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Leveraging Time Series Analysis and Machine Learning to Quantify Intra and Inter Trajectory Heterogeneity in Particle Tracking Experiments[1]

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Microscopy hardware is now capable of producing high accuracy position vs. time data characterizing fluorescently tagged molecules in live cells. However, analytical methods for efficiently quantifying molecular motion parameters from the raw 3D (or 2D) single particle tracking (SPT) data are underdeveloped. "Downstream" trajectory analysis methods have only begun to efficiently and reliably harness the wealth of statistical kinetic information buried in SPT time series. The lack of analytical methods is due in part to the numerous challenges facing the translation the noisy position measurement information encoded in image stacks into unambiguous and readily interpretable biophysical information quantities (e.g., instantaneous effective diffusivity, forces, molecular friction, etc.). Some of these challenges are caused by: the inherently stochastic (and often nonlinear) nature of the dynamics of molecules in live cells, the highly crowded and heterogeneous time changing micro-environment of live cells influencing the dynamics of tagged molecules, and artifacts induced by the measurement device (e.g.localization error and motion blur). This talk will demonstrate how the merging of ideas from high frequency financial time series analysis, machine learning, and nonparametric Bayesian statistics can address these challenges, overcome limitations inherent in classic SPT methods, and provide insight into various single particle tracking experiments. We will describe and illustrate the new SPT trajectory analysis methods and discuss how the methods can be used to more reliably estimate data-driven and physically interpretable models.

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