Thermodynamic uncertainty relation for Markov jump processes

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Many complex biomolecular dynamics can be modeled as Markov jump processes on a suitable graph. In such Markov processes, near-equilibrium fluctuations are completely characterized by dissipation due to one general principle: the fluctuation-dissipation theorem. However, far from equilibrium generally it is difficult to infer information about dissipation. Recently, a new universal principle has been proposed [1][2] for Markov jump processes, which states that even at arbitrarily far away from equilibrium, fluctuation still regulates dissipation. Here we review recent progress in this topic and rederive a relation within this principle called 'thermodynamic uncertainty relation'.

INTRODUCTION

Biomolecular systems like enzymatic reactions, molecular motors, and transcription machinery can be modeled as Markov jump processes. In such systems, it is generally difficult for the experimenter to measure the dissipation rate across all the mesoscopic configurations modeled as Markov states. Therefore, it is desirable to have a way to infer information about dissipation from the easier-to-measure current fluctuation around the steady state. Indeed, there is a long history of using fluctuation to infer dissipation in the near-equilibrium regime: the fluctuation-dissipation theorem allows one to use near-equilibrium fluctuation to deduce the non-equilibrium response of the system within the linear response framework. In this term paper, we review the recent progress in Markov jump processes that use dynamical current fluctuations to infer dissipation rate in the non-equilibrium dynamics [1][2][3]. This recently proposed connection between fluctuation and dissipation can be thought of a non-equilibrium generalization of the fluctuation-dissipation theorem, which only holds in the near-equilibrium regime. While the fluctuation-dissipation theorem is an equality that relates the two quantities that it is named after, the far-from-equilibrium analog is an inequality stating that the fluctuation sets a lower bound on the dissipation rate.

In this paper, we first review the formalism of Markov process, and apply large deviation theory to constraint current fluctuation in such processes. We then focus on a single edge, by approximating the flow along this edge as a Poisson process, we obtain its so-called Level 2.5 large deviation function. Then we show that under saddle point approximation, we can analytically solve the large deviation function for the entire graph. We then truncate the Taylor series at small thermodynamic force, and show that the first term bounds the entire series, thus obtaining a bound on the large deviation function for the entire Markov chain. This is the central inequality for the non-equilibrium analog of the fluctuation-dissipation theorem, which contains all vector quantities (with components being the edges of the graph). We can weaken the bound by summing over weighted edges of the graph, and obtain a scalar version, called the 'thermodynamic uncertainty relation' for current fluctuations in the Markov chain, which states that the fluctuation of the currents normalized by the mean is bounded the dissipation rate. The 'thermodynamic uncertainty relation' has already found many useful applications in biomolecular systems [4][5][6], and can be used as a guide for further experimental design.

Markov jump processes on a graph

A Markov state usually represents a collection of some coarse-grained physical microstates. The probability of occupying state x at time t is denoted as $p_t(x)$, and we use bold symbol $\boldsymbol{p_t}$ to denote the vector quantity with components being $p_t(x)$. We use $r(x, y)$ to represent the transition rate between Markov states x and y. Then the current flowing from x to y is given by $j^{p_t}(x, y) = p_t(x)r(x, y) - p_t(y)r(y, x)$. The state $p_t(x)$ evolves according to the Master equation

$$\frac{\partial p_t(x)}{\partial t} = \sum_{y \neq x} j^{p_t}(x, y). \tag{1}$$

When the condition $r(y, x) > 0$ whenever $r(x, y) > 0$ is satisfied, the Markov chain will eventually evolve to some steady-state distribution $\boldsymbol{\pi} = \lim_{t\to\infty} \boldsymbol{p}_t$. The steady-state distribution $\boldsymbol{\pi}$ in general need not satisfy the detail-balanced condition $\boldsymbol{j}^{\pi} = 0$ (see Fig.1 for an illustration of Markov chain).

When the detailed-balance is broken, it is customary to use the thermodynamic force $F^p(x, y)$ to characterize the extent of its brokenness,

$$F^p(x, y) = \ln \frac{p(x)r(x, y)}{p(y)r(y, x)}. \tag{2}$$

In the steady-state, the dissipation rate for the edge xy is given by $\sigma^{\pi}(x, y) = j^{\pi}(x, y)F^{\pi}(x, y)$, and the dissipation rate across the entire Markov chain is

$$\Sigma^{\pi} = \sum_{x<y} \sigma^{\pi}(x, y) = \sum_{x<y} j^{\pi}(x, y)F^{\pi}(x, y), \tag{3}$$

where $x < y$ is to avoid double-counting.

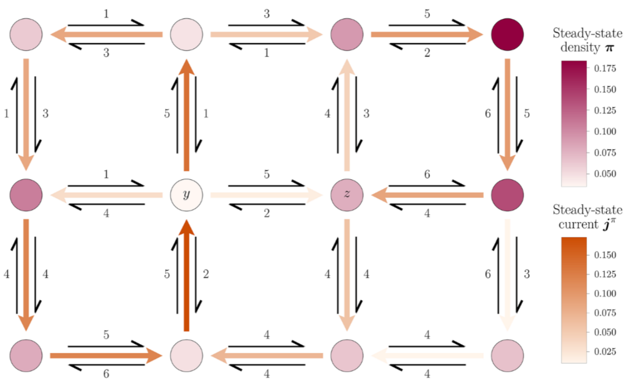

FIG. 1. An illustration for a Markov jump processes on a graph [3]. Each Markov state (circles in the figure) is shaded according to its steady-state density $\boldsymbol{\pi}$. Black arrows represent the transition rates between states, and the shaded arrows denote current $\boldsymbol{j}^\pi$.

Flows between Markov states and the large deviation function

In a single realization of the Markov jump process, the average flow from a state x to y over some long observation time T is given by

$$q(y,z) = \frac{1}{T}\int_0^T dt\delta_{x(t^-),y}\delta_{x(t^+),z}, \tag{4}$$

where $x(t^-)$ denotes the state immediately before time t and $x(t^+)$ immediately after time t. There is considerable correlation between successive jumps along a single edge, which is characterized by the correlation time-scale τ_{cor}. However, for $T \gg \tau_{cor}$, the jumps are essentially memoryless and can be approximated by a Poisson process. Therefore, in a particular realization, the probability of observing Q jumps from y to z is given by $P(Q) = \lambda^Q e^{-\lambda}/Q!$. Demanding that the average number of jumps λ to be the same as the expected number for a given distribution $p(y)$, we have $\lambda = Tp(y)r(y,z)$.

We can also identify $Q = q(y,z)T$, so that for $T \gg \tau_{cor}$,

$$P(p(y), q(y,z)) \asymp \frac{(Tp(y)r(y,z))^{Tq(y,z)}e^{-Tp(y)r(y,z)}}{(Tq(y,z))!}, \tag{5}$$

where we use $\asymp$ to denote 'asymptotic to".

On the other hand, the probability distribution for $q(y,z)$ and $p(y)$ represents the fluctuations away from the corresponding steady-state distributions in finite observation time. For large T, the distribution satisfies the large deviation form

$$P(p(y), q(y,z)) \asymp e^{-TI(p(y),q(y,z))}, \tag{6}$$

where $I(p(y), q(y,z))$ is the large deviation function that quantifies the fluctuations away from steady-state.

Equating Eqn.(5) and Eqn.(6), we obtain the form of large deviation function

$$I(p(y), q(y,z)) = p(y)r(y,z) - q(y,z) + q(y,z)\ln\frac{q(y,z)}{p(y)r(y,z)}. \tag{7}$$

To obtain the large deviation function $I(\boldsymbol{p},\boldsymbol{q})$, we need to not only sum over all the $I(p(y), q(y,z))$ for individual edges, but also impose probability conservation $\sum_z (q(y,z) - q(z,y)) = 0, \forall y$. Therefore, we have

$$I(\boldsymbol{p},\boldsymbol{q}) = \begin{cases} \sum_{y<z} I(p(y), q(y,z)) & \boldsymbol{q} \text{ conserves probability} \\ \infty & \text{otherwise.} \end{cases} \tag{8}$$

Similarly, the current fluctuations $P(p(y), j(y,z))$ are governed by the large deviation function $I(p(y), j(y,z))$ asymptotically. Its probability $P(p(y), j(y,z))$ is obtained by marginalizing over $q(y,z)$ and $q(z,y)$ under the constraint $j(y,z) = q(y,z) - q(z,y)$. For large T, each individual jump is essentially uncorrelated, so we can treat the forward and backward process independently, $I(p(y), j(y,z)) \simeq [I(p(y), q(y,z)) + I(p(z), q(y,z))]|_{j(y,z)=q(y,z)-q(z,y)}$. The large T limit allows us to perform a saddle point approximation such that the marginalization over $q(y,z)$ is dominated by the smallest term,

$$\begin{aligned} &\sum_{q(y,z)} I(p(y), j(y,z)) \\ &\simeq \inf_{q(y,z)} I(p(y), q(y,z)) + I(p(z), q(y,z) - j(y,z)). \end{aligned} \tag{9}$$

This function is minimized at

$$q_\star(y,z) = \frac{1}{2}[j(y,z) + \sqrt{j(y,z)^2 + a^p(y,z)^2}], \tag{10}$$

where $a^p(y,z) \equiv 2(p(y)p(z)r(y,z)r(z,y))^{1/2}$. We can plug the minimizer $q_\star(y,z)$ into Eqn.(9) to obtain

$$\begin{aligned} &\Psi(p(y), p(z), j(y,z)) \\ &\equiv \sum_{q(y,z)} I(p(y), j(y,z)) \\ &\simeq \sqrt{j^p(y,z)^2 + a^p(y,z)^2} - \sqrt{j(y,z)^2 + a^p(y,z)^2} \\ &\quad + j(y,z)\left(\operatorname{arcsinh}\frac{j(y,z)}{a^p(y,z)} - \operatorname{arcsinh}\frac{j^p(y,z)}{a^p(y,z)}\right). \end{aligned} \tag{11}$$

Therefore, we arrive at the large deviation function for current fluctuations

$$I(\boldsymbol{p},\boldsymbol{j}) = \begin{cases} \sum_{y<z} \Psi(p(y), p(z), j(y,z)) & \boldsymbol{j} \text{ conserves probability} \\ \infty & \text{otherwise.} \end{cases} \tag{12}$$

A bound on large deviation function

We can rewrite Ψ in terms of thermodynamic force F^p (Eqn.(2)), noticing that $j^p a^p = \sinh(F^p/2)$,

$$\begin{aligned}\Psi =& j^p\Bigg[\coth\frac{F^p}{2} - \frac{\bar{j}F^p}{2} + \bar{j}\text{arcsinh}\left(\bar{j}\sinh\frac{F^p}{2}\right) \\ &- \sqrt{\bar{j}^2 + \text{csch}^2\frac{F^p}{2}}\Bigg],\end{aligned} \tag{13}$$

where $\bar{j} \equiv j/j^p$. We can now Taylor expand Ψ in small F^p,

$$\Psi = j^p\left[\frac{(\bar{j}-1)^2F^p}{4} - \frac{(\bar{j}^2-1)^2(F^p)^3}{192} + \mathcal{O}((F^p)^5)\right]. \tag{14}$$

It turns out that the first term Ψ_{quad} bounds the entire series,

$$\Psi \le \Psi_{\text{quad}} \equiv \frac{(\bar{j}-1)^2F^pj^p}{4} = \frac{(\bar{j}-1)^2\sigma^p}{4}, \tag{15}$$

as we can easily verify that the remainder $\Delta \equiv \Psi_{\text{quad}} - \Psi$ satisfies

$$\frac{\partial\Delta}{\partial\bar{j}} = j^p\left[\text{arcsinh}\left(\bar{j}\sinh\frac{F^p}{2}\right) - \frac{\bar{j}F^p}{2}\right], \tag{16}$$

which implies that Δ is monotonically increasing with $\bar{j}-1$. So for $\bar{j} > 1$, $\Delta > \Delta|_{\bar{j}=1} = 0$. Therefore, we obtained a bound on the large deviation function itself (for $\boldsymbol{j}$ that conserves probability)

$$\begin{aligned}I(\boldsymbol{p},\boldsymbol{j}) \le I_{\text{quad}}(\boldsymbol{p},\boldsymbol{j}) &\equiv \sum_{y<z}\frac{(\bar{j}(y,z)-1)^2\sigma^p(y,z)}{4} \\ &= \sum_{y<z}\frac{\sigma^p(y,z)}{4j^p(y,z)^2}(j(y,z)-j^p(y,z))^2.\end{aligned} \tag{17}$$

Note that by construction $I_{\text{quad}}(\boldsymbol{p},\boldsymbol{j})$ has the same curvature as the full $I(\boldsymbol{p},\boldsymbol{j})$, and that at steady-state $I(\boldsymbol{\pi},\boldsymbol{j^\pi}) = I_{\text{quad}}(\boldsymbol{\pi},\boldsymbol{j^\pi}) = 0$, $I_{\text{quad}}(\boldsymbol{p},\boldsymbol{j})$ is the tightest quadratic upper bound on $I(\boldsymbol{p},\boldsymbol{j})$.

Thermodynamic uncertainty relation as a corollary

The bound on large deviation function $I(\boldsymbol{p},\boldsymbol{j})$ Eqn.(17) contains all vector quantities, and is difficult to use in practice because experiments usually cannot resolve all the details in a system with large number of Markov states. Therefore, a scalar version of this bound is desirable as it allows one to sum over all the edges on the graph and directly infer information about the system as a whole. Let's consider the scalar current j_d

$$j_d = \boldsymbol{j}\cdot\boldsymbol{d} \equiv \sum_{y<z} j(y,z)d(y,z), \tag{18}$$

which is an edge-weighted sum of individual currents $j(y,z)$. One has the freedom to choose different $\boldsymbol{d}$ to suit different purposes. For example, choosing $\boldsymbol{d} = \boldsymbol{F^p}$ makes the scalar current same as dissipation rate. The probability distribution for the scalar current also adopts the large deviation form, $P(j_d) \asymp e^{-TI(j_d)}$. Similar to the calculation of marginalizing over $q(y,z)$ to obtain Ψ, we can perform a saddle point approximation and write

$$I(j_d) \simeq \inf_{\boldsymbol{p},\boldsymbol{j}|\boldsymbol{j}\cdot\boldsymbol{d}=j_d} I(\boldsymbol{p},\boldsymbol{j}). \tag{19}$$

And in particular,

$$\begin{aligned}I(j_d) \le I(\boldsymbol{\pi},\frac{j_d}{j_d^\pi}\boldsymbol{j}^\pi) &\le I_{\text{quad}}(\boldsymbol{\pi},\frac{j_d}{j_d^\pi}\boldsymbol{j}^\pi) \\ &= \frac{1}{4}\left(\frac{j_d}{j_d^\pi}-1\right)^2\sum_{y<z}\sigma^\pi(y,z) \\ &= \frac{(j_d-j_d^\pi)^2\Sigma^\pi}{4(j_d^\pi)^2},\end{aligned} \tag{20}$$

where $j_d^\pi = \boldsymbol{j}^\pi\cdot\boldsymbol{d}$, and in the second inequality we have used Eqn.(17). Note that $\text{var}(j_d) = 1/I''(j_d)$, so we have $1/\text{var}(j_d) = I''(j_d) \le \Sigma^\pi/2(j_d^\pi)^2$, or

$$\frac{2(j_d^\pi)^2}{\text{var}(j_d)} \le \Sigma^\pi. \tag{21}$$

Eqn.(21) is called the 'thermodynamic uncertainty relation' because its familiar form of variance normalized by the mean-squared.

Discussion

In this paper, we review the newly proposed relation between fluctuation and dissipation in Markov jump processes that holds arbitrarily far from equilibrium [1]-[3]. We show that the bound on large deviation function (Eqn.(17)) is the tightest quadratic upper bound, and its weaken form for scalar current leads to the 'thermodynamic uncertainty relation' (Eqn.(21)). Although this uncertainty relation is not the strongest bound we can write down for such Markov processes, the benefit is that it avoids the calculation of individual entropy production rate σ^π and focus on the system as a whole. These newly discovered relations can be applied to study interesting far from equilibrium many-body dynamics like biophysical/biochemical processes that can be modeled as Markov jumps.

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