Simulating diffusion in crowded environments with multifractional Brownian motion

André Leier[1], Tatiana T. Marquez-Lago[2], and Kevin Burrage[3]

***Short Abstract* — Many studies from both experimental and simulation perspectives have attempted to deepen our understanding of spatial crowding in molecular cell biology. Much of the focus has been on continuous time random walks (CTRWs), but some very recent work has suggested that, in some cases, fractional Brownian motion (FBM) may be a good descriptor of spatial crowding effects. In this contribution, we present results from a recent study [1] using FBM and multifractional Brownian motion (MFBM) to simulate diffusion of a tracked particle in the presence of crowding molecules and physical obstacles. Our comparison is based on standard statistical measures and highlights how well (M)FBM represents such motion.**

***Keywords* — Spatial crowding, anomalous diffusion, (multi-) fractional Brownian motion, random walks.**

I. Background

UNDIRECTED diffusion of molecules is a common motion process within cells. Based on experimental data such as time-lapse microscopy, such motion has many times been characterized as highly anomalous [2], referring to a mean-square displacement (MSD) $\langle x^2 \rangle \sim t^{\alpha}$ where $0 < \alpha < 1$. Even though the mechanisms leading to subdiffusive motion in cells are not entirely understood, excluded volume effects inside the crowded cell have already been identified as one cause for subdiffusion [3].

When modeling anomalous diffusion, one has the choice between spatial models that explicitly account for crowding molecules and/or obstacles, and those devoid of such spatial details. The latter type is used to capture only the essential dynamics while significantly reducing computational time. In this way, subdiffusive dynamics of molecules have been represented by time-fractional differential equations, or, equivalently, have been described by CTRWs with appropriate Mittag-Leffler waiting time distribution and normal spatial jump distributions [4,5]. Recently, FBMs have also been used to simulate anomalous diffusion, for instance in crowded environments [6], and it has been shown that CTRWs might be less appropriate for representing certain subdiffusive processes than FBMs [6,7].

FBM is driven by a Gaussian process with zero-mean and a covariance function that depends on the so-called Hurst exponent *H*. A natural generalization of FBM is achieved by replacing *H* by a time-dependent Hölder function *H(t)* leading to what has been termed multifractional Brownian motion (MFBM).

II. Results

We have performed a series of simulation studies showing how to characterise anomalous diffusion in two types of crowded environments, with immovable obstacles or with diffusing crowding molecules, through FBM and MFBM. Particle tracking data, mimicking experimental data, was first generated by using Smoldyn. We then attempted to obtain (M)FBM paths that match the statistical properties given by MSD and time averaged MSD of our sample data. While diffusion around immovable obstacles can be reasonably characterized by a single Hurst exponent, diffusion in the presence of crowding molecules seems to exhibit multifractional properties in form of a different short and long-time behaviour. Since the MSD is not necessarily a robust metric for inferring complex spatial information, we also compared corresponding radial PDFs in the scenario of crowding molecules and found a close match in the radial distributions of experimental and MFBM paths.

[1]Okinawa Institute of Science and Technology, 1919-1 Tancha, Onna-son, Kunigami, Okinawa 904-0412, Japan. E-mail: andre.leier@oist.jp

[2]Integrative Systems Biology Unit, Okinawa Institute of Science and Technology, 1919-1 Tancha, Onna-son, Kunigami, Okinawa 904-0412, Japan. E-mail: tatiana.marquez@oist.jp

[3]University of Oxford, Department of Computer Science, Wolfson Building, Parks Road, Oxford, OX1 3QD, United Kingdom, and Queensland University of Technology, Brisbane 4001, Australia. E-mail: kevin.burrage@comlab.ox.ac.uk

References

[1] Marquez-Lago TT, Leier A, Burrage, B (accepted for publication; 2012) Anomalous diffusion and multifractional Brownian motion: simulating molecular crowding and physical obstacles in Systems Biology. *IET Syst Biol*. **6**(3).

[2] Wachsmuth M, Waldeck W, Langowski J (2000) Anomalous diffusion of fluorescent probes inside living cell nuclei investigated by spatially-resolved fluorescence correlation spectroscopy. *J Mol Biol* **298**(4), pp. 677-689.

[3] McGuffy SR, Elcock AH (2010). Diffusion, Crowding & Protein Stability in a Dynamic Molecular Model of the Bacterial Cytoplasm. *PLoS Comput Biol* **6**(3): e1000694.

[4] Hilfer R., Anton L (1995) Fractional master equations and fractal time random walks. *Phys Rev E Stat Phys* **51**(2), pp. R848-R851.

[5] Metzler R, Klafter J (2000) The Random walker's guide to anomalous diffusion: a fractional dynamics approach. *Phys Reports* **339**, pp. 1–77.

[6] Szymanski J, Weiss M. (2009) Elucidating the Origin of Anomalous Diffusion in Crowded Fluids. Phys Rev Lett **103**, 038102.

[7] Burov S, Jeon JH, Metzler R, Barkai E (2011) Single particle tracking in systems showing anomalous diffusion: the role of weak ergodicity breaking. *Phys Chem Chem Phys* **13**(5), pp. 1800-1812.