FCS and anomalous diffusion model as tool to report modifications in molecular interactions

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Abstract

Diffusion of transcription factor (FT) plays a key role in the control of their target search. Dynamic proteins in the nucleus classically display a subdiffusive behavior which can be modelled with an anomalous diffusion [1], yet the underlying physical mechanisms are still debated. We propose to address this question by monitoring of HEXIM1, a multifunction factor implied in transcription regulation. By studying photon fluctuations of fluorescently-labelled HEXIM1-GFP with FCS (fluorescence correlation spectroscopy), we explored the contribution of interactome of FT to the generation of anomalous diffusion. We show that HEXIM1 interactions with 7SK RNA and with positive transcription elongation factor b (P-TEFb) determine HEXIM1 anomalous diffusion.

Moreover, numerical simulations allowed us to establish that, in a regime where interactions change very slowly relative to the residence time, the proportions of distinct oligomeric HEXIM1 subpopulations define the apparent anomaly parameter of the whole population. Altogether our data open new prospects in which the alpha coefficient in anomalous diffusion becomes a rule to track and report modifications in molecular interactome.

[1] Wachsmuth M, Waldeck W, Langowski J. Anomalous diffusion of fluorescent probes inside living cell nuclei investigated by spatially-resolved fluorescence correlation spectroscopy. J Mol Biol. 2000 May 12;298(4):677-89.