image Mean Square Displacement: a powerful tool for the characterization of intracellular dynamics of nanoparticles

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At a cellular level, the interactions among living matter and nanoparticle-based drug delivery systems highly regulate their dynamics and strongly affect their therapeutic efficiency.[1] Thus, manifold fluorescence techniques (including Single Particle Tracking (SPT) and Image Correlation Spectroscopy (ICS)) are increasingly being employed to study intracellular motions of fluorescence-labelled objects with high spatial and temporal resolution. However, none of these experimental tools has been specifically developed to take into account a spatial distribution of directed motions, commonly arising from the active transport of the labelled particles along cytoskeletal networks. To fulfil this gap, here we show how to characterize two-dimensional dynamics driven by Brownian diffusion and flow terms that are uniformly distributed in an angular range. Overall information about the investigated dynamics is obtained by decoupling the flow contributions, to quantify both the net displacement of the ensemble and the strength of the driving speed. These interdependent terms are related to the intrinsic anisotropy of the particle flow and its eventual symmetry, which arises when an angular dispersion affects the directionality of motion. The proposed approach exploits general concepts of the spatiotemporal image correlation analysis,[2] extends the image-derived mean square displacement method[3] and recovers dynamic and geometric features, which are commonly achieved through single particle analyses. In detail, starting from a time series of the collected fluorescence images, a spatiotemporal correlation function is computed and studied over the entire domain of the lag-variables (Fig. 1). Numeric simulations and in vitro experiments (Fig. 2) validated the method and demonstrate high stability in the measurement procedure, accurate description of the particle dynamics and low sensitivity to background. Furthermore, this procedure does not require the extraction of single particle tracks neither threshold-based criterions for the characterization of motion and provides a rapid measurement of the ensemble behaviour. Finally, despite this work focuses on directed motions and Brownian diffusions, we point out that the capabilities of the original approach[3] are preserved, thus confined motions and anomalous diffusions can be detected and the corresponding dynamic parameters can be measured. Therefore, we argue that this study will contribute to advance our understanding about the movement of nanoparticles in cells, their interactions with the biological environment and the subsequent effects on their therapeutic efficiency.

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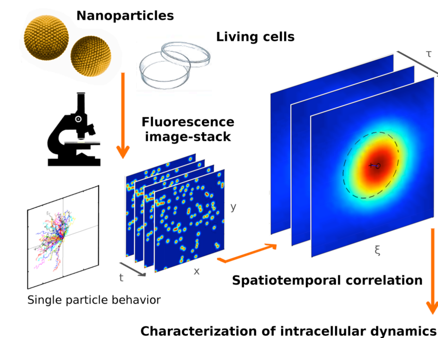

Figure 1. General scheme of an image correlation analysis: a fluorescence image time series is acquired and processed to get the autocorrelation function, which gives information about the investigated dynamics.