Correlation between speed and turning naturally arises in simulations of persistent random walks with sub-sampled trajectories

Vitaly V. Ganusov[1], Viktor Zenkov[2] and Barun Majumder[1]

***Abstract*— Mechanisms regulating cell movement are not fully understood. One feature of cell movement that determines how far cells displace from an initial position is persistence, the ability to perform movements in a direction similar to the previous movement direction. Persistence is thus determined by turning angles between two sequential displacements and be characterized by an average turning angle or persistence time. Recent studies found that a cell's average speed and turning are negatively correlated, suggesting a fundamental cell-intrinsic program whereby cells with a lower turning ability (i.e., larger persistence time) are intrinsically faster (or faster cells turn less). By simulating correlated or persistent random walks (PRWs) using two different frameworks (one based on von Mises-Fisher (vMF) distribution and another based on Ornstein-Uhlenbeck (OU) process) we show that the negative correlation between speed and turning naturally arises when cell trajectories are sub-sampled, i.e., when the frequency of sampling is lower than frequency at which cells make movements. This effect is strongest when the sampling frequency is on the order of magnitude with the typical cell persistence time and when cells vary in the persistence time. Both conditions are observed for datasets of T cell movements in vivo that we have analyzed. In simulations the correlation arises due to randomness of cell movements resulting in highly variable persistence times for individual cells that with sub-sampling leads to large variability of average cell speeds. Interestingly, previously suggested methodology of calculating displacement of cell cohort s with different speeds resulted in similar results whether or not there is a cell-intrinsic correlation between cell speed and persistence. For both vMF- and OU-based simulations of PRWs we could find parameter values (distribution of persistence times, speeds, and sampling frequency) that matched experimentally measured correlations between speed and turning for two datasets of T cell movement in vivo suggesting that such simple correlations are not fully informative on the intrinsic link between speed and persistence. Our results thus suggest that sub-sampling may contribute to (and perhaps fully explains) the observed correlation between speed and turning at least for some cell trajectory data and emphasize the role of sampling frequency in inference of critical cellular mechanisms of cell motility such as speeds (doi: 10.1101/2020.12.30.424897).**

***Index Terms*— Persistent random walks, von Mises-Fisher, Universal Coupling between Speed and Persistence, Ornstein-Uhlenbeck process**

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[1]Department of Microbiology, University of Tennessee, Knoxville, TN 37996, USA Email: vitaly.ganusov@gmail.com

[2]Department of Electrical Engineering and Computer Science, University of Tennessee, Knoxville, TN 37996, USA

I. Purpose

Immune cells often exhibit correlated/persistent random walks in vivo. What determines the ability of cells to exhibit correlated random walks remains poorly understood. Authors of several recent studies accurately measured movement of cells in 2D (*in vitro*) or in 3D (*in vivo*) over time and found that there is a strong positive correlation between average cell persistence, defined as the persistence time or the cosine of turning angles, and average cell speed [1], [2], [3]; this is equivalent to the negative correlation between average turning angle per cell and cell speed. These studies suggested that such correlation arises via a cell-intrinsic program.

II. Results

We performed simulations of persistent random walks using two different frameworks: von Mises-Fisher distribution-based simulations and simulations based on stochastic implementation of the Ornstein-Uhlenbeck process. In cases when speed and turning for individual cells were not correlated but trajectories were sub-sampled we found a strong, statistically significant correlation between average speed and average turning angle per cell. A similar correlation was observed between average speed and average persistence time of cells in the population. The results were relatively robust to parameter choices; however, for this effect to arise the sub-sampling frequency had to occur at the rate similar to a typical persistence time in the population.

III. Conclusion

Our results suggest that Universal Coupling between Speed and Persistence for cells of different biological systems may arise as an artifact of sub-sampled persistent random walks.

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