

*Chapter 8*

# FRACTIONAL REACTION-TRANSPORT EQUATIONS ARISING FROM EVANESCENT CONTINUOUS TIME RANDOM WALKS

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## Abstract

Continuous time random walks (CTRWs) describe a particular class of renewal processes used to model a wide variety of phenomena such as the motion of charge carriers in disordered systems, the dynamics of financial markets, the motion of diffusing particles in crowded environments, and certain anomalous relaxation phenomena in dielectric systems. It is well known that, on long time scales, a CTRW described by a separable probability density function (pdf) for the jump length of a particle and its waiting time between consecutive jumps yields a variety of fractional diffusion equations for suitable (and yet rather general) choices of both pdfs. Such fractional diffusion equations give rise to a broad range of behaviors for the mean square displacement of the particle, ranging from subdiffusive to superdiffusive. In this work we show that fractional equations with interesting solutions may also be obtained when the above CTRW is combined with a rather general class of death processes (evanescence), including a simple first-order process typical of radioactive decay. A general feature of the resulting fractional equations is that the parameters describing the decay process explicitly appear in the transport term, as opposed to heuristic fractional equations lacking a rigorous mesoscopic justification. In the subdiffusive case, we consider

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two applications of interest. First, we compute the survival probability of an immobile target surrounded by one or more subdiffusive traps that may spontaneously disappear in the course of their motion. The second example concerns a biologically relevant problem, namely, the formation of stationary morphogen concentration gradients by means of morphogen synthesis, anomalous diffusion, and degradation.

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## 1. Introduction

The importance of fractional calculus for the theoretical description of anomalous transport has been highlighted by recent research on the connection between renewal processes underlying Continuous Time Random Walks (CTRWs) and fractional diffusion equations. CTRWs are paradigmatic models of stochastic transport that incorporate memory effects reflecting complex features of real-world systems, e.g., transport in complex media [1] and stochastic dynamics of financial markets [2–4]. It is by now a well-known fact that a CTRW with a suitable choice of jump statistics yields fractional diffusion equations that can be solved by standard techniques. The boundary and initial conditions depend on the specific application of interest.

In the simplest case one is interested in the propagator solution of the fractional diffusion equation, which characterizes the diffusive spread of a particle starting at the origin of an infinite volume. In the particular case where the spatial and temporal dependences of the single-step probability density of the CTRW are uncoupled and the corresponding waiting time distribution is long-tailed, the behavior of the mean square displacement (MSD) of the propagator solution depends on the choice of the jump length distribution. If the latter is assumed to follow an inverse power law, sublinear or superlinear behavior of the MSD as a function of time may occur, resulting in the emergence of anomalous subdiffusive or superdiffusive transport in the long time regime.

Researchers working in the field of stochastic transport are quite familiar with the passage from the integral equations describing the arrival and sojourn probability densities of a continuous time random walker to a fractional diffusion equation. However, it is not infrequent to encounter serious misconceptions in the literature when the transported species is allowed to undergo a chemical reaction or a transformation in the course of its motion, as is the case, for instance, for a diffusing radionuclide in a complex medium. In this case, it is tempting to write an evolution equation with separate transport and reaction terms, whereby the transport term is exactly the same as in the absence of the chemical reaction. However, this heuristic approach is plainly wrong, since a rigorous derivation of the equations for particle concentrations from the CTRW probability density equations shows that both terms are mathematically intertwined [5–12], and the reaction rate parameters often appear explicitly in the transport term (even for very simple reaction processes of birth and death type). Failing to take the above into account may result in fractional reaction-transport equations that yield unphysical results, such as negative particle concentrations.

Instead of a heuristic approach, a procedure is required whereby the fractional equations obtained when a reaction is at play are substantiated by the proper CTRW integral equations for the probability densities. The resulting equations may then be shown to fulfill elementary consistency properties that prevent an ill-behaved evolution of the system. In several instances we shall see that the fractional reaction-transport equations may be cast in the form of pure transport equations by a suitable transformation of the concentration variable, much in the spirit of Danckwerts' solution for a Fickian reaction-diffusion equation with a linear loss term [13, 14]. Physically, this means that if one constantly feeds back the amount of reactant lost in the reaction process by multiplying the concentration by a proper time dependent factor, then a pure transport process is obtained (alternatively, one can view this as a rescaling of the concentration in terms of the survival probability of the particle). As it turns out, in the case of anomalous diffusion such a transformation does not work if the transport term is not made to depend on the reaction rate constant.

The aim of this work is to recapitulate previous results obtained in different contexts where the derivation of fractional reaction-transport equations is required. In particular, these results refer to relatively simple reactions, namely, first-order death processes (also called evanescence process). Despite their apparent simplicity, the combination of these reactions with anomalous transport gives rise to fractional equations that are not particularly intuitive. Our focus lies in the derivation of the equations in terms of the Riemann-Liouville fractional derivative, but we also discuss two applications, namely, the survival probability of a particle surrounded by evanescent traps, and the properties of morphogen profiles giving rise to embryogenic cellular differentiation.

The plan of this presentation is as follows. In Sec. 2 we derive an integral equation for the probability density of a particle subject to a rather general class of death processes. In Sec. 3 we consider special cases of the above equation, leading to a fractional reaction-subdiffusion equation and a reaction-superdiffusion equation, as well as to a bifractional reaction diffusion equation. Two applications of the resulting reaction-subdiffusion equation are addressed in Sec. 4. Finally, Sec. 5 is devoted to a summary of our main findings.

## 2. Integral Equation for a CTRW with Evanescence

Our starting point is a particle performing a CTRW in continuum space (we adopt this type of description for concreteness, but on-lattice approaches do not pose difficulties of principle). The particle jumps take place in negligible time after a randomly distributed waiting time during which the particle remains immobile, as opposed to creeper models where the particle moves continuously and switches direction after a random time after the last change in direction. The probability density that a CTRWer located at  $\mathbf{r}_0$  when  $t = 0$  is at position  $\mathbf{r}$  at time  $t$  is denoted by  $w(\mathbf{r}, t | \mathbf{r}_0, 0)$ . In order to obtain the desired integral equation for this quantity it is necessary to introduce the probability density  $\Psi(\mathbf{r} - \mathbf{r}', t - t')$  for the walker to jump in a single step from  $\mathbf{r}'$  to  $\mathbf{r}$  after having waited a time interval  $t - t'$  at position  $\mathbf{r}'$ . Note that we restrict  $\Psi$  to depend only on the difference between the initial position and the final position after the jump, as well as on the difference between the start and the end of the waiting time interval, i.e., we assume translational and temporal invariance of the random walk. The waiting time probability density  $\psi(t)$  and the probability density  $\chi(\mathbf{r})$

for a single step displacement are respectively obtained by integration, i.e.,

$$\psi(t) = \int d\mathbf{r}' \Psi(\mathbf{r}', t), \quad (1)$$

and

$$\chi(\mathbf{r}) = \int_0^\infty dt' \Psi(\mathbf{r}, t'). \quad (2)$$

The specific forms of the above probability densities determine whether the transport is “normal” or “anomalous”. In the latter case one can distinguish between subdiffusive and superdiffusive transport. However, in our case we must bear in mind that the walker disappears at a certain rate in the course of its motion (in physical systems, this death process can for instance be the result of a radioactive or photoemissive decay). Therefore, the above jump statistics are conditional on the walker’s survival and must be weighted by a suitable survival function. To this end, let us specify the manner in which the death process proceeds by introducing the probability  $\Xi(\mathbf{r}, \mathbf{r}'; t, t')$  that the particle has not evanesced during the stepping process described by  $\Psi(\mathbf{r} - \mathbf{r}', t - t')$ .

As is customary in the derivation of fractional equations in the absence of evanescence, we next introduce  $q_n(\mathbf{r}, t | \mathbf{r}_0, 0)$ , the probability density that the particle arrives at position  $\mathbf{r}$  at time  $t$  exactly after making its  $n$ th jump, given that it was initially at  $\mathbf{r}_0$  [6]. For  $n = 0$  one must recover the initial condition, that is,

$$q_0(\mathbf{r}, t | \mathbf{r}_0, 0) = \delta(\mathbf{r} - \mathbf{r}_0) \delta(t). \quad (3)$$

The probability density that the particle steps onto position  $\mathbf{r}$  exactly at time  $t$  is obtained by summing over  $n$ :

$$q(\mathbf{r}, t | \mathbf{r}_0, 0) \equiv \sum_{n=0}^{\infty} q_n(\mathbf{r}, t | \mathbf{r}_0, 0). \quad (4)$$

One can then write the following equation for the  $q_n$ ’s:

$$q_{n+1}(\mathbf{r}, t | \mathbf{r}_0, 0) = \int d\mathbf{r}' \int_0^t dt' \Psi(\mathbf{r} - \mathbf{r}', t - t') q_n(\mathbf{r}', t' | \mathbf{r}_0, 0) \Xi(\mathbf{r}, \mathbf{r}'; t, t'). \quad (5)$$

This equation states that the probability density for the particle to arrive at location  $\mathbf{r}$  at time  $t$  on the  $(n + 1)$ st step is given by the probability density for the particle to arrive at any point  $\mathbf{r}'$  at any earlier time  $t'$  on the  $n$ th step and then to step from  $\mathbf{r}'$  to  $\mathbf{r}$  at time  $t$ , provided that the particle does not die in the interval between the  $n$ th and  $(n + 1)$ st steps. The usual integral equation without evanescence is immediately recovered upon setting  $\Xi$  equal to unity. We now take advantage of the fact that  $\Psi$  has been assumed to not depend on  $n$ ; summing over  $n$  we obtain the following integral equation:

$$\begin{aligned} q(\mathbf{r}, t | \mathbf{r}_0, 0) &= \int d\mathbf{r}' \int_0^t dt' \Psi(\mathbf{r} - \mathbf{r}', t - t') \\ &\times q(\mathbf{r}', t' | \mathbf{r}_0, 0) \Xi(\mathbf{r}, \mathbf{r}'; t, t') + q_0(\mathbf{r}, t | \mathbf{r}_0, 0). \end{aligned} \quad (6)$$

The next step in our route to a fractional reaction-transport equation is to write an equation relating  $w$  and  $q$ . To this end, we introduce  $\Xi(\mathbf{r}, \mathbf{r}'; t, t')$  as the probability that the

particle does not die between the times  $t'$  and  $t$  as it moves from  $\mathbf{r}'$  to  $\mathbf{r}$ , with no reference to steps. We can then write the exact relation

$$w(\mathbf{r}, t | \mathbf{r}_0, 0) = \int_0^t dt' \Phi(t - t') q(\mathbf{r}, t' | \mathbf{r}_0, 0) \Xi(\mathbf{r}, \mathbf{r}; t, t'), \tag{7}$$

where

$$\Phi(t) = 1 - \int_0^t dt' \psi(t') = \int_t^\infty dt' \psi(t') \tag{8}$$

stands for the probability that the particle does not take a step in the time interval between 0 and  $t$ . Equation (7) is intuitively clear. It simply states that the probability density for the particle to be at  $\mathbf{r}$  at time  $t$  is the probability that it arrived at that location at time  $t' < t$  and then neither moved nor died until time  $t$ .

Note that  $\Xi(\mathbf{r}, \mathbf{r}'; t, t')$  is in general different from the function  $\Xi(\mathbf{r}, \mathbf{r}'; t, t')$ . We recall that the latter is the probability that the particle does not die in a waiting time interval exactly delineated by two steps (and none in between), one taking it to location  $\mathbf{r}'$  and the other to location  $\mathbf{r}$ . If particles die at a constant rate independent of position and of stepping times, then  $\Xi$  and  $\Xi$  are equal. However, if, for example, particles die only when they take a step, then these probabilities are different. For this reason, Eq. (6) and Eq. (7) cannot be easily combined with one another to obtain an integral equation for  $w(\mathbf{r}, t | \mathbf{r}_0, 0)$  unless one assumes that  $\Xi$  and  $\Xi$  are equal. We shall do so hereafter.

The other (admittedly debatable) assumption needed to obtain a fractional reaction-transport equation is that the survival function  $\Xi$  can be written as follows:

$$\Xi(\mathbf{r}, \mathbf{r}'; t, t') = \frac{\varphi(\mathbf{r}, t)}{\varphi(\mathbf{r}', t')} \tag{9}$$

with a suitably defined function  $\varphi(\mathbf{r}, t)$ . This assumption is not as limiting as might appear at first glance, since it can be shown to embrace many special cases that have been treated in the literature. The possibilities that  $\varphi$  depends explicitly on the walker density  $w$  or that it is prescribed by an external mechanism not related to the intrinsic properties of the walker are not excluded (see discussion in 3.1 and 3.2).

The simplest type of evanescence is an exponential, location-independent decay,  $\varphi(\mathbf{r}, t) = \exp(-\lambda t)$ , implying that  $\Xi(\mathbf{r}, \mathbf{r}'; t, t') = \exp[-\lambda(t - t')]$ . Thus,  $\Xi$  depends only on the time difference. This case was considered early on in the literature [5], possibly because of its great practical importance, notably for the description of decay processes uncoupled from transport as is often the case for a population of diffusing particles that decay into other species by light or particle emission [15].

We are now in the position to obtain an integral equation for  $w$  by taking Eqs. (6) and (7) as a starting point. To begin with, we implement the replacements  $t \rightarrow t'$  and  $t' \rightarrow t''$  in Eq. (6). Then we multiply by  $\Phi(t - t') \Xi(\mathbf{r}, \mathbf{r}; t, t')$ , integrate over  $t'$ , and use Eq. (7) to

write

$$\begin{aligned}
 w(\mathbf{r}, t | \mathbf{r}_0, 0) = & \\
 & \int_0^t dt' \Phi(t-t') \Xi(\mathbf{r}, \mathbf{r}; t, t') \left( \int d\mathbf{r}' \int_0^{t'} dt'' \Psi(\mathbf{r}-\mathbf{r}', t'-t'') q(\mathbf{r}', t'' | \mathbf{r}_0, 0) \Xi(\mathbf{r}, \mathbf{r}'; t', t'') \right) \\
 & + \int_0^t dt' \Phi(t-t') \Xi(\mathbf{r}, \mathbf{r}; t, t') q_0(\mathbf{r}, t' | \mathbf{r}_0, 0). \tag{10}
 \end{aligned}$$

Next, we insert the special form given by Eq. (9) and perform a series of simple manipulations, whereby the double convolution structure of the resulting equations with respect to space and time is exploited (details can be found in ref. [10]). Finally, one is left with the desired integral equation:

$$w(\mathbf{r}, t | \mathbf{r}_0, 0) = \int d\mathbf{r}' \int_0^t dt' \Psi(\mathbf{r}-\mathbf{r}', t-t') w(\mathbf{r}', t' | \mathbf{r}_0, 0) \frac{\varphi(\mathbf{r}, t)}{\varphi(\mathbf{r}', t')} + \Phi(t) \frac{\varphi(\mathbf{r}, t)}{\varphi(\mathbf{r}, 0)} \delta(\mathbf{r}-\mathbf{r}_0). \tag{11}$$

The above equation takes into account all the possible ways in which the particle can be at location  $\mathbf{r}$  at time  $t$  by carrying out detailed bookkeeping of the positions  $\mathbf{r}'$  at prior times  $t'$  from which the particle may later arrive at  $\mathbf{r}$ . The second term on the right hand side is needed to account for the possibility that the particle was initially at  $\mathbf{r}$  and has not moved by time  $t$ .

Equation (11) is central to the present work; shortly we shall see that it allows one to deduce various fractional reaction-diffusion equations for different forms of  $\Psi(\mathbf{r}-\mathbf{r}', t-t')$ .

### 3. Fractional Diffusion Equations with Evanescence

In order to use Eq. (11) to derive various fractional reaction-transport equations, we start by making the simplifying assumption that the waiting time and the jump length distributions are uncoupled, that is,

$$\Psi(\mathbf{r}, t) = \psi(t)\chi(\mathbf{r}). \tag{12}$$

The assumption of decoupling is needed at this stage to make Eq. (11) more tractable from a mathematical point of view. Decoupling is admittedly not fulfilled in many real-world systems, e.g., a grasshopper is likely to need a longer recovery time if she is to perform a longer jump. However, dealing with coupled CTRW schemes in the presence of reactions is a very challenging problem beyond the scope of the present work.

With the above assumption, one can use the techniques employed by various authors to obtain fractional diffusion equations for a conventional, non-evanescent CTRW [16–18]. In particular, when  $\psi(t)$  has long tails and  $\chi(\mathbf{r})$  does not, one arrives at a fractional subdiffusion equation. When, on the other hand,  $\chi(\mathbf{r})$  has long tails but  $\psi(t)$  does not, a fractional superdiffusion equation is found. The most “anomalous” case occurs when both have long tails, which leads to a bifractional equation. In what follows we consider a transport process *with a superimposed evanescence process* and find equations that are not trivial superpositions of the reaction and the transport terms, as would be the case for a Markovian walker.

In view of the form of Eq. (11), it turns out to be convenient to work with a ratio introduced earlier in ref. [10], namely,

$$\eta(\mathbf{r}, t | \mathbf{r}_0, 0) = \frac{w(\mathbf{r}, t | \mathbf{r}_0, 0)}{\varphi(\mathbf{r}, t)} \quad (13)$$

rather than with  $w(\mathbf{r}, t | \mathbf{r}_0, 0)$  itself. One now proceeds as in the non-evanescent case, namely, one takes the Fourier (for space)-Laplace (for time) transform of Eq. (11) and finds

$$u\hat{\eta}(\mathbf{q}, u) = u\hat{\chi}(\mathbf{q})\tilde{\psi}(u)\hat{\eta}(\mathbf{q}, u) + \left(1 - \tilde{\psi}(u)\right) \frac{e^{i\mathbf{q}\cdot\mathbf{r}_0}}{\varphi(\mathbf{r}_0, 0)}, \quad (14)$$

where  $\mathbf{q}$  is the wave vector variable of the Fourier transform and  $u$  stands for the Laplace variable (the functions with a hat are Fourier transforms and those with a tilde are Laplace transforms).

### 3.1. Fractional Subdiffusive Equation with Evanescence

The first example we shall explore involves the waiting time distribution

$$\psi(t) \sim \frac{\kappa}{\tau_D} \left(\frac{t}{\tau_D}\right)^{-\gamma-1}, \quad (15)$$

with  $0 < \gamma < 1$ . Here  $\kappa$  is a dimensionless constant and  $\tau_D$  is a characteristic mesoscopic time (but not a first moment). By construction, all the integer moments of the above long-tailed waiting time distribution diverge. When combined with a jump distance distribution with finite moments,  $\psi(t)$  gives rise to subdiffusive behavior of the particle. In the limit of small  $u$ , the Laplace transform of  $\psi(t)$  reads as follows:

$$\tilde{\psi}(u) \sim 1 - \mathcal{A}u^\gamma, \quad (16)$$

with  $\mathcal{A} = \gamma^{-1}\kappa\Gamma(1-\gamma)\tau_D^\gamma$ .

In contrast to the waiting time distribution, we shall assume that the jump distance distribution is “normal”, i.e., that it has finite moments. In the limit of small  $q = |\mathbf{q}|$  we can perform the following expansion:

$$\hat{\chi}(\mathbf{q}) \sim 1 - \frac{\sigma^2\mathbf{q}^2}{2} + \mathcal{O}(\mathbf{q}^4), \quad (17)$$

where

$$\sigma^2 = \int d\mathbf{r} \mathbf{r}^2 \chi(\mathbf{r}) \quad (18)$$

is the second moment of the jump length distribution. Substitution of the expansions (16) and (17) into Eq. (14) and neglect of a term of  $\mathcal{O}(u\mathbf{q}^2)$  yields

$$u\hat{\eta}(\mathbf{q}, u) - \frac{e^{i\mathbf{q}\cdot\mathbf{r}_0}}{\varphi(\mathbf{r}_0, 0)} = -u^{1-\gamma} \frac{\sigma^2\mathbf{q}^2}{2\mathcal{A}} \hat{\eta}(\mathbf{q}, u). \quad (19)$$

The corresponding double inversion with respect to the Fourier and Laplace variables gives

$$\frac{\partial\eta(\mathbf{r}, t | \mathbf{r}_0, 0)}{\partial t} = K_\gamma \mathcal{D}_t^{1-\gamma} \nabla_{\mathbf{r}}^2 \eta(\mathbf{r}, t | \mathbf{r}_0, 0), \quad (20)$$

where the anomalous diffusion coefficient is given by

$$K_\gamma = \frac{\sigma^2}{2\mathcal{A}}. \quad (21)$$

The integro-differential operator  ${}_0D_t^{1-\gamma}$  introduced in Eq. (20) is defined via the relation

$$\mathcal{L}_{u \rightarrow t}^{-1} \{u^{1-\gamma} \tilde{y}(u)\} = {}_0D_t^{1-\gamma} y(t), \quad (22)$$

where  $\mathcal{L}_{u \rightarrow t}^{-1}$  denotes the inverse Laplace transform and  $y(t)$  is a time-dependent function. The operator  ${}_0D_t^{1-\gamma}$ , called the Grünwald-Letnikov fractional derivative, is closely related to the Riemann-Liouville operator  ${}_0D_t^{1-\gamma}$ , defined as follows:

$${}_0D_t^{1-\gamma} y(t) = \frac{1}{\Gamma(\gamma)} \frac{\partial}{\partial t} \int_0^t dt' \frac{y(t')}{(t-t')^{1-\gamma}}. \quad (23)$$

When applied to sufficiently regular functions  $y(t)$  fulfilling the condition  $\lim_{t \rightarrow 0} \int_0^t d\tau (t-\tau)^{\gamma-1} y(\tau) = 0$ , the operators  ${}_0D_t^{1-\gamma}$  and  ${}_0D_t^{1-\gamma}$  can be shown to be equivalent (see [19, p. 76]). In practice, this condition is satisfied for all the situations we are interested in here. Thus we shall use the Riemann-Liouville operator.

In terms of the probability density  $w$ , Eq. (20) explicitly yields the fractional reaction-subdiffusion equation

$$\frac{\partial w(\mathbf{r}, t | \mathbf{r}_0, 0)}{\partial t} = \varphi(\mathbf{r}, t) K_\gamma {}_0D_t^{1-\gamma} \nabla_{\mathbf{r}}^2 \frac{1}{\varphi(\mathbf{r}, t)} w(\mathbf{r}, t | \mathbf{r}_0, 0) + \frac{\dot{\varphi}(\mathbf{r}, t)}{\varphi(\mathbf{r}, t)} w(\mathbf{r}, t | \mathbf{r}_0, 0). \quad (24)$$

Equation (24) describes the combination of subdiffusive transport and a class of evanescence processes that, despite the requirement (9), is much more general than would appear at first glance. It actually includes the possibility of a density-dependent reaction rate constant, or an external feedback mechanism resulting in enhancement of the evanescent reaction. While Eq. (24) has been formulated for a single walker, it is straightforward to show that if one initially has one walker or an ensemble of identical walkers, the concentration or number density  $\rho(\mathbf{r}, t)$  satisfies Eq. (24). For a one-particle system, there is a trivial connection between  $\rho(\mathbf{r}, t)$  and  $w(\mathbf{r}, t | \mathbf{r}_0, 0)$ , namely

$$\rho(\mathbf{r}, t) = \int d\mathbf{r}_0 p(\mathbf{r}_0) w(\mathbf{r}, t; \mathbf{r}_0, 0), \quad (25)$$

where  $p(\mathbf{r}_0)$  is the distribution of all possible initial positions for the walker.

At this stage, a technical remark is in order. In deriving Eq. (24) we have followed the standard route used for the case without reaction, namely, an expansion of the relevant integral equation in Fourier-Laplace space. In order for this procedure to be valid in the presence of the evanescence process, the latter has been implicitly assumed to be slow enough so as to allow the walker to perform a sufficiently large number of steps and thus have access to the regime of long times and large displacements, corresponding to small wavevectors and Laplace variables in Fourier-Laplace space.

In passing, we mention that it is possible to derive a reaction-transport equation with a Caputo fractional derivative [19, p. 78] as an alternative to equation (24). Both equations are valid under the same conditions. The equation with the Caputo derivative reads

$$\frac{\partial^\gamma w(\mathbf{r}, t | \mathbf{r}_0, 0)}{\partial t^\gamma} = K_\gamma \nabla_{\mathbf{r}}^2 \frac{w(\mathbf{r}, t | \mathbf{r}_0, 0)}{\varphi(\mathbf{r}, t)}. \quad (26)$$



### 3.2. Subdiffusion with Specific Types of Evanescence

The simplest type of evanescence contained in Eq. (24) is the exponential case,  $\varphi(\mathbf{r}, t) \propto \exp(-\lambda t)$ . With this choice, the results of Sokolov et al. [5] and Henry et al. [6] are recovered. However, significantly more complex forms of evanescence are also included. For instance, the case of a position dependent reactivity is immediately obtained if one takes  $\varphi(\mathbf{r}, t) \propto \exp(-\lambda(\mathbf{r})t)$ . We consider the following particular choice:

$$\varphi(\mathbf{r}, t) = \exp \left\{ \int_{\tau}^t \Re[\rho(\mathbf{r}, t')] dt' \right\}. \quad (27)$$

The time  $\tau$  in Eq. (27) is an arbitrary reference time. In the language of ref. [8], this corresponds to an evanescence reaction that follows a local law of mass action of the form  $\dot{\rho} = \Re(\rho)\rho$ . The rate coefficient

$$\Re[\rho(\mathbf{r}, t)] = \left[ \frac{\dot{\rho}}{\rho} \right]_{\text{Reaction}} < 0 \quad (28)$$

is thus given by the logarithmic derivative of  $\varphi(\mathbf{r}, t)$ . In general, the rate coefficient may depend on the density itself, thus leading to an interesting nonlinear problem. To make the connection with previous work, we note that substitution of Eq. (27) with the specific choice  $\tau = 0$  into our general equation (24) for the one-dimensional case, and subsequent integration over the initial condition, yields Eq. (23) in ref. [8].

A simplified version of the above problem arises if the rate coefficient depends *only* on the global density

$$\bar{\rho}(t) = \frac{1}{V} \int d\mathbf{r} \rho(\mathbf{r}, t), \quad (29)$$

where  $V$  stands for the system volume. One then has

$$\Re(\bar{\rho}(t)) = \frac{1}{\bar{\rho}} \frac{d\bar{\rho}}{dt}, \quad (30)$$

and (taking  $\tau = 0$ )

$$\varphi(\mathbf{r}, t) = \varphi(t) = \exp \left\{ \int_0^t \Re(\bar{\rho}(t')) dt' \right\} = \frac{\bar{\rho}(t)}{\bar{\rho}(0)}. \quad (31)$$

In this case,  $\varphi(t)$  has a clear physical interpretation. In a single-particle system this can be interpreted as the survival probability of the particle up to time  $t$ . In a many-particle system, it can be interpreted as the fraction of surviving particles. As a result of Eq. (9), the probability  $\Xi(t, t')$  that a randomly chosen evanescent particle present in the system at time  $t'$  survives up to time  $t$  is  $\bar{\rho}(t)/\bar{\rho}(t')$ . This is consistent with what one would expect from the interpretation of  $\Xi(t, t')$  as a conditional probability: the survival probability  $\bar{\rho}(t)/\bar{\rho}(0)$  of a given particle up to time  $t$  must be equal to the probability  $\Xi(t, t')$  that it does not die during the interval  $(t', t)$  provided that it survived up to time  $t'$ , times the probability  $\bar{\rho}(t')/\bar{\rho}(0)$  for this condition to be fulfilled. Using Eq. (31) in Eq. (24), one finds that the kinetics of individual particles subject to a density-dependent homogeneous rate coefficient is dictated by the reaction-subdiffusion equation

$$\frac{\partial w(\mathbf{r}, t | \mathbf{r}_0, 0)}{\partial t} = \bar{\rho}(t) K_{\gamma} D_t^{1-\gamma} \nabla_{\mathbf{r}}^2 \frac{1}{\bar{\rho}(t)} w(\mathbf{r}, t | \mathbf{r}_0, 0) + \frac{\dot{\bar{\rho}}(t)}{\bar{\rho}(t)} w(\mathbf{r}, t | \mathbf{r}_0, 0). \quad (32)$$

In Sec. 4, we show that Eq. (32) can be used to set up the boundary value problem for the survival probability of an evanescent diffusing particle in the presence of a fully absorbing target. One can subsequently use this equation to compute the survival probability of the target, both in the presence of a single evanescent diffusive particle and of a collection thereof. Such target problems are of great importance in biological systems where diffusive transport is at play.

Finally, we note that, in more general terms, Eq. (24) also allows for the possibility of an *external* control mechanism of the evanescence reaction not necessarily coupled to the instantaneous particle population. Indeed, one can prescribe a reactivity field  $\Re(\mathbf{r}, t) < 0$  and subsequently set  $\varphi(\mathbf{r}, t) = \exp \left\{ \int_0^t \Re(\mathbf{r}, t') dt' \right\}$ , which is then the survival probability of the particle up to time  $t$  given that it stays at  $\mathbf{r}$  all the time (immobile reactant limit). Consequently, our assumption (9) implies that the probability for a particle to vanish during the time interval  $(t', t)$  if it is known to be at position  $\mathbf{r}'$  at time  $t'$  and at position  $\mathbf{r}$  at time  $t$  depends only on the instantaneous values of the local rate coefficient at the start and end points via the ratio of the associated survival probabilities for particles respectively fixed at  $\mathbf{r}'$  and  $\mathbf{r}$ . The survival probability does not depend on the particular trajectory of the particle between these two points.

### 3.3. Fractional Superdiffusive Equation with Evanescence

In Section 3.1 we derived a rather general reaction-subdiffusion equation using a waiting time distribution with long tails together with a “normal” distribution of displacements. In contrast, we now consider a “normal” waiting time distribution along with a distribution of displacements that has long tails. In this case, the transport turns out to be superdiffusive.

The waiting time distribution we consider has a finite mean  $\tau$ , implying that the small  $u$  behavior of the Laplace transform (corresponding to long times) is

$$\tilde{\psi}(u) \sim 1 - \tau u. \quad (33)$$

The jump length distribution is assumed to behave as follows:

$$\chi(\mathbf{r}) \sim \frac{\sigma^\mu}{r^{1+\mu}} \quad (34)$$

with  $1 \leq \mu \leq 2$  and  $r = |\mathbf{r}|$ . As a result of this choice, the variance diverges. The Fourier transform of the jump length distribution is

$$\hat{\chi}(\mathbf{q}) \sim 1 - \sigma^\mu q^\mu, \quad (35)$$

where  $q = |\mathbf{q}|$ . Once again taking Eq. (14) as a starting point, one straightforwardly obtains (upon retention of the leading terms)

$$u \hat{\eta}(\mathbf{q}, u) - \frac{e^{i\mathbf{q} \cdot \mathbf{r}_0}}{\varphi(\mathbf{r}_0, 0)} = -\frac{\sigma^\mu}{\tau} q^\mu \hat{\eta}(\mathbf{q}, u), \quad (36)$$

or, inverting the time Laplace transform,

$$\frac{\partial}{\partial t} \hat{\eta}(\mathbf{q}, t) = -\frac{\sigma^\mu}{\tau} q^\mu \hat{\eta}(\mathbf{q}, t). \tag{37}$$

Let  $\partial^\mu / \partial r^\mu$  be the operator defined by the Fourier transform property,

$$\mathfrak{F} \left\{ \frac{\partial^\mu f(\mathbf{r})}{\partial r^\mu} \right\} = -q^\mu f(\mathbf{q}). \tag{38}$$

We can thus write

$$\frac{\partial \eta(\mathbf{r}, t | \mathbf{r}_0, 0)}{\partial t} = K \frac{\partial^\mu}{\partial r^\mu} \eta(\mathbf{r}, t | \mathbf{r}_0, 0), \tag{39}$$

where we have introduced the anomalous diffusion coefficient

$$K = \frac{\sigma^\mu}{\tau}. \tag{40}$$

For a one-dimensional system,  $\partial^\mu / \partial r^\mu = \partial^\mu / \partial x^\mu$  is identical to the Riesz operator [16–18].

Undoing the transformation (13), we obtain the following fractional reaction-superdiffusion equation:

$$\frac{\partial w(\mathbf{r}, t | \mathbf{r}_0, 0)}{\partial t} = \varphi(\mathbf{r}, t) K \frac{\partial^\mu}{\partial r^\mu} \frac{1}{\varphi(\mathbf{r}, t)} w(\mathbf{r}, t | \mathbf{r}_0, 0) + \frac{\dot{\varphi}(\mathbf{r}, t)}{\varphi(\mathbf{r}, t)} w(\mathbf{r}, t | \mathbf{r}_0, 0). \tag{41}$$

### 3.4. Bifractional Equation with Evanescence

Finally, in this subsection we combine subdiffusion and superdiffusion by choosing a waiting time distribution that lacks finite moments (and thus leads to subdiffusion by itself) with a jump distance distribution that also lacks moments (and thus leads to superdiffusion by itself). Our methodology directly lends itself to this combination.

We choose the waiting time distribution of Eq. (15) whose Laplace transform is given in Eq. (16), and the jump distribution Eq. (34) whose Fourier transform is given in Eq. (35). The steps to follow are now essentially the same as in the previous sections, with appropriate care given to the retention of the leading contributions. After some algebra we find

$$\frac{\partial \eta(\mathbf{r}, t | \mathbf{r}_0, 0)}{\partial t} = K {}_0D_t^{1-\gamma} \frac{\partial^\mu}{\partial r^\mu} \eta(\mathbf{r}, t | \mathbf{r}_0, 0). \tag{42}$$

Undoing the transformation (13), we obtain the fractional reaction-sub/superdiffusion equation,

$$\frac{\partial w(\mathbf{r}, t | \mathbf{r}_0, 0)}{\partial t} = \varphi(\mathbf{r}, t) K {}_0D_t^{1-\gamma} \frac{\partial^\mu}{\partial r^\mu} \frac{1}{\varphi(\mathbf{r}, t)} w(\mathbf{r}, t | \mathbf{r}_0, 0) + \frac{\dot{\varphi}(\mathbf{r}, t)}{\varphi(\mathbf{r}, t)} w(\mathbf{r}, t | \mathbf{r}_0, 0). \tag{43}$$

This is our third mesoscopic result and is unique in that it combines both subdiffusion and superdiffusion in a single equation. The behavior of the rescaled mean square displacement depends on the relative values of  $\gamma$  and  $\mu$ .

## 4. Applications

We now turn to two specific examples where the reaction-subdiffusion equation (32) proves to be useful. The first one concerns the survival probability of an immobile target that is surrounded by one or more subdiffusively moving particles (also called traps) that disappear spontaneously in the course of their motion. The second example refers to the formation of morphogen gradients, which are crucial in embryogenesis.

### 4.1. The Target Problem with Evanescent Traps

#### 4.1.1. The Single-trap Problem

We consider a target of radius  $R$  centered at the origin  $\mathbf{r} = 0$  of a  $d$  dimensional volume  $V$  and an evanescent subdiffusive point trap placed at an initial position  $\mathbf{r}_0$  inside  $V$ . In three dimensions the target is spherical, in two dimensions it is circular, and in one dimension it is a line. Unless otherwise specified, the survival probability of the trap will hereafter be assumed to decay exponentially,  $\varphi(t) = e^{-\lambda t}$ , in the absence of the target. In other words, the associated (global) number density  $\bar{\rho}(t)$  obeys the following first-order differential equation:

$$\dot{\bar{\rho}}(t) \equiv \frac{d\bar{\rho}(t)}{dt} = -\lambda \bar{\rho}(t). \quad (44)$$

Since the trap may evanesce as it moves, the behavior of the trap is described by Eq. (32). The target is impenetrable and is killed by the trap as soon as the latter hits the target surface. We are interested in the survival probability  $Q_{1,tg}(\mathbf{r}_0, t; R)$  of the target up to time  $t$ . The trap will also be assumed to disappear as soon as it hits the target (pairwise annihilation). The survival probability  $Q_1(\mathbf{r}_0, t; R) = \int w(\mathbf{r}, t | \mathbf{r}_0; 0) d\mathbf{r}$  of the trap can be shown to be related to  $Q_{1,tg}(\mathbf{r}_0, t; R)$  by the following equation [20, 21]:

$$Q_{1,tg}(\mathbf{r}_0, t; R) = Q_1(\mathbf{r}_0, t; R) + \lambda \int_0^t Q_1(\mathbf{r}_0, t'; R) dt'. \quad (45)$$

The survival probability of the target is greater than that of the trap, as the trap has a second decay channel due to the spontaneous death process described by Eq. (44). Now, the strategy to obtain  $Q_{1,tg}(\mathbf{r}_0, t; R)$  consists of first solving the boundary value problem

$$\frac{\partial Q_1(\mathbf{r}_0, t; R)}{\partial t} = e^{-\lambda t} K_\gamma {}_0D_t^{1-\gamma} e^{\lambda t} \nabla_{\mathbf{r}_0}^2 Q_1(\mathbf{r}_0, t; R) - \lambda Q_1(\mathbf{r}_0, t; R) \quad (46a)$$

$$Q_1(\mathbf{r}_0, 0; R) = 1, \quad (46b)$$

$$Q_1(R, t; R) = 0, \quad (46c)$$

$$Q_1(\mathbf{r}_0 \rightarrow \infty, t; R) = e^{-\lambda t}. \quad (46d)$$

The detailed solution can be found in ref. [21]. In dimensions  $d = 1, 3$  one arrives at the following long-time expression:

$$Q_{1,tg}(r_0, \infty; R) - Q_{1,tg}(r_0, t; R) \sim - \left( \frac{R}{r_0} \right)^{(d-1)/2} \frac{1}{\Gamma(1 - \frac{\gamma}{2})} \frac{r_0 - R}{\lambda^{1+\frac{\gamma}{2}} \ell_\gamma} t^{-1-\frac{\gamma}{2}} e^{-\lambda t}, \quad (47)$$

where  $\ell_\gamma = (4K_\gamma/\lambda^\gamma)^{1/2}$  is a length scale associated with the typical distance explored by the trap before decaying spontaneously. The asymptotic survival probability of the target in  $d = 1, 3$  is

$$Q_{1,tg}(r_0, \infty; R) = 1 - \left( \frac{R}{r_0} \right)^{(d-1)/2} e^{-2(r_0-R)/\ell_\gamma}. \quad (48)$$

In  $d = 2$  the long-time decay is more complex. It has the following form:

$$Q_{1,tg}(r_0, t; R) \sim Q_{1,tg}(r_0, \infty; R) + \frac{2}{\gamma} \ln \left( \frac{r_0}{R} \right) \frac{e^{-\lambda t}}{\lambda t \ln^2(\alpha_\gamma t)} \quad (49)$$

with  $\alpha_\gamma = (4K_\gamma/R^2)^{1/\gamma}$  and

$$Q_{1,tg}(r_0, \infty; R) = 1 - \frac{\mathcal{K}_0(2r_0/\ell_\gamma)}{\mathcal{K}_0(2R/\ell_\gamma)}, \quad (50)$$

where  $\mathcal{K}_\nu$  stands for a modified Bessel function of the second kind of order  $\nu$ .

Note that in  $d = 1, 2$  the target has a finite survival probability due to the evanescence of the trap. In contrast, if the trap were non-evanescent ( $\lambda = 0$ ), the target would eventually be killed with certainty because of the compact space exploration of a random walker in one and two dimensions.

#### 4.1.2. The Many-trap Problem

Let us now extend the results in Section 4.1.1 to the case where the target centered at  $\mathbf{r} = 0$  is surrounded by a collection of  $N_0$  point traps moving independently of one another. The traps are assumed to be evanescent and randomly distributed in a spherical volume  $V$  (or circular area or line, depending on dimension) around  $\mathbf{r} = 0$ . At time  $t = 0$  they begin to move (and decay) according to Eq. (32). As in the single trap problem, we assume that whenever any of the traps hits the target, both reaction partners are annihilated. Our goal is once again to compute the survival probability  $Q_{tg}(t)$  of the target, that is, the probability that none of the traps has collided with the target surface up to time  $t$ .

Since the traps are statistically independent, we can write the solution in terms of the single-trap problem discussed previously. One has

$$Q_{tg}(t; R) = \left[ \frac{1}{V} \int_{r_0 > R} Q_{1,tg}(\mathbf{r}_0, t; R) d\mathbf{r}_0 \right]^{N_0}. \quad (51)$$

We focus on the thermodynamic limit  $N_0 \rightarrow \infty, V \rightarrow \infty$ , which implies fixing the initial global trap density  $\bar{\rho}_0 \equiv \bar{\rho}(0) = \lim_{N_0, V \rightarrow \infty} N_0/V$ . We already know the solution for  $Q_{1,tg}$  in the infinite volume case, so in that limit we find

$$Q_{tg}(t; R) = \exp \left\{ -\bar{\rho}_0 R^d \sigma(t, R) \right\}, \quad (52)$$

where we have introduced the auxiliary quantity

$$\sigma(t; R) \equiv \frac{1}{R^d} \int_{r_0 > R} [1 - Q_{1,tg}(\mathbf{r}_0, t; R)] d\mathbf{r}_0. \quad (53)$$

We note that the quantity  $R^d \sigma(t, R)$  is directly related to the average volume explored by a *single* evanescent trap up to time  $t$ , see e.g., refs. [22] and [23].

One can now employ the explicit expressions of the Laplace transform of  $Q_{1,tg}$ , perform the integration over  $\mathbf{r}_0$ , and finally make use of Tauberian theorems to find the long-time behavior of  $Q_{tg}$ . In terms of  $\sigma(t; R) = -(\bar{\rho}_0 R^d)^{-1} \ln Q_{tg}(t; R)$  one has

$$\sigma(\infty; R) - \sigma(t; R) \propto \begin{cases} t^{\gamma/2-1} e^{-\lambda t}, & d = 1, \\ \ln^{-1}(\alpha_\gamma t) t^{\gamma-1} e^{-\lambda t}, & d = 2, \\ t^{\gamma-1} e^{-\lambda t}, & d = 3, \end{cases} \quad (54)$$

with  $\sigma(\infty; R) = \ell_\gamma/R$  for  $d = 1$ ,  $\sigma(\infty; R) = (2\pi\ell_\gamma/R)(1 + \ell_\gamma/2R)$  for  $d = 3$  and  $\sigma(\infty; R) = 2\pi(\ell_\gamma/2R) \mathcal{K}_1(2R/\ell_\gamma)/\mathcal{K}_0(2R/\ell_\gamma)$  for  $d = 2$  (details can be found in refs. [20] and [21]). These are particular cases of the general  $d$ -dimensional expression

$$\sigma(\infty; R) = S_d \frac{\ell_\gamma}{2R} \frac{\mathcal{K}_{d/2}(2R/\ell_\gamma)}{\mathcal{K}_{d/2-1}(2R/\ell_\gamma)}, \quad (55)$$

where  $S_d = 2\pi^{d/2}/\Gamma(d/2)$  denotes the surface of a  $d$ -dimensional hypersphere of unit radius. Thus, the asymptotic survival probability of the target is *finite* in all dimensions despite the infinite initial number of traps. The physical reason for this is the evanescent character of the traps, in the absence of which the final survival probability of a target surrounded by a collection of uncorrelated traps is zero in all dimensions. In the absence of evanescence, the target is eventually killed in all spatial dimensions [24].

Interestingly, the survival probability  $Q_{tg}(t; R)$  obtained from Eq.(55) displays non-monotonic behavior as a function of dimensionality. Figure 1 displays a plot of  $\sigma(\infty; R)$  as a function of  $d$  for three different values of the dimensionless parameter  $z = 2R/\ell_\gamma$ . It is seen that  $\sigma(\infty; R)$  first increases and then decreases with increasing  $d$ , implying the opposite behavior of  $Q_{tg}(t; R)$ . We note the behavior in the limit  $d \rightarrow \infty$ . Using the asymptotic expansion

$$\mathcal{K}_\alpha(z) \sim \frac{\Gamma(\alpha)}{2} \left( \frac{2}{z} \right)^\alpha, \quad (56)$$

valid for  $\alpha > 0$  and  $0 < z \ll \sqrt{\alpha + 1}$ , one sees that  $\sigma(\infty; R)$  tends to zero in this limit, implying  $Q_{tg}(t; R) \rightarrow 1$ . For large values of  $d$ , the traps are more likely to perform long excursions and die in the course of these excursions before they are able to hit the target.

It is also possible to obtain the long time expression for  $\sigma(\infty; R)$  in the case of a general global density decay  $\bar{\rho}(t)$ . To this end, Eq. (45) must be replaced by the more general equation

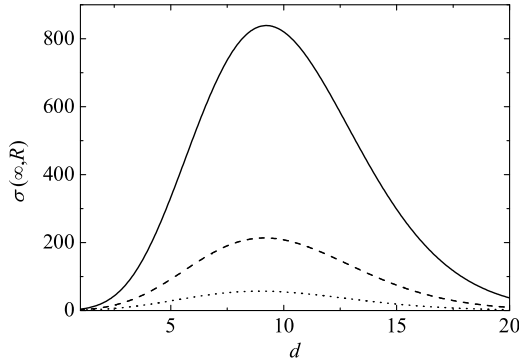


Figure 1. Behavior of  $\sigma(\infty; R)$  as a function of  $d$   $z = 0.5$  (solid line),  $z = 1$  (dashed line) and  $z = 3$  (dotted line).

$$Q_{1,tg}(r, t; R) = Q_1(r, t; R) - \int_0^t Q_1(r, t'; R) \frac{\dot{\bar{\rho}}(t')}{\bar{\rho}(t')} dt'. \quad (57)$$

Using this equation in the definition (53) in combination with (32), one finds

$$\sigma(t; R) = S_d \frac{K_\gamma}{R} \int_0^t \left[ {}_0D_{t'}^{1-\gamma} \frac{1}{\bar{\rho}(t')} \frac{\partial Q_1(r, t'; R)}{\partial r} \Big|_{r=R} \right] \bar{\rho}(t') dt', \quad (58)$$

where the Gauss theorem was used to convert the volume integral resulting from Eq. (53) into a surface integral. From the specific form of  $Q_1$  for  $d = 1$  one finds [20, 21]

$$\sigma(t; R) = \frac{1}{\bar{\rho}_0 R} \frac{2\sqrt{K_\gamma}}{\Gamma(\gamma/2)} \int_0^t \bar{\rho}(t') t'^{\gamma/2-1} dt'. \quad (59)$$

Likewise, using the expression for  $Q_1$  for  $d = 3$  we obtain [20, 21]

$$\sigma(t; R) = \frac{4\pi\sqrt{K_\gamma}}{\bar{\rho}_0 R \Gamma(\gamma/2)} \int_0^t \bar{\rho}(t') t'^{\gamma/2-1} dt' + \frac{4\pi K_\gamma}{\bar{\rho}_0 R^2 \Gamma(\gamma)} \int_0^t \bar{\rho}(t') t'^{\gamma-1} dt'. \quad (60)$$

In contrast, for  $d = 2$  only a long-time expression is available (provided that  $\bar{\rho}(t)$  decays sufficiently fast):

$$\sigma(\infty; R) - \sigma(t; R) \sim \frac{4\pi K_\gamma}{\bar{\rho}_0 R^2 \Gamma(\gamma + 1)} \int_t^\infty \frac{\bar{\rho}(t') t'^{\gamma-1}}{\ln(\alpha_\gamma t')} dt', \quad (61)$$

where to the best of our knowledge the exact expression for  $\sigma(\infty; R)$  is in general unknown.

## 4.2. Morphogen Gradient Formation

Morphogens are special signaling molecules that are secreted at a specific location in the embryo and subsequently disseminate through the tissue. One current understanding of the

morphogenesis process suggests that different target genes in an embryonic cell are activated above certain concentration thresholds, resulting in a different development and fate of different cells depending on the local morphogen concentration that they sense [25, 26]. According to this mechanism, cell differentiation in embryos thus requires the preexistence of a morphogen gradient controlled by the morphogen secretion rate, the transport properties of morphogens, and their degradation pathways. Traditional synthesis-diffusion-degradation models are based on the classical reaction-diffusion equation

$$\frac{\partial \rho(x, t)}{\partial t} = D \frac{\partial^2}{\partial x^2} \rho(x, t) - \lambda \rho(x, t), \quad (62)$$

where  $\rho(x, t)$  is the local concentration of morphogens,  $\lambda$  is the degradation rate constant, and  $D$  is the diffusion coefficient in the case of ordinary Brownian motion (because of the high degree of symmetry in experiments, one often restricts the analysis to an effectively one-dimensional setting as above). However, the dissemination process of morphogens is more complex than a Fickian diffusion process. Indeed, some of the transport routes are likely to involve binding and unbinding to surface receptors and transcytosis in the complex intracellular environment [25], resulting in long characteristic waiting times. There is also reason to believe that the distribution of those waiting times displays significant dispersion, a rather common feature in biological systems. Under these circumstances a phenomenological description in terms of a CTRW with a long-tailed waiting time distribution and a concomitant degradation process becomes a plausible picture. In ref. [27], a mesoscopic reaction-transport model was developed that becomes equivalent to Eq. (32) in the case of a constant degradation rate  $\lambda$ . In this case, one can go beyond the ordinary diffusion case described by Eq. (62) by using the equation<sup>1</sup>

$$\frac{\partial \rho(x, t)}{\partial t} = e^{-\lambda t} K_{\gamma} D_t^{1-\gamma} \frac{\partial^2}{\partial x^2} e^{\lambda t} \rho(x, t) - \lambda \rho(x, t). \quad (63)$$

The above equation is solved assuming a constant injection  $j_0$  of secreted morphogens at, say,  $x = 0$ . Typically, one neglects other boundary effects and assumes that one is dealing with an infinite system. The solution of the corresponding boundary value problem can be expressed in terms of the propagator solution  $G(x, t)$  corresponding to the deterministic initial condition  $\rho(x, t) = \delta(x)$ . The solution reads

$$\rho(x, t) = j_0 \int_0^t G(x, t - t') dt'. \quad (64)$$

Our formulation yields stationary concentration profiles  $\rho_s(x) = \lim_{t \rightarrow \infty} \rho(x, t)$ . Note that this is by no means a universal feature; in our model, we have assumed that degradation may occur at any time. Models assuming that morphogen degradation occurs only at the time of a jump have also been implemented [28, 29], but in general they do not lead to a steady state solution [28]. Returning to our case, the stationary profile can easily be found from the solution of the corresponding boundary value problem in Laplace space and the subsequent application of the final value theorem. Details can be found in refs. [11] and [27]. One finds exponentially decaying stationary profiles of the form [27]

<sup>1</sup>Note the interesting feature that Eq. (63) can be cast into a pure transport equation by means of a rescaling of the concentration, i.e.,  $u(x, t) = e^{\lambda t} \rho(x, t)$ .



$$\rho_s(x) = \frac{j_0 \lambda^{\gamma/2-1}}{2 \sqrt{K_\gamma}} \exp[-|x|/\Lambda], \quad 0 < \gamma < 1, \quad (65)$$

where the decay length is  $\Lambda = \sqrt{K_\gamma/\lambda^\gamma}$ .

Equation (65) generalizes the well-known stationary exponential profile found for normal diffusion [26], which is simply this result if one takes  $\gamma = 1$  and sets  $K_1 \equiv D$ . This shows that the same characteristic decay length may be obtained with different combinations of the parameters  $K_\gamma$ ,  $\lambda$  and  $\gamma$ , which are difficult to measure individually. We thus conclude that the exponentially decaying experimentally observed profiles are not only compatible with Fickian diffusion, but also with non-Markovian generalizations thereof.

Moreover, in ref. [27] it has been shown that if the characteristic degradation time  $\lambda^{-1}$  is large in comparison with the typical stepping time  $\tau_D$  of the underlying CTRW, the robustness of the profile against fluctuations in the morphogen secretion rate  $j_0$  increases with decreasing  $\gamma$ . In the small  $\gamma$  regime, it would appear that subdiffusion enhances the stability of the concentration profile. Needless to say, a mechanism for dampening the effects of accidental fluctuations in the morphogen secretion rate is crucial for a proper development of the embryo.

A question of interest in the above context is whether similar results are obtained when the rate constant of the evanescence process becomes density-dependent, a non-linear problem that is also described by our equations. Recent research has focused on the form of the morphogen concentration profiles in this case [30, 31]. These interesting studies concern specific realizations of the microscopic reaction and transport processes. The next step will be to ascertain the influence of the model details on the robustness of the concentration profiles by performing comparative studies.

## 5. Summary and Outlook

In this work we have presented the derivation of rather general reaction-subdiffusion and reaction-superdiffusion equations starting from a CTRW description of particles that die as they walk, or as they wait to walk. The reaction term describing the death or evanescence of the particles may in general depend on both position and time. An explicit dependence of the rate constant on the particle density is not excluded either, hence the problem is in general a nonlinear one. The final form of the resulting fractional reaction-transport equations is not particularly intuitive, as the reaction rate constant appears explicitly in the transport term.

Two interesting applications of our reaction-subdiffusion equation have been considered, namely, the survival probability of a target surrounded by one or many decaying subdiffusive particles, and the formation of stationary morphogen gradients. However, our fractional equations can be applied to many other interesting problems by considering different initial conditions and boundary conditions.

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