

## Introduction

There are various models of intermittent particle transport (including intracellular transport) (Holcman 2007; Lagache et al. 2009; Bénichou et al. 2011; Thiel et al. 2012; Bressloff and Newby 2013; Bressloff 2014). We propose a mean-field model of intermittent particle transport, where a particle may be in one of two phases: the first is an active (ballistic) phase, when a particle runs with constant velocity in some direction, and the second is a passive (diffusive) phase,

when the particle diffuses freely. The particle can instantly change the phase of motion. When the particle is in the active phase the rate of transition to the passive phase depends, in general, on time from the beginning of the run, so the distribution of the free path is not exponential. When the particle is in the passive phase the transition rate is constant, and diffusion is non-anomalous Brownian. Reasoning is similar to that of (Rukolaine 2016).

## The model

### Basic equations

Particles (individuals) move in the  $d$ -dimensional space  $\mathbb{R}^d$ . They can be in one of two phases: the first is an active (or ballistic) phase, when a particle runs with constant velocity in some direction, and the second is a passive phase, when the particle diffuses freely. The particle can instantly change the phase of motion. *When the particle is in the active phase the rate of transition to the passive phase depends, in general, on time from the beginning of the run.* The densities of the particles in the active and passive phases are denoted by  $\xi \equiv \xi(\mathbf{r}, t, \mathbf{v}, \tau)$  and  $\vartheta \equiv \vartheta(\mathbf{r}, t)$ , respectively, where  $\mathbf{r}$  and  $t$  are the space and time variables, respectively,  $\mathbf{v} \in \mathbb{V}$  is the velocity vector, and  $\tau$  is time from the beginning of the run.

where  $\alpha \equiv \alpha(\mathbf{r})$  is the rate of transition from the passive to active phase,  $T$  is the transition kernel such that

$$T \geq 0 \quad \text{and} \quad \int_{\mathbb{V}} T(\mathbf{r}, \mathbf{v}) d\mathbf{v} = 1.$$

The density  $\vartheta$  obeys the diffusion equation

$$\partial_t \vartheta - D \Delta \vartheta = -\alpha \vartheta + \int_{\mathbb{V}} \int_0^\infty \gamma(\mathbf{r}, \mathbf{v}, \tau) \xi(\mathbf{r}, t, \mathbf{v}, \tau) d\tau d\mathbf{v},$$

where  $D$  is the diffusion coefficient. The first term on the right-hand side expresses the loss of diffusing particles due to transition to the active phase, the second term is the source of diffusing particles due to transition from the active phase.

Initial conditions are

$$\xi|_{t=0} = \chi(\mathbf{r}, \mathbf{v}) \delta(\tau),$$

where  $\delta(\cdot)$  is the Dirac delta function, and

$$\vartheta|_{t=0} = \vartheta_0(\mathbf{r}).$$

The initial condition for  $\xi$  means that at the moment  $t = 0$  all the active particles are at the beginning of the run.

The density  $\xi$  obeys the equation

$$\partial_t \xi + \mathbf{v} \cdot \nabla \xi + \gamma \xi = 0,$$

where  $\gamma \equiv \gamma(\mathbf{r}, \mathbf{v}, \tau)$  is the transition rate. This equation describes noninteracting particles running at the point  $\mathbf{r}$  with the velocity  $\mathbf{v}$  so that they become diffusing particles with the rate  $\gamma$ .

The density of particles at the beginning of the run is given by

$$\xi|_{\tau=0} = \alpha T(\mathbf{r}, \mathbf{v}) \vartheta,$$

### Transformed equations

We define the density

$$\psi(\mathbf{r}, t, \mathbf{v}) = \int_0^\infty \xi(\mathbf{r}, t, \mathbf{v}, \tau) d\tau.$$

The densities  $\psi$  and  $\vartheta$  obeys the coupled equations

$$\partial_t \psi + \mathbf{v} \cdot \nabla \psi = -\mathcal{M} \psi(\mathbf{r}, t, \mathbf{v}) + \alpha T(\mathbf{r}, \mathbf{v}) \vartheta, \quad (1)$$

$$\partial_t \vartheta - D \Delta \vartheta = \int_{\mathbb{V}} \mathcal{M} \psi(\mathbf{r}, t, \mathbf{v}) d\mathbf{v} - \alpha \vartheta. \quad (2)$$

The memory operator  $\mathcal{M}$  is given by

$$\mathcal{M} \psi(\mathbf{r}, t, \mathbf{v}) = \int_0^t \phi(\mathbf{r}, \mathbf{v}, \tau) \psi(\mathbf{r} - \mathbf{v}\tau, t - \tau, \mathbf{v}) d\tau,$$

the memory kernel  $\phi$  is defined through its Laplace transform by

$$\mathcal{L} \phi(\mathbf{r}, \mathbf{v}, s) \stackrel{\text{def}}{=} \frac{\mathcal{L} p(\mathbf{r}, \mathbf{v}, s)}{\mathcal{L} S(\mathbf{r}, \mathbf{v}, s)}$$

$$(\mathcal{L} f)(s) = \int_0^\infty e^{-st} f(t) dt,$$

$$S(\mathbf{r}, \mathbf{v}, \tau) = \exp \left\{ - \int_0^\tau \gamma(\mathbf{r} - \mathbf{v}(\tau - \tau'), \mathbf{v}, \tau') d\tau' \right\}$$

## Asymptotic solution

### Assumptions

- The transition rates  $\alpha$  and  $\gamma$  do not depend on  $\mathbf{r}$ . The transition rate  $\gamma$  is also independent of the direction of the particle movement (i. e.,  $\gamma$  depends on the velocity  $\mathbf{v}$  rather than the direction  $\Omega = \mathbf{v}/v$ ). Therefore the same is valid for the survival probability  $S$ , density  $p$  and memory kernel  $\phi$ .
- The time of a run has the finite mean

$$\langle \tau_a \rangle \equiv \langle \tau_a \rangle(v) = \int_0^\infty \tau p(v, \tau) d\tau$$

and second moment

$$\langle \tau_a^2 \rangle \equiv \langle \tau_a^2 \rangle(v) = \int_0^\infty \tau^2 p(v, \tau) d\tau.$$

- The mean time of a run  $\langle \tau_a \rangle$  is small of order  $\varepsilon$ , where  $\varepsilon$  is a small parameter, therefore the transition rate  $\gamma$  is represented as

$$\gamma(v, \tau) = \frac{1}{\varepsilon} \bar{\gamma} \left( v, \frac{\tau}{\varepsilon} \right),$$

where  $\bar{\gamma}$  does not depend on  $\varepsilon$ . This implies the representations

$$S(v, \tau) = \bar{S} \left( v, \frac{\tau}{\varepsilon} \right), \quad p(v, \tau) = \frac{1}{\varepsilon} \bar{p} \left( v, \frac{\tau}{\varepsilon} \right), \\ \phi(v, \tau) = \frac{1}{\varepsilon^2} \bar{\phi} \left( v, \frac{\tau}{\varepsilon} \right),$$

### Asymptotic solution

Eqs. (1) and (2) are recast as

$$\partial_t \psi + \mathbf{v} \cdot \nabla \psi = -\frac{1}{\varepsilon} \mathcal{M}_\varepsilon \psi(\mathbf{r}, t, \mathbf{v}) + \frac{\bar{\alpha}}{\varepsilon} \left[ \bar{T}(\mathbf{r}, \mathbf{v}) + \varepsilon \bar{T}(\mathbf{r}, \mathbf{v}) \right] \vartheta, \quad (3)$$

$$\partial_t \vartheta - \varepsilon \bar{D} \Delta \vartheta = \frac{1}{\varepsilon} \int_{\mathbb{V}} \mathcal{M}_\varepsilon \psi(\mathbf{r}, t, \mathbf{v}) d\mathbf{v} - \frac{\bar{\alpha}}{\varepsilon} \vartheta, \quad (4)$$

where

$$\mathcal{M}_\varepsilon \psi(\mathbf{r}, t, \mathbf{v}) = \int_0^t \frac{1}{\varepsilon} \bar{\phi} \left( v, \frac{\tau}{\varepsilon} \right) \psi(\mathbf{r} - \mathbf{v}\tau, t - \tau, \mathbf{v}) d\tau.$$

The densities are represented in the form

$$\psi(\mathbf{r}, t, \mathbf{v}) = \psi^o(\mathbf{r}, t^o, \mathbf{v}) + \psi^i(\mathbf{r}, t^i, \mathbf{v}), \\ \vartheta(\mathbf{r}, t) = \vartheta^o(\mathbf{r}, t^o) + \vartheta^i(\mathbf{r}, t^i),$$

where

$$t^o = \varepsilon t \quad \text{and} \quad t^i = t/\varepsilon$$

are slow time and fast time, respectively,  $\psi^o$ ,  $\vartheta^o$  and  $\psi^i$ ,  $\vartheta^i$  are outer and inner solutions, respectively. The inner solutions approximate  $\psi$  and  $\vartheta$  in the initial layer, i. e., for  $0 < t \lesssim O(\varepsilon)$ , while the outer solutions approximate them outside of the initial layer, i. e., for  $t \gtrsim O(\varepsilon)$ . We derive here only the outer solutions. The inner solutions can be derived in the same way as in (Rukolaine 2016).

The memory kernel has the asymptotic expansion

$$\frac{1}{\varepsilon} \bar{\phi} \left( v, \frac{\tau}{\varepsilon} \right) \sim \bar{\phi}_0 \delta(\tau) + \bar{\phi}_1 \delta'(\tau) \varepsilon + \dots \quad \text{as } \varepsilon \rightarrow 0$$

(the expansion is considered in the weak sense) with the coefficients

$$\bar{\phi}_0 \equiv \bar{\phi}_0(v) = \frac{1}{\langle \bar{\tau}_a \rangle}, \quad \bar{\phi}_1 \equiv \bar{\phi}_1(v) = \frac{\langle \bar{\tau}_a^2 \rangle}{2 \langle \bar{\tau}_a \rangle^2} - 1,$$

where

$$\langle \bar{\tau}_a \rangle \equiv \langle \bar{\tau}_a \rangle(v) = \int_0^\infty \tau \bar{p}(v, \tau) d\tau$$

where  $\bar{S}$ ,  $\bar{p}$  and  $\bar{\phi}$  do not depend on  $\varepsilon$ .

- The mean time in the passive phase  $\langle \tau_a \rangle$  is small of order  $\varepsilon$ . Since  $\langle \tau_a \rangle = 1/\alpha$ , this means that

$$\alpha = \frac{\bar{\alpha}}{\varepsilon},$$

where  $\bar{\alpha}$  does not depend on  $\varepsilon$ .

- The diffusion coefficient  $D$  is small of order  $\varepsilon$ :

$$D = \varepsilon \bar{D},$$

where  $\bar{D}$  does not depend on  $\varepsilon$ .

- The transition kernel has the form

$$T(\mathbf{r}, \mathbf{v}) = \bar{T}(\mathbf{r}, \mathbf{v}) + \varepsilon \bar{T}(\mathbf{r}, \mathbf{v}),$$

where  $\bar{T}$  and  $\bar{T}$  do not depend on  $\varepsilon$ ,

$$\bar{T} \geq 0 \quad \text{and} \quad \int_{\mathbb{V}} \bar{T}(\mathbf{r}, \mathbf{v}) d\mathbf{v} = 1.$$

We suppose also that  $\bar{T}(\mathbf{r}, -\mathbf{v}) = \bar{T}(\mathbf{r}, \mathbf{v})$ , which is met if  $\bar{T}$  is isotropic, i. e.,  $\bar{T} = |\mathbb{V}|^{-1}$ . The normalization of  $T$  and  $\bar{T}$  implies

$$\int_{\mathbb{V}} \bar{T}(\mathbf{r}, \mathbf{v}) d\mathbf{v} = 0.$$

- The "space" of velocities  $\mathbb{V}$  is bounded and rotationally invariant.

$$\text{and} \quad \langle \bar{\tau}_a^2 \rangle \equiv \langle \bar{\tau}_a^2 \rangle(v) = \int_0^\infty \tau^2 \bar{p}(v, \tau) d\tau.$$

We assume that the outer solutions have the asymptotic expansions

$$\psi^o \sim \psi_0^o + \psi_1^o \varepsilon + \psi_2^o \varepsilon^2 + \dots \quad \text{as } \varepsilon \rightarrow 0,$$

$$\vartheta^o \sim \vartheta_0^o + \vartheta_1^o \varepsilon + \vartheta_2^o \varepsilon^2 + \dots \quad \text{as } \varepsilon \rightarrow 0.$$

Substituting the asymptotic expansions into Eqs. (3), (4), and equating coefficients of like powers of  $\varepsilon$  yields the system of equations of the second kind for  $\psi_i^o$  and  $\vartheta_i^o$ . The use of the Fredholm alternative and the solvability condition yields the representation of the zeroth-order densities (the quasi-steady state approximation)

$$\begin{pmatrix} \psi_0^o \\ \vartheta_0^o \end{pmatrix} = \begin{pmatrix} \langle \bar{\tau}_a \rangle \bar{T}(\mathbf{r}, \mathbf{v}) \\ \langle \bar{\tau}_a \rangle \end{pmatrix} \rho(\mathbf{r}, t^o),$$

where  $\langle \bar{\tau}_a \rangle = 1/\bar{\alpha}$ .

The density  $\rho \equiv \rho(\mathbf{r}, t)$  satisfies the drift-diffusion equation

$$\partial_t \rho - \nabla \cdot (D_{\text{eff}} \nabla \rho) + \mathbf{u} \cdot \nabla \rho = 0,$$

where

$$C = \int_{\mathbb{V}} \langle \tau_a \rangle \bar{T}(\mathbf{r}, \mathbf{v}) d\mathbf{v} + \langle \tau_a \rangle,$$

the effective diffusion coefficient is

$$D_{\text{eff}} = \frac{1}{C} \left[ D \langle \tau_a \rangle + \int_{\mathbb{V}} \frac{\langle \tau_a^2 \rangle}{2} \bar{T}(\mathbf{r}, \mathbf{v}) v v^T d\mathbf{v} \right]$$

the drift velocity is

$$\mathbf{u} = \frac{1}{C} \int_{\mathbb{V}} \langle \tau_a \rangle [T(\mathbf{r}, \mathbf{v}) - \bar{T}(\mathbf{r}, \mathbf{v})] \mathbf{v} d\mathbf{v}.$$

The initial condition is

$$\rho|_{t=0} = \int_{\mathbb{V}} \bar{T}(\mathbf{r}, \mathbf{v}) \bar{\phi}_0(v) \chi(\mathbf{r}, \mathbf{v}) d\mathbf{v} + \bar{\alpha}(\mathbf{r}) \vartheta_0(\mathbf{r}).$$

## Asymptotic solution

### A special case: the one-speed model

Let  $v \equiv |\mathbf{v}| = \text{const}$  (i. e.,  $\mathbb{V} = v\mathbb{S}^{d-1}$ ) and the nonperturbed term  $\bar{T}$  of the transition kernel is isotropic, i. e.,  $\bar{T}(\mathbf{r}, \Omega) = |\mathbb{V}|^{-1}$ , then  $C = \langle \tau_a \rangle + \langle \tau_a \rangle$ , and

$$D_{\text{eff}} = \frac{1}{\langle \tau_a \rangle + \langle \tau_a \rangle} \left[ D \langle \tau_a \rangle + \frac{\langle \tau_a^2 \rangle v^2}{2d} \right],$$

$$\mathbf{u} = \frac{\langle \tau_a \rangle v}{\langle \tau_a \rangle + \langle \tau_a \rangle} \int_{\mathbb{S}^{d-1}} [T(\mathbf{r}, \Omega) - \bar{T}(\mathbf{r}, \Omega)] \Omega d\Omega.$$

Limiting cases: If the active phase is negligibly

short compared to the passive phase ( $\langle \tau_a \rangle \ll \langle \tau_d \rangle$ ), then

$$D_{\text{eff}} \rightarrow D \quad \text{and} \quad \mathbf{u} \rightarrow 0.$$

If the passive phase is negligibly short compared to the active phase ( $\langle \tau_a \rangle \ll \langle \tau_d \rangle$ ), then

$$D_{\text{eff}} \rightarrow \frac{\langle \tau_a^2 \rangle v^2}{2d \langle \tau_a \rangle} \quad \text{and} \\ \mathbf{u} \rightarrow v \int_{\mathbb{S}^{d-1}} [T(\mathbf{r}, \Omega) - \bar{T}(\mathbf{r}, \Omega)] \Omega d\Omega$$

### The importance of being corrected

A correction to the diffusion coefficient  $D_{\text{eff}}$  due to non-exponential distribution of free paths may be significant. Consider the one-speed model. Suppose for simplicity that  $\langle \tau_d \rangle = 0$  (the passive phase is negligibly short) and  $T(\mathbf{r}, \Omega) = \bar{T}(\mathbf{r}, \Omega) = |\mathbb{V}|^{-1}$  (reorientation is isotropic). Then  $\mathbf{u} = 0$  and  $D_{\text{eff}} = \langle \tau_a^2 \rangle v^2 / (2d \langle \tau_a \rangle)$ .

Fig. 1(a) shows two probability density functions (PDFs): the first is the exponential PDF

$$p(\tau) = \gamma e^{-\gamma\tau}$$

and the second is the power-like PDF

$$p(\tau) = \frac{\gamma\alpha}{\alpha-1} \left[ 1 + \frac{\gamma\tau}{\alpha-1} \right]^{-(\alpha+1)}$$

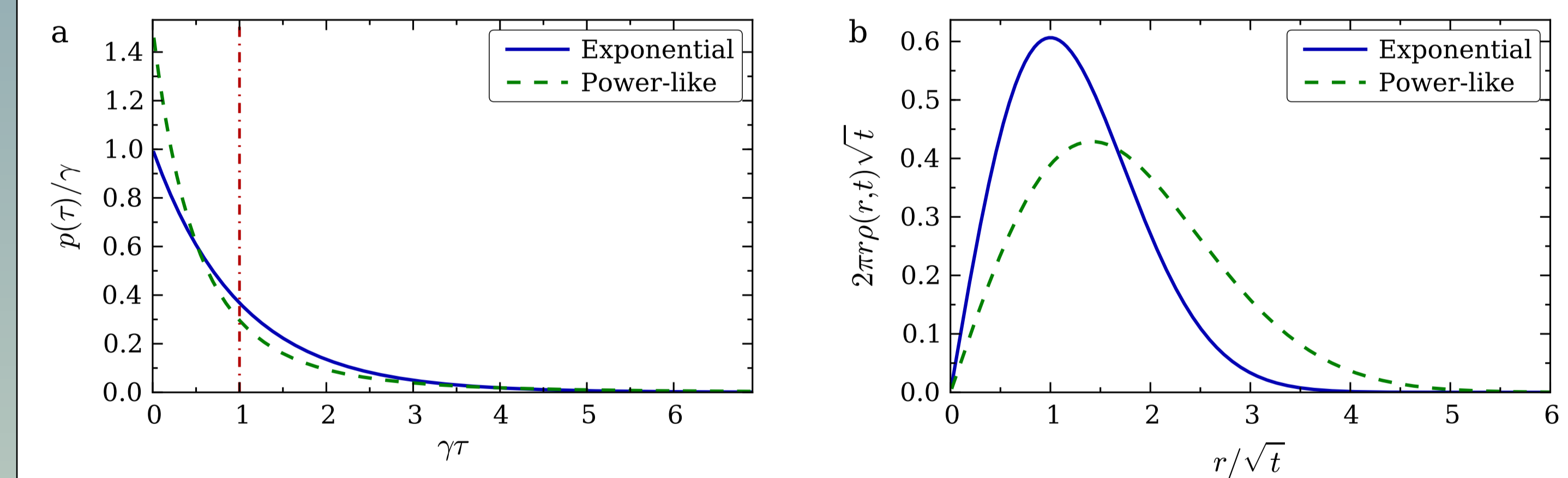


Figure 1: (a) The exponential and power-like PDFs with the same mean (shown by the vertical dashdot line). (b) Corresponding solutions to the initial value problem (5), (6).

## Concluding remarks

- The use of the exponential distribution of free paths, when it is actually non-exponential, may lead to significant errors in results of modelling.
- The model admits straightforward extension to the case when absorption (degradation) of particles and sources are present.

- Extension of the model to non-Cartesian geometries is possible. For example, it can be extended to intracellular vesicular transport in spherical geometry.

## References

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