Field:

Biology / Life Science

Session Topic:

Experimental evolution to understand and engineer life

Speaker:

MIZUUCHI Ryo, Waseda University

Title: Exploring life's origins through experimental evolution

How did life originate from non-living matter about four billion years ago? It is widely believed that simple self-replicating molecules gradually evolved into complex living systems. To study the evolutionary history of life, researchers often rely on fossil records or comparisons of the genomes of living organisms. However, simple molecular systems did not leave behind fossils, and genome comparisons can only reveal evolutionary events that occurred after the emergence of the last universal common ancestor—an already complex cell that gave rise to all known life. To overcome these limitations, we are working to experimentally evolve primitive molecular systems in the laboratory, allowing us to directly "witness" possible evolutionary processes that may have taken place before life began.

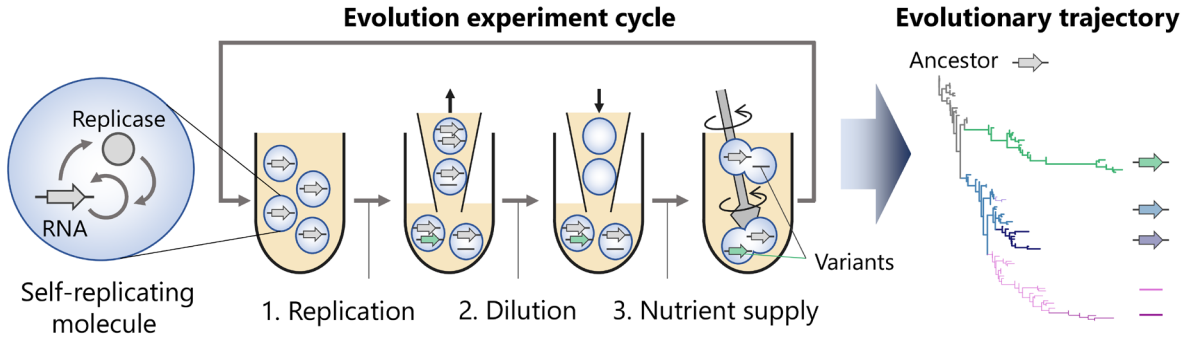
We have developed several evolvable molecular systems based on our understanding of the origins of life. One such system contains a self-replicating RNA that encodes a replicase, a protein that copies the RNA and is synthesized by a translation system [1]. When encapsulated in cell-like compartments and subjected to repeated experimental cycles of replication, dilution, and nutrient supply, the RNA can evolve spontaneously toward increased complexity. During these experiments, replication errors introduce mutations, generating RNA variants with different properties. Some variants may replicate more efficiently and increase in frequency by outcompeting others, representing a form of evolution. Using this RNA replication system, we have observed various evolutionary behaviors, including adaptation, diversification, cooperation, and functional integration, all contributing to the development of more complex replicating systems [1–3]. We are currently conducting new evolutionary experiments to further explore potential pathways that could have led to the origins of life.

References:

[1] Mizuuchi, R., Furubayashi, T., Ichihashi N. Evolutionary transition from a single RNA replicator to a multiple replicator network. *Nature Communications*, 13, 1460 (2022).

[2] Mizuuchi, R., Ichihashi, N. Sustainable replication and coevolution of cooperative RNAs in an artificial cell-like system. *Nature Ecology & Evolution*, 2, 1654–1660 (2018).

[3] Ueda, K., Mizuuchi, R., Ichihashi, N. Emergence of linkage between cooperative RNA replicators encoding replication and metabolic enzymes through experimental evolution. *PLOS Genetics*, 19, e1010471 (2023).



An overview of experimental evolution using a molecular system. A self-replicating molecule (RNA, in our case) is subjected to repeated cycles of replication, dilution, and nutrient supply. During these cycles, variant RNAs can arise and may come to dominate the RNA population depending on their replication efficiency. The diagram on the right is called a phylogenetic tree, which depicts evolutionary relationships among detected RNAs; the tip of each line represents a different RNA.

Glossary:

- **RNA:** Ribonucleic acid, a molecule that can encode genetic information (such as proteins). RNA is a polymer composed of four types of monomers (called nucleotides). While DNA is the primary genetic information carrier in most organisms today, some viruses use RNA instead. It is believed that primitive genetic systems were also based on RNA.
- **Translation system:** A set of molecules that synthesize proteins encoded by RNA. This "translation" process is a fundamental biological mechanism shared by all extant life.
- **Mutation:** A change in part of an RNA (or DNA) sequence, such as the replacement, deletion, or insertion of nucleotides. In our experiment, mutations occur due to replication errors.

Background Review Article:

- Szathmáry, E., and Maynard Smith, J., The major evolutionary transitions. *Nature*, 374, 227-232 (1995).
- Yukawa, K., Mizuuchi, R., Ichihashi, N., How prebiotic complexity increases through Darwinian evolution. *Current Opinion in Systems Biology*, 34, 100456 (2023).

Field:

Chemistry / Material Science

Session Topic:

Experimental and Computational Exploration of Three-Dimensional Biological Structures

Speaker:

YAMAMOTO Junpei, The University of Osaka

Title: Cinematography of enzymatic reactions at atomic resolutions

Determination of the actual structures of biomolecules and organelles that consist of a cell, a fundamental unit of organisms, provides indispensable information and deeper insights into the understanding of biological systems in organisms. After the first determination of the three-dimensional structure of myoglobin – a molecule responsible for oxygen storage – via X-ray crystallography by Prof. John Kendrew [1], more than 200,000 structures have now been solved and registered in the Protein Data Bank. Using the coordinates of the biomolecules as training data, computational prediction of the unsolved structures of biomolecules has been achieved [2], leading to development of new pharmaceutical drugs.

Recent trends in structural biology can be divided into two major directions: one is toward chemistry, which details how proteins/enzymes move during their function, and the other is toward biology, which seeks to understand the whole biological system, i.e. how these biomolecules and organelles are connected and work together. Computational studies complement the experimental observations and even extend the limitations of experiments.

Over the past decade, a sophisticated experimental technique has been developed for real-time visualization of chemical reactions in biomolecules at near-atomic resolutions. This technique, called time-resolved serial femtosecond X-ray crystallography (TR-SFX), using an X-ray free-electron laser (XFEL) can capture kinetically resolvable intermediates as snapshots, providing a time evolution of the three-dimensional molecular structure during a reaction [3]. By flipping through the snapshots, we can produce a molecular film of the reaction. Experimental and computational cinematography of enzymatic reactions will pave the way for a new era of enzymology.

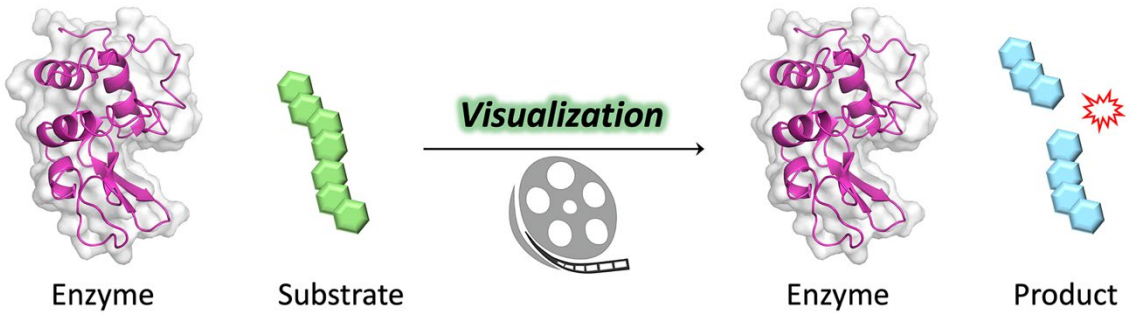


Figure. Graphical abstract of filming enzymatic reactions. Here, the lysozyme (PDB: 2LYS) reaction is shown as an example of enzymatic reactions.

References:
[1] Kendrew et al. *Nature* 181, 662-666 (1958)
[2] Jumper et al. *Nature* 596, 583-589 (2021)
[3] Maestre-Reyna et al. *Science* 382, eadd7795 (2023)

Glossary:
- X-ray crystallography【X 線結晶構造解析】: the experimental science to determine the atomic and molecular structure of a crystal. When X-rays are incident on a crystal, the beam can be diffracted in specific directions. By measuring the angles and intensities of the diffraction patterns, we can reconstruct a three-dimensional map of the density of electrons in the crystal, thus providing the atomic model structures of the molecule in the crystal.

- X-ray free electron laser【X 線自由電子レーザー】: an advanced light source producing extremely brilliant and short pulses of X-ray enough to resolve chemical bonds and reactions. Currently, the TR-SFX experiment can be performed in five facilities, i.e Linac Coherent Light Source in US, European XFEL in Germany, SwissFEL in Switzerland, SPring-8 Angstrom Compact Free Electron Laser in Japan, Pohang Accelerator Laboratory XFEL in South Korea. In addition, Shanghai XFEL in China will be launched soon.

Field:

Chemistry / Material Science

Session Topic:

Experimental and Computational Exploration of Three-Dimensional Biological Structures

Speaker:

KOSUGI Takahiro, National Institutes of Natural Sciences

Title: Computational Protein Structure Prediction and Design

Protein structure research has entered a transformative new era. Proteins are macromolecules composed of 20 different types of amino acids and folded into specific three-dimensional structures determined by their amino acids sequences. Over half a century has passed since the first success of experimental structure determination by using crystal structural analysis, and then a substantial number of protein structures have been elucidated experimentally (experimental structures > 200,000). This extensive repository of experimental structure data has been trained using advanced machine learning, resulting in the development of high-performance protein structural prediction algorithm, AlphaFold [1]. Although the task of predicting folded structures from an astronomical number of possible conformations was considered unattainable at one time, it is now possible to easily obtain a huge number of highly reliable predicted structures (predicted structures > 200 million).

Computational protein design has also advanced significantly by insights derived from extensive experimental structural data [2]. Using the technologies, many kinds of de novo designed proteins and rationally redesigned native proteins have been reported to date. The technologies for creation of proteins with novel structures and functions promise applications to a wide range of research fields or industries. We also have recently reported de novo design of adenosine triphosphate (ATP) hydrolase [3] and design of allosteric sites into a rotary molecular motor by restoring the lost functions [4]. These

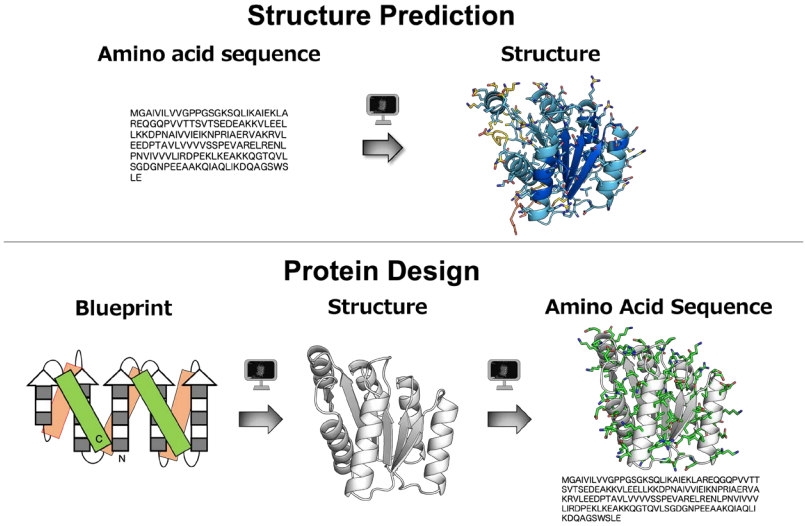


Fig. 1 Protein structure prediction (top) and design (bottom)

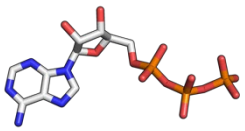
achievements were realized through the analysis of previously solved structures and the structural determination of our designed proteins.

Both experimentally determined and computationally predicted structures are opening up a bright future for broad fields.

References:
[1] Jumper, J. et al. Nature 596, 583-589 (2021).
[2] Huang, P.-S.; Boyken, S. E. and Baker D. Nature 537, 320-327 (2016).
[3] Kosugi, T.; Tanabe, M.; Koga, N. Protein Sci. in press.
[4] Kosugi, T.; Iida, T.; Tanabe, M.; Iino, R. and Koga, N. Nat. Chem. 15, 1591-1598 (2023).

- **Adenosine Triphosphate (ATP):** 【アデノシン三リン酸】

ATP is called energy currency of the cell and provides energy to drive and support many process in living cells.

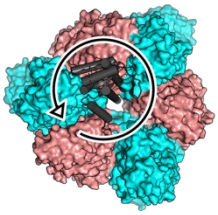


- **Allosteric site:** 【アロステリック部位】

A substance binds to this site distant from a functional site, resulting in regulation of the protein function.

- **Rotary molecular motor:** 【回転型分子モーター】

Rotary molecular motor rotates using chemical energy generated by ATP hydrolysis.



Field:
Earth Science / Environment

Session Topic:
Resourcing society: metals for the future

Speaker:
YASUKAWA, Kazutaka, The University of Tokyo

Title: Critical metal resources on the seafloor as a key to a sustainable future

Achieving a carbon-neutral society is an urgent challenge in addressing the ongoing climate change. Most of low-carbon technologies rely on critical metals such as rare-earth elements (REE) used in powerful magnets for electric vehicles and wind-power generator, or cobalt (Co) and nickel (Ni) for high-capacity lithium-ion batteries.
However, these conventional, onshore mineral resources have severe problems, including oligopoly and resource nationalism, human rights violation (e.g., child labor), and environmental pollutions (e.g., radioactive wastes from light REE deposits associated with magmatic activity).

In recent years, seafloor mineral resources have attracted attention as a new source for such industrially critical metals. Especially, deep-sea sediments enriched in REE, called "REE-rich mud" [1], and "ferromanganese (Fe-Mn) nodules" that were precipitated from seawater and contain high concentrations of Co, Ni, or Cu [2] are widely distributed in the world ocean (Fig. 1). They have tremendous resource potential [2,3]. Developing these seafloor mineral resources will be implemented by nations or companies with good compliance, which can avoid severe issues involved with current onshore mines and, thus, can be a foundation of a sustainable future.

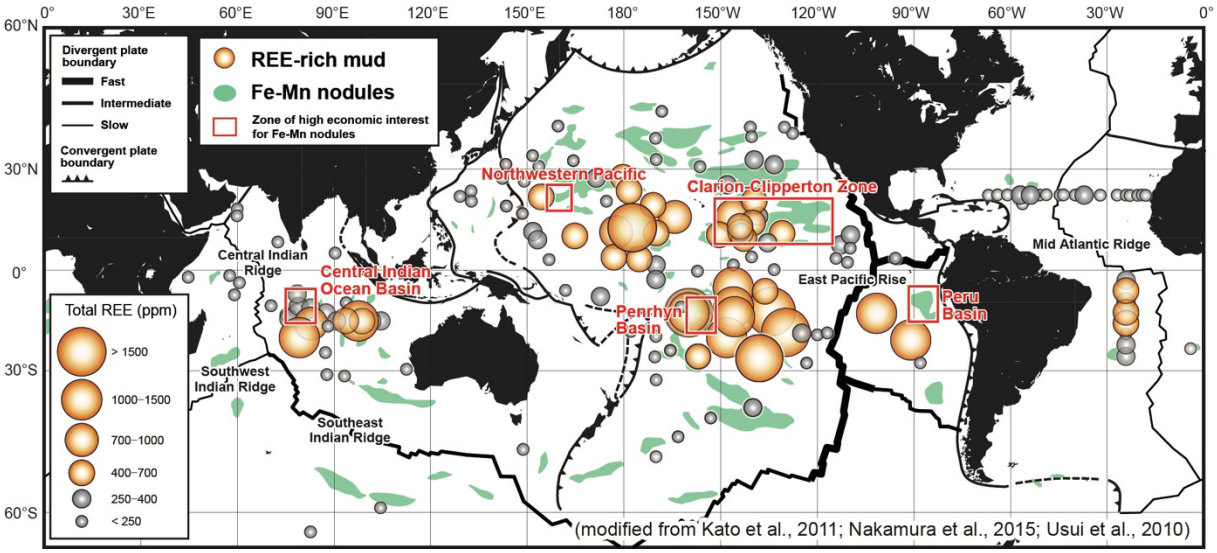


Figure 1. Global distribution of REE-rich mud (less than 2 m below seafloor) and ferromanganese nodules.

References:

[1] Kato et al. (2011) Deep-sea mud in the Pacific Ocean as a potential resource for rare-earth elements. *Nature Geoscience* 4, 535-539.

[2] Hein et al. (2020) Deep-ocean polymetallic nodules as a resource for critical materials. *Nature Reviews Earth & Environment* 1, 158-169.

[3] Takaya et al. (2018) The tremendous potential of deep-sea mud as a source of rare-earth elements. *Scientific Reports* 8, 5763.

Field:

Math / Applied Math / Informatics

Session Topic:

Singular Learning Theory

Speaker:

Kenji Nagata, National Institute for Materials Science, Japan.

Title: Introduction of Singular Learning Theory and Algebraic Geometry

It is fresh in our minds that the Nobel Prizes in Physics and Chemistry for 2024 were awarded in the field of AI[1]. The main technology of those prizes was the proposal and utilization of deep neural networks. The term "Learning Theory" in this session title refers to the field of mathematics and statistics that attempts to theoretically analyze the learning efficiency and learning performance of such deep neural networks.

In learning from given data, the amount of data naturally leads to the stability of the estimation. This is similar to the behavior of thermodynamics with respect to temperature. At low temperatures, the motion of atoms and other elements tends to be smaller, and the overall system tends to have a stable structure like a solid. Such a picture can be equated with the fact that estimation becomes stable when more data is available, leading to a theoretical clarification of the learning properties of statistical models. By taking advantage of this fact, conventional Learning Theory has been advanced by utilizing Gaussian approximation around one point of model parameter when there is a sufficient amount of data.

However, a problem arises when trying to utilize it directly for neural network training. In neural networks, there is no one-to-one correspondence between parameters and model behavior. Therefore, the model parameters are not fixed at a single point when there is a sufficiently large amount of data. Furthermore, the parameter set forms a manifold including singular points in the parameter space. The learning theory of such neural networks requires a departure from analysis centered on Gaussian approximation. This is a very difficult subject. The name "Singular Learning Theory" was coined as a field to discuss learning theory for models with such singularities. Professor Sumio Watanabe, a pioneer in this field, used algebraic geometry as a technique for this analysis[2]. Algebraic geometry is a field of mathematics that discusses manifolds as solutions to (polynomial) = 0. It has a high affinity as a technique for handling manifolds in the parameter space of neural networks.

In this talk, I will introduce Prof. Sumio Watanabe's contributions to Singular Learning Theory. As an example, I will introduce his work on Bayesian inference, in which he clarified the asymptotic behavior of Bayesian free energy under the condition that the number of data is sufficiently large[2], and the information criterion, WAIC[3] and WBIC[4], which were proposed based on his theory.

References:

[1] https://www.nobelprize.org/all-nobel-prizes-2024/
[2] S. Watanabe, Neural Computation, Vol.13, No.4, pp.899-933, 2001.
[3] S. Watanabe, Journal of machine learning research, Vol.11, No.12, pp.3571-3594, 2010.
[4] S. Watanabe, Journal of machine learning research, Vol.14, pp. 867-897, 2013.

Field:
Math / Applied Math / Informatics

Session Topic:
Singular Learning Theory

Speaker:
Keisuke Yano, The Institute of Statistical Mathematics

Title: On assessing generalization performance in various predictive scenarios

Assessing generalization performance is a central concern in data-science research. Since Akaike introduced the information criterion (AIC), many techniques, most notably cross validation, have been developed to estimate out-of-sample predictive accuracy. Yet, the recent success of deep neural networks has put singular learning machines, whose parameterizations are not uniquely determined, and unfortunately, classical criteria often break down in this setting.

Watanabe's Widely Applicable Information Criterion (WAIC) [1] provides the first theoretically sound assessment tool for singular models. WAIC relies only on the posterior variances of sample-wise log-likelihoods, so it can be obtained from a single Bayesian simulation on the full data set; this avoids the repeated retraining required by conventional cross validation.

In this talk, I survey several recent extensions of WAIC that accommodate modern predictive scenarios: Weighted inference like covariate-shift adaptation; Learning with over-parameterized models that has overabundant model parameters [3]; Evaluation with general loss functions that move beyond log-likelihood to task-specific risk measures [4].

References:
[1] S. Watanabe. Equations of states in singular statistical estimation. *Neural Networks*, 23:20–34, 2010.
[2] Y. Iba and K. Yano, Posterior Covariance Information Criterion for Weighted Inference, *Neural Computation*, vol. 35, 1340–1361, 2023.
[3] A. Okuno and K. Yano, A generalization gap estimation for overparameterized models via Langevin functional variance, *Journal of Computational and Graphical Statistics*, vol. 32, 1287-1295, 2023.
[4] Posterior Covariance Information Criterion for arbitrary loss functions (with Y. Iba; arXiv:2206.05887; in minor revision)

Field:
Medical / Neuroscience

Session Topic:
Non-conventional organismal biology

Speaker:
Kyoko Miura, Kumamoto University / Kyushu University

Title: Unlocking biological time: insights from the naked mole-rat and the turquoise killifish

With the rapid advances in next-generation sequencing and genome editing technologies, research on non-conventional or 'non-model' organisms has expanded significantly in recent years. These developments are opening new avenues to explore biological phenomena that were previously difficult to study using standard laboratory animals alone. This session highlights two fascinating non-model animals that exhibit unique ways of controlling biological time. The naked mole-rat, the longest-lived rodent, shows little sign of aging and is highly resistant to age-related diseases such as cancer and Alzheimer's disease–maintaining a youthful state for most of its life. Meanwhile, the turquoise killifish is a small fish that can enter a long-term dormant state in response to environmental changes, effectively 'pausing time' during early development. Studying these unusual animals provides valuable insights into how living organisms manage biological time.
In this talk, I will introduce recent advances in non-conventional organism research and present our study on the mechanisms of aging and disease resistance in the naked mole-rat.

References:
[1] The Naked Mole-Rat as a Model for Healthy Aging. Oka K, Yamakawa M, Kawamura Y, Kutsukake N and Miura K. *Annu. Rev, Anim. Biosci* 15:11:207-226. 2023.
[2] Cellular senescence induction leads to progressive cell death via the INK4a-RB pathway in naked mole-rats. Kawamura Y, Oka K, Miura K. et al. *EMBO J.* 15;42(16):e111133. 2023

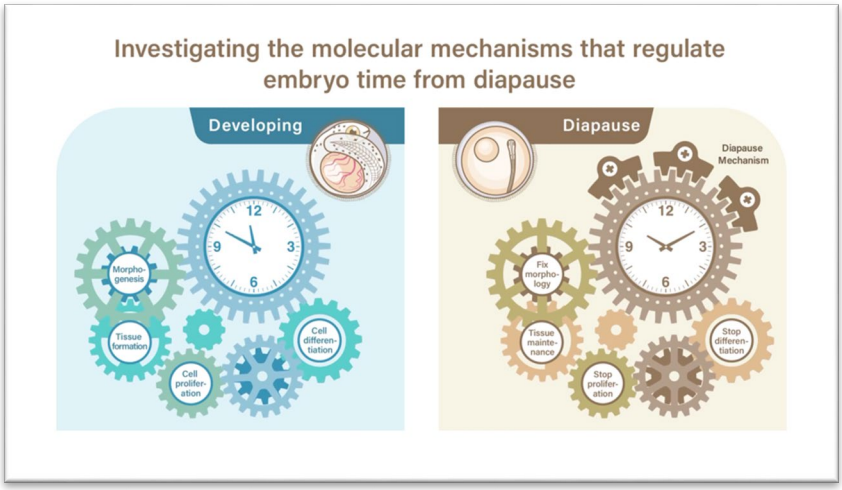
Field:
Medical / Neuroscience

Session Topic:
Non-conventional organismal biology

Speaker:
Masayuki Oginuma, RIKEN Cluster for Pioneering Research / Center for Biosystems Dynamics Research (BDR)

Title: Chrono-Developmental Biology: Exploring the Blueprint of Time via Killifish Diapause

Organisms possess a remarkable "blueprint of time" that orchestrates embryonic development—from fertilization to body formation—according to a precisely regulated genetic clock. However, the molecular mechanisms underlying this temporal regulation remain largely unknown. The African turquoise killifish Nothobranchius furzeri, which inhabits ephemeral ponds, has evolved the ability to enter diapause—a unique developmental arrest that pauses this embryonic clock for extended periods. Our laboratory is focused on uncovering the molecular basis of diapause, a highly specialized mechanism for suspending embryonic time. We have established a rapid and efficient method for functional analysis of genes in the turquoise killifish, allowing us to investigate the genetic regulation of embryonic timing in unprecedented detail. By analyzing the dynamics and functions of candidate genes involved in diapause, we aim to elucidate the full picture of the "blueprint of time." Ultimately, we seek to extend our findings to understand temporal regulation across diverse species. In this meeting, I will present novel findings on embryonic clock mechanisms revealed through studies of diapause.



References:
[1] Oginuma M, Nishida M, Ohmura-Adachi T, et al. Rapid reverse genetics systems for Nothobranchius furzeri, a suitable model organism to study vertebrate aging. *Scientific Reports*, 12(1), 11628 (2022)

Field:

Physics / Astrophysics

Session Topic:

Quantum Information Science and Technology 2025

Speaker:

Kosuke Mitarai, Graduate School of Engineering Science / Center for Quantum Information and Quantum Biology, Osaka University

Title: Simulating Quantum Systems with Quantum Computers: New Approaches for Understanding Materials and Fundamental Physics

How do materials behave at the atomic scale? How do electrons interact to give rise to the properties of matter? These questions are fundamental to physics, chemistry, and materials science, yet solving quantum many-body problems on classical computers becomes exponentially difficult as system size increases. This is because the number of quantum states that must be considered grows exponentially with the number of interacting particles.

Quantum computers, which operate based on quantum mechanics, offer a promising alternative. Unlike classical computers, which use bits (0s and 1s), quantum computers use qubits, which can exist in multiple states simultaneously. This allows them to explore quantum interactions in ways that classical methods cannot.

Despite their potential, today's quantum computers are still in their early stages, facing limitations in qubit count and computational accuracy. To make quantum simulation practical, we are developing new algorithms for both near-term devices and future large-scale quantum computers.

For current and near-term quantum devices, we focus on Quantum-Selected Configuration Interaction (QSCI) [1], a hybrid quantum-classical method that reduces computational cost by selecting only the most relevant electronic configurations in quantum chemistry calculations. For future large-scale quantum computers, we explore Quantum Signal Processing for Perturbation Theory [2], which systematically incorporates higher-order corrections, and Schwinger model simulations [3], which estimate computational resources needed for fundamental physics problems. These studies provide insights into how quantum computers might one day surpass classical methods.

By explaining these challenges and advancements, this talk aims to provide an accessible introduction to the role of quantum computing in materials science, chemistry, and fundamental physics.

References:

[1] K. Kanno, M. Kohda, R. Imai, S. Koh, K. Mitarai, W. Mizukami, Y. O. Nakagawa, "Quantum-Selected Configuration Interaction: Classical Diagonalization of Hamiltonians in Subspaces Selected by Quantum Computers," *arXiv:2302.11320* (2023).

[2] K. Mitarai, K. Toyoizumi, W. Mizukami, "Perturbation Theory with Quantum Signal Processing," *Quantum*, **7**, 1000-1000 (2023).

[3] K. Sakamoto, H. Morisaki, J. Haruna, E. Itou, K. Fujii, K. Mitarai, "End-to-End Complexity for Simulating the Schwinger Model on Quantum Computers," *Quantum*, **8**, 1474 (2024).