Quantification of Directional Motility by a Characteristic Directionality Time

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Abstract

Many cell types can bias their direction of locomotion by coupling to external cues. Characteristics such as how fast a cell migrates and the coordination of its migration path can both be quantified to provide metrics that determine which biochemical and biomechanical effects direct cell migration, and how long and how fast a cell migrates. A recent analytical model has been derived for a 1-D correlated random walk to demonstrate that the functional form of the characteristic directionality time is an appropriate metric of directional persistence. Furthermore, TAD persistence and SI do not take the resulting quantitative analysis should describe the underlying processes that occur in the system. In this work, we extend the random walk to two dimensions to demonstrate that the characteristic directionality time for random walks on 2-D substrates in the presence of a chemotactic gradient is a sensitive measure of directional bias. In this example, chemotactic cells on 100 kPa substrates migrate more directionally than those on 10 kPa, that is, 0.760 kDa (2.2 kDa) at 100 kPa

Time Interval Independent Metrics

Analytical Modeling

A new model for measuring directionality time is discussed, an empirical exponential fit against experimental data of neutrophils directionally migrating towards a chemoattractant. Time averages of the ensemble averaged angular bias,  , showed no significant nonergodic processes. Another round of more realistic nonergodic simulations is underway to determine the modification term, .

Reconciling Analytical Mode with in vitro Measurements

Simulations were used to answer the following questions:
1. Does directionality time measured from analytical and empirical fitting correlate to similar parameters that mediate directional bias?
2. Under what conditions is the usage of directionality time fitting appropriate?
3. Can the components, , be calculated directly from the data, without a specific MSD model?

The primary objective is to determine if directionality time is a true measure of directionality that is comparable from one dataset to the next.

Simulations followed the same rules outlined by the 2D biased random walk (analytical modeling panel) with two additional components: 1) crawling speeds of both sets were similar (see MSD plot), but trajectories on the 10 kPa gel were more wiggly than those on 100 kPa. 2) Migration is said to be directional when the mean squared displacement, , is scaled as a sensitive measure of both the time directionality, , and the angular bias factor, . Measurements with the analytical model depended less on parameter , therefore, the analytical model better describes the fact that random motion does not result from noise.

Summary and Work in Progress

- Directionality time is the time scale at which kinematic motion transitions from random to ballistic and is measured through MSD fitting in log-log coordinates.
- Directionality time is a more reliable measure of kinematic persistence than time interval dependent measures such as turning angle distribution metrics and straightness indices.
- To measure directionality time, we propose an empirical model, and also use several biased random walk models to derive an analytical model, .
- Deviations between real data and the idealized analytical model are accounted for by tracking changes in the log-log MSD slope to ergodic and kinematic variances (a work in progress).
- We would like to apply the model to other 2D datasets.
- Does the same directionality time model hold for 3D trajectories?

Acknowledgements

This work was supported by grants from the NIH (GM-065196 and AI-071592) to JXT; NIH MCIR Graduate Fellowship (A.L.) (Grant Assistance in Areas of National Need) from the U.S. Department of Education (X.M.O.), and allocations to the Department of Surgery by Rhode Island Hospital.

References