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Transport equations for subdiffusion with nonlinear particle interaction

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HIGHLIGHTS

- A microscopic stochastic model for subdiffusion with nonlinear interaction (volume filling and adhesion) is developed.
- Macroscopic governing differential equations are derived which are consistent with the microscopic stochastic model.
- Examples of stationary particle densities are computed which are subject to anomalous aggregation and nonlinear interaction.

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ABSTRACT

We show how the nonlinear interaction effects 'volume filling' and 'adhesion' can be incorporated into the fractional subdiffusive transport of cells and individual organisms. To this end, we use microscopic random walk models with anomalous trapping and systematically derive generic *non-Markovian and nonlinear* governing equations for the mean concentrations of the subdiffusive cells or organisms. We uncover an interesting interaction between the nonlinearities and the non-Markovian nature of the transport. In the subdiffusive case, this interaction manifests itself in a nontrivial combination of nonlinear terms with fractional derivatives. In the long time limit, however, these equations simplify to a form without fractional operators. This provides an easy method for the study of aggregation phenomena. In particular, this enables us to show that volume filling can prevent "anomalous aggregation," which occurs in subdiffusive systems with a spatially varying anomalous exponent.

1. Introduction

Stochastic models for the diffusive motion of biological cells and organisms are well established in the mathematical biology community. Random walk models, stochastic differential equations and their governing nonlinear partial differential equations have been very successful from a mathematical modelling standpoint. They provide tractable means to incorporate various taxis effects such as the directed transport along the concentration gradient of external signals (Othmer and Hillen, 2002; Hillen and Painter, 2009; Stevens, 2000), particle generation and degradation rates which depend on particle concentrations (Murray, 2007; Oelschläger, 1989), density dependent dispersal rates (Méndez et al., 2012; Murray, 2007), volume exclusion effects (Painter and Hillen, 2002; Simpson and Baker, 2011; Fernando et al., 2010), and adhesion between particles (Anguige, 2011; Armstrong et al., 2006; Johnston et al., 2012). A defining feature of most such nonlinear reaction–diffusion-taxis equations is that the macroscopic transport processes involving diffusion and advection are derived from microscopic Markovian random walk models; see the excellent review by Stevens and Othmer (1997). However, this does not fit well with anomalous non-Markovian subdiffusive systems, for which the transport operators are non-local in time and the mean squared displacement of individual particles grows proportionally to t^{μ}, where $0<\mu<1$ (Metzler and Klafter, 2000). Anomalous transport occurs microscopically on the level of individual cells, e.g. for the transport of macromolecules within living cells (Golding and Cox, 2006; Tolić-Nørrelykke et al., 2004; Weiss et al., 2004; Banks and Fradin, 2005). Moreover, it has been found that the motion of individual cells is anomalously diffusive (Dieterich et al., 2008; Mierke et al., 2011; Fedotov et al., 2013).

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The main mathematical models for subdiffusive dynamics are the Continuous Time Random Walk (CTRW) and fractional Brownian motion (fBm). Both processes are non-Markovian, unlike Brownian motion. The CTRW appears to be the most popular model for anomalous dynamics (Metzler and Klafter, 2000), presumably because it admits a tractable PDE formalism (Barkai et al., 2000; Henry et al., 2010). However, it should be noted that most articles on anomalous transport deal with linear fractional PDEs without particle interactions. Unlike for Markovian dynamics, it is challenging to incorporate nonlinearities into the subdiffusive PDEs. For instance, even if the particle death rate is bounded below, by naively adding a degradation term to the PDE one can achieve negative particle concentrations (Henry et al., 2006). Transport equations for CTRWs with nonlinear reactions have only recently been derived (Mendez et al., 2010; Angstmann et al., 2013). Apart from an article by one of the authors (Fedotov, 2013), to our knowledge, particle interactions have not yet been incorporated into the CTRW framework. The challenge is to take into account non-linear effects: volume exclusion (Painter and Hillen, 2002) and adhesion (Anguige, 2011) together with subdiffusive transport.

The main purpose of this article is to systematically derive generic *non-Markovian and non-linear* integro-differential equations for the mean concentration of particles such as randomly moving cells or individual organisms. Our aims are: (i) to understand the interaction of non-Markovian transport and nonlinearities due to volume filling and adhesion effects and (ii) to find the stationary solutions of nonlinear non-Markovian transport equations that describe aggregation phenomena.

On our way towards goal (i), we give a formalism which connects nonlinearly interacting microscopic CTRWs with nonlinear and non-Markovian diffusion equations. As it turns out, our formalism also applies to the situation where the anomalous exponent μ, which governs the trapping behaviour of the CTRW, varies in space (Chechkin et al., 2005). This situation is very significant for biology because it may explain the widespread phenomenon of anomalous accumulation of bacteria in particular patches. One example is the aggregation of phagotrophic protists (Fenchel and Blackburn, 1999), where "cells become immobile in attractive patches, which will then eventually trap all cells." Another example is the formation of nodules on the roots of nitrogen-fixing plants that contain the colony of nitrogen-fixing bacteria (Wadhams and Armitage, 2004).

It is well known that the movement of bacteria in environments with varying favorability is in the most cases determined by chemokinesis rather than chemotaxis. The reason for this is that typically the bacteria/cells are too small to sense the macroscopic gradient of a chemotactic substance $S(x)$ (Erban and Othmer, 2005). Hence a model for the random motility of microorganisms should take into account the dependence of the transition probability γ on the nonuniformly distributed concentration $S(x)$, rather than the dependence of a cell's jump direction on the gradient $\partial S/\partial x$. With this in mind, CTRWs with space-varying anomalous exponent μ arise very naturally as models for chemokinesis: suppose that $\mu=\mu(S(x))$ is a decreasing function of a favourable substance with concentration $S(x)$. Then the transition probability γ (i.e. the probability of a jump away from x) equals

$$\gamma(\tau,S(x))=\frac{\mu(S(x))}{\tau_0+\tau},$$

where τ is the residence time and τ_0 is a constant (see Eq. (14)). Hence the rate at which a bacterium jumps away from a favourable environment at x is small, which leads to the phenomenon of anomalous aggregation (Fedotov and Falconer, 2012).

The setup is as follows: In Section 2 we quickly reiterate the derivation of nonlinear Markovian transport equations from microscopic stochastic models. Section 3 contains a quick overview over the anomalous sub-diffusion literature and fractional diffusion equations. In Section 4 we use the structured density approach and recover Markovian methods for CTRWs; this allows for the derivation of nonlinear differential equations involving subdiffusion. Finally, in Section 5 we give examples of stationary solutions to nonlinear fractional PDEs that describe the aggregation phenomenon.

2. Markovian transport with nonlinear particle interaction

In this section, we briefly review the standard derivation of nonlinear diffusion equations, starting from a microscopic random walk model. For simplicity, we consider a one dimensional lattice of sites x which are evenly spaced with spacing h. We study the dynamics of the concentration $\rho(x,t)$ of particles (e.g. cells and bacteria). We assume that particles perform instantaneous jumps to neighbouring lattice sites. We write $T^+(x,t)$ and $T^-(x,t)$ for the rates of jumps to the right resp. left. Rates are instantaneous and may vary in space x and in time t. The total jump rate is then $T(x,t):=T^+(x,t)+T^-(x,t)$. The master equation for $\rho(x,t)$ reads

$$\frac{\partial\rho(x,t)}{\partial t}=T^+(x-h,t)\rho(x-h,t)+T^-(x+h,t)\rho(x+h,t)-T(x,t)\rho(x,t). \tag{1}$$

Transport models for diffusion, chemotaxis, volume filling and adhesion have been studied by Anguige (2011), Anguige and Schmeiser (2009) and Painter and Hillen (2002). A general model which accommodates all the above effects is given by

$$T^{\pm}(x,t)=\lambda_0(1-[S(x\pm h,t)-S(x,t)])q(\rho(x\pm h,t))a(\rho(x\mp h,t)) \tag{2}$$

Here, λ_0 is the rate parameter, and $S(x,t)$ is a spatio-temporally varying external signal (e.g. a chemoattractant or chemorepellent concentration). The functions $q(\rho)$ and $a(\rho)$ model volume filling and adhesion phenomena; they are decreasing with respect to the concentration density $\rho(x,t)$ and map to values in $[0,1]$. The volume filling function $q(\rho(x,t))$ can be interpreted as the probability that a particle will be accommodated at x, should it attempt to jump there at time t. With the remaining probability $1-q(\rho(x,t))$, it will not find enough room at x and hence will not jump. Similarly, the adhesive effect is modelled with the function $a(\rho(x,t))$: Given that a particle attempts to jump from x to $x+h$ at time t, it succeeds in jumping there with probability $a(\rho(x-h,t))$. With probability $1-a(\rho(x-h,t))$, it will stay "glued" to the particles at position $x-h$ and thus not jump.

Eq. (1) governs the evolution of the concentration $\rho(x,t)$ on the discrete lattice. We perform a Taylor expansion in the lattice spacing h (see appendix) and consider the spatiotemporal scaling limit:

$$h\downarrow 0,\quad \lambda_0\uparrow\infty,\quad h^2\lambda_0\to D_0. \tag{3}$$

The particle concentration is then governed by the nonlinear advection–diffusion equation:

$$\frac{\partial\rho}{\partial t}=\frac{\partial}{\partial x}\left[D(\rho)\frac{\partial\rho}{\partial x}-\rho v(\rho)\right] \tag{4}$$