Exact solution for the Anisotropic Ornstein-Uhlenbeck Process

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Abstract

Active Matter models commonly consider particles with overdamped dynamics subject to a force (speed) with constant modulus and random direction. Some models include also random noise in particle displacement (Wiener process) resulting in a diffusive motion at short time scales. On the other hand, Ornstein-Uhlenbeck processes consider Langevin dynamics for the particles velocity and predict a motion that is not diffusive at short time scales. However, experiments show that migrating cells may present a varying speed as well as a short-time diffusive behavior. While Ornstein-Uhlenbeck processes can describe the varying speed, Active Matter models can explain the short-time diffusive behavior. Isotropic models cannot explain both: short-time diffusion renders instantaneous velocity ill-defined, hence impeding dynamical equations that consider velocity time-derivatives. On the other hand, both models apply for migrating biological cells and must, in some limit, yield the same observable predictions. Here we propose and analytically solve an Anisotropic Ornstein-Uhlenbeck process that considers polarized particles, with a Langevin dynamics for the particle’s movement in the polarization direction while following a Wiener process for displacement in the orthogonal direction. Our characterization provides a theoretically robust way to compare movement in dimensionless simulations to movement in dimensionful experiments, besides proposing a procedure to deal with inevitable finite precision effects in experiments or simulations.

Key words: Ornstein-Uhlenbeck process, Modified Fürth Equation, Anisotropic persistent random walk.

1 Introduction

Single cell migration on flat surfaces has been observed and quantified for over a century [1,2]. Since then, cell movement has been often described by Fürth equation, that gives cell’s Mean
Square Displacement (MSD) as a function of the time interval $\Delta t$ between the acquisition of the cell’s positions used to calculate displacement:

$$MSD_{\text{Fürth}} = 4D \left[ \Delta t - P \left( 1 - \exp(-\Delta t/P) \right) \right],$$

(1)

where $D$ is the diffusion coefficient (for long time intervals, $MSD_{\text{Fürth}} \sim 4D\Delta t$) with the factor 4 accounting for the movement in two dimensions. At short time intervals, $MSD_{\text{Fürth}} \sim \frac{2D}{P} \Delta t^2,$ hence presenting a ballistic motion and allowing a sound definition for instantaneous velocity (as opposed to a Wiener process). The persistence time $P$ signals the transition from ballistic to diffusive motion $[3,4,5,6,7,8]$. Eq.(1) is the solution of an Ornstein-Uhlenbeck process for a particle motion, that is,

$$\frac{d\vec{v}}{dt} = -\gamma \vec{v} + \vec{\xi}(t)$$

$$\frac{d\vec{r}}{dt} = \vec{v} ,$$

(2)

where $\vec{r}$ and $\vec{v}$ are, respectively, the particle’s position and instantaneous velocity, $\gamma$ stands for a dissipation term, that consumes kinetic energy, and $\vec{\xi}(t)$ is a two-dimensional white noise vector from which the particle gathers kinetic energy. Trajectories can be obtained from solving Eqs.(2), from which $MSD$ can be calculated. Classical Brownian particles on a liquid surface are described by the same set of equations where the $\gamma$ term is the usual viscosity and $\vec{\xi}(t)$ stands for the impulse the particle receives from the numerous collisions with the fluid molecules. However, migrating cells are neither isotropic nor inert particles put into movement by the interaction with the thermal motion of the components of its environment. Besides the reinterpretation of each term in Eqs.(2), some further adjustments are required to account for deviations for the $MSD$ from the Fürth equation. Thomas and collaborators [9] demonstrated that eukaryotic single-cell migration shows Ornstein-Uhlenbeck-like statistics for intermediate and long-time scales but diffusive statistics for short-time scales. Because the instantaneous velocity of the cells is divergent, the inferred velocity and diffusion constant depend on the time interval between position measurements, impeding consistent comparisons between experiments. Computer simulations of 3D crawling cells using the Cellular Potts Model Compucell3D also show short-time diffusive movement [10]. Since experiments and simulations always have some shortest interval between position measurements, we need metrics to quantify movement that are independent of this minimum. Another valuable tool to investigate cell migration is the Velocity AutoCorrelation Function (VACF), defined as the average scalar product of velocity at a given time with velocity after a time interval $\Delta t$. For stationary processes, it may be calculated from the $MSD$ second time derivative. However, when time intervals are small, the inevitable finite precision in measurements leads to a marked decrease in the modulus of $VACF$, as compared to the values predicted by the $MSD$ second time derivative. This velocity correlation loss will be observable in any system that presents the same short-time diffusive behavior [9].

Many Active Matter models also apply to migrating, biological cells. In general, in these models the particle’s speed $v_0$ is kept constant while its direction may change due to a white noise term. In this case, the $MSD$ is also given by Eq.(1). The interpretation is that the particle’s acquire speed due to internal activity, which is completely lost in a short (infinitesimal) time interval and re-acquired in the next time interval: the particle is active, but its dynamics is said to be overdamped. The movement direction, denoted by an angle $\theta$ in respect to the reference frame, keeps memory from the previous time instant, being stochastically changed by small
amounts. It may happen that an additional, white noise term is added to the displacement
equation, that is,

\[
\begin{align*}
\dot{v}(t) &= v_0 \\
\frac{d\theta}{dt} &= \beta(t) \\
\frac{d^2 r}{dt^2} &= v_0 \vec{p}(t) + \vec{\omega}(t),
\end{align*}
\]

where \( \vec{r} \) is the particle’s position, \( \vec{p}(t) = (\cos \theta , \sin \theta) \), and \( \beta(t) \) and \( \vec{\omega}(t) \) are white noise
terms with adequate units. When \( \vec{\omega}(t) \) is assumed different from zero, instantaneous velocity
is not well-defined, since \( \lim_{\Delta t \to 0} \frac{\vec{r}(t+\Delta t)-\vec{r}(t)}{\Delta t} \) diverges. In other words, \( v_0 \) is not measured as
displacement over time interval for vanishing time intervals and is not a proper velocity, but
rather a model parameter, associated to the cell’s internal activity. The effect of adding a non-
zero \( \vec{\omega}(t) \) results in a short time interval diffusion, that translates into \( MSD \sim \Delta t \) as \( \Delta t \to 0 \).

While \( v(t) \) is kept constant in Eqs.(3), a non-zero \( \vec{\omega}(t) \) does not harm the rigor of the
equations, although it turns inadequate the name for \( v(t) \) and requires defining new measurement
protocols. On the other hand, both Ornstein-Uhlenbeck process and Active Matter models apply to migrating cells and, at least in some limit, should agree in measurement
protocols and observable results. When neither \( \vec{\omega}(t) \) nor the short-time diffusive regime
presented by \( MSD \) curves are taken into account, this conciliation is easily accomplished by
changing the first equation in Eqs.(3) by an Ornstein-Uhlenbeck equation for velocity. On the
other hand, since the diffusive regime for short time intervals must be accounted for, \( \vec{\omega}(t) \) is
non-zero and the consequent instantaneous velocity ill-definition impedes assuming an
equation that involves its time-derivative.

Here we propose to bypass this apparent contradiction by explicitly considering the
anisotropy of migrating cells. We consider dynamical equations where the particle has a
polarization degree of freedom. The polarization direction continuously changes as described by
the \( \theta \)-equation in Eqs.(3), and, at each instant, the particle’s speed in the polarization direction
obeys an Ornstein-Uhlenbeck process while in the orthogonal direction(s) the particle’s
displacement is ruled by a Wiener process. Below, we propose and analytically solve this mixed
model. We show that its \( MSD \) curves have a short-time scale diffusive regime as do Active Matter models with non-zero \( \vec{\omega}(t) \) \cite{11,12,13} and eukaryotic migrating cells \cite{7,9}. We
numerically solve the model equations, to verify the analytical solutions and obtain trajectories. 
Finally, we show how finite precision in the numerical solutions or in experiment measurements
can lead to observed differences in \( VACF \) for short-time intervals.

2 The model

We assume that a particle has an internal orientational degree of freedom, given by a
polarization vector, \( \vec{p}(t) = (\cos \theta(t), \sin \theta(t)) \). In a biological cell, this orientation might
define the direction of cell polarization \cite{14}, in an animal, the vector pointing from tail to head.
We begin by defining polarization dynamics as

\[
[\theta(t+\Delta t) - \theta(t)] = \int_t^{t+\Delta t} \beta_\perp(t) \, dt,
\]

\( \beta_\perp(t) \) is the particle’s internal activity. The effect of adding a non-
zero \( \beta_\perp(t) \) results in a short time interval diffusion, that translates into \( MSD \sim \Delta t \) as \( \Delta t \to 0 \).
where $\beta_\perp(t)$ is a Gaussian white noise. The statistics of movement parallel and perpendicular to $\vec{p}(t)$ differ. In the polarization direction, we assume that for a small time interval $\Delta t$ the change in cell’s velocity may be written as

$$v_{\parallel}^{\text{final}}(t) = \left[(1 - \gamma \Delta t)v_{\parallel}^{\text{initial}}(t) + \int_t^{t+\Delta t} \xi_\parallel(t) dt \right],$$

(5)

where $\gamma$ is the dissipation and $\xi_\parallel(t)$ is also a Gaussian white noise, with adequate units. $v_{\parallel}^{\text{initial}}(t)$ and $v_{\parallel}^{\text{final}}(t)$ are the velocities, respectively, at the beginning and at the end of time interval $\Delta t$. At the end of that small time interval, we assume that the polarization direction changes, from $\vec{p}(t)$ to $\vec{p}(t + \Delta t)$, and the initial parallel velocity at the beginning of the subsequent time interval is taken as the projection of $v_{\parallel}^{\text{final}}(t)\vec{p}(t)$ on $\vec{p}(t + \Delta t)$, that is,

$$v_{\parallel}^{\text{initial}}(t + \Delta t) = v_{\parallel}^{\text{final}}(t)(\vec{p}(t) \cdot \vec{p}(t + \Delta t)).$$

(6)

In Eq.(6) we hypothesize that the actin filaments dynamics is subject to noise that may randomly change the rear-to-front axis that defines migrating cells polarization, obtained from Eq.(4). We also hypothesize that these direction changes reduce cell speed, since a migrating cell’s speed is universally coupled to its cytoskeleton organization [14]. Here we assume that the conserved fraction of speed may be described by the projection of the new polarization direction on the previous one. Eq. (6) gives the particle’s speed $v_{\parallel}^{\text{initial}}(t + \Delta t)$ at the beginning of the subsequent time interval along $\vec{p}(t + \Delta t)$ (the speed ‘memory’) as the component of the particle’s speed at the end of the previous time interval projected onto the new axis.

Eqs.(5) and (6) can be put in unique equation for a a well-defined speed $v_{\parallel}(t)$, as

$$v_{\parallel}(t + \Delta t)\vec{p}(t + \Delta t) = \left[(1 - \gamma \Delta t)v_{\parallel}(t) + \int_t^{t+\Delta t} \xi_\parallel(t) dt \right](\vec{p}(t) \cdot \vec{p}(t + \Delta t))\vec{p}(t + \Delta t),$$

(7)

One critical point in the rigor for Eq.(7) lays in the fact that the dynamics for polarization direction, $\vec{p}(t) = (\cos \theta(t), \sin \theta(t))$, follows Eq.(4), that is a Wiener process for which it is not possible to consider an infinitesimal time interval where the variables are constant. However, in Eq.(7) the relevant quantity is $\vec{p}(t) \cdot \vec{p}(t + \Delta t) = \cos \Delta \theta(t) \sim 1 - \frac{(\Delta \theta)^2}{2}$ and $(\Delta \theta)^2 \sim \Delta t$. Hence, in Eq.(7), we can assume that $\vec{p}(t)$ is constant during $\Delta t$. In supplementary materials online, we show in detail that our assumption of an infinitesimal time interval for $v_{\parallel}(t)$ dynamics, given in Eq.(7), is justified.

The particle position in the direction orthogonal to the polarization obeys a Wiener process:

$$[r_\perp(t + \Delta t) - r_\perp(t)] \vec{n}(t) = \vec{n}(t) \int_t^{t+\Delta t} \xi_\perp(t) dt,$$

(8)

where $\vec{n}(t) = (\sin(\theta(t)), -\cos(\theta(t)))$ is a unit vector perpendicular to $\vec{p}(t)$.

$\xi_\parallel(t), \xi_\perp(t),$ and $\beta_\perp(t)$ are Gaussian white noises (with different units). $\xi_\parallel(t)$ is independent of the two other terms, but we consider that $\xi_\parallel(t)$ and $\beta_\perp(t)$ are related: we assume that fluctuations in the actin-network dynamics in the lamellipodia are responsible for both stochastic change in the rear-to-front direction, as well as to the random displacements in the $\vec{n}(t)$ direction. We assume

$$\xi_\parallel(t) = \sqrt{q} \beta_\perp(t),$$

(9)
with $\sqrt{q}$ given in units of length. The noise terms are given in terms of their second moment, as follows:

\begin{align}
\langle \xi_\parallel(t) \rangle &= 0, & \langle \xi_\parallel(t) \xi_\parallel(t') \rangle &= g \delta(t - t'), \tag{10a} \\
\langle \beta_\perp(t) \rangle &= 0, & \langle \beta_\perp(t) \beta_\perp(t') \rangle &= 2k \delta(t - t'), \tag{10b} \\
\langle \xi_\perp(t) \rangle &= 0, & \langle \xi_\perp(t) \xi_\perp(t') \rangle &= 2qk \delta(t - t'), \tag{10c}
\end{align}

where $g$, $k$, and $qk$ have units of $[\text{length}]/\text{time}^3$, $1/\text{time}$, and $[\text{length}]/\text{time}$, respectively.

We summarize our model in Fig.1: it considers a particle with two spatial degrees of freedom and one internal polarization degree of freedom that breaks spatial symmetry. The particle follows a Langevin-like dynamics for speed in the instantaneous polarization direction and, in its perpendicular direction, a Wiener process for displacement. There are two independent sources of noise: one acts on the speed dynamics in the polarization direction and the second acts on the polarization direction itself, linked to a random displacement in the direction orthogonal to the polarization. The change in polarization acts as a further term for loss of time correlation in velocity and, as we show below, reduces the persistent time of the movement.

Figure 1. Sketch for the model. At the beginning of a small time interval $\Delta t$, the cell has initial speed $v_{\parallel \text{initial}}(t)$ and polarization direction $\vec{p}(t)$. At the end of the interval the parallel-to-polarization speed changes to $v_{\parallel \text{final}}(t)$, as prescribed in Eq.(5), and its polarization changes to $\vec{p}(t + \Delta t)$, such that $\vec{p}(t) \cdot \vec{p}(t + \Delta t) = \cos \Delta \theta$, with $\Delta \theta$ evolving as prescribed by Eq.(4) (as a Wiener process). The turning in polarization reduces speed, from $v_{\parallel \text{final}}(t)$ to $v_{\parallel \text{initial}}(t + \Delta t)$ (Eq.(6)). Additional to the displacement in the parallel-to-polarization axis, we also assume a random displacement in the perpendicular-to-polarization axis (Eq.8).
3 Numeric solutions

To verify our analytic results we have numerically solved the dynamics represented by Eqs. (3)-(6), that have 4 parameters \((q, \gamma, g, \text{ and } k)\). We built a C language program using the Euler-Maruyama method for integrating stochastic differential equations [15]. When we analyze the movement (below) we find that by rescaling the parallel and perpendicular length scales and the time scale we can eliminate three parameters, leaving a single parameter dependence on \(k\). As we analytically show below, by solving Eqs. (4,7, and 8) we obtain MSD curves that reproduce the empirically proposed functions proposed as the Modified Fürth Equation in Ref. [9], shown in Eq.(22), below. The Modified Fürth Equation, when written using non-dimensional variables, represents a single-parameter family of curves where the free parameter is called excess diffusion coefficient, is denoted by \(S\), and is linked to the time duration of the short-time-diffusion regime, a consequence of assuming Eq.(8). \(MSD_{\text{Fürth}}\) given in Eq.(1), represents the member of this family of curves with \(S = 0\). The relations between \(q, \gamma, g, \text{ and } k\) with the observable parameters \(S, P, \text{ and } D\) are given in Eqs. (23), while the length and time scales are \(\sqrt{\frac{2DP}{1-5}}\) and \(P\), as in Ref. [9].

Without loss of generality, we consider all parameters constant \((q = 0.1, \gamma = 1 \text{ and } g = 10 )\) except for \(k\): by adequately varying \(k\) \((0.04405, 0.2625, 0.965, \text{ and } 1.7425\) which correspond to values of \(S = 0.001,0.01,0.1 \text{ and } 0.3\), all observed dynamics of migrating cells become apparent, while the other parameters define length and time scales of the system.

As in a usual Langevin problem, our model supports a stationary state, where average speed, MSD and VACF curves do not change in time. Initial cell polarization angles are randomly and uniformly distributed in \([0, 2\pi]\) and \(v_\parallel(t = 0)\) is initialized at two different values: at the stationary state \(\sqrt{\langle v_\parallel^2 \rangle}\) (Eq. 16, below), aiming at stationary MSD and VACF measurements, and \(v_\parallel(t = 0) = 10^3\), to address transient decay to the stationary state.

Each time step of the dynamics consists of the following: \(i\) we choose a Gaussian random number with standard deviation equals to \(2k\) and update the polarization \(\theta\) according to Eq. (4); \(ii\) we choose an independent Gaussian random number with standard deviation equal to \(g\) and update \(v_\parallel\) and project it onto the new direction, according to Eq. (5 and 6); \(iii\) \(r_\perp\) is obtained from the variation in angle (Eqs. 8 and 9); \(iv\) cell positions are updated. These steps are repeated (we used \(dt = 10^{-4}\)) and we take an average over 10 independent cells.
4 Analytical solutions for MSD and VACF.

Below we present exact solutions for this model’s MSD, speed and VACF. We obtained our analytical solutions at time $T$ by considering $n$ steps each of duration $\Delta t = \frac{T}{n}$ then taking the limit $\Delta t \to 0$, while $n \to \infty$, such that $T$ remains finite.

4.1 Analytical forms for $\langle v_i^2(n\Delta t) \rangle$ and the persistence time $P$.

In what follows, we write $\vec{p}_j \equiv \vec{p}(j\Delta t)$. We apply Eq. (7), to obtain the speed in the direction of the instantaneous polarization axis. We first calculate $v_i(\Delta t)\vec{p}(\Delta t)$ in terms of $v_i(0)\vec{p}(0)$:

$$v_i(\Delta t)\vec{p}(\Delta t) = \left[ (1 - \gamma \Delta t) v_i(0) + \int_0^{\Delta t} \xi_i(t) \, dt \right] (\vec{p}_0 \cdot \vec{p}_1) \vec{p}_1 \, ,$$

we then iterate Eq. (7) $n = \frac{T}{\Delta t}$ times to obtain $v_i(T)\vec{p}(T)$ in terms of $v_i(0)\vec{p}(0)$.
\[ v_{\parallel}(n\Delta t) \hat{p}_n = (1 - \gamma \Delta t)^n v_{\parallel_0} \prod_{i=0}^{n-1} [\hat{p}_i, \hat{p}_{i+1}] \hat{p}_n \]

\[ + \sum_{j=0}^{n-1} \int_{j\Delta t}^{(j+1)\Delta t} ds \xi(s) (1 - \gamma \Delta t)^{n-(j+1)} \prod_{i=j}^{n-1} [\hat{p}_i, \hat{p}_{i+1}] \hat{p}_n. \]  

(12)

From Eq. (12), we calculate \( \langle v_{\parallel}^2(n\Delta t) \rangle \) as follows:

\[ \langle v_{\parallel}^2(n\Delta t) \rangle = (1 - \gamma \Delta t)^{2n} v_{\parallel_0}^2 \left( \prod_{i=0}^{n-1} [\hat{p}_i, \hat{p}_{i+1}]^2 \right) \]

\[ + g \sum_{j=0}^{n-1} \int_{j\Delta t}^{(j+1)\Delta t} ds (1 - \gamma \Delta t)^{2(n-(j+1))} \left( \prod_{i=j}^{n-1} [\hat{p}_i, \hat{p}_{i+1}]^2 \right), \]

(13)

where we used Eq. (10a) for the average over \( \xi_{\parallel}(t) \). To calculate the average over the stochastic changes in \( \hat{p}_i \), we use that \( [\hat{p}_{i-1}, \hat{p}_j] = \cos(\theta((j-1)\Delta t) - \theta(j\Delta t)) = \cos(\Delta \theta) \). For small \( \Delta t \), \( \cos(\Delta \theta) \sim 1 - \frac{1}{2}(\Delta \theta)^2 \) and \( \cos^2(\Delta \theta) \sim 1 - (\Delta \theta)^2 \). Using Eq. (10b), we have \( (\Delta \theta)^2 = 2k\Delta t \) and

\[ \langle v_{\parallel}^2(n\Delta t) \rangle = v_{\parallel_0}^2 (1 - \gamma \Delta t)^{2n}(1 - k\Delta t)^{2(n-1)} \]

\[ + g \left[ (1 - \gamma \Delta t)^{2(n-1)}(1 - k\Delta t)^{2(n-1)} + \ldots + 1 \right]. \]

(14)

Taking the limit \( \Delta t \rightarrow 0 \), with \( n = \frac{T}{\Delta t} \), we find:

\[ \langle v_{\parallel}^2(T) \rangle = \frac{g}{2(\gamma + k)} + \left( v_{\parallel_0}^2 - \frac{g}{2(\gamma + k)} \right) \exp[-2(\gamma + k)T]. \]

(15)

If we assume an initial condition equal to the asymptotic solution, \( v_{\parallel_0}^2 = \frac{g}{2(\gamma + k)} \), we get:

\[ \langle v_{\parallel_{st}}^2 \rangle = \frac{g}{2(\gamma + k)}. \]

(16)

The relaxation time \( R \), defined as:

\[ R = (\gamma + k)^{-1}, \]

(17)

determines the rate at which the average squared speed approaches its asymptotic value. To compare with numerical solutions, we estimate the squared speed from the mean velocity over finite time intervals \( \varepsilon \), that is, \( \langle v_{\parallel}^2(T) \rangle \approx \frac{\langle [\hat{v}(T+\varepsilon) - \hat{v}(T)]^2 \rangle}{\varepsilon^2} \) which, for small \( \varepsilon \) decomposes into:

\[ \frac{\langle [\hat{v}(T+\varepsilon) - \hat{v}(T)]^2 \rangle}{\varepsilon^2} = \langle v_{\parallel}^2 \rangle + \frac{\langle r_{\parallel}(T+\varepsilon) - r_{\parallel}(T) \rangle^2}{\varepsilon^2} \]

(18).

Figure 3 presents \( \frac{\langle [\hat{v}(T+\varepsilon) - \hat{v}(T)]^2 \rangle}{\varepsilon^2} - \frac{g}{2(\gamma + k)} \) as a function of time, for initial conditions with \( v_{\parallel_0} = 10^3 \) and for different values of \( k \). The symbols correspond to numerically calculated trajectories. The solid line is the analytical prediction, given by subtracting Eq.(16) from Eq.(15). Notice that

\[ \lim_{T \rightarrow \infty} \left( \frac{\langle [\hat{v}(T+\varepsilon) - \hat{v}(T)]^2 \rangle}{\varepsilon^2} - \frac{g}{2(\gamma + k)} \right) = \frac{2kq}{\varepsilon} \]

as predicted.
Figure 3. Semi-log plots of \( \frac{(\mathbf{r}(T + \varepsilon) - \mathbf{r}(T))^2}{\varepsilon^2} \) versus \( T \), for \( q = 0.1, g = 10, \gamma = 1 \), and \( k \) as indicated. \( R \) depends on \( k \) according to Eq. (17). Symbols correspond to estimates obtained from numerical integration of 10 replicas. Solid lines correspond to the analytical solutions obtained from Eq. (18).

4.2 Analytical forms for the Mean Square Displacement (MSD)

We obtain the mean squared displacement by first calculating the displacement in each time interval \( \Delta t \), from \( T = 0 \) to \( T = n \Delta t \), then summing over the displacements, taking the square of this expression, and finally averaging different trajectories, which is equivalent to the average over noise terms, since we consider the stationary solution. The Supplementary Materials Online provide details on these calculations.

After \( n \) iterations (\( n > 0 \)) the particle’s displacement:

\[
\mathbf{r}(n\Delta t) - \mathbf{r}(0) = v_0 \Delta t \left[ \hat{p}_0 + \Theta(n - 1) \sum_{j=0}^{n-1} (1 - \gamma \Delta t)^{n-j-1} \prod_{m=0}^{n-j-2} [\hat{p}_m \cdot \hat{p}_{m+1}] \hat{p}_{n-j-1} \right] \\
+ \Delta t \Theta(n - 2) \sum_{j=0}^{n-2} \int_{j\Delta t}^{(j+1)\Delta t} ds \xi_\parallel(s) \sum_{i=0}^{n-j-2} (1 - \gamma \Delta t)^{n-i-j-2} \prod_{m=j}^{n-i-2} [\hat{p}_m \cdot \hat{p}_{m+1}] \hat{p}_{n-i-1} \\
+ \sum_{j=0}^{n-1} \int_{j\Delta t}^{(j+1)\Delta t} ds \xi_\perp(s) [(j + 1)\Delta t - s] \hat{p}_j + \sum_{j=0}^{n-1} \int_{j\Delta t}^{(j+1)\Delta t} ds \xi_\perp(s) \hat{n}_j. \tag{19}
\]

Where \( \Theta(n - 2) = 0 \) if \( n < 2 \) and \( \Theta(n - 2) = 1 \) otherwise. Squaring Eq. (19) and averaging over noise, we get:

\[
MSD = \langle (\mathbf{r}(T + \Delta T) - \mathbf{r}(T))^2 \rangle = \frac{g}{(\gamma + 2k)(\gamma + k)} [\Delta T - \frac{1}{\gamma + 2k} (1 - e^{-(\gamma + 2k)\Delta T})] + 2qk\Delta T. \tag{20}
\]
The Fürth equation is the MSD for the Langevin equation:

\[
MSD_{\text{Fürth}} = 2D \left[ \Delta T - P \left( 1 - e^{-\Delta T/P} \right) \right].
\]  

(21)

We can rewrite Eq.(20) as a modified Fürth equation:

\[
MSD_{\text{ModifiedFürth}} = 2D \left[ \frac{\Delta T}{1 - S} - P \left( 1 - e^{-\Delta T/P} \right) \right],
\]  

(22)

as proposed by Thomas et al. [9], where we identify:

\[
D = \frac{g}{2(y + 2k)(y + k)},
\]  

(23a)

\[
P = \frac{1}{y + 2k},
\]  

(23b)

and

\[
S = \frac{2qk(y + 2k)(y + k)}{g + 2qk(y + 2k)(y + k)}.
\]  

(23c)

Active matter models considering noise added to displacement yield MSD curves that are isomorphic to Eq.(22) [11]. In these models, when isotropic noise added to displacement is assumed, it is necessary to avoid a dynamical equation that considers velocity derivatives.

Unlike the classical Ornstein-Uhlenbeck process, our model yield different values for persistence time \( P \) (Eq. 23b) as compared to relaxation time \( R \), defined in Eq. (17). \( S \) and \( D \) depend on both parameters as given in Eqs.(23).

When \( k = 0 \), our model results in the one-dimensional Fürth equations for both MSD and \( \langle v_\parallel^2(T) \rangle \) relaxation, with \( S = 0 \), \( P = \frac{1}{y^*} \), and \( D = \frac{g}{2y^*} \). When \( k > 0 \), but \( q = 0 \), our model’s MSD curve is the same as that of the Fürth equation, but their \( \langle v_\parallel^2 \rangle \) relaxation time \( (R) \) differ. For \( k > 0 \) and \( q > 0 \), our model’s MSD and \( \langle v_\parallel^2 \rangle \) relaxation differ from those of the Fürth equation.

As observed in Ref. [9], for small \( \Delta T \), Eq. (22) yields:

\[
\lim_{\Delta T \to 0} MSD_{\text{ModifiedFürth}} \sim \frac{2SD}{1 - S} \Delta T,
\]  

(24)

indicating that at short-time intervals, the particle’s motion is diffusive with an effective diffusion constant \( D_{\text{fast}} = \frac{SD}{1 - S} = qk \). For long-time intervals, we find:

\[
\lim_{\Delta T \to \infty} MSD_{\text{ModifiedFürth}} \sim \frac{2D}{1 - S} \Delta T,
\]  

(25)

indicating a long-time diffusive behavior, with an effective diffusion constant \( D_{\text{slow}} = \frac{D}{1 - S} \).

Together, these diffusion constants give physical meaning to the parameter \( S \): \( S = \frac{D_{\text{fast}}}{D_{\text{slow}}} \).

Following Ref. [9], we call \( S \) the excess diffusion coefficient. The \( MSD_{\text{ModifiedFürth}} \) in Eq. (22) has three regimes: a fast-diffusive regime for short time intervals \( (\Delta T < SP) \), a ballistic-like, intermediate-time-interval regime \( (SP < \Delta T < P) \), and a slow diffusive, long-time-interval regime \( (\Delta T > P) \). Fortuna and collaborators [10] found in their numerical simulations that \( S = \)
\( \frac{D_{\text{fast}}}{D + D_{\text{fast}}} \), while we show that this behavior is an exact consequence of the definition of \( D_{\text{fast}} \) and Eqs. (23).

Below, following Ref. [9], we use \( \sqrt{\frac{2DP}{1-S}} \) as a length scale and \( P \) as a time scale to rewrite Eq. (23) as:

\[
\langle |\Delta \rho|^2 \rangle = \Delta \tau - (1 - S)(1 - e^{-\Delta \tau}),
\]

where \( \Delta \tau = \frac{\Delta T}{P} \) and \( \langle |\Delta \rho|^2 \rangle = \left(\frac{\text{MSD}}{1-S}\right) \) are non-dimensional quantities. The link of these scales with the original model parameters are given by Eqs. (17) and (23). Eq.(26) provides supports the choices we made for the numerical solution, discussed in Section 3. Figure 4 presents plots for \( \langle |\Delta \rho|^2 \rangle \) versus \( \Delta \tau \) for different values of \( S \): the larger \( S \), the larger the value of \( \Delta \tau \) for which is the short-time behavior is diffusive.

![Log-log plot of \( \langle |\Delta \rho|^2 \rangle \) versus \( \Delta \tau \) for \( q = 0.1, g = 10, \gamma = 1 \), and four values of \( S \). Solid lines correspond to Eq. (22), while the dots are averages over 10 numerical trajectories. Error bars for the simulations are not shown because they are smaller than the dot size.](image)

3.3 Analytical forms for the Velocity auto-correlation functions

The diffusive behavior of the position at short-time intervals for \( S > 0 \) implies that the instantaneous velocity diverges. The instantaneous velocity in natural units, \( \tilde{u}(\tau) \), is:

\[
\tilde{u}(\tau) = \lim_{\delta \to 0} \frac{\tilde{\rho}(\tau + \delta) - \tilde{\rho}(\tau)}{\delta} = \lim_{\delta \to 0} \frac{\Delta \tilde{\rho}_\parallel + \Delta \tilde{\rho}_\perp}{\delta} = u(t) \tilde{\rho}(t) + \lim_{\delta \to 0} \frac{\Delta \rho_\perp}{\delta} \tilde{n}(t),
\]

(27)
where $\Delta \vec{\rho}_\parallel$ and $\Delta \vec{\rho}_\perp$ are non-dimensional displacements respectively parallel and orthogonal to the polarization. When $k > 0$ and $q > 0$, displacement in the orthogonal direction, $\lim_{\delta \to 0} \frac{\Delta \vec{\rho}_\perp}{\delta}$ goes to infinity, since $\Delta \vec{\rho}_\perp$ follows a Wiener process, while $u_\parallel(\tau)$ is well-defined. An experiment cannot always measure $\Delta \vec{\rho}_\parallel$ and $\Delta \vec{\rho}_\perp$ separately. In what follows we define two different correlation functions, where the finite time precision is explicitly taken into account.

To analyze the divergence of the instantaneous speed $|\vec{u}(\tau)|$, we define to mean velocity over a finite time interval $\delta$, as:

$$\bar{u}(\tau, \delta) = \frac{\vec{\rho}(\tau + \delta) - \vec{\rho}(\tau)}{\delta}.$$  \hspace{1cm} (28)

Figure 5 shows $\left\langle |\vec{u}(\tau, \delta)| \right\rangle$ vs $\delta$ for numerical calculations: the mean speed $\left\langle |\vec{u}(\tau, \delta)| \right\rangle$ diverges as $\delta \to 0$.

![Figure 5](image.png)

*Figure 5. Log-log plot, with time and length rescaled by $P$ and $\sqrt{2DP}$, of the average mean speed $\left\langle |\vec{u}(\tau, \delta)| \right\rangle$, obtained by averaging 10 replicas of numerical trajectories, as a function of the time interval $\delta$, for $q = 0.1$, $g = 10$, $\gamma = 1$, and four values of $S$ (corresponding to four values of $k$). Note that $\left\langle |\vec{u}(\tau, \delta)| \right\rangle$ diverges as $\delta \to 0$.\*
4.3.1 Analytical forms for the Langevin velocity autocorrelation function: VACF

We first observe that:

\[
\begin{aligned}
\left( v_i(T) \ddot{p}(T) + \lim_{\delta \to 0} \frac{\Delta r_\perp(T)}{\delta} \dddot{h}(T) \right) \cdot \left( v_i(T + \Delta T) \ddot{p}(T + \Delta T) + \lim_{\delta \to 0} \frac{\Delta r_\perp(T + \Delta T)}{\delta} \dddot{h}(T + \Delta T) \right) \\
= \langle v_i(T) \ddot{p}(T) \cdot v_i(T + \Delta T) \ddot{p}(T + \Delta T) \rangle, 
\end{aligned}
\]

(29)
because \( \Delta r_\perp(T) \) obeys a Wiener process.

We define VACF to be:

\[
VACF(\Delta T) = \langle v_i(T) \ddot{p}(T) \cdot v_i(T + \Delta T) \ddot{p}(T + \Delta T) \rangle 
\]

(30)
We partition the finite time interval \( \Delta T = n \Delta t \) with an infinite number \( n \) of infinitesimal time intervals \( \Delta t \) (such that \( \Delta T \) remains finite), sum over it and find (see supplementary materials online):

\[
VACF(\Delta T) = \langle v_{\text{esta}}^2(T) \rangle e^{-\gamma \Delta T} = \langle v_{\text{esta}}^2 \rangle e^{-\Delta T/P}.
\]

(31)
That is the expected result: As the asymptotic solution is stationary, \( VACF(\Delta T) \) is equal to half the second derivative of the MSD curve. Since this second derivative is the same for both Eqs. (21) (original Fürth MSD) and (22) (modified Fürth MSD), VACF results in the same function for both models. The result is an exponential decay with a decay constant given by \( P \) (and not \( R \)).

3.3.2 Mean velocity autocorrelation function \( \psi(\delta, \Delta t) \): Finite-precision measurements

Eq. (31) implies that in the stationary state \( \lim_{\Delta T \to 0} VACF(\Delta T) = \langle v_{\text{esta}}^2 \rangle \). Experiments and simulations often diverge from Eq. (31), due to two different effects, which we discuss below.

3.3.2.1 Instantaneous velocity is ill-defined for Wiener motion

The definition of instantaneous velocity (Eq. (27)), like the experimental and computational procedure for estimating \( \ddot{u} \) consists in measuring displacements for decreasing time intervals \( \delta \) and taking the ratio \( \frac{\Delta \rho_\perp(\delta)}{\delta} \). For a Wiener process, the displacement \( \Delta \rho_\perp(\delta) \) does not converge to 0 as \( \delta \to 0 \), so the estimated velocity diverges.

However, when \( \delta > S \), the measured particle displacement is in the intermediate-time interval regime, meaning that the particle movement is ballistic and \( u_\parallel \delta > \Delta \rho_\perp \). In this case, \( \ddot{u}(\tau) \approx u_\parallel(\tau) \ddot{h}(\tau) \) and estimating VACF using \( \ddot{u}(\tau) \) instead of \( u_\parallel(\tau) \ddot{h}(\tau) \) will agree with the prediction of Eq. (31).

On the other hand, when \( \delta < S \), the second term on the right-hand side of Eq. (27) dominates and the estimated value for velocity is \( \ddot{u}(\tau) \approx \frac{\Delta \rho_\perp(\tau)}{\delta} \ddot{h}(\tau) \), yielding an estimate of VACF that goes to zero for decreasing \( \Delta \tau \), since \( \Delta \rho_\perp \) follows a Wiener process.

Here, we define the mean velocity autocorrelation function (in non-dimensional quantities) as:

\[
\psi(\delta, \Delta \tau) = \langle \ddot{u}(\tau, \delta) \cdot \ddot{u}(\tau + \Delta \tau, \delta) \rangle,
\]

(32)
using Eq. (27). For infinite precision measurements we trivially find
ψ(δ, Δτ) = \frac{(1 - e^{-γδ})(1 - e^{-(γ+2k)δ})}{γ(γ+2k)δ^2} \langle u_{\text{lista}}^2 \rangle e^{-Δτ}.

(33)

For high precision measurements, small values of δ imply ψ(δ, Δτ) \sim \langle u_{\text{lista}}^2 \rangle e^{-Δτ}, that is, ψ(δ, Δτ) tends to VACF(Δτ). For finite precision measurements, however, ψ(δ, Δτ) decreases with decreasing Δτ, when Δτ < S, due to the poor estimate of \langle u_{\text{lista}}^2 \rangle. If we degrade the precision of our estimate of the mean velocity by truncating the estimate to a fixed number of decimal digits, we see that as ψ(δ, Δτ) decreases as Δτ decreases (Figure 6).

![Figure 6. Log-log plot, in natural units, of \psi(\delta, \Delta \tau) versus \Delta \tau for q = 0.1, g = 10, γ = 1, k = 0.04405 (S = 0.001), for δ = 0.001 and different precision for the calculation of the mean displacement. For lower precision, measurements of position or velocity ψ(\delta, \Delta \tau) decreases as Δτ decreases.](image)

3.3.2.2 Too short-time intervals Δτ.

Since δ is not infinitesimal, we must guarantee that Δτ > δ to prevent the time intervals [τ, τ + δ] and [τ + Δτ, τ + Δτ + δ] from overlapping. Since we use these intervals to estimate, respectively, \overline{u}(τ, δ) and \overline{u}(τ + Δτ, δ), when Δτ < δ the overlap of time intervals introduces a correlation between the displacements used to calculate these quantities. That happens even when the accuracy of measurement is high (Figure 7). For low precision measurements of displacement and Δτ < δ (not shown), as Δτ decreases ψ(δ, Δτ) may first decrease, then increase to reach \psi(δ, Δτ = 0) = \langle \overline{u}(τ, δ) \rangle^2, that is its maximum value.
Log-log plot, in natural units, of \( \psi(\delta, \Delta \tau) \) versus \( \Delta \tau \) for \( q = 0.1, g = 10, \gamma = 1, k = 0.04405 \) (\( S = 0.001 \)), for different values of \( \delta > \Delta \tau \). Solid lines correspond to analytical calculations using Eq. (33), and the dots correspond to numerical solutions averaged over 10 trajectories. \( \delta \) values indicated in the figure.

5 Discussion and conclusions

Migrating cells are anisotropic and their speed is persistent. In its original form, Ornstein-Uhlenbeck processes stem from isotropic Langevin models with well-defined instantaneous velocities. Active Matter models are anisotropic. In models where the cell speed follows some dynamics in one direction and cell displacement is ruled by a Wiener process, instantaneous velocity is ill-defined. Not surprisingly, Active Matter models have generally avoided dynamical equations for velocity, assuming overdamped particles. However, both Ornstein-Uhlenbeck and Active Matter models apply to migrating cells on flat surfaces. In some limit, they must yield the same observable results.

Here we proposed and solved an Anisotropic Ornstein-Uhlenbeck process that has a well-defined instantaneous velocity in the instantaneous direction of an internal polarization, taken as a further degree of freedom. This model considers a Langevin equation for velocity in the polarization direction and a Wiener process for displacements in the perpendicular direction. The main results are i) analytical calculations, verified by numerical solutions for the empirical \( MSD \) and \( VACF \) curves obtained for experiments and CompuCell3D simulations, ii) \( MSD \) curves show a diffusive regime for short-time intervals as found in experiments and simulations, iii) procedures that take into account finite precision for measuring speed and velocity, and iv) the definition of time and length scales (as in Ref. [9]), that enables comparison of movement statistics between experiments and between experiments and simulations.
In previous works, Eq.(22) was used to fit 12 different sets of migrating cell experiments, from 5 different laboratories [9], as well as CompuCell3D simulations of migrating cells [10], and the observed behaviors for MSD, speed, and velocity autocorrelation functions agree with our analytical calculations.

This statistical analysis applies to any particles moving under an Anisotropic Ornstein-Uhlenbeck process and therefore are useful for quantification both of Active Matter and biological models and experiments.

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Supplementary Materials for
Exact solution for the anisotropic Ornstein-Uhlenbeck Process

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Analytic solutions

Velocity in the instantaneous polarization direction

Starting at $t = 0$ with speed $v_{\parallel 0}$ (we assume speed can be negative) in the direction of the cell polarization $\vec{p}_{0}$, using Eq.(1) in the main text, we can write the velocity in the direction of the cell polarization at the first infinitesimal time interval $\Delta t$ as

$$v_{\parallel}(\Delta t)\vec{p}(\Delta t) = \left[ (1 - \gamma\Delta t) v_{\parallel 0} + \int_{0}^{\Delta t} \xi_{\parallel}(t)\, dt \right] (\vec{p}(0) \cdot \vec{p}(\Delta t)) \, \vec{p}(\Delta t). \tag{1}$$

By continuing iterations, the velocity at time $T = n \Delta t$ is

$$v_{\parallel}(n\Delta t)\vec{p}(n\Delta t) =$$

$$v_{\parallel 0}(1 - \gamma\Delta t)^n \left[ \vec{p}_{0}(\vec{p}(\Delta t),\vec{p}(2\Delta t)) \ldots [\vec{p}(n-1)\Delta t,\vec{p}(n\Delta t)] \vec{p}(n\Delta t) \right.$$

$$+ \int_{0}^{\Delta t} ds \xi_{\parallel}(s) (1 - \gamma\Delta t)^{n-1} \left[ \vec{p}_{0}(\vec{p}(\Delta t)) \ldots [\vec{p}(n-1)\Delta t,\vec{p}(n\Delta t)] \vec{p}(n\Delta t) \right.$$\n
$$+ \int_{\Delta t}^{2\Delta t} ds \xi_{\parallel}(s) (1 - \gamma\Delta t)^{n-2} \left[ \vec{p}(\Delta t),\vec{p}(2\Delta t) \ldots [\vec{p}(n-1)\Delta t,\vec{p}(n\Delta t)] \vec{p}(n\Delta t) \right.$$\n
$$+ \ldots$$\n
$$+ \int_{(n-1)\Delta t}^{n\Delta t} ds \xi_{\parallel}(s) [\vec{p}(n-1)\Delta t,\vec{p}(n\Delta t)] \vec{p}(n\Delta t). \tag{2}$$

Observe that at each time step the realignment of the polarization axis implies that only the component of the velocity in the direction of the new polarization is partially conserved.

We will calculate each of the terms in the above in separate. But first we need to deal with the scalar products between cell polarization at different time instants.

Cell polarization vectors are unitary. Hence $\vec{p}_{i} \cdot \vec{p}_{j} = \cos(\theta_{i} - \theta_{j})$, where $\theta_{j}$ is the angle between the direction of $\vec{p}_{j}$ and the abscissas axis. We define $\Delta \theta_{i,j} = \theta_{i} - \theta_{j}$.
Here we assume that the change in polarization direction is due to the noise perpendicular to the instantaneous polarization direction. This noise is also responsible for displacements in the perpendicular direction. Hence, for a small time interval $\Delta t$, we assume that the change in direction is a Wiener process, such that $(\langle \Delta \theta_{i,i+1} \rangle_{\parallel}^2)_{\parallel} = k \Delta t$. Observe also that $\xi_1$ and $\beta_{\perp}$ are not correlated, hence the average over the two noises decouples.

We are interested in the $\Delta t \to 0$ limit, which means that the scalar product between consecutive polarization vectors may be taken up to first order in $\Delta t$. In this case the following approximations apply:

$$\cos \Delta \theta_{i,i+1} = 1 - \frac{(\Delta \theta_{i,i+1})^2}{2}$$

$$\cos^2 \Delta \theta_{i,i+1} = 1 - (\Delta \theta_{i,i+1})^2$$

Also, for any pair $(i,j)$, with $i < j$ we have

$$\Delta \theta_{i,j} = \Delta \theta_{i,i+1} + \Delta \theta_{i+1,i+2} + \ldots + \Delta \theta_{j-1,j}$$

and hence

$$\langle \cos \Delta \theta_{i,j} \rangle_{\parallel} \approx \langle \cos \Delta \theta_{i,i+1} \rangle_{\parallel} \langle \cos (\Delta \theta_{i+1,i+2} + \Delta \theta_{i+2,i+3} + \ldots + \Delta \theta_{j-1,j}) \rangle_{\parallel}$$

$$- \langle \sin \Delta \theta_{i,i+1} \rangle_{\parallel} \langle \sin (\Delta \theta_{i+1,i+2} + \Delta \theta_{i+2,i+3} + \ldots + \Delta \theta_{j-1,j}) \rangle_{\parallel}$$

$$\approx \langle \cos \Delta \theta_{i,i+1} \rangle_{\parallel} \langle \cos (\Delta \theta_{i+1,i+2} + \Delta \theta_{i+2,i+3} + \ldots + \Delta \theta_{j-1,j}) \rangle_{\parallel}$$

$$\approx \langle 1 - k \Delta t \rangle_{\parallel}^{j-i}$$

Also, in the limit $\Delta t \to \infty$,

$$\langle \cos^2 \Delta \theta_{i,j} \rangle_{\parallel} \approx (1 - k \Delta t)^{2(j-i)}$$.

Using this approximation we can calculate $< v_{\parallel} >$. Since the terms containing noise averages vanish, we have

$$< v_{\parallel} > = v_{\parallel 0} (1 - \gamma \Delta t)^n (1 - k \Delta t)^n,$$

which, using $T = n \Delta t$, in the limit $n \to \infty$, it can be written as

$$< v_{\parallel} > = v_{\parallel 0} \exp \left[ - (\gamma + k) T \right].$$

So, for $T \to \infty$,

$$< v_{\parallel} > = 0.$$

We calculate now the square of the velocity and take the average over the noise:

$$\langle v_{\parallel}^2(n \Delta t) \rangle = v_{\parallel 0}^2 (1 - \gamma \Delta t)^{2n} \langle \langle \bar{p} \cdot \bar{p} (\Delta t) \rangle^2 \langle \bar{p} (\Delta t) \rangle^2 \langle \bar{p} (2 \Delta t) \rangle^2 \ldots \langle \bar{p} (n - 1 \Delta t) \rangle \langle \bar{p} (n \Delta t) \rangle^2 \rangle$$

$$+ g \int_0^{\Delta t} ds \langle (1 - \gamma \Delta t)^{2(n-1)} \langle \bar{p} \cdot \bar{p} (\Delta t) \rangle^2 \langle \bar{p} (n - 1 \Delta t) \rangle \rangle$$

$$+ g \int_{\Delta t}^{2 \Delta t} ds \langle (1 - \gamma \Delta t)^{2(n-2)} \langle \bar{p} (\Delta t) \rangle \langle \bar{p} (2 \Delta t) \rangle^2 \ldots \langle \bar{p} (n - 1 \Delta t) \rangle \rangle$$

$$+ \ldots$$

$$+ g \int_{(n-1) \Delta t}^{n \Delta t} ds \langle \bar{p} (n - 1 \Delta t) \rangle \langle \bar{p} (n \Delta t) \rangle^2 \rangle,$$

where we have used that

$$\langle \xi_1(t) \xi_2(t') \rangle = g \delta(t - t')$$

and that crossed terms where the integral limits are not the same are zero.

Also, $\langle \bar{p} (j - 1 \Delta t) \rangle \langle \bar{p} (j \Delta t) \rangle = \cos (\dot{\theta}(j - 1 \Delta t) - \dot{\theta}(j \Delta t)) = \cos (\Delta \theta)$, since polarization are unitary vectors. Assuming
small $\Delta t$, $\cos(\Delta \theta) \sim 1 - \frac{1}{2} (\Delta \theta)^2$ and $\cos^2(\Delta \theta) \sim 1 - (\Delta \theta)^2$. Here we assume that the change in polarization direction is due to the Wiener process perpendicular to the polarization axis, that is, averaging over the perpendicular noise, at each time interval of duration $\Delta t$, $\langle (\Delta \theta)^2 \rangle = 2k\Delta \theta$. Using this result in Eq. (11) and solving the integrals we have

$$
\langle v_{\parallel}^2(n \Delta t) \rangle = v_0^2 (1 - \gamma \Delta t)^{2n} (1 - k \Delta t)^{2n} + g \left[ (1 - \gamma \Delta t)^{2n-1} (1 - k \Delta t)^{2(n-1)} + \ldots + 1 \right].
$$

(13)

Using that $T = n \Delta t$, and taking the limit for $\Delta t \to 0$ and $n \to \infty$ such that $T$ is finite, we arrive at

$$
\langle v_{\parallel}^2(T) \rangle = \frac{g}{2(\gamma + k)} + \left( v_0^2 - \frac{g}{2(\gamma + k)} \right) \exp[-2(\gamma + k) T].
$$

(14)

The transient is avoided by making $v_0^2 = \frac{g}{2(\gamma + k)}$ from the start.

**Mean square displacement**

Mean square displacement is obtained by first calculating the displacement in each time interval $\Delta t$, from $t = 0$ to $t = n \Delta t = \Delta T$, then summing over time, taking the square of this expression and finally averaging over noise. In this section we will shorten notation, using $\vec{p}(n \Delta t) = \vec{p}_n$.

**Displacement in each time interval**

We assume that for $0 \leq t \leq \Delta t$ the cell polarization $\vec{p}_0$ remains constant. We can write

$$
\vec{r}(\Delta t) - \vec{r}(0) = v_{\parallel 0} \Delta t \vec{p}_0 + \int_0^{\Delta t} ds (\Delta t - s) \xi_\parallel(s) \vec{p}_0 + \int_0^{\Delta t} ds \xi_\perp(s) \vec{n}_0
$$

(15)

At $t = \Delta t$, the cell polarization suffers a turn, going from $\vec{p}_0$ to $\vec{p}_1 = \vec{p}(\Delta t)$. For the following interval, the initial value for the velocity is taken as $v_{\parallel}(\Delta t) \vec{p}_0$. For the time interval $\Delta t \leq \Delta t$ the displacement is

$$
\vec{r}(2\Delta t) - \vec{r}(\Delta t) = \Delta t (v_{\parallel}(\Delta t) \vec{p}_1) + \int_{\Delta t}^{2\Delta t} ds (\Delta t - s) \xi_\parallel(s) \vec{p}_1 + \int_{\Delta t}^{2\Delta t} ds \xi_\perp(s) \vec{n}_1,
$$

(16)

where we can use that

$$
v_{\parallel}(\Delta t) = (1 - \gamma \Delta t) v_{\parallel 0} \vec{p}_0 + \int_0^{\Delta t} ds \xi_\parallel(s) \vec{n}_0
$$

(17)

and obtain

$$
\vec{r}(2\Delta t) - \vec{r}(\Delta t) = (1 - \gamma \Delta t) \Delta t v_{\parallel 0} (\vec{p}_0, \vec{p}_1) \vec{p}_1 + \Delta t \int_0^{\Delta t} ds \xi_\parallel(s) (\vec{p}_0, \vec{p}_1) \vec{n}_1 + \int_{\Delta t}^{2\Delta t} ds (\Delta t - s) \xi_\parallel(s) \vec{n}_1 + \int_{\Delta t}^{2\Delta t} ds \xi_\perp(s) \vec{n}_1.
$$

(18)

Analogously,

$$
\vec{r}(3\Delta t) - \vec{r}(2\Delta t) = (1 - \gamma \Delta t)^2 \Delta t v_{\parallel 0} (\vec{p}_0, \vec{p}_1) (\vec{p}_1, \vec{p}_2) \vec{p}_2 + \Delta t \int_0^{\Delta t} ds \xi_\parallel(s) (1 - \gamma \Delta t) (\vec{p}_0, \vec{p}_1) (\vec{p}_1, \vec{p}_2) \vec{p}_2 + \Delta t \int_{\Delta t}^{2\Delta t} ds \xi_\parallel(s) (\vec{p}_1, \vec{p}_2) \vec{p}_2
$$

(19)
\[ + \int_{2\Delta t}^{3\Delta t} ds (\Delta t - s) \xi_\parallel(s) \vec{p}_2 \]
\[ + \int_{2\Delta t}^{3\Delta t} ds \xi_\perp(s) \vec{n}_2. \] (19)

and also
\[
\vec{r}(4\Delta t) - \vec{r}(3\Delta t) = (1 - \gamma \Delta t)^3 \Delta t \nu_{00} (\vec{p}_0, \vec{p}_2) (\vec{p}_1, \vec{p}_2) (\vec{p}_2, \vec{p}_3) \vec{p}_3 \\
+ \Delta t \int_{0}^{\Delta t} ds \xi_\parallel(s) (1 - \gamma \Delta t)^2 (\vec{p}_0, \vec{p}_1) (\vec{p}_1, \vec{p}_2) (\vec{p}_2, \vec{p}_3) \vec{p}_3 \\
+ \Delta t \int_{\Delta t}^{2\Delta t} ds \xi_\parallel(s) (1 - \gamma \Delta t) (\vec{p}_1, \vec{p}_2) (\vec{p}_2, \vec{p}_3) \vec{p}_3 \\
+ \Delta t \int_{2\Delta t}^{3\Delta t} ds \xi_\parallel(s) (\vec{p}_2, \vec{p}_3) \vec{p}_3 \\
+ \int_{3\Delta t}^{4\Delta t} ds (\Delta t - s) \xi_\parallel(s) \vec{p}_3 \\
+ \int_{3\Delta t}^{4\Delta t} ds \xi_\perp(s) \vec{n}_3. \] (20)

Now we can infer the general rule and hence
\[
\vec{r}(n\Delta t) - \vec{r}((n-1)\Delta t) = (1 - \gamma \Delta t)^{n-1} \Delta t \nu_{00} (\vec{p}_0, \vec{p}_1) (\vec{p}_1, \vec{p}_2) \ldots (\vec{p}_{n-2}, \vec{p}_{n-1}) \vec{p}_{n-1} \\
+ \Delta t \int_{0}^{\Delta t} ds \xi_\parallel(s) (1 - \gamma \Delta t)^{n-2} (\vec{p}_0, \vec{p}_1) (\vec{p}_1, \vec{p}_2) \ldots (\vec{p}_{n-2}, \vec{p}_{n-1}) \vec{p}_{n-1} \\
+ \Delta t \int_{\Delta t}^{2\Delta t} ds \xi_\parallel(s) (1 - \gamma \Delta t)^{n-3} (\vec{p}_1, \vec{p}_2) (\vec{p}_2, \vec{p}_3) \ldots (\vec{p}_{n-2}, \vec{p}_{n-1}) \vec{p}_{n-1} \\
\ldots \\
+ \Delta t \int_{(n-2)\Delta t}^{(n-1)\Delta t} ds \xi_\parallel(s) (\vec{p}_{n-2}, \vec{p}_{n-1}) \vec{p}_{n-1} \\
+ \int_{(n-1)\Delta t}^{n\Delta t} ds (\Delta t - s) \xi_\parallel(s) \vec{p}_{n-1} \\
+ \int_{(n-1)\Delta t}^{n\Delta t} ds \xi_\perp(s) \vec{n}_{n-1}. \] (21)

To find the total displacement, from \( t = 0 \) to \( t = n\Delta t \) we sum over the individual time steps. We get
\[
\vec{r}(n\Delta t) - \vec{r}(0) = \nu_{00} \Delta t \left[ (1 - \gamma \Delta t)^{n-1} (\vec{p}_0, \vec{p}_1) (\vec{p}_1, \vec{p}_2) \ldots (\vec{p}_{n-2}, \vec{p}_{n-1}) \vec{p}_{n-1} \\
+ (1 - \gamma \Delta t)^{n-2} (\vec{p}_0, \vec{p}_1) (\vec{p}_1, \vec{p}_2) \ldots (\vec{p}_{n-3}, \vec{p}_{n-2}) \vec{p}_{n-2} \\
+ \ldots \\
+ \vec{p}_0 \right] \\
+ \Delta t \int_{0}^{\Delta t} ds \xi_\parallel(s) \left[ (1 - \gamma \Delta t)^{n-2} (\vec{p}_0, \vec{p}_1) (\vec{p}_1, \vec{p}_2) \ldots (\vec{p}_{n-2}, \vec{p}_{n-1}) \vec{p}_{n-1} \\
+ (1 - \gamma \Delta t)^{n-3} (\vec{p}_0, \vec{p}_1) (\vec{p}_1, \vec{p}_2) \ldots (\vec{p}_{n-3}, \vec{p}_{n-2}) \vec{p}_{n-2} \\
+ \ldots \\
+ (\vec{p}_0, \vec{p}_1) \vec{p}_1 \right] \\
+ \ldots \\
+ \int_{(n-1)\Delta t}^{n\Delta t} ds \xi_\parallel(s) \left[ (1 - \gamma \Delta t)^{n-2} (\vec{p}_0, \vec{p}_1) (\vec{p}_1, \vec{p}_2) \ldots (\vec{p}_{n-2}, \vec{p}_{n-1}) \vec{p}_{n-1} \\
+ (1 - \gamma \Delta t)^{n-3} (\vec{p}_0, \vec{p}_1) (\vec{p}_1, \vec{p}_2) \ldots (\vec{p}_{n-3}, \vec{p}_{n-2}) \vec{p}_{n-2} \\
+ \ldots \\
+ (\vec{p}_0, \vec{p}_1) \vec{p}_1 \right]. \]
\[ + \int_{0}^{\Delta t} ds \xi_{\parallel}(s) (\Delta t - s) \tilde{p}_{0} + \Delta t \int_{\Delta t}^{2\Delta t} ds \xi_{\parallel}(s) \left[ (1 - \gamma \Delta t)^{n-3} \left( \tilde{p}_{1} \tilde{p}_{2} \tilde{p}_{3} \cdots \tilde{p}_{n-2} \tilde{p}_{n-1} \right) \tilde{p}_{n-1} \right. \\
+ (1 - \gamma \Delta t)^{n-4} \left( \tilde{p}_{1} \tilde{p}_{2} \tilde{p}_{3} \cdots \tilde{p}_{n-3} \tilde{p}_{n-2} \right) \tilde{p}_{n-2} \\
+ \cdots \\
+ \left. (\tilde{p}_{1} \tilde{p}_{2} \tilde{p}_{3}) \tilde{p}_{3} \right] + \int_{\Delta t}^{2\Delta t} ds \xi_{\parallel}(s) (\Delta t_{2} - s) \tilde{p}_{1} + \cdots + \Delta t \int_{(n-1)\Delta t}^{(n-2)\Delta t} ds \xi_{\parallel}(s) (\tilde{p}_{n-2} \tilde{p}_{n-1}) \tilde{p}_{n-1} + \\
\int_{(n-2)\Delta t}^{(n-1)\Delta t} ds \xi_{\parallel}(s) (\Delta t_{n-1} - s) \tilde{p}_{n-2} + \\
\int_{(n-1)\Delta t}^{n\Delta t} ds \xi_{\parallel}(s) (\Delta t_{n} - s) \tilde{p}_{n-1} + \\
\int_{0}^{n\Delta t} ds \xi_{\perp}(s) \tilde{n}_{0} + \cdots + \int_{(n-1)\Delta t}^{n\Delta t} ds \xi_{\perp}(s) \tilde{n}_{n-1} \right] \tag{22} \]

**Square displacement and average over noises**

To obtain the MSD we must square Eq. (22) and then average the noises. In this process, the square of each term is added to crossed terms. Some of the crossed terms vanish due to the noise average: (i) any crossed term containing the term that depends on \( \nu_{0} \); (ii) the crossing of terms integrated in different time intervals; and (iii) terms crossing \( \xi_{\parallel}(s) \) and \( \beta_{\perp}(s) \). We may define the following quantities:

\[ J^{2} = \nu_{0}^{2} (\Delta t)^{2} \left\langle \left( 1 - \gamma \Delta t \right)^{n-1} \left( \tilde{p}_{0} \tilde{p}_{1} \tilde{p}_{2} \cdots \tilde{p}_{n-2} \tilde{p}_{n-1} \right) \tilde{p}_{n-1} \right. \\
+ (1 - \gamma \Delta t)^{n-2} \left( \tilde{p}_{0} \tilde{p}_{1} \tilde{p}_{2} \cdots \tilde{p}_{n-3} \tilde{p}_{n-2} \right) \tilde{p}_{n-2} + \cdots \\
+ (1 - \gamma \Delta t) \left( \tilde{p}_{0} \tilde{p}_{1} \tilde{p}_{2} \right) \left( \tilde{p}_{1} + \tilde{p}_{0} \right)^{2} \left\rangle \right\rangle \xi_{\parallel}, \beta_{\perp}, \tag{23} \]

where \( \langle \rangle \) stands for the average over the noise in the polarization direction, \( \xi_{\parallel} \), and in the direction perpendicular to it, \( \xi_{\perp} \), respectively.

Also,

\[ J^{2}(k; \Delta t) = \left\langle \left( \Delta t \int_{(k-1)\Delta t}^{k\Delta t} ds \xi_{\parallel}(s) \left[ (1 - \gamma \Delta t)^{n-k-1} \left( \tilde{p}_{k-1} \tilde{p}_{k} \tilde{p}_{k+1} \cdots \tilde{p}_{n-2} \tilde{p}_{n-1} \right) \tilde{p}_{n-1} \right. \\
+ (1 - \gamma \Delta t)^{n-k-2} \left( \tilde{p}_{k-1} \tilde{p}_{k} \tilde{p}_{k+1} \cdots \tilde{p}_{n-3} \tilde{p}_{n-2} \right) \tilde{p}_{n-2} + \cdots + (\tilde{p}_{k-1} \tilde{p}_{k}) \tilde{p}_{k} \right] + \right. \\
+ \int_{(k-1)\Delta t}^{k\Delta t} ds \xi_{\parallel}(s) (k \Delta t - s) \tilde{p}_{k-1} \left\rangle \right\rangle \xi_{\parallel}, \beta_{\perp}, \tag{24} \]

and

\[ K^{2} = \left\langle \left[ \int_{0}^{n\Delta t} ds \xi_{\perp} \right]^{2} \right\rangle \xi_{\parallel}, \xi_{\perp} \tag{25} \]
Using the above definitions, we can write

\[
MSD = \lim_{\Delta t \to 0, n \to \infty} \left\langle |\vec{r}(n \Delta t) - \vec{r}(0)|^2 \right\rangle_{\xi_0} = \lim_{\Delta t \to 0, n \to \infty} I^2 + \sum_{k=1}^{n} J^2(k \Delta t) + K^2
\]  

(26)

\[I^2\] calculation

In Eq. (23) we write all scalar products as angles:

\[
I^2 = v^2_{00}(\Delta t)^2 \left( \left( 1 - \gamma \Delta t \right)^{n-1} \cos \Delta \theta_{0,1} \cos \Delta \theta_{1,2} \ldots \cos \Delta \theta_{n-2,n-1} \vec{p}_{n-1}
+ (1 - \gamma \Delta t)^{n-2} \cos \Delta \theta_{0,1} \cos \Delta \theta_{1,2} \ldots \cos \Delta \theta_{n-3,n-2} \vec{p}_{n-2}
+ \ldots
\right)_{\xi_0} \nonumber
\]

(27)

\[
I^2 = v^2_{00}(\Delta t)^2 \left( \left( \sum_{i=0}^{n-1} (1 - \gamma \Delta t)^i \prod_{m=1}^{i} \cos \Delta \theta_{m-1,m} \vec{p}_m \right)^2 \right)_{\xi_0} \nonumber
\]

(28)

The noise at different time intervals are not correlated. Hence, using Eq.(7),

\[
I^2 = v^2_{00}(\Delta t)^2 \left( \sum_{i=0}^{n-1} (1 - \gamma \Delta t)^i (1 - k \Delta t)^{2i} \right)_{\xi_0} \nonumber
\]

(29)

These are sums of geometric progressions. After some manipulations

\[
I^2 = \frac{v^2_{00}}{(\gamma + 2k)(\gamma + k)} \left[ \gamma + (\gamma + 2k) e^{-2(\gamma + k)\Delta T} - 2(\gamma + k) e^{-(\gamma + 2k)\Delta T} \right]
\]

(30)

Eq.(14) gives the asymptotic value of the square velocity \(v^2_{00}\) as \(\frac{g}{2(\gamma + k)}\). We take the initial velocity as this asymptotic value. \(I^2\) may then be written as

\[
I^2 = \frac{g}{2(\gamma + 2k)(\gamma + k)} \left[ \gamma + (\gamma + 2k) e^{-2(\gamma + k)\Delta T} - 2(\gamma + k) e^{-(\gamma + 2k)\Delta T} \right]
\]

(31)

Observe that when \(k = 0\),

\[
I^2(k = 0) = \frac{g}{2\gamma^4} \left[ \gamma + \gamma e^{-2(\gamma)\Delta T} - 2\gamma e^{-(\gamma)\Delta T} \right]
\]

\[
= \frac{g}{2\gamma^3} \left[ 1 - e^{-(\gamma)\Delta T} \right]^2
\]

(32)
**J^2 calculation**

In Eq. (24) we write all scalar products as cosines:

\[
J^2(k, \Delta t) = \left\langle \left\{ \Delta t \int_{(k-1)\Delta t}^{k\Delta t} ds \xi(s) \left[ (1 - \gamma \Delta t)^{n-k-1} \cos \Delta \theta_{k-1,k} \cos \Delta \theta_{k,k+1} \ldots \cos \Delta \theta_{n-2,n-1} \vec{p}_{n-1} \\
+ (1 - \gamma \Delta t)^{n-k-2} \cos \Delta \theta_{k-1,k} \cos \Delta \theta_{k,k+1} \ldots \cos \Delta \theta_{n-3,n-2} \vec{p}_{n-2} \\
+ \ldots \\
+ \cos \Delta \theta_{k-1,k} \vec{p}_k \right] \right\} \right\rangle_{\xi, \beta, \perp},
\]

(33)

\[
J^2(k, \Delta t) = \left\langle \left\{ \Delta t \int_{(k-1)\Delta t}^{k\Delta t} ds \xi(s) \left[ (1 - \gamma \Delta t)^{n-k-1} \cos \Delta \theta_{k-1,k} \cos \Delta \theta_{k,k+1} \ldots \cos \Delta \theta_{n-2,n-1} \vec{p}_{n-1} \\
+ (1 - \gamma \Delta t)^{n-k-2} \cos \Delta \theta_{k-1,k} \cos \Delta \theta_{k,k+1} \ldots \cos \Delta \theta_{n-3,n-2} \vec{p}_{n-2} \\
+ \ldots \\
+ \cos \Delta \theta_{k-1,k} \vec{p}_k \right] \right\} \right\rangle_{\xi, \beta, \perp}
+ 2\left\langle \int_{(k-1)\Delta t}^{k\Delta t} ds \xi(s) \left[ (1 - \gamma \Delta t)^{n-k-1} \cos \Delta \theta_{k-1,k} \cos \Delta \theta_{k,k+1} \ldots \cos \Delta \theta_{n-2,n-1} \vec{p}_{n-1} \\
+ (1 - \gamma \Delta t)^{n-k-2} \cos \Delta \theta_{k-1,k} \cos \Delta \theta_{k,k+1} \ldots \cos \Delta \theta_{n-3,n-2} \vec{p}_{n-2} \\
+ \ldots \\
+ \cos \Delta \theta_{k-1,k} \vec{p}_k \right] \right\} \right\rangle_{\xi, \beta, \perp}
\]

(34)

After long, tedious, and straightforward calculation, the sum over \( k \), in the limit of \( \Delta t \to 0 \), we have

\[
\sum_{i=0}^{n} J^2(i\Delta t) = \frac{g}{(\gamma + k)(\gamma + 2k)} \Delta T \\
+ \frac{g}{2(\gamma + k)^2} \left( 1 - e^{-2(\gamma + k)\Delta T} \right) \\
- \frac{2g}{\gamma (\gamma + 2k)^2} \left( 1 - e^{-(\gamma + 2k)\Delta T} \right)
\]

(35)

**K^2 calculation**

This calculation is rather straightforward.

\[
\langle \xi_\perp(s) \xi_\perp(s') \rangle = q \langle \beta_\perp(s) \beta_\perp(s') \rangle = 2qk \delta(s - s')
\]

(36)

The expression for \( K^2 \) is

\[
K^2 = 2qk\Delta T
\]

(37)

The estimate of \( q \) will be presented in what follows.
**MSD final expression**

Using Eqs. (31), (35), and (37) in Eq.(22) squared, we have

\[ MSD = \frac{g}{(\gamma + 2k)(\gamma + k)} \left[ \Delta T - \frac{1}{\gamma + 2k} \left( 1 - e^{-(\gamma + 2k)\Delta T} \right) \right] + 2qk\Delta T \] (38)

that may be rewritten as

\[ MSD = \frac{g}{(\gamma + 2k)^2(\gamma + k)} \left[ (1 + Q)(\gamma + 2k)\Delta T - \left( 1 - e^{-(\gamma + 2k)\Delta T} \right) \right] \] (39)

where

\[ Q = \frac{2qk}{g(\gamma + 2k)(\gamma + k)}. \] (40)

We can define the natural time unit \( P \) as

\[ P = \frac{1}{(\gamma + 2k)} \] (41)

and define \( \Delta \tau = \Delta T/P \) and \( S = \frac{Q}{1+Q} \). The MSD now is

\[ MSD = \frac{g}{(\gamma + 2k)^2(\gamma + k)(1-S)} \left[ \Delta \tau - (1-S)(1-e^{-\Delta \tau}) \right]. \] (42)

or

\[ \langle \langle \mathbf{\tilde{r}} \rangle \rangle^2 = \left[ \Delta \tau - (1-S)(1-e^{-\Delta \tau}) \right]. \] (43)

where

\[ \langle \langle \mathbf{\tilde{r}} \rangle \rangle^2 = \frac{MSD}{m^2(\gamma + 2k)^2(\gamma + k)(1-S)} \] (44)

We finally arrive at

\[ \langle \langle \mathbf{\tilde{r}} \rangle \rangle^2 = \left[ \Delta \tau - (1-S)(1-e^{-\Delta \tau}) \right]. \] (45)

which is exactly the modified Fürth Equation, proposed by Thomas and collaborators. Observe that if \( k = 0 \)

\[ MSD = \frac{g}{\gamma^2} \left[ \Delta T - \frac{1}{\gamma} \left( 1 - e^{-\gamma \Delta T} \right) \right], \] (46)

that is, the original Fürth equation.

Also, in the \( \Delta T \to 0 \) limit of Eq. (38) is

\[ MSD \approx 2qk\Delta T, \] (47)

while for \( \Delta T \to \infty \)

\[ MSD \approx \frac{g(1+Q)}{(\gamma + 2k)(\gamma + k)} \Delta T \] (48)

**Velocity Auto Correlation Functions**

**VACF**

The velocity auto correlation function can be obtained by calculating the product between two velocities for all time intervals and taking the average with respect to time for all the summed terms. Here we will consider only the velocity in the direction of the cell polarization: in this instantaneous direction it is well defined.

By assuming that \( T + \Delta T = (n + \Delta n)\Delta t \):

\[ VACF(\Delta T) = \langle v_i(T + \Delta T)\mathbf{\bar{p}}(T + \Delta T) \cdot v_i(T)\mathbf{\bar{p}}(T) \rangle \]

\[ = \langle v_i((n + \Delta n)\Delta t)\mathbf{\bar{p}}((n + \Delta n)\Delta t) \cdot v_i(n\Delta t)\mathbf{\bar{p}}(n\Delta t) \rangle \] (49)
Observe that here $\Delta T$ is not an infinitesimal quantity as $\Delta t$. Also, we will eventually take the limit $\Delta n \to \infty$, such that when $\Delta t \to 0$, $\Delta T$ remains finite.

Using equation 2 for $T$ and $\Delta T$, we obtain:

$$VACF(\Delta T) = \left\langle \left(1 - \gamma \Delta t\right)^n \left[ \bar{p}_0 \cdot \bar{p}(\Delta t) \cdot \bar{p}(2\Delta t) \ldots \bar{p}(n \Delta t) \right] \bar{p}(n \Delta t) \rightangle$$
$$+ \int_0^{\Delta t} \bar{d} \xi_1 \left(1 - \gamma \Delta t\right)^{n-1} \left[ \bar{p}_0 \cdot \bar{p}(\Delta t) \right] \left[ \bar{p}(n \Delta t) \right] \bar{p}(n \Delta t)$$
$$+ \int_{\Delta t}^{2\Delta t} \bar{d} \xi_1 \left(1 - \gamma \Delta t\right)^{n-2} \left[ \bar{p}(\Delta t) \cdot \bar{p}(2\Delta t) \ldots \bar{p}(n \Delta t) \right] \bar{p}(n \Delta t)$$
$$+ \ldots$$
$$+ \int_{(n-1)\Delta t}^{n\Delta t} \bar{d} \xi_1 \left[ \bar{p}(n \Delta t) \right] \bar{p}(n \Delta t)$$
$$\left(1 - \gamma \Delta t\right)^{n+\Delta n} \left[ \bar{p}_0 \cdot \bar{p}(\Delta t) \right] \left[ \bar{p}(n \Delta t) \right] \bar{p}(n \Delta t)$$
$$\ldots$$

\[ (50) \]
Through the multiplication of both terms and also the averaging of the integral terms we get

\[
VACF(\Delta T) = \nu_0^2 (1 - \gamma \Delta t)^{2n+\Delta n} \left\langle \left[ \nu_0 \cdot \nu(\Delta t) \right]^2 \ldots \left[ \nu(n-1) \cdot \nu(n \Delta t) \right]^2 \right\rangle \\
\times \left[ \nu(n \Delta t) \cdot \nu((n + 1) \Delta t) \ldots \nu((n + \Delta n) \Delta t) \right] \right\rangle \\
+ g \int_0^{\Delta t} ds \xi(s) \left( 1 - \gamma \Delta t \right)^{2n-1+\Delta n} \left\langle \left[ \nu_0 \cdot \nu(\Delta t) \right]^2 \ldots \left[ \nu(n-1) \cdot \nu(n \Delta t) \right]^2 \right\rangle \\
\times \left[ \nu(n \Delta t) \cdot \nu((n + 1) \Delta t) \ldots \nu((n + \Delta n) \Delta t) \right] \right\rangle \\
+ \ldots \\
+ g \int_{(n-1)\Delta t}^{n\Delta t} ds \xi(s) \left( 1 - \gamma \Delta t \right)^{\Delta n} \left\langle \left[ \nu(n \Delta t) \cdot \nu((n + \Delta n) \Delta t) \right] \right\rangle \right\rangle 
\] (51)

The crossed terms resulting from the multiplication, vanish due to the fact that the multiplication of two white noises different instants have zero correlation. We also use Eq.(33), that is

\[
\langle \cos \Delta \theta_{ij} \rangle_{\perp} \approx (1 - k \Delta t)^{|j-i|},
\]

or making the same assumptions made in section (i) we reach the equation:

\[
VACF(\Delta T) = \nu_0^2 (1 - \gamma \Delta t)^{2n+\Delta n} (1 - k \Delta t)^{2(n-1)+\Delta n} \\
+ g \left[ (1 - \gamma \Delta t)^{2(n-1)+\Delta n} (1 - k \Delta t)^{2(n-1)+\Delta n} + \ldots \right] \\
+ \left( 1 - \gamma \Delta t \right)^{\Delta n} (1 - k \Delta t)^{2\Delta n-1/2} \right]\right\rangle 
\] (52)

Using that \( \nu_0^2 = \frac{g}{2(\gamma + k)} \) we can conclude that:

\[
VACF(\Delta T) = \left( 1 - \gamma \Delta t \right)^{\Delta n} (1 - k \Delta t)^{2\Delta n-1/2} \langle \nu^2(T) \rangle \right\rangle 
\] (53)

Due to the fact that \( T = n \Delta t, \Delta T = \Delta n \Delta t \) and \( \Delta n \to \infty \) we have:

\[
VACF(\Delta T) = \langle \nu^2(T) \rangle \left( 1 - \gamma \frac{\Delta T}{\Delta n} \right)^{\Delta n} \left( 1 - k \frac{\Delta T}{\Delta n} \right)^{2\Delta n-1/2} \\
= \langle \nu^2(T) \rangle \exp \left\{ - (\gamma + 2k) \Delta T \right\} 
\] (54)
Mean Velocity Auto Correlation Function $\psi^*(\Delta T, \epsilon)$

The mean velocity is defined as

$$\bar{v}(T, \epsilon) = \frac{\bar{r}(T + \epsilon) - \bar{r}(T)}{\epsilon}, \quad (55)$$

Observe that both parallel and perpendicular displacements are considered in the above equation. The average velocity auto correlation function is defined as

$$\psi^*(\Delta T, \epsilon) = \langle \bar{v}(T, \epsilon) \cdot \bar{v}(T + \Delta T, \epsilon) \rangle$$

(56)

To calculate we must partition the time intervals involved. We write all time intervals as multiples of the infinitesimal interval $\Delta t$, and we use the following convention: $T + \epsilon = T + n \Delta t$, $T + \Delta T = T + (m + n) \Delta T$, and $T + \Delta T + \epsilon = T + (m + 2n) \Delta T$. Inspecting Eq. (22), written for displacements in the intervals $[T, T + \epsilon]$ and $[T + \Delta T, T + \Delta T + \epsilon]$, we verify that using Eq. (22) produces crossed terms that have $\xi_{||}$ and/or $\xi_{\perp}$. All these products vanish due to the average over noise implicit in the definition of $\psi^*(\Delta T, \epsilon)$. After averaging over noise, we have

$$\psi^*(\Delta T, \epsilon) = \frac{\Delta t^2}{\epsilon^2} \langle v_{||}(T + \Delta T) v_{||}(T) \rangle \left( \sum_{j=1}^{n} (1 - \gamma \Delta t)^{n-j} (1 - k \Delta t)^{n-j} \bar{p}_{m+2n-j} \right)$$

$$\cdot \left( \sum_{i=1}^{n} (1 - \gamma \Delta t)^{n-i} (1 - k \Delta t)^{n-i} \bar{p}_{n-i} \right)$$

(57)

$$= \frac{\Delta t^2}{\delta^2} \langle v_{||}(T + \Delta T) v_{||}(T) \rangle \left( \sum_{j=1}^{n} \sum_{i=1}^{n} (1 - \gamma \Delta t)^{2n-j-i} (1 - k \Delta t)^{2n-j-i} \bar{p}_{m+2n-j} \cdot \bar{p}_{n-i} \right)$$

We use that $\langle \bar{p}_0 \cdot \bar{p}_{m+n} \rangle = (1 - k \Delta t)^{m+n}$ to write that

$$\psi^*(\Delta T, \epsilon) = \frac{\Delta t^2}{\delta^2} \langle v_{||}(T + \Delta T) \bar{p}_{m+n} \cdot v_{||}(T) \bar{p}_0 \rangle \sum_{j=1}^{n} (1 - \gamma \Delta t)^{n-j} (1 - k \Delta t)^{2(n-j)}$$

(58)

Taking that $n \to \infty$ such that $\epsilon$ is finite and using that the sums in the above equations are sums of geometrical series,

$$\psi^*(\Delta T, \epsilon) = \frac{(1 - e^{-\gamma \epsilon})(1 - e^{-(\gamma + 2k)\epsilon})}{\epsilon^2 \gamma (\gamma + 2k)} VACF(\Delta T)$$

(59)

Observe that $\lim_{\epsilon \to 0} \psi(\Delta T, \delta) = VACF(\Delta T)$, as it should. From the above equation, it is straightforward to obtains the mean velocity auto correlation function $\psi(\Delta T, \delta)$ given in natural units.