Non-Gaussian normal diffusion in a fluctuating corrugated channel

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A Brownian particle floating in a narrow corrugated (sinusoidal) channel with fluctuating cross section exhibits non-Gaussian normal diffusion. Its displacements are distributed according to a Gaussian law for very short and asymptotically large observation times, whereas a robust exponential distribution emerges for intermediate observation times of the order of the channel fluctuation correlation time. For intermediate to large observation times, the particle undergoes normal diffusion with one and the same effective diffusion constant. These results are analytically interpreted without having recourse to heuristic assumptions. Such a simple model thus reproduces recent experimental and numerical observations obtained by investigating complex biophysical systems.

I. INTRODUCTION

Recent observations [1–6] of particle diffusion in fluctuating crowded environments manifestly contradict the common belief that normal diffusion is associated with a Gaussian distribution of spatial displacements. Indeed, if for simplicity, we restrict ourselves to one dimensional (1D) geometries, the displacement, $\Delta x(t) = x(t) - x(0)$, of a standard overdamped Brownian particle suspended in a homogeneous Newtonian fluid [7] (i) grows with time according to the Einstein-Stokes law, $\langle \Delta x^2(t) \rangle = 2Dt$; and (ii) is distributed according to a rescaled Gaussian probability density function (pdf), $p(\Delta x/\sqrt{t})$ with half-variance D. Under these circumstances, the random variable $\Delta x(t)$ is said to undergo Gaussian normal (or Fickian) diffusion.

There is no *a priori* reason why the diffusion of a tracer in a time varying inhomogeneous medium should be Fickian. In real biophysical systems, with increasing the observation time the rescaled displacement distributions, $p(\Delta x/\sqrt{t})$, often develop prominent exponential tails, whereas the tracers start diffusing linearly in time. Such transient tails disappear only for asymptotically large observation times (at times hardly accessible to real experiments [1]), when finally the Δx distributions turn Gaussian, as predicted by the central limit theorem, without appreciably changing the underlying diffusion mechanism. Persistent diffusive transients of this type have been detected in diverse experimental setups [1–3,8–10]. Extensive numerical simulations confirmed the occurrence

of this remarkable phenomenon in crowded environments consisting of slowly diffusing or changing microscopic constituents (filaments [1,3], large hard spheres [4–6], clusters [11,12], and other heterogeneities [13]).

The current interpretation of picture above postulates the existence of one or more relaxation processes affecting the suspension medium or the confining geometry, where the tagged particle diffuses [1]. As long as the fixed time interval, t, over which $\Delta x(t)$ is measured is of the order of the relaxation time constant(s), τ, the particle displacement can obey a non-Gaussian statistics. Through what mechanism, under these conditions the particle's diffusion retains its normal character, may vary from case to case. To this purpose, a popular paradigm revolves around the heuristic notion of *diffusing diffusivity* [14], whereas the environmental fluctuations are modeled by means of an *ad hoc* random particle diffusion constant, $D(t)$. On assuming that $D(t)$ is an Ornstein-Ulenbeck process with average D and time constant τ, the distribution $p(\Delta x/\sqrt{t})$ changes from exponential for $t \ll \tau$ to Gaussian for $t \gg \tau$. In both time regimes, the displacement diffusion is normal, with $\langle \Delta x^2(t) \rangle = 2Dt$ [14]. This phenomenological description, together with its more refined variations [15–21], may qualitatively interpret a conspicuous body of diverse experimental observations, but sheds little light on the underlying microscopic mechanisms.

In this paper, we investigate both numerically and analytically the directed diffusion of an overdamped Brownian particle in a narrow quasi-1D corrugated channel [22,23] of fluctuating width. Such a time variable geometry is inspired to cell biology [24,25] and models the key ingredient of the phenomenon under study, namely slow environmental fluctuations. The relevant stochastic model is detailed in Sec. II. The simulation results of Sec. III reproduce the essentials of non-Gaussian normal diffusion [14] without having recourse to the paradigm of diffusing diffusion: (1) the distribution of the particle displacements along the channel is Gaussian

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for observation times either much shorter (local diffusion) or much longer than the correlation time of the channel fluctuation (channel diffusion), and exponential for a rather wide interval of intermediate observation times. (2) A normal diffusion law with the same channel diffusion constant extends from intermediate to large observation times, thus implying a nontrivial relationship between displacement pdf's. The compatibility of normal diffusion with different displacement statistics is discussed in Sec. IV. (3) These effects are robust as long as fluctuations randomly open and close the channel constrictions. As remarked in the concluding Sec. V, the compartmentalization of particle's diffusion thus emerges as a prerequisite of non-Gaussian normal diffusion.

II. FLUCTUATING CHANNEL MODEL

The dynamics of an overdamped (or massless) Brownian particle in a channel is modeled by the Langevin equation $\dot{\mathbf{r}}(t) = \sqrt{D_0}\boldsymbol{\xi}(t)$, where $\mathbf{r} = (x, y)$ are the particle's coordinates and the translational fluctuations $\boldsymbol{\xi}(t) = [\xi_x(t), \xi_y(t)]$ are zero-mean, white Gaussian noises with autocorrelation functions $\langle \xi_i(t)\xi_j(0) \rangle = 2\delta_{i,j}\delta(t)$, with $i, j = x, y$. The strength of $\xi_i(t)$ is the free-particle diffusion constant, D_0, which is typically proportional to the temperature of the suspension fluid. Without loss of generality, we considered a two-dimensional (2D) sinusoidal channel with axis oriented along x and symmetrically confined transverse coordinate, $|y| \leqslant w(x, t)$, where

$$w(x, t) = (y_L/2)[\varepsilon^2 + (1 - \varepsilon^2)\sin^2(\pi x/x_L)]. \quad (1)$$

Here, y_L and x_L are respectively the maximum width and the length of the unit channel cell, and $\varepsilon^2 y_L$ is the fluctuating width of the pores located at $x = 0 \bmod(\pi)$. We assume for simplicity that $\varepsilon(t)$ obeys the Ornstein-Uhlenbeck equation

$$\dot{\varepsilon} = -(\varepsilon - \varepsilon_0)/\tau + \sqrt{D_\varepsilon/\tau^2}\xi_\varepsilon(t), \quad (2)$$

where the noise $\xi_\varepsilon(t)$ has the same statistics of, but is uncorrelated with the thermal noises, $\boldsymbol{\xi}(t)$. Unless stated otherwise, we set $\varepsilon_0 = 0$, so that the average pore width is $\langle \varepsilon^2 \rangle y_L$ with $\langle \varepsilon^2 \rangle \doteq \sigma_\varepsilon^2 = D_\varepsilon/\tau$. In order to ignore hydrodynamic effects [23], we addressed the case of pointlike particles in highly viscous suspension fluids. Accordingly. we assumed that, for small channel fluctuations, the varying pressure exerted by the walls on the fluid does not sensibly modulate the particle's diffusion constant, D_0, neither in space nor in time. In practice, to modulate the effective width of the channel pores without incurring this difficulty, one can simply apply a tunable external gating potential [23].

We numerically integrated the particle Langevin equation in the free space inside the channel by means of a Milstein algorithm [26]; we imposed reflecting boundary conditions at the channel's walls, $y = \pm w(x, t)$, and took stochastic averages over not fewer than 10^5 particle's trajectories with random initial conditions.

III. THE CASE OF OPENING-CLOSING PORES

The statistics of the particle displacement, $\Delta x(t)$, depends on the observation time, t, as shown in Fig. 1, where three different pdf regimes are clearly
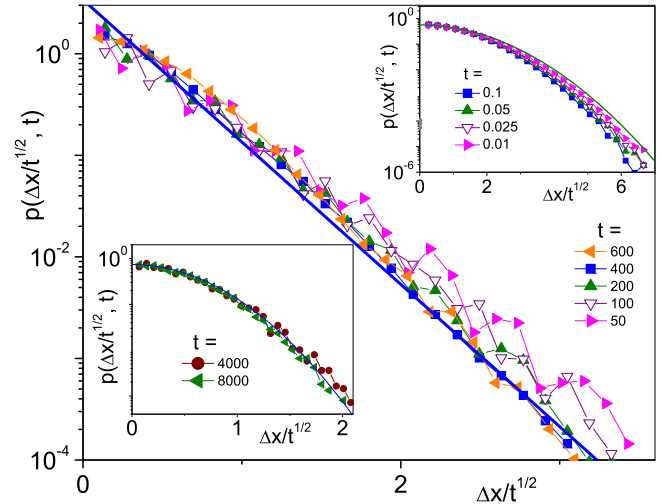

FIG. 1. Diffusion regimes in a fluctuating channel. The rescaled displacement pdf's, $p(\Delta x/\sqrt{t})$, are computed for short, large, and intermediate observation times t, respectively, in the top-right inset, bottom-left inset, and main panel. Simulation parameters are: $y_L = 1$, $x_L = \pi$, $D_0 = 1$, $D_\varepsilon = 3$, $\varepsilon_0 = 0$, and $\tau = 200$. The relevant Gaussian and Laplace distributions are represented by solid curves. The half-variance of the Gaussian fitting curves in the insets are $B = D_0 = 1$ (top right) and $B = D = 0.145$ (bottom left); the exponential decay constant is $\alpha = 0.325$ (main panel). The parameters α and B are defined in the text.

distinguishable: two distinct Gaussian distributions, $p(\Delta x/\sqrt{t}) = (4\pi B)^{-1/2}\exp(-\Delta x^2/4Bt)$, at very short and large t values (insets) and an exponential (or Laplace) distribution, $p(\Delta x/\sqrt{t}) = (2\alpha)^{-1}\exp(-\Delta x/\alpha\sqrt{t})$, over an extended intermediate t range. The short-t Gaussian regime describes the free Brownian diffusion inside a single channel cell, far from the walls, which occurs for time intervals not larger than $\tau_L = \min\{x_L^2/8D_0, y_L^2/8D_0\}$. Under these circumstances, the fitting parameter B turned out to coincide with D_0, as expected [7].

For larger observation times, the particle becomes sensitive to confinement [22]. The escape from one cell into the adjacent ones requires diffusing through narrow pores, a mechanism that takes relatively long waiting times. On extending the approximate techniques of Ref. [27] to the case of fluctuating pores, one estimates a characteristic mean-first exit time (MFET)

$$\tau_0 = \frac{x_L^2}{8D_0}\frac{1}{\langle |\varepsilon| \rangle} = \frac{x_L^2}{8D_0}\sqrt{\frac{\pi\tau}{2D_\varepsilon}}. \quad (3)$$

Here, τ_0 is the time the particle takes to diffuse from inside a cell up to the center of its left or right exit pore. Accordingly, the time constant of the corresponding discrete intercell jumping process is $2\tau_0$ and the channel diffusion constant is thus well approximated by [23,27]

$$D = x_L^2/4\tau_0. \quad (4)$$

On the other hand, the correlation time of the fluctuating pore width, $\varepsilon^2(t)$, is 2τ, see Eq. (2). In view of these timescales, one is led to anticipate that the three distinct regimes of the
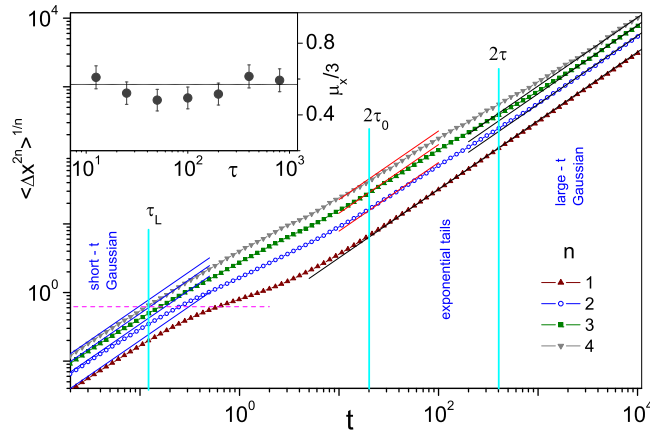
FIG. 2. Normal diffusion in a fluctuating channel: time dependence of $\langle \Delta x^{2n} \rangle^{1/n}$ for different n. Simulation parameters are: $y_L = 1$, $x_L = \pi$, $D_0 = 1$, $\varepsilon_0 = 0$, $D_\varepsilon = 3$, and $\tau = 200$. The parallel straight lines represent the expected values for the higher order moments ($n > 1$) in terms of the fitted normal diffusion law for $\langle \Delta x^2(t) \rangle$ in the Gaussian and exponential regimes (see text). The vertical lines delimit the three pdf regimes of Fig. 1 and are positioned respectively at $t = \tau_L, 2\tau_0$ and 2τ. (Inset:) Ratio $\mu_x/3 \simeq \alpha^2/B$ vs τ at large t. The numerical quantifier μ_x is defined in Sec. IV and was computed here for $t = 2\tau$; for an ideal exponential transient $\mu_x/3 = \pi/2 - 1$ (horizontal line).

rescaled pdf illustrated in Fig. 1 must hold for observation times $t \ll \tau_L$, $2\tau_0 \lesssim t \lesssim 2\tau$ and $t \gg 2\tau$, respectively.

In the asymptotic regime, $t \gg 2\tau$, the particle diffusion along the channel is normal (i.e., $\langle \Delta x^2 \rangle$ is a linear function of t, Fig. 2), which allows a direct numerical determination of the constant D of Eq. (4). Moreover, the intercell jumping process yields a Gaussian distribution of the discretized particle displacements (Brownian random walker [7]). This suggests that asymptotically $B = D$, as discussed below.

The exponential transient, $2\tau_0 \lesssim t \lesssim 2\tau$, thus bridges two Gaussian limits, $t \to 0$ with $B = D_0$, and $t \to \infty$ with $B = D$. Most remarkably, the same Laplace law (i.e., one decay constant α) fits all $\Delta x/\sqrt{t}$ distributions over about one decade of observation times. The similarity with recent experimental observations is apparent [1–6]. The short-t Gaussian regime cannot be reproduced by the diffusing diffusion model of Ref. [14], as there the intracell diffusion time, τ_L, was implicitly set to zero. We notice that the exponential transient interval can be expanded by decreasing σ_ϵ^2 while increasing τ. In the present case, however, this condition leads soon to extremely long simulation runs.

A defining property of channel diffusion is featured in Fig. 2. One normal diffusion law with the same diffusion constant, D, fits all numerical data for $\langle \Delta x^2(t) \rangle$ with $t \gtrsim 2\tau_0$, i.e., in correspondence with both the Laplace and the asymptotic Gaussian distributions. To assess the Gaussian nature of the normal diffusion for $t \to 0$ and $t \to \infty$, we explicitly computed a few higher moments $\langle \Delta x^{2n} \rangle$ with $n \geqslant 1$, also reported in Fig. 2. We checked that in both limits $\langle \Delta x^{2n} \rangle^{1/n} = [(2n-1)!!]^{1/n} \langle \Delta x^2 \rangle$, as expected for Gaussian Δx distributions. Instead, for the Laplace pdf's fitted in Fig. 1, one would expect $\langle \Delta x^{2n} \rangle^{1/n} = [(2n!)/2^n]^{1/n} \langle \Delta x^2 \rangle$. The agreement between these latter estimates and the actual
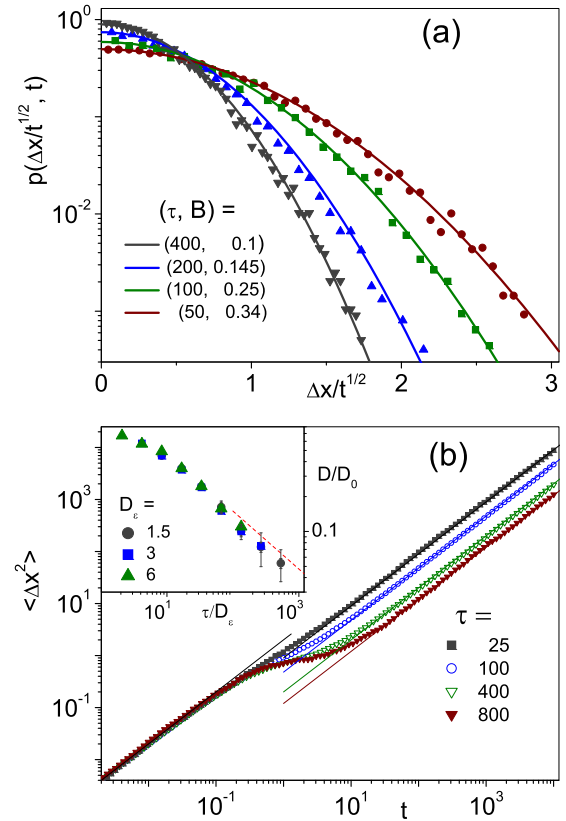

FIG. 3. Role of the fluctuation time correlation: (a) displacement pdf, $p(\Delta x/\sqrt{t})$, and (b) diffusion, $\langle \Delta x^2 \rangle$ vs t for increasing τ. Simulation parameters are: $y_L = 1$, $x_L = \pi$, $D_0 = 1$, $\varepsilon_0 = 0$, and $D_\varepsilon = 3$. The straight lines on the right-hand side of (b) are the linear fits employed to extract the D constant, whereas the solid lines in (a) are the corresponding Gaussian curves, $p(\Delta x/\sqrt{t})$, defined in the text, with $B = D$. For short t, all curves in (b) collapse on one linear branch with diffusion constant D_0, also denoted by a straight line. (Inset) D vs τ for different D_ε (see legend). All other simulation parameters are as in the main panel.

diffusion data in the intermediate t domain is qualitative good, only, which we attributed to the deviations from the Laplace distributions, apparent at $\Delta x/\sqrt{t} \ll \alpha$.

On the other hand, the Laplace and the large-t Gaussian fitting pdf curves introduced above, yield the same channel diffusion constant, D, only under the condition $\alpha^2 = B$. However, the inset of Fig. 2 shows that, for the parameters of Fig. 1, $0.8 < \alpha/\sqrt{B} < 0.9$. The ratio $\alpha/\sqrt{B}$ thus serves as a measure of the exponential character of the displacement statistics across the normal diffusion transient dominated by channel fluctuations. An estimate of this ratio is obtained in Sec. IV.

The role of the timescale τ is further illustrated in Fig. 3. As the MFET of Eq. (3) increases like $\tau^{1/2}$, for large τ the diffusion curves $\langle \Delta x^2(t) \rangle$ develop a plateau in the range $\tau_L \ll t \ll \tau_0$. During this time interval, the diffusing particle "fills up" the 2D channel cell where it was initially injected, attaining a temporary maximum displacement $\langle \Delta x^2 \rangle \simeq \bar{x}^2$, where $\bar{x} = \pi/4$ is the average half-width of the cell $w(x)$, Eq. (1), for $\sigma_\varepsilon \to 0$. This diffusion plateau is represented in Fig. 2 by a horizontal line.

The numerical estimates of the channel diffusion constant, D, for $t \gtrsim 2\tau_0$ and the fitting parameter B of the Gaussian Δx pdf for $t \gg 2\tau$ were anticipated to coincide. Simulation data. like those reported in Fig. 3, confirmed our expectations, within the statistical error, for all choices of the simulation parameters. Moreover, on combining Eqs. (3) and (4), one expects that $D/D_0 = 2(2D_\varepsilon/\pi\tau)^{1/2}$, also in fairly close agreement with the numerical data plotted in the inset of Fig. 3(b).

Finally, we notice that on lowering τ the slopes of the normal diffusion branches for $t \ll \tau_L$ and $t \gtrsim 2\tau_0$ tend to coincide, that is D (and B) tend to D_0. This is due to the fact that the average pore width, $\langle\varepsilon^2\rangle y_L$, grows like D_ε/τ. As a result, for $\langle\varepsilon\rangle \geqslant 1$ the effective channel bottlenecks are no longer located at $x = 0\,\mathrm{mod}\{\pi\}$, but rather at $x = \pi/2\,\mathrm{mod}\{\pi\}$, and have fixed width, y_L. Accordingly, from Eq. (3), $\tau_0 = x_L^2/8D_0$ and the channel diffusion constant of Eq. (4) is $D = D_0$.

IV. EXPONENTIAL NORMAL DIFFUSION

In Sec. III, we showed that on increasing the observation time larger than twice the MFET, (i) the displacement distribution evolves from Laplacian to Gaussian, and (ii) the same normal diffusion law holds for any t. A simple argument, first introduced in Ref. [14], can be generalized to support these conclusions.

Let us model a particle trajectory in the x direction as the sum of random small steps, Δx_i, taken at discretized times, $t_i = i\Delta t$, where $i = 1,\ldots N$, and $\Delta t = 1$, for simplicity. The position of the particle at time N is, therefore, $x_N = \sum_{i=1}^N \Delta x_i$. Accordingly,

$$\langle x_N^2 \rangle = \sum_{i=1}^N \langle \Delta x_i^2 \rangle + 2 \sum_{i \neq j}{}' \langle \Delta x_i \Delta x_j \rangle, \tag{5}$$

where $\sum_{i\neq j}'$ stays for $\sum_{i=1}^{N-1}\sum_{j=1+1}^N$. Contrary to the standard model of Brownian random walker [7], normal diffusion at time N sets in under the generic condition that the *step directions are uncorrelated*, $\langle\Delta x_i \Delta x_j\rangle = 0$, that is for mirror-symmetric distributions, $p(\Delta x_i)$, with variances, $\langle\Delta x_i^2\rangle$, possibly different, but of the same order.

Following the authors of Ref. [14], one can further assume that during each unit time step the particle's diffusion is normal with time-dependent constant, D_i, i.e.,

$$p(\Delta x_i) = (4\pi D_i)^{-1/2} \exp\left(-\Delta x_i^2/4D_i\right),$$

with unspecified D_i distribution, $p(D_i)$. It follows immediately that

$$\langle x_N^2 \rangle = 2\langle D \rangle N, \tag{6}$$

and

$$\langle x_N^4 \rangle - 3\langle x_N^2 \rangle^2 = 12(\langle D^2 \rangle - \langle D \rangle^2)N$$
$$+ 24 \sum_{i \neq j}{}' (\langle D_i D_j \rangle - \langle D_i \rangle \langle D_j \rangle), \tag{7}$$

where $\langle D \rangle \equiv \langle D_i \rangle$ for the relevant choice of $p(D_i)$.

Suppose now that two particle steps, Δx_i and Δx_j, are statistically uncorrelated, i.e., $\langle D_i D_j \rangle = \langle D_i \rangle \langle D_j \rangle$, only for $|i - j| > \tau$. We then distinguish two limiting cases:

(i) $N \gg \tau$, where

$$\mu_x = \frac{\langle x_N^4 \rangle - 3\langle x_N^2 \rangle^2}{\langle x_N^2 \rangle^2} = \frac{3\mu_D}{N} \to 0, \tag{8}$$

with $\mu_D = (\langle D^2 \rangle - \langle D \rangle^2)/\langle D \rangle^2$. A vanishing μ_x hints at a Gaussian x_N distribution as obtained from numerical simulation.

(ii) $N \ll \tau$, where

$$\mu_x = \frac{\langle x_N^4 \rangle - 3\langle x_N^2 \rangle^2}{\langle x_N^2 \rangle^2} \simeq 3\mu_D. \tag{9}$$

$\mu_x = 3$ would correspond to an exponential distribution of x_N; the coefficient μ_D is thus a measure of the deviation of the actual x_N distribution from the ideal Laplace distribution.

To apply the argument above to the model under study, the time step Δt has to be taken not shorter than τ_0, i.e., the argument does not hold for the intracell diffusion. The corresponding coefficient μ_D can be estimated analytically by adapting the procedure of Ref. [27] to the case of a fluctuating channel, namely,

$$\mu_D \simeq \frac{\langle\varepsilon^2\rangle - \langle\varepsilon\rangle^2}{\langle\varepsilon\rangle^2} = \frac{\pi}{2} - 1. \tag{10}$$

On the other hand, on adopting the Laplace distribution $p(\Delta x/\sqrt{t})$ for x_N and the normal diffusion law, $\langle\Delta x^2\rangle = 2Dt$, instead of Eq. (6), that is, $\langle D \rangle = D = B$, numerator and denominator of μ_x can be calculated explicitly to obtain

$$\mu_x = \frac{3\alpha^4}{B^2}. \tag{11}$$

Finally, on comparing Eqs. (9)–(11), one estimates $\alpha/B^{1/2} \simeq 0.86$, in fairly close agreement with the numerical data reported in the inset of Fig. 2.

V. CONCLUSIONS

So far, by setting $\varepsilon_0 = 0$ in Eq. (2) we assumed that the fluctuations of the channel cause the opening and closing of its pores. Of course, in most cases the pores remain open at all times, with $\varepsilon_0 > 0$ and slightly fluctuating cross-section. Therefore we investigated how the non-Gaussian normal diffusion mechanism depends on ε_0. In the main frame of Fig. 4, we plotted the rescaled displacement pdf's at $t = 2\tau$ for the simulation parameters of Fig. 1, except that ε_0 is increased from 0 up to well above σ_ε. One sees immediately that on widening the pores, the rescaled pdf's change from exponential at $\varepsilon_0 = 0$, see Fig. 1, to Gaussian with $B = D$, for $\varepsilon_0 \gtrsim \sigma_\varepsilon$. The dependence of D on ε_0 in the absence and presence of channel fluctuations is compared in the inset of Fig. 4. For $\varepsilon_0 \gtrsim \sigma_\varepsilon$, the diffusion constant grows insensitive to the fluctuation strength, D_ε. The obvious conclusion is that non-Gaussian normal diffusion only occurs when the fluctuations of the channel walls are strong enough to actually open and close the pores. Note that in the absence of channel fluctuations, $D_\varepsilon = 0$, our data for D are well fitted by Eq. (4), with τ_0 given by the first Eq. (3) upon replacing $\langle\varepsilon\rangle$ with ε_0 [27].
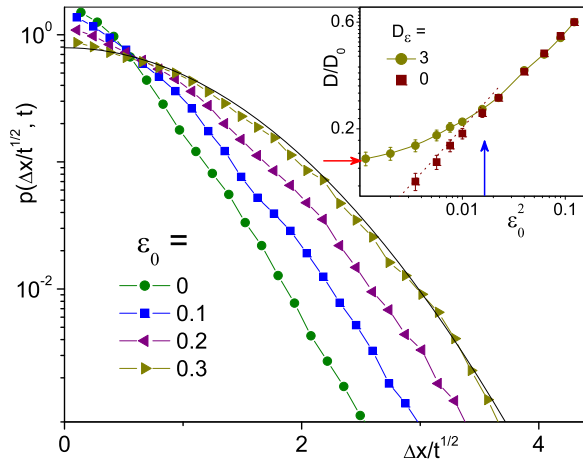
FIG. 4. Role of the fixed pore width ε_0: $p(\Delta x/\sqrt{t})$ at $t = 2\tau$ for increasing ε_0 (see legend). Other simulation parameters are: $y_L = 1$, $x_L = \pi$, $D_0 = 1$, $D_\varepsilon = 3$, and $\tau = 200$. The solid curve represents a normalized Gaussian distribution with $B = D$, D being fitted from the normal diffusion data (inset). (Inset) Channel diffusion constant, D, as a function of ε_0 in the presence ($D_\varepsilon = 3$) and absence ($D_\varepsilon = 0$) of channel fluctuations. The dashed line is the analytical prediction $D/D_0 = 2\varepsilon_0$ [27]; the values $\varepsilon_0^2 = \sigma_\varepsilon^2$ and D/D_0 at $\varepsilon_0 = 0$ are denoted by a vertical and a horizontal arrow, respectively.

The results of Fig. 4 illustrate the importance of diffusion compartmentalization during intermediate observation time

intervals, $2\tau_0 \lesssim t \lesssim 2\tau$. For $\varepsilon_0 > \sigma_\varepsilon$, the tagged particle diffuses along the channel at all times, with only weakly correlated open-pore crossings; hence a Gaussian displacement distribution. In sharp contrast, for $\varepsilon_0 < \sigma_\varepsilon$, the pore crossings of the trapped particle grow more and more time correlated; hence the exponential tails of $p(\Delta x/\sqrt{t})$ discussed in Sec. IV. This description is consistent with the subordination mechanism advocated in Ref. [20].

The microscopic model investigated in this paper, despite its simplicity, was proven to reproduce most of the intriguing properties of the phenomenon known as non-Gaussian normal diffusion. Such a phenomenon has emerged as ubiquitous in soft matter physics, which suggests a number of promising generalizations of the present model by incorporating additional sources of randomness [28], for instance, by decorrelating channel's pore spacing and fluctuations [29] or exciting size and configurational fluctuations of the diffusing particles [30], each on a suitably long timescale. Their combined action is expected to make the conclusions of the present study even more robust.

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