Anomalous diffusion in models of fluorescence recovery after photobleaching

S. B. Yuste[1,2], K. Lindenberg[3], A. Baumgaertner[1], and E. Abad[2,4]
[1]Departamento de Física, Facultad de Ciencias, Universidad de Extremadura, E-06071 Badajoz, Spain
[2]Instituto de Computación Científica Avanzada (ICCAEx), Universidad de Extremadura, Spain
[3]Department of Chemistry and Biochemistry, and BioCircuits Institute, University of California San Diego, 9500 Gilman Drive, La Jolla, CA 92093-0340, USA
[4]Departamento de Física Aplicada, Centro Universitario de Mérida, Universidad de Extremadura, E-06800 Mérida, Spain

Anomalous diffusion, in particular subdiffusion, is frequently invoked as a mechanism of motion in dense biological media and may have a significant impact on the kinetics of binding/unbinding events at the cellular level. Here, we extend a previously developed model for FRAP experiments to account for anomalous diffusion [1]. Our particular implementation of subdiffusive transport is based on a continuous time random walk (CTRW) description of the motion of fluorescent particles, as CTRWs lend themselves particularly well to the inclusion of binding/unbinding events. In order to model switching between bound and unbound states of fluorescent subdiffusive particles, we derive a fractional reaction-subdiffusion equation of rather general applicability. Using suitable initial and boundary conditions, this equation is then incorporated in the model describing 2D kinetics of FRAP experiments. We find that this model can be used to obtain excellent fits to experimental data. Moreover, recovery curves corresponding to different radii of the circular bleach spot can be fitted by a single set of parameters. While not enough evidence has been collected to claim with certainty that the underlying transport mechanism in FRAP experiments is one that leads to anomalous diffusion, the compatibility of our results with experimental data fuels the discussion as to whether normal diffusion or some form of anomalous diffusion is the appropriate model and as to whether anomalous diffusion effects are important to fully understand the outcome of FRAP experiments.

In the above context, we also address the problem of diffusion on a comb whose teeth display a varying length [2]. Specifically, the length ℓ of each tooth is drawn from a probability distribution displaying power law behavior at large ℓ, $P(\ell) \sim \ell^{-(1+\alpha)}$, $(\alpha > 0)$. We first focus on the computation of the anomalous diffusion coefficient for the subdiffusive motion along the backbone. This quantity is subsequently used as an input to compute concentration recovery curves mimicking fluorescence recovery after photobleaching experiments in comb-like geometries such as spiny dendrites. Our method is based on the mean-field description provided by the well-tested Continuous Time Random Walk approach for the random comb model, and the obtained analytical result for the diffusion coefficient is confirmed by numerical simulations of a random walk with finite steps in time and space along the backbone and the teeth. Finally, we show that recovery curves obtained with the help of the analytical expression for the anomalous diffusion coefficient cannot be fitted perfectly by a model based on scaled Brownian motion, i.e., a standard diffusion equation with a time-dependent diffusion coefficient. However, differences between the exact curves and such fits are small, thereby providing justification for the practical use of models relying on scaled Brownian motion as a fitting procedure for recovery curves arising from particle diffusion in comb-like systems.

[1] S. B. Yuste, E. Abad, and K. Lindenberg, A reaction-subdiffusion model of fluorescence recovery after photobleaching (FRAP), J. Stat. Mech. **2014**, P11014 (2014).

[2] S. B. Yuste, E. Abad, and A. Baumgaertner, Anomalous diffusion and dynamics of fluorescence recovery after photobleaching in the random-comb model, Phys. Rev. E **94**, 012118 (2016).