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Assessing the limits of hidden Markov model analysis for multi-state particle tracks in living systems DYLAN YOUNG, Clarkson Univ — Particle tracking offers significant insight into the molecular mechanics that govern the behavior of living cells. The analysis of molecular trajectories that transition between different motive states, such as diffusive, driven and tethered modes, is of considerable importance, with even single trajectories containing significant amounts of information about a molecule's environment and its interactions with cellular structures such as the cell cytoskeleton, membrane or extracellular matrix. Hidden Markov models (HMM) have been widely adopted to perform the segmentation of such complex tracks, however robust methods for failure detection are required when HMMs are applied to individual particle tracks and limited data sets. Here, we show that extensive analysis of hidden Markov model outputs using data derived from multi-state Brownian dynamics simulations can be used for both the optimization of likelihood models, and also to generate custom failure tests based on a modified Bayesian Information Criterion. In the first instance, these failure tests can be applied to assess the quality of the HMM results. In addition, they provide critical information for the successful design of particle tracking experiments where trajectories containing multiple mobile states are expected.

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