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The motion of cell-surface proteins analyzed with a hidden Markov model

Single particle tracks of tagged cell-surface proteins frequently show deviations from random Brownian diffusion. Such deviations are usually transient and are variously attributed to membrane heterogeneities, the presence of rigid obstacles, or interaction with other membrane-bound or cytosolic proteins. We analyze the dynamics of a diffusing cell-surface protein that interacts with a homogeneously distributed binding partner, such as intracellular cytoskeletal tethers. The system is parametrized by 2D diffusion coefficients of the protein in its free and bound states, and transition probabilities between the two states. Tracks of single protein molecules are considered to be the outcome of a hidden Markov model, whose underlying Markovian state sequence (free or bound) is not observable, while the particle position at each observation time is recorded. In this formulation, the likelihood of the observed sequence of displacements in a track is a function of the four model parameters. We maximize this likelihood function with respect to the model parameters to estimate their best-fit values and assign statistical error bounds to these estimates. Our analysis reveals important kinetic parameters for the underlying physical system that are not easily discernible with a traditional single particle tracking analysis. We apply our analysis to experimentally observed tracks of the adhesion molecule LFA-1 on the surface of T cells.