

An anomalous diffusion approach to stochastic modeling for single molecule tracking of receptors and proteins at cell surface

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The Nobel Prize in Physiology or Medicine 2009 was awarded for the discovery of how chromosomes are protected by telomeres and the enzyme telomerase. The Nobel Prize in Chemistry 2012 was given for studies of G-protein-coupled receptors and the Nobel Prize in Chemistry 2014 was presented for the development of superresolved fluorescence microscopy. Definitely, the research behind these Nobel Prizes - awarded within a short few years period - have caused a dramatic increase of experimental and theoretical achievements in the study of living cells around the world.

Ultimately the accessibility of quantitative data prompted many statistical physicists and applied mathematicians to turn their attention to the study of single biological cells and the physiological processes running off therein. For example, G protein-coupled receptors mediate the biological effects of many hormones and neurotransmitters and are major pharmacological targets, [1-4]. However, how receptors and G proteins interact and couple at the plasma membrane is not well understood.

A phenomenon observed in recent single-molecule experiments is anomalous diffusion, which largely departs from the classical Brownian diffusion theory since the mean-squared displacement (MSD) is nonlinear. The most popular theoretical models that are commonly employed are: continuous-time random walk (CTRW), fractional Brownian motion (FBM), fractional Langevin equation (FLE) and autoregressive fractionally integrated moving average (ARFIMA).

Using single-molecule imaging data one can visualize motion of individual receptors and G proteins at the surface of living cells [2]. Here, we provide a detailed anomalous diffusion classification based on MSD analysis [5] for some exemplary experimental data from [2].

[1] K. L. Pierce, R.T. Premont, R.T. & R.J. Lefkowitz, Seven-transmembrane receptors, *Nat. Rev. Mol. Cell. Biol.* 3, 639-650 (2002).

[2] D. Calebiro, et al. Single-molecule analysis of fluorescently labeled G-protein-coupled receptors reveals complexes with distinct dynamics and organization, *Proc. Natl. Acad. Sci. U.S.A.* 110, 743-748 (2013).

[3] R. O. Dror, et al. Structural basis for nucleotide exchange in heterotrimeric G proteins, *Science* 348, 1361-1365 (2015).

[4] B. T. DeVree, et al. Allosteric coupling from G protein to the agonist-binding pocket in GPCRs, *Nature* 535, 182-186 (2016).

[5] K. Burnecki, E. Kepten, Y. Garini, G. Sikora, & A. Weron, Estimating the anomalous diffusion exponent for single particle tracking data with measurement errors, *Sci. Rep.* 5, 11306 (2015).

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