

Universal response inequalities beyond steady states via trajectory information geometry

Jiming Zheng^{*} and Zhiyue Lu[†]

Department of Chemistry, *University of North Carolina-Chapel Hill*, North Carolina



(Received 26 April 2024; revised 28 May 2025; accepted 27 June 2025; published 25 July 2025)

Fluctuation-dissipation relations elucidate the response of near-equilibrium systems to environmental changes, with recent advances extending response theory to nonequilibrium steady states. However, a general response theory for systems evolving far from steady states has remained elusive. This letter presents a complete trajectory information geometric framework that generalizes response theory for nonstationary Markov processes. By constructing the full trajectory probability manifold and identifying a globally orthogonal coordinate system defined by transition rates, we derive a diagonal Fisher information metric that enables explicit calculations in this high-dimensional space. From the local metric structure, we obtain a Cramér-Rao-type inequality that bounds the linear response of arbitrary nonstationary observables. Furthermore, by analyzing the global geometry of this manifold, we derive a universal nonperturbative (nonlinear) response inequality in terms of geodesic length. This geometric framework reveals deep connections between dynamical activity, observable variance, and system sensitivity, and it encompasses or anticipates several recent results as special cases. Our approach offers new design principles for responsive behaviors in far-from-equilibrium systems.

DOI: [10.1103/scg2-qkxv](https://doi.org/10.1103/scg2-qkxv)

Introduction. Beyond thermal equilibrium, biological and chemical systems demonstrate complex responsiveness to the changes of their surroundings. Unraveling the principles governing the sensitivity and robustness of systems toward external perturbations is crucial for understanding and designing lifelike behaviors in complex systems, while the linear response theory near equilibrium [1,2] captures the response of systems toward perturbations near thermal equilibrium. In the past few decades, there have been attempts to extend the linear response theory beyond thermal equilibrium, including violation of fluctuation-dissipation relation [3,4], results obtained under Gaussian approximation [5], generalization of Einstein relation [6], and many other works [7–11]. Yet, there is still a gap between exact formal response theories and the tangible dynamical properties of systems. Recently, two groups have made prominent results in deriving intuitive bounds on the nonequilibrium responsiveness of stochastic systems [12–14]. However, these recent intuitive results are only applicable to systems restricted to the nonequilibrium steady states (NESS), which can not capture a system’s transient response beyond stationary. Today, a general framework for understanding the responsiveness of systems far from NESS remains elusive.

In this work, we present a set of universal response relations: Eqs. (7)–(9) and (11) for both linear and nonlinear responses of non-equilibrium systems. Here, linear response refers to the response toward infinitesimally small changes

of its surroundings, whereas nonlinear response refers to system’s response toward large-amplitude stimuli. In both cases, our theory is applicable to systems that evolve arbitrarily far from NESS. Moreover, this theory explicitly relates a system’s responsiveness to its kinetic properties, providing direct insight into how dynamical characteristics govern the sensitivity to environmental conditions. This universal theory has the potential to transform our understanding of complex responsiveness of nonequilibrium systems and pave the way for the design of rich response features, such as sensitivity [15–17], adaptation [18–20], and robustness [21–25], into far-from-equilibrium systems.

The key of the new theory is the construction of information geometry [26–29] in the space of Markovian trajectory probability distributions. Our approach differs from previous information-geometry thermodynamic theories [28,29] by focusing on trajectory probabilities [30] instead of state probabilities. This perspective enables the theory to describe systems evolving far from steady states, significantly expanding the scope of response theory to nonequilibrium and nonstationary relaxation processes.

Setup. Consider a Markov process described by a graph $\mathbb{G} = (\{\mathbf{v}_v\}, \{\mathbf{e}_e\})$ with N_v vertices $\{\mathbf{v}_v\}$ and N_e undirected edges $\{\mathbf{e}_e\}$. One can assign each edge $\mathbf{e}_e$ a forward and a reverse direction, with their corresponding transition probability rates denoted by (R_{e+}, R_{e-}) . These rates can be alternatively denoted by the two vertices of the edge—the transition rate from v' to v is $R_{e+} = R_{vv'}$, and equivalently $R_{e-} = R_{v'v}$. Here we call the v' the head of the forward edge; $h(e+) = v'$ and v the tail of the forward edge $t(e+) = v$, as shown in Fig. 1(b). The dynamics of the Markov system are represented by the master equation

$$\frac{d\mathbf{p}(t)}{dt} = \mathbf{R} \cdot \mathbf{p}(t), \quad (1)$$

^{*}Contact author: jiming@unc.edu

[†]Contact author: zhiyuelu@unc.edu

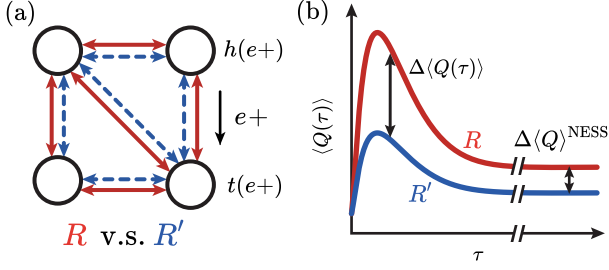


FIG. 1. (a) Markov system illustrated by a graph, where the transition of each directed edge (e.g., $e+$) jumps from the head vertex $h(e+)$ to the tail $t(e+)$. (b) System's response to an external change is quantified by comparing the dynamics of the original system R with the changed system R' . The transient response is captured by $\Delta\langle Q(\tau) \rangle = |\langle Q[X_\tau] \rangle' - \langle Q[X_\tau] \rangle|$, where $Q(\tau)$ represents a time-dependent observable. As $\tau \rightarrow \infty$, both systems approach their respective NESS, and the response converges to $\Delta\langle Q \rangle^{\text{NESS}}$.

where $\mathbf{p}(t) = (p_1(t), \dots, p_{N_v}(t))^T$ is the column vector of probability distributions on vertices at time t and $R = \{R_{vv'}\}_{N_v \times N_v}$ is the rate matrix with diagonal elements $R_{vv} = -\sum_{v', v' \neq v} R_{vv'}$.

For a Markov system under the influence of external input or environmental conditions, its transition rates can be dependent on the control parameters (or environmental parameters). To generally describe this dependence, we denote the rate matrix $R(\xi)$ as a function of all external control parameters:

$$\xi = (\xi_1, \dots, \xi_{N_p})^T, \quad (2)$$

which is a column vector with N_p control parameters. Examples of environmental parameters ξ_i include but are not limited to temperature, pressure, pH, chemical concentration, electric field, etc. Under this description, alternation in the control parameter ξ changes the system's probability transition rates $R(\xi)$, which may result in changes in its dynamics.

To construct a theoretical framework for system's environmental responsiveness, especially if the system evolves in time rather than maintaining the NESS, we focus on the system's probability distribution stochastic trajectories. The trajectory distribution contains more information [30] than the solution of the master equation-state probability $\mathbf{p}(t)$. Here, a trajectory with time length τ can be denoted by a sequence of n jump events at time $\{t_i\}$:

$$X_\tau = ((x_0, t_0), (x_1, t_1), \dots, (x_n, t_n)), \quad (3)$$

where $x_i \in \{v_v\}$, the initial time is denoted by $t_0 = 0$, and $t_n \leq \tau$ is the time when the last jump occurs before τ . The probability of the trajectory X_τ can be represented by the following product: $\mathcal{P}[X_\tau] = \mathcal{P}[X_\tau|x_0] \cdot p_{x_0}(0)$, where $p_{x_0}(0)$ is the initial state probability and $\mathcal{P}[X_\tau|x_0]$ is the conditional path probability of X_τ given the initial state x_0 . The conditional path probability can also be represented by [31]

$$\mathcal{P}[X_\tau|x_0] = \prod_{i=1}^n R_{x_i x_{i-1}} \prod_{i=0}^n e^{\int_{t_i}^{t_{i+1}} R_{x_i x_i} dt}, \quad (4)$$

where $t_{n+1} = \tau$ is the time length of the trajectory.

The central result of this letter is the environmental responsiveness of Markov systems without the restriction of

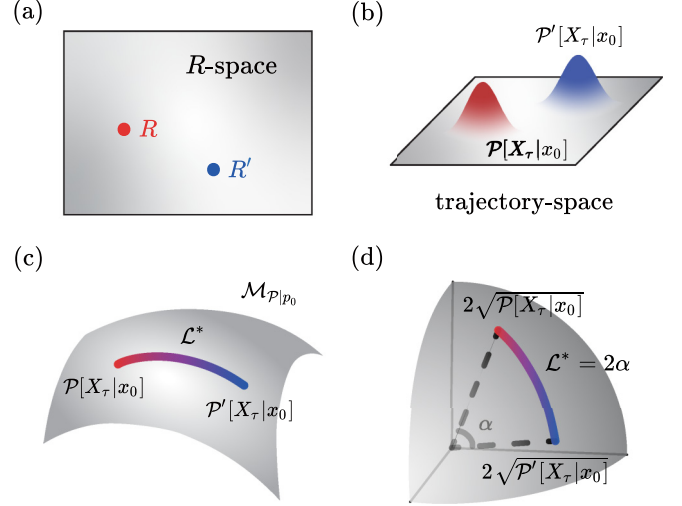


FIG. 2. Four equivalent representations of nonstationary Markov processes. (a) In the space parametrized by rate matrices, the original and changed dynamics are shown by distinct two points. (b) In the trajectory space, the original and changed dynamics (R or R') are represented by their corresponding probability distributions of trajectories conditioned by an initial state distribution $\mathbf{p}(0)$. (c) On the manifold of trajectory probability distributions $\mathcal{M}_{\mathcal{P}|p_0}$, the two dynamics are represented by two points: $\mathcal{P}[X_\tau|x_0]$ and $\mathcal{P}'[X_\tau|x_0]$. The shortest path between them is the geodesic $\mathcal{L}^*$. (d) The manifold $\mathcal{M}_{\mathcal{P}|p_0}$ is isometrically embedded to the positive orthant of a radius-2 hypersphere of dimension $2N_e$, thus the geodesic length between two points becomes an arc length $\mathcal{L}^* = 2\alpha$.

NESS. Without losing generality, the environmental change can be arbitrary alternations of ξ and the response can be denoted by the trajectory-averaged changes of arbitrary observable $\langle Q[X_\tau] \rangle$. Here the angular brackets denote an average over the ensemble of trajectories generated from the Markov dynamics $R(\xi)$. We consider the system's response toward two types of environmental changes: (i) perturbative change or linear response, $|\partial_{\xi_p} \langle Q(\tau) \rangle|$, which captures the infinitesimal change of the nonstationary observable caused by the infinitesimal environmental perturbation; and (ii) finite change or nonlinear response, $\Delta\langle Q(\tau) \rangle = |\langle Q(\tau) \rangle' - \langle Q(\tau) \rangle|$, which quantifies the difference in the system's nonstationary outputs between two finitely different environmental conditions ξ' and ξ .

Information geometry. To build a general theory, we construct information geometry [26,27] for the space of trajectory probabilities, where the Fisher information metric is chosen as the metric tensor for the parametric probability distributions.

Given a Markov graph and an initial state distribution $\mathbf{p}(0)$, the rate matrix $R(\xi)$ fully determines the trajectory probability distribution conditioned by the initial $\mathbf{p}(0)$. This correspondence between the rate matrix and conditional path probability is shown by Figs. 2(a) and 2(b). As a result, the manifold $\mathcal{M}_{\mathcal{P}|p_0}$ of conditional path probabilities $\mathcal{P}[X_\tau|x_0]$, as shown by Fig. 2(c), can be fully represented by transition rate matrix R . Since the degree of freedom for R is $2N_e$, the resulting conditional path probability manifold $\mathcal{M}_{\mathcal{P}|p_0}$ is $2N_e$ -dimensional. In other words, Figs. 2(a) and 2(c) share the same dimensionality, and every point on the manifold

uniquely specifies an evolution process (i.e., a distribution of trajectories). One can alternatively represent the conditional path probability manifold by embedding it on a hypersphere of radius 2 [27], illustrated by Fig. 2(d). The hypersphere representation provides a geometric argument for the nonlinear responsiveness relation.

As mentioned above, the natural and complete choice of the coordinate system for the $2N_e$ -dimension manifold $\mathcal{M}_{\mathcal{P}|p_0}$ is the set of all transition rates $\{R_{e+}\} \cup \{R_{e-}\}$. We refer to this choice as transition rate coordinates. With the help of the trajectory KL divergence recently derived in [30],

$$D_{\text{KL}}[\mathcal{P}[X_\tau|x_0]||\mathcal{P}'[X_\tau|x_0]] = \int_0^\tau \sum_{e\pm} R_{e\pm} p_{h(e\pm)} \left(\ln \frac{R_{e\pm}}{R'_{e\pm}} + \frac{R'_{e\pm}}{R_{e\pm}} - 1 \right) dt, \quad (5)$$

whose second-order derivatives (Hessian matrix) gives the geometric foundation of this work—the Fisher information metric

$$g(\{R_{e+}\}, \{R_{e-}\}) = \text{diag} \left\{ \left\{ \frac{\mathcal{A}_{e+}}{R_{e+}^2} \right\}, \left\{ \frac{\mathcal{A}_{e-}}{R_{e-}^2} \right\} \right\}, \quad (6)$$

where $\mathcal{A}_{e+} = \int_0^\tau R_{e+} p_{h(e+)}(t) dt$ denotes the directed activity on the directed edge $e+$ [32]. $\mathcal{A}_{e+}$ is the expectation value of the number of directed transitions along edge $e+$ within the time duration τ [33], which was shown to play an important role in various thermodynamic relations by recent studies [11,34–38].

The diagonal form of the Fisher information metric implies that the contribution of response on each edge is additive and statistically independent, as explained in detail in the more recent work [39]. Geometrically, it also implies that the transition rate coordinate system serves as an orthogonal basis everywhere, making it straightforward to transform to other coordinate systems (e.g., the explicit environmental parameter coordinate system ξ). Taking advantage of the orthogonal basis, it is also straightforward to define and evaluate various geometric quantities on the manifold. For example, the line element ds^2 in terms of transition rates is then given by $ds^2 = \sum_{e\pm} \frac{\mathcal{A}_{e\pm}}{R_{e\pm}^2} dR_{e\pm}^2$. For an infinitesimal displacement along any axis of the transition rate coordinates, e.g., R_{e+} , the line element is simply $ds^2 = \frac{\mathcal{A}_{e+}}{R_{e+}^2} dR_{e+}^2$. The geodesic between any two points on the manifold is the path of minimum curve length, illustrated by $\mathcal{L}^*$ in two representations of the manifold, Figs. 2(c) and 2(d).

Within the general framework of information geometry, this work describes system's nonstationary responses to both perturbative and finite environmental changes, i.e., (i) linear response beyond stationarity and (ii) nonlinear response relations.

Linear response beyond stationarity. By applying the Cramér-Rao inequality [40,41] to the trajectory Fisher information metric defined in Eq. (6), we obtain the first central result of this work: the thermodynamic bound for the response magnitude of any observable Q to the perturbation. The result takes two forms. When considering system's response to the perturbation of a single transition rate, the responsiveness

relation can be expressed by

$$\left| \frac{\partial \langle Q(\tau) \rangle}{\partial R_{e\pm}} \right| \leq \sqrt{\text{Var}[Q]} \cdot \frac{\sqrt{\mathcal{A}_{e\pm}}}{R_{e\pm}}, \quad (7)$$

where the only change is applied to a single directed edge R_{e+} (or R_{e-}), while all other transition rates remain intact. Here, the expectation value of the observable is the ensemble average over all stochastic trajectories of time length τ : $\langle Q(\tau) \rangle = \int \mathcal{D}[X_\tau] \mathcal{P}[X_\tau] Q[X_\tau]$. Under different choices of the exact form for $Q[X_\tau]$, the definition can generally represent either a trajectory observable (time-accumulated quantity) or a transient observable. To realize a transient observable at any time t , one can introduce a delta function peaked at time t into $Q[X_\tau]$. Formal discussions on different types of transient observables and their corresponding numerical results can be found in Sec.II in the SM. If one chooses $Q[X_\tau]$ as a time accumulation observable, our response relations can provide NESS response relations. The linear response inequality Eq. (7) can also be derived from the Dechant-Sasa response relation [9]. See Sec.VI of the SM for the alternative derivation.

In general, Eq. (7) implies that the responsiveness of an observable is bounded by the product between the square root of observable variance $\text{Var}[Q] \equiv \langle Q(\tau)^2 \rangle - \langle Q(\tau) \rangle^2$ and the square root of the scaled dynamical activity of the perturbed transition rates. Also, in alignment with intuition, this result indicated that the directed edge with larger activities may result in a stronger response toward the perturbation of its rate.

More conveniently, the above response relation can be formulated in terms of environmental-variable responsiveness relation. Through coordinate transformation into the environmental coordinate ξ in Eq. (2), the responsiveness bound to any chosen environmental variable change $\delta \xi_i$ can be obtained:

$$\left| \frac{\partial \langle Q \rangle}{\partial \xi_i} \right| \leq \sqrt{\text{Var}[Q]} \cdot \sqrt{\sum_{e\pm} \frac{\mathcal{A}_{e\pm}}{R_{e\pm}^2} \left(\frac{\partial R_{e\pm}}{\partial \xi_i} \right)^2}, \quad (8)$$

where $\frac{\partial R_{e\pm}}{\partial \xi_i}$ denotes the transition rate's dependence on the environmental variable ξ_i while fixing all other environmental conditions. An illustrative example of the application of this relation to illustrate the system's environmental responsiveness can be found in the example at the end of this letter. More formal analysis on the change of coordinate system to study system's responses to dissipative thermodynamic driving forces can also be found in Sec. III in the SM.

Nonlinear responsiveness relations. Based on the geometry of the whole manifold $\mathcal{M}_{\mathcal{P}|p_0}$, we can obtain the *second central result*, universal responsiveness relations toward finite environmental condition change ξ to ξ' . For comparison, the linear-responsiveness relations only utilize the local geometric property of the manifold.

First, the following geometric nonlinear responsiveness relation holds:

$$\arctan \frac{|\langle Q(\tau) \rangle' - \langle Q(\tau) \rangle|}{\sqrt{\text{Var}[Q]} + \sqrt{\text{Var}'[Q]}} \leq \frac{\mathcal{L}^*(\tau)}{2} \leq \frac{\mathcal{L}(\tau)}{2}, \quad (9)$$

where $\mathcal{L}^*$ is the geodesic length between the two path distributions for the two environmental conditions ξ and ξ' . Geometrically, the ratio $\mathcal{L}^*/2 = \alpha$ is the angle shown in

Fig. 2(d); and the second inequality in Eq. (9) comes from the fact that the geodesic length $\mathcal{L}^*$ is shorter than any other curve length $\mathcal{L}$. Here we define a curve length $\mathcal{L}$ by accumulated difference on all the changed rates:

$$\mathcal{L}(\tau) = \int_R^{R'} \sqrt{\sum_{e\pm} \frac{\mathcal{A}_{e\pm}}{R_{e\pm}^2} (dR_{e\pm})^2}. \quad (10)$$

By combining Eqs. (9) and (10) and Jensen's inequality [42], one can further obtain an alternative dynamical nonlinear responsiveness relation that explicitly reveals the connection between system's responsiveness and its dynamical rate changes:

$$\arctan \frac{|\langle Q(\tau) \rangle' - \langle Q(\tau) \rangle|}{\sqrt{\text{Var}[Q]} + \sqrt{\text{Var}'[Q]}} \leq \sqrt{\tau} \sum_{e\pm} |\sqrt{R'_{e\pm}} - \sqrt{R_{e\pm}}|. \quad (11)$$

The geometric and dynamical nonlinear responsiveness relations, Eqs. (9) and (11), reveal that observables of two different Markov dynamics are bounded by the fluctuations of the observables and a geometric length $\mathcal{L}\tau$. Furthermore, the alternative bound replaced the geometric length by a simple term that scales with the square root of time duration and the square root of the difference in transition rates. Notice that in both inequalities, the right-hand side only involves the transitions whose rate differs for the two Markov systems. Additionally, our result reveals that the difference between the two Markov system dynamics, reflected by an observable $Q[X_\tau]$, is geometrically bounded by an angle α [see Fig. 2(d)]. This geometric argument is elaborated below.

Geometric proof of nonlinear response relation. Let us consider alternative representations of the space of conditional trajectory probabilities as illustrated by Fig. 2. Notice that each trajectory probability density $\mathcal{P}[X_\tau; R]$ is a map from the product space of the Hilbert space of trajectories Ω and the $2N_e$ -dimensional rate parameter space Ξ to a positive real number, i.e., $\mathcal{P}[X_\tau; R] : \Omega \times \Xi \rightarrow \mathbb{R}^+$. For two different rate matrices R and R' , the corresponding trajectory densities are represented by $\mathcal{P} \equiv \mathcal{P}[X_\tau; R]$ and $\mathcal{P}' \equiv \mathcal{P}[X_\tau; R']$. Inspired by Ref. [27], we define their corresponding θ -scaled half density via a map $\pi_\theta^{1/2} : \mathcal{P} \mapsto \rho \equiv \theta \sqrt{\mathcal{P}}$ with a positive real number θ . Here $\pi_\theta^{1/2}$ is a diffeomorphism and preserves the geodesic.

The map $\pi_\theta^{1/2}$ provides us with an alternative representation of the trajectory probability manifold $\mathcal{M}_{\mathcal{P}|p_0}$ with the fisher information metric as a hypersphere in Euclidean space with radius θ . In the half-density representation, the inner product is defined by integrating over the trajectory Hilbert space Ω :

$$(\rho, \rho') = \int \rho \rho' \mathcal{D}[X_\tau]. \quad (12)$$

Thus, due to normalization over trajectory space Ω , the self inner product for each ρ must be $(\rho, \rho) \equiv \|\rho\|^2 = \theta^2$. In other words, all ρ 's lives on the positive orthant of the radius- θ hypersphere of dimension $2N_e$ as shown in Fig. 2(d).

By choosing $\theta = 2$, the map $\pi_2^{1/2}$ becomes an isometric diffeomorphism. In other words, the geodesic length on the hypersphere between ρ and ρ' coincides with the geodesic length $\mathcal{L}^*$ between $\mathcal{P}$ and $\mathcal{P}'$. Geometrically, by representing

the former as the arc length on the great circle with radius $\theta = 2$, we have $\mathcal{L}^* = 2\alpha$, where α is the geodesic angle as shown in Fig. 2(d).

Under this geometric analysis, one can further obtain

$$\cos \alpha = \frac{(\rho, \rho')}{\|\rho\| \cdot \|\rho'\|} = \int_\Omega \sqrt{\mathcal{P}} \sqrt{\mathcal{P}'} \mathcal{D}[X_\tau]. \quad (13)$$

By combining this with the inequality for Hellinger distance from [43], we arrive at

$$\cos \alpha \leq \left[\left(\frac{\langle Q(\tau) \rangle' - \langle Q(\tau) \rangle}{\sqrt{\text{Var}'[Q]} + \sqrt{\text{Var}[Q]}} \right)^2 + 1 \right]^{-1/2}. \quad (14)$$

By rearrangements, we can obtain the nonlinear response inequality Eq. (9). More details of the derivation can be found in Sec. IV-A in the SM.

From this geometry perspective, one can consider the non-perturbative (nonlinear) response relations, Eqs. (9) and (11), as extensions of the linear response relation, Eq. (7). The nonlinear relation reduces to the linear case in the limit of $R' \rightarrow R$. In this case, the geodesic shrinks to a point and the geodesic length $\mathcal{L}^*$ reduces to the local Fisher information metric, Eq. (6), and the linear-response relation Eqs. (7) and (8) is recovered.

Discussion: Zoology of thermodynamic information geometry. This Letter provides a trajectory-ensemble information geometric framework with four equivalent representations (shown in Fig. 2) and a complete orthogonal coordinate basis [as shown by Eq. (6)]. The trajectory-ensemble framework is inherently different from previous state-ensemble information geometric theories [28,29,44], and short-time trajectory theory [45]. Our trajectory-ensemble theory is capable of describing nonequilibrium and nonstationary Markov processes.

This new framework defines information geometry on the full manifold of the Markov trajectory ensembles, $\mathcal{P}[X_\tau]$, which can be obtained by combining the manifold of conditional distributions of trajectories $\mathcal{M}_{\mathcal{P}|p_0}$ with the initial state ensemble manifold $\mathcal{M}_p$ [46]. The metric for the manifold $\mathcal{P}[X_\tau]$ is the product metric $g_p \oplus g_{\mathcal{P}|p_0}$. Here, we focus on the property of the conditional trajectory manifold $\mathcal{M}_{\mathcal{P}|p_0}$.

Our geometric framework offers a complete description of the manifold $\mathcal{M}_{\mathcal{P}|p_0}$. In this framework, it is not necessary to include the trajectory length τ as a parameter. This is because the time coordinate is dependent on the transition rate coordinates $(\{R_{e+}\} \cup \{R_{e-}\})$. In other words, measuring a system within a longer time period is equivalent to measure a system with faster transition rates, i.e., $\mathcal{P}[X_\tau; \{\theta R_{e\pm}\}] = \mathcal{P}[X_{\theta\tau}; \{R_{e\pm}\}]$ for $\theta \in (0, +\infty)$, as pointed out by the relevant work [35,47]. This time-rescaling equivalence illustrates that the trajectory information geometry in the recent works [38,47] can be reduced from the new complete geometric framework by scaling all the transition rates with the same factor θ , where the length $\mathcal{L}$ is related to $\frac{1}{2} \int_0^\tau \frac{\sqrt{A}}{t} dt$. In other words, the recently developed trajectory information geometry analysis [38,47] can be considered as one-dimensional restricted studies of the complete $2N_e$ -dimensional geometric framework proposed by this Letter. Moreover, one can reduce our results Eq. (7) to the kinetic uncertainty relation [35] by using the equivalence property.

Here, we conjecture that the responsiveness inequality may be better saturated when the observable Q is strongly correlated with the transition events of the perturbed edge, as illustrated in the Sec. VII in the SM. More technical discussions of the saturation condition for the inequalities are provided in Sec. V in the SM.

Notice that the local geometric property of the trajectory manifold, Eq. (6), obtained by the Fisher information of classical Markov trajectories, agrees with previous works on the quantum Fisher information for Lindblad equation [48,49]. In the future, it is useful to explore if the information geometric framework developed for classical Markov systems in this work, especially the nonlinear responsiveness relations, Eqs. (9) and (11), can be extended by considering quantum information geometry approaches [50].

Application: Responsiveness design principle. Our responsiveness relation provides a general theoretical principle to guide the design of a system's nonstationary response to environmental condition changes. This relation connects experimentally accessible measurements (observable Q) with system's inherent transition statistics:

$$\eta_i^Q \equiv \frac{(\partial_{\xi_i} \langle Q \rangle)^2}{\text{Var}[Q]} \leq \mathcal{A} \cdot \sum_{e\pm} a_{e\pm}^2(\xi_i) \frac{\mathcal{A}_{e\pm}}{\mathcal{A}} \quad (15)$$

$$= \mathcal{A} \cdot \overline{a_i^2} \equiv \eta_i^{\text{Bound}}, \quad (16)$$

where η_i^Q denotes the sensitivity-to-noise ratio for observable Q with respect to control parameter ξ_i , $a_{e\pm}(\xi_i) \equiv \partial_{\xi_i} \ln R_{e\pm}$ is the logarithm sensitivity of each transition's rate with respect to the control variable ξ_i , $\mathcal{A}$ is the total activity, $\mathcal{A}_{e\pm}/\mathcal{A}$ is the fraction of transitions from each edge, and $\overline{a_i^2}$ is the statistical average of the logarithm rate sensitivity for all observed transition events. This result aligns with intuition: the parameter sensitivity of a nonequilibrium process depends on the total activity $\mathcal{A}$ and the average logarithmic rate sensitivity of observed transitions. By further choosing an observational time scale to maintain a constant activity $\mathcal{A}$, the system's sensitivity only depends on the average logarithmic rate sensitivity of observed edges, $\overline{a_i^2}$.

This result can be illustrated with a thermal system described by the generalized Arrhenius law

$$R_{e\pm} = C_e e^{-\beta(B_e - E_{h(e\pm)}) + \beta w_{e\pm}}, \quad (17)$$

where $\beta = 1/k_B T$ is the inverse temperature, B_e denotes energy barrier for edge e , C_e and c_e are constants for edge e , $E_{h(e\pm)}$ denotes the energy of the head of the directed transition edge $e\pm$, and $w_{e\pm}$ denotes the nonequilibrium work applied to assist transition $e\pm$ that breaks the detailed balance. In this case, the logarithm rate sensitivity for inverse temperature is the generalized activation energy $a_{e\pm} = w_{e\pm} - (B_e - E_{h(e\pm)})$. To design a system with ultralow (or high) temperature sensitivity, one needs to minimize (or maximize) $\eta_{\beta}^{\text{Bound}}$ via optimizing the energy landscapes and the external driving patterns. Moreover, to create a system sensitive to one variable (ξ_i) but robust to another (ξ_j), one can focus on maximizing the ratio between their respective sensitivity bounds $\eta_i^{\text{Bound}}/\eta_j^{\text{Bound}}$.

Conclusion. In summary, this work presents a set of universal responsiveness relations for nonstationary Markov processes under either infinitesimal or finite-amplitude perturbations. These relations explicitly reveal the connection between any observable's environmental response, the variance of the measured observable, and the dynamical features of the system. It provides a powerful tool for understanding and predicting the environmental responsiveness of complex systems far from equilibrium, with a wide range of potential applications in biological sensory processes and synthetic responsive materials. The illustrative example reveals that the explicit responsiveness relations presented in this work may lead to practical design principles to help the design and optimization of stochastic sensors, biological or synthetic, with desired time-dependent sensitivity or robustness. Detailed derivations can be found in the Supplemental Materials [51].

Acknowledgments. This work is funded by the U.S. National Science Foundation Grant DMR-2145256. The authors appreciate discussions and suggestions on the manuscript from Prof. Chris Jarzynski and from attendees at the Frontiers of Non-equilibrium Physics 2024 workshop held in July 2024 at Kyoto University, Japan. We also appreciate the careful read and valuable suggestions from the reviewers.

-
- [1] R. Kubo, The fluctuation-dissipation theorem, *Rep. Prog. Phys.* **29**, 255 (1966).
 - [2] R. Kubo, Statistical-mechanical theory of irreversible processes. I. General theory and simple applications to magnetic and conduction problems, *J. Phys. Soc. Jpn.* **12**, 570 (1957).
 - [3] T. Harada and S. Shin-ichi, Equality connecting energy dissipation with a violation of the fluctuation-response relation, *Phys. Rev. Lett.* **95**, 130602 (2005).
 - [4] C. Maes and M. H. van Wieren, Time-symmetric fluctuations in nonequilibrium systems, *Phys. Rev. Lett.* **96**, 240601 (2006).
 - [5] K. Sato, Y. Ito, T. Yomo, and K. Kaneko, On the relation between fluctuation and response in biological systems, *Proc. Natl. Acad. Sci. USA* **100**, 14086 (2003).
 - [6] M. Baiesi, C. Maes, and B. Wynants, The modified sutherland-einstein relation for diffusive non-equilibria, *Proc. Roy. Soc. A* **467**, 2792 (2011).
 - [7] C. Maes and B. Wynants, On a response formula and its interpretation, *Markov Proc. Related Fields* **16**, 45 (2010).
 - [8] P. E. Harunari, S. Dal Cengio, V. Lecomte, and M. Poletini, Mutual linearity of nonequilibrium network currents, *Phys. Rev. Lett.* **133**, 047401 (2024).
 - [9] A. Dechant and S.-I. Sasa, Fluctuation-response inequality out of equilibrium, *Proc. Natl. Acad. Sci. USA* **117**, 6430 (2020).
 - [10] C. Maes, Response theory: A trajectory-based approach, *Front. Phys.* **8**, 229 (2020).
 - [11] M. Baiesi, C. Maes, and B. Wynants, Fluctuations and response of nonequilibrium states, *Phys. Rev. Lett.* **103**, 010602 (2009).
 - [12] J. A. Owen, T. R. Gingrich, and J. M. Horowitz, Universal thermodynamic bounds on nonequilibrium response with biochemical applications, *Phys. Rev. X* **10**, 011066 (2020).

- [13] T. Aslyamov and M. Esposito, Nonequilibrium response for markov jump processes: Exact results and tight bounds, *Phys. Rev. Lett.* **132**, 037101 (2024).
- [14] T. Aslyamov and M. Esposito, A general theory of static response for markov jump processes, *Phys. Rev. Lett.* **133**, 107103 (2024).
- [15] T. Mora, Physical limit to concentration sensing amid spurious ligands, *Phys. Rev. Lett.* **115**, 038102 (2015).
- [16] W. Bialek and S. Setayeshgar, Physical limits to biochemical signaling, *Proc. Natl. Acad. Sci. USA* **102**, 10040 (2005).
- [17] D. Hartich, A. C. Barato, and U. Seifert, Sensory capacity: An information theoretical measure of the performance of a sensor, *Phys. Rev. E* **93**, 022116 (2016).
- [18] B. Wark, B. N. Lundstrom, and A. Fairhall, Sensory adaptation, *Current Opinion Neurobiol.* **17**, 423 (2007).
- [19] G. Lan, P. Sartori, S. Neumann, V. Sourjik, and Y. Tu, The energy–speed–accuracy trade-off in sensory adaptation, *Nat. Phys.* **8**, 422 (2012).
- [20] D. Conti and T. Mora, Nonequilibrium dynamics of adaptation in sensory systems, *Phys. Rev. E* **106**, 054404 (2022).
- [21] C. S. Pittendrigh, On temperature independence in the clock system controlling emergence time in drosophila, *Proc. Natl. Acad. Sci. USA* **40**, 1018 (1954).
- [22] *Circadian Rhythms in Bacteria and Microbiomes*, edited C. H. Johnson and M. J. Rust (Springer, Cham, Switzerland, 2021), Vol. 409.
- [23] J. B. Hogenesch and H. R. Ueda, Understanding systems-level properties: Timely stories from the study of clocks, *Nat. Rev. Genet.* **12**, 407 (2011).
- [24] N. Ay and D. C. Krakauer, Geometric robustness theory and biological networks, *Theory Biosci.* **125**, 93 (2007).
- [25] H. Fu, C. Fei, Q. Ouyang, and Y. Tu, Temperature compensation through kinetic regulation in biochemical oscillators, *Proc. Natl. Acad. Sci.* **121**, e2401567121 (2024).
- [26] S.-I. Amari, *Information Geometry and its Applications* (Springer, Japan, 2016), Vol. 194.
- [27] N. Ay, J. Jost, H. Vân Lê, and L. Schwachhöfer, *Information Geometry* (Springer, Cham, Switzerland, 2017), Vol. 64.
- [28] S. Ito, Stochastic thermodynamic interpretation of information geometry, *Phys. Rev. Lett.* **121**, 030605 (2018).
- [29] G. E. Crooks, Measuring thermodynamic length, *Phys. Rev. Lett.* **99**, 100602 (2007).
- [30] A. Pagare, Z. Zhang, J. Zheng, and Z. Lu, Stochastic distinguishability of Markovian trajectories, *J. Chem. Phys.* **160**, 171101 (2024).
- [31] U. Seifert, Stochastic thermodynamics, fluctuation theorems and molecular machines, *Rep. Prog. Phys.* **75**, 126001 (2012).
- [32] For systems evolving under time-dependent rate matrix, the Fisher information is discussed in the Sec. I in the SM.
- [33] C. Maes, Frenesy: Time-symmetric dynamical activity in nonequilibria, *Phys. Rep.* **850**, 1 (2020).
- [34] J. P. Garrahan, Simple bounds on fluctuations and uncertainty relations for first-passage times of counting observables, *Phys. Rev. E* **95**, 032134 (2017).
- [35] I. Di Terlizzi and M. Baiesi, Kinetic uncertainty relation, *J. Phys. A: Math. Theor.* **52**, 02LT03 (2019).
- [36] N. Shiraishi, K. Funo, and K. Saito, Speed limit for classical stochastic processes, *Phys. Rev. Lett.* **121**, 070601 (2018).
- [37] P. E. Harunari, A. Dutta, M. Poletini, and É. Roldán, What to learn from a few visible transitions’ statistics? *Phys. Rev. X* **12**, 041026 (2022).
- [38] Y. Hasegawa, Thermodynamic correlation inequality, *Phys. Rev. Lett.* **132**, 087102 (2024).
- [39] J. Zheng and Z. Lu, Spatial correlation unifies nonequilibrium response theory for arbitrary markov jump processes, [arXiv:2501.01050](https://arxiv.org/abs/2501.01050).
- [40] C. R. Rao, Information and the accuracy attainable in the estimation of statistical parameters, in *Breakthroughs in Statistics: Foundations and Basic Theory* (Springer, New York, NY, 1992), pp. 235–247.
- [41] H. Cramér, *Mathematical Methods of Statistics* (Princeton University Press, Princeton, NJ, 1999), Vol. 26.
- [42] J. L. W. V. Jensen, Sur les fonctions convexes et les inégalités entre les valeurs moyennes, *Acta Math.* **30**, 175 (1906).
- [43] T. Nishiyama, A tight lower bound for the hellinger distance with given means and variances, [arXiv:2010.13548](https://arxiv.org/abs/2010.13548).
- [44] D. A. Sivak and G. E. Crooks, Thermodynamic metrics and optimal paths, *Phys. Rev. Lett.* **108**, 190602 (2012).
- [45] S. Ito, Geometric thermodynamics for the fokker–planck equation: Stochastic thermodynamic links between information geometry and optimal transport, *Inf. Geom.* **7**, 441 (2024).
- [46] The full manifold is locally the product manifold $\mathcal{M}_p \times \mathcal{M}_{\mathcal{P}|p_0}$.
- [47] Y. Hasegawa, Unifying speed limit, thermodynamic uncertainty relation and heisenberg principle via bulk–boundary correspondence, *Nat. Commun.* **14**, 2828 (2023).
- [48] K. Macieszczak, M. Guță, I. Lesanovsky, and J. P. Garrahan, Dynamical phase transitions as a resource for quantum enhanced metrology, *Phys. Rev. A* **93**, 022103 (2016).
- [49] J. P. Garrahan and M. Guță (private communication).
- [50] M. Guță and J. Kiukas, Information geometry and local asymptotic normality for multi-parameter estimation of quantum markov dynamics, *J. Math. Phys.* **58** (2017).
- [51] See Supplemental Material at <http://link.aps.org/supplemental/10.1103/scg2-qkxv> for detailed derivations and discussions of the responsiveness bounds.