Inferring dissipation from the violation of Fluctuation-Dissipation Theorem for Markov systems

Shou-Wen Wang1,2

1Department of Engineering Physics, Tsinghua University, Beijing, 100086, China
2Beijing Computational Science Research Center, Beijing, 100094, China

(Dated: October 31, 2017)

The Harada-Sasa equality elegantly connects the dissipation of a moving object with its measurable violation of the Fluctuation-Dissipation Theorem (FDT). Although proven for Langevin processes, its application to Markov processes has remained unclear, especially when the local dissipation contributes asymmetrically to the forward and backward transitions. Here, we show that, while the FDT violation persists surprisingly in the high frequency limit due to this asymmetry, the Harada-Sasa equality is restored by neglecting this high frequency violation, and furthermore, by assuming that not only the dissipation per jump is small, as compared to the thermal energy unit, but also its variation along the observed direction. In fact, these assumptions lead to an effective Langevin dynamics, thus rationalizing the result. The symmetric case is unique, as it has a much smaller deviation from the Harada-Sasa equality, thus allowing for larger discreteness.

Introduction. The recent development of technology has allowed direct observation and manipulation of objects at the scale of micrometer or even nanometer. This reveals a strongly fluctuating world, and opens up a new field to explore experimentally tiny systems that operate out of equilibrium. Among various experimental systems, molecular motors are super stars 1–3, while colloid particles contained in laser traps are also commonly used to verify theoretical observations 4. Please refer to recent reviews for more details about recent experimental progress 5,7.

An important way to investigate a stochastic system is to study its spontaneous fluctuation and the elicited response. For the recorded velocity \( \dot{x}_t \) of a particle, its spontaneous fluctuation is captured by the temporal correlation function: \( C_x(t - \tau) = \langle (\dot{x}_t - \dot{x}_\tau)(\dot{x}_t - \dot{x}_\tau) \rangle_{ss} \), with \( \langle \cdot \rangle_{ss} \) denoting the average over the stationary ensemble. On the other hand, the response to a small external perturbation is given by \( R_x(t - \tau) = \delta(\dot{x}_t)/\delta h_{\tau} \), with \( h_{\tau} \) the external force applied to the particle at time \( \tau \). For equilibrium systems, these two functions are closely related through the fundamental Fluctuation-Dissipation Theorem (FDT) 8,10, which in the Fourier space reads

\[
\tilde{C}_x(\omega) = 2T \tilde{R}_x(\omega),
\]  

where prime gives the real part of the response spectrum. The violation of this relation indicates that the system is driven out of equilibrium, which has been exploited to understand glassy systems 11,12, hair bundles 13 and the cytoskeleton network 14. The connection between response and fluctuation in non-equilibrium steady state has been clarified recently 15,19.

For systems described by Langevin equations, Harada and Sasa have shown that the violation of FDT gives the dissipation rate \( \dot{q} \) for this observed variable 20,22:

\[
\langle \dot{x} \rangle^2_{ss} + \int_{-\infty}^{\infty} \left[ \tilde{C}_x(\omega) - 2T \tilde{R}_x(\omega) \right] d\omega = \frac{\dot{q}}{\gamma},
\]  

with \( \gamma \) the friction coefficient. This Harada-Sasa equality is valid generally, regardless of the inertia effect and nonlinearity. When the friction has memory effect, modification is needed 23. This relation has been applied successfully to infer the energetics of molecular motors 24,25. It is also a promising tool to estimate dissipation of stochastic systems when having access to only a subset of variables, according to our recent study 26. It has also been generalized to study spatially extended stochastic systems in the context of active matter 27,28.

Seemingly very general, yet it is not valid for arbitrary Markov processes, a much more general description of stochastic systems 29. Theoretically, Langevin processes can be understood as a special class of Markov jumping processes that has a continuous state space. Indeed, Lippiello et al. have shown that the Harada-Sasa equality is recovered in the context of Markov jumping processes when entropy production in the medium, i.e., dissipation divided by temperature, is small for each jump 30, a salient feature of Langevin processes. However, they have assumed that the local dissipation contributes symmetrically to the forward and backward transitions. In fact, breaking of this symmetry has been suggested as necessary to explain the experimentally observed velocity or efficiency of molecular motors 31,35. This problem has also been encountered recently in an experimental effort to apply the Harada-Sasa equality to kinesin 36. Understanding the validity of Harada-Sasa equality for general Markov processes with asymmetric dissipation is the main goal of this article.

Here, we show generally that, due to this asymmetry, the FDT violation does not vanish in the high frequency domain, leading to a divergent integral on the left hand side of Eq. (2). However, by neglecting the high frequency violation, the Harada-Sasa equality can be restored, provided that not only the medium entropy production per jump is small, but also its variation in the state space. This is consistent with the observation that
an effective Langevin description emerges under these assumptions. The symmetric case is unique, as it gives a much smaller deviation from the Harada-Sasa equality, thus allowing for larger discreteness.

One-dimensional (1-d) hopping model. Let us consider a simple example with such an asymmetry. In FIG. 1(a), we illustrate a particle hopping along a discrete lattice with a lattice constant \( d \). Each state is labeled by an integer \( n \), and it has a well-defined energy \( U_n \). The transition rates are assumed to satisfy

\[
\begin{align*}
    w_n^+ &= w_0 \exp \left( \left( + \frac{1}{2} \frac{U_n - U_{n+1}}{T} \right) \right), \\
    w_n^- &= w_0 \exp \left( \left( - \frac{1}{2} \frac{U_n - U_{n+1}}{T} \right) \right),
\end{align*}
\]

(3a)

(3b)

where \( T \) is the temperature of the bath. The Boltzmann constant is set to be 1 throughout this article. \( \theta \) is the asymmetric load-sharing factor that controls how local dissipation contributes to the forward and backward transitions. Symmetric case corresponds to \( \theta = 0 \). It can be checked immediately that the local detailed balance of energy is satisfied, i.e., \( w_n^+/w_n^- = \exp[(U_n - U_{n+1})/T] \), regardless of what \( \theta \) is. In fact, Eq. (3) is the same as the Arrhenius equation if we take \( \theta = -\Delta U_n^+/\Delta U_n \), as explained in FIG. 1(b), which is in general non-zero, thus asymmetric. In particular, \( \theta = 0.5 \) \((0.5) \) corresponds to the case that there is no activation energy in the forward (backward) transition, which is assumed in several recent studies on molecular motors \[31\,32\].

We assume that \( U_n \) is sampled from a smooth function \( U(x) \), i.e., \( U_n = U(nd) \), and that \( U(x) = U(x + L) + \Delta \mu \) is a periodic function tilted by an energy input \( \Delta \mu \) for each period, thus driving the system out of equilibrium. This is illustrated in FIG. 2(a). The dynamics of this system is governed by the following master equation

\[
\partial_t P_n = w_n^+ P_{n-1} + w_n^- P_{n+1} - (w_n^+ + w_n^-) P_n,
\]

(4)

where \( P_n \) is the probability at the \( n \)th state, normalized over each spatial period. Below, we focus on the consequence of a finite \( \theta \) in this system.

In Supplemental Material \[37\], we show that the dynamics of this discrete system can be mapped to that of the following Fokker-Planck equation when \( d/L \ll 1 \):

\[
\partial_t \rho = D \left\{ \frac{\partial}{\partial x} \left[ \frac{1}{T} \frac{\partial U}{\partial \rho} \right] + \frac{\partial^2 \rho}{\partial x^2} + \theta O \left( \frac{d}{L} \right) \right\} + O \left( \frac{d^2}{L^2} \right),
\]

(5)

where \( \rho(x,t) \) is the corresponding probability distribution, which is related to the original distribution via \( \rho(nd,t) = P_n(t)/d \), and \( D \equiv w_0 d^2 \) is the effective diffusion constant. In the region \( d/L \ll 1 \), an effective description emerges that is independent of the microscopic details, as is shown numerically in FIG. 2(b). Interestingly, while the discreteness \( d/L \) contributes only a second-order correction, the asymmetry gives a first-order one, thus much larger. This is confirmed numerically in FIG. 2(c). Here, we have shown that such an asymmetric system can be mapped to a Langevin process, which is the counterpart of Fokker-Planck equation.

On the other way around, to construct a microscopic model for a system that is known to be described by this Fokker-Planck equation, Eq. (5) also indicates that we are allowed to use a small \( d \) that reasonably represents \( U(x) \), and also include a non-zero \( \theta \). The microscopic transition rates will increase as a smaller \( d \) is used, since \( w_0 = D/d^2 \) and \( D \) is fixed here.

Now, we consider the violation of FDT. Consider such a perturbation: \( U_n \rightarrow U_n - (nd) \hbar \), which corresponds to

FIG. 1. (a) The 1-d hopping model. (b) Generation of the asymmetric load sharing factor \( \theta \) due to asymmetric positioning of the metastable state away from the medium energy \((U_n + U_{n+1})/2\) of the two stable states. The sketched energy landscape corresponds to \( \theta < 0 \), while \( \theta > 0 \) if \( U_n < U_{n+1} \).

FIG. 2. (a) The periodic energy landscape \( U_n \), constructed from \( U(x) = -\sin(2\pi x/L) - \Delta \mu x/L \) at a given lattice constant \( d \). The landscapes for different \( d \)'s are shifted vertically for illustration. (b) The rescaled stationary distribution \( P_n^\ast/d \). The red line gives \( \rho^\ast(x) \) from the corresponding Fokker-Planck equation. (c) The deviation of \( P_n^\ast/d \) from \( \rho^\ast(x) \) at the position \( x_* \), \( 0.5 \) indicated in (b). The red curve is a quadratic fitting for \( \theta = 0 \). (d) The correlation spectrum \( C_Q(\omega) \) and the (real part) response spectrum \( R_{Q}(\omega) \) for the velocity \( Q_t = \dot{v}_t d \), obtained at \( d = 0.1 \) and \( \theta = -0.1 \). A finite violation of FDT exists in the high frequency limit. Other parameters: \( D = 1, T = 1, L = 1, \Delta \mu = 2.5 \).
More, FIG. 3(b) shows that the relative violation, i.e., \( \tilde{V}_D(\infty) \), converges to zero when \( d/L \ll 1 \), as suggested by Eq. (7). These features are consistent with the prediction based on Eq. (5).

To avoid the divergence, we might just shift the response spectrum such that the FDT is restored in the high frequency limit, and then compute Eq. (6) again. This defines a modified FDT violation integral, denoted as \( I^* \). For a sufficiently small \( d/L \), this operation amounts to setting a high frequency cutoff. With this modification, we find that the Harada-Sasa equality survives for this modified FDT violation integral in the parameter region \( d/L \ll 1 \):

\[
\gamma I^* = \Delta \mu \big[ 1 + \theta O \left( \frac{d}{T} \right) + O \left( \frac{d^2}{T^2} \right) \big],
\]

with \( \gamma = T/D \) the effective friction coefficient. The dissipation rate \( \dot{q} = \Delta \mu \langle \dot{q} \rangle_{ss} / L \) for this system, with \( L \langle \dot{q} \rangle_{ss} \) setting the average time to complete a cycle. In FIG. 3(c), we show that the dissipation rate \( \dot{q} \) converges to the same value for all \( \theta \) when \( d/L \ll 1 \), as is also the case for \( I^* \). FIG. 3(c) also implies that a constant input \( \Delta \mu \) leads to a larger drifting velocity when a smaller number of states (a larger \( d \)) and a forward bias (\( \theta > 0 \)) are used. FIG. 3(d) shows that the Harada-Sasa equality is restored for all \( \theta \) when \( d/L \ll 1 \). While the leading deviation from the Harada-Sasa equality is of the order \( d/L \) due to the asymmetry \( \theta \), the symmetric case has a deviation of the second order, thus much smaller in the region \( d/L \ll 1 \), as is shown in the inset of FIG. 3(d). Below, we generalize all these observations to general Markov systems with an asymmetric load-sharing factor. In particular, Eq. (7) and Eq. (8) will be derived from general equations (13) and (16) for Markov processes.

**General Markov systems.**—Consider a general Markov process with \( N \) states. The transition from state \( n \) to state \( m (1 \leq n, m \leq N) \) happens with rate \( w_{nm} \). The probability \( P_n(t) \) at state \( n \) and time \( t \) evolves according to the following master equation

\[
\frac{d}{dt} P_n(t) = \sum_m M_{nm} P_m(t),
\]

where \( M \) is assumed to be an irreducible transition rate matrix determined by \( M_{nm} = w_{nm} - \delta_{nm} \sum_k w_{nk} \). The \( j \)-th left and right eigenmodes, denoted as \( x_j(n) \) and \( y_j(n) \) respectively, satisfy the characteristic equations \( \sum_m M_{nm} x_j(m) = -\lambda_j x_j(n) \) and \( \sum_m y_j(m) M_{mn} = -\lambda_j y_j(n) \), where the minus sign is introduced to have an “eigenvalue” \( \lambda_j \) with a positive real component [29]. These eigenvalues are arranged in the ascending order by their real part, i.e., \( \text{Re}(\lambda_1) \leq \text{Re}(\lambda_2) \leq \cdots \). This system has a unique stationary distribution \( P_{ss}^{\text{ss}} \) that satisfies \( \sum_m P_{ss}^{\text{ss}} = 1 \). For the ground state associated with \( \lambda_1 = 0 \), \( y_1(n) \) should be constant and \( x_1(m) \) be proportional to \( P_{ss}^{\text{ss}} \). Here, we fix \( y_1 = 1 \) and \( x_1(m) = P_{ss}^{\text{ss}} \). For this system, we can always find a set of eigenmodes that...
satisfy the orthogonal relations \( \sum_m x_j(m)y_{j'}(m) = \delta_{j,j'} \) and completeness relations \( \sum_j x_j(n)y_{j}(m) = \delta_{m,n} \), which we use in the following analysis. For equilibrium systems, we have \( x_j(m) = y_j(m)P_{m\to m}^q \). Therefore, the right eigenmodes are sufficient for describing the system’s dynamics. However, for non-equilibrium systems, both left and right eigenmodes are necessary.

We assume that, under an external perturbation \( h \), the modified transition rate, denoted as \( \tilde{w}_m \), satisfies

\[
\tilde{w}_m = w_m^n \exp \left[ h(\theta_m^n + \frac{1}{2} \frac{Q_m - Q_n}{T} ) \right],
\]

which is a generalization of Eq. (3). Here, \( Q_m \) is a conjugate variable to perturbation \( h \), and \( \theta_m^n \) is a load-sharing factor that satisfies \( \theta_m^n = -\theta_m^m \). \( \theta_m^n \) may vary for different transitions. We are interested in the correlation and response spectrum of the velocity observable \( \dot{Q}_t = dQ_n/dt \). The strategy is to project these spectra onto the eigenspace. We introduce the projection coefficients:

\[
\alpha_j = \sum_n Q_n x_j(n), \quad \beta_j = \sum_n Q_n y_j(n) P_{n\to n}^q, \quad \phi_j = \sum_n B_n y_j(n),
\]

where \( B_n \) captures the effect from perturbation, and is given by \( B_n = \sum_m (\theta_m^n J_m^\nu + A_m^n)(Q_n - Q_m)/T \). Here, \( A_m^n = (w_m^n P_{n\to n}^s + w_m^n P_{m\to s}^s)/2 \) is the dynamical activity between state \( n \) and \( m \), while \( J_m^\nu = w_m^n P_{n\to m}^s - w_m^m P_{m\to n}^s \) is the net flux from state \( n \) to \( m \). Then, we obtain

\[
\tilde{C}_Q(\omega) = \sum_{j=2}^N 2\alpha_j \beta_j \lambda_j \left[ 1 - \frac{1}{1 + (\omega/\lambda_j)^2} \right],
\]

\[
\tilde{R}_Q(\omega) = \sum_{j=2}^N \alpha_j \phi_j \left[ 1 - \frac{1 + i(\omega/\lambda_j)}{1 + (\omega/\lambda_j)^2} \right],
\]

with \( i \) the imaginary unit. This approach has been used in our previous article to discuss the FDT violation spectrum in Markov systems with timescale separation [29]. See Supplemental Material [37] for more details.

We first analyze the situation in the high frequency limit. According to Eq. (11), \( \tilde{C}_Q(\infty) = \sum_{j=2}^N 2\alpha_j \beta_j \lambda_j \) and \( \tilde{R}_Q(\infty) = \sum_{j=2}^N \alpha_j \phi_j \). Using the definitions of these coefficients, we obtain

\[
\tilde{C}_Q(\infty) = \sum_{n,m}(Q_n - Q_m)^2 A_m^n,
\]

\[
\tilde{R}_Q(\infty) = \frac{1}{2T} \sum_{n,m}(Q_n - Q_m)^2 \left( \theta_m^n J_m^\nu + A_m^n \right).
\]

In obtaining Eq. (12b), we note that \( \sum_j x_j(n)\lambda_j y_j(m) = -M_{n,m} \), and that any summation over the full state space is invariant under the switching of the label, i.e., \( n \leftrightarrow m \). Because \( \theta \) is introduced only at the stage of perturbation in this general setup, the correlation spectrum does not depend on \( \theta \), while the response spectrum does. More specifically, \( \tilde{C}_Q(\infty) \) is only a measure of the local fluctuation, which only depends on the dynamical activity \( A_m^n \), while \( \tilde{R}_Q(\infty) \) has an additional dependence on the local flux \( J_m^\nu \) in the presence of an asymmetric load-sharing factor. For the 1-d hopping model in the region \( d \ll L \), we should have \( |J_{n+1}^\nu|/A_{n+1}^\nu \ll 1 \), i.e., the transitions are dominated by futile back-and-forth jumps, thus resulting in a small relative violation in the high frequency limit, as discussed earlier.

The high frequency FDT violation is given by

\[
\mathcal{V}_\infty = -\sum_{n,m} \theta_m^n J_m^\nu (Q_m - Q_n)^2.
\]

Eq. (7) can be easily derived from Eq. (13), noting that the flux \( J \) is constant in this 1-d hopping model, which is given by \( \langle \dot{Q} \rangle_{ss}/L \). If we assume that the state space can be partitioned into different blocks, with \( Q_m \) being the same for each block and \( \theta_m^n \) the same between two given blocks, this leads to a simplification of Eq. (13), with \( n \) and \( m \) replaced by the labels for the corresponding blocks, and \( J_m^n \) by the total flux between the two blocks. See Fig. 1 for relevant network structures, where we have \( \mathcal{V}_\infty \propto \langle \dot{Q} \rangle_{ss} \). For such models, we could have \( \mathcal{V}_\infty = 0 \) even if the system remains out of equilibrium.

The FDT violation spectrum, according to Eq. (11), can be generally written as

\[
\tilde{C}_Q(\omega) - 2T \tilde{R}_Q(\omega) = 2 \sum_{j=2}^N \alpha_j \beta_j \frac{T \phi_j - \beta_j \lambda_j}{1 + (\omega/\lambda_j)^2} + \mathcal{V}_\infty.
\]

On the right hand side, although the individual coefficients may have imaginary components, the summation over all the eigenmodes results in a real violation spectrum [37]. By neglecting \( \mathcal{V}_\infty \) and then integrating over the frequency domain, we obtain the modified FDT violation integral: \( I^* = \sum_j \lambda_j \alpha_j \langle T \phi_j - \beta_j \lambda_j \rangle \) [53]. Note that \( \langle T \phi_j - \beta_j \lambda_j \rangle \) is a key quantity in the violation spectrum. Using the definitions of these coefficients, we obtain

\[
T \phi_j - \beta_j \lambda_j = \sum_{n,m} y_{j}(n) J_m^n \left( \frac{Q_n + Q_m}{2} + \theta_m^n (Q_m - Q_n) \right).
\]

For equilibrium systems, the flux \( J_m^n \) vanishes due to detailed balance. This leads to \( T \phi_j = \beta_j \lambda_j \) for all eigenmodes, and thus the validity of FDT according to Eq. (14). On the other hand, \( \lambda_j \alpha_j = -\sum_n \nu_n x_j(n) \), with \( \nu_n = \sum_m w_m^n (Q_m - Q_n) \), the average change rate of \( Q_t \) when it starts from state \( n \). Combining these relations, we finally obtain the analytical expression for the modified FDT violation integral:

\[
I^* = \sum_{n,m} \nu_m J_m^n \left( \frac{Q_n + Q_m}{2} + \theta_m^n (Q_m - Q_n) \right).
\]

Noting that \( \sum_m J_m^n = 0 \) due to stationarity, we can subtract \( \sum_{n,m} \nu_n J_m^n Q_n \) (which is zero) from \( I^* \), and symmetrize the resulting expression to obtain

\[
I^* = \sum_{n,m} \left( \frac{\nu_n + \nu_m}{4} + \frac{\nu_n - \nu_m}{2} \right) J_m^n (Q_m - Q_n).
\]
Evidently from this equation, the violation of FDT only comes from transitions that change the observable \( Q_n \), as it should, and it is proportional to the local net flux \( J_n^{m+1} \), the signature of non-equilibrium systems.

Below, based on the modified integral \( I^* \) in Eq. (16), we reveal basic assumptions that are needed for the Harada-Sasa equality to hold for Markov jumping systems with an asymmetric load-sharing factor. We first consider the 1-d hopping model, which gives

\[
I^* = d \sum_n \left( \frac{\bar{\nu}_n + \bar{\nu}_{n+1}}{2} + \theta(\bar{\nu}_n - \bar{\nu}_{n+1}) \right) J_n^{m+1}. \tag{17}
\]

Here, \( \bar{\nu}_n = d(w_n^+ - w_n^-) \). We introduce \( \epsilon_n \equiv \ln[w_n^+ / w_{n+1}^-] \) as the entropy produced in the medium per jump. Since \( U_n \) is sampled from a smooth function \( U(x) \), we have \( \epsilon_n \approx -\frac{d^2}{2} \partial_x U \big|_{x=n} \). We also note that the relative variation \( \eta_n \equiv (\epsilon_{n+1} - \epsilon_n) / \epsilon_n \approx d^2 \partial_x U / \partial_x U \big|_{x=n} \). As both \( \epsilon_n \) and \( \eta_n \) are small for \( d/L \ll 1 \), we can expand Eq. (17) in Taylor series of \( d \), and obtain

\[
I^* = w_0 d^2 \sum_n J_n^{m+1} \epsilon_n \left(1 + \theta O \left( \frac{d}{L} \right) + O \left( \frac{d^2}{L^2} \right) \right). \tag{18}
\]

The details of the calculation is presented in Supplemental Material. Identifying \( \bar{q} = T \sum_n \bar{J}_n \) as the dissipation rate of the stochastic motion of \( Q_t \) and \( \gamma = T/(w_0 d^2) \) as the effective friction coefficient, we obtain the Harada-Sasa equality (3) discussed before. We note that this result cannot be generalized to the case with a heterogeneous \( \theta_m \). Throughout the derivation, we did not assume that \( J_n^{m+1} \) is constant, a characteristic property of 1-d systems. Hence, the results can be generalized straightforwardly to higher dimensions, as discussed below.

In general, the dissipation rate through the stochastic motion of \( Q_t \) is defined to be

\[
\dot{q} \equiv T \sum_{n,m} (1 - \delta_{Q_m Q_n}) J_n^m \epsilon_n^m, \tag{19}
\]

where \( \epsilon_n^m = \ln[w_n^m / w_{n+1}^m] \) is the medium entropy production for the transition from state \( n \) to \( m \), and \( (1 - \delta_{Q_m Q_n}) \) is a weight that only counts transitions that change the observable. The same argument leading to Eq. (3) can be generalized for the networks in FIG. 4, where the same value of \( Q_p = pd \) is shared by all the states within the same colored block. These models may describe molecular motors that hop along a discrete lattice with several internal chemical states. The model for sensory adaptation in *E. coli* also takes a similar form \( (39) \). The perturbed rates of the blue transitions that change the observable are assumed to satisfy

\[
\begin{align}
\dot{w}_n^m &= w_0 \exp \left( \theta \frac{1}{2} \left( \frac{Q_n - Q_m}{T} \right) \right), \tag{20a} \\
\dot{w}_m^n &= w_0 \exp \left( \theta \frac{1}{2} \left( \frac{Q_n - Q_m}{T} \right) \right), \tag{20b}
\end{align}
\]

which essentially mimics Eq. (3), except that we do not assume an energy landscape \( U_n \). We also do not assume anything about the red transitions within each colored block. With \( \epsilon \) and its variation in the neighboring region, i.e., \( \eta \), being small, the Harada-Sasa equality also emerges. The difference of network topologies in FIG. 4 is captured by the effective friction coefficient \( \gamma = 4T/(kw_0 d^2) \), with \( k \) the number of blue transitions out of a node. Again, the symmetric case only incurs a second-order correction in terms of \( d \). Under these assumptions, the dynamics of \( Q_t \) for these models can be approximated by a corresponding Langevin process, in which the emergent energy landscape has a dependence on the internal chemical state, as compared with the 1-d hopping model. These results suggest that the Harada-Sasa equality is generally valid for models that can be cast into the universality class of Langevin equations.

**Conclusion.**—Here, we have studied the FDT violation of a general Markov process with an asymmetric load-sharing factor \( \theta \). We find that the violation of FDT could persist even in the high frequency limit due to this asymmetry, which is in sharp contrast with our intuition that a physical system reaches equilibrium in the high frequency limit. This implies that Markov processes may not faithfully describe a physical system in the high frequency region. Nevertheless, this high-frequency-limit violation vanishes in many cases when the observable has a zero drifting velocity. By ignoring this high-frequency-limit violation, we show that the Harada-Sasa equality is recovered provided that \( \epsilon \), the entropy production in the medium per jump, is not only small itself, but also has a small local variation in the state space. We also show that the system can be described by a Langevin process under these assumptions, thus consolidating the existing connection between Harada-Sasa equality and Langevin processes. The symmetric case only has a second-order deviation (\( \sim \epsilon^3 \)) from either the effective Langevin description or the Harada-Sasa equality, as compared with the first-order deviation for the asymmetric case. Recently, various forms of generalized FDT that go beyond symmetric perturbation have been discussed \( (10, 10, 11) \). It would be interesting to place our study of FDT violation in that context in the future work.

The author thanks Kyogo Kawaguchi for motivating this project and helpful suggestions, and Macro Baiesi,
Ben Machta for their helpful discussion. I also thank my supervisor Leihan Tang for his generous support for my independent research. The work was partially supported by the NSFC under Grant No. U1430237 and 11635002.

∗ wangsw13@mails.tsinghua.edu.cn

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[37] See Supplemental Material for deriving the Fokker-Planck equation (5), the correlation and response spectrum Eq. (11), the violation formula (14), discussion on the case with an infinite state space, and more details about deriving the Harada-Sasa equality.
[38] We note that $\langle \dot{Q} \rangle_{ss} = 0$ in this system due to its finite state space. However, we expect Eq. (16) to work even for systems with an infinite state space, as suggested by our numerics for the 1-d hopping model and an analytical example in Supplemental Material.
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SUPPLEMENTAL MATERIAL

Derivation of the Fokker-Planck equation

Consider the 1-d hopping process described by the master equation (4) in the Main Text. Assume that the dimensionless energy $U(x)/T$ changes slowly over the distance $d$, i.e.,

$$d \ll \left| \frac{T}{\partial_x U} \right|, \quad d \ll \sqrt{\left| \frac{T}{\partial^2_x U} \right|},$$

(S1)

which is the manifestation of the assumption $d/L \ll 1$ in the Main Text. Then, both the distribution $P_n(t)$ and the transition rates $w_n^\pm$ change roughly continuously in the state space, which are readily approximated by continuous function $\rho(x,t)$ and $W^\pm(x)$, respectively. They are related via

$$P_n(t) = \rho(nd,t) d, \quad w_n^\pm = W(nd)^\pm.$$

(S2)

We treat $d/L$ as a small parameter, and expand the following quantities in Taylor series around $x = nd$:

$$w_n^+ P_n - w_{n-1}^- P_{n-1} = \frac{\partial}{\partial x} \left[ W^+(x)\rho(x) \right] d^2 - \frac{1}{2} \frac{\partial^2}{\partial x^2} \left[ W^+(x)\rho(x) \right] d^3 + \frac{1}{6} \frac{\partial^3}{\partial x^3} \left[ W^+(x)\rho(x) \right] d^4 + O\left( w_0 \frac{d^5}{L^5} \right), \quad (S3a)$$

$$w_{n+1}^- P_n - w_n^- P_n = \frac{\partial}{\partial x} \left[ W^-(x)\rho(x) \right] d^2 + \frac{1}{2} \frac{\partial^2}{\partial x^2} \left[ W^-(x)\rho(x) \right] d^3 + \frac{1}{6} \frac{\partial^3}{\partial x^3} \left[ W^-(x)\rho(x) \right] d^4 + O\left( w_0 \frac{d^5}{L^5} \right). \quad (S3b)$$

Combined with Eq. (4) in the Main Text, we obtain

$$\partial_t \rho = \frac{\partial}{\partial x} \left[ (W^+ - W^-)\rho \right] d + \frac{\partial^2}{\partial x^2} \left[ \frac{W^+ + W^-}{2} \rho \right] d^2 - \frac{\partial^3}{\partial x^3} \left[ \frac{W^+ - W^-}{6} \rho \right] d^3 + O\left( w_0 \frac{d^4}{L^4} \right),$$

(S4)

where $\rho(nd,t) = P_n(t)/d$ absorbs one $d/L$. On the other hand, according to Eq. (3) in the Main Text and that $W^\pm(nd) = w_n^\pm$, we have

$$W^+(x) - W^-(x) = w_0 \left[ \epsilon + 3\theta^2 (\frac{1}{24} + \frac{\theta^2}{2}) \epsilon^3 + O(\epsilon^4) \right], \quad (S5a)$$

$$W^+(x) + W^-(x) = w_0 \left[ 2 + 2\theta \epsilon + \frac{1}{4} + \theta^2 \epsilon^2 + O(\epsilon^3) \right]. \quad (S5b)$$

with $\epsilon = -\frac{\partial U}{\partial x} \frac{d}{T} \propto d/L$. Keeping only the leading order terms, we have

$$\partial_t \rho = w_0 d^2 \frac{\partial}{\partial x} \left[ \frac{1}{T} \frac{\partial U}{\partial x} \rho \right] + w_0 d^2 \frac{\partial^2 \rho}{\partial x^2} + \theta O\left( w_0 \frac{d^3}{L^3} \right) + O\left( w_0 \frac{d^4}{L^4} \right). \quad (S6)$$

Derivation and discussion concerning the correlation and response spectrum

Below, we derive Eq. (11) in the Main Text, the expansion of the correlation and response spectrum in the eigenspace, and present a rigorous proof of the FDT violation formula (14).

Correlation spectrum

Noting that the correlation function for $Q_t$ satisfies $C_Q(t - \tau) \equiv \langle [Q_t - \langle Q \rangle_{ss}] [Q_\tau - \langle Q \rangle_{ss}] \rangle_{ss}$, we have

$$C_Q(t - \tau) = \frac{\partial^2 C_Q(t - \tau)}{\partial \tau \partial t}. \quad (S7)$$
It is easier to calculate $C_Q(t - \tau)$ first. Assuming $t \geq \tau$, it satisfies

$$C_Q(t - \tau) = \sum_{n, n'} Q_n Q_{n'} P(t - \tau; n, n') P_{n'}^{ss} - \langle Q \rangle_{ss}^2,$$

(S8)

where $P(t - \tau; n, n')$ is the propagator, or the probability for reaching state $n$ at time $t$, given that the system starts from state $n'$ at time $\tau$. In the eigenspace,

$$P(t - \tau; n, n') = \sum_j y_j(n') e^{-\lambda_j |t - \tau|} x_j(n).$$

(S9)

Indeed, it is the solution of the corresponding master equation (9) in the Main Text, given the initial condition $P(0; n, n') = \delta_{nn'}$. Inserting this relation back to Eq. (S8) and introducing the projection of $Q$ on the $j$-th eigenmode, i.e., $\alpha_j \equiv \sum_n Q_n x_j(n)$ and $\beta_j \equiv \sum_n Q_n y_j(n) P_{n'}^{ss}$, we obtain the expansion of correlation function in the eigenspace:

$$C_Q(t - \tau) = \sum_{j=2}^N \alpha_j \beta_j e^{-\lambda_j |t - \tau|}.$$

(S10)

The contribution of the first eigenmode is counteracted by $\langle Q \rangle_{ss}^2$. Stationarity of the system guarantees that $C_Q(t - \tau) = C_Q(\tau - t)$. Therefore, Eq. (S10) obtained from $t \geq \tau$ is also applicable for $t < \tau$. We use the following convention for Fourier transform:

$$\tilde{f}(\omega) = \int_{-\infty}^{\infty} f(t) \exp(\omega t) dt, \quad f(t) = \int_{-\infty}^{\infty} \tilde{f}(\omega) \exp(-\omega t) \frac{d\omega}{2\pi}.$$

(S11)

Combining Eq. (S7), Fourier transformation and Eq. (S10), we finally obtain the velocity correlation spectrum (11a) in the Main Text.

**Response spectrum**

The response spectrum can be obtained by studying the response of the system to a periodic perturbation. Consider $h_t = h_0 \exp(-i\omega t)$ with $h_0$ a small amplitude and $i$ the imaginary unit. Expanded in Taylor series, the modified transition rate matrix $\tilde{M}$ is given by

$$\tilde{M} = M + M^* h_0 \exp(-i\omega t) + O(h_0^2),$$

(S12)

where $M^* \equiv \partial_h \tilde{M}|_{h \to 0}$. On the other hand, the modified distribution can also be expanded up to the first order:

$$\tilde{P}_m = P_{mm}^{ss} + P_m^* h_0 \exp(-i\omega t) + O(h_0^2),$$

(S13)

with $P_m^* \equiv \partial_h \tilde{P}_m|_{h \to 0}$. Since $d\tilde{P}_m/dt = \sum_n \tilde{M}_{mn} \tilde{P}_n$ and $\sum_n M_{mn} P_{m'}^{ss} = 0$, we obtain in a Matrix form

$$P^* = -\frac{1}{M + i\omega} M^* P^{ss}.$$

(S14)

For the observable $Q_t$, its response spectrum is given by

$$\tilde{R}_Q(\omega) = \sum_n Q_n P_n^* = \sum_{j=2}^N \alpha_j \phi_j - i\omega,$$

(S15)

where $\phi_j \equiv \sum_n B_n y_j(n)$ with $B_n \equiv \sum_m M_{nm}^* P_{m'}^{ss}$. By using the transformation $R_Q(t) = dR_Q/dt$ or $\tilde{R}_Q(\omega) = -i\omega \tilde{R}_Q(\omega)$, we obtain the velocity response spectrum (11b) in the Main Text.
For the FDT violation spectrum (14) in the Main Text, although the individual coefficients may have imaginary components, the summation over all the eigenmodes results in a real violation spectrum, as shown below.

Now, we prove that the following summation

\[ \sum_{j=2}^{N} \alpha_j \phi_j \left[ 1 - \frac{1}{1 + (\omega/\lambda_j)^2} \right] \]

gives a real function over frequency domain, although each component can be a complex function. For the first quantity, inserting the definition of the projection coefficients \( \alpha_j \) and \( \phi_j \), we obtain

\[ \sum_{j=2}^{N} \alpha_j \phi_j \left[ 1 - \frac{1}{1 + (\omega/\lambda_j)^2} \right] = \sum_{j=1}^{N} \alpha_j \phi_j \left[ 1 - \frac{1}{1 + (\omega/\lambda_j)^2} \right] \]

\[ = \sum_{n,m} Q_n \left( \sum_{j=1}^{N} x_j(n) \left[ 1 - \frac{\lambda_j^2}{\lambda_j^2 + \omega^2} \right] y_j(m) \right) B_m \]

\[ = \sum_{n,m} Q_n \left( 1 - \frac{M^2}{M^2 + \omega^2} \right)_{nm} B_m, \]

which indeed is a real function (\( M \) is a real matrix). Here, \((\cdot)_{nm}\) takes the entry of the matrix at \( n\)-th row and \( m\)-th column. The above calculation has used a critical relation

\[ \sum_{j=1}^{N} x_j(n)f(\lambda_j)y_j(m) = \left( f(M) \right)_{nm}, \]

where \( f(\cdot) \) is an analytical function. It can be proved as follows

\[ \sum_{j=1}^{N} x_j(n)f(\lambda_j)y_j(m) = \sum_{j=1}^{N} \sum_{k} \left( f(M) \right)_{nk} x_j(k)y_j(m) \]

\[ = \sum_{k} \left( f(M) \right)_{nk} \left[ \sum_{j=1}^{N} x_j(k)y_j(m) \right] \]

\[ = \sum_{k} \left( f(M) \right)_{nk} \delta_{km}. \]

Then summation over \( k \) gives the desired relation in Eq. (S18).

Similarly, we can show that

\[ \sum_{j=2}^{N} \alpha_j \phi_j \left[ \frac{\omega/\lambda_j}{1 + (\omega/\lambda_j)^2} \right] \]

is a real function, and thus the real part of the response spectrum is given by

\[ \tilde{R}_Q'(\omega) = \sum_{j=2}^{N} \alpha_j \phi_j \left[ 1 - \frac{1}{1 + (\omega/\lambda_j)^2} \right]. \]

This justifies the violation spectrum (14) in the Main Text.

**Markov systems with an infinite state space**

Here we present an analytical result for a simple model with an infinite state space to demonstrate that Eq. (16) in the Main Text works even for systems with an infinite size. Consider again the 1-d hopping model, but with
a homogeneous forward and backward rate, denoted as $w_+$ and $w_-$, respectively. The key feature of this non-equilibrium model is its translational invariance. Indeed, the probability distribution is the same for all states. If we take the probability $P = 1$ for each state, then the flux $J = w_+ - w_-$. For the observable $Q_n = nd$, we have $\bar{\nu} = \langle \bar{Q} \rangle = d(w_+ - w_-)$. Then, according to Eq. (16), we have

$$I^* = d^2(w_+ - w_-)^2. \tag{S20}$$

On the other hand, they can be directly computed from their definition if we know the functional form of $\tilde{C}_\bar{Q}(\omega)$ and $\tilde{R}_\bar{Q}(\omega)$. In fact, these two spectra are constant in the frequency domain due to translational invariance of the model. Therefore, after shifting the response spectrum to restore the FDT artificially in the high frequency limit, the FDT will be satisfied also in the whole frequency domain. Hence, the modified FDT violation integral is given by

$$I^* = \langle \tilde{Q} \rangle_{s s}^2 = d^2(w_+ - w_-)^2, \tag{S21}$$

which agrees exactly with Eq. (S20), thus confirming the generality of Eq. (16). We defer to a future work for a more rigorous proof of Eq. (16) for the case with an infinite state space.

The explicit expression of the correlation and response spectrum can be constructed by first evaluating their respective values in the high frequency limit from Eq. (12) in the Main Text, and then extend these values to the low frequency domain due to the translational invariance of the model. This gives

$$\tilde{C}_\bar{Q}(\omega) = (w_+ + w_-)d^2, \tag{S22a}$$

$$\tilde{R}_\bar{Q}(\omega) = \frac{\theta(w_+ - w_-)d^2}{T} + \frac{(w_+ + w_-)d^2}{2T}. \tag{S22b}$$

They can be derived directly for the continuum version of this 1-d hopping model:

$$\gamma \dot{x}_i = f_0 + h_t + \eta_t, \tag{S23}$$

where $f_0$ is a constant force inherent to the system, $h_t$ the external force to be turned on if perturbation is needed, and $\eta_t$ the zero-mean Gaussian white noise that satisfies

$$\langle \eta_t \eta_{t'} \rangle = 2T\gamma \delta(t-t'). \tag{S24}$$

In this case, the stationary velocity is $\langle \dot{x} \rangle_{s s} = f_0/\gamma$, and the both the fluctuation and response spectrum can be obtained directly from the Fourier transform of Eq. (S23), which gives

$$\tilde{C}_\dot{x}(\omega) = 2D, \tag{S25a}$$

$$\tilde{R}_\dot{x}(\omega) = \frac{1}{\gamma}, \tag{S25b}$$

with $D = T/\gamma$ the diffusion constant here. The FDT is automatically satisfied in all frequency domain in this continuum model.

**Deriving the Harada-Sasa equality**

Following Eq. (17), we are interested in how $\bar{\nu}_n + \bar{\nu}_{n+1}$ and $\bar{\nu}_n - \bar{\nu}_{n+1}$ behave when $\epsilon_n$ is small. Applying Taylor expansion, we obtain

$$\bar{\nu}_n + \bar{\nu}_{n+1} = w_0d\left[\exp\left(\theta + \frac{1}{2}\epsilon_n\right) - \exp\left(\theta - \frac{1}{2}\epsilon_{n-1}\right)\right] + \left[\exp\left(\theta + \frac{1}{2}\epsilon_{n+1}\right) - \exp\left(\theta - \frac{1}{2}\epsilon_n\right)\right],$$

with $\epsilon$ capturing the overall amplitude of $\epsilon_n$. On the other hand, we have

$$\bar{\nu}_n - \bar{\nu}_{n+1} = w_0d\left[\exp\left(\theta + \frac{1}{2}\epsilon_n\right) - \exp\left(\theta - \frac{1}{2}\epsilon_{n+1}\right)\right] - \left[\exp\left(\theta + \frac{1}{2}\epsilon_{n+1}\right) + \exp\left(\theta - \frac{1}{2}\epsilon_n\right)\right].$$
Combining these two together, we obtain
\[ \bar{\nu}_n + \bar{\nu}_{n+1} + \theta(\bar{\nu}_n - \bar{\nu}_{n+1}) = w_0 d \left( \epsilon_n + \frac{\epsilon_{n-1} + \epsilon_{n+1}}{2} - 2\theta^2 (\epsilon_n - \frac{\epsilon_{n-1} + \epsilon_{n+1}}{2}) + \theta (\epsilon_n^2 + \frac{\epsilon_{n-1}^2 + \epsilon_{n+1}^2}{2}) \right) \]
\[ - \left( \frac{\theta}{4} + \theta^3 \right) (\epsilon_n^2 - \frac{\epsilon_{n-1}^2 + \epsilon_{n+1}^2}{2}) + \left( \frac{1}{8} + \theta^2 \right) (\epsilon_{n+1}^2 - \epsilon_{n-1}^2) + O(\epsilon^3) \].
\[
(S26)
\]

Now, we assume \( \epsilon_n = \epsilon f(nd) \), with \( f(x) \) a continuous function and \( \epsilon \propto d \). The motivation of this assumption is that there is an underlying smooth energy landscape, as discussed in the Main Text. From Taylor expansion, we obtain
\[ \epsilon_{n\pm} = \epsilon \left[ f(nd) \pm \frac{\partial f}{\partial x} d + \frac{1}{2} \frac{\partial^2 f}{\partial x^2} d^2 + O(\frac{d^3}{L^3}) \right]. \]

Therefore, we have
\[
\begin{align*}
\epsilon_{n+1} + \epsilon_{n-1} &= 2\epsilon_n + O(\frac{\epsilon^2}{L^2}), \\
\epsilon_{n+1} - \epsilon_{n-1} &= 2\epsilon \frac{\partial f}{\partial x} d + O(\frac{\epsilon^3}{L^3}), \\
\epsilon_{n+1}^2 + \epsilon_{n-1}^2 &= 2\epsilon^2 + O(\frac{\epsilon^2}{L^2}), \\
\epsilon_{n+1}^2 - \epsilon_{n-1}^2 &= 4\epsilon^2 \frac{\partial f}{\partial x} d + O(\frac{\epsilon^3}{L^3}).
\end{align*}
\]
\[
(S27) \quad (S28) \quad (S29) \quad (S30)
\]

Plugging these relations into Eq. (S26), we finally obtain
\[ \bar{\nu}_n + \bar{\nu}_{n+1} + \theta(\bar{\nu}_n - \bar{\nu}_{n+1}) = 2w_0 d \epsilon_n \left( 1 + \theta O\left( \frac{d}{L} \right) + O\left( \frac{d^2}{L^2} \right) \right). \]
\[
(S31)
\]

This result leads to Eq. (18) in the Main Text, which then gives the Harada-Sasa equality (8).