論 文 の 内 容 の 要 旨

論文題目　Estimation of entropy production by machine learning
（機械学習によるエントロピー生成の推定）

氏　　名　大坪　舜

In the last two decades, our understanding of thermodynamics of small systems has developed substantially, being formulated as stochastic thermodynamics. For example, when a pulling experiment of a folded RNA is conducted, the dissipated work fluctuates from sample to sample even if the experimental condition is fixed. This is in contrast to conventional thermodynamics. To take such stochasticity into account, thermodynamic quantities are defined at the level of single realizations. This formulation has enabled us to discover universal laws that hold for nonequilibrium processes far from equilibrium.

Among such laws, a notable example is the fluctuation theorem, which states that the entropy production is the logarithm of the ratio between forward and backward transition probabilities, representing the time-reversal symmetry breaking. A closely related concept is information thermodynamics, which reveals the interplay between the thermodynamic entropy and information flow. Finally, yet another fundamental relation called the thermodynamic uncertainty relation (TUR) has been discovered recently. The TUR is a tradeoff relation between the entropy production and the fluctuation of currents, and thus gives a tight constraint on possible realization of currents.

On another front, living systems are primary examples where nonequilibrium is essential. Especially, cellular processes are often enhanced by nonequilibrium driving to perform their function. Recent developments in experiments enable us to observe such cellular activities at the level close to elementary stochastic processes. For example, primary cilia, hairlike organelles protruding from the surface of eukaryotic cells, show apparently random behavior. A recent study has shown that its nonequilibrium activity is detectable as circulating probability currents in some phase space mapped from the real space dynamics, and thus the motion of primary cilia is not thermal.

To quantify such nonequilibrium activity beyond the qualitative classification of thermal or active, the estimation of the entropy production is demanded. However, its estimation from experimental data is still not an easily tractable problem. For example, the estimation of the forward and backward transition probabilities requires full details of the stochastic dynamics, and thus the direct use of the fluctuation theorem is not practical.

The present thesis is devoted to develop a framework for estimating the entropy production solely on the basis of time-series data using variational approaches with machine learning. Especially, we consider to apply the TUR for the estimation. This approach has been recently proposed, where the main idea is as follows: (i) view the TUR as an inequality that gives a lower bound on the entropy production, (ii) find an optimal current that maximizes the lower bound, and (iii) use the lower bound as an estimate of the entropy production. This variational approach is expected to be data efficient since it requires only the mean and the variance of a single fluctuating current. In addition, it has been numerically suggested that this method can give the exact estimate by taking the short-time limit of the optimizing current (short-time TUR).

There are three fundamental remaining issues in the previous researches. First, the equality condition of the short-time TUR has not been analytically studied, and thus its range of applicability has been unclear. Second, only a few previous studies actually consider the maximization process in numerical setups that are applicable to practical situations. Third, its practical effectiveness is not well understood: for example, whether this approach works well at high-dimensional or non-stationary setups.

To overcome these issues and to go beyond, we present two main results in this thesis. In the first part, we resolve the above issues and develop a practical estimation method for stationary dynamics. In the second part, we theoretically reveal the relationship between several variational representations of the entropy production including the short-time TUR. Then, an estimation method for non-stationary dynamics is provided. Our method is of practical significance since all it requires are trajectory data without prior knowledge of the system parameters. In addition, we find that our method performs well even in high-dimensional, non-linear, and non-stationary dynamics. Below, we explain these points in more detail.

In the first part of this thesis, we formulate the short-time TUR and analytically study the equality condition. As a result, we show that the short-time TUR can give the exact estimate of the entropy production in overdamped Langevin dynamics, while this is not the case in general Markov jump processes. In addition, we show that the short-time TUR holds for the partial entropy production of subsystems under autonomous interaction, which reveals the hierarchy of the estimation when the optimizing currents are partially masked.

On the basis of the above theoretical result, we develop a practical estimator of the entropy production for overdamped Langevin dynamics in the stationary state by combining the short-time TUR with machine learning techniques such as the gradient ascent. The learning estimator works solely on the basis of trajectory data without requiring prior knowledge of the parameters of the underlying dynamics. We numerically demonstrate that the learning estimator performs well even in nonlinear and high-dimensional Langevin dynamics. We also discuss the estimation in Markov jump processes and develop a learning estimator for them. It is found that the learning estimator is robust against the choice of the sampling interval of trajectory data, while the exact estimation is shown to be impossible in general.

The estimation of the entropy production in non-stationary dynamics is yet another important but largely unexplored issue. In the second part of this thesis, we extend the learning algorithm developed in the first part to non-stationary dynamics. First, we establish the theoretical relationship between two variational representations of the entropy production: one is the short-time TUR, and the other is Neural Estimator for Entropy Production (NEEP) which has been proposed after the short-time TUR. Especially, we show that the short-time TUR gives a tighter bound on the entropy production than the NEEP in Langevin dynamics by deriving an intermediate variational representation of them. In addition, we reveal that the NEEP is related to a dual representation of the Kullback-Leibler divergence, and show that the NEEP is also applicable to non-stationary dynamics.

Next, we develop an efficient algorithm for the non-stationary estimation on the basis of the variational representations. For the non-stationary estimation, an ensemble of trajectories sampled from repeated experiments is necessary, in contrast to the stationary case where a single long trajectory is enough. To take advantage of this setup, we propose a method that finds the optimal currents continuously in time using a feedforward neural network, namely using the optimal current at one time to help finding the optimal currents in the near time. Indeed, we numerically find that the estimate of our method converges not only by increasing the number of trajectories but also by increasing the number of time instances contained in each trajectory, which is of practical importance since preparing a large number of trajectories may not be easy.

Meanwhile, as a side issue to the foregoing main two results, we study information-thermodynamic efficiencies of F_1-ATPase (or F_1). F_1 is a molecular motor, which rotates and converts chemical energy into mechanical work reversibly and very efficiently. According to recent experiments, the F_1 keeps the internal heat dissipation close to zero. A theoretical study has shown that a reaction-diffusion model of the F_1 reproduces its energetics, suggesting that the feedback structure plays a certain role. Since a feedback usually entails information flow, F_1 is interesting from the information-thermodynamic perspective. However, a quantitative understanding of the interplay between heat dissipation and information flow has been lacking. In this thesis, we numerically study the information flow and the information-thermodynamic dissipation, which is a partial entropy production defined by heat dissipation minus information flow, on the basis of the reaction-diffusion model. We show that in the free rotation setup, the rotational degree of freedom plays a role of Maxwell's demon, which acquires information of the internal state. From this perspective, the small internal heat dissipation can be understood as a consequence of the feedback control by Maxwell's demon.

In summary, we have made a platform for applying machine learning to the estimation of the entropy production by variational methods. Our method has been shown to perform well even in high-dimensional, non-linear and non-stationary dynamics, and thus is applicable to a broad class of stochastic dynamics. Its application to real experimental data including biological ones is an important future issue. In addition, we have theoretically established the variational representations of the entropy production. We expect that these representations are useful for the future searching of universal laws regarding the entropy production far from equilibrium.