

## Move, Dither, Move, Dither. On the Structure of Random Walks and Single-Particle Trajectories

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### 1. Introduction

Paths in single-particle tracking experiments and simulated random walks often include what might be called periods of motion and periods of dithering. These periods are often interpreted as directed motion (in cell biophysics, diffusion superimposed on bulk flow of membrane or cytoplasm; transport by cytoskeletal motors) and confinement (by cytoskeletal corrals, chromatin corrals, or lipid domains). **The general question is: When are these apparent types of motion real, and when are they merely fluctuations in a random walk?** More quantitatively, what is the probability that such a feature of prescribed length occurs by chance in a pure random walk with no mechanisms of directed motion or confinement?

The **fundamental principle** in interpreting single-particle trajectories is that a **pure random walk is the control and null hypothesis**. In order to make any claim about a putative physical or biological event in an observed single-particle trajectory, one must evaluate the probability that the event could have occurred by chance in the corresponding pure random walk.

### 2. Descriptors

Characterization of 2D random walks is based on pairs of descriptors of the random walk: a measure of extent and a measure of asymmetry. For 3D random walks, a measure of extent and two measures of asymmetry are used. One set of descriptors is based on the eigenvalues of the radius of gyration tensor, a standard way of characterizing random walks and polymers [1]. The extent descriptor is the squared radius of gyration, that is, the sum of the eigenvalues. It is scaled by time. The asymmetry descriptor is the asphericity, in 2D the ratio of the difference of the eigenvalues to their sum. This is dimensionless and it is independent of time for moderate or large times. In 3D the second asymmetry descriptor is the prolateness. Another set of descriptors is based on the convex hull. The extent descriptor is the area  $A$  scaled by time, and the asymmetry descriptor is the perimeter  $P$ , used in dimensionless form  $P/\sqrt{4\pi A}$ , normalized to 1 for a circle. Results are presented as 1D histograms of the descriptors and 2D histograms of pairs of descriptors. The correlation of the descriptors is also examined.

A key point is that long dithering or moving events are rare in themselves. But in examining a trajectory for these events, we do not specify the starting point of the event, and all that we specify about the duration is that it be above some minimum threshold of

detectability. The large number of potential starting points and durations of these events compensates for their rarity.

An essential feature of the approach is to separate three distinct aspects of the problem. First, we separate characterization from trajectory segmentation, and treat only characterization here. Second, we separate characterization from the effect of noise, and assume that the particle positions are exactly known. In practical applications to experimental single-particle trajectories, the random noise in the position measurement must be taken into account.

### **3. Applications**

Two applications are considered. First is the basic characterization of random walks. The statistical self-similarity of a random walk implies that if dithering or moving events occur, and whatever descriptors are used to identify them, they occur on all time scales. Second, the analysis provides new tests to identify directed and confined motion in single-particle trajectories, and to distinguish anomalous from normal diffusion. In anomalous diffusion due to fractional Brownian motion, the moves are shorter and the dithers are longer and denser than in normal diffusion.

### **References**

[1] J Rudnick and G Gaspari, Elements of the Random Walk, Cambridge University Press, Cambridge, 2004.

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