

Time-dependent trajectory of a one-dimensional Gaussian non-Markovian observable does not reveal its nonequilibrium character

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When analyzing experimental or simulation time-series data, the question arises whether it is possible to tell from the mere observation of the time-dependent trajectory of a one-dimensional observable whether the system is in equilibrium or not. We here consider the nonequilibrium version of the generalized Langevin equation for a Gaussian non-Markovian observable and show that (i) the multipoint joint distribution solely depends on the two-point correlation function and that (ii) for any nonequilibrium process an equilibrium process with uniquely determined parameters can be found that produces the same two-point correlation function. Since the multipoint joint distribution completely characterizes the dynamics of an observable, we conclude that the nonequilibrium character of a system, in contrast to its non-Markovianity, cannot be read off from the one-dimensional trajectory of a Gaussian observable. These findings are relevant for human cancer and algae cells, whose single-cell velocity distributions have been found to be Gaussian within the data accuracy.

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I. INTRODUCTION

The field of nonequilibrium (NEQ) statistical mechanics has steadily developed for decades [1–14]. In this development, projection techniques have played a key role, since they allow to systematically derive the equation of motion, the so-called generalized Langevin equation (GLE), for arbitrary observables of interest [15–29]. The GLE contains, besides a deterministic force term, memory-friction and random-force terms which account for non-Markovian dissipation and fluctuation effects, respectively. The extraction of all GLE parameters from simulation or experimental time-series data is well established [20,28–35]. GLEs thus furnish a practical connection between fundamental concepts of statistical mechanics and experimental time-series data, the latter becoming progressively available through novel experimental approaches such as single-molecule and high-resolution optical techniques [36–43]. In the past, GLEs were amply used to study protein folding dynamics [44–47], barrier crossing dynamics [48–52], motion of living cells [53,54], spectroscopy [55–57], dynamical networks [58], and data predictability [59].

In this paper NEQ refers to systems that even in their stationary state are not described by equilibrium (EQ) statistical-mechanics laws and violate the fluctuation-dissipation theorem (FDT), according to which the observable linear-response function is proportional to the time derivative of its two-point correlation function [8]. In the standard treatment, the GLE is derived from a time-independent Hamiltonian [15–17] and

hence does not apply to such NEQ systems. A number of works dealt with generalizations of the projection framework to time-dependent and transient scenarios [60–69], but the resulting GLEs are typically too complex to be dealt with in practical applications. This is why in applications to driven NEQ systems, it has become standard practice to use modified GLEs that violate the FDT by construction [12,14,41,52–54,70–78]. The same starting point is taken in this paper. We consider a GLE as derived by Mori projection but assume a random force whose two-point correlation function is not proportional to the memory-friction kernel, thereby violating the FDT. The question whether from the time-dependent trajectory of a scalar, i.e., one-dimensional, observable one can infer that the data come from a NEQ system has been the focus of several recent works [71–73,79], many of which assumed a Markovian model [80–87]. Our answer for a Gaussian general non-Markovian observable, based on the exact derivation of the multipoint distribution, is negative. This provides important insight not only for the analysis of experimental NEQ systems whose trajectories happen to be Gaussian, but also for the future development of methods from which the NEQ character of a system can be clearly identified.

II. RESULTS

To proceed, the Mori GLE for a general scalar observable $A(t)$ reads [15–17]

$$\ddot{A}(t) = -K(A(t) - \langle A \rangle) - \int_{t_0}^{\infty} ds \Gamma(t-s) \dot{A}(s) + F(t), \quad (1)$$

where the stiffness of the effective harmonic potential is denoted as K , $F(t)$ is the random force, which results from the interactions with the many-body surrounding, and $\Gamma(t)$ is the single-sided friction memory kernel, i.e., $\Gamma(t) = 0$ for $t < 0$; note that there is no mass variable in front of the acceleration

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$\ddot{A}(t)$, which affects the physical units of the parameters in the equation. The time at which the projection onto the initial probability distribution (taken to be the canonical distribution) is performed is denoted as t_0 (for details of the derivation see [69]). Strictly speaking, $F(t)$ is a phase-space dependent deterministic function with well-defined initial conditions at $t = t_0$, Eq. (1) is thus deterministic and time-reversible. As usual, we instead treat $F(t)$ as a random force characterized solely by its two-point correlation according to

$$\langle F(s)F(t) \rangle = \Gamma_R(t - s) = \Gamma_R(s - t). \quad (2)$$

In EQ, it follows for the Mori GLE that $\Gamma_R(t) = \langle \dot{A}^2 \rangle \Gamma(|t|)$; note that this relation does not hold for other GLEs that have been derived recently even in EQ [28,88] and therefore is equivalent to the FDT only for a restricted subset of GLEs. In this paper we treat the more general case $\Gamma_R(t) \neq \langle \dot{A}^2 \rangle \Gamma(|t|)$ that is widely used as a model for NEQ systems. In order to derive the multipoint distribution explicitly, the Mori GLE in Eq. (1), which is linear in $A(t)$, is a suitable model for Gaussian observables (i.e., observables whose joint distribution at different times can be written as a multivariate Gaussian process) as considered by us. We note in passing that the Mori GLE in Eq. (1) is exact even for non-Gaussian observables, unless one approximates the random-force distribution as Gaussian.

The question we address is whether from a sufficiently long time-dependent trajectory of the scalar Gaussian observable $A(t)$, that follows from the GLE defined by Eqs. (1) and (2), one can extract the GLE parameters, namely K , $\Gamma(t)$ and $\Gamma_R(t)$. A more modest question is whether one is able to tell from the trajectory whether it comes from a NEQ GLE with $\Gamma_R(t) \neq \langle \dot{A}^2 \rangle \Gamma(|t|)$. To answer both questions we derive the multipoint joint distribution for $A(t)$ and show that it is determined solely in terms of the two-point correlation function of $A(t)$. We also show that the two-point correlation function of the NEQ GLE with $\Gamma_R(t) \neq \langle \dot{A}^2 \rangle \Gamma(|t|)$ is identical to the two-point correlation function of a substitute EQ GLE with $\Gamma_R(t)/\langle \dot{A}^2 \rangle_{\text{eq}} = \Gamma(|t|) = \Gamma_{\text{eq}}(|t|)$ with a uniquely determined single-sided effective EQ kernel $\tilde{\Gamma}_{\text{eq}}(t)$. Since the multipoint distribution constitutes a complete description of the dynamics of an observable, by combining these two results we conclude that the scalar trajectory of a Gaussian NEQ observable does not reveal its NEQ character. This is a nontrivial and relevant finding, since a few NEQ scalar observables, such as the center-of-mass motion of human cancer cells [53] and algae cells [54] as well as high-pass filtered weather and financial data [89], have been shown to follow Gaussian processes to high accuracy. It thus follows that for these observables the obvious fact that they are NEQ cannot be conclusively inferred just by observation of a sufficiently long trajectory of the observable. In this context it is important to realize that an observable can be Gaussian even when the entire many-body system is described by a non-Gaussian Hamiltonian, meaning that other observables and system coordinates may very well exhibit non-Gaussian fluctuations. So our results are not limited to Gaussian systems but only to Gaussian observables, which is an important distinction. The reason why for some complex systems, such as human cancer cells [53] or algae cells [54], which certainly are described by non-Gaussian

many-body Hamiltonians, the single-cell center-of-mass velocity displays Gaussian behavior is not clear. Presumably, this has to do with the fact that the center-of-mass position of a cell results from the summation of many independently fluctuating components, similar in spirit to the central-limit theorem. Having said that, it should be clear that one would expect residual non-Gaussianity in the distribution tails, which however is difficult to detect because of the omnipresent noise in such biological system. Likewise, it is quite possible that other observables characterizing human cancer and algae cells exhibit more prominent non-Gaussian behavior.

To proceed, by Fourier transforming Eq. (1) according to $\tilde{A}(\nu) = \int_{-\infty}^{\infty} dt e^{-i\nu t} A(t)$, we obtain the linear response relation as

$$\tilde{A}(\nu) - 2\pi\delta(\nu)\langle A \rangle = \tilde{\chi}(\nu)\tilde{F}(\nu), \quad (3)$$

where the Fourier-transformed response function (which is causal and thus single-sided in the time-domain) is determined by

$$1/\tilde{\chi}(\nu) = K - \nu^2 + i\nu\tilde{\Gamma}(\nu). \quad (4)$$

In deriving Eq. (3) we have shifted the projection time into the far past, $t_0 \rightarrow -\infty$. By doing so, the observable distribution and dynamics become for systems with finite relaxation times independent of the phase-space distribution imposed at time t_0 and rather depend on the random-force distribution only [69].

In order to derive the FDT we calculate the two-point correlation function

$$C(t - t') = \langle (A(t) - \langle A \rangle)(A(t') - \langle A \rangle) \rangle \quad (5)$$

for general times $t, t' \gg t_0$ by averaging over $F(t)$. By combining Eqs. (5) with (2) and (3), the Fourier-transformed correlation function results as [53]

$$\tilde{C}(\nu) = \tilde{\chi}(\nu)\tilde{\chi}(-\nu)\tilde{\Gamma}_R(\nu). \quad (6)$$

For an EQ system with $\Gamma_R(t)/\langle \dot{A}^2 \rangle_{\text{eq}} = \Gamma(|t|) \equiv \Gamma_{\text{eq}}(|t|)$ the correlation function can be written as

$$\begin{aligned} \tilde{C}_{\text{eq}}(\nu) &= \tilde{\chi}_{\text{eq}}(\nu)\tilde{\chi}_{\text{eq}}(-\nu)\langle \dot{A}^2 \rangle_{\text{eq}}[\tilde{\Gamma}_{\text{eq}}(\nu) + \tilde{\Gamma}_{\text{eq}}(-\nu)] \\ &= \langle \dot{A}^2 \rangle_{\text{eq}} \left[\frac{\tilde{\chi}_{\text{eq}}(-\nu)}{i\nu} - \frac{\tilde{\chi}_{\text{eq}}(\nu)}{i\nu} \right] \\ &= -\frac{2\langle \dot{A}^2 \rangle_{\text{eq}} \tilde{\chi}_{\text{eq}}''(\nu)}{\nu}, \end{aligned} \quad (7)$$

where the EQ response function is defined in analogy to Eq. (4) as $1/\tilde{\chi}_{\text{eq}}(\nu) = K_{\text{eq}} - \nu^2 + i\nu\tilde{\Gamma}_{\text{eq}}(\nu)$. In the last step in Eq. (7) we used that the time-domain response function is real and thus $\tilde{\chi}_{\text{eq}}'(\nu) = \tilde{\chi}_{\text{eq}}'(-\nu)$ and $\tilde{\chi}_{\text{eq}}''(\nu) = -\tilde{\chi}_{\text{eq}}''(-\nu)$, where we split $\tilde{\chi}_{\text{eq}}(\nu)$ into its real and imaginary parts according to $\tilde{\chi}_{\text{eq}}(\nu) = \tilde{\chi}_{\text{eq}}'(\nu) + i\tilde{\chi}_{\text{eq}}''(\nu)$. In contrast to the NEQ result in Eq. (6), $\tilde{C}_{\text{eq}}(\nu)$ splits into its two single-sided time-domain parts proportional to $\tilde{\chi}_{\text{eq}}(\nu)$ and $\tilde{\chi}_{\text{eq}}(-\nu)$. Eq. (7) is the FDT in the frequency domain and it obviously only holds in the EQ case for $\Gamma_R(t)/\langle \dot{A}^2 \rangle_{\text{eq}} = \Gamma(|t|)$. The mean square of the observable $A(t)$ follows from the correlation function as

$\langle \dot{A}^2 \rangle_{\text{eq}} = C_{\text{eq}}(0) = \int dv \tilde{C}_{\text{eq}}(v) = \langle \dot{A}^2 \rangle_{\text{eq}} / K_{\text{eq}}$, together with the relation $\langle \dot{A}^2 \rangle_{\text{eq}} = -\ddot{C}_{\text{eq}}(0) = \int dv v^2 \tilde{C}_{\text{eq}}(v)$ this allows to determine K_{eq} from $\tilde{C}_{\text{eq}}(v)$.

We next split the NEQ and EQ correlation functions into their single-sided components according to $C(t) = C^+(t) + C^+(-t)$ and $C_{\text{eq}}(t) = C_{\text{eq}}^+(t) + C_{\text{eq}}^+(-t)$, where $C^+(t) \equiv \theta(t)C(t)$ and $C_{\text{eq}}^+(t) \equiv \theta(t)C_{\text{eq}}(t)$ and $\theta(t)$ denotes the Heavy-side function. With this, the Fourier transform of $C_{\text{eq}}^+(t)$ follows from Eq. (7) as

$$\tilde{C}_{\text{eq}}^+(v) = -\frac{\langle \dot{A}^2 \rangle_{\text{eq}}}{iv} (\tilde{\chi}_{\text{eq}}(v) - \tilde{\chi}_{\text{eq}}(0)). \quad (8)$$

Note that a similar decomposition of Eq. (6) is not possible, because it cannot be straightforwardly split into its causal and anticausal parts (see Supplemental Material (SM) Sec. I [90] for an explicit illustration).

Now we ask whether for a given NEQ correlation function $\tilde{C}(v)$ we can find a matching EQ correlation function $\tilde{C}_{\text{eq}}(v)$ that satisfies $\tilde{C}_{\text{eq}}(v) = \tilde{C}(v)$ [in which case we would also have $\langle \dot{A}^2 \rangle_{\text{eq}} = \langle \dot{A}^2 \rangle = -\ddot{C}(0)$ and $\langle A^2 \rangle_{\text{eq}} = \langle A^2 \rangle = C(0)$]. In fact, by combining the equivalent assumption for the single-sided correlation functions, $\tilde{C}_{\text{eq}}^+(v) = \tilde{C}^+(v)$, with Eq. (8) and the EQ version of Eq. (4), we find after rearranging

$$iv\tilde{\Gamma}_{\text{eq}}(v) = v^2 - K_{\text{eq}} + \frac{K_{\text{eq}}}{1 - iv\tilde{C}^+(v)/\langle A^2 \rangle}, \quad (9)$$

where $K_{\text{eq}} = \langle \dot{A}^2 \rangle_{\text{eq}} / \langle A^2 \rangle_{\text{eq}} = \langle \dot{A}^2 \rangle / \langle A^2 \rangle$ (but in general $K_{\text{eq}} \neq K$). In essence, Eq. (9) shows that for every single-sided NEQ correlation function $\tilde{C}^+(v)$ that is produced by the NEQ GLE in Eqs. (1) and (2), there is an EQ GLE with a memory kernel $\tilde{\Gamma}_{\text{eq}}(v)$ determined by Eq. (9) that displays the identical correlation function; in other words, from the two-point correlation function one cannot decide whether a system is NEQ or EQ. As an illustration, in SM Sec. I [90] we explicitly calculate the EQ GLE parameters that match the two-point correlation of a simple NEQ model with Markovian friction and exponentially decaying noise correlation. Since the two-point correlation function of the NEQ system is well-behaved and physically sound, we expect the parameters of the effective EQ substitute model, K_{eq} and $\tilde{\Gamma}_{\text{eq}}(v)$, to correspond to a physically sound model as well. However, an effective temperature of the EQ model cannot be straightforwardly determined, unless one assumes an effective mass for the observable $A(t)$, which would allow to calculate the effective temperature from the mean-squared velocity $\langle \dot{A}^2 \rangle$ using an analog of the equipartition theorem.

One could think that the two-point correlation function is only a partial description of a system, we therefore check whether the N -point distribution function allows to infer the NEQ properties of an observable. To proceed, we define the N -point joint probability distribution of $A(t)$ according to continuum probability calculus as

$$\rho(\{A_N, t_N\}) = \left\langle \prod_{k=1}^N \delta(A_k - A(t_k)) \right\rangle. \quad (10)$$

For the delta functions we use their Fourier representation and obtain

$$\rho(\{A_N, t_N\}) = \prod_{k=1}^N \int_{-\infty}^{\infty} \frac{dq_k}{2\pi} e^{i \sum_{k=1}^N q_k A_k} \times \left\langle \exp \left(-i \sum_{k=1}^N q_k A(t_k) \right) \right\rangle. \quad (11)$$

We next use the linear response relation in Eq. (3), which is exact for a Gaussian observable, and express the average over the random force $F(t)$ in Eq. (11) by a Gaussian path integral according to

$$\langle X(F) \rangle = \int_{-\infty}^{\infty} \frac{\mathcal{D}F(\cdot)}{\mathcal{N}_F} X(F) \times \exp \left(-\frac{1}{2} \int_{-\infty}^{\infty} ds ds' F(s) F(s') \Gamma_R^{-1}(s - s') \right), \quad (12)$$

where $\mathcal{N}_F$ is a normalization constant and $\Gamma_R^{-1}(s)$ is the functional inverse of the random-force kernel defined in Eq. (2) according to $\int ds \Gamma_R^{-1}(t - s) \Gamma_R(s - t') = \delta(t' - t)$. Since we consider a Gaussian variable $A(t)$, non-Gaussian fluctuations of $F(t)$ need not be considered here. Performing the Gaussian path integrals, the N -point distribution follows in matrix notation as

$$\rho(\{A_N, t_N\}) = \frac{\exp \left(-\sum_{j,k=1}^N (A_j - \langle A \rangle) I_{jk}^{-1} (A_k - \langle A \rangle) / 2 \right)}{\sqrt{\det 2\pi I}}, \quad (13)$$

where the matrix

$$I_{jk} = C(t_j - t_k) \quad (14)$$

is solely determined in terms of the two-point correlation function defined in Eq. (6), details of the derivation are given in the SM Sec. II [90]. From Eq. (13) we see that if the random force $F(t)$ is described by a Gaussian process, as assumed in Eq. (12), then also the observable $A(t) - \langle A \rangle$ is a Gaussian process determined by the correlation function $C(t)$ defined in Eq. (6). Since the correlation function $C(t)$ is identical to an EQ correlation function $C_{\text{eq}}(t)$ with a memory kernel defined in Eq. (9), and since the N -point joint distribution for general N completely defines the trajectory statistics, we conclude that there is no way to tell whether a process is NEQ or EQ from a one-dimensional trajectory of a general Gaussian observable. Multipoint distributions involving $A(t_k)$ and velocities $\dot{A}(t_k)$ also only depend on $C(t)$ and derivatives thereof, as shown in SM Sec. III [90], so our conclusion also holds if one considers more general multipoint joint distributions including observable velocities.

While the N -point distribution of a Gaussian NEQ trajectory does not reveal its NEQ character, it can very well be used to characterize its non-Markovianity. To make this notion concrete, we consider the three-point distribution function $\rho(A_3, t_3; A_2, t_2; A_1, t_1)$, which according to Eq. (13) is

determined by the inverse covariance matrix

$$I^{-1} = \frac{\begin{pmatrix} J^2 - I_{23}^2 & I_{13}I_{23} - JI_{12} & I_{12}I_{23} - JI_{13} \\ I_{13}I_{23} - JI_{12} & J^2 - I_{13}^2 & I_{12}I_{13} - JI_{23} \\ I_{12}I_{23} - JI_{13} & I_{12}I_{13} - JI_{23} & J^2 - I_{12}^2 \end{pmatrix}}{\det I}, \quad (15)$$

where we introduced the short-hand notation $J \equiv C(0) = \langle A^2 \rangle$ for the mean square of A . There are different ways of defining the Markovian property, we here use the factorization of the three-point conditional distribution into the product of two two-point conditional distributions according to [8]

$$\rho(A_3, t_3; A_2, t_2 | A_1, t_1) = \rho(A_3, t_3 | A_2, t_2) \rho(A_2, t_2 | A_1, t_1), \quad (16)$$

where the conditional three- and two-point distributions are defined as $\rho(A_3, t_3; A_2, t_2 | A_1, t_1) \equiv \rho(A_3, t_3; A_2, t_2; A_1, t_1) / \rho(A_1, t_1)$ and $\rho(A_3, t_3 | A_2, t_2) \equiv \rho(A_3, t_3; A_2, t_2) / \rho(A_2, t_2)$ and the single-point distribution follows from Eq. (13) as $\rho(A_1, t_1) = \exp(-(A_1 - \langle A \rangle)^2 / (2J)) / \sqrt{2\pi J}$ and obviously is independent of time. It is easy to see that the Markovian condition Eq. (16) can only be satisfied if the off-diagonal entries $I_{13}^{-1} = I_{31}^{-1}$ of the inverse covariance matrix in Eq. (15) vanish, i.e., if $I_{12}I_{23} - JI_{13} = 0$ holds [this condition is necessary and sufficient and follows from the fact that a term that involves the product $(A_1 - \langle A \rangle)(A_3 - \langle A \rangle)$ does not appear on the right side of Eq. (16)]. Using the definition Eq. (14) the Markovian condition can thus be written as

$$C(t_3 - t_1) = C(t_3 - t_2)C(t_2 - t_1)/C(0), \quad (17)$$

which is only satisfied if the correlation function is a single exponential, $C(t) = C(0)e^{-t/\tau}$, as is well known. We conclude that the only trajectory property one can deduce from the multipoint distribution is its non-Markovianity by the violation of Eq. (16) (equivalent to deviations of the correlation function $C(t)$ from a single exponential decay) but not its NEQ character.

We finally point out some subtle properties of the stochastic NEQ model defined by Eqs. (1) and (2) that are important when extracting the memory kernel from time-series data by turning the stochastic GLE for $A(t)$ into a nonstochastic Volterra equation for $C(t)$. To proceed, we multiply the GLE in Eq. (1) by $\dot{A}(t')$ and average over the random force, by which we obtain

$$-\ddot{C}(t - t') = K\dot{C}(t - t') + \int_{-\infty}^{t-t_0} ds \Gamma(s) \ddot{C}(t - t' - s) + \langle \dot{A}(t') F(t) \rangle. \quad (18)$$

For a system that follows Hamiltonian dynamics and for most standard GLEs, the average $\langle \dot{A}(t_0) F(t) \rangle$ vanishes, i.e., the observable velocity at the projection time t_0 is orthogonal to the random force [28]. Therefore, by choosing $t' = t_0$ and using $\langle \dot{A}(t_0) F(t) \rangle = 0$, the random force drops out and one obtains after single-sided Fourier transformation

$$\tilde{C}^+(\nu) = \frac{\ddot{C}(0)\tilde{\chi}(\nu)}{i\nu} + \frac{C(0)}{i\nu} \quad (19)$$

with $\tilde{\chi}(\nu)$ given by Eq. (4), details are presented in SM Sec. IV [90]. Equation (19) is identical to Eq. (8), the equation for the EQ GLE, and will therefore yield the parameters

of the EQ and not of the NEQ system. How come? For a stochastic GLE with a random force according to Eq. (2), we find from Eq. (3) and for $t_0 \rightarrow -\infty$ a nonvanishing velocity-random-force coupling

$$\langle \dot{A}(t') F(t) \rangle = \frac{d}{dt'} \int_{-\infty}^{\infty} ds \chi(s) \Gamma_R(t - t' + s). \quad (20)$$

Inserting Eq. (20) into Eq. (18) one recovers for $t_0 \rightarrow -\infty$ after Fourier transforming Eq. (6), the exact expression for the two-point correlation function for the NEQ GLE, see SM Sec. IV [90] for details. Still, while the Volterra Eq. (18) yields the NEQ correlation function for the stochastic GLE defined by Eqs. (1) and (2) when accounting for the term $\langle \dot{A}(t_0) F(t) \rangle$, it does not allow to separately deduce the response function $\tilde{\chi}(\nu)$ and the random force correlator $\tilde{\Gamma}(\nu)$ from the correlation function $C(t)$. Thus, one cannot deduce the NEQ character of an observable using the Volterra equation, regardless of whether one accounts for the presence of the term $\langle \dot{A}(t_0) F(t) \rangle$ in Eq. (18) or not.

III. CONCLUSIONS

In conclusion, from the time-dependent trajectory of a one-dimensional Gaussian observable described by Eqs. (1) and (2), it cannot be decided whether the observable characterizes a NEQ or an EQ system, regardless of how the trajectory is processed. From this follows that also the system entropy production cannot be unambiguously inferred from a one-dimensional Gaussian NEQ trajectory. In contrast, the non-Markovianity of an observable follows from the trajectory by using standard criteria. For the GLE studied here, NEQ can only be obtained for nonvanishing memory, because the EQ relation $\Gamma_R(t) = \langle \dot{A}^2 \rangle \Gamma(|t|)$ is for a Markovian system with $\Gamma_R(t) \sim \delta(t)$ and $\Gamma(|t|) \sim \delta(t)$ trivially satisfied by the resulting value of $\langle \dot{A}^2 \rangle$. We note that for EQ systems one has $\langle \dot{A}^2 \rangle = k_B T / m$ and $\langle A^2 \rangle = k_B T / K$ according to an analog of the equipartition theorem, where $k_B T$ is the heat-bath temperature and m is the effective observable mass; if only the trajectory of $A(t)$ is known, $\langle A^2 \rangle$ and $\langle \dot{A}^2 \rangle$ follow directly but $k_B T$, K and m cannot be separately determined. But, obviously, the opposite is not true, a non-Markovian system is not necessarily NEQ. Thus, non-Markovianity and NEQ are properties of an observable that are distinct but impossible to disentangle solely based on scalar trajectory information. Note that we did not assume that the entire system is Gaussian, but only that the observable $A(t)$ is Gaussian, which is a subtle but important distinction: In fact, the center-of-mass motion of cancer and algae cells, which obviously are NEQ systems, is Gaussian within data accuracy when analyzed on a single-cell level [53,54] and therefore is a nontrivial experimental example of the impossibility to deduce the NEQ character of a Gaussian scalar observable. Another well-known example of a Gaussian NEQ system is the active Ornstein-Uhlenbeck process, which has been shown to be equivalent to a non-Markovian equilibrium system with a negative exponentially decaying memory function [91].

Thus, to deduce the NEQ properties of a system one needs to (i) apply an external force and detect violation of the FDT Eq. (7) [36,43,74,92], (ii) simultaneously observe more than one observable and detect violation of the detailed balance condition [14,93], for example for a system of many interact-

ing active Ornstein-Uhlenbeck particles, (iii) simultaneously measure trajectories of the observable and the applied force [94], or (iv) measure the response to a change of relevant system parameters (such as the viscosity, which mostly modifies the solution friction kernel [95], or ATP) that in EQ would not (or only mildly) modify the observable behavior [75,96].

Non-Gaussian NEQ observables are interesting but much more complex than Gaussian observables [70,76–78,97,98], since for these the relation $\Gamma_R(t) = \langle \dot{A}^2 \rangle \Gamma(|t|)$ can be broken already for EQ systems if the GLE projects out the exact nonlinear potential-of-mean force [28,88]. Likewise, the coupling between nonlinearities, non-Markovianity and nonequilibrium for a vectorial observable needs to be fully unravelled in the future.

Very recently it has been shown that for a many-body system defined by a time-dependent Hamiltonian that includes an external NEQ force which couples linearly to an observable, the resulting GLE nevertheless obeys the FDT if the observable described by the GLE is Gaussian [69]. Our results reported here are in line with those findings but constitute a considerable generalization, as no explicit form of the underlying NEQ Hamiltonian is assumed.

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