HAMLET How to Apply Machine Learning to Experimental & Theoretical PHYSICS
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Achieving sub-temporal resolution in the analysis of two-state single-molecule trajectories

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While spatial resolution in flourescence microscopy and related fields during the last two decades reached the nanometer scale, the time resolution has remained essentially unchanged and is set by the camera system's imaging time. Yet adequate time resolution is crucial for accurate information acquisition about, for instance, dynamical processes in cells.

In a reaction-difffusion process in a cell a given molecule will undergo an alterating process: unbound (free molecule) to bound (molecule bound into a complex) and back. The two states (bound and unbound) are in general characterized by different diffusion constants, and the transitions between the two states are characterized by two rates (bound-to-unbound) and (bound-to-unbound).

The analysis of experimentally acquired trajctories for such two-state trajectories is often done using a discrete-time hidden Markov model, thus implicitly assuming that the observations generated by the hidden states are near-perfectly resolved, which is seldom the case in practise. The matter is brought to its head for rapid kinetics, where sub-time events that happen during imaging time are commonplace. To deal with type of rapid switching dynamics, we introduce a Bayesian parameter estimation procedure combined with a novel algorithm that efficiently calculates the exact probability of observed trajectories, including the many "unseen" switching events during imaging. Our method is based on an analytic derivation of generalised transition probabilities - transition-accretion probabilities - that probabilistically capture unseen switching behaviour during data acquisition. We do in-silico parameter inference where we compare this sub-time hidden Markov model to the standard variant (applicable to slow kinetics) as well as to an approximative method recently proposed (applicable to rapid kinetics). We find that our method works well irrespective of the temporal resolution of the setup.

Broad physics domain

single particle trajectory analysis

AI/ML technique(s) to be presented

Bayesian inference, model selction

Authors: CLARKSON, Erik (Lund University); AMBJÖRNSSON, Tobias (Lund University)

Presenter: AMBJÖRNSSON, Tobias (Lund University)

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