Tracer particles in two-dimensional elastic networks diffuse logarithmically slow

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Abstract
Several experiments on tagged molecules or particles in living systems suggest that they move anomalously slow—their mean squared displacement (MSD) increase slower than linearly with time. Leading models aimed at understanding these experiments predict that the MSD grows as a power law with a growth exponent that is smaller than unity. However, in some experiments the growth is so slow (fitted exponent $\sim 0.1$–0.2) that they hint towards other mechanisms at play. In this paper, we theoretically demonstrate how in-plane collective modes excited by thermal fluctuations in a two dimensional membrane lead to logarithmic time dependence for the tracer particle’s MSD.

Keywords: diffusion, membrane, single-particle tracking, logarithmic dynamics

(Some figures may appear in colour only in the online journal)

1. Introduction

In crowded environments, such as living cells, macromolecules often diffuse slower than expected. A simple way to see this is to measure the macromolecule’s mean squared displacement: in dilute systems, we know that it grows linearly with time, whereas in crowded systems it often grows sub-linearly. Sub-linear behaviour has been seen in several single-molecule experiments that track, for example, fluorescently labelled mRNA molecules in the cell volume \cite{1}, lipid granules in membranes of yeast \cite{2}, and membrane proteins in human kidney.
cells [3]. Apart from biological systems, there are also several cases in artificial crowded fluids, such as dextran solutions [4] and colloidal suspensions near the glass transition [5].

Because the dynamics in these examples deviates from an ordinary diffusion process, it is often referred to as anomalous, [6]. To model these, many theorists and experimentalists use either fractional Brownian motion (FBM) or continuous time random walk (CTRW), and in some cases diffusion on fractals (e.g. [7]). FBM is a generalised Gaussian process with slowly decaying correlations [8], and CTRW describes a particle that jumps in random directions, where the time between consecutive jumps is drawn from a general waiting time distribution (possibly with a diverging first moment) [9].

These frameworks share two important features. (i) They describe a diffusion process of a single-particle, and (ii) the mean-squared displacement \( \langle \Delta r^2(t) \rangle \) grows as a sub-linear power law as a function of time \( t \), that is \( \langle \Delta r^2(t) \rangle \propto t^\alpha \) for \( \alpha < 1 \). Because of this, a common way to analyse single particle trajectories is to calculate \( \langle \Delta r^2(t) \rangle \), fit it to a power-law, and then extract diffusion constants and growth exponents \( \alpha \). However, in some cases it is not clear that a power-law is the best functional form, especially not for many-particle systems.

To better understand what other types of functional forms that may be useful, and how the system’s collective modes can influence the motion of a single particle, we investigate a simple physical system: a tracer particle that moves stochastically in a two dimensional elastic solid membrane. We model the membrane as a beads-on-a-string network and consider over-damped dynamics. Independently of whether the damping comes from friction against a solid support or interactions with a surrounding viscous fluid, we find that the tracer particle’s in-plane \( \langle \Delta r^2(t) \rangle \) does not grow as a power-law, but rather as a logarithm.

With fluid on both sides, our model could be used to describe a fluorescently labeled protein attached to the cell’s cytoskeleton (a network of thread-like protein fibres) while at the same time anchored in a fluid lipid membrane. On length scales longer than the mesh size of the network, this case is effectively the same as a two dimensional solid. Thus, our model complements FBM and CTRW frameworks to better understand slower than Brownian diffusion processes of fluorescently labeled single particles in membranes.

2. Elastic network model

We model the membrane as a two dimensional isotropic elastic network with beads interacting as a Hooke’s law material. Apart from elastic forces, each bead experiences stochastic forces from thermal fluctuations and drag forces from the media that surrounds the membrane. We will let the membrane interact with a solid surface on one side, leading to friction with membrane-wall friction constant \( \zeta \), and a viscous fluid (viscosity \( \eta \)) on the other side, leading to hydrodynamic interactions between different parts of the membrane (see figure 1). To transform this setup to a membrane with fluid on both sides, one simply set \( \zeta = 0 \) and double the viscosity \( \eta \rightarrow 2\eta \) in all equations below.

We assume thermal initial conditions, label each bead by \( n = (n_x, n_y) \), and denote \( u(n,t) = (u_x(n,t), u_y(n,t)) \) as the displacement vector with respect to the beads’ equilibrium positions at time \( t \). We will also assume that the magnitude of \( u(n,t) \) during \( t \) is smaller than the size of the membrane but larger than nearest-bead distances. This allow us to consider the membrane as infinite and \( n \) as a continuous variable. Based on these assumptions, we formulate the equation of motion

\[
\int_{-\infty}^{\infty} d^2 n' \; B(n - n') \cdot \frac{\partial u(n',t)}{\partial t} = \mu \nabla^2 u(n,t) + (\lambda + \mu) \nabla (\nabla \cdot u(n,t)) + w(n,t) \tag{1}
\]
where $\nabla_n = (\frac{\partial}{\partial n_1}, \frac{\partial}{\partial n_2}, \frac{\partial}{\partial n_3})$, and $\lambda$ and $\mu$ are the first and second Lamé parameters that describe the membrane’s elastic properties \cite{10, 11}. $B(n - n')$ is the friction tensor—which is the mobility tensor, or better known as Oseen tensor—and includes bead-support friction and hydrodynamic interactions between beads (the explicit expression is given in Fourier space below). Further, $\mathbf{w}(\mathbf{n}, t)$ is a zero-mean, white Gaussian white noise. The correlations of $\mathbf{w}(\mathbf{n}, t)$ is determined by the fluctuation-dissipation theorem to be:

$$\langle w_\alpha(n, t) w_\beta(n', t') \rangle = 2k_B T \delta(t - t') B_{\alpha\beta}(n - n'),$$

where $\langle ... \rangle$ denotes ensemble average and $k_B T$ is thermal energy.

To proceed we write the displacement in terms of Fourier modes as

$$\mathbf{u}(\mathbf{n}, t) = \int_{-\infty}^{\infty} \frac{d^2 q}{(2\pi)^2} \int_{-\infty}^{\infty} \frac{d\omega}{2\pi} \mathbf{u}(\mathbf{q}, \omega) e^{i\mathbf{q} \cdot \mathbf{n} - i\omega t}$$

where $\mathbf{q} = |\mathbf{q}|$. This transforms equation (1) into

$$-i\omega B(\mathbf{q}) \cdot \mathbf{u}(\mathbf{q}, \omega) = -\mu q^2 \mathbf{u}(\mathbf{q}, \omega) - (\lambda + \mu) \mathbf{q} [\mathbf{q} \cdot \mathbf{u}(\mathbf{q}, \omega)] + \mathbf{w}(\mathbf{q}, \omega)$$

To solve equation (4), it is convenient to split the displacement vector and friction tensor into in-plane longitudinal ($l$) and in-plane transverse ($t$) directions

$$\mathbf{u}(\mathbf{q}, \omega) = u_l(\mathbf{q}, \omega) \hat{l} + u_t(\mathbf{q}, \omega) \hat{t}$$

$$B(\mathbf{q}) = B_l(q) \hat{q} \hat{l} + B_t(q) \hat{q} \hat{t}$$

where $\hat{t}$ is orthogonal to $\hat{q} = \mathbf{q}/|\mathbf{q}|$. After splitting, equation (4) can be written as

\[ \]
To calculate the tensor elements $B(q)$ and $B'(q)$, we must consider two effects. One comes from hydrodynamic friction between the beads: as a bead moves, it changes the velocity field of the surrounding liquid that feeds back on the other beads in the membrane. The other effect comes from the solid support. While the contribution from the solid support simply adds a constant to $B(q)$ and $B'(q)$, the hydrodynamic part is more complicated. In [12] it was shown that the hydrodynamic coupling is proportional to $\eta q$. Combining the two contributions yields

$$B(q) = \xi + 2\eta q$$

(9)

$$B'(q) = \xi + \eta q$$

(10)

These tensor relations together with equations (7) and (8) form the starting point for further analysis.

Before moving on, we point out that the authors of [13] analyse an equation similar to equation (1) but for out-of-plane membrane fluctuations. This contrasts our equations that describe in-plane fluctuations, but it is in any case interesting to note that equation (1) overlaps with the equations in [13] if we set $\lambda + \mu = 0$.

3. In-plane tracer particle fluctuations in a membrane

To analyse a tracer particle’s in-plane fluctuations in the membrane, we study how a tagged piece of the membrane (i.e. a bead in the elastic network) explores space. In the model, the particle cannot detach from the membrane, and nearest-neighbour bonds are maintained over experimental time scales. In particular we calculate the mean squared displacement (MSD) $\langle \delta u_n(t)^2 \rangle = \langle (u(n, t) - u(n, 0))^2 \rangle$ in the membrane’s plane. We will assume that the system is in a stationary state, which means that $\langle u(n, t) \cdot u(n, t') \rangle = \langle u(n, t) \rangle \langle u(n, t') \rangle$, and leads to

$$\langle \delta u_n(t)^2 \rangle = 2\langle (u(n, 0) \cdot u(n, 0)) - \langle u(n, t) \cdot u(n, 0) \rangle \rangle.$$  

(11)

As before we split the correlation $\langle u(n, t) \cdot u(n, t') \rangle$ into its longitudinal part, $C'(t) = \langle u'(t)u'(0) \rangle$, and corresponding transverse part:

$$\langle u(n, t) \cdot u(n, t') \rangle = C'(t - t') + C'(t + t'),$$

(12)

where in terms of $C(t)$ and $C'(t)$ the $\langle \delta u_n(t)^2 \rangle$ is

$$\langle \delta u_n(t)^2 \rangle = 2\langle C'(0) - C'(t) \rangle + [C'(0) - C'(t)].$$

(13)

First we calculate $C'(t)$. To achieve this, we use $u'(q, \omega)$ from equation (8) and the noise autocorrelation function

$$\langle w_i(q, \omega)w_j(q', \omega') \rangle = 2k_B T(2\pi)^3 \delta(\omega + \omega')\delta(q + q')B_{ij}(q).$$

(14)

This leads to
\[ C'(t - t') = \int_{-\infty}^{\infty} \frac{d^2q}{(2\pi)^2} \int_{-\infty}^{\infty} \frac{dq}{2\pi} e^{-i\omega(t-t')} \frac{2k_B T}{B'(q)} \frac{1}{\mu \omega^2 q^2 B'(q)^2 + \omega^2} \]
\[ = \frac{k_B T}{\mu} \int_{-\infty}^{\infty} \frac{d^2q}{(2\pi)^2} \frac{e^{-\mu \omega^2 q^2 B'(q)}}{q^2}. \quad (15) \]

for \( t > t' \). Based on this we find
\[ C'(0) - C'(t) = \frac{k_B T}{\mu} \int_{0}^{\infty} \frac{dq}{2\pi} \frac{1 - e^{-\mu \omega^2 q^2 B'(q)}}{q} \equiv \frac{\Delta'}{2}. \quad (16) \]

where \( \Delta' \) is the transverse contribution to the \( \langle \Delta u_n(t)^2 \rangle \).

To calculate \( \Delta' \) we must work out the integral over \( q \). But for large \( q \), the integrand is proportional to \( 1/q \) and therefore diverges. To overcome this we note that our continuum theory only holds down to a length scale of the order of the distance between the beads. Therefore we introduce a cutoff \( \Lambda \) which is on the order of one over this distance. The dynamics at wave numbers larger than \( \Lambda \) will be fast and therefore will just contribute a constant to the asymptotic long time behavior of the MSD. Including this constant in the final result will correspond to an adjustment of the value of \( \Lambda \). With the cutoff, equation (16) reads
\[ \Delta' = \frac{k_B T}{\mu} \int_{0}^{\Lambda} \frac{dq}{\pi} \frac{1 - e^{-\mu \omega^2 q^2 B'(q)}}{q} \quad (17) \]

The corresponding expression for \( \Delta' \) is the same but with \( \mu \) replaced by \( \lambda + 2\mu \) and \( \eta \) by \( 2\eta \).

To find the long time dynamics of \( \langle \Delta u_n(t)^2 \rangle \), we need to find the asymptotic behavior of \( \Delta' \) and \( \Delta' \). To that end, we investigate two cases: \( \xi \neq 0 \) and \( \xi = 0 \). These correspond to a membrane that is supported by a solid interface on one side and viscous liquid on the other (\( \xi \neq 0 \)), and liquid on both sides (\( \xi = 0 \), but then with \( \eta \rightarrow 2\eta \) to reflect the doubling of the liquid).

3.1. Case \( \xi \neq 0 \)

Let us first consider our setup with solid support (\( \xi = 0 \)). If we let \( \mu \xi t \) in equation (17) we get
\[ \Delta' = \frac{k_B T}{\mu} \int_{0}^{\Lambda} \frac{dy}{\pi} \frac{1 - e^{-\mu \omega^2 y^2 B'(y)}}{y} \quad (18) \]

We now split the integration into two parts, according to whether \( y \) is above or below a parameter \( \epsilon \) that we choose such that \( 1 \ll \epsilon \ll \min(\sqrt{\mu \xi t}, \Lambda \sqrt{\mu \xi t}) \). For \( y > \epsilon \) we can approximate \( B'(y) \sqrt{\mu \xi t} \sim \xi \) and for \( y > \epsilon \) we can ignore the exponential term in the numerator. This gives
\[ \Delta' \sim \frac{k_B T}{\pi \mu} \left( \int_{0}^{\epsilon} \frac{dy}{y} - \int_{\epsilon}^{\Lambda \sqrt{\mu \xi t}} \frac{dy}{y} \right) \quad (19) \]

From these integrals we find when \( \epsilon \gg 1 \) that
\[ \Delta' \sim \frac{k_B T}{2\pi \mu} \left[ \ln \left( \frac{\mu \Lambda^2}{\xi} \right) + \gamma \right] \quad (20) \]
where $\gamma = 0.577 \ldots$ is Euler’s constant. Again, to get the longitudinal part $\Delta l$ we replace $\mu$ by $\lambda + 2\mu$ in $\Delta t$. Adding $\Delta l$ and $\Delta t$ in equation (13) gives the asymptotic behavior

$$\langle du(t)^2 \rangle \sim \frac{k_B T (\lambda + 2\mu)}{\pi \mu (\lambda + 2\mu)} \left[ \ln (t/\tau_{\xi=0}) + \gamma \right]$$

with a characteristic time scale:

$$\tau_{\xi=0} = \frac{\xi}{\mu \lambda^2}$$

Thus, when the membrane is on a solid support, the tracer particle’s MSD is asymptotically proportional to the logarithm of time, $\langle du(t)^2 \rangle \propto \ln t$.

3.2. Case 2: $\xi = 0$

In the absence of a solid support, we set $\xi = 0$. Equation (17) then becomes (after replacing $\eta$ with $2\eta$ since we now have fluid on both sides)

$$\Delta l = \frac{k_B T}{\mu} \int_0^\Lambda dq \frac{1 - e^{-q/(2\eta)}}{\pi q}$$

This integral can be evaluated directly and has the asymptotic behaviour

$$\Delta l \sim \frac{k_B T}{\pi \mu} \left[ \ln \left( \frac{\mu \Lambda t}{2\eta} \right) + \gamma \right]$$

As before, we get $\Delta l$ by letting $\mu \to \lambda + 2\mu$ and doubling the viscosity: $2\eta \to 4\eta$. For large times, we find that

$$\langle du(t)^2 \rangle \sim \frac{k_B T (\lambda + 3\mu)}{\pi \mu (\lambda + 2\mu)} \left[ \ln (t/\tau_{\xi=0}) + \gamma \right]$$

with a characteristic time scale

$$\tau_{\xi=0} = \frac{2\eta}{\mu \lambda}$$

Thus, like for a supported membrane ($\xi \neq 0$) the MSD grows logarithmically with time for long times. Note, however, that the result above differ from the $\xi = 0$—case by a factor of $\frac{1}{2}$. Also, whereas the characteristic time scales are independent on $\eta$ for $\xi \neq 0$, this is not the case without solid support, see equations (20) and (25). Thus, in the presence of a solid support the support-bead friction dominates the dynamics and in this case, for long enough times, the tracer particle motion is insensitive to the hydrodynamic coupling between beads.

4. Summary and concluding remarks

In this paper we show that the mean squared displacement of a tracer particle in a solid membrane moves logarithmically slow. This model could serve as a complement to other models.
that are used to interpret single-particle tracking experiments, foremost fractional Brownian motion and continuous time random walks. For example, it could shed new light on the molecular dynamics simulation of lipids in lipid membranes [14], where fitting a power-law yields a very small exponent ($\alpha \approx 0.16$).

Apart from our model and [13], there are more 2D models that exhibit logarithmic behaviour. For example Edward-Wilkinson growth for granular aggregates [15]. This model describes how the height profile of a growing surface develops in a reference frame that moves with the surface’s average growth speed. The relative height $h(r, t)$ is governed by the diffusion equation $\partial h(r, t) / \partial t = \Delta_c h(r, t) + \eta(t)$ with gaussian white noise $\eta(t)$, compare our equation (1). Calculating the fluctuations in 2D gives $\langle h(r, t)^2 \rangle \propto \log t$.

Even though our system is far from granular aggregation, our model can mathematically be seen as a generalisation of the Edward-Wilkinson model or an alteration to previous generalisations (e.g. the 2D XY model [16]): we add non-local couplings between spatial points due to hydrodynamic interactions between beads. This leads to several interesting results. Apart from the logarithm, we find that the tracer particle’s motion does not depend on the hydrodynamic coupling for long times, when the membrane has a solid support (however, for short and intermediate times it depends on the viscosity of the surrounding medium). Without solid support, the long-time effect of the hydrodynamic coupling is weak and enters only through a characteristic time scale in the logarithm.

Going into one dimension, there are several other physical systems that belong to the Edward-Wilkinson universality class. For example, a tracer particle that diffuse together with other particles that it cannot pass (without hydrodynamic interactions), so-called single-file diffusion [17], or monomer diffusion in a Rouse polymer [18]. In these cases we interpret $h(x, t)$ as the position of particle (or monomer) $x$, and one can show that $\langle h(x, t)^2 \rangle$ grows as $\sqrt{t}$ rather than $\log t$.

Even though the Edward-Wilkinson equation is useful for hard-core interacting particles in 1D, it fails to describe diffusing hard-core particles in higher dimensions. In 2D and 3D the particles may easily pass each other and $\langle h(x, t)^2 \rangle$ therefore grows linearly with time. This contrasts the Edward-Wilkinson equation that predicts $\log t$ behaviour in 2D, and that $\langle h(x, t)^2 \rangle$ is constant in 3D.

The logarithmic dynamics in our model stems from collective motion of the membrane. Such collective behaviour cannot be described by FBM and CTRW that are single-particle models with power-law dynamics. However, we point out that there are several single-particle processes different from ours that exhibit logarithmic time evolution. Here are three examples: (i) Sinai diffusion [19] where a particle moves in an energy landscape with power-law distributed energy barriers, (ii) extreme value problems such as record statistics [20] where the logarithm comes from the increasing difficulty to break new records, (iii) the average number of cities visited by a hitchhiker up to time $t$ [21]. See also [21] for more examples of logarithmic time evolution.

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