, and demonstrate that sleep quality is crucial for these mechanisms to function effectively.

Sleep and the heart-brain axis

Cameron McAlpine

Icahn School of Medicine at Mount Sinai, USA

ABSTRACT

The brain and heart are vital co-dependent organs and hubs of the nervous and circulatory systems respectively. Communication between these organs is critical to health and occurs through neuronal innervation and vascular supply of immune cells and molecules. The heart-brain axis is calibrated by many factors and among the most important is sleep. Indeed, sleep is essential for cardiovascular and brain health. Yet, the bidirectional brain-body axes that connect sleep and cardiovascular pathologies are incompletely understood. Relying on mouse models and human trials, we interrogate interoceptive and immunoceptive mechanisms by which the heart regulates sleep and how sleep and its associated brain outputs modulate immune and cardiovascular function during atherosclerosis and myocardial infarction.

Session 4 **15:30 - 16:15**

Sleep, Dragons, CPGs

Lorenz Fenk

Max Planck Institute for Biological Intelligence, GERMANY

ABSTRACT

Sleep occupies roughly a third of our life time, yet an understanding of its mechanisms and functions, its evolution, or of how precisely it differs from awake states, remains rudimentary. Typically associated with physical inactivity and rest, the sleeping brain expresses rich patterns of activity that are relatively unconstrained by active behaviour and sensory input, providing a unique window into the functional organization and internal dynamics of neural circuits. I will discuss our neuroethological approach and describe a series of recent experiments that reveal the complex dynamics of sleep activity in the brain of a reptile, the Australian dragon *Pogona vitticeps*. I will conclude by providing evidence that the ultradian sleep rhythm—in this vertebrate at least—is the output of a central pattern-generator (CPG), and thus of a class of circuits usually known to control motor rhythms and action.

Genetic evidence for two independent sleep homeostats in zebrafish

Jason Rihel

University College London, UK

ABSTRACT

The nature of sleep homeostasis remains poorly explained. We previously demonstrated in zebrafish that neurons that express the inhibitory neuropeptide, Galanin, are a critical output arm of the sleep homeostat, as animals that lack Galanin fail to respond to increases in sleep pressure driven by either neuronal activity or forced wakefulness. Another proposed regulator of sleep homeostasis is the kinase, Sik3. Gain of function Sik3 mutations in rodents lead to continuous sleep need throughout the day and night, while loss of Sik3 function in many species leads to decreased sleep. If Sik3 encodes sleep pressure, does this also signal via the Galanin sleep-regulatory pathway? To test this, we first generated both gain and loss of function mutants of *sik3* and confirmed that these reproduce the sleep phenotypes observed in rodents. However, these sleep phenotypes do not require Galanin but instead depend upon functional Neuropeptide VF signalling. Moreover, acute modulation of neuronal activity induces normal rebound sleep in the complete absence of Sik3. Together, these data show that dual signals for sleep need act through independent neuronal circuits—one driven by brain-wide neuronal activity via the Galanin circuit and one driven by metabolic/nutritional state in a Sik3 dependent manner via non-Galanin circuits. Having separate channels that signal and release homeostatic sleep pressure would give animals greater flexibility to modulate sleep need when environmentally or metabolically challenged.

Session 4 | **17:00 - 17:45**

The evolution of social behaviors in nature and under domestication

Andrés Bendesky

Columbia University, USA

ABSTRACT

What mechanisms underlie the vast diversity of social behaviors we observe in nature? I will present how we leverage extreme variation in social behaviors between populations of a species and between closely-related species of vertebrates to discover the genetic, neuronal, and endocrine bases of this variation. This work has identified unifying principles and a few surprises about the evolution of social behavior.

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