Mini-Workshop on Frontiers in Biophysics

July 1st, 2024
Room 233, Faculty of Science Bldg.1, Hongo campus,
The University of Tokyo
Supported by Universal Biology Institute

Program

13:00-13:05   Opening

13:05-13:45   Anne-Florence Bitbol (EPFL)
               "Optimization and historical contingency in protein
               sequences

13:45-14:25   Yuichi Wakamoto (Univ. Tokyo)
               "Physiological adaptation and homeostasis against
               environmental and genetic perturbations"

14:25-15:05   Arvind Murugan (Univ. Chicago)
               "Neural computation through learned phase diagrams"

15:05-15:20   Coffee break

15:20-16:00   Kenshi Suzuki (Univ. Tokyo)
               TBA

16:00-16:40   Namiko Mitarai (Niels Bohr Institute)
               "The spatiotemporal dynamics of phage predation and
               competition"

16:40-17:20   Tetsuhiro Hatakeyama (Tokyo Tech.)
               "Evolvability of the toxin-adaptation system"

Abstract

Optimization and historical contingency in protein sequences
Anne-Florence Bitbol (EPFL)

Abstract: Protein sequences are shaped by functional optimization on the one hand and by evolutionary history, i.e. phylogeny, on the other hand. A multiple sequence alignment of homologous proteins contains sequences which evolved from the same ancestral sequence and have similar structure and function. In such an alignment, correlations in amino-acid usage at different sites can arise from structural and functional constraints due to coevolution, but also from historical contingency.

Correlations arising from phylogeny often confound coevolution signal from functional or structural optimization, impairing the inference of structural contacts from sequences. I will show that inferred Potts models are more robust than local statistics to these effects, which may explain their success. I will argue that phylogenetic correlations can also provide useful information for some inference tasks, especially to infer interaction partners from sequences among the paralogs of two protein families. In this case, signal from phylogeny and signal from constraints combine constructively.

Protein language models have recently been applied to sequence data, greatly advancing structure, function and mutational effect prediction. Language models trained on multiple sequence alignments capture coevolution and structural contacts, but also phylogenetic relationships. I will discuss a method we recently proposed that leverages these models to predict which proteins interact among the paralogs of two protein families, and improves the prediction of the structure of some protein complexes. Finally, I will show that these models have promising generative properties.

Physiological adaptation and homeostasis against environmental and genetic perturbations
Yuichi Wakamoto (Univ. Tokyo)

Abstract: Exposing biological cells to environmental and genetic stresses can exert global changes in gene expression and metabolic profiles. These changes can vary even among genetically identical cells, and a fraction of cells eventually adapt and reach the states that permit cells long-term survival or even stable proliferation. To understand the mechanisms of cellular adaptation, we need to answer the following crucial questions: (1) What factors determine which cells adapt and which do not? (2) Are adapted states to an identical stress solitary or plural? (3) Which parts of the molecular profile in cells are altered during adaptation? In this workshop, we present experimental results on the adaptation of Escherichia coli against environmental and genetic perturbations. We show the time-dependent significance of the expression noise of the resistant protein for survival and adaptation against antibiotic stress, the commonality and diversity of the adapted states, and the role of stoichiometry recovery of core components in adaptation. Finally, we present the characteristic stoichiometry-conserving architecture in gene expression profiles preserved from bacteria to human cells and discuss its role in simultaneous realization of adaptability and homeostasis.

Neural computation through learned phase diagrams
Arvind Murugan (Univ. Chicago)

Abstract: Our model for learning is based on neural networks, i.e., networks of linear threshold devices. Even physical realizations of neural computation, such as molecular or electrical circuits, effectively mimic these network architectures at an element-by-element level. Here, we explore an alternative paradigm for neural computation - inevitable collective physical processes that can learn in Hebbian-inspired ways without being designed to mimic a neural network element-by-element. Through theory and experiment, we show how nucleation in molecular systems can learn to recognize complex patterns in chemical or mechanical stimuli. Our work suggests that exploiting ubiquitous physical phenomena, such as nucleation, is an underexplored powerful route to neural computation without neurons.

The spatiotemporal dynamics of phage predation and competition
Namiko Mitarai (Niels Bohr Institute)

Abstract: Phages and bacteria manage to coexist and sustain ecosystems, despite limited resources for bacteria growth and heavy predation by various phages. In this seminar, we focus on the role of spatial structure in phage attack on bacterial population. We discuss the dynamics of phages infecting a dense bacterial colony outside, focusing on how much superinfection of the bacteria on the surface can protect the bacteria close to the centre of the colony. We then discuss how the T-even phage's ability to respond to secondary infection, called lysis inhibition, provides competitive advantages to the phage, and how it can affect the phage epidemic in a lawn of bacteria.

References:
- Eriksen, Rasmus Skytte, et al. "The dynamics of phage predation on a microcolony." Biophysical Journal 123.2 (2024): 147-156.
- Hvid, Ulrik, and Namiko Mitarai. "Competitive advantages of secondary adsorption-triggered lysis inhibition for T-even phages." bioRxiv (2024): 2024-02.

Evolvability of the toxin-adaptation system
Tetsuhiro Hatakeyama (Tokyo Tech.)

Abstract: In microbial communities, many cooperative interactions have been reported, working among different species and clonal cells. Besides, competitive interactions working among cells with different genotypes have mainly been reported, and those among clonal cells would be difficult to evolve, in general. However, we found an elaborate response of the yeast community against glucose depletion, in which the first adapted cells kill the latecomer cells. During glucose depletion, yeast cells release autotoxins, which can even kill the clonal cells of the ones producing them. Although these autotoxins were likely to induce mass suicide, some cells differentiated to adapt to the autotoxins without genetic changes. If nondifferentiated latecomers tried to invade the habitat, autotoxins damaged or killed the latecomers, but the differentiated cells could selectively survive.

Furthermore, we found distant yeast species maintain this toxin-adaptation system with the same autotoxins; this is puzzling because the well-known toxin-immunity system is generally weak in cheaters, which do not produce toxins but benefit from those produced by others. In this case, different toxins continue to evolve, as in an arms race, so that different species use different toxins. To address the question of the stability of the toxin-adaptation system, we analyze the evolutionary stability of the system using population dynamics. Under constant conditions, the toxin-adaptation system cannot evolve; under continuous starvation conditions, cheaters outcompete adaptive cells with the toxin-adaptation system. In continuous nutrient-rich conditions, the adaptive cells cannot beat sensitive cells that have neither toxin nor immunity. However, the toxin-adaptation system is stably maintained when the environment switches stochastically between starvation and nutrient-rich conditions, with the average duration of nutrient-rich conditions being much longer than that of starvation.

This suggests that the same toxin-adaptation system can evolve and be stably maintained in distant species under fluctuating environments with frequent starvation but will decline when the environment is stable.