ASHBi SEMINAR

Deciphering Biological Principles by Machine Learning and Mathematical Modeling

Dr Tetsuya J Kobayashi

Associate Professor,
Institute of Industrial Science, the University of Tokyo

Date: Wednesday, 10th February 2021
Time: 3:00PM–4:00PM
Venue: Zoom Online Meeting

Understanding biological principles is the ultimate goal of life science.Recent technological advancements in quantitative and comprehensive measurements primarily bioimaging and sequencing provide dynamic and detailed information on complex biological phenomena more than ever. To decipher such intricate data, informatics and mathematics are now indispensable. In this talk, I would like to show two examples how we can use machine learning and mathematics for this purpose.

In the first part, after touching on a general overview how machine learning has been and should be used in life science, I will show an application of deep neural network to unveil the regulatory laws in size regulation of microbes. This example demonstrates how machine learning can assist us in searching for rules and relations among multiple observables and their combinations.

In the second part, by using bacterial chemotaxis as an example, I want to share the idea that finding rules to reproduce observed phenomena is not the goal for understanding biological principles. A set of biological molecules, reactions and their dynamical rules implements a certain biological functions, and mathematics is necessary to grasp the functional aspects of dynamical rules. I will show how we can use information theory to clarify the functional optimality of the biochemical network for chemotaxis.

Finally, I may introduce our new attempts if time remains.

Organizer: Prof Yasuaki Hiraoka

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ASHBi SEMINAR

How gene regulation shaped the evolution of modern and archaic humans

Dr David Gokhman

Postdoctoral Research Fellow,
Department of Biology, Stanford University

Date: Thursday, 18th February 2021
Time: Noon–1:00PM
Venue: Zoom Online Meeting

To study human evolution, it is imperative to compare our genetics to that of our closest extinct relatives – the Neanderthal and Denisovan. Particularly important is gene regulation, as regulatory changes are thought to be the main driver of phenotypic differences between closely related organisms. However, ancient samples are degraded, and mapping their gene regulatory marks is largely impossible. To address this, we developed a method to reconstruct a key gene regulatory mark – DNA methylation – from ancient samples. We used these reconstructed DNA methylation maps to identify regulatory differences between modern and archaic humans. We found that genes affecting the voice box have gone through particularly extensive changes. We then turned to use these maps to shed light on the little-understood Denisovan. We present a method for reconstruction of anatomical profiles using DNA methylation patterns and data from monogenic diseases. We then apply it to the Denisovan and offer a putative morphological profile. We conclude that DNA methylation can be used as a tool to reconstruct anatomical features, including some that do not survive in the fossil record. Finally, we use massively parallel reporter assays (MPRAs) to measure the regulatory effects of each of the 14,000 single-nucleotide variants that separate modern from archaic humans. Overall, 1,791 (13%) of these loci showed active regulatory activity, and 407 (23%) of these drove differential expression between human groups. Differentially active sequences were associated with vocal tract and brain anatomy and function. Together, these works provide insight into the recent evolution of human gene regulation.

Organizer: Dr Fumitaka Inoue
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ASHBi SEMINAR

Formation, function, and regeneration of corticospinal circuits underlying skilled movements

Dr Yutaka Yoshida

Lab Director,
Burke Neurological Institute / Weill Cornell Medicine

Professor(Adjunct),
Okinawa Institute of Science and Technology Graduate School (OIST)

Date: Thursday, 4th March 2021
Time: 2:00PM–3:00PM
Venue: Zoom Online Meeting

Our lab is interested in understanding the neural circuits underlying locomotion and skilled motor behaviors in mammals. The motor neuron activity integral to these neural circuits is regulated by synaptic inputs from three main pathways: local interneuron circuits, proprioceptive sensory feedback, and descending fibers from the brain, including the corticospinal (CS) tract.

In this presentation, I will particularly focus on CS circuits. CS neurons control motor neuron activity for skilled movements such as reaching and grasping. We found how species-specific CS circuits may be formed during development. Manual dexterity in higher primates is superior to that of other animals. This trait emerged in part together with the appearance of cortico-motoneuronal (CM) connections during the evolution of the mammalian CS system, and was thought to be unique to higher primates. However, we identified CM connections in early postnatal mice, which are eventually eliminated by Sema6D-PlexA1 signaling. *PlexA1* mutant mice maintain CM connections into adulthood, resulting in superior manual dexterity compared to controls. Furthermore, we showed that species-specific regulation of *PlexA1* expression by Fezf2 may be crucial to the evolution of enhanced fine motor control in higher primates. We also demonstrated how the activity dependent, non-apoptotic Bax/Bak-caspase pathway regulates reorganization of CS motor circuits during development in mice. We further show how axonal projections of CS neurons are regulated by a repellent signaling pathway in the spinal cord. Finally, we demonstrate how CS neurons in the motor and sensory cortex differentially control skilled movements through distinct spinal interneuron connections.

In addition to the formation and function of motor circuits, we are also interested in the regeneration and reorganization of neural circuits following spinal cord injury (SCI). Time permitting, I will briefly talk about our SCI research including roles of semaphorins in inhibition of regeneration of injured CS axons at the end of my talk.

Organizer: Prof Tadashi Isa

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