Anomalous transport and nonlinear fractional subdiffusive equations

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Ginzburg Conference on Physics

Content

1. INTRODUCTION
   - Reaction-advection-diffusion PDE's, fractional PDE's and underlying random processes
   - Subdiffusion in spiny dendrites and proteins on cell membrane
   - Fractional PDE's and random walks

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   - Reaction-advection-diffusion PDE's, fractional PDE's and underlying random processes
   - Subdiffusion in spiny dendrites and proteins on cell membrane
   - Fractional PDE's and random walks
2. NON-LOCAL IN SPACE AND TIME REACTION-TRANSPORT EQUATIONS
   - Subdiffusive Fokker-Planck equation with space dependent anomalous exponent
   - Fractional PDE's with nonlinear reactions
   - Example: Anomalous chemotaxis

Reaction-Advection-Diffusion Equation for Density ρ

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• Fractional PDE with anomalous transport (Levy flights, subdiffusion, etc.):

$$\tau_\gamma D_t^\gamma \rho = -D_\alpha (-\Delta)^{\frac{\alpha}{2}} \rho + r(\rho)\rho, \qquad x \in \mathbb{R}^3$$

where $D_t^\gamma \rho$ is the Caputo derivative and the Laplacian Δ is replaced by a Riesz fractional operator: $-(-\Delta)^{\frac{\alpha}{2}}$.

Is it a good model for reaction-transport?

Anomalous transport: subdiffusion

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Subdiffusion:

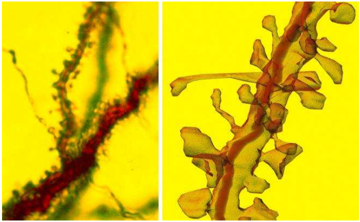
$$\mathbb{E}X^2(t) \sim t^\gamma \qquad 0 < \gamma < 1$$

Biology contains a wealth of subdiffusive phenomena, for example, proteins diffuse across cell membranes.
Subdiffusion in hydrology: the travel times of contaminants in groundwater are much longer than is expected from the classic diffusion.

What is the macroscopic equation for the concentration ρ?

Subdiffusion in dendritic spines

Spiny Dendrites:



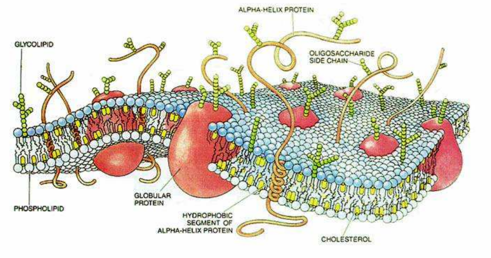
Dendritic spines are essential elements of most brain regions because they form a surface for receiving synaptic inputs. Transport of biologically inert particles (fluorescein dextran) in spiny dendrites is subdiffusive (Neuron 52, 635 (2006)):

$$\mathbb{E}X^2(t) \sim t^{\gamma} \qquad 0 < \gamma < 1$$

Non-Markovian model: Fedotov, Mendez, Phys.Rev.Lett. 101, 218102 (2008); Phys. Rev. E 82, 041103 (2010)

Subdiffusion of proteins on cell membrane

A variety of proteins are scattered throughout the flexible matrix of phospholipid molecules, somewhat like icebergs floating in the ocean.



Basic reasons for anomalous diffusion:

1) obstruction by mobile and immobile proteins;
2) transient binding to immobile or mobile species (lipid-protein and protein-protein interactions);
3) confinement by membrane skeletal corrals;
4) interaction of proteins with lipid microdomains (lipid rafts).

Probabilistic solution of advection-diffusion PDE

Probabilistic solution of the initial-value problem (macroscopic)

$$\frac{\partial \rho}{\partial t} + v\left(x,t\right) \cdot \nabla \rho = D \Delta \rho, \qquad \rho(x,0) = \rho_0(x) \qquad x \in \mathbb{R}^3$$

is given by the formula

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$$\rho(x,t) = \mathbb{E}_x \rho_0(X(t)),$$

where $X(t)$ is a solution of the (microscopic) SDE:

$$dX(s) = -v(X(s), t-s)\, ds + (2D)^{1/2} dW(s), \quad 0 < s < t$$

W(s) is the standard three-dimensional Wiener process (M. Freidlin)

Continuous time random walk (CTRW)

Let $X(t)$ denote the position of a particle:

$$X(t) = \sum_{i=1}^{N(t)} Z_i, \tag{1}$$

where $N(t)$ is a *renewal* or *counting process*. $X(t)$ is called a continuous time random walk (CTRW).

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Generalized Master equation for the mean-field density $\rho(x,t)$:

$$\frac{\partial \rho(x,t)}{\partial t} = \int_0^t K(t-s)\left[\int \rho(x-z,s)w(z)dz - \rho(x,s)\right] ds \tag{2}$$

R. Metzler and J. Klafter, Phys. Rep. **339**, 1 (2000).

Parabolic scaling vs anomalous scaling

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Assume that the pdf $\phi(t)$ of the waiting time has a finite first moment and the dispersal kernel $w(z)$ has a finite variance.

If we apply the parabolic scaling (long-time large-scale limit) $x \to \frac{x}{\varepsilon}, \quad t \to \frac{t}{\varepsilon^2}$ then the density

$$\rho(x,t) = \lim_{\varepsilon\to 0} \rho^{\varepsilon}(x,t) = \lim_{\varepsilon\to 0} \rho\left(\frac{x}{\varepsilon}, \frac{t}{\varepsilon^2}\right)$$

obeys the macroscopic diffusion equation

$$\frac{\partial \rho}{\partial t} = D\frac{\partial^2 \rho}{\partial x^2}.$$

Anomalous diffusion

Assume that the pdf of the waiting time $\phi(\tau)$ decreases like $\tau^{-\gamma-1}$ as $\tau \to \infty$ (infinite mean waiting time) and the dispersal kernel $w(z)$ has heavy tails $|z|^{-1-\alpha}$ (infinite variance).

$$\rho(x,t) = \lim_{\varepsilon \to 0} \rho^{\varepsilon}(x,t) = \lim_{\varepsilon \to 0} \rho\left(\frac{x}{\varepsilon}, \frac{t}{\varepsilon^{\frac{\alpha}{\gamma}}}\right)$$

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obeys the macroscopic space-time fractional diffusion equation

$$\frac{\partial^{\gamma}\rho}{\partial t^{\gamma}} = D_{\alpha,\gamma}\frac{\partial^{\alpha}\rho}{\partial |x|^{\alpha}}, \quad 0<\alpha<2$$

where

$$\frac{\partial^{\gamma}\rho}{\partial t^{\gamma}} := \frac{1}{\Gamma(1-\gamma)}\int_0^t \frac{\rho_s'(x,s)\,ds}{(t-s)^{\gamma}}, \qquad 0<\gamma<1$$

is the Caputo fractional derivative,

$$\frac{\partial^{\alpha}\rho}{\partial |x|^{\alpha}} := \Gamma(1+\alpha)\frac{\sin(\pi\alpha/2)}{\pi}\int_0^{\infty}\frac{\rho(x-z,t)-2\rho(x,t)+\rho(x+z,t)}{z^{1+\alpha}}dz$$

is the symmetric Riesz fractional derivative.

Fractional Fokker-Planck (FFP) equation

Let $p(x,t)$ be the PDF for finding the particle in the interval $(x, x+dx)$ at time t, then

$$\frac{\partial p}{\partial t} = \mathcal{D}_t^{1-\mu} L_{FP}\, p \tag{4}$$

with $L_{FP}\, p = -\partial \left(v_\mu(x) p \right) \partial x + \partial^2 \left(D_\mu(x) p \right) / \partial x^2$.

The Riemann-Liouville derivative $\mathcal{D}_t^{1-\mu}$ is defined as

$$\mathcal{D}_t^{1-\mu} p\,(x,t) = \frac{1}{\Gamma(\mu)} \frac{\partial}{\partial t} \int_0^t \frac{p\,(x,u)\, du}{(t-u)^{1-\mu}} \tag{5}$$

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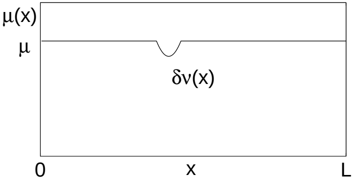
The difference between standard Fokker-Planck equation and FFP equation is the rate of relaxation of $p\left(x,t\right) \to p_{st}(x)$. In the anomalous subdiffusive case the relaxation process is very slow and it is described by a Mittag-Leffler function $E_\mu\left(-\lambda_n t^\mu\right)$ with the power-law decay $t^{-\mu}$ as $t \to \infty$ (R. Metzler and J. Klafter, 2000) .

Fractional Fokker-Planck (FFP) equation

Our main result is that the subdiffusive fractional equations with constant μ in a bounded domain $[0, L]$ are not structurally stable with respect to the non-homogeneous variations of parameter μ.

$$\mu(x) = \mu + \delta\nu(x) \tag{6}$$



The space variations of the anomalous exponent lead to a drastic change in asymptotic behavior of $p(x, t)$ for large t.

S. Fedotov and S. Falconer, Phys. Rev. E, 85, 031132, 2012

Subdiffusive Fokker-Planck equation

FFP equation with varying anomalous exponent

$$\frac{\partial p}{\partial t} = -\frac{\partial \left(v_\mu(x) \mathcal{D}_t^{1-\mu(x)} p \right)}{\partial x} + \frac{\partial^2 \left(D_\mu(x) \mathcal{D}_t^{1-\mu(x)} p \right)}{\partial x^2} \tag{7}$$

with the fractional diffusion coefficient $D_\mu(x)$ and fractional drift $v_\mu(x)$.

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We put the reflecting barriers at $x = 0$ and $x = L$ and consider constant exponent μ and diffusion D_μ. Then the FFP equation (7) admits the stationary solution in the form of the Gibbs-Boltzmann distribution

$$p_{st}(x) = C \exp\left[-U(x)\right], \quad U(x) = \frac{1}{D_\mu} \int^x v_\mu(z) dz \tag{8}$$

When the anomalous exponent μ depends on the space variable x, the Gibbs-Boltzmann distribution is not a long time limit of the fractional Fokker-Planck equation.

Monte Carlo simulations

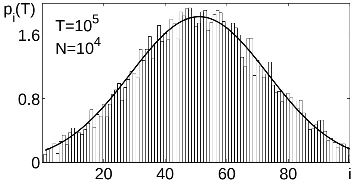

Figure: Long time limit of the solution to the system with $\mu_i = 0.5$ for all i. Gibbs-Boltzmann distribution is represented by the line.

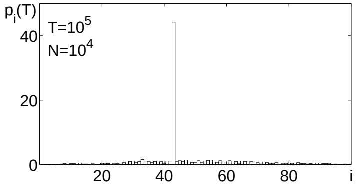

Figure: The parameters are $\mu_i = 0.5$ for all i except $i = 42$ for which $\mu_{42} = 0.3$.

Fractional PDE's with reactions.

The main challenge is to implement the non-linear kinetic term into non-Markovian transport equations involving CTRW.

We assume that the chemical reaction follows the mass action law and reaction term is of the form $r(\rho)\rho$. It is also convenient to represent the non-linear reaction rate $r(\rho)$ as the difference between the birth rate $r^{+}(\rho)$ and the death rate $r^{-}(\rho)$

$$r(\rho) = r^{+}(\rho) - r^{-}(\rho). \tag{9}$$

Now we consider two different models for reaction and transport process.
S. Fedotov, Phys. Rev. E 81, 011117 (2010)

Model A: Nonlinear Master equation

One can obtain nonlinear Master equation for the density $\rho(x,t)$ which is non-local in space and time

$$\frac{\partial\rho}{\partial t} = \int_0^t K(t-\tau)\Big(\int_{\mathbb{R}} \rho(x-z,\tau)\, e^{\int_\tau^t r(\rho(x-z,u))du} w(z)\, dz$$

$$-\rho(x,\tau)\, e^{\int_\tau^t r(\rho(x,u))du}\Big)d\tau + r(\rho)\,\rho.$$

Transport and the reaction are not separable!

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Fractional reaction-transport equation:

$$\frac{\partial \rho}{\partial t} = \Delta e^{\int_0^t r(\rho(x,u))du} D_t^{1-\gamma}[\rho e^{-\int_0^t r(\rho(x,u))du}] + r(\rho)\rho. \qquad (10)$$

In a linear case, this equation has been derived by Sokolov, et al, PRE, 2006 and Henry, et al, PRE, 2006

Model B: Reaction-transport Master equation

We assume that the particles created with the rate $r^{+}(\rho)\,\rho$ have zero age.
We interpret the density $j(x,t)$ as a zero-age density of particles arriving at the point x exactly at time t.

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$$-\rho(x,\tau)\, e^{-\int_\tau^t r^{-}(\rho(x,u))du}\Big) d\tau + r^{+}(\rho)\,\rho - r^{-}(\rho)\,\rho.$$

If we expand the expression in the brackets for small z, we obtain

$$\frac{\partial \rho}{\partial t} = \frac{\sigma^2}{2}\frac{\partial^2}{\partial x^2}\int_0^t K(t-\tau)\,\rho(x,\tau)\, e^{-\int_\tau^t r^{-}(\rho(x,u))du} d\tau + r^{+}(\rho)\,\rho - r^{-}(\rho)\,\rho. \quad (11)$$

Model B describes the situation when newborn particles have been given new waiting time (Vlad, Ross (2002); Yadav, Horsthemke (2006).

Anomalous Transport and Nonlinear Reactions in Two-State Systems

Two-state Markovian random process: we assume that the transition probabilities γ_1 and γ_2 are constants.

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Master equations for the mean density of particles in state 1 (mobile), $\rho_1(x,t)$, and the density of particles in state 2 (immobile), $\rho_2(x,t)$, are

$$\frac{\partial \rho_1}{\partial t} = L_x \rho_1 - \gamma_1 \rho_1 + \gamma_2 \rho_2, \tag{12}$$

$$\frac{\partial \rho_2}{\partial t} = r_2\left(\rho_2\right)\rho_2 - \gamma_2 \rho_2 + \gamma_1 \rho_1, \tag{13}$$

where the reaction rate $r_2\left(\rho_2\right)$ depends on the local density of particles ρ_2. Here L_x is the transport operator acting on x-coordinate.

Non-Markovian model for the transport and reactions of particles in two-state systems

Nonlinear Master equations:

$$\frac{\partial \rho_1}{\partial t} = L_x \rho_1 + j_1(x,t) - j_2(x,t), \tag{14}$$

$$\frac{\partial \rho_2}{\partial t} = r_2(\rho_2)\,\rho_2 + j_2(x,t) - j_1(x,t), \tag{15}$$

where the densities $j_1(x,t)$ and $j_2(x,t)$ describe the exchange flux of particles:

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$$j_1(x,t) = \int_0^t K_2(t-t')\rho_2(x,t')e^{\int_{t'}^{t} r_2(\rho_2(x,s))ds}dt', \tag{16}$$

$$j_2(x,t) = \int_0^t \int_{\mathbb{R}} K_1(t-t')p(x-z,t-t')\rho_1(z,t')dzdt', \tag{17}$$

where $K_i(t)$ is the memory kernel defined as $\tilde{K}_i(s) = \frac{\tilde{\psi}_i(s)}{\tilde{\Psi}_i(s)}$.

Anomalous chemotaxis

The chemotaxis is a directed migration of cells toward a more favorable environment

The flux of cells

$$J = \chi \frac{\partial S}{\partial x}\rho - \frac{\sigma^2 \gamma(S(x))}{2}\frac{\partial \rho}{\partial x} \tag{18}$$

where $S(x)$ is the chemotactic substance and χ is the chemotactic sensitivity.

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The anomalous cell flux (SF, Phys. Rev. E 83, 021110 (2011)):

$$\begin{aligned} J &= -\frac{\sigma^2}{2}\frac{\partial S}{\partial x}\frac{\partial \mu}{\partial S}\frac{\partial}{\partial \mu} g_\mu^{-1}(x)\mathcal{D}_t^{1-\mu(S(x))}\rho \\ &\quad -\frac{\sigma^2}{2} g_\mu^{-1}(x)\mathcal{D}_t^{1-\mu(S(x))}\frac{\partial \rho}{\partial x}. \end{aligned} \tag{19}$$

Here we introduced the *anomalous chemotactic sensitivity* $\partial\mu/\partial S$ as a derivative of the anomalous exponent μ.
$\mathcal{D}_t^{1-\mu(S(x))}$ is the Riemann-Liouville fractional derivative.

Anomalous chemotaxis

The anomalous flux leads to

$$\rho(x,t) \to \delta(x - x_M) \qquad as \qquad t \to \infty. \tag{20}$$

Here x_M is the point in space where the anomalous exponent $\mu(S(x))$ has a minimum. It means that all cells aggregate into a tiny region of space forming high density system at the point $x = x_{M.}$ This phenomenon can be referred to as anomalous aggregation.

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Another example of dense aggregation is MOSCOW

Conclusions

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• A research associate position is available at the University of Manchester for applied mathematician or theoretical physicist to work with Prof. Sergei Fedotov on the project "Anomalous reaction-transport equations: applications to the theory of cancer spreading and subdiffusion in dendrites".

Salary : £29,249 to £35,938 p.a.
Duration: three years
Closing date: 14 June 2012