diffusion-fundamentals

The Open-Access Journal for the Basic Principles of Diffusion Theory, Experiment and Application

Lateral Diffusion of Proteins in Cell Membrane: The Anomalous Case

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Abstract:

We present a method describing the lateral movement of proteins in cell membranes as observed in FRAP experiments. We extend earlier results derived for normal diffusion [1] to account for the case of anomalous subdiffusion. Our analytic closed forms are compared to computer simulations of anomalous diffusion and both show excellent agreement. The approach sheds light on the behavior of proteins in such complex systems and provides a tool to analyze experimental results.

FRAP Method:

FRAP experiments measure the lateral mobility of proteins in a membrane. In these experiments a certain kind of proteins which a considerable part of is located in the membrane are tagged with a fluorescence probe. A small spot on a membrane is illuminated by a laser beam and the total fluorescence returning from the tagged proteins is measured. These proteins are then photobleached by a brief exposure to an intense focused laser beam. The subsequent recovery is monitored by the same, but attenuated laser beam. Recovery occurs by replenishment of fluorophores in the bleached spot due to lateral transport from the surrounding membrane surface. The lateral transport process can be written as a diffusion equation with a flow term [1]:

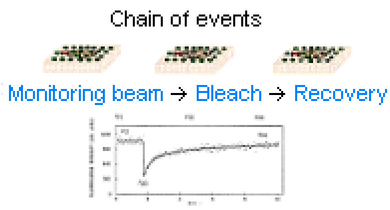

Figure 1:scheme of FRAP experiment

$$\frac{\partial C_K(r,t)}{\partial t} = D\nabla^2 C_K(r,t) - V_0 \frac{\partial C_K(r,t)}{\partial x} \tag{1}$$

The fluorescence measured can then be written as:

$$F(t) = \frac{q}{A}\int I(r) C_K(r,t) d^2 r \tag{2}$$

Diffusion, Anomalous Diffusion and Fractional Calculus:

The main characteristic that distinguishes anomalous from normal diffusion is the behavior of the mean squared displacement (MSD) as a function of time. For normal behavior the MSD grows linearly with time while for an anomalous process it grows sublinearly. It has been shown [2] that one can rewrite the diffusion equation for the anomalous case in the following way:

$$\frac{\partial C(r,t)}{\partial t} = {}_0D_t^{1-\alpha}(D\nabla^2 C(r,t) - V_0[\partial C(r,t)/\partial x]) , \quad 0<\alpha<1 \qquad (3)$$

where the ${}_0D_t^{1-\alpha}$ is the Riemann-Liouville operator:

$$ {}_0D_t^{-\alpha} f(t) = \int_0^t ds \frac{(t-s)^{\alpha-1}}{\Gamma(\alpha)} f(s) \qquad (4)$$

It has also been shown [2,3] that there exists a relationship between the anomalous and normal behaviors presented as:

$$C_\alpha(x,t) = \int_0^\infty dsA(s,t)C_1(x,t) \qquad (5)$$

where $C_\alpha(x,t)$ and $C_1(x,s)$ are the solutions of the fractional diffusion equation, Eq (3), and normal diffusion equation, Eq (1) respectively. A(s,t) is a one sided Levy function [2].

Calculation and Simulation:

All our calculations have been done for the case of pure diffusion (V_0=0 in Eq (1)). We calculated the anomalous curves for some special cases: $\alpha = 1/2, \alpha = 1/3$. We also simulated the FRAP experiment directly for anomalous diffusion.
The simulation was based on continuous time random walk theory that leads to fractional diffusion equation [2].

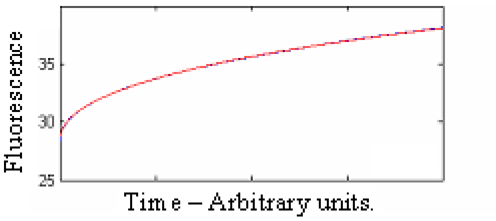

Figure 2: Anomalous fluorescence recovery $\alpha = 1/3$.

Discussion:

We presented a new method to achieve fluorescent recovery curves for anomalous diffusion when dealing with FRAP experiments. We have to emphasize that both the diffusion equation and the fractional diffusion equation give an average behavior. In normal FRAP experiment one sometimes has two types of populations: mobile and immobile. When describing the problem in the above anomalous diffusion framework we assume only one type of population out of which some of the proteins get stuck (and therefore are practically immobile) for a very long time.

[1] D. Axelrod ,D.E.Koppel, J.Schlessinger, E.Elson amd W.W.Webb – Mobility measurement by analysis of fluorescence photobleaching recovery kinetics. (biophysical journal 1976 vol. 16).

[2] R.Metzler and J.Klafter – The random walk's guide to anomalous diffusion: a fractional dynamics approach. (Physics reports vol. 339 December 2000)

[3] I. M. Sokolov - Solutions of a class of no-Markovian Fokker-Plank equations (PRE 66 2002).