Time Series Analysis of Particle Tracking Data for Molecular Motion on the Cell Membrane

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***Short Abstract* — Single particle tracking is an important method to probe the dynamic behavior of individual proteins and lipids in cell membranes. We introduce the use of time series analysis to better understand the motion of membrane proteins. It is common to compare the motion to independent identically-distributed random walks. We first show that that the tracks are significantly autocorrelated so the jumps in the walk are not independent, which complicates the analysis. We fit the probability distributions of jump sizes with several models. One model implies that the motion is fractal. The mean squared displacement for biological data can show a power law behavior. In this case, we introduce the notion of an instantaneous diffusion constant to better understand the motion.**

***Keywords* — Single Particle Tracking, Molecular Motion, Cell Membrane**

Biophysicists use single particle tracking (SPT) methods to probe the dynamic behavior of individual proteins and lipids in cell membranes. The mean squared displacement (MSD) has proven to be a powerful tool for analyzing the data and drawing conclusions about membrane organization, including features like lipid rafts, protein islands and confinement zones defined by cytoskeletal barriers. Here we implement time series analysis as a new analytic tool to analyze further the motion of membrane proteins. The experimental data track the motion of 40nm gold particles bound to Class I major histocompatibility complex (MHCI) molecules on the membranes of mouse hepatoma cells.

Our first novel result is that the tracks are significantly autocorrelated. Because of this, we developed linear autoregressive models to elucidate the autocorrelations. Estimates of the signal to noise ratio for the models show that the autocorrelated part of the motion is significant. Next we fit the probability distributions of jump sizes with four different models. The first model is a general Weibull distribution that shows that the motion is characterized by an excess of short jumps as compared to a normal random walk. We also fit the data with a chi distribution which provides a natural estimate of the dimension d of the space in which a random walk is occurring. For the biological data, the estimates satisfy $1 < d < 2$, implying that particle motion is not confined to a line but also does not occur freely in the plane. The dimension gives a quantitative estimate of the amount of nanometer scale obstruction met by a diffusing molecule. We introduce a new distribution and use the generalized extreme value distribution to show that the biological data also have an excess of long jumps as compared to normal diffusion. These fits provide novel estimates of the microscopic diffusion constant.

Previous MSD analyzes of SPT data have provided evidence for nanometer-scale confinement zones that restrict lateral diffusion, supporting the notion that plasma membrane organization is highly structured. Our demonstration that membrane protein motion is autocorrelated and is characterized by an excess of both short and long jumps reinforces the concept that the membrane environment is heterogeneous and dynamic. Autocorrelation analysis and modeling of the jump distributions are powerful new techniques for the analysis of SPT data and the development of more refined models of membrane organization.

The time series analysis also provides several methods of estimating the diffusion constant in addition to the constant provided by the mean squared displacement. The mean squared displacement for most of the biological data shows a power law behavior rather the the linear behavior of Brownian motion. In this case, we introduce the notion of an instantaneous diffusion constant. All of the diffusion constants show a strong consistency for most of the biological data.

Acknowledgements: This work was supported by NIH grants P20 GM067594 R01 GM49814, and R01 AI051575.

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