

Information Thermodynamics of the Transition-Path Ensemble

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The reaction coordinate describing a transition between reactant and product is a fundamental concept in the theory of chemical reactions. Within transition-path theory, a quantitative definition of the reaction coordinate is found in the committor, which is the probability that a trajectory initiated from a given microstate first reaches the product before the reactant. Here we develop an information-theoretic origin for the committor and show how selecting transition paths from a long ergodic equilibrium trajectory induces entropy production which exactly equals the information that system dynamics provide about the reactivity of trajectories. This equality of entropy production and dynamical information generation also holds at the level of arbitrary individual coordinates, providing parallel measures of the coordinate's relevance to the reaction, each of which is maximized by the committor.

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Understanding the mechanism for a transition between metastable states of a system is of fundamental interest to the natural sciences. Reaction theories seek to derive the rate constant from underlying system dynamics and have led to increased insight into the reaction mechanism, the sequence of elementary steps by which a reaction occurs. A notable example is transition-state theory and its extensions [1–3], which conceptualize the activated complex (or transition-state species) as a key dynamical intermediate and makes use of its properties (e.g., free energy relative to the reactant) to derive an approximate rate constant for large classes of reactions. The transition state is one identifiable state along the reaction coordinate, a one-dimensional collective variable that preserves all quantitative and qualitative aspects of a reaction under projection of the multidimensional dynamics [4,5].

Motivated by rare-event sampling methods [6], transition-path theory [7] was developed to quantitatively describe the entire reaction and determine its rate constant, without assumptions of metastability for the reactant and product or any specific details of the reaction mechanism (e.g., the presence of a single transition state). This statistical description relies on the definition of the committor function q_ϕ (also called the commitment or splitting probability), the probability that a trajectory initiated from microstate ϕ reaches the product before returning to the reactant. The committor maps the state space onto the interval $q_\phi \in [0, 1]$ and has been called the “true” or “ideal” one-dimensional reaction coordinate [4,8–11]. The committor allows calculation of the reaction rate from a one-dimensional description [12] and identifies the transition-state ensemble as states making up the $q_\phi = 0.5$ isocommittor surface [13].

In this Letter, we derive a novel information-theoretic justification of the committor as the reaction coordinate.

We show how selecting the transition-path ensemble (the set of trajectories from reactant to product) from a long ergodic equilibrium trajectory results in entropy production that precisely equals the information generated by system dynamics about the reactivity of trajectories.

The components of entropy production and information generation due to an arbitrary system coordinate are also equal; this reveals equivalent thermodynamic and information-theoretic measures of the suitability of low-dimensional collective variables that encode information relevant for describing reaction mechanisms. The committor is a single coordinate that preserves all system entropy production and distills all system information about reactivity, giving further support for its role as the reaction coordinate.

Information-theoretic formulation of the committor as reaction coordinate.—Consider a multidimensional system Φ evolving according to Markovian dynamics governed by the master equation [14] $d_t p(\phi) = \sum_{\phi'} T_{\phi\phi'} p(\phi')$, where $T_{\phi\phi'}$ is the transition rate from state $\phi' \rightarrow \phi$ and $p(\phi)$ is the probability of state ϕ . We assume the transition rates obey detailed balance [14], and the system is in equilibrium with its environment so that $p(\phi) = \pi(\phi)$, the equilibrium probability of ϕ . We study the transition-path ensemble (TPE), the set of trajectories that leave one subset of states $A \in \Phi$ and next visit a distinct subset $B \in \Phi \setminus A$ before A . In most applications, A and B are metastable states separated by a dynamical barrier; following Refs. [15,16], we only assume that A and B do not overlap and lack direct transitions, i.e., $T_{\phi\phi'} = 0$ for $\phi' \in A$ and $\phi \in B$.

The TPE can be formed by selecting from a long ergodic equilibrium supertrajectory, the trajectory segments that leave A and reach B before A . Transition paths are therefore

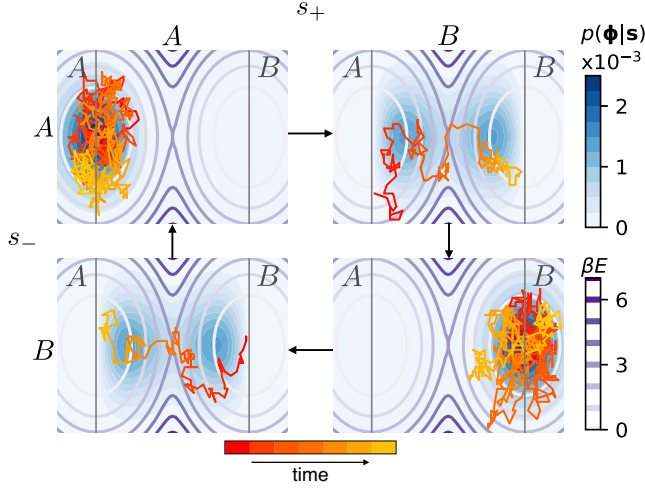


FIG. 1. Partitioning a long ergodic equilibrium supertrajectory into subensembles based on trajectory outcome S_+ and origin S_- . Contours: example double-well potential energy. Heat map: probability distribution $p(\boldsymbol{\phi}|s)$ of system state conditioned on trajectory subensemble s . Solid curves: representative trajectories from each subensemble. The forward (reverse) TPE in the top-right (bottom-left) panel has net flux of trajectories from $A \rightarrow B$ ($B \rightarrow A$). The top-left (bottom-right) panel shows the stationary subensemble from $A \rightarrow A$ ($B \rightarrow B$).

selected based on the trajectory outcome S_+ [the next mesostate (A or B) visited by the system] and origin S_- (the mesostate most recently visited by the system). This partitions the supertrajectory into four trajectory subensembles, each with particular $s \equiv (s_-, s_+)$: The forward (reverse) transition-path ensemble is the set of trajectory segments with $s = (A, B)$ [$s = (B, A)$], and the stationary subensemble from $A \rightarrow A$ ($B \rightarrow B$) has $s = (A, A)$ [$s = (B, B)$], as depicted in Fig. 1. Every trajectory segment in the forward TPE has a corresponding equally probable time-reversed trajectory segment in the reverse TPE.

At any time during the equilibrium supertrajectory, we define random variables Φ and S , respectively, denoting the current system state and trajectory subensemble, with $p(\boldsymbol{\phi}, s)$ the joint distribution that the system is currently in state $\boldsymbol{\phi}$ and is currently on a trajectory segment with respective origin and outcome $s = \{s_-, s_+\}$. Since the system dynamics are Markovian, the trajectory outcome and origin are conditionally independent given current state $\boldsymbol{\phi}$, so the joint distribution can be factored as $p(\boldsymbol{\phi}, s) = \pi(\boldsymbol{\phi})p(s_+|\boldsymbol{\phi})p(s_-|\boldsymbol{\phi})$ [15]. The conditional probabilities of trajectory outcome and origin given current state $\boldsymbol{\phi}$ are

$$p(S_+ = B|\boldsymbol{\phi}) = q_\phi^+, \quad (1a)$$

$$p(S_- = A|\boldsymbol{\phi}) = q_\phi^-. \quad (1b)$$

Here, q_ϕ^+ is the forward committor, the probability that the system currently in state $\boldsymbol{\phi}$ will next reach B before A , and q_ϕ^- is the backward committor, the probability that the system (currently in $\boldsymbol{\phi}$) was more recently in mesostate A than in B . The committors obey boundary conditions $q_\phi^+ = 0$ and $q_\phi^- = 1$ for $\boldsymbol{\phi} \in A$, and $q_\phi^+ = 1$ and $q_\phi^- = 0$ for $\boldsymbol{\phi} \in B$. Since the system is in equilibrium and the transition rates obey detailed balance $q_\phi^- = 1 - q_\phi^+$ [15], a single committor (without loss of generality, the forward committor q_ϕ^+) provides information about both the outcome and origin of the trajectory segment, so we refer to q_ϕ^+ as the reaction coordinate.

During the equilibrium supertrajectory, the system continually evolves from A to B and B to A , completing a unidirectional cycle through each subensemble with stochastic transition times depending on underlying microscopic dynamics. Transition-path theory [7,16,17] derives quantitative properties (reaction rate and free-energy difference) of the $A \rightarrow B$ reaction from the equilibrium probability flux of subensemble transitions

$$\nu_S = \sum_{\boldsymbol{\phi} \notin A, \boldsymbol{\phi}' \in A} T_{\boldsymbol{\phi}\boldsymbol{\phi}'} \pi(\boldsymbol{\phi}') q_\phi^+, \quad (2)$$

and the respective marginal probabilities $p(s_+)$ and $p(s_-)$:

$$k_{AB} = \frac{\nu_S}{p(S_- = A)} = \frac{\nu_S}{p(S_+ = A)}, \quad (3a)$$

$$k_{BA} = \frac{\nu_S}{p(S_- = B)} = \frac{\nu_S}{p(S_+ = B)}, \quad (3b)$$

$$\beta \Delta F_{AB} = \ln \frac{p(S_- = A)}{p(S_- = B)} = \ln \frac{p(S_+ = A)}{p(S_+ = B)}, \quad (3c)$$

where k_{AB} (k_{BA}) is the rate constant for the $A \rightarrow B$ ($B \rightarrow A$) transition, and $\Delta F_{AB} \equiv F_B - F_A$ is the free-energy difference. Mesoscopic reaction properties are therefore derived from information about the subensembles, specifically the proportion of time spent in each subensemble and how frequently the subensemble switches.

The reaction coordinate should be maximally informative about the current subensemble. This is precisely quantified by mutual information, a nonlinear statistical measure of the relationship between two random variables, specifically quantifying the reduction of uncertainty [given by Shannon entropy $H(X) \equiv -\sum_x p(x) \ln p(x)$] about one random variable from measuring another [18]:

$$I(S; \Phi) \equiv \sum_{\boldsymbol{\phi}, s} p(\boldsymbol{\phi}, s) \ln \frac{p(\boldsymbol{\phi}, s)}{\pi(\boldsymbol{\phi})p(s)}, \quad (4)$$

where $p(s) = \sum_{\phi} p(\phi, s)$ is the marginal probability that the system is currently on a trajectory segment with outcome and origin $s = (s_-, s_+)$. Operationally, $p(s)$ can be estimated from the proportion of time τ_s spent in subensemble s during a supertrajectory of length τ , $p(s) = \lim_{\tau \rightarrow \infty} \tau_s / \tau$. If the committor depends only on a one-dimensional coordinate $X \in \Phi$ (i.e., $q_{\phi} = q_x$), then X is a sufficient statistic for the mutual information between trajectory subensemble and full system state, i.e., $I(S; \Phi) = I(S; X)$. In this sense, the committor is the “optimal” reaction coordinate, since it is maximally informative about the trajectory subensemble given a measurement of system state. This is our first major result.

Physically, the trajectory outcome and origin (and hence, the committors) represent uncertainty in the state of the environment. Classical mechanics assumes a constant-energy universe (system Φ plus environment Ψ) governed by deterministic dynamics so that the outcome and origin of the trajectory initiated from a given state of system and environment are deterministic (and can be determined by integrating the state of the universe forward and backward in time until the system reaches A or B), i.e., $p(s|\phi, \psi)$ is either 0 or 1. This partitions the state space of the universe into four quadrants corresponding to each trajectory subensemble, with each state (ϕ, ψ) belonging to only one subensemble; thus, the uncertainty about the trajectory subensemble given a state of the universe is zero, $H(S|\Phi, \Psi) \equiv -\sum_{\phi, \psi, s} p(\phi, \psi, s) \ln p(s|\phi, \psi) = 0$. In this case, the mutual information between the universe and trajectory subensemble is the uncertainty about the trajectory subensemble, $I(S; \Phi, \Psi) = H(S) - H(S|\Phi, \Psi) = H(S)$; the measurement of the state of the universe fully determines the trajectory outcome and origin. However, we typically do not resolve the microstate of the environment, instead coarse-graining its interaction with the system into friction and fluctuations [14]. Measurement of the system state alone does not fully determine the trajectory outcome and origin, which become random variables with positive conditional Shannon entropy $H(S|\Phi) \equiv -\sum_{s, \phi} p(\phi, s) \ln p(s|\phi) > 0$ reflecting uncertainty in the state of the environment that is relevant to classification of the current subensemble.

Transition-path thermodynamics.—The joint dynamics of (Φ, S) is given by the master equation

$$d_t p(\phi, s) = \sum_{\phi', s'} T_{\phi\phi'}^{ss'} p(\phi', s'), \quad (5)$$

where the $(\phi', s') \rightarrow (\phi, s)$ transition rate is (see Supplemental Material I [19])

$$T_{\phi\phi'}^{ss'} = \begin{cases} T_{\phi\phi'}^s \equiv T_{\phi\phi'} \frac{p(s_+|\phi)}{p(s_+|\phi')}, & s' = s, \\ T_{\phi\phi'} p(S_+ = B|\phi), & \begin{cases} \phi' \in A, \phi \notin A, \\ s' = (A, A), s = (A, B), \end{cases} \\ T_{\phi\phi'} p(S_+ = A|\phi), & \begin{cases} \phi' \in B, \phi \notin B, \\ s' = (B, B), s = (B, A), \end{cases} \\ T_{\phi\phi'} / p(S_+ = A|\phi'), & \begin{cases} \phi' \notin A, \phi \in A, \\ s' = (B, A), s = (A, A), \end{cases} \\ T_{\phi\phi'} / p(S_+ = B|\phi'), & \begin{cases} \phi' \notin B, \phi \in B, \\ s' = (A, B), s = (B, B), \end{cases} \\ -\sum_{\substack{\phi'' \neq \phi' \\ s'' \neq s'}} T_{\phi''\phi'}^{s''s'}, & \phi = \phi', s = s', \\ 0 & \text{otherwise.} \end{cases} \quad (6)$$

The top transition does not change the subensemble and biases transitions within subensemble s toward states with higher probability of trajectory outcome s_+ . The middle four transitions switch subensembles and are unidirectional, contributing to the probability flux ν_S [Eq. (2) and Supplemental Material Eq. (S9) [19]]. These joint dynamics are Markovian: Since the underlying system dynamics are Markovian, the transition rates (6) do not depend on the trajectory origin s_- , and the outcome s_+ does not induce dependence on earlier system states. Considered alone, system dynamics are at equilibrium and microscopically reversible; adding the trajectory outcome and origin variables (that are not functions of system state and explicitly depend on the past and future) breaks time-reversal symmetry, producing absolutely irreversible trajectory-subensemble transitions and time-asymmetric system transitions within a given subensemble.

To quantify the time asymmetry for a particular $\phi' \rightarrow \phi$ transition in subensemble s , we combine (6), Bayes’ rule, and the equilibrium detailed-balance relation $T_{\phi\phi'} \pi(\phi') = T_{\phi'\phi} \pi(\phi)$ to derive a local detailed-balance relation,

$$\frac{T_{\phi\phi'}^s p(\phi'|s)}{T_{\phi'\phi}^s p(\phi|s)} = \frac{p(s_-|\phi') p(s_+|\phi)}{p(s_-|\phi) p(s_+|\phi')}. \quad (7)$$

The $A \rightarrow A$ (and analogously, $B \rightarrow B$) stationary subensemble has $s_+ = s_- = A$, and due to system detailed balance $p(s_- = A|\phi) = p(s_+ = A|\phi)$, so the rhs is unity and detailed balance holds for transitions within stationary subensembles. The reactive subensembles (forward or reverse TPE) have different trajectory outcome and origin so the rhs side differs from unity, leading to a detailed-balance-breaking flux (and hence, entropy production) along particular transitions within these subensembles.

Within a fixed subensemble s , the net trajectory flux is

$$J_{\phi\phi'}^s = T_{\phi\phi'}^s p(\phi', s) - T_{\phi'\phi}^s p(\phi, s) \quad (8a)$$

$$= [p(s_-|\phi')p(s_+|\phi) - p(s_-|\phi)p(s_+|\phi')]T_{\phi\phi'}\pi(\phi'). \quad (8b)$$

The second equality follows from $p(\phi, s) = p(s|\phi)\pi(\phi)$; the conditional independence of s_+ and s_- given state ϕ , i.e., $p(s_+, s_-|\phi) = p(s_+|\phi)p(s_-|\phi)$; and substitution for $T_{\phi'\phi}^s$ using (6). The stationary subensembles ($A \rightarrow A$ and $B \rightarrow B$) have no net flux because each trajectory segment and its time-reversed counterpart occur at equal rates within the same subensemble. In contrast, the forward and reverse TPEs have net trajectory flux since each transition path and its time-reversed counterpart occur in different subensembles. (Our procedure of effectively replicating the state space and introducing opposing fluxes in the replicas by modification of the transition rates bears similarity to irreversible Markov chains obeying skew detailed balance used to speed convergence to a stationary distribution [20].)

We decompose (see Supplemental Material II [19]) the change in joint entropy $H(\Phi, S) \equiv -\sum_{\phi, s} p(\phi, s) \ln p(\phi, s)$ at steady state [21,22] into

$$0 = d_t H(\Phi, S) \quad (9a)$$

$$= \underbrace{\sum_s p(s) \sum_{\phi, \phi'} T_{\phi\phi'}^s p(\phi'|s) \ln \frac{T_{\phi\phi'}^s p(\phi'|s)}{T_{\phi'\phi}^s p(\phi|s)}}_{\langle \dot{\Sigma} \rangle} - 2 \underbrace{\sum_{\phi, \phi', s_+} T_{\phi\phi'}^{s_+} p(\phi', s_+) \ln \frac{p(s_+|\phi)}{p(s_+|\phi')}}_{i^\Phi(S_+; \Phi)}, \quad (9b)$$

where $\langle \dot{\Sigma} \rangle = \sum_s p(s) \dot{\Sigma}_s$ is the subensemble-weighted average of the irreversible entropy production rate $\dot{\Sigma}_s$ conditioned on subensemble s , which quantifies the time irreversibility of system dynamics within that subensemble. $i^\Phi(S_+; \Phi) \geq 0$ is the rate of change in mutual information between the trajectory outcome and system state due to system dynamics in a fixed subensemble [23]. Rearranging Eq. (9b) gives (see Supplemental Material III [19])

$$0 \leq \langle \dot{\Sigma} \rangle = 2i^\Phi(S_+; \Phi) \quad (10a)$$

$$= i^\Phi(S_+; \Phi) - i^\Phi(S_-; \Phi), \quad (10b)$$

where $i^\Phi(S_-; \Phi) \leq 0$ is the rate of change in mutual information between trajectory origin and system state due to Φ dynamics in a fixed subensemble. These information rates reflect the dependence of the trajectory outcome and origin variables on the past and future states of the system: As the

system evolves, uncertainty about the outcome S_+ diminishes, increasing the information the current system state carries about S_+ , while uncertainty (given current system state Φ) about the origin S_- increases, decreasing information Φ carries about the S_- .

Since the stationary subensembles have no entropy production ($\dot{\Sigma}_{s=(A,A)} = \dot{\Sigma}_{s=(B,B)} = 0$), Eq. (10a) reduces to an equation for a single subensemble,

$$0 \leq p_R \dot{\Sigma}_R = \dot{i}^\Phi(S_+; \Phi). \quad (11)$$

This equates the rate $\dot{i}^\Phi(S_+; \Phi)$ of generating information about the outcome with the product of the entropy production rate of a reactive subensemble $\dot{\Sigma}_R = \dot{\Sigma}_{s=(A,B)} = \dot{\Sigma}_{s=(B,A)}$ and that subensemble's marginal probability $p_R = p(S=(A,B)) = p(S=(B,A))$. Although the supertrajectory is at equilibrium with no entropy production, $\dot{\Sigma}_R$ physically represents the dissipation that would be necessary in a system evolving according to the TPE's detailed-balance-breaking transition rates [top line of Eq. (6) for $s_- \neq s_+$]. Equation (11) is our second major result: The entropy production in a reactive subensemble equals the information generated about the reactivity of trajectories.

When the state space Φ is continuous, we derive (see Supplemental Material IV [19]) a Fisher-information metric $\mathcal{I}(\phi)$ that imposes an information geometry on the state space [24,25]. The metric measures distance on the reaction coordinate (committor) as the system evolves and thereby defines a reaction-coordinate length \mathcal{L}_{AB} . From this, the TPE entropy production is

$$\dot{\Sigma}_R \approx \frac{\mathcal{L}_{AB}^2}{2\tau_R}, \quad (12)$$

where τ_R is the mean duration of a transition path. This relates the TPE entropy production to the squared length between A and B along the reaction coordinate.

Bipartite dynamics.—We now demonstrate how the TPE entropy production quantitatively measures the relevance of an arbitrary coordinate to the reaction. We assume bipartite dynamics [26,27], essentially that instantaneous transitions only happen in either a one-dimensional coordinate X or in all other degrees of freedom Y making up the system state $\Phi = (X, Y)$:

$$T_{xx',yy'} = \begin{cases} T_{xx',y}, & x \neq x', y = y', \\ T_{x,yy'}, & x = x', y \neq y', \\ -\sum_{\substack{x'' \neq x' \\ y'' \neq y'}} T_{x''x',y''y'}, & x = x', y = y', \\ 0 & \text{otherwise.} \end{cases} \quad (13)$$

Dynamics that do not obey the bipartite assumption introduce further complications in unambiguously partitioning the entropy production between coordinates [28].

Combining Eqs. (1), (8a), and (9b) gives the full TPE entropy production as a function of the forward committor,

$$p_R \dot{\Sigma}_R = \frac{1}{2} \sum_{\phi, \phi'} T_{\phi\phi'} \pi(\phi') (q_{\phi}^+ - q_{\phi'}^+) \ln \frac{q_{\phi}^+(1 - q_{\phi'}^+)}{q_{\phi'}^+(1 - q_{\phi}^+)}, \quad (14)$$

which splits into contributions from the two transition types:

$$p_R \dot{\Sigma}_R = p_R \dot{\Sigma}_R^X + p_R \dot{\Sigma}_R^Y \quad (15a)$$

$$\begin{aligned} &= \frac{1}{2} \sum_{x, x', y} T_{xx'y} \pi(x', y) (q_{xy}^+ - q_{x'y}^+) \ln \frac{q_{x'y}^+(1 - q_{xy}^+)}{q_{xy}^+(1 - q_{x'y}^+)} \\ &+ \frac{1}{2} \sum_{x, y, y'} T_{xyy'} \pi(x, y') (q_{xy}^+ - q_{xy'}^+) \ln \frac{q_{xy}^+(1 - q_{xy'}^+)}{q_{xy'}^+(1 - q_{xy}^+)}. \end{aligned} \quad (15b)$$

The same decomposition holds for the information rate [23], so that TPE entropy production due to X dynamics is equal to the information rate (due to X dynamics) between Φ and S_+ :

$$p_R \dot{\Sigma}_R^X = \dot{I}^X(S_+; \Phi). \quad (16)$$

This is our third major result: The entropy production due to dynamics of coordinate X equals the mutual information generated by X dynamics, thereby quantifying the relevance of X transitions to identifying the current subensemble and highlighting those transitions that are ‘‘correlated’’ with reactive trajectories and therefore important to the reaction mechanism.

In particular, for X^* determining the committor and Y^* orthogonal degrees of freedom that are therefore not relevant to the reaction ($q_{xy} = q_x$), the entropy production rate due to Y^* dynamics is [simplifying Eq. (15b)]

$$\dot{\Sigma}_R^{Y^*} = \sum_{x, y, y'} T_{x,yy'} \pi(x, y') (q_x^+ - q_x^+) \ln \frac{q_x^+(1 - q_x^+)}{q_x^+(1 - q_x^+)} \quad (17a)$$

$$= 0. \quad (17b)$$

Therefore, $\dot{\Sigma}_R^{Y^*} = \dot{\Sigma}_R$. This is additional confirmation that the committor is the reaction coordinate, in that it provides a thermodynamically complete coarse-grained representation of the transition-path ensemble, fully accounting for its entropy production [22].

We illustrate with overdamped dynamics in a double-well energy landscape [Fig. 2(a); details in Supplemental Material V [19]]. To exemplify the typical situation where the reaction coordinate is not known *a priori* and coordinates are thus chosen based on convenience or intuition, fixed system coordinates (x, y) lie at an angle θ to the correct reaction coordinate, the linear coordinate passing

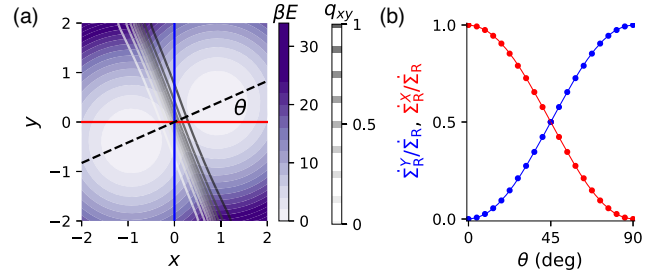


FIG. 2. (a) Double-well energy landscape (purple) with fixed x axis (red solid) and y axis (blue solid), and rotated reaction coordinate (black dashed). Gray contours: forward committor. (b) Share of TPE entropy production due to coordinate X (red dots) and Y (blue dots), as a function of reaction-coordinate angle θ . Red solid: $\cos^2 \theta$. Blue solid: $\sin^2 \theta$.

through both energy minima. For $\theta = 0^\circ$, X is the reaction coordinate, Y is an orthogonal bath mode [29], and X dynamics fully capture the TPE entropy production without Y contribution. Figure 2(b) shows that as the underlying energy landscape is rotated relative to system coordinates, the X -coordinate entropy production decreases and Y -coordinate entropy production increases, with equal contribution at $\theta = 45^\circ$. The entropy production for each coordinate is proportional to the squared Euclidean distance between A and B projected onto each coordinate $\dot{\Sigma}_R^X(\theta) \propto \cos^2 \theta$ and $\dot{\Sigma}_R^Y(\theta) \propto \sin^2 \theta$.

Discussion.—We have derived the information thermodynamics of a system undergoing reactions between distinct state-space subsets A and B , making a fundamental connection between transition-path theory, information theory, and stochastic thermodynamics. Partitioning a long ergodic equilibrium trajectory into reactive and nonreactive subensembles results in entropy production for system dynamics in the reactive subensembles (physically representing the dissipation needed to implement the detailed-balance-breaking transition rates of the TPE), which in turn identifies transitions that are relevant to the overall reaction mechanism. This rigorous equality between TPE entropy production and informativeness of dynamics also holds for an arbitrary coordinate, revealing parallel stochastic-thermodynamic and information-theoretic measures of the relevance of collective variables to the system reaction that are each maximized by the committor.

This work has implications for the identification of important collective variables and analysis of reaction mechanisms. While the committor provides a microscopically detailed reaction coordinate that maps each system microstate to a scalar value, it does not immediately identify physically meaningful collective variables (e.g., internal molecular coordinates) that are relevant to the reaction [4,5,30]. Our results have indicated that relevant coordinates are identified by entropy production in the transition-path ensemble; thus, partitioning the entropy production between multiple relevant collective variables

for which one has physical intuition can provide a low-dimensional model that allows increased insight into the reaction mechanism.

More concretely, this connection we have established between transition-path theory and stochastic thermodynamics suggests a novel method for rigorously grounded inference of reaction coordinates: generate an ensemble of transition paths using transition-path sampling [6,31] or related algorithms [32–34]; estimate entropy production along chosen coordinates [35–37] or identify linear combinations of coordinates producing the most entropy using dissipative components analysis [38]; use these most dissipative coordinates to enhance sampling of transition paths, and through further iteration identify system coordinates producing the most entropy in the transition-path ensemble and hence of most relevance to the reaction.

Machine-learning approaches to solve for high-dimensional committor coordinates [39–41] or find low-dimensional reaction models that retain predictive power [42,43] are active areas of research [44]. The information-theoretic and thermodynamic perspectives on reactive trajectories described in this Letter provide guidance to the development of data-intensive automated methods to infer these models and their corresponding reaction mechanisms.

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