

Force-Free Kinetic Inference of Entropy Production

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Estimating entropy production, which quantifies irreversibility and energy dissipation, remains a significant challenge despite its central role in nonequilibrium physics. We propose a novel method for estimating the mean entropy production rate σ that relies solely on position traces, bypassing the need for flux or microscopic force measurements. Starting from a recently introduced variance sum rule, we express σ in terms of measurable steady-state correlation functions that we link to previously studied kinetic quantities, known as “traffic” and “inflow rate.” Under realistic constraints of limited access to dynamical degrees of freedom, we derive efficient bounds on σ by leveraging the information contained in the system’s traffic, enabling partial but meaningful estimates of σ . We benchmark our results across several orders of magnitude in σ using two models: a linear stochastic system and a nonlinear model for spontaneous hair-bundle oscillations. Our approach offers a practical and versatile framework for investigating entropy production in nonequilibrium systems.

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Stochastic modeling is essential for describing complex phenomena characterized by randomness and fluctuations. Their breaking of time-reversal symmetry and energy dissipation are quantified by the “entropy production” [1–6]. The irreversibility of stochastic traces can be directly used to infer the entropy production rate σ in a nonequilibrium steady state (NESS) [7–10]. However, estimating σ exploiting violations of time-reversal symmetry typically requires observing stochastic trajectories whose length scales exponentially with σ , posing practical limitations. Recent advances offer an alternative approach by bounding entropy production using information-theoretic methods, leading to the development of thermodynamic uncertainty relations [11–29]. Alternative methods require perturbation experiments to exploit the violation of the fluctuation-dissipation theorem [30,31] by directly applying the Harada-Sasa relation [32]. Another possibility could be to directly measure microscopic forces or probability fluxes and use their relation with dissipation [33,34], but this is challenging in most cases. Moreover, in many realistic scenarios, the system under study can only be partially observed, which further complicates the inference process. For discrete systems, this typically corresponds to observing coarse-grained or lumped mesostates, which aggregate numerous microstates whose individual transitions remain unobservable [35–46]. For continuous processes, limited information may result from spatial coarse graining [47–50] or from the partial observation of a subset of the Markovian

degrees of freedom [51–54]. While central to understanding irreversible processes, estimating entropy production remains a challenging and active area of ongoing research.

In this Letter, we present a framework to estimate σ directly from stochastic trajectories, without requiring force measurements or inference of irreversibility, and applicable even under partial observation. We consider steady-state dynamics of multiple degrees of freedom (d.o.f.) $\{x_t^i\}$ governed by the overdamped Langevin equation,

$$\dot{x}_t = \mu F(x_t) + \sqrt{2D}\xi_t, \quad (1)$$

with potentially nonconservative forces $F(x_t)$ and white noise with mean $\langle \xi_t^i \rangle = 0$ and covariance $\langle \xi_t^i \xi_s^j \rangle = \delta^{ij} \delta(t-s)$. This effective description is valid in the overdamped regime, which is typical for mesoscopic systems where inertia is negligible compared to viscous damping, as commonly encountered in biological and soft matter systems. More generally, such a continuous description may emerge as a coarse-grained limit of an underlying discrete stochastic process with fast microscopic dynamics. Under broad conditions, these processes admit a diffusion approximation, ensuring that the inferred entropy production still provides a meaningful lower bound on the total dissipation [37]. The system may be in contact with different thermal baths T^i encoded in a diagonal temperature matrix $\mathbf{T}$. The mobility matrix μ is related to the diffusion matrix by the Einstein relation $D = k_B T \mu$. According to stochastic energetics [33], in a NESS σ corresponds to the amount of heat dissipated in the environment per unit time,

$$\sigma = \sum_i \frac{\langle \Delta Q^i \rangle}{k_B T^i} = \sum_i \frac{1}{k_B T^i} \langle F_t^i \circ \dot{x}_t^i \rangle, \quad (2)$$

where $\langle \Delta Q^i \rangle$ is the average heat injected into the i th heat bath at temperature T^i and $\circ$ denotes the Stratonovich product.

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This formula often exposes two main empirical problems: (i) it requires measuring the forces acting on the relevant d.o.f. (which is challenging in most cases), and (ii) it often clashes with the impossibility of observing all relevant d.o.f.

In [55,56] we derived a formula for σ starting from the variance sum rule (VSR) involving the second derivative of the position correlation function and the covariances of microscopic forces. Expressed in terms of correlation functions and following Einstein's summation convention, it takes the following form:

$$\sigma = \frac{1}{2} (D^{-1})^{ij} (-\ddot{C}_x^{ij}(0) + C_{\mu F}^{ij}(0)), \quad (3)$$

where $C_O^{ij}(t) \equiv \langle O_i^j(t) O_0^i \rangle - \langle O_i^j \rangle \langle O_0^i \rangle$ is the connected correlation matrix for the observable O and $\ddot{C}_O(0) \equiv \partial_t^2 C_O(t)|_{t=0^+}$ is its second derivative evaluated at zero. Equation (3) shows that the curvatures of the position correlation functions at short times are highly informative about dissipation. Still, the difficulties in estimating mobility and forces in experiments hinder the direct application of this formula. For example, in [55], we analyzed experimental measurements of red blood cell flickering, where only a single degree of freedom was observable and direct measurements of cellular forces were not accessible. To overcome these limitations, a reduced form of the VSR was employed to fit the experimental data, and, similar to [53,57], modeling was necessary to compensate for the lack of information about the underlying system.

Starting from the VSR, we derive a new formula for σ [see Eq. (5) below] that does not rely on the evaluation of forces. First, we deal with cases where all relevant d.o.f. are visible, even if forces are not directly measurable. When some d.o.f. are not detectable, we derive bounds on σ , enabling a partial yet informative estimation process. Rather than relying on microscopic forces, our method estimates effective forces from the experimentally accessible probability density function (PDF) $p(\mathbf{x}_t)$. In a NESS, the effective potential is $\phi(\mathbf{x}_t) = -\log p(\mathbf{x}_t) + C$, with C a constant dependent on the PDF's normalization, and its gradient, multiplied by $-k_B T$, acts as an effective force. We thus reformulate Eq. (3) in terms of effective forces using the “mean local velocity” $\nu(\mathbf{x}_t)$, obtained from the Fokker-Planck equation associated with Eq. (1),

$$\nu(\mathbf{x}_t) = \mu \mathbf{F}(\mathbf{x}_t) + D \nabla \phi(\mathbf{x}_t), \quad (4)$$

which connects real forces $\mathbf{F}(\mathbf{x}_t)$ to $-\nabla \phi(\mathbf{x}_t)$. This leads, as shown in Sec. S1 of [58], to a novel expression for σ ,

$$\sigma = -(D^{-1})^{ij} \ddot{C}_x^{ij}(0) + D^{ij} C_{\nabla \phi}^{ij}(0), \quad (5)$$

where all terms are directly inferred from position traces. Indeed, the diffusion matrix, D^{ij} , can be directly extracted from the position correlation matrix, $C_x^{ij}(t)$, via

$$D^{ij} = -\dot{C}_x^{(ij)}(0), \quad (6)$$

where $C^{(ij)} = (C^{ij} + C^{ji})/2$ denotes the symmetrized matrix and $\dot{C}_x(0) \equiv \partial_t C_x(t)|_{t=0^+}$ (see Sec. S5 in [58]). The linear short-time behavior of $C_x(t)$ is a signature of overdamped dynamics, as underdamped systems exhibit a ballistic (quadratic) onset instead (see Sec. S5A [58]); this provides a direct way to verify that the overdamped approximation is appropriate for the system under study. The second term on the right-hand side of Eq. (5) corresponds to the inflow rate

$$\mathcal{G} = D^{ij} C_{\nabla \phi}^{ij}(0), \quad (7)$$

a time-symmetric quantity obeying fluctuation relations [59] and recently used to study the information content of stochastic traces [60]. $\mathcal{G}$ can be determined from effective force measurements, which involves estimating $p(\mathbf{x}_t)$ using a kernel density estimator and computing the gradient $\nabla \phi(\mathbf{x}_t)$ with standard numerical tools; see Sec. S11 in [58] for more details. The connection between σ and $\mathcal{G}$ was first established in [61], with the traffic $\mathcal{T}$, a key kinetic quantity also commonly referred to as “dynamical activity” or “frenesy” [62–64], providing the link between the two. This relationship is given by

$$\sigma = 4\mathcal{T} + \mathcal{G}, \quad (8)$$

and, together with (5), leads to the identification

$$\mathcal{T} = -(D^{-1})^{ij} \ddot{C}_x^{ij}(0)/4. \quad (9)$$

The traffic represents the symmetric component of the stochastic action associated with the Langevin process. While its original definition [61] [see Eq. (S17) in [58]] is based on microscopic forces, the new formulation (9) enables direct estimation from position measurements. To summarize, since both $\mathcal{G}$ and $\mathcal{T}$ can be expressed in terms of derivatives of position correlation functions $C_x(t)$ and effective force covariances $C_{\nabla \phi}(0)$, both terms in (8) can be accurately evaluated from position traces. In the following examples, we show that $\mathcal{T}$ typically tracks the behavior of σ more closely than $\mathcal{G}$. The inflow rate $\mathcal{G}$ reflects how the steady-state distribution is shaped by the forces, acting as a measure of local compression or spreading of probability, and is more reflective of static features of the system. In contrast, $\mathcal{T}$ encodes time-symmetric dynamical fluctuations and reflects local kinetic activity. As shown in Sec. S3 of [58], this distinction becomes crucial in strongly driven regimes, where $\mathcal{T}$ continues to grow with dissipation while $\mathcal{G}$ remains comparatively small.

To illustrate our approach, we consider two representative systems: (i) the analytically tractable Ornstein-Uhlenbeck process, and (ii) a nonlinear model of spontaneous hair-bundle oscillations in bullfrog ears [65]. While the former enables full theoretical analysis, the latter highlights biological applicability. Across both, we identify parameter regimes

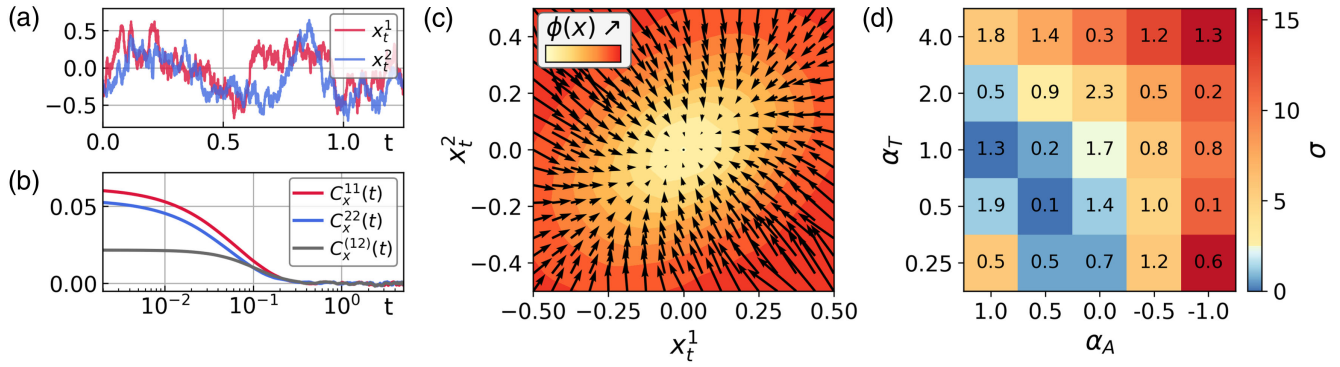


FIG. 1. (a) Stochastic traces of x_t^1 and x_t^2 , sampled at 4 kHz over a duration of 500 s. (b) Corresponding correlation functions for both d.o.f. (c) Effective forces $-\nabla\phi$ (black arrows) pointing from regions of high ϕ (red areas) to regions of smaller ϕ (yellow areas). Parameters for panels (a)–(c) are $A_{11} = A_{22} = -20$, $A_{12} = -10$, $T = \alpha_T = 1$, and $\alpha_A = 0.5$. (d) Heat map of σ as a function of the dissipative parameters α_A and α_T . Numbers written over the heat map indicate the accuracy $\pi(\bar{\sigma}) = |\sigma - \bar{\sigma}|/\Delta\bar{\sigma}$ of our estimates $\bar{\sigma}$.

where entropy production σ varies significantly, and show that this variability is largely captured by the traffic $\mathcal{T}$, which remains accessible even under partial observation, unlike $\mathcal{G}$.

As a first example, we consider the Ornstein-Uhlenbeck process [66],

$$\dot{x}_t = Ax_t + \sqrt{2D}\xi_t, \quad (10)$$

where $D = k_B T\mu$ and A is the drift matrix. A general discussion of this model is provided in the End Matter; here, we focus on the two-dimensional realization of Eq. (10) to test the predictive power of Eq. (5). This system, often referred to as the Brownian gyrator [54,67–71], is defined by the drift and diffusion matrices

$$A = \begin{pmatrix} A_{11} & A_{12} \\ \alpha_A A_{12} & A_{22} \end{pmatrix}, \quad D = \begin{pmatrix} T & 0 \\ 0 & \alpha_T T \end{pmatrix}, \quad (11)$$

where, for simplicity, we set $\mu = 1$ and $k_B = 1$. The entropy production rate σ can be calculated analytically (see Sec. S6B in [58]) and reads as follows:

$$\sigma = \frac{A_{12}^2(\alpha_A - \alpha_T)^2}{\alpha_T \mathcal{G}}. \quad (12)$$

From Eq. (12), one sees that α_A and α_T are directly related to dissipation. When these parameters differ, mechanical forces and heat fluxes are not balanced, resulting in the generation of probability currents. The magnitude of these currents scales with A_{12}^2/α_T and is modulated by the inflow rate, $\mathcal{G} = -(A_{11} + A_{22})$. We thus generated simulated data by fixing $\mathcal{G} = 40$ and $A_{12} = 10$, and considered 25 different combinations of the dissipative parameters α_A and α_T . For each pair, we simulated a single long trajectory [see Fig. 1(a) for an example] compatible with typical experimental recordings. From these, we derived correlation functions [Fig. 1(b)], as well as $p(x_t)$ and the effective forces $-\nabla\phi(x_t)$ [Fig. 1(c)], which were used to estimate the entropy production from Eq. (5) as $\sigma_{\text{est}} = \bar{\sigma} \pm \Delta\bar{\sigma}$, where $\Delta\bar{\sigma}$ denotes the statistical uncertainty. Briefly, a single trajectory is split

into subtrajectories, the inference is applied independently, and the results are combined via a weighted average. Technical details are provided in Sec. S11 of [58]. We emphasize that the analysis pipeline involves specific methodological choices and is not unique. We have also tested the robustness of our approach to measurement noise, a key practical consideration when performing inference from experimental data [60,72,73], as detailed in Sec. S12 of [58].

For each estimate σ_{est} we assess the quality of the prediction by evaluating the accuracy coefficient $\pi(\bar{\sigma}) = |\sigma - \bar{\sigma}|/\Delta\bar{\sigma}$ that quantifies how far, in units of statistical error $\Delta\bar{\sigma}$, the estimate $\bar{\sigma}$ is from the true value σ . The latter is evaluated from the analytical expression (12). Figure 1(d) shows the accuracy π obtained for all simulated traces, while σ is shown in the underlying heat map. The inference process yields reliable results: the estimates are well-aligned with the true values, with only moderate deviations relative to their statistical uncertainty. Across all traces, the average accuracy is $\langle\pi\rangle \approx 0.93$, indicating consistent performance of the method within estimated error bounds.

As a second example, we examine a nonlinear model of spontaneous hair-bundle oscillations in bullfrog ears [65], where estimating the entropy production from experimental traces remains an open problem [53,57]. The model captures the interplay between mechanosensitive ion channels, molecular motors, and calcium feedback through two coupled degrees of freedom, namely the bundle position x_t^1 and the motor position x_t^2 , governed by

$$\begin{aligned} \dot{x}_t^1 &= -\mu_1 \partial_{x^1} V_t + \sqrt{2k_B T \mu_1} \xi_t^1, \\ \dot{x}_t^2 &= -\mu_2 \partial_{x^2} V_t - \mu_2 F_t^{\text{act}} + \sqrt{2k_B T^{\text{eff}} \mu_2} \xi_t^2, \end{aligned} \quad (13)$$

where $V_t = V(x_t^1, x_t^2) = V_E(x_t^1, x_t^2) + V_G(x_t^1, x_t^2)$ describes the mechanical interactions within the system, including elastic forces (V_E) and the gating dynamics of mechanosensitive ion channels (V_G) [74–76]. Active, nonequilibrium driving arises through

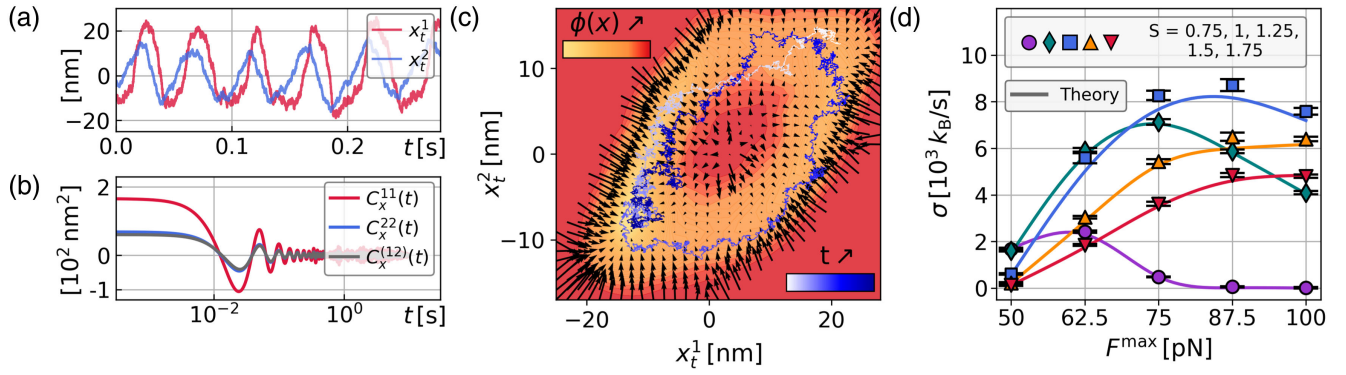


FIG. 2. (a) Time series of x_t^1 and x_t^2 for the hair-bundle model, recorded at a sampling rate of 100 kHz over a 10 s interval. (b) Autocorrelation and cross-correlation functions computed for both d.o.f. (c) Effective forces $-\nabla\phi$ (black arrows) pointing from regions of higher ϕ (orange areas) to regions of smaller ϕ (yellow areas). The area where the PDF $p(x_t)$ is very small (and ϕ is very high) has been highlighted in red. Effective forces have not been shown in this area for visualization purposes. A section of the stochastic trajectory is also depicted on top of the effective potential contour plot. For panels (a)–(c), $F^{\max} = 100$ and $S = 1$. (d) Relationship between σ and $F^{\max}$ for different values of S ($S = 0.75, 1, 1.25, 1.5, 1.75$). Solid lines represent the true σ while markers indicate estimated values with associated uncertainties. Note how the estimation procedure demonstrates high reliability across several orders of magnitude of σ .

$$F_t^{\text{act}} = F^{\max}(1 - SP_0(x_t^1, x_t^2)), \quad (14)$$

with $F^{\max}$ the maximal motor force and S the calcium-feedback strength. The gating probability $P_0(x_t^1, x_t^2)$ follows a two-state equilibrium model whose nonlinear dependence on bundle displacement mediates feedback between channel opening and active motor activity [77]. Further details are provided in the End Matter. While $T^{\text{eff}} \approx 1.5T$ characterizes enhanced fluctuations due to active processes, the main contributors to entropy production are the activity parameters $F^{\max}$ and S . Following the approach in [53], we focus on the effect of $F^{\max}$ and S on σ , as they directly modulate the nonequilibrium driving forces. To explore a wide range of σ values ($1k_B/s$ to $10^4k_B/s$), we simulated 25 traces with varying $F^{\max}$ and S , keeping all other parameters fixed as in [53]. Trace lengths (10 s) and sampling rate (10^5 Hz) match typical experimental conditions. We then applied the same subtrajectory-based procedure as in the linear system to compute estimates and uncertainties, using correlation functions and their $t=0$ derivatives for $\mathcal{T}$, and kernel density estimation with numerical differentiation for $\mathcal{G}$ [Fig. 2(c)].

As shown in Fig. 2(d), the predicted values $\bar{\sigma}$ (symbols) closely match the true values σ (solid lines). Since the system is nonlinear, the latter were numerically computed using Eq. (2). The accuracy of these estimates can be validated by the relative error, defined as $\delta(\bar{\sigma}) = |\sigma - \bar{\sigma}|/\sigma$. In all cases, the average error remains low at $\langle\delta\rangle \approx 0.05$, except for instances where $\sigma < 20k_B/s$, where small denominators distort the error measure. The quality of these estimates is further supported by the accuracy metric $\pi(\bar{\sigma}) = |\sigma - \bar{\sigma}|/\Delta\bar{\sigma}$, with $\langle\pi\rangle \approx 1.67$ and shown in more detail in Fig. S6(a) in [58]. Crucially, the quality of our estimates remains unaffected by the average ion channel opening probability $\langle P_0 \rangle$ [Fig. S6(b) [58]]. In contrast, approaches based on trace irreversibility may encounter

challenges when $\langle P_0 \rangle \approx 0.5$ [53]. Another key observation is that, similar to the linear model, $\mathcal{G}$ remains relatively constant [$\mathcal{G} \approx 100k_B/s$ to $500k_B/s$, see Fig. S6(d) in [58]] despite large variations in $F^{\max}$ and S , while σ spans orders of magnitude (1 to $10^4k_B/s$). This indicates that even in this highly nonlinear system, $\mathcal{T}$ captures most of the information about the dissipative components of the dynamics.

Our approach can be extended to the cases of partial observations. This is particularly relevant since, in most systems, only a subset of dynamical d.o.f., denoted by $\mathcal{S}$, is accessible. In such cases, we can use an intermediate result of Eq. (5) (see Sec. S1 in [58]),

$$-\ddot{C}_x^{ii}(0) \leq C_\nu^{ii}(0) = \langle(\nu^i)^2\rangle, \quad (15)$$

where ν^i is the i th component of the mean local velocity (4). For any $i \in \mathcal{S}$, if $\ddot{C}_x^{ii}(0) < 0$, it implies $C_\nu^{ii}(0) > 0$, therefore implying a nonequilibrium state. This provides a practical criterion for detecting nonequilibrium under partial observation. For a one dimensional Gaussian trace this is particularly challenging [78]: time reversal tests fail [79,80], and in one dimension probability currents are not observable unless the topology is nontrivial, which rules out current based methods such as the thermodynamic uncertainty relation. When $\mathbf{D} = k_B T \boldsymbol{\mu}$, our approach offers a complementary route to characterize nonequilibrium when irreversibility based methods are insufficient.

When the diffusion matrix is diagonal, Eq. (5) not only enables nonequilibrium detection but also provides an effective lower bound on σ . This is particularly relevant in systems like the hair-bundle model (13), where direct observation of certain degrees of freedom, such as the motor coordinate x_t^2 , is experimentally challenging. Moreover, having prior knowledge that the system can be effectively described by a model with a diagonal diffusion matrix facilitates the practical application of this bound. More in detail, as shown in

Sec. S4 in [58], it is useful to decompose σ as

$$\sigma = \sum_i \sigma_i = \sum_i (4\mathcal{T}_i + \mathcal{G}_i). \quad (16)$$

Each component σ_i is defined by $\sigma_i = \langle (\nu^i)^2 \rangle / D^{ii} \geq 0$, $\mathcal{T}_i = -\ddot{C}_x^{ii}(0)/(4D^{ii})$, and $\mathcal{G}_i = D^{ii}C_{\nabla\phi}^{ii}(0) = D^{ii}\text{Var}(\partial_i\phi) \geq 0$. From this, it follows that

$$4\mathcal{T}_i = \sigma_i - \mathcal{G}_i \leq \sigma_i \leq \sigma, \quad (17)$$

implying that any positive traffic component $\mathcal{T}_i > 0$ guarantees $\sigma > 0$, indicating the system is out of equilibrium and providing a lower bound to the entropy production rate. This observation thus provides a practical method for detecting nonequilibrium and bounding σ potentially from a single stochastic trace. More in general, for a subset $\mathcal{S}$ of observed d.o.f., one can select only positive traffic components and obtain a partial estimate of σ , namely

$$\sigma_{\mathcal{S}} = \sum_{i \in \mathcal{S}} \max(4\mathcal{T}_i, 0) \leq \sigma. \quad (18)$$

Similar kinetic bounds on σ have been previously reported in [81], though Eq. (18) has the advantage of being experimentally accessible. We note that estimating $\mathcal{G}$ requires knowledge of the PDF of the entire system, making it impossible to derive from partial observations alone. The Gaussian system defined by (11), despite its simplicity, offers valuable insights when applying Eq. (17) under the minimal assumption of a diagonal diffusion matrix. Figure 3(a) illustrates the relation between $4\mathcal{T}_1$ and σ for various parameters in (11), demonstrating that a higher ratio between the temperatures of the two thermal baths (α_T) tightens the bound, allowing for more precise nonequilibrium detection. Furthermore, the condition $\mathcal{T}_1 > 0$ corresponds to the absence of an equilibrium solution for the 2D linear system leading to the observed correlation function $C_x^{11}(t)$ (see Sec. S8 in [58] for details). In our previous work [55], red blood cell flickering traces were Gaussian and yielded $\mathcal{T}_1 \lesssim 0$ for the observed degree of freedom, requiring a specific model for thermodynamic characterization. Section S9 of [58] analyzes the detectability of σ under partial observation in linear systems, including the red blood cell case from [55].

For the model (13), our bound yields the results shown in Fig. 3(b). The colors of the heat map represent σ , while the numbers indicate the fraction of σ estimated using our method, specifically $4\mathcal{T}_1/\sigma$. In the more active regions of parameter space, the estimator recovers roughly half of σ , yielding inferred dissipation about 3 orders of magnitude larger than the values reported in [50,53]. This shows that the method is able to capture a substantial fraction of entropy production and is well suited to study biological systems under partial observation.

To conclude, this Letter introduces Eq. (5) to estimate the entropy production rate σ directly from stochastic trajectories without forces or steady-state currents.

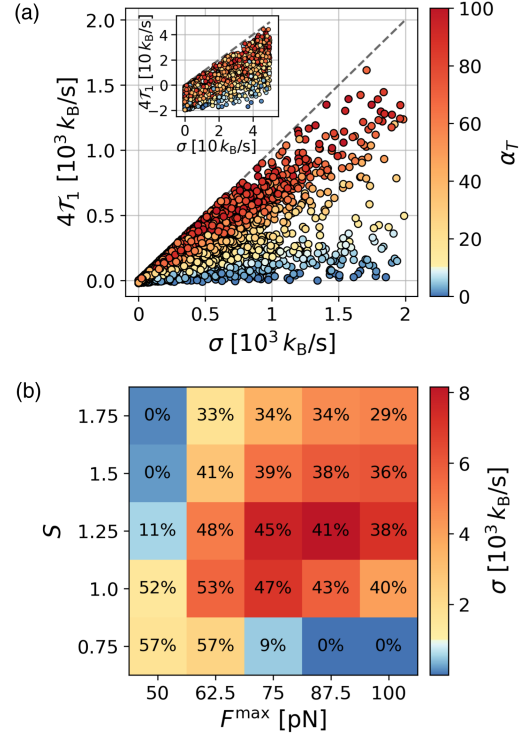


FIG. 3. (a) Scatter plot of $4\mathcal{T}_1$ vs σ , illustrating the lower bound (17) for randomly sampled parameters: $A_{11} \in [-20, -1]$, $A_{22} \in [-20, -1]$, $A_{12} \in [-10, 0]$, $\alpha_A \in [-50, 1]$, and $\alpha_T \in [0.1, 100]$. Color bar indicates α_T , showing how increasing thermal bath asymmetry tightens the bound. (b) Heat map of σ as a function of $F^{\max}$ and S . Numerical values in the heat map correspond to the fraction $4\mathcal{T}_1/\sigma$, representing the proportion of σ estimated by the bound.

Unlike current-based approaches, we infer σ from kinetic information, such as the short-time curvature (traffic) of correlation functions. This is important for experiments that record only positions. Other practical advantages are that (i) our approach applies under partial observation (we find evidence of tight bounds in cases where the thermodynamic uncertainty relation performs poorly, as discussed in Sec. S9B in [58]), and (ii) even applies when only a single degree of freedom is observed, where currents are not detectable. We illustrate this both in Gaussian systems coupled to multiple thermal baths, where detecting and quantifying nonequilibrium from a single degree of freedom is notoriously challenging [78–80], and in a biological model of hair cells, where we infer dissipation from a single measured coordinate [Fig. 3(b)]. We also provide practical procedures to estimate the traffic from the data (Sec. S12 in [58]) and demonstrate robustness to measurement noise (Sec. S13 in [58]). Overall, our approach offers a powerful and versatile framework for analyzing dissipation in nonequilibrium diffusive systems, including single particle tracking and microrheology [82], active matter systems [83], and for biological settings with partial observation [65].

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Data availability—The data that support the findings of this article are not publicly available. The data are available from the author upon reasonable request.

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- [1] C. Maes, On the origin and the use of fluctuation relations for the entropy, *Sémin. Poincaré* **2**, 29 (2003).
 - [2] U. Seifert, Stochastic thermodynamics, fluctuation theorems and molecular machines, *Rep. Prog. Phys.* **75**, 126001 (2012).
 - [3] L. Peliti and S. Pigolotti, *Stochastic Thermodynamics: An Introduction* (Princeton University Press, Princeton, NJ, 2021).
 - [4] G. Gallavotti and E. G. D. Cohen, Dynamical ensembles in nonequilibrium statistical mechanics, *Phys. Rev. Lett.* **74**, 2694 (1995).
 - [5] Gavin E. Crooks, Entropy production fluctuation theorem and the nonequilibrium work relation for free energy differences, *Phys. Rev. E* **60**, 2721 (1999).
 - [6] J. Kurchan, Fluctuation theorem for stochastic dynamics, *J. Phys. A* **31**, 3719 (1998).
 - [7] D. Andrieux, P. Gaspard, S. Ciliberto, N. Garnier, S. Joubaud, and A. Petrosyan, Entropy production and time asymmetry in nonequilibrium fluctuations, *Phys. Rev. Lett.* **98**, 150601 (2007).
 - [8] J. Li, J.M. Horowitz, T.R. Gingrich, and N. Fakhri, Quantifying dissipation using fluctuating currents, *Nat. Commun.* **10**, 1666 (2019).
 - [9] I.A. Martínez, G. Bisker, J.M. Horowitz, and J.M. Parrondo, Inferring broken detailed balance in the absence of observable currents, *Nat. Commun.* **10**, 3542 (2019).
 - [10] S. Ro, B. Guo, A. Shih, Trung V. Phan, Robert H. Austin, D. Levine, Paul M. Chaikin, and S. Martiniani, Model-free measurement of local entropy production and extractable work in active matter, *Phys. Rev. Lett.* **129**, 220601 (2022).
 - [11] Andre C. Barato and U. Seifert, Thermodynamic uncertainty relation for biomolecular processes, *Phys. Rev. Lett.* **114**, 158101 (2015).
 - [12] P. Pietzonka, F. Ritort, and U. Seifert, Finite-time generalization of the thermodynamic uncertainty relation, *Phys. Rev. E* **96**, 012101 (2017).
 - [13] K. Macieszczak, K. Brandner, and Juan P. Garrahan, Unified thermodynamic uncertainty relations in linear response, *Phys. Rev. Lett.* **121**, 130601 (2018).
 - [14] D.M. Busiello and S. Pigolotti, Hyperaccurate currents in stochastic thermodynamics, *Phys. Rev. E* **100**, 060102(R) (2019).
 - [15] Y. Hasegawa and T. Van Vu, Fluctuation theorem uncertainty relation, *Phys. Rev. Lett.* **123**, 110602 (2019).
 - [16] Y. Hasegawa and T. Van Vu, Uncertainty relations in stochastic processes: An information inequality approach, *Phys. Rev. E* **99**, 062126 (2019).
 - [17] J.M. Horowitz and T.R. Gingrich, Thermodynamic uncertainty relations constrain non-equilibrium fluctuations, *Nat. Phys.* **16**, 15 (2020).
 - [18] S. Otsubo, S. Ito, A. Dechant, and T. Sagawa, Estimating entropy production by machine learning of short-time fluctuating currents, *Phys. Rev. E* **101**, 062106 (2020).
 - [19] G. Falasco, M. Esposito, and J.-C. Delvenne, Unifying thermodynamic uncertainty relations, *New J. Phys.* **22**, 053046 (2020).
 - [20] I.D. Terlizzi and M. Baiesi, A thermodynamic uncertainty relation for a system with memory, *J. Phys. A* **53**, 474002 (2020).
 - [21] Sreekanth K. Manikandan, D. Gupta, and S. Krishnamurthy, Inferring entropy production from short experiments, *Phys. Rev. Lett.* **124**, 120603 (2020).
 - [22] T. Van Vu, V. Tuan Vo, and Y. Hasegawa, Entropy production estimation with optimal current, *Phys. Rev. E* **101**, 042138 (2020).
 - [23] N. Shiraishi, Optimal thermodynamic uncertainty relation in Markov jump processes, *J. Stat. Phys.* **185**, 19 (2021).
 - [24] V. Tuan Vo, T. Van Vu, Y. Hasegawa *et al.*, Unified thermodynamic-kinetic uncertainty relation, *J. Phys. A* **55**, 405004 (2022).
 - [25] S.K. Manikandan, S. Ghosh, A. Kundu, B. Das, V. Agrawal, D. Mitra, A. Banerjee, and S. Krishnamurthy, Quantitative analysis of non-equilibrium systems from short-time experimental data, *Commun. Phys.* **4**, 258 (2021).
 - [26] S. Otsubo, S.K. Manikandan, T. Sagawa, and S. Krishnamurthy, Estimating time-dependent entropy production from non-equilibrium trajectories, *Commun. Phys.* **5**, 11 (2022).
 - [27] C. Dieball and A. Godec, Direct route to thermodynamic uncertainty relations and their saturation, *Phys. Rev. Lett.* **130**, 087101 (2023).
 - [28] P. Pietzonka and F. Coghi, Thermodynamic cost for precision of general counting observables, *Phys. Rev. E* **109**, 064128 (2024).
 - [29] D. Lucente, M. Baldovin, F. Cecconi, M. Cencini, N. Cociagli, A. Puglisi, M. Viale, and A. Vulpiani, Conceptual and practical approaches for investigating irreversible processes, *New J. Phys.* **27**, 041201 (2025).
 - [30] H. Turlier, D. A. Fedosov, B. Audoly, T. Auth, N. S. Gov, C. Sykes, J.-F. Joanny, G. Gompper, and T. Betz, Equilibrium physics breakdown reveals the active nature of red blood cell flickering, *Nat. Phys.* **12**, 513 (2016).
 - [31] Shou W. Wang, Inferring energy dissipation from violation of the fluctuation-dissipation theorem, *Phys. Rev. E* **97**, 052125 (2018).
 - [32] T. Harada and Shin I. Sasa, Equality connecting energy dissipation with violation of fluctuation-response relation, *Phys. Rev. Lett.* **95**, 130602 (2005).
 - [33] K. Sekimoto, Langevin equation and thermodynamics, *Prog. Theor. Phys. Suppl.* **130**, 17 (1998).
 - [34] F.S. Gnesotto, F. Mura, J. Gladrow, and C.P. Broedersz, Broken detailed balance and non-equilibrium dynamics in living systems: A review, *Rep. Prog. Phys.* **81**, 066601 (2018).

- [35] É. Roldán and Juan M. R. Parrondo, Entropy production and Kullback-Leibler divergence between stationary trajectories of discrete systems, *Phys. Rev. E* **85**, 031129 (2012).
- [36] G. Bisker, M. Poletini, T. R. Gingrich, and J. M. Horowitz, Hierarchical bounds on entropy production inferred from partial information, *J. Stat. Mech.* (2017) 093210.
- [37] D. M. Busiello, J. Hidalgo, and A. Maritan, Entropy production for coarse-grained dynamics, *New J. Phys.* **21**, 073004 (2019).
- [38] Dominic J. Skinner and J. Dunkel, Estimating entropy production from waiting time distributions, *Phys. Rev. Lett.* **127**, 198101 (2021).
- [39] Dominic J. Skinner and J. Dunkel, Improved bounds on entropy production in living systems, *Proc. Natl. Acad. Sci. U.S.A.* **118**, e2024300118 (2021).
- [40] G. Teza and Attilio L. Stella, Exact coarse graining preserves entropy production out of equilibrium, *Phys. Rev. Lett.* **125**, 110601 (2020).
- [41] A. Ghosal and G. Bisker, Entropy production rates for different notions of partial information, *J. Phys. D* **56**, 254001 (2023).
- [42] Pedro E. Harunari, A. Dutta, M. Poletini, and É. Roldán, What to learn from a few visible transitions' statistics?, *Phys. Rev. X* **12**, 041026 (2022).
- [43] J. Van der Meer, B. Ertel, and U. Seifert, Thermodynamic inference in partially accessible Markov networks: A unifying perspective from transition-based waiting time distributions, *Phys. Rev. X* **12**, 031025 (2022).
- [44] K. Blom, K. Song, E. Vouga, A. Godec, and D. E. Makarov, Milestoning estimators of dissipation in systems observed at a coarse resolution, *Proc. Natl. Acad. Sci. U.S.A.* **121**, e2318333121 (2024).
- [45] M. Baiesi, T. Nishiyama, and G. Falasco, Effective estimation of entropy production with lacking data, *Commun. Phys.* **7**, 264 (2024).
- [46] Jonas H. Fritz, B. Ertel, and U. Seifert, Entropy estimation for partially accessible Markov networks based on imperfect observations: Role of finite resolution and finite statistics, *Phys. Rev. E* **111**, 044106 (2025).
- [47] T. R. Gingrich, G. M. Rotskoff, and J. M. Horowitz, Inferring dissipation from current fluctuations, *J. Phys. A* **50**, 184004 (2017).
- [48] C. Dieball and A. Godec, Mathematical, thermodynamical, and experimental necessity for coarse graining empirical densities and currents in continuous space, *Phys. Rev. Lett.* **129**, 140601 (2022).
- [49] C. Dieball and A. Godec, Coarse graining empirical densities and currents in continuous-space steady states, *Phys. Rev. Res.* **4**, 033243 (2022).
- [50] A. Ghosal and G. Bisker, Inferring entropy production rate from partially observed Langevin dynamics under coarse-graining, *Phys. Chem. Chem. Phys.* **24**, 24021 (2022).
- [51] É. Roldán and Juan M. R. Parrondo, Estimating dissipation from single stationary trajectories, *Phys. Rev. Lett.* **105**, 150607 (2010).
- [52] F. S. Gnesotto, G. Gradziuk, P. Ronceray, and C. P. Broedersz, Learning the non-equilibrium dynamics of Brownian movies, *Nat. Commun.* **11**, 5378 (2020).
- [53] É. Roldán, J. Barral, P. Martin, J. M. Parrondo, and F. Jülicher, Quantifying entropy production in active fluctuations of the hair-cell bundle from time irreversibility and uncertainty relations, *New J. Phys.* **23**, 083013 (2021).
- [54] D. M. Busiello, M. Ciarchi, and I. Di Terlizzi, Unraveling active baths through their hidden degrees of freedom, *Phys. Rev. Res.* **6**, 013190 (2024).
- [55] I. D. Terlizzi, M. Gironella, D. Herrera-Aguilar, T. Betz, F. Monroy, M. Baiesi, and F. Ritort, Variance sum rule for entropy production, *Science* **383**, 971 (2024).
- [56] I. Di Terlizzi, M. Baiesi, and F. Ritort, Variance sum rule: Proofs and solvable models, *New J. Phys.* **26**, 063013 (2024).
- [57] G. Tucci, E. Roldán, A. Gambassi, R. Belousov, F. Berger, R. G. Alonso, and A. J. Hudspeth, Modeling active non-Markovian oscillations, *Phys. Rev. Lett.* **129**, 030603 (2022).
- [58] See Supplemental Material at <http://link.aps.org/supplemental/10.1103/fsph-437v> for “Force-free entropy production estimation from stochastic traces.”
- [59] M. Baiesi and G. Falasco, Inflow rate, a time-symmetric observable obeying fluctuation relations, *Phys. Rev. E* **92**, 042162 (2015).
- [60] A. Frishman and P. Ronceray, Learning force fields from stochastic trajectories, *Phys. Rev. X* **10**, 021009 (2020).
- [61] C. Maes, K. Netočný, and B. Wynants, Steady state statistics of driven diffusions, *Physica (Amsterdam)* **387A**, 2675 (2008).
- [62] M. Baiesi and C. Maes, Life efficiency does not always increase with the dissipation rate, *J. Phys. Comm.* **2**, 045017 (2018).
- [63] I. Di Terlizzi and M. Baiesi, Kinetic uncertainty relation, *J. Phys. A* **52**, 02LT03 (2019).
- [64] C. Maes, Frenesy: Time-symmetric dynamical activity in nonequilibria, *Phys. Rep.* **850**, 1 (2020).
- [65] P. Martin, D. Bozovic, Y. Choe, and A. J. Hudspeth, Spontaneous oscillation by hair bundles of the bullfrog's sacculus, *J. Neurosci.* **23**, 4533 (2003).
- [66] Jeffrey B. Weiss, Fluctuation properties of steady-state Langevin systems, *Phys. Rev. E* **76**, 061128 (2007).
- [67] A. Crisanti, A. Puglisi, and D. Villamaina, Nonequilibrium and information: The role of cross correlations, *Phys. Rev. E* **85**, 061127 (2012).
- [68] V. Dotsenko, A. Maciołek, O. Vasilyev, and G. Oshanin, Two-temperature Langevin dynamics in a parabolic potential, *Phys. Rev. E* **87**, 062130 (2013).
- [69] V. Mancois, B. Marcos, P. Viot, and D. Wilkowski, Two-temperature Brownian dynamics of a particle in a confining potential, *Phys. Rev. E* **97**, 052121 (2018).
- [70] S. Cerasoli, V. Dotsenko, G. Oshanin, and L. Rondoni, Asymmetry relations and effective temperatures for biased Brownian gyrators, *Phys. Rev. E* **98**, 042149 (2018).
- [71] S. A. M. Loos and S. H. Klapp, Irreversibility, heat and information flows induced by non-reciprocal interactions, *New J. Phys.* **22**, 123051 (2020).
- [72] F. Ferretti, V. Chardès, T. Mora, Aleksandra M. Walczak, and I. Giardina, Building general Langevin models from discrete datasets, *Phys. Rev. X* **10**, 031018 (2020).

- [73] David B. Brückner, P. Ronceray, and Chase P. Broedersz, Inferring the dynamics of underdamped stochastic systems, *Phys. Rev. Lett.* **125**, 058103 (2020).
- [74] J.-Y. Tinevez, F. Jülicher, and P. Martin, Unifying the various incarnations of active hair-bundle motility by the vertebrate hair cell, *Biophys. J.* **93**, 4053 (2007).
- [75] J. Barral, F. Jülicher, and P. Martin, Friction from transduction channels' gating affects spontaneous hair-bundle oscillations, *Biophys. J.* **114**, 425 (2018).
- [76] V. Bormuth, J. Barral, J.-F. Joanny, F. Jülicher, and P. Martin, Transduction channels' gating can control friction on vibrating hair-cell bundles in the ear, *Proc. Natl. Acad. Sci. U.S.A.* **111**, 7185 (2014).
- [77] B. Nadrowski, P. Martin, and F. Jülicher, Active hair-bundle motility harnesses noise to operate near an optimum of mechanosensitivity, *Proc. Natl. Acad. Sci. U.S.A.* **101**, 12195 (2004).
- [78] D. Lucente, A. Baldassarri, A. Puglisi, A. Vulpiani, and M. Viale, Inference of time irreversibility from incomplete information: Linear systems and its pitfalls, *Phys. Rev. Res.* **4**, 043103 (2022).
- [79] F. Zamponi, F. Bonetto, L. F. Cugliandolo, and J. Kurchan, A fluctuation theorem for non-equilibrium relaxational systems driven by external forces, *J. Stat. Mech.* (2005) P09013.
- [80] L. Caprini, U. M. B. Marconi, A. Puglisi, and A. Vulpiani, The entropy production of Ornstein–Uhlenbeck active particles: A path integral method for correlations, *J. Stat. Mech.* (2019) 053203.
- [81] C. Maes, Frenetic bounds on the entropy production, *Phys. Rev. Lett.* **119**, 160601 (2017).
- [82] J. Gieseler, J. R. Gomez-Solano, A. Magazzù, I. P. Castillo, L. P. García, M. Gironella-Torrent, X. Viader-Godoy, F. Ritort, G. Pesce, A. V. Arzola, K. Volke-Sepúlveda, and G. Volpe, Optical tweezers—From calibration to applications: A tutorial, *Adv. Opt. Photonics* **13**, 74 (2021).
- [83] P. J. Foster, J. Bae, B. Lemma, J. Zheng, W. Ireland, P. Chandrakar, R. Boros, Z. Dogic, D. J. Needleman, and J. J. Vlassak, Dissipation and energy propagation across scales in an active cytoskeletal material, *Proc. Natl. Acad. Sci. U.S.A.* **120**, e2207662120 (2023).

End Matter

Multivariate Ornstein-Uhlenbeck model—We consider the multivariate Ornstein-Uhlenbeck process [66],

$$\dot{\mathbf{x}}_t = \mathbf{A}\mathbf{x}_t + \sqrt{2\mathbf{D}}\boldsymbol{\xi}_t, \quad (\text{A1})$$

where $\mathbf{x}_t \in \mathbb{R}^n$ is the state vector, $\mathbf{A}$ is the drift matrix, $\mathbf{D}$ the diffusion matrix, and $\boldsymbol{\xi}_t$ a vector of independent Gaussian white noises with $\langle \xi_t^i \xi_{t'}^j \rangle = \delta^{ij} \delta(t - t')$. The process is dynamically stable provided all eigenvalues of $\mathbf{A}$ have negative real parts, $\Re(\lambda_i) < 0$ for all i . The diffusion matrix relates to mobility and temperature as

$$\mathbf{D} = k_B \mathbf{T} \boldsymbol{\mu}, \quad (\text{A2})$$

where $\boldsymbol{\mu}$ is the mobility tensor and $\mathbf{T}$ may encode local effective temperatures associated with different thermal reservoirs. The drift matrix can be written as

$$\mathbf{A} = \boldsymbol{\mu}(-\mathbf{K} + \boldsymbol{\psi}), \quad (\text{A3})$$

where $\mathbf{K}$ is a symmetric positive-definite matrix and $\boldsymbol{\psi}$ is an antisymmetric matrix. The symmetric matrix $\mathbf{K}$ may be associated with an effective quadratic potential, while $\boldsymbol{\psi}$ may represent non conservative forces. No particular physical meaning needs to be ascribed to $\mathbf{K}$ and $\boldsymbol{\psi}$ unless additional structure is specified for $\boldsymbol{\mu}$.

Nonequilibrium conditions arise either from asymmetries in $\boldsymbol{\psi}$ or from temperature heterogeneity encoded in $\mathbf{T}$. The inflow rate, defined as the negative trace of the drift matrix, reads

$$\mathcal{G} = -\text{Tr}(\mathbf{A}) = \text{Tr}(\boldsymbol{\mu}\mathbf{K}) \quad (\text{A4})$$

and depends only on the symmetric part of the drift, because $\text{Tr}(\boldsymbol{\mu}\boldsymbol{\psi}) = 0$ when $\boldsymbol{\mu}$ is symmetric and $\boldsymbol{\psi}$ antisymmetric. Consequently, the inflow is insensitive to the sources of nonequilibrium, such as rotational or non-reciprocal couplings and temperature differences. This property extends to the case where $\boldsymbol{\psi}$ is nonsymmetric but has vanishing diagonal elements, provided that $\boldsymbol{\mu}$ (and thus $\mathbf{D}$) is diagonal, since any diagonal elements in $\boldsymbol{\psi}$ can be absorbed into $\mathbf{K}$ without loss of generality (see Sec. S6 of [58] for more details). When $\boldsymbol{\mu}$ is diagonal, the matrix $\mathbf{K}$ can be associated to conservative forces arising from a quadratic potential while the nonsymmetric $\boldsymbol{\psi}$ corresponds to nonreciprocal forces that drive the system out of equilibrium. For this case, and from Eq. (8), it also follows that for a fixed potential, increases in entropy production σ due to $\boldsymbol{\psi}$ must captured by the traffic $\mathcal{T}$.

Hair-bundle model—The spontaneous oscillations of hair bundles in the auditory organs of bullfrogs are driven by the interplay of mechanosensitive ion channels, molecular motor activity, and calcium-feedback mechanisms [53,65,74–76]. These dynamics are effectively captured by a nonlinear model with two coupled degrees of freedom: the bundle position x^1 and the center of mass of the molecular motors x^2 .

The stochastic equations of motion read

$$\begin{aligned} \dot{x}_t^1 &= -\mu_1 \partial_{x^1} V_t + \sqrt{2k_B T \mu_1} \xi_t^1, \\ \dot{x}_t^2 &= -\mu_2 \partial_{x^2} V_t - \mu_2 F_t^{\text{act}} + \sqrt{2k_B T^{\text{eff}} \mu_2} \xi_t^2, \end{aligned} \quad (\text{B1})$$

where μ_1 and μ_2 are mobility coefficients and $V_t = V(x_t^1, x_t^2)$ is the total potential energy. The potential

includes an elastic $[V_E(x^1, x^2)]$ contribution and a gating $[V_G(x^1, x^2)]$ contribution,

$$V_E(x^1, x^2) = \frac{k_{gs}}{2}(x^1 - x^2)^2 + \frac{k_{sp}}{2}(x^1)^2, \quad (\text{B2})$$

$$V_G(x^1, x^2) = -Nk_B T \ln \left[\exp \left(\frac{k_{gs} D (x^1 - x^2)}{Nk_B T} \right) + A \right], \quad (\text{B3})$$

so that $V(x^1, x^2) = V_E(x^1, x^2) + V_G(x^1, x^2)$. Here, k_{gs} and k_{sp} are stiffness coefficients, D is the gating swing of a transduction channel, and

$$A = \exp \left[\frac{\Delta G + k_{gs} D^2 / (2N)}{k_B T} \right], \quad (\text{B4})$$

where ΔG denotes the free-energy difference between open and closed channel states, and N is the number of transduction elements.

The system is driven out of equilibrium by molecular motor activity, represented by an effective temperature T^{eff}

and a nonconservative active force

$$F_t^{\text{act}} = F^{\text{max}}(1 - SP_0(x_t^1, x_t^2)), \quad (\text{B5})$$

where F^{max} is the maximal motor force and S quantifies the strength of calcium-mediated feedback on the motors. The gating probability of the mechanosensitive ion channels is

$$P_0(x^1, x^2) = \frac{1}{1 + A \exp \left[-\frac{k_{gs} D (x^1 - x^2)}{Nk_B T} \right]}, \quad (\text{B6})$$

which represents the open probability of a two-state equilibrium model of channel gating. In this model, the free-energy difference between open and closed states depends linearly on the displacement $x^1 - x^2$. In practice, $P_0(x^1, x^2)$ couples channel gating to bundle motion, mediating feedback between mechanical displacement and active motor forces. This feedback loop underlies the self-sustained oscillations characteristic of active hair-bundle dynamics [77].