

STANFORD UNIVERSITY
DEPARTMENT OF STATISTICS
DEPARTMENTAL SEMINAR

4:15 p.m., Tuesday, March 2, 2004
Sequoia Hall Room 200
(Cookies at 3:45 in 1st Floor Lounge)

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Statistical Analysis of Single Molecule Experimental Data

Abstract:

Recent advances in experimental technologies allow scientists to follow biochemical processes on a single molecule basis, which provide much richer information about chemical dynamics than traditional ensemble averaged experiments, but also raise many new statistical challenges. This article provides the first likelihood-based statistical analysis of the single-molecule fluorescence lifetime experiment designed to probe the conformational dynamics of a single DNA hairpin molecule. The conformational change is initially modeled as a continuous-time two-state Markov chain, which has to be indirectly inferred from changes in photon emissions on top of the unobservable molecular Brownian diffusion. Beyond the simple two-state model, a competing model that models the energy barrier between the states of the DNA hairpin as an Ornstein-Uhlenbeck process has been suggested in the literature. We first derive the likelihood function of the simple two-state model using a matrix discretization method, and then generalize the method to handle complications such as unobserved molecular diffusions and the fluctuating energy barrier. The data augmentation technique and Markov chain Monte Carlo methods are developed to sample from the desired posterior distribution. The Bayes factor calculation together with posterior estimates of relevant parameters indicate that the fluctuating barrier model fits the data better than the simple two-state model.

This work is joint with Sunney Xie and Jun Liu