Symposium 16: Understanding and modeling cerebellar functions (Sat July 31, 9-11AM JST)
Chair: Shogo Ohmae (Baylor College of Medicine) and Olivia Kim (Princeton)

9:00-9:30 Shogo Ohmae (Baylor College of Medicine, Houston, USA)
The temporal-difference error signals of the climbing fibers and their origins during cerebellar learning in mice

9:30-10:00 Olivia A. Kim (Princeton University, Princeton, USA)
Inhibition of the inferior olive is sufficient for extinction of cerebellar motor learning

10:00-10:30 Yunliang Zang (Brandeis University, Waltham, USA)
Multiplexed coding in cerebellar Purkinje neurons

10:30-11:00 Tadashi Yamazaki (Univ of Electro-Communication, Tokyo)
High-performance simulation of cerebellar neurons and microcircuits

Symposium 16 Speaker 1
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The temporal-difference error signals of the climbing fibers and their origins during cerebellar learning in mice

Recently, it has been revealed that the climbing fibers, which play the role of teachers during motor learning of the cerebellum, signal advanced and diverse information. As a pioneering work, we reported that the climbing fibers convey higher-order signals, which are markedly similar to the responses of dopamine neurons during reinforcement learning and sufficient for Temporal Difference learning (Ohmae and Medina 2015), by sending two types of error signals to the cerebellum: a retrospective error signal driven by sensory feedback after an unexpected event occurs, and a prospective error signal of unknown origin that provides the cerebellum with a prediction of the upcoming sensory event before it occurs. Here, we use eyeblink conditioning in mice to demonstrate that the prospective signal of climbing fibers has a motor-related component (*motor-CF*), which is causally linked to the predictive defensive action generated by the mouse in anticipation of an aversive airpuff stimulus to the eye. Furthermore, we used simultaneous recording and targeted electrical and optogenetic stimulation to identify a ponto-cerebellar pathway that is sufficient and necessary for generating the prospective *motor-CF* signal. Altogether, our results reveal a hardwired recurrent circuit that allows the cerebellum to activate its own climbing fiber input and essentially become its own teacher. Finally, I will discuss theoretically what role this contribution of the cerebellum itself to the teaching signal can play in the information processing of the cerebellum.

Symposium 16 Speaker 2
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Inhibition of the inferior olive is sufficient for extinction of cerebellar motor learning

Negative prediction error (NPE) signals trigger extinction, a form of inhibitory learning that suppresses learned behaviors when they are no longer useful. There have been reports of NPE signals in multiple brain regions. For instance, in the olivo-cerebellum, pauses in Purkinje cell complex spikes are correlated with NPEs during cerebellar-dependent delay eyeblink conditioning. This observation has led the field to posit that complex spike pauses are the neural NPE that triggers cerebellar extinction learning. In order to test this hypothesis, we used a viral approach to drive expression of channelrhodopsin (ChR2) in the deep cerebellar nucleus (DCN), which sends a GABAergic projection to the source of the complex spikes, the inferior olive. Stimulating these GABAergic terminals in the inferior olive could induce a complex spike pause. Mice expressing ChR2 in the DCN were trained on the delay eyeblink conditioning task, in which a tone was paired with an airpuff to the eye. After mice had learned to blink in response to the tone to protect the eye from the airpuff, photostimulatuion was presented simultaneously with the airpuff. In spite of continued airpuff presentation, mice gradually learned to stop performing the protective eyeblink response. The timecourse of this learning was remarkably similar to the timecourse of normal extinction learning, suggesting that photostimulation mimicked the NPE signals that occur during normal extinction. Thus, our results demonstrate that GABAergic cerebello-olivary neurons can generate a powerful NPE signal that is is capable of causing extinction of conditioned eyelid responses.

Symposium 16 Speaker 3

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Multiplexed coding in cerebellar Purkinje neurons

Neuronal firing patterns are crucial to underpin circuit level behaviors. In cerebellar Purkinje neurons, both spike rates and pauses are used for behavioral coding, but the cellular mechanisms causing code transitions is unclear. We use a well-validated Purkinje neuron model to explore the coding strategy that individual Purkinje neurons use to process parallel fiber inputs. We find increasing input intensity shifts Purkinje neurons from linear rate-coders to burst-pause timing-coders by triggering localized dendritic spikes. We validate dendritic spike properties with experimental data, elucidate spiking mechanisms, and predict spiking thresholds with and without inhibition. Both linear and burst-pause computations use individual branches as computational units, which challenges the traditional view of Purkinje neurons as linear point neurons. Dendritic spike thresholds can be regulated by voltage state, compartmentalized channel modulation, between-branch interaction and synaptic inhibition to expand the dynamic range of linear computation or burst-pause computation. In addition, co-activated parallel fiber inputs between branches can modify somatic maximum spike rates and pause durations to make them carry analog signals. Our results provide new insights into the strategies used by individual neurons to expand their capacity of information processing.

Symposium 16 Speaker 4
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High-performance simulation of cerebellar neurons and microcircuits

Performance of computers have been steadily increasing over decades. Currently, at the national project level, Supercomputer Fugaku, the Japanese flagship supercomputer and the world's fastest supercomputer as of June 2021, can perform basic calculations 0.5 x 10^18 times per second. At the laboratory level, Graphics Processing Units (GPUs) are affordable yet powerful and useful devices for parallel computing.
These allow us to build large-scale and realistic neural network models of the brain.
In particular, the cerebellum is a promising target for such simulation due to the large amount of available experimental data from molecular level to behavioral level.
Integrating multi-scale experimental data into a single spiking network model on powerful computers will provide a useful means to understand the computational principle of the cerebellum. In this talk, I would like to introduce our recent results obtained in my lab. First, reinforcement learning is a recent hot topic in cerebellar research. We have extended the classical Marr-Albus-Ito model, which is a supervised learning machine, by incorporating syanaptic plasticity at parallel fiber synapses on molecular layer interneurons, and demonstrated that the resulting model could act as a reinforcement learning machine known as an actor-critic method. I will explain how the model is implemented and works. Second, neurons in the cerebellum have characteristic morphological structures. For example, Purkinje cells have large dendritic trees spanning in 2D, whereas granule cells have only 4 short dendrites. Moreover, recent studies indicate that morphological structures could play important roles in information processing at the individual neuron level. I will explain our recent progress on multi-compartment modeling of cerebellar neurons and microcircuits.