Global effective fluctuation-dissipation relation in particle dynamics and Brownian motion

Chiara Pezzotti and Massimiliano Giona[*]

Dipartimento di Ingegneria Chimica, Materiali, Ambiente La Sapienza Università di Roma Via Eudossiana 18, 00184 Roma, Italy

(Received 11 December 2025; accepted 7 April 2026; published 25 August 2026)

We introduce the concept of a global effective fluctuation-dissipation relation for thermal particle motion in heterogeneous and disordered systems. The relation connects two effective quantities: the diffusivity, determined from the long-time scaling of the particle mean-square displacement at thermal equilibrium, and the effective friction factor, associated with the linear scaling of the particle terminal velocity in the presence of a constant external force with the intensity of the force itself. The global effective fluctuation-dissipation relation is identically fulfilled by hydromechanic models of fluid-particle interactions in heterogeneous media, i.e., whenever the friction factor either is a function of the particle position or represents a stochastic process. Conversely, models in which heterogeneity is described via a potential landscape do not fulfill this property in general but solely in the limit of small external forces or small intensities of the equilibrium potential.

DOI: 10.1103/zl8y-r5vx

I. INTRODUCTION

The study of transport phenomena in biological systems [1,2], both in intracellular [3] and in extracellular [4] environments, and the growing interest in soft-matter applications, such as the transport of liposomes and lipid particles [5], have increasingly focused attention on the analysis of random motion (diffusion) in complex and crowded fluid environments, commonly referred to as heterogeneous fluids [6]. Hereafter, a fluid is termed heterogeneous if it contains suspended macromolecular structures and/or dispersed soft (e.g., liposomes, vesicles) or rigid particles. Typical examples are suspensions, polymer solutions, and hydrogels.

Compared to particle transport in homogeneous media, such as a single-phase, single-component fluid, a range of diverse phenomena emerge in heterogeneous systems. These include subdiffusive motion [7,8], anisotropic effects [9], and Fickian yet non-Gaussian diffusion [10–12], among others. In general, the heterogeneity originates from the suspension of macromolecular structures or nano/microparticles within an otherwise homogeneous liquid phase, leading to interactions with the tagged particle.

From a physical point of view, these complex interactions can be accounted for in different ways: (1) by considering hydromechanical models in which the friction factor, and as a consequence the particle diffusivity, depends on the particle position or (2) by considering the interaction with the other suspended objects via some interaction potentials [13,14].

[*]Contact author: massimiliano.giona@uniroma1.it

In hydromechanical models, assuming a Stokesian description of solvent hydrodynamics (in which the momentum balance equation in the fluid is described by means of the Stokes equations for a Newtonian and incompressible fluid equipped with either slip or no-slip boundary conditions at the particles' external surfaces and the force acting on each particle is the integral over its external surface of the normal component of the overall stress tensor of the fluid [15,16]), the confinement induced by surrounding macromolecular structures and nano/microscale objects on the tagged particle results in a position-dependent friction factor, which generally has a tensorial nature [15,16]. Therefore, the heterogeneity is essentially hydrodynamic in origin: It breaks the homogeneity of the fluid-particle interactions, and its position dependence is a direct consequence of confinement effects that modify the Stokesian friction tensor [15]. This is also the case of the stochastic models characterizing the theory of dissipative particle dynamics, in which a position-dependent friction accounts for the hydrodynamic interactions among the particles [17,18]. Similarly, the Stokesian dynamics introduced by Brady and Bossis to simulate suspensions involves position-dependent friction kernels [19,20]. Moreover, position-dependent friction is widely used to describe heterogeneous friction landscapes experienced by passive or active particles, including anomalous effects [21–24]. Beyond these particle-based descriptions, confinement effects can also be investigated within a lattice Boltzmann framework [25].

Coupled with this mean-field description of the interactions, thermal fluctuations must also be taken into account, leading to the consideration of the various fluctuation-dissipation relations that govern thermal particle motion.

Following Kubo [26], in the case of a homogeneous fluid, the fluctuation-dissipation relations of the first and second kinds describe, respectively, the equilibrium correlation properties of the particle velocity and the thermal force (see also Ref. [27]). As a consequence of the first fluctuation-dissipation relation (the classical Stokes-Einstein relation for

Newtonian fluids in Stokes regime), a global fluctuation-dissipation relation is established, connecting the long-term particle diffusivity to the hydromechanic long-term friction factor. If the particle dynamics is characterized by memory effects [see, e.g., Eq. (9)], the long-term friction factor corresponds to the integral of the dissipative memory kernel [see Eq. (11)], and thus the asymptotic diffusive regime is defined for timescales larger that the characteristic relaxation time of the memory kernel. In homogeneous viscoelastic fluids, this has been generalized to account for the rheological conditions that may lead to anomalous diffusive scalings, and this is referred to as the generalized Stokes-Einstein relation [28–30].

In a heterogeneous fluid, such as a suspension, within a Stokesian description of the hydrodynamics, a local fluctuation-dissipation relation can be established, connecting the local pointwise friction factor to the local value of the diffusivity [31]. However, the concept of the local diffusivities is altogether different from the notion of an effective diffusion coefficient that sets up in the long term and that is a functional of the entire diffusivity field. In a similar way, the knowledge of the local friction factor does not provide a quantitative prediction of the effective resistance exerted by the fluid when a force is applied to the particle.

These observations lead to a global fluctuation-dissipation relation involving the effective transport and mechanical properties characterizing particle motion in a heterogeneous fluid, involving the effective long-term transport and mechanical properties.

The definition of this effective global fluctuation-dissipation relation is the main focus of this article, examining a range of physically relevant situations where the validity of such a relation may or may not be ensured. This analysis has no counterpart in homogeneous fluids, as the effective global fluctuation-dissipation relation in that case simply reduces to the global Stokes-Einstein equation *sic et simpliciter*.

The article is organized as follows. Section I reviews briefly the different fluctuation-dissipation relations for particle motion at thermal equilibrium, introducing the concept of global effective fluctuation-dissipation relation in heterogeneous fluids. Section II provides the main analytical results for hydrodynamic models and for particle motion in a periodic potential landscape, i.e., for the two main classes of models describing, from different perspectives, the effects of heterogeneities. The proofs of the results presented in Sec. II are postponed to the Appendixes, making use of homogenization theory [32] for the effective transport coefficients. Section III analyzes other models of transport and the validity of the global effective fluctuation-dissipation relation previously stated. A stochastic hydromechanic model and particle dynamics in a random system of partially reflecting barriers are considered. The concluding Sec. IV discusses some other implications of the present analysis in related fields such as in the analysis of molecular dynamics experiments.

In order to properly frame the concept of effective global fluctuation-dissipation relation, it is useful to overview the different known fluctuation-dissipation results for particle motion in a fluid, and how they depend on the level of complexity/generality of the hydrodynamic description of the fluid-particle interactions.

A. Fluctuation-dissipation relations

Consider the motion of a particle of mass m in a fluid at constant temperature T. Several fluctuation-dissipation relations can be established. For the sake of notational simplicity, we adopt a scalar (one-dimensional) formalism that can be easily extended to the tensorial (three-dimensional) case.

To begin with, consider the Stokes-Einstein case, i.e., the description of particle motion in a Newtonian, macroscopically quiescent, fluid under the Stokes regime:

$$m\frac{dv(t)}{dt} = -\eta\, v(t) + R(t), \tag{1}$$

where η is the friction factor and $R(t)$ the thermal/hydrodynamic force at equilibrium. The global Stokes-Einstein fluctuation-dissipation relation dictates that the particle diffusivity D, defined by the long-term linear scaling of the particle mean-square displacement

$$D = \lim_{t\to\infty} \frac{\langle (x(t)-x_0)^2\rangle}{2\,t}, \tag{2}$$

where $dx(t)/dt = v(t)$, $x(t=0) = x_0$, is related to η by the relation

$$D\,\eta = k_B\,T, \tag{3}$$

where k_B is the Boltzmann constant.

The Kubo fluctuation-dissipation relation of the first kind (FD1k for short) involves the properties of the particle velocity autocorrelation function at equilibrium:

$$C_{vv}(t) = \langle v(t)\, v(0)\rangle_{\text{eq}} \tag{4}$$

and states that $C_{vv}(t)$ is the solution of the equation

$$m\,\frac{dC_{vv}(t)}{dt} = -\eta\, C_{vv}(t), \quad C_{vv}(0) = \langle v^2\rangle_{\text{eq}} = \frac{k_B\,T}{m}. \tag{5}$$

Obviously, in the Stokes-Einstein case, $C_{vv}(t)$ is exponential:

$$C_{vv}(t) = \langle v^2\rangle_{\text{eq}}\ e^{-\eta\,t/m} \tag{6}$$

and, applying the Green-Kubo theorem (D equals the integral of the velocity autocorrelation function), Eq. (3) follows [26]. It should be noted, in passing, that the connection between the FD1k and the global fluctuation-dissipation relation is not a matter of direct mathematical implication; indeed, there exist cases in which the global relation is satisfied, whereas FD1k fails [33].

The Kubo fluctuation-dissipation relation of the second kind (FD2k for short) involves the correlation properties of the thermal/hydrodynamic force $R(t)$ at equilibrium and, in the Stokes-Einstein case, it reduces to the condition

$$\langle R(t)\, R(0)\rangle_{\text{eq}} = 2\,k_B\,T\,\eta\,\delta(t), \tag{7}$$

implying that $R(t)$ is a white-noise process. In the Gaussian approximation, this leads to $R(t) = \sqrt{2\,k_B\,T\,\eta}\,dw(t)/dt$; i.e., $R(t)$ is proportional to the distributional derivative of a Wiener process $w(t)$.

Generalizing the hydrodynamic description, thus assuming that fluid-particle interactions are characterized by memory effects (and this occurs either as a consequence of a more refined characterization of the solvent hydrodynamics via the time-dependent Stokes equation in place of the instantaneous one or due to rheological effects such as linear viscoelasticity), the particle equation of motion modifies as

$$m \frac{dv(t)}{dt} = -\int_0^t h(t-\tau)\, v(\tau)\, d\tau + R(t), \tag{8}$$

i.e., in the form of a generalized Langevin equation characterized by a continuous memory kernel $h(t)$. In this case, Kubo's FD1k takes the form

$$m \frac{dC_{vv}(t)}{dt} = -\int_0^t h(t-\tau)\, C_{vv}(\tau)\, d\tau,$$
$$C_{vv}(0) = \langle v^2 \rangle_{\mathrm{eq}} \tag{9}$$

and FD2k becomes

$$\langle R(t)\, R(0)\rangle_{\mathrm{eq}} = k_B\, T\, h(t). \tag{10}$$

In this setting, the global fluctuation-dissipation relation involves the long-time friction factor and attains the form

$$D \int_0^\infty h(t)\, dt = k_B\, T. \tag{11}$$

This result can be generalized to fluid-dynamic interaction leading to anomalous diffusive properties in particle motion corresponding, in the hydromechanic picture, to a memory kernel $h(t)$ possessing long-term power-law scaling, $h(t) \sim t^{-\kappa}$, $\kappa \in (0, 1)$, for large t. This extension is of great conceptual relevance, as it connects rheological properties of the solvent fluid (the relaxation modulus) to the macrotransport properties of the diffusing particles in it, and is referred to as the generalized Stokes-Einstein relation [34].

The generalization of fluctuation-dissipation properties to nonequilibrium systems, with particular attention to nonequilibrium steady states, has been carried out by several authors [35–42]. We return to the analysis of these models at the end of Sec. I B as they display strong analogies with the pulling experiment considered for estimating the effective friction factor.

The extension of the fluctuation-dissipation relations to heterogeneous systems is a delicate issue. Here, we consider the Stokesian case [43] where the solvent fluid hydrodynamics is described by means of the Stokes equation, and the fluid-particle hydromechanics involves exclusively the friction. For notational simplicity, we refer to a scalar description.

Heterogeneity implies that the Stokesian friction factor becomes a function of the particle position, i.e.,

$$\frac{dx(t)}{dt} = v(t), \quad m \frac{dv(t)}{dt} = -\eta(x(t))\, v(t) + R(t, x(t)). \tag{12}$$

Adopting a Gaussian description for the thermal force, this implies

$$R(t, x) = 2\, k_B\, T\, \eta(x) \frac{dw(t)}{dt}, \tag{13}$$

which is a direct extension of Eq. (7). In this heterogeneous case, it is also possible to provide a "local" form of the global fluctuation-dissipation relation. Indicating with $D(x)$ the local (pointwise) diffusion coefficient entering the overdamped approximation of Eq. (12), i.e.,

$$dx(t) = \sqrt{2\, D(x(t))} \odot dw(t) \tag{14}$$

where the nonlinear Langevin equation (14) should be interpreted *à la* Hänggi-Klimontovich (we use the notation $dx(t) = f(x(t)) \odot dw(t)$, where $dw(t)$ are increments of a Wiener process to indicate the Hänggi-Klimontovich interpretation of the resulting stochastic integral $\int_0^t f(x(\tau))\, dw(\tau)$, to mark the difference with $dx(t) = f(x(t)) w(t)$ that corresponds to the Ito formulation [44]), then [21,31,45]

$$D(x)\, \eta(x) = k_B\, T. \tag{15}$$

Equations (14) and (15) correspond to the overdamped approximation of Eqs. (12) and (13). Observe that Eq. (14) is to be interpreted in the Hänggi-Klimontovich meaning, consistently with the Stratonovich interpretation of Eqs. (12) and (13). For details, see Ref. [46]. It corresponds to the Langevin equation *à la* Ito

$$dx(t) = D'(x(t))\, dt + \sqrt{2\, D(x(t))} dw(t), \tag{16}$$

where $D'(x) = dD(x)/dx$, for which the associated Fokker-Planck equation for the probability density function $p(x, t)$ reads

$$\frac{\partial p(x,t)}{\partial t} = \frac{\partial}{\partial x}\left(D(x) \frac{\partial p(x,t)}{\partial x} \right). \tag{17}$$

B. Effective global fluctuation-dissipation relation

In the heterogeneous case, it is possible to introduce a further global relation connecting particle transport properties and the mechanical resistivity of the medium to particle motion, relating the effective diffusivity D_e to an effective friction factor η_e, thus connecting the outcomes of two conceptually different experiments.

Consider Eqs. (12) and (13) in the Wiener representation of the thermal force

$$m\, dv(t) = -\eta(x(t))\, v(t)\, dt + \sqrt{2\, k_B\, T\, \eta(x(t))}\, dw(t). \tag{18}$$

The dependence of $\eta(x)$ on x comes from the hydrodynamic interactions of the particle with the other obstacles (i.e., other particles and/or macromolecular objects) [47,48], which, in the present approximation, are assumed to be static. Because of its hydromechanic nature, $\eta(x)$ is lower bounded by an η_0 corresponding to the friction factor in the free-space fluid phase removing all the suspended obstacles, $\eta(x) \geqslant \eta_0$. This result stems from the energy dissipation principle in a viscous flow [15,49]. Because of this property, the effective diffusion coefficient D_e,

$$D_e = \lim_{t\to\infty} \frac{\langle (x(t) - x_0)^2 \rangle}{2\, t}, \tag{19}$$

can be always be defined: D_e is greater than zero if diffusion is regular in the long term, while $D_e = 0$ in the anomalous case. While Eq. (19) is the standard experimental way for estimating D_e from microparticle trajectory analysis, it may suffer some problems when some possible convective contributions may be present, disrupting the linear scaling. For this reason, it is more convenient to consider theoretically the more conservative definition of D_e as

$$D_e = \lim_{t\to\infty} \frac{\langle (x(t) - \langle x(t) \rangle)^2 \rangle}{2\, t}, \tag{20}$$

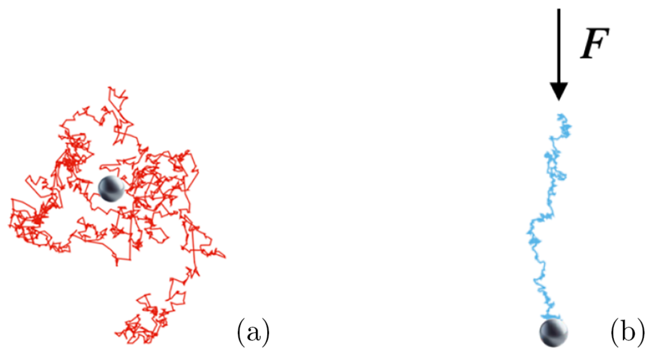

FIG. 1. Pictorial representation of the diffusion experiment [panel (a)] and of the pulling experiment [panel (b)] to obtain D_e and η_e, respectively.

which filters out the superposition of possible long-term convective biases and coincides with Eq. (19) in the purely diffusive case.

Next, consider the mechanical experiment of pulling the particle in the same fluid via a constant force F. This simply implies to add an additional term to Eq. (18),

$$m\,dv(t) = -\eta(x(t))\,v(t)\,dt + \sqrt{2\,k_B\,T\,\eta(x(t))}\,dw(t) + F\,dt. \tag{21}$$

The main mechanical quantity of interest is the long-term particle velocity (settling velocity) V_e,

$$V_e = \lim_{t\to\infty} \langle v(t)\rangle = \frac{F}{\eta_e}, \tag{22}$$

which defines the effective friction factor η_e via the proportionality relation expressed by Eq. (22). Figure 1 shows a pictorial representation of the two experiments (diffusive and pulling experiments).

If the results of these two different experiments at constant T fulfill the relation

$$D_e\,\eta_e = k_B\,T, \tag{23}$$

we say that the global effective fluctuation-dissipation relation is satisfied.

As can be observed, the global effective fluctuation-dissipation relation is a property involving the long-term transport and mechanical coefficients that account for the overall particle interactions with a heterogeneous and complex fluid.

So far we have considered a hydromechanical model of particle motion in a heterogeneous fluid medium. Another classical approach worth attention described heterogeneities by means of a potential energy landscape specified by a potential $U(x)$, while the friction factor can be assumed constant. In this case, Eq. (21) is replaced by

$$m\,dv(t) = -\eta\,v(t)\,dt - U'(x) + \sqrt{2\,k_B\,T\,\eta}\,dw(t) + F\,dt, \tag{24}$$

where $U'(x) = dU(x)/dx$, and Eq. (18) follows simply by setting $F = 0$. In this model, the potential $U(x)$ describes the heterogeneous equilibrium interactions of the tagged particle with the remaining macromolecular/particle structures [50–52]. The meaning of D_e and η_e remains unaltered.

Intrinsically, Eq. (24) represents a nonequilibrium system corresponding to the underdamped case of similar systems considered in Refs. [36–42], as an external force F is applied determining a net motion as $\langle v(t)\rangle \neq 0$. However, in the representation adopted in Ref. [36] by Speck and Seifert, Eq. (24) can instead be regarded as the perturbation of an equilibrium dynamics associated with the potential $U(x)$, where the perturbation is encoded in an additional force term denoted by $f_p(t)$; in the present case, $f_p(t) = F$. Specifically, the nonequilibrium steady states considered in Ref. [36] correspond to states characterized by a steady-state marginal position distribution violating the canonical Boltzmann density. However, in the present case the unperturbed dynamics is characterized by an equilibrium marginal Boltzmann distribution as regards the particle position, associated with probability fluxes (currents) that are identically vanishing; i.e., here F is a perturbation and not the out-of-equilibrium driving force as in Ref. [36].

Whether Eq. (24) is interpreted as describing a nonequilibrium steady state, or as the mechanical response of an equilibrium system subjected to an external forcing, is ultimately of minor physical relevance and largely a matter of perspective. What matters instead are the properties of this class of systems in the light of the global, effective fluctuation-dissipation relation. Indeed, Eq. (24) has been used (for $F = 0$) to model the equilibrium behavior of a particle in heterogeneous environments [see Sec. III B].

II. MAIN RESULTS

In this section, we provide the main results connected to global effective properties D_e and η_e. Specifically, for the hydrodynamic model [Eqs. (18) and (21)], the global effective fluctuation-dissipation relation is intrinsically fulfilled, while this is not the case for the potential model [Eq. (24)], unless in the limit for vanishingly small F or small intensities of the equilibrium potentials.

To begin with, consider the hydrodynamic model where $\eta(x) = \eta_0\,\beta(x)$, $\beta(x) \geqslant 1$, and its nondimensional formulation rescaling time is the characteristic momentum relaxation time $t_c = m/\eta_0$ and velocity is the thermal velocity $V_c = \sqrt{k_B\,T/m}$, where the characteristic length is set equal to $L_c = V_c\,t_c$. We use the same symbols, namely, t, x, v, to indicate the corresponding nondimensional quantities. In this nondimensional setting, Eq. (18) becomes

$$dv(t) = -\beta(x(t))\,v(t)\,dt + \sqrt{2\,\beta(x(t))}\,dw(t). \tag{25}$$

In order to get the expression for the effective diffusion coefficient, it is sufficient to consider the overdamped approximation of Eq. (25) [46], namely,

$$dx(t) = \sqrt{\frac{2}{\beta(x(t))}} \odot dw(t), \tag{26}$$

the density function $p(x,t)$ of which fulfills the Fokker-Planck equation

$$\frac{\partial p(x,t)}{\partial t} = \frac{\partial}{\partial x}\left(\frac{1}{\beta(x)}\,\frac{\partial p(x,t)}{\partial x}\right), \tag{27}$$

$x \in \mathbb{R}$, and the position dependent diffusivity is $D(x) = 1/\beta(x)$. Consider for $\beta(x)$ a periodic function of the position $\beta(x+L)=\beta(x)$ for some $L>0$. We have the following preposition.

Proposition 1. The effective diffusion coefficient for Eq. (26) in a periodic friction landscape is given by

$$D_e = \left[\frac{1}{L}\int_0^L \beta(x)\,dx\right]^{-1}, \tag{28}$$

and if a constant force F is applied, the effective friction factor is

$$\eta_e = \frac{1}{L}\int_0^L \beta(x)\,dx \tag{29}$$

Dim: The proof of this result is reported in Appendixes A and B. ■

One can generalize this result by considering a random uncorrelated friction profile

$$\beta(x) = \sum_{h=-\infty}^{\infty} \beta_h\,\chi_h(x), \tag{30}$$

where β_h, $h=\ldots,-1,0,1,\ldots$, are independent and identically distributed random variables defined by the probability density function $p_\beta(\beta)$, $\beta\in[1,\infty)$ and $\chi_h(x)$ is the characteristic function of the hth interval:

$$\chi_h(x) = \begin{cases} 1, & x\in(h-1,h],\\ 0, & \text{otherwise.}\end{cases} \tag{31}$$

We refer to this model as a random uncorrelated friction landscape. We have the following result:

Proposition 2. The effective diffusion of a particle moving according to Eq. (26) in a random uncorrelated friction landscape is

$$D_e = \left[\int_1^\infty \beta\,p_\beta(\beta)\,d\beta\right]^{-1} = \frac{1}{\langle\beta\rangle} \tag{32}$$

and, in the presence of a constant force applied,

$$\eta_e = \langle\beta\rangle \tag{33}$$

Dim: Consider a periodization of a realization of the random uncorrelated friction model with period L_p. Without loss of generality, set $L_p/2$ equal to an integer. From Proposition 1 we have

$$D_e|_{\text{periodization}} = \left[\frac{1}{L_p}\int_{-L_p/2}^{L_p/2}\beta(x)\,dx\right]^{-1} = \left[\frac{1}{L_p}\sum_{-L_p/2}^{L_p/2}\beta_h\right]^{-1}. \tag{34}$$

The random uncorrelated friction model is recovered for $L_p\to\infty$. Thus, by the law of large numbers,

$$\begin{aligned} D_e &= \lim_{L_p\to\infty}\left[\frac{1}{L_p}\sum_{-L_p/2}^{L_p/2}\beta_h\right]^{-1}\\ &= \frac{1}{\lim_{L_p\to\infty}\sum_{-L_p/2}^{L_p/2}\beta_h}\\ &= \left[\int_1^\infty \beta\,p_\beta(\beta)\,d\beta\right]^{-1}. \end{aligned} \tag{35}$$

In an analogous way, the expression for η_e Eq. (33) follows. ■

Observe that in the proof of Proposition 2 the uncorrelated nature of β_h's has been enforced in connection with the use of the law of large numbers. This result can be extended by removing the condition of independence assuming that $\langle\beta_h\beta_k\rangle \leqslant C^{|h-k|}$ with $0\leqslant C\leqslant 1$, i.e., an exponential decay of the spatial correlation function with the position [53]. Under this condition, the result of Proposition 2 is valid for any random friction pattern for which the local values of friction are bounded away from zero.

Therefore, the results of Propositions 1 and 2, with this further generalization, lead to the following theorem.

Theorem 1. In the presence of a periodic or random friction landscape, such that $\beta(x)>0$, the global effective fluctuation-dissipation relation $D_e\,\eta_e=1$ is fulfilled.

Dim: This follows immediately from Eqs. (28), (29), (32), and (33). ■

Next, turning attention to models of heterogeneity described by means of a potential landscape $U(x)$ [Eq. (24)], consider its overdamped approximation

$$dx(t) = \frac{F-U'(x)}{\eta}\,dt + \sqrt{2D}\,dw(t), \tag{36}$$

where $D=k_BT/\eta$. We have the following theorem:

Theorem 2. The effective diffusion and friction coefficients of a particle moving according to Eq. (36) in the presence of a periodic potential $U(x+L)=U(x)$ are

$$D_e = \frac{D}{U_+U_-},\quad U_\pm = \frac{1}{L}\int_0^L e^{\pm U(x)/k_BT}\,dx \tag{37}$$

and

$$\eta_e = \eta_e(F) = \eta\,F\left[\int_0^L \big(F-U'(x)\big)w_{0,U,F}(x)\,dx\right]^{-1}, \tag{38}$$

where the density $w_{0,U,F}(x)$ is defined by Eq. (C15). Thus, in general, $D_e\,\eta_e\neq 1$.

Dim: Equations (37) and (38) are derived in Appendix C. As regards the generic failure of validity of the global effective fluctuation-dissipation relation, this immediately follows from the functional form of η_e, which is not the reciprocal of D_e, and moreover, η_e is not uniquely defined as it depends nonlinearly on the intensity F of the applied force, via the dependence of the density $w_{0,U,F}(x)$ on F. ■

While, in general, the global effective fluctuation-dissipation relation is not satisfied for potential models of equilibrium behavior, a weaker result holds, namely, that it is fulfilled in the limit of vanishing pulling force F.

Theorem 3. For the potential model Eq. (36) in the presence of a periodic potential $U(x+L)=U(x)$, we have

$$V_e = \frac{1}{\eta\,U_+U_-}F + O(F^2), \tag{39}$$

where $O(F^2)$ is a quantity vanishing quadratically to zero with F for $F\to 0$.

Dim: See Appendix C. ■

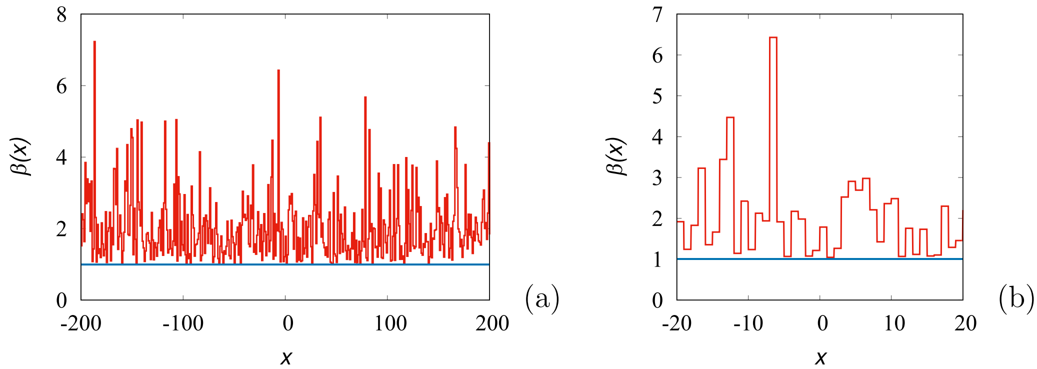

FIG. 2. Representation of a portion of a random uncorrelated friction landscape defined by the exponential distribution [Eq. (40)] with $\lambda = 1$ [panel (a)]. Panel (b) depicts a more resolved close-up.

A. Examples

In this section, we analyze some examples and case studies. To begin with, consider the hydromechanic setting, i.e., Eq. (25) including, in the case of the pulling experiment, a nondimensional constant force F. As a model for $\beta(x)$, consider a random uncorrelated friction landscape, the statistics of which is defined by an exponential density function

$$p_\beta(\beta) = \lambda\, e^{-\lambda\,(\beta-1)}, \quad \beta \in [1, \infty) \tag{40}$$

depending on the parameter $\lambda > 0$. Observe that $\beta(x) \geqslant 1$, as in the nondimensional formulation the time variable has been rescaled with respect to the momentum relaxation time in the free space, and the presence of particles and macromolecular objects determines an higher friction with respect to the case of unconstrained hydrodynamic interactions. For the exponential uncorrelated model, we have

$$\langle \beta \rangle = \frac{1+\lambda}{\lambda}. \tag{41}$$

Figure 2 depicts a realization of these friction landscapes. Stochastic simulations have been performed using the full dynamic model (underdamped) [Eq. (25)], considering a large domain $x \in [-L_{\max}, L_{\max}]$ with $L_{\max} = 10^6$, localizing the initial ensemble of $N_p = 10^5$ particles in a uniform random way in a smaller portion $x_0 \in [-L_i, L_i]$ with $L_i = 10^4$, in order to avoid boundary effects for the timescales considered. The particle initial velocities were randomly selected from the equilibrium Maxwellian distribution with $\langle v_0^2 \rangle = 1$. In the present nondimensional formulation, the global effective fluctuation-dissipation relation reads $D_e\, \eta_e = 1$.

In the diffusion experiment, no external forces are applied, and from the linear long-term scaling of the mean-square displacement $\sigma_x^2(t) = \langle (x(t) - x_0)^2 \rangle$, depicted in Fig. 3, the values of D_e are obtained.Next, using the same setup, a constant external force F is applied to the particles, and from the long-term linear scaling of $\langle v(t) \rangle / F$, the values of $1/\eta_e$ are obtained. These results are reported in Fig. 4. Combining the results of these two simulation experiments, the validity of the global effective fluctuation-dissipation relation can be tested. Data are reported in Fig. 5, for D_e, η_e and for the product $D_e\, \eta_e$ as a function of the parameter λ of the exponential distribution. As can be observed, the agreement with

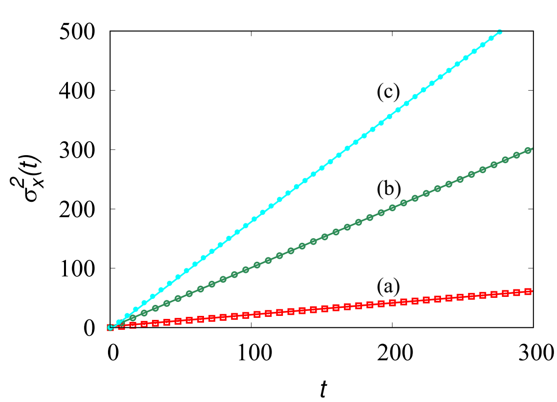

FIG. 3. $\sigma_x^2(t)$ vs t in a random uncorrelated friction landscape, possessing an exponential distribution [Eq. (40)], obtained from the stochastic dynamics [Eq. (25)] for different values of λ. Symbols represent the results of the stochastic simulations, and lines are the long-term fitting curves $\sigma_x^2(t) = 2\,D_e\,t + b$, where b is a constant. Line (a) and symbols (□) refer to $\lambda = 0.1$, line (b) and symbols (○) refer to $\lambda = 1$, and line (c) and symbols (•) refer to $\lambda = 10$.

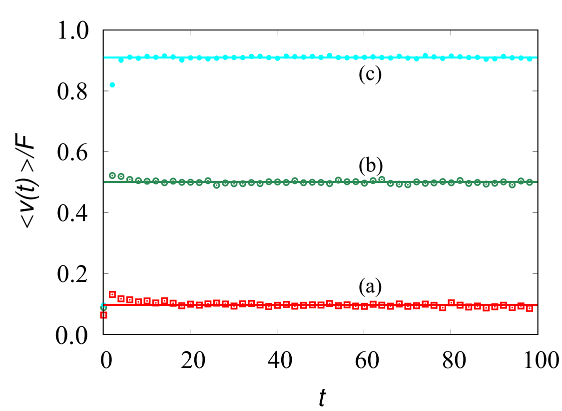

FIG. 4. $\langle v(t) \rangle / F$ vs t in a random uncorrelated friction landscape possessing an exponential distribution [Eq. (40)], obtained from the stochastic dynamics [Eq. (25)] in which a constant force F has been added, for different values of λ. Symbols are the results of the stochastic simulations, and lines are the long-term fitting curves $\langle v(t) \rangle / F = 1/\eta_e$. Line (a) and symbols (□) refer to $\lambda = 0.1$, line (b) and symbols (○) refer to $\lambda = 1$, and line (c) and symbols (•) refer to $\lambda = 10$.

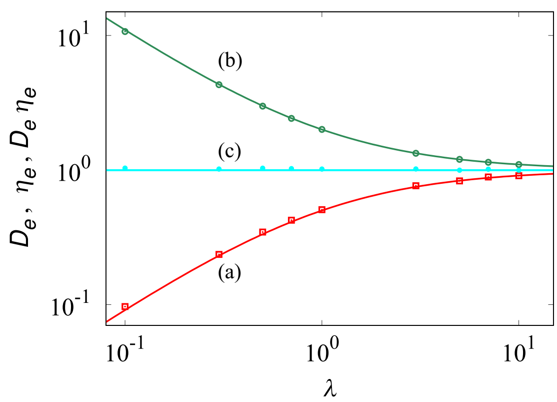

FIG. 5. D_e [line (a) and symbols]), η_e [line (b) and symbols], and $D_e\,\eta_e$ [line (c) and symbols] vs λ for the motion in a random uncorrelated friction landscape by the exponential distribution [Eq. (40)]. Symbols are the results of stochastic simulations, line (a) corresponds to $1/\langle\beta\rangle$, line (b) corresponds to $\langle\beta\rangle$, where $\langle\beta\rangle$ is given by Eq. (41), and line (c) corresponds to the global effective result $D_e\,\eta_e = 1$.

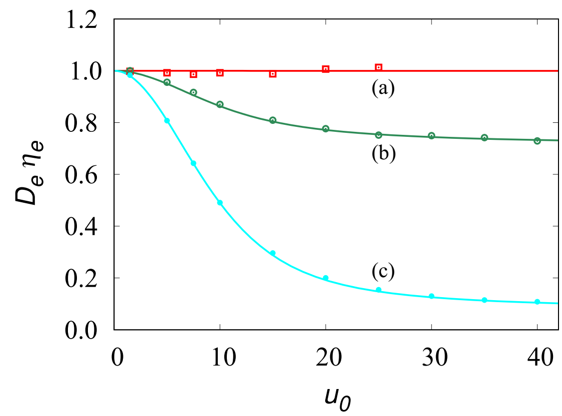

FIG. 6. Product $D_e\,\eta_e$ vs u_0 for the sinusoidal potential model [Eq. (42)] with $\phi'(x) = \cos(2\pi x)$. Symbols depict the results of stochastic simulations, and solid lines represent the homogenization result stemming from Eqs. (37) and (38). Line (a) and symbols (□) refer to $f = 0.1$, line (b) and symbols (○) refer to $f = 3$, and line (c) and symbols (•) refer to $f = 10$.

the results of Proposition 2 and Theorem 1 is excellent. This is not merely a confirmation of a mathematical property, as these propositions have been proved within the overdamped approximation, while the stochastic simulations depicted in Fig. 5 refer to the full underdamped model [Eq. (25)].

Next, turn attention to the potential model, where $U(x)$ is periodic with period L in its overdamped approximation [Eq. (36)]. Rescaling time by $t_c = L^2/D$ the spatial coordinate by $L_c = L$, Eq. (36) attains the nondimensional form (keeping the same symbols for the nondimensional quantities x and t)

$$\frac{dx(t)}{dt} = f - u_0\,\phi'(x) + \sqrt{2}\xi(t), \tag{42}$$

where $\phi'(x) = d\phi(x)/dx$, $|\phi'(x)| \leqslant 1$ and $\xi(t) = dw(t)/dt$ is the distributional derivative of a Wiener process $w(t)$. If U_0 is the maximum value attained by the dimensional potential $U(x) = U_o\,\phi(x)$, then $u_0 = U_0\,t_c/\eta\,L_c^2$, $f = F\,t_c/\eta\,L_c$. Let us now consider a sinusoidal potential $\phi'(x) = \cos(2\,\pi x)$. The simulations in the underdamped case therefore refer to the nondimensional formulation

$$\frac{dv(t)}{dt} = -v(t) + f - u_0\,\phi'(x) + \sqrt{2}\xi(t). \tag{43}$$

Figure 6 depicts the product of $D_e\eta_e$, which in the present nondimensional formulation should be equal to 1 if the global effective fluctuation-dissipation relation was satisfied, obtained from diffusive ($f = 0$) and mechanical ($f \neq 0$) simulations, as a function of u_0, for different intensities of the pulling force f. Data refer to the simulation of Eq. (43). Solid lines are the analytical predictions based on Eqs. (37) and (38), and symbols represent the result of stochastic simulations with an ensemble of 10^5 particles initially distributed uniformly in $x \in [0, 1]$. As predicted by Theorems 2 and 3, the global effective fluctuation-dissipation relation is not satisfied unless in the limit for $f \to 0$ for any u_0 (and obviously also in the limit for $u_0 \to 0$ for any f). Indeed, the origin of the failure of the global effective fluctuation-dissipation relation is related to the intrinsic nonlinear relation between the settling velocity V_e and the applied force, induced by the interplay of F with the equilibrium potential $U(x)$.

This is clearly evident from the data depicted in Fig. 7 showing the values of D_e and η_e as a function of the intensity of the pulling force f.

III. FURTHER APPLICATIONS

In this section, we consider two other applications, associated with (1) a stochastic hydromechanic model and (2) the motion of particles in a random system of partially reflecting mirrors.

A. Stochastic hydromechanic model

Consider the classical Stokes-Einstein hydromechanic model in which the friction is a stochastic process. In nondimensional form, the dynamics is expressed by the equa-

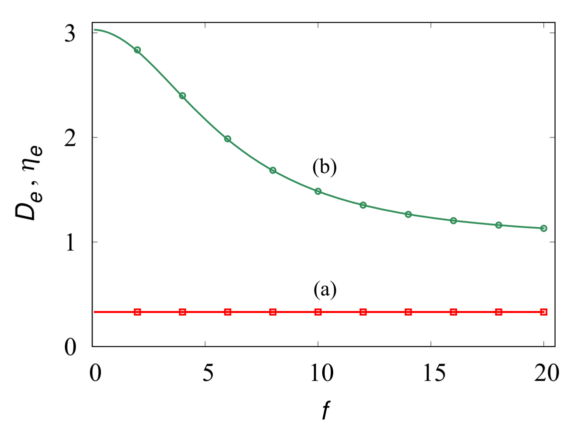

FIG. 7. D_e [line (a)] and η_e [line (b)] as a function of the pulling force f for the sinusoidal model with Eq. (42) with $\phi'(x) = \cos(2\pi x)$ and $u_0 = 10$, $\ell = 1$. Symbols represent the results of stochastic simulations, and lines represent the homogenization predictions [Eqs. (37) and (38)].

tion

$$\frac{dv(t)}{dt} = -\beta(t)\,v(t) + F + \sqrt{2\,\beta(t)}\,\xi(t), \tag{44}$$

where $\xi(t)$ is the distributional derivative of a one-dimensional Wiener process and $\beta(t) \geqslant 0$ is a Markov process attaining two values $\beta_1 = 1$ and $\beta_2 > 1$, and characterized by a uniform transition rate λ as regards the transitions among the two states (see also [54]). The statistical description of Eq. (44) involves the two partial densities $p_h(v,t)$, $h = 1, 2$, that satisfy the balance equation

$$\begin{aligned}\frac{\partial p_1(v,t)}{\partial t} &= \beta_1 \frac{\partial (v\,p_1(v,t))}{\partial v} - F\frac{\partial p_1(v,t)}{\partial v}\\ &\quad + \beta_1 \frac{\partial^2 p_1(v,t)}{\partial v^2} - \lambda[p_1(v,t) - p_2(v,t)],\\ \frac{\partial p_2(v,t)}{\partial t} &= \beta_2 \frac{\partial (v\,p_2(v,t))}{\partial v} - F\frac{\partial p_2(v,t)}{\partial v}\\ &\quad + \beta_2 \frac{\partial^2 p_2(v,t)}{\partial v^2} + \lambda[p_1(v,t) - p_2(v,t)].\end{aligned} \tag{45}$$

The overall velocity density $p(v,t) = p_1(v,t) + p_2(v,t)$ is the sum of two partial densities. Let $p_h^*(v)$ be the equilibrium densities, and define the moment hierarchies $m_h^{(n)}(v,t) = \int_{-\infty}^{\infty} v^n p_h(v,t)\,dv$ and let $m_h^{(n,*)}$ be the stationary values toward which the hierarchy converges in the long-term limit. We are interested in the effective velocity V_e defined by equilibrium first-order moment,

$$V_e = m_1^{(1,*)} + m_2^{(1,*)} = \frac{F}{\eta_e}. \tag{46}$$

The evolution equation for the first-order moments follows from Eq. (44), namely,

$$\begin{aligned}\frac{dm_1^{(1)}(t)}{dt} &= -\beta_1\, m_1^{(1)}(t) - \lambda\big[m_1^{(1)}(t) - m_2^{(1)}(t)\big] + F\, m_1^{(0)}(t),\\ \frac{dm_2^{(1)}(t)}{dt} &= -\beta_2\, m_2^{(1)}(t) + \lambda\big[m_1^{(1)}(t) - m_2^{(1)}(t)\big] + F\, m_2^{(0)}(t).\end{aligned} \tag{47}$$

In the long-term limit, the first-order moments converge toward their stationary values $m_h^{(1,*)}$, $h = 1, 2$. Since $m_1^{(*,0)} = m_2^{(*,0)} = 1/2$, the stationary first-order moments are the solution of the linear system

$$\begin{aligned}-\beta_1\, m_1^{(1,*)} - \lambda\big[m_1^{(1,*)} - m_1^{(1,*)}\big] + \frac{F}{2} &= 0,\\ -\beta_2\, m_2^{(1,*)} + \lambda\big[m_1^{(1,*)} - m_1^{(1,*)}\big] + \frac{F}{2} &= 0.\end{aligned} \tag{48}$$

By solving this system, the value of the effective friction factor η_e, defined by Eq. (46), is given as follows:

$$\eta_e = \frac{2[\beta_1\,\beta 2 + \lambda\,(\beta_1 + \beta_2)]}{\beta_1 + \beta_2 + 4\,\lambda}. \tag{49}$$

Next, consider the effective diffusivity, i.e., the motion in the absence of an external force, $F = 0$. Using the Green-Kubo theorem, the effective diffusivity can be obtained from the integral of the velocity autocorrelation function $C_{vv}(t)$,

$$C_{vv}(t) = \int_{-\infty}^{\infty}\int_{-\infty}^{\infty} v\, v_0\, p(v,t\,|\,v_0)\, p^*(v_0)\, dv\, dv_0, \tag{50}$$

where $p^*(v_0)$ is the equilibrium velocity density and $p(v,t\,|\,v_0)$ the condition density of having the value v of the velocity at time t if the initial condition at time $t = 0$ is v_0. Equation (50) can be reformulated as

$$C_{vv}(t) = \int_{-\infty}^{\infty} v_0\, m^{(1)}(t\,|\,v_0)\, p^*(v_0)\, dv_0, \tag{51}$$

where $m^{(1)}(t\,|\,v_0) = m_1^{(1)}(t\,|\,v_0) + m_2^{(1)}(t\,|\,v_0)$ and $m_h^{(1)}(t\,|\,v_0)$ are the partial moments, satisfying Eq. (47) with $F = 0$ and equipped with the initial condition, $m_h^{(1)}(t\,|\,v_0) = v_0$, $h = 1, 2$. Setting $C_{vv}^h(t) = \int_{-\infty}^{\infty} v_0\, m_h^{(1)}(t\,|\,v_0)\, p^*(v_0)\, dv_0$, so that $C_{vv}(t) = C_{vv}^1(t) + C_{vv}^2(t)$, these partial correlation functions satisfy the same linear dynamics for $m_h^{(1)}(t\,|\,v_0)$, but with the initial conditions $C_{vv}^h(0) = \langle v^2\rangle_{\rm eq}/2 = 1/2$, since $\langle v^2\rangle_{\rm eq} = 1$ in the present nondimensional formulation, i.e.,

$$\begin{aligned}\frac{dC_{vv}^1(t)}{dt} &= -\beta_1\, C_{vv}^1(t) - \lambda\big[C_{vv}^1(t) - C_{vv}^2(t)\big],\\ \frac{dC_{vv}^2(t)}{dt} &= -\beta_2\, C_{vv}^2(t) + \lambda\big[C_{vv}^1(t) - C_{vv}^2(t)\big].\end{aligned} \tag{52}$$

Solving this system in the Laplace domain, $\widehat{C}_{vv}^h(s) = \int_0^{\infty} e^{-st} C_{vv}^h(t)\, dt$, the values $\widehat{C}_{vv}^h(0)$ at $s = 0$ provide the diffusion coefficient (Green-Kubo theorem),

$$D_e = \widehat{C}_{vv}^1(0) + \widehat{C}_{vv}^2(0) = \frac{\beta_1 + \beta_2 + 4\,\lambda}{2\,[\beta_1\,\beta_2 + \lambda\,(\beta_1 + \beta_2)]}. \tag{53}$$

From Eqs. (49)–(53), it follows that $D_e\,\eta_e = 1$, i.e., that the global effective fluctuation-dissipation relation is fulfilled for any value F. Moreover, this result can be generalized to any continuous distribution of β values.

B. Diffusion in a random mirror chessboard

In this section, we consider another diffusive motion of solute particles in a heterogeneous two-dimensional medium made by unit cells $Q_{h,k} = \{(x,y)\,|\,(h-1) < x < h,\ (k-1) < y < k \quad h, h \in \mathbb{Z}\}$. Particles move homogeneously, and the momentum transfer is characterized by a constant friction factor. Each of the four boundaries of each square unit cell consists, with probability $p_{\rm mir}$ by a mirror (membrane), that with probability p_r reflects back the solute particle touching it [11,55,56]. In nondimensional terms, particle dynamics in the presence of a constant force $\mathbf{F} = (F, 0)$ can be described by the equations

$$\begin{aligned}d\mathbf{x}(t) &= \mathbf{v}(t)\, dt,\\ d\mathbf{v}(t) &= -\mathbf{v}(t)\, dt + \mathbf{F}\, dt + \sqrt{2}\, d\mathbf{w}(t)\\ &\quad + d\mathbf{R}(\mathbf{x}(t), \mathbf{v}(t); p_{\rm mir}, p_r),\end{aligned} \tag{54}$$

where $\mathbf{x}(t) = (x(t), y(t))$, $\mathbf{v}(t) = (v(t), w(t))$, $d\mathbf{w}(t) = (dw_1(t), dw_2(t))$ are the increments of a two-dimensional Wiener process and $d\mathbf{R}(\mathbf{x}(t), \mathbf{v}(t); p_{\rm mir}, p_r)$ accounts for the random reflection/transmission process described above at the boundaries of each unit cell, if it consists of a mirror. Consequently, if no mirror is present at some cell boundary,

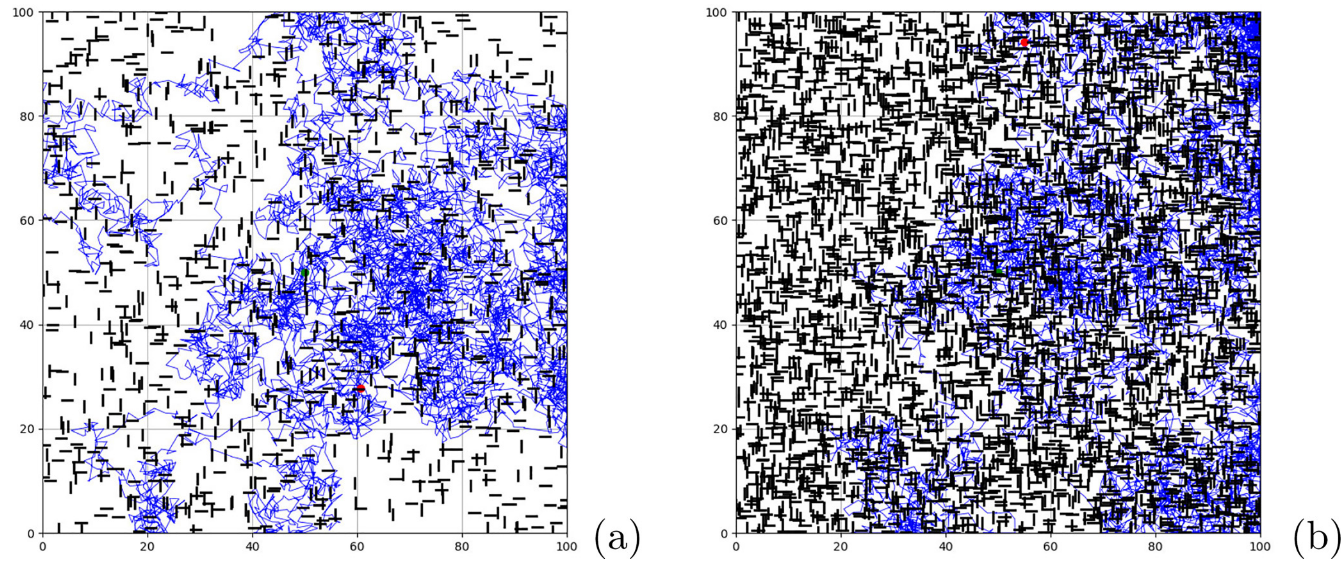

FIG. 8. Orbits of diffusing particles (blue lines) in the random mirror model ($p_r = 1$). The mirrors are depicted as black segments. Panel (a) refers to $p_{\rm mir} = 0.2$ and panel (b) refers to $p_{\rm mir} = 0.9$.

$d\mathbf{R}(\mathbf{x}(t), \mathbf{v}(t); p_{\rm mir}, p_r) = 0$. This model of particle diffusion in a random landscape of mirrors is characterized by two parameters, the probability $p_{\rm mir}$, defining statistically the mirror configuration, and the probability p_r associated with the occurrence of a perfect reflection, once a particle hits a boundary mirror. Figures 8(a) and 8(b) depict two configurations of this system and some particle orbits in the case $p_r = 1$.

Figure 9 reports the results for the effective particle diffusion coefficient D_e as a function of p_r for different values of $p_{\rm mir}$, obtained from stochastic simulations of Eq. (54) with $F = 0$, considering the long-term scaling of the particle mean-square displacement for an ensemble of 10^5 particles, the initial positions of which were randomly distributed and the initial velocities of which were taken from the equilibrium Maxwellian distribution with $\langle v \rangle_{\rm eq} = 1$.

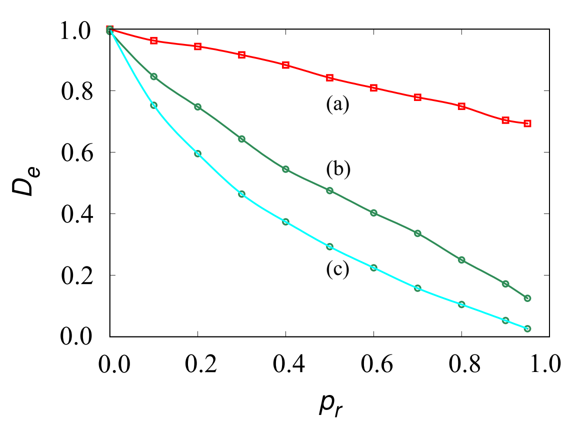

FIG. 9. Diffusion in a random mirror chessboard: D_e vs the reflection probability p_r for different values of $p_{\rm mir}$: (a) $p_{\rm mir} = 0.1$, (b) $p_{\rm mir} = 0.5$, and (c) $p_{\rm mir} = 0.9$, obtained from stochastic simulations of Eq. (54) with $F = 0$.

Next, consider a nonvanishing external force $F \neq 0$ and the mechanical experiment of pulling the particle, out of which the effective friction factor η_e can be estimated, from the long-term behavior $\langle v(t) \rangle = F/\eta_e$.

Figures 10(a)–10(c) depict the behavior of D_e versus $1/\eta_e$ for different configurations (values of $p_{\rm mir}$) and for values of p_r ranging from 0.1 to 0.95. Specifically, η_e has been estimated from the pulling experiments in the presence of forces of different intensities. If F is small ($F \leqslant 1$), one recovers a substantial agreement with the global effective fluctuation-dissipation relation (i.e., $D_e \simeq 1/\eta_e$), and this result is quantitatively more accurate for smaller values of F. Conversely, if F is large enough, the global effective fluctuation-dissipation relation grossly fails [see panel (c) and the data for $F = 10$].

This phenomenon can be easily explained, since V_e is a nonlinear function of the pulling force F, as in the potential model analyzed in the preceding paragraphs. More precisely, as depicted in Fig. 11, for small values of F the linearity between V_e and F is recovered, while, as F increases, V_e saturates toward a limit value independent of F.

These features can be explained by means of a simple toy model. Consider the purely random motion of a particle over the real line, characterized by the friction factor β, in the presence of an external constant force F, experiencing at random time intervals τ_i external kicks that invert its velocity. It is reasonable to assume the time interval between two consecutive kicks as independent random variables characterized by an exponential distribution possessing mean value $1/\lambda$. The momentum transfer in this model is defined by the equation

$$dv(t) = -\beta\, v(t)\, dt + F\, dt + \sqrt{2\,\beta}\, dw(t) + dK_\lambda(t, v(t)), \tag{55}$$

where the term $dK_\lambda(t, v(t))$ accounts for the random kicks inverting particle velocity. The statistical description of this process involves the generalized Fokker-Planck equation for

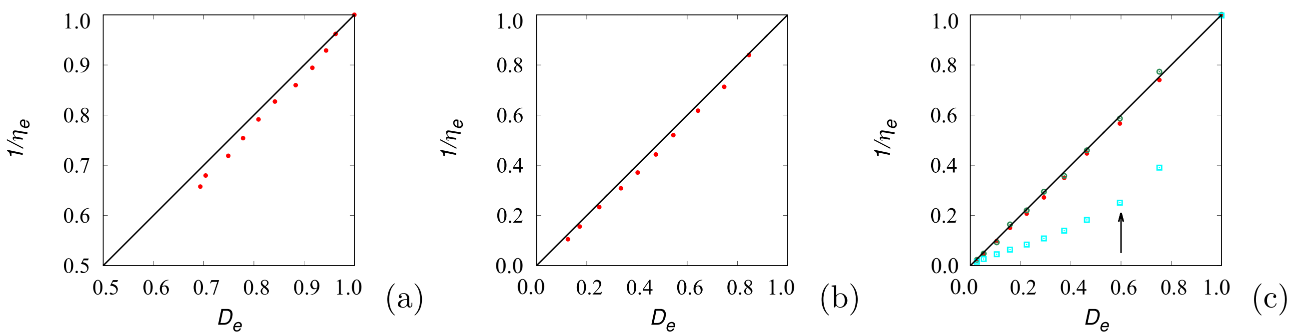

FIG. 10. $1/\eta_e$ vs D_e (symbols) for the random mirror model. Panel (a) refers to $p_{\rm mir} = 0.1$, panel (b) refers to $p_{\rm mir} = 0.5$, and panel (c) refers to $p_{\rm mir} = 0.9$. The solid lines represent $1/\eta_e = D_e$. All the data refer to stochastic simulation of diffusion and particle pulling with a constant force $F = 1$, but symbols (○) and (□) in panel (c) correspond to $F = 0.1$ and $F = 10$, respectively. The dataset with $F = 10$ in panel (c) is also marked by an arrow.

the probability density $p(v, t)$,

$$\frac{\partial p(v,t)}{\partial t} = \frac{\partial(\beta\, v\, p(v,t))}{\partial v} - F\, \frac{\partial p(v,t)}{\partial v} + \beta\, \frac{\partial^2 p(v,t)}{\partial v^2} - \lambda\, p(v,t) + \lambda\, p(-v,t). \tag{56}$$

Considering the first-order moment of $p(v, t)$, the mean velocity V_e at steady state satisfies the equation $0 = -\beta\, V_e + F - \lambda\, V_e - \lambda V_e$, and thus

$$V_e = \frac{F}{\beta + 2\,\lambda}. \tag{57}$$

This model represents a simplified description of the momentum transfer occurring in the random mirror model discussed above, and the kicks correspond to the reflections at the mirrors. In this adaptation, we have to consider that in the random mirror model the frequency of kicks (i.e., λ) depends on F, as collisions with the mirrors become more frequent as the pulling force increases. More precisely, the collision frequency can be assumed to be a linear function of F. Therefore, we have $\lambda = \alpha\, F$, where $\alpha > 0$, that substituted into Eq. (57) yields

$$V_e = \frac{F}{\beta + 2\,\alpha\, F}, \tag{58}$$

displaying a linear behavior for $F \ll \beta/2\alpha$, and a saturation for $F \to \infty$ at the limit value $1/2\alpha$.

In point of fact, Eq. (58) accurately reproduces the data obtained in the random mirror model. To check this, consider the double reciprocal plot of expression (58), which provides a linear behavior of $1/V_e$ vs $1/F$, $1/V_e = 2\,\alpha + \beta/F$, out of which the actual values of β and α can be easily estimated. This double-reciprocal representation is depicted in Fig. 12, and the solid lines reported in Fig. 11 correspond to the graph of Eq. (58), where the parameters α and β have been estimated using linear least squares from the double-reciprocal graph in each system configuration.

IV. CONCLUDING REMARKS

This article has added a further brick in fluctuation-dissipation theory as regards heterogeneous fluids, expressed by the global effective fluctuation-dissipation relation, and

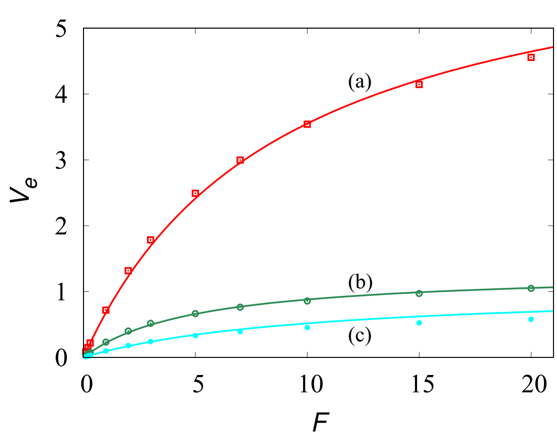

FIG. 11. V_e vs F for different configurations of the random mirror model with $p_r = 0.8$. Symbols represent the results of the stochastic simulations, and the solid lines represent Eq. (58). Symbols (□) and line (a) refer to $p_{\rm mir} = 0.1$, symbols (○) and line (b) refers to $p_{\rm mir} = 0.5$, and symbols (•) and line (c) refers to $p_{\rm mir} = 0.9$.

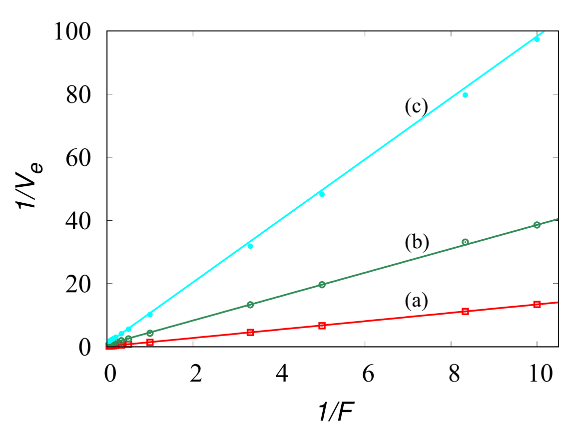

FIG. 12. Double reciprocal plot $1/V_e$ vs $1/F$ of the data reported in Fig. 11. Symbols (□) and line (a) refer to $p_{\rm mir} = 0.1$, symbols (○) and line (b) refers to $p_{\rm mir} = 0.5$, and symbols (•) and line (c) refers to $p_{\rm mir} = 0.9$.

involving the transport and mechanical properties of a particle interacting with the surrounding fluid.

For Stokesian hydromechanic models, in which the friction factor becomes a function of the position as a consequence of the hydromechanic constraints represented by the other macromolecules/particles immersed in the fluid, the global effective fluctuation-dissipation relation holds in general. This is true either in the static case, where $\eta(x)$ is simply a time-independent function of the particle position, or including some form of stochastic fluctuations of the particle friction factor, as addressed in Sec. III using a Markovian transition model. The hydromechanic model of Brownian and microparticle dynamics in heterogeneous fluids in which the presence of suspended particles and macromolecular objects determines a hydrodynamic confinement, hindering the motion of a tagged particle and resulting in a position-dependent friction factor, is a sufficient condition for the fulfillment of the global effective fluctuation-dissipation relation.

This is not the case of potential models, in which the interactions with the other suspended objects, macromolecular complexes, and polymers are described by some periodic interaction potential. This failure is intrinsically due to the nonlinear dependence of the terminal settling velocity V_e on the intensity F of the pulling force. We have discussed the possible and different interpretations of the pulling experiment to determine η_e in the light of nonequilibrium states. Any interpretation, especially considering the observation by Speck and Seifert [36], is reasonable and deserves attention. Nevertheless, our conclusions do not depend on this choice: They indicate that no matter how small the pulling force F is, deviations from the global effective fluctuation-dissipation relation occur by a factor order of F^2, while hydromechanic models in which medium heterogeneity is described via a position-dependent landscape fulfill analytically this relation. This result is particularly interesting in the analysis of those molecular dynamic simulations (both in equilibrium and in nonequilibrium conditions) where, apart from the analysis of the mean-square displacement of the tagged molecular object, the mechanical experiment of pulling it via an external force is performed for estimating η_e via the value of the terminal velocity V_e. Indeed, in the analysis of polymer dynamics in polymeric fluids under a shear stress, deviations from the global fluctuation-dissipation relation have been observed, still awaiting a theoretical explanation [57].

There are also other interesting realms where the validity of the global effective fluctuation-dissipation relation should be analyzed in order to draw a more definite conclusion about its general validity: specifically, (1) the extension of the present analysis to hydromechanic heterogeneous models in which the fluid-particle interactions display memory effects. This occurs whenever one considers fluid-inertial effects (generalized Basset forces) on particle motion. This problem involves the application of the theory developed in Refs. [33,34,58]; (2) the analysis of problems involving the motion of active particles where position-dependent effects in the coarse-grained modeling of the system might arise [59].

Of course, the fundamental and decisive test for any theory is the experimental one. While a wealth of diffusive experiments involving hard and soft particles in complex fluids and suspensions have been performed, the mechanical counterpart of pulling a microparticle via a constant force in a complex fluid has never been thoroughly considered in connection with fluctuation-dissipation properties, and we welcome the development of these experiments in order to assess the validity of the global effective relation.

ACKNOWLEDGMENT

This work was supported by Sapienza University of Rome through the project SAP_RICERCA_2024_GRANDIPROGETTI_PALOCCI_C_01—“Multicomponent miRNA–lipid nanovectors by microfluidic synthesis: Unravelling structure–performance relationships” (Ateneo 2024 PALOCCI).

DATA AVAILABILITY

The data that support the findings of this article are not publicly available. The data are available from the authors upon reasonable request.

APPENDIX A: DERIVATION OF D_e

In this Appendix, we provide an analytic expression for the effective diffusion coefficient D_e in a periodic friction landscape. Consider the diffusion equation

$$\frac{\partial p(x,t)}{\partial t} = \frac{\partial}{\partial x}\left(D(x)\, \frac{\partial p(x,t)}{\partial x}\right), \tag{A1}$$

$x \in \mathbb{Z}$, in the presence of a periodic diffusivity landscape $D(x+L) = D(x)$, where $p(x,t)$ is normalized probabilistically, i.e., $\int_{-\infty}^{\infty} p(x,t)\,dx = 1$.

Introduce a local cell coordinate $\xi \in [0, L]$, so that $x = k\,L + \xi$, $k \in \mathbb{Z}$, and the local moments $m^{(n)}(\xi, t)$, $n = 0, 1, 2, \ldots$,

$$m^{(n)}(\xi, t) = \sum_{k=-\infty}^{\infty} (k\,L + \xi)^n\, p(k\,L + \xi, t), \tag{A2}$$

so that the global moments $M^{(n)}(t)$ can be expressed as integrals of the local ones over the unit periodicity cell,

$$M^{(n)}(t) = \int_{-\infty}^{\infty} x^n\, p(x,t)\,dx = \int_0^L m^{(n)}(\xi, t)\,d\xi, \quad n = 0, 1, 2, \ldots \tag{A3}$$

Obviously, $M^{(0)}(t) = 1$, and in the long term the scaling of the lower-order moments provides the long-term transport coefficients, i.e., the effective velocity V_e and the effective diffusion coefficient D_e

$$\frac{dM^{(1)}}{dt} = V_e + r_1(t),$$
$$\frac{dM^{(2)}}{dt} - 2\,M^{(1)}\,\frac{dM^{(1)}}{dt} = 2\,D_e + r_2(t), \tag{A4}$$

where $r_1(t)$ and $r_2(t)$ decay to zero for $t \to \infty$. The evolution equations for the local moments follow from Eq. (A1), namely,

$$\frac{\partial m^{(n)}(\xi,t)}{\partial t} = \mathcal{L}_\xi[m^{(n)}(\xi,t)] - n\frac{\partial (D(\xi)\, m^{(n-1)}(\xi,t))}{\partial \xi} - n\, D(\xi)\,\frac{\partial m^{(n-1)}(\xi,t)}{\partial \xi} + n\,(n-1)\, m^{(n-2)}(\xi,t) \tag{A5}$$

defined within the unit periodicity cell $\xi \in (0, L)$, and equipped with periodic boundary conditions,

$$m^{(n)}(0,t) = m^{(n)}(L,t), \quad n = 0, 1, 2, \dots, \tag{A6}$$

where $\mathcal{L}_\xi$ is the local cell diffusion operator

$$\mathcal{L}_\xi[f(\xi,t)] = \frac{\partial}{\partial \xi}\left(D(\xi)\,\frac{\partial f(\xi,t)}{\partial \xi}\right), \quad \xi \in (0, L). \tag{A7}$$

Equation (A5) expresses compactly the dynamics of the local moment hierarchy, with the convection that, for $n = 0, 1, 2$, the terms containing negative-order moments equal zero.

The evolution of the zeroth-order moment is simply $\partial m^{(0)}(\xi,t)/\partial t = \mathcal{L}_\xi[m^{(0)}(\xi,t)]$, and in the long-term limit $m^{(0)}(\xi,t)$ converges to the unique stationary cell density $w_0(\xi)$,

$$w_0(\xi) = \frac{1}{L}. \tag{A8}$$

Next, consider the first-order local moment, evolving according to the equation

$$\frac{\partial m^{(1)}(\xi,t)}{\partial t} = \mathcal{L}_\xi[m^{(1)}(\xi,t)] - \frac{\partial (D(\xi)\, m^{(0)}(\xi,t))}{\partial \xi} - D(\xi)\,\frac{\partial m^{(0)}(\xi,t)}{\partial \xi}. \tag{A9}$$

As $m^{(0)}(\xi,t)$ approaches the uniform stationary density $w_0(\xi)$, it is easy to see that

$$\lim_{t\to\infty} \frac{dM^{(1)}(t)}{dt} = \lim_{t\to\infty} \int_0^L \frac{\partial m^{(1)}(\xi,t)}{\partial t}\, d\xi = 0, \tag{A10}$$

i.e., the effective velocity V_e is vanishing. In the long-term limit, $m^{(1)}(\xi,t)$ approaches a stationary profile $m_1^*(\xi)$, solution of the equation

$$\frac{d}{d\xi}\left(D(\xi)\,\frac{dm_1^*(\xi)}{d\xi}\right) = \frac{1}{L}\,\frac{dD(\xi)}{d\xi}; \tag{A11}$$

thus,

$$\frac{dm_1^*(\xi)}{d\xi} = \frac{1}{L} + \frac{A}{D(\xi)}, \tag{A12}$$

where A is a constant, admitting the solution

$$m_1^*(\xi) = \frac{\xi}{L} + A\int_0^\xi \frac{d\xi}{D(\xi)} + B, \tag{A13}$$

where

$$A = -\left[\int_0^L \frac{d\xi}{D(\xi)}\right]^{-1} \tag{A14}$$

by periodicity and B is an arbitrary constant. Finally, consider the second-order local moment $m^{(2)}(\xi,t)$, evolving according to the equation

$$\frac{\partial m^{(2)}(\xi,t)}{\partial t} = \mathcal{L}_\xi[m^{(2)}(\xi,t)] - 2\,\frac{\partial (D(\xi)\, m^{(1)}(\xi,t))}{\partial \xi} - 2\,D(\xi)\,\frac{\partial m^{(1)}(\xi,t)}{\partial \xi} + 2\,D(\xi)\,\frac{\partial m^{(0)}(\xi,t)}{\partial \xi}. \tag{A15}$$

In the long-term limit, because of the periodicity of the local moment, we have

$$\frac{d}{dt}\int_0^L m^{(2)}(\xi,t)\, d\xi = -\,2\int_0^L D(\xi)\,\frac{dm_1^*(\xi)}{d\xi}\, d\xi - 2\int_0^L D(\xi)\, d\xi \tag{A16}$$

and thus, since $dM^{(1)}/dt \to 0$ for $t \to \infty$, the expression for D_e is given as follows:

$$D_e = -\int_0^L D(\xi)\left(\frac{1}{L} + \frac{A}{D(\xi)}\right) d\xi + \frac{1}{L}\int_0^L D(\xi)\, d\xi = -A\,L = \left[\frac{1}{L}\int_0^L \frac{d\xi}{D(\xi)}\right]^{-1}. \tag{A17}$$

Since in the nondimensional formulation $D(\xi) = 1/\beta(\xi)$, Eq. (A17) can be rewritten in nondimensional terms as

$$D_e = \frac{1}{\langle\beta\rangle_L}, \quad \langle\beta\rangle_L = \frac{1}{L}\int_0^L \beta(\xi)\, d\xi. \tag{A18}$$

APPENDIX B: PROOF OF THEOREM 1

The Fokker-Planck equation for the probability density $p(x,t)$ associated with the overdamped approximation of Eq. (26) in the presence of a constant force F is given by

$$\frac{\partial p(x,t)}{\partial t} = -\frac{\partial}{\partial x}\left(\frac{F}{\beta(x)}\, p(x,t)\right) + \frac{\partial}{\partial x}\left(\frac{1}{\beta(x)}\,\frac{\partial p(x,t)}{\partial x}\right), \tag{B1}$$

where $\beta(x)$ is a periodic friction landscape, $\beta(x+L) = \beta(x)$. As in Appendix A, consider the local moments $m^{(n)}(\xi,t)$, $\xi \in (0, L)$ that satisfy the system of evolution equations,

$$\frac{\partial m^{(n)}(\xi,t)}{\partial t} = \mathcal{L}_{\xi,F}[m^{(n)}(\xi,t)] + \frac{n\,F}{\beta(\xi)}\, m^{(n-1)}(\xi,t) - n\,\frac{\partial}{\partial \xi}\left(\frac{m^{(n-1)}(\xi,t)}{\beta(\xi)}\right) \tag{B2}$$

$$- \frac{n}{\beta(\xi)}\,\frac{\partial m^{(n-1)}(\xi,t)}{\partial \xi} + \frac{n\,(n-1)}{\beta(\xi)}\, m^{(n-2)}(\xi,t), \tag{B3}$$

involving the cell operator

$$\mathcal{L}_{\xi,F}[f(\xi,t)] = -F\,\frac{\partial}{\partial \xi}\left(\frac{f(\xi,t)}{\beta(\xi)}\right) + \frac{\partial}{\partial \xi}\left(\frac{1}{\beta(\xi)}\,\frac{\partial f(\xi,t)}{\partial \xi}\right) \tag{B4}$$

equipped with periodic boundary conditions at $x = 0, L$. In the presence of an external force F, the stationary cell density

$w_{0,F}(\xi)$, toward which the zeroth-order local moment converges in the long-term limit, satisfies the equation

$$\frac{d}{d\xi}\left[-\frac{F}{\beta(\xi)}\,w_{0,F}(\xi)+\frac{1}{\beta(\xi)}\,\frac{dw_{0,F}(\xi)}{d\xi}\right]=0, \tag{B5}$$

i.e.,

$$-\frac{F}{\beta(\xi)}\,w_{0,F}(\xi)+\frac{1}{\beta(\xi)}\,\frac{dw_{0,F}(\xi)}{d\xi}=B, \tag{B6}$$

the solution of which is

$$w_{0,F}(\xi)=A\,e^{F\,\xi}+B\,e^{F\,\xi}\int_0^{\xi}e^{-F\,\xi'}\beta(\xi')\,d\xi', \tag{B7}$$

where the two constants A and B are determined by periodicity, $w_{0,F}(0)=w_{0,F}(L)$,

$$A=A\,e^{F\,L/k_BT}+B\,e^{F\,L/k_BT}I,\quad I=\int_0^L e^{-F\,\xi'}\beta(\xi')\,d\xi', \tag{B8}$$

i.e.,

$$(e^{F\,L}-1)A+e^{F\,L/k_BT}\,I\,B=0, \tag{B9}$$

and by normalization, $\int_0^L w_{0,F}(\xi)\,d\xi=1$,

$$\frac{e^{F\,L}-1}{F}A+B\,I^*=1,$$
$$I^*=\int_0^L e^{F\,\xi}\,d\xi\int_0^{\xi}e^{-F\,\xi'}\,\beta(\xi')\,d\xi', \tag{B10}$$

Reworking by parts the integral defining I^* in Eq. (B10), one obtains

$$I^*=\frac{1}{F}e^{F\,L}\,I-\frac{1}{F}\int_0^L\beta(\xi)\,d\xi, \tag{B11}$$

which, substituted into Eq. (B10), making also use of Eq. (B9), provides

$$-\frac{B}{F}\,\langle\beta\rangle_L\,L=1,\quad \langle\beta\rangle_L=\frac{1}{L}\int_0^L\beta(\xi)\,d\xi. \tag{B12}$$

Next, consider the first-order local moment, the dynamics of which is given by

$$\begin{aligned}\frac{\partial m^{(1)}(\xi,t)}{\partial t}&=\mathcal{L}_{\xi,F}[m^{(1)}(\xi,t)]+\frac{F}{\beta(\xi)}\,m^{(0)}(\xi,t)\\&\quad-\frac{\partial}{\partial\xi}\left(\frac{m^{(0)}(\xi,t)}{\beta(\xi)}\right)-\frac{1}{\beta(\xi)}\,\frac{\partial m^{(0)}(\xi,t)}{\partial\xi}.\end{aligned} \tag{B13}$$

Enforcing periodicity, we have in the long-term limit

$$\begin{aligned}\frac{dM^{(1)}}{dt}&=V_e=\int_0^L\left[\frac{F}{\beta(\xi)}\,w_{0,F}(\xi)-\frac{1}{\beta(\xi)}\,\frac{\partial w_{0,F}(\xi)}{d\xi}\right]d\xi\\&=-B\,L,\end{aligned} \tag{B14}$$

where we have used Eq. (B6). Making use of Eq. (B12), we finally obtain

$$V_e=\frac{F}{\langle\beta\rangle_L} \tag{B15}$$

The comparison of Eqs. (A6) and (B15) proves Theorem 1.

APPENDIX C: PROOF OF THEOREM 3

In this Appendix, we consider the model [Eq. (36)] in the presence of constant friction and a rough energy landscape, defined by a periodic potential $U(x+L)=U(x)$.

Consider the diffusive problem, i.e., $F=0$. The Fokker-Planck equation for the probability density function $p(x,t)$ reads

$$\frac{\partial p(x,t)}{\partial t}=\frac{1}{\eta}\,\frac{\partial(U'(x)\,p(x,t))}{\partial x}+D\frac{\partial^2 p(x,t)}{\partial x^2}=\mathcal{L}_{x,U}[p(x,t)], \tag{C1}$$

where $U'(x)=dU(x)/dx$ and $D\,\eta=k_BT$. The estimate of D_e proceeds, as in the previous Appendixes, by considering the local moments $m^{(n)}(\xi,t)$ that satisfy the system of equations

$$\begin{aligned}\frac{\partial m^{(n)}(\xi,t)}{\partial t}&=\mathcal{L}_{\xi,U}[m^{(n)}(\xi,t)]-\frac{n\,U'(\xi)}{\eta}\,m^{(n-1)}(\xi,t)\\&\quad-2\,n\,D\frac{\partial m^{(n-1)}(\xi,t)}{\partial\xi}\\&\quad+n\,(n-1)\,Dm^{(n-2)}(\xi,t),\quad \xi\in(0,L),\end{aligned} \tag{C2}$$

where $\mathcal{L}_{\xi,U}$ is the cell operator defined by Eq. (C1) with $x=\xi$, equipped with periodic boundary conditions at $\xi=0,L$. For $n=0$, one recovers the invariant cell density function $w_{0,U}(\xi)$, solution of the steady problem $\mathcal{L}_{\xi,U}[w_{0,U}(\xi)]=0$ with periodic boundary conditions and probabilistic normalization:

$$w_{0,U}(\xi)=A\,e^{-U(\xi)/k_BT},\quad A=\left[\int_0^L e^{-U(\xi)/k_BT}d\xi\right]^{-1}=\frac{1}{I_-}. \tag{C3}$$

From the evolution equation for the first-order local moment, it is straightforward to verify that the effective velocity is vanishing for $t\to\infty$. Therefore, $m^{(1)}(\xi,t)$ attains a steady profile $m_1^*(\xi)$ in the long-term limit, expressed by

$$\begin{aligned}m_1^*(\xi)&=C\,e^{-U(\xi)/k_BT}+A\,\xi\,e^{-U(\xi)/k_BT}\\&\quad+Be^{-U(\xi)/k_BT}\int_0^{\xi}e^{U(\xi')/k_BT}d\xi',\end{aligned} \tag{C4}$$

where the constant C is arbitrary and the constant B is uniquely defined by imposing the periodicity condition $m_1^*(0)=m_1^*(L)$. This leads to the condition

$$L\,A+I_+\,B=0,\quad I_+=\int_0^L e^{U(\xi)/k_BT}d\xi. \tag{C5}$$

From the evolution equation of the second-order local moment

$$\begin{aligned}\frac{\partial m^{(2)}}{\partial t}&=\mathcal{L}_{\xi,U}[m^{(2)}(\xi,t)]-2\,\frac{U'(\xi)}{\eta}\,m^{(1)}(\xi,t)\\&\quad-4\,D\frac{\partial m^{(1)}(\xi,t)}{\partial\xi}+2\,D\,m^{(0)}(\xi,t)\end{aligned} \tag{C6}$$

and from $V_e=0$, it follows that the effective diffusivity D_e can be expressed as

$$D_e=-\frac{1}{\eta}\int_0^L U'(\xi)\,m_1^*(\xi)\,d\xi+D=D^*+D, \tag{C7}$$

where, considering the expression for $m_1^*(\xi)$ [Eq. (C4)], we have

$$D^* = \underbrace{-\frac{A}{\eta}\int_0^L \xi\, U'(\xi)\, e^{-U(\xi)/k_BT} d\xi}_{T_1} \underbrace{-\frac{B}{\eta}\int_0^L U'(\xi)\, e^{-U(\xi)/k_BT}\, d\xi \int_0^\xi e^{U(\xi')/k_BT}\, d\xi'}_{T_2}, \quad \text{(C8)}$$

where

$$T_1 = D\,A \int_0^L \xi \frac{d\,(e^{-U(\xi)/k_BT})}{d\xi}\, d\xi = D\,A\,L e^{-U(L)/k_BT} - D,$$
$$T_2 = D\,B \int_0^L \frac{d\,(e^{-U(\xi)/k_BT})}{d\xi}\, d\xi \int_0^\xi e^{U(\xi')/k_BT}\, d\xi' = D\,B e^{-U(L)/k_BT} I_+ - D\,B\,L, \quad \text{(C9)}$$

Substituting these expressions into Eq. (C9) and enforcing condition (C5), one finally obtains

$$D_e = D + D^* = -D\,B\,L = -\frac{D\,L^2}{I_-\,I_+} = \frac{D}{U_-\,U_+},$$
$$U_\pm = \frac{1}{L}\int_0^L e^{\pm U(\xi)/k_BT}\, d\xi. \quad \text{(C10)}$$

Next, consider the same problem is the presence of a constant force F. Applying the local moment analysis also to this case, it follows that the effective velocity attains the expression

$$V_e = \frac{1}{\eta}\int_0^L [F - U'(\xi)]\, w_{0,U,F}(\xi)\, d\xi, \quad \text{(C11)}$$

where $w_{0,U,F}(\xi)$ is the stationary cell density, i.e., the probabilistically normalized solution of the transport cell problem $\mathcal{L}_{\xi,F,U}[w_{0,F,U}(\xi)] = 0$, where

$$\mathcal{L}_{\xi,F,U}[f(\xi)] = -\frac{F}{\eta}\frac{df(\xi)}{d\xi} + \frac{1}{\eta}\frac{d(U'(\xi)\, f(\xi))}{d\xi} + D\frac{d^2 f(\xi)}{d\xi^2}, \quad \text{(C12)}$$

the solution of which is

$$w_{0,F,U}(\xi) = A\, e^{(F\xi - U(\xi))/k_BT} + B e^{(F\xi - U(\xi))/k_BT} \times \int_0^\xi e^{-(F\xi' - U(\xi'))/k_BT}\, d\xi', \quad \text{(C13)}$$

where A and B are two constants to be determined for the periodicity, leading to the relation

$$A(e^{FL} - 1) + B e^{FL} I = 0, \quad I = \int_0^L e^{-(F\xi - U(\xi))/k_BT}\, d\xi, \quad \text{(C14)}$$

and from normalization

$$w_{0,F,U}(\xi) = \Gamma^{-1}\, e^{(F\xi - U(\xi))/k_BT} \times \left[1 - \frac{(1 - e^{-F\,L/K_BT})}{I}\int_0^\xi e^{-(F\xi' - U(\xi'))/k_BT}\, d\xi'\right], \quad \text{(C15)}$$

where the constant $\Gamma^{-1} = A$ is defined by the normalization condition $\int_0^L w_{0,F,U}(\xi)\, d\xi = 1$

$$\Gamma = \int_0^L e^{(F\xi - U(\xi))/k_BT}, d\xi - \frac{(1 - e^{-F\,L/K_BT})}{I} \times \int_0^L e^{(F\xi - U(\xi))/k_BT}\, d\xi \int_0^\xi e^{-(F\xi' - U(\xi'))/k_BT}\, d\xi'. \quad \text{(C16)}$$

Finally, let us consider the behavior of V_e defined by Eq. (C11) for small values of F. We have

$$\frac{V_e\,\eta}{F} - 1 = -\int_0^L U'(\xi) w_{0,U}^{(1)}(\xi) d\xi + O(F^2), \quad \text{(C17)}$$

where $w_{0,U}^{(1)}(\xi)$ is the derivative of $w_{0,F,U}(\xi)$ with respect to F at $F = 0$,

$$w_{0,U}^{(1)}(\xi) = \left.\frac{\partial w_{0,F,U}(\xi)}{\partial F}\right|_{F=0}. \quad \text{(C18)}$$

Since $(1 - e^{-F\,L/K_BT})/I = (L/k_BT I_+)F + O(F^2)$, and considering that the integral of $U'(\xi) e^{-U(\xi)/k_BT}$ over the unit cell is vanishing, we have

$$-\int_0^L U'(\xi)\, w_{0,U}^{(1)}(\xi)\, d\xi$$
$$= \frac{1}{I_-}\left[\int_0^L \xi \frac{d e^{-U(\xi)/k_BT}}{d\xi}\, d\xi - \frac{L}{I_+}\int_0^L \frac{d e^{-U(\xi)/k_BT}}{d\xi}\, d\xi \int_0^\xi e^{U(\xi')/k_BT}\, d\xi'\right]$$
$$= \frac{1}{I_-}\left[\xi\, e^{-U(\xi)/k_BT}\Big|_0^L - \int_0^L e^{-U(\xi)/k_BT}\, d\xi - \frac{L}{I_+}\left(e^{-U(\xi)/k_BT}\int_0^\xi e^{-U(\xi')/k_BT}\, d\xi\Big|_0^L - L\right)\right]$$
$$= \frac{1}{I_-}\left[L\, e^{-U(L)/k_BT} - I_- \frac{L}{I_+}(e^{-U(L)/k_BT}\, I_+ - L)\right]$$
$$= -1 + \frac{L^2}{I_-\,I_+}. \quad \text{(C19)}$$

Thus,

$$\frac{\eta\, V_e}{F} - 1 = -1 + \frac{L^2}{I_-\,I_+} + O(F), \quad \text{(C20)}$$

which implies

$$\frac{V_e}{F} = \frac{1}{\eta\, U_-\, U_+} + O(F) \quad \text{(C21)}$$

corresponding to the content of Theorem 3.

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