Abstract Book

DAIKIN International Symposium on Physics of Intelligence

-- Statistical Mechanics and Machine Learning: A Powerful Combination for Data Analysis --

ISPI2024: Nov. 6-8, 2024 @Koshiba Hall, The University of Tokyo

Institute for Physics of Intelligence

DAIKIN

JST JPMJCR1912 "Deciphering intracellular phenomena through information flow"

Statistical Physics of Generative Diffusion

Marc Mézard
Università Bocconi

Abstract: Generative models, in which one trains an algorithm to generate samples ‘similar’ to those of a data base, is a major new direction developed in machine learning in the recent years. In particular, generative models based on diffusion equations have become the state of the art, notably for image generation. However, the reasons for this spectacular technological success are not well understood, and neither are its limitations.

After an introduction to this topic, the talk will focus on the behavior of generative diffusion in the high-dimensional limit, where data are formed by a very large number of variables. Using methods from statistical physics, and through a detailed analysis of two well-controlled high-dimensional cases, we explain the various phase transitions that take place during the dynamics of generation. Implications for practical design of score functions guiding the diffusion will also be discussed.

Infinite-Fold Way of Meta-Scaling

Sho Yaida
Meta

Abstract: Large neural networks perform extremely well in practice, providing the backbone of modern machine learning. Training such models to their best capacities, however, involves carefully tuning lots of knobs called hyperparameters. In this talk, I will present principled ways to scale these hyperparameters so as to ensure that empirical insights obtained at small scales nicely transfer to large scales.

Hierarchical data structures through the lenses of diffusion models

Antonio Sclocchi
École polytechnique fédérale de Lausanne

Abstract: The success of deep learning with high-dimensional data relies on the fact that natural data are highly structured. A key aspect of this structure is hierarchical compositionality, yet quantifying it remains a challenge.

In this talk, we explore how diffusion models can serve as a tool to probe the hierarchical structure of data. We consider a context-free generative model of hierarchical data and show the distinct behaviors of high- and low-level features during a noising-denoising process. Specifically, we find that high-level features undergo a sharp transition in reconstruction probability at a specific noise level, while low-level features recombine into new data from different classes. This behavior of latent features leads to correlated changes in real-space variables, resulting in a diverging correlation length at the transition.

We validate these predictions in experiments with real data, using state-of-the-art diffusion models for both images and texts. Remarkably, both modalities exhibit a growing correlation length in changing features at the transition of the noising-denoising process.

Overall, these results highlight the potential of hierarchical models in capturing non-trivial data structures and offer new theoretical insights for understanding generative AI.

Spatial heterogeneity of deep learning

Hajime Yoshino
Osaka University

Abstract: In this talk, we discuss our recent studies on multi-layer perceptrons (MLP) from the statistical mechanics perspective. On one hand, we built a minimalistic model amenable to detailed theoretical and numerical analysis. Specifically, we studied the two standard learning scenarios used in the statistical mechanics of machine learning, namely the random scenario (random constraint satisfaction problem) and the teacher-student scenario (Bayes optimal statistical inference), applied to MLP. Using the replica method we found that the design space of the MLP (the Gardner volume [1]) becomes very heterogeneous in the real space when it is over-parameterized: It is more strongly constrained closer to the input/output boundaries like in (crystalline or glassy) solids while remaining more free like a liquid in the center [2,3]. The thickness of the solid phases grows logarithmically with the number of training data, which implies exponential growth of the capacity with the depth of the network. We also performed numerical simulations of the machine learning by the MLP in the random/teacher-student scenario and more realistic tasks (classification/de-noising) based on MNIST image data.
The numerical results suggest that simple stochastic learning algorithms (Monte Carlo [3] and SGD) exhibit long-time, diffusive dynamics over a nearly flat energy landscape where the ensemble of the typical machines exhibits spatial heterogeneity.

This talk is based on collaborations with A. G. Cavaliere, Y. Orito, and T. Yoshida.

[1] Elisabeth Gardner, J. Phys. A 21, 257 (1988).
[2] Hajime Yoshino, SciPost Phys. Core 2, 005 (2020).
[3] Hajime Yoshino, Phys. Rev. Research 5, 033068 (2023).

Modeling biological networks using Natural Language Processing (NLP)

Mariko Okada
Imperial College London & Osaka University

Abstract: Mathematical analysis of gene regulatory networks is important for understanding the mechanism of cell fate decision and human diseases. In particular, the gene activity dynamics arising from the networks have been reported to be useful as biomarkers for human diseases. However, various bottlenecks exist in the construction of mathematical models of the regulatory networks. Among these, the identification of the network structure has so far required the reading of a huge number of papers, which has been the most manpower-intensive step. Therefore, our group is trying to develop a method to identify gene-gene interactions and regulatory networks using natural language processing (NLP) from the information in the scientific papers. In particular, large language model (LLM)-based methods have proven to be useful in identifying large-scale cellular networks in a context-dependent manner (. In this presentation, I will introduce a few examples of our NLP-based modelling approach.

References

Imoto H, Yamashiro S, Okada M. A text-based computational framework for patient-specific modeling for classification of cancers. iScience, 10.1016/j.isci.2022.103944, 2022.

Arakane K, Ormersbach F, Imoto H, Okada M. Extending BioMASS to construct mathematical models from external knowledge. Bioinformatics Advances, 4(1) vbae042, 2024.

Tsutsui M, Okada M. DynProfiler: A Python package for comprehensive analysis and interpretation of signaling dynamics leveraged by deep learning techniques. Bioinformatics Advances, in press, 2024.

Gene expression network analysis of thymic T-cell differentiation using interaction information

Shinsuke Uda, Atsushi Hatano[A]

Yamaguchi University, Niigata University[A]

Abstract: The precursors of thymic T-cells, which are the command centers of the immune system, differentiate and mature in the thymus. The understanding of the differentiation process of thymic T-cells has been understood well at the cellular level. However, it remains poorly understood at the genetic level. To reveal the differentiation process at the genetic level, we acquired the two data sets at the single cell level and analyzed the data set from an information theoretic approach. The two data sets consist of the gene expression data set and the membrane protein expression data set, which were acquired by next generation sequencer and fluorescence-activated cell sorting, respectively. We inferred the gene interaction networks by interaction information and extracted characteristic genes and gene interactions based on network statistics, which was obtained from the network structure, for each differentiated cell type. The characteristic genes were suggested to be involved in cell differentiation by statistical clustering method. In addition, the part of characteristic gene interactions suggested the possibility related to immune system.

Intracelluar information analysis in RAS-MAPK signaling

Yasushi Sako
RIKEN

Abstract: The RAS-MAPK system is a protein reaction network in animal cells, controlling the cell fates including proliferation, differentiation, and cell death responding to various extracellular signaling molecules. Dysregulation of this system causes genetic diseases and cancer affecting diverse tissues. To better understand the regulation mechanism of this system, we employed information flow analysis based on transfer entropy (TE) between the activation dynamics of two proteins, SOS and RAF, direct upstream and downstream molecules for a key element, RAS. SOS is an activator of RAS and RAF is a RAS effector that leads MAPK activation. TE calculation has been difficult for intracellular reactions because it requires a huge data set and strong computational power. However, we recently have reported a method for TE assessment applicable to relatively small numbers of time sequences utilizing a Gaussian approximation of the response distributions (Imaizumi et al. 2022). We stimulated HeLa cells with epidermal growth factor (EGF) to stimulate the RAS-MAPK system and calculated the TE time courses. Significant levels of information flow were found from SOS to RAF (forward) and RAF to SOS (backward). The backward flow was caused by feedback regulations. In addition, the property of the TE wave suggested multiple-track information flows. This suggestion was supported in the analyses for the input (EGF dose) dependency, and the responses to a MEK inhibitor and a SOS mutation found in a genetic disease. Our findings demonstrate that reaction network analysis based on TE holds significant promise for molecular pharmacology and pathology applications.

Physical modeling of embryonic transcriptomes identifies collective modes of gene expression

Dominic Skinner
École polytechnique fédérale de Lausanne

Abstract: Starting from one totipotent cell, complex multicellular organisms form through a series of differentiation and morphogenetic events, culminating in a multitude of cell types arranged in a functional and intricate spatial pattern. To do so, cells coordinate with each other, resulting in dynamics which follow a precise developmental trajectory, constraining the space of possible embryo-to-embryo variation. Using recent single-cell sequencing data of early ascidian embryos, we leverage natural variation together with modeling and inference techniques from statistical physics to investigate development at the level of a complete interconnected embryo. After developing a robust and biophysically motivated approach to identifying distinct transcriptomic states or cell types, a statistical analysis reveals correlations within embryos and across cell types demonstrating the presence of collective variation. From these intra-embryo correlations, we infer minimal networks of cell-cell interactions using spin glass-like models, which reveal collective modes of gene expression.

Learning and active mechanics

Vincenzo Vitelli
University of Chicago

Abstract: Physical learning is an emerging paradigm in science and engineering whereby materials acquire desired macroscopic behaviors by exposure to examples. So far, it has been applied to static properties such as elastic moduli and self-assembled structures encoded in minima of an energy landscape. In this talk, I discuss extensions of this paradigm to dynamic functionalities, such as motion and shape change, that are instead encoded in limit cycles or pathways of a dynamical system. Two ingredients are needed to learn time-dependent behaviors irrespective of experimental platforms: (i) learning rules with time delays and (ii) exposure to examples that break time-reversal symmetry during training. After providing a hands-on demonstration of these requirements using programmable LEGO toys, I will turn to realistic particle-based simulations where the training rules are not programmed on a computer. Instead, they emerge from active physico-chemical processes involving the causal propagation of fields, like in recent experiments on moving oil droplets with chemotactic signaling. Such trainable particles can self-assemble into structures that move or change shape on demand, either by retrieving the dynamic behavior previously seen during training, or by learning on the fly. This rich phenomenology is captured by a modified Hopfield spin model amenable to analytical treatment. The principles illustrated here provide a step towards von Neumann's dream of engineering synthetic living systems that adapt to the environment.

Image-based inference for epithelial mechanics

Kaoru Sugimura, Shuji Ishihara
The University of Tokyo

Abstract: Measuring forces and mechanical properties of cells is essential to decipher the mechanical control of tissue development and repair. We have formulated Bayesian force inference and mechanical parameter inference, both utilizing image data of epithelial cells to infer physical quantities. In addition, we have employed Bayesian inversion stress microscopy for stress measurements on a monolayer of mammalian epithelial cells. These methods have been validated for accuracy and robustness through tests using synthetic and in vivo data. In this symposium, I will discuss how these methods have helped elucidate the mechanisms underlying cell rearrangement and cell competition.

Emergent time scales of epistasis in protein evolution

Francesco Zamponi
Sapienza University

Abstract: We introduce a data-driven epistatic model of protein evolution, capable of generating evolutionary trajectories spanning very different time scales reaching from individual mutations to diverged homologs. Our in silico evolution encompasses random nucleotide mutations, insertions and deletions, and models selection using a fitness landscape, which is inferred via a generative probabilistic model for protein families. I will show that the proposed framework accurately reproduces the sequence statistics of both short-time (experimental) and long-time (natural) protein evolution, suggesting applicability also to relatively data-poor intermediate evolutionary time scales, which are currently inaccessible to evolution experiments. Our model uncovers a highly collective nature of epistasis, gradually changing the fitness effect of mutations in a diverging sequence context, rather than acting via strong interactions between individual mutations. This collective nature triggers the emergence of a long evolutionary time scale, separating fast mutational processes inside a given sequence context, from the slow evolution of the context itself. The model quantitatively reproduces epistatic phenomena such as contingency and entrenchment, as well as the loss of predictability in protein evolution observed in deep mutational scanning experiments of distant homologs. It thereby deepens our understanding of the interplay between mutation and selection in shaping protein diversity and novel functions, allows one to statistically forecast evolution, and challenges the prevailing independent-site models of protein evolution, which are unable to capture the fundamental importance of epistasis.

Unified Understanding of Nonlinear Rheology in Jammed Amorphous Solids

Takeshi Kawasaki
Nagoya University

Abstract: Amorphous solids exhibit elastic behavior under slow strain, maintaining linear elasticity until a yield point is reached, beyond which they transition to a plastic state. However, near the jamming transition density, their behavior changes significantly. In addition to elastic responses at very small strains, these materials may exhibit shear softening, shear melting, or shear hardening before ultimately yielding. Such complex nonlinear responses are observed even in frictionless and athermal systems [1].

In this talk, beginning with fundamental concepts of the jamming transition, I present recent work on a unified understanding of these nonlinear responses through extensive numerical simulations. Here we studied two- and three-dimensional jammed packings under athermal quasi-static (AQS) shear strain for frictionless particles interacting via harmonic or Hertzian potentials. Different initial packing configurations were prepared through mechanical training before applying strain. Notably, we found that while both stress and pressure are highly sensitive to strain and initial conditions, their ratio reveals shear softening behavior over an exceptionally wide strain range up to the yield point, regardless of the initial configurations. This finding suggests that shear softening is a central mechanism governing criticality near the jamming transition. Additionally, we provide a simple scaling argument to explain these results. Our study offers a comprehensive perspective on the complex nonlinear rheology near the jamming transition and addresses previous debates on scaling relationships in this regime [2].

[1] J. Boschan, D Vågberg, E. Somfai, and B. P. Tighe, Soft Matter 12, 5450 (2016).
[2] T. Kawasaki and K. Miyazaki, Phys. Rev. Lett. 132, 268201 (2024).

Vortex reversal is a precursor of confined bacterial turbulence

Daiki Nishiguchi
Institute of Science Tokyo

Abstract: Being intrinsically out-of-equilibrium, active matter systems, composed of interacting self-propelled particles, exhibit a remarkable tendency to self-organization and the onset of collective behavior. One of the most visible manifestations of their collective dynamics is the emergence of self-sustained spatiotemporal chaotic flows termed active turbulence. It is observed in a wide variety of active matter systems such as concentrated suspensions of motile bacteria, epithelial cell sheets, and Janus particles. Active turbulence possesses a characteristic length scale of vortices, which allows organizing their motion into stable vortex arrays under geometrical confinements or in the presence of periodic obstacles that are comparable to the vortex size. However, a fundamental question of how such regular vortices transit to chaotic motion in unconstrained systems remains elusive.

In this talk, I will begin by reviewing our current understanding of how active turbulence is transformed into stabilized vortices. I will then introduce our recent work addressing the reverse process: how such vortex order become destabilized, ultimately leading back to turbulence [D. Nishiguchi et al. arXiv:2407.05269 (2024)]. By combining large-scale experiments, high-resolution computer modeling, and analytical theory, we have discovered a generic sequence of transitions occurring in bacterial suspensions confined in cylindrical wells of varying radii. As the confinement is weakened by increasing the well's radius, we observed that persistent vortex motion is destabilized and transit to periodic vortex reversals, four-vortex pulsations, and then well-developed active turbulence. The reversals were also captured as a periodic oscillation of vortices in our numerical simulations and analytical theory. Our findings indicate that the vortex reversal is a precursor of turbulence-like behavior in bacterial and related active systems.

Exploration of Novel Proteins Based on Design Principles

Nobuyasu Koga
Osaka University

Abstract: Protein molecules carry out their functions based on the three-dimensional structures specified by their amino acid sequences. The space of protein sequences is astronomically vast, and the proteins discovered by nature constitute only a tiny fraction of the entire protein sequence space. We have developed principles and methods based on the structural data of naturally occurring proteins and physicochemistry to design proteins from scratch. We have successfully designed a variety of protein structures, including those with topologies not found in nature, with atomic resolution. Furthermore, we also designed an ATPase with P-loop motif, based on the design principles. The presentation will highlight these researches and discuss future prospects.

Learning Multiscale Genome and Cellular Organization

Jian Ma
Carnegie Mellon University

Abstract: Despite significant advancements in high-throughput data acquisition in genomics and cell biology, our understanding of the diverse cell types within the human body remains limited. In particular, the principles governing intracellular molecular spatial organization and interaction, as well as cellular spatial organization within complex tissues, are still largely unclear. A major challenge lies in developing computational methods capable of integrating heterogeneous and multiscale molecular, cellular, and tissue information. In this talk, I will discuss our recent work on creating integrative approaches to advance regulatory genomics using single-cell spatial epigenomics. These methods hold the potential to reveal new insights into fundamental genome structure, gene regulation, and cellular function within complex tissues, across a wide range of biological contexts in both health and disease.

Learning in intelligence systems

Hiroshi Makino
Keio University

Abstract: Recent years have seen a resurgence of interactions between artificial intelligence (AI) and neuroscience. AI research has the potential to provide new theories and hypotheses about how the brain solves computational problems, while neuroscience could contribute new algorithms and neural network architectures that endow machines with cognitive abilities resembling those of humans and other animals. Despite this, direct comparisons between artificial and biological intelligent systems remain limited. Here, we explore behaviors and neural representations in both systems across a variety of behavioral paradigms, spanning different domains of intelligence. By training both mice and artificial deep reinforcement learning (RL) agents on the same tasks and analyzing the resulting task representations in their respective neural networks, we found that learning in the mouse cortex exhibits key features similar to those of deep RL algorithms. For instance, after conducting a systematic hyperparameter search and evaluating thousands of deep RL models, we found that AI models optimized for behavioral outcomes more closely recapitulated the neural representation patterns observed in biological systems. Moreover, by formulating AI-derived theoretical predictions and empirically testing them in mice, we discovered that the brain composes novel behaviors through a simple arithmetic combination of pre-acquired action-value representations and a stochastic policy. These results underscore the remarkable parallels in behavior and neural representations between the two systems and demonstrate the value of comparative approaches. Our interdisciplinary methodology may define new research trajectories for AI and neuroscience, deepening our understanding of the brain while enhancing machine intelligence through neuroscience-inspired algorithms.

Dynamic landscapes during cellular growth and diversification

Gautum Reddy
Princeton University

Abstract: The complexity of gene regulatory networks in multicellular organisms makes interpretable low-dimensional models highly desirable. An attractive geometric picture, attributed to Waddington, visualizes the differentiation of a cell into diverse functional types as gradient flow on a dynamic potential landscape, but it is unclear under what biological constraints this metaphor is mathematically precise. In this talk, I will show that gene regulatory strategies that guide the growth and development of a single cell to a target distribution of cell types are described by time-dependent potential landscapes, under certain specific growth-control tradeoffs. The theory highlights a conceptual link between nonequilibrium thermodynamics and cellular decision-making during development.

Decoding layers of spatial and temporal organization in multicellular systems

Mor Nitzan
Hebrew University of Jerusalem

Abstract: Gene expression profiles of cellular populations, generated by single-cell RNA sequencing, contain rich information about biological states and collective multicellular behavior that are lost during the experiment or not directly accessible, including cell type, cell cycle phase, gene regulatory patterns, cell-cell communication, and location within the tissue-of-origin. In this talk I will discuss several methods, based on a combination of spectral, machine learning, and dynamical systems approaches, to disentangle and enhance particular spatiotemporal signals that cellular populations encode, and interpret their manifestation across space and time in tissues.

Computing with Neural Manifolds: Towards a Multi-Scale Understanding of Biological and Artificial Neural Networks

SueYeon Chung
New York University & Flatiron Institute

Abstract: Recent breakthroughs in experimental neuroscience and machine learning have opened new frontiers in understanding the computational principles governing neural circuits and artificial neural networks (ANNs). Both biological and artificial systems exhibit an astonishing degree of orchestrated information processing capabilities across multiple scales - from the microscopic responses of individual neurons to the emergent macroscopic phenomena of cognition and task functions. At the mesoscopic scale, the structures of neuron population activities manifest themselves as neural representations. Neural computation can be viewed as a series of transformations of these representations through various processing stages of the brain. The primary focus of my lab's research is to develop theories of neural representations that describe the principles of neural coding and, importantly, capture the complex structure of real data from both biological and artificial systems.

In this talk, I will present three related approaches that leverage techniques from statistical physics, machine learning, and geometry to study the multi-scale nature of neural computation. First, I will introduce new statistical mechanical theories that connect geometric structures that arise from neural responses (i.e., neural manifolds) to the efficiency of neural representations in implementing a task. Second, I will employ these theories to analyze how these representations evolve across scales, shaped by the properties of single neurons and the transformations across distinct brain regions. Finally, I will demonstrate how insights from the theories of neural representations can elucidate why certain ANN models better predict neural data, facilitating model comparison and selection.

Speaker Bio: SueYeon Chung is an Assistant Professor in the Center for Neural Science at NYU, with a joint appointment in the Center for Computational Neuroscience at the Flatiron Institute, an internal research division of the Simons Foundation. She is also an affiliated faculty member at the Center for Data

Science and Cognition & Perception Program at NYU. Prior to joining NYU, she was a Postdoctoral Fellow in the Center for Theoretical Neuroscience at Columbia University, and BCS Fellow in Computation at MIT. Before that, she received a Ph.D. in applied physics at Harvard University, and a B.A. in mathematics and physics at Cornell University. She received the Klingenstein-Simons Fellowship Award in Neuroscience in 2023, and the Sloan Research Fellowship in 2024. Her main research interests lie at the intersection between statistical physics, neuroscience and machine learning, with a particular focus on understanding and interpreting neural computation in biological and artificial neural networks by employing methods from neural network theory, statistical physics, and high-dimensional statistics.

A temporal signaling code to specify immune responses

Alexander Hoffmann
University of California, Los Angeles

Abstract: Immune sentinel cells must initiate the appropriate immune response upon sensing the presence of diverse pathogens. Our studies have revealed that immune sentinel cells have evolved a temporal code in the dynamics of the stimulus-responsive transcription factor NFκB.

I will present recent studies that unraveled several aspects of this temporal code, e.g. 1) using an information theoretic approach to identify the codewords, termed “signaling codons”, 2) using a machine learning approach to characterize their reliability and points of confusion, 3) using dynamical systems modeling to characterize the molecular circuits that allow for their encoding, and 4) the development of ‘digital twin’ macrophages that allow us to investigate the molecular basis and biological roles of heterogeneity.

NFκB Signaling: information theory, signaling codons

Adelaja, A., Taylor, B., Sheu, K.M., Liu, Y., Luecke, S., Hoffmann, A. 2021 Six distinct NFκB signaling codons convey discrete information to distinguish stimuli and enable appropriate macrophage responses. Immunity, 54, pp.916-930. e7. PMID: 33979588

Tang, Y., Adelaja, A., Ye, X, Deeds, E., Wollman, R., Hoffmann, A. 2021. Quantifying information accumulation encoded in the dynamics of biochemical signaling. Nature Communications 12, pp. pp.1272. PMID: 33627672, PMC7904837

Decoding signaling codons to specify immune response gene expression and epigenetic memory

Sen S., Cheng, Z., Sheu, K., Chen, E.Y.H., Hoffmann, A. 2020 Gene Regulatory Strategies that Decode the Duration of NFkB Dynamics Contribute to LPS- versus TNF-Specific Gene Expression. Cell Systems, 10, pp.1-14. PMID:31972132,

PMC7047529

Cheng, Q.J., Ohta, S., Sheu, K.M., Spreafico, R., Adelaja, A., Taylor, B., Hoffmann, A. 2021 NFκB dynamics determine the stimulus-specificity of epigenomic reprogramming in macrophages. Science, 372, pp.1349-1353; PMID: 34140389.

Pharmacologic manipulation of the code

Behar, M., Barken, D., Werner, S.L., Hoffmann, A. 2013 The Dynamics of Signaling as a Pharmacological Target. Cell, 155, pp.448-461. PMID: 24120141, PMC3856316

Infinite Limits of Deep Neural Networks and Scaling Laws

Cengiz Pehlevan
Harvard University

Abstract: I will review recent developments in obtaining a mean-field description of the high-dimensional learning dynamics of deep neural networks. These mean-field theories result from various infinite limits, including width, depth and attention-heads. I will present applications of these ideas to neural scaling laws in lazy and feature-learning regimes.

Why do we die from cancer? A multi-omics approach

Shinpei Kawaoka
Tohoku University & Kyoto University

Abstract: Cancer remains one of the leading causes of death globally. In Japan alone, about 380,000 people die from cancer each year, making up 25% of total deaths. Our research group is tackling the fundamental question: why do we die from cancer? We seek to understand how cancer disrupts overall bodily functions. To do this, we use a multi-omics approach, comparing samples from healthy and cancer-affected individuals. Multi-omics measures genes, proteins, metabolites, hormones, and more to provide a comprehensive view of biological states. Unlike hypothesis-driven studies, multi-omics seeks to identify molecules that may explain observed phenomena in a less-biased manner. For instance, we demonstrated that breast cancer can remotely reprogram circadian gene expression in the liver (PMID: 28388556). Additionally, we found that intestinal tumors alter liver cholesterol metabolism, leading to liver inflammation (PMID: 29592890). Through these analyses, we identified Nicotinamide-N-methyltransferase (Nnmt) as a key enzyme mediating cancer's effects on the host (PMID: 35705545 & 37014628). We also use spatial gene expression analyses, combining gene expression data with tissue histology, to examine livers from cancer-bearing mice (PMID: 36694005) and human lymph nodes with breast cancer metastasis (PMID: 39173531). These studies revealed cancer's role in disrupting liver zonation (spatially regulated gene expression in the liver) and immune cell exclusion in lymph nodes. Furthermore, time-series blood analyses in breast cancer patients uncovered a set of cytokines predictive of treatment outcomes (PMID: 38238427). In this study, the importance of time-series datasets was highlighted. In summary, we are leveraging less-biased multi-omics techniques to better understand how cancer undermines organismal homeostasis. My presentation will highlight these findings, with particular focus on challenges in data collection, analysis, and interpretation.

Nonequilibrium thermodynamics and optimal transport for diffusion models

Sosuke Ito
The University of Tokyo

Abstract: Diffusion models are a class of generative models that have recently been widely used. Diffusion models were introduced inspired by nonequilibrium thermodynamics [1], and techniques from optimal transport theory have been used [2]. Here we discuss the relationships between nonequilibrium thermodynamics and optimal transport theory [3-5], and their application to diffusion models [6]. We introduce a thermodynamic trade-off relation for diffusion models, which gives a fundamental bound on the accuracy of the data. We also discuss an optimal protocol for generating accurate data based on the thermodynamic trade-off relation, and relationships between the optimal protocol and the existing well-used methods.

[1] J. Sohl-Dickstein, E. Weiss, N. Maheswaranathan & S. Ganguli, In International conference on machine learning (pp. 2256-2265) PMLR (2015)
[2] Y. Lipman, R. T. Chen, H. Ben-Hamu, M. Nickel & M. Le, M. In The Eleventh International Conference on Learning Representations (2023).
[3] M. Nakazato, S. Ito, Physical Review Research, 3(4), 043093 (2021).
[4] A. Dechant, S-I. Sasa, S. Ito, Physical Review Research, 4(1), L012034 (2022).
[5] S. Ito, Information Geometry, 7(Suppl 1), 441-483 (2024).
[6] K. Ikeda, T. Uda, D. Okanohara & S. Ito, arXiv:2407.04495 (2024).

Information-Theoretic Measure of Time Irreversibility

Sunghan Ro
Massachusetts Institute of Technology

Abstract: Understanding how complex systems evolve over time is crucial for the study of learning. While time irreversibility can provide valuable insights into system evolution, its measurement remains challenging due to the high dimensionality of state spaces of complex systems. In this talk, I will present an information-theoretic measure of time irreversibility that can be adopted to analyze systems with many degrees of freedom, including biological and active many-body systems. The measure evaluates the Kullback-Leibler divergence between forward and backward realizations of system state transitions using cross-parsing algorithms. I will demonstrate how this measure can be employed to characterize time-irreversible events by applying it to data from numerical simulations and experimental observations of E. coli in a rectifying device.

Neural Canonical Transformations

Lei Wang
Chinese Academy of Sciences

Abstract: Canonical transformations play a fundamental role in simplifying and solving physical systems, yet designing and implementing them can be particularly challenging in many-particle settings. By reinterpreting canonical transformations through the lens of learnable diffeomorphisms, we uncover a fruitful connection to flow models from generative modeling. The key challenge is then to incorporate physical constraints such as symplecticity, unitarity, and permutation equivariance into these flow transformations. In this talk, I will present the design and application of neural canonical transformations across several physical problems, including identifying nonlinear modes of peptides, computing equations of state for electron gases, and solving vibrational spectra of molecules and solids.