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Models of single molecule dynamics from single photon detections: a Bayesian nonparametric approach

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Fluorescence time traces report on dynamical properties of biomolecules. The basic unit of information contained therein is the individual photon. Single photons carry instantaneous information from the biomolecule, from which they are emitted, to the detector on rapid, sub-microsecond, timescales. Thus, from confocal microscopy it is theoretically possible to monitor biomolecular dynamics from hundreds to thousands of photons arrivals at those timescales. In practice, however, signals are stochastic and to deduce information through traditional means, such as fluorescence correlation spectroscopy (FCS) and related techniques, fluorescence signals are collected and temporally auto-correlated over several minutes. Here, we exploit novel mathematical tools, namely Bayesian nonparametrics, that allow us to deduce in a principled fashion the same information normally deduced from FCS but from the direct analysis of significantly smaller datasets starting from individual photon arrivals. We discuss the implications of this method in helping dramatically reduce phototoxic damage on the sample and the ability to monitor out-of-equilibrium processes.