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Fourier Imaging Correlation Spectroscopy for Studies of Sub-Cellular Dynamics and Biomolecular Conformation Transition Pathways[1]

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Novel high signal-to-noise spectroscopic experiments that probe the dynamics of fluorescently labeled macromolecules have the potential to reveal complex intracellular biochemical mechanisms, or the slow relaxations of soft matter systems. Fourier imaging correlation spectroscopy (FICS) is a phase-selective approach to fluorescence fluctuation spectroscopy that employs a unique route to elevate signal levels while acquiring detailed information about microscopic coordinate trajectories. In this talk, I will illustrate the broad applicability of this approach by discussing two recent studies. The anomalous sub-diffusive dynamics of mitochondria in budding yeast are characterized using FICS, and provide detailed, length-scale dependent information about the influence of specific cytoskeletal elements on the movements of this organelle. We find that non-equilibrium forces associated with actin polymerization lead to a 1.5-fold enhancement of the long-time mitochondrial diffusion coefficient, and a transient sub-diffusive temporal scaling of the mean-square displacement. These non-equilibrium dynamics are a predominant factor in driving mitochondrial transport. In another set of experiments, polarization-modulated FICS simultaneously captures information about the internal conformation fluctuations and molecular translational dynamics of the fluorescent protein DsRed. By implementing a four-point correlation analysis, we construct two-dimensional spectral densities and joint distribution functions that determine temporal correlations of center-of-mass and anisotropy coordinates over successive time intervals. These four-point functions reveal statistically meaningful transition pathways between different optical conformations of the DsRed protein. The FICS method is well suited to investigate the dynamics of a broad range of heterogeneous systems, which include the molecular motions of glass forming liquids.

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