

Comment

Redundancy, extreme statistics and geometrical optics of Brownian motion

Comment on “Redundancy principle and the role of extreme statistics in molecular and cellular biology” by Z. Schuss et al.

S. Redner^{a,*}, B. Meerson^{b,*}

^a Santa Fe Institute, 1399 Hyde Park Road, Santa Fe, NM, 87501, USA

^b Racah Institute of Physics, Hebrew University of Jerusalem, Jerusalem 91904, Israel

Received 16 January 2019; accepted 24 January 2019

Available online 31 January 2019

Communicated by M. Frank-Kamenetskii

The authors of [1] promote the idea that many diffusion-limited reaction processes in molecular and cellular biology are determined by extreme effects. That is, the reaction kinetics is controlled not by the typical time for a reactant to reach a reaction site, but rather, by the time for the first of many particles to arrive. If the number of reactants is very large, there can be a profound difference between the typical arrival time and the first arrival time. As argued in [1], this difference has striking implications for the kinetics of a wide variety of diffusion-limited reactions.

To appreciate the origin of these extreme effects, it is helpful to start with a simple example. Consider the average time for a diffusing particle in one dimension, initially at $L > 0$, to *first* reach a target that is located at the origin—the first-passage time. As is well known, the particle is sure to eventually reach the target, but the average first-passage time is infinite [2,3]. This dichotomy is one of reason why diffusion processes are so fascinating, both from the theoretical and the practical perspective. Physically, this divergent first-passage time stems from the contribution of trajectories that wander arbitrarily far from the target before eventually reaching it. Mathematically, the divergence arises because the distribution of first-passage times,

$$f(t) = \frac{L}{\sqrt{4\pi Dt^3}} e^{-L^2/4Dt}, \quad (1)$$

has a long-time tail that decays at $t^{-3/2}$. This leads to all positive integer moments of the first-passage distribution being divergent. The probability that the particle reaches the target by time t is $F(t) = \int_0^t f(t')dt' = \text{erfc}(L/\sqrt{4Dt})$. As $t \rightarrow \infty$, $F(t) \simeq 1 - L/\sqrt{\pi Dt}$; that is, the probability that the particle *eventually* reaches the target equals 1. Thus a diffusing particle is sure to reach the target, even though the average time for this event is infinite.

Suppose now that two particles start at the same point $L > 0$. What is the average time for the first of these two particles to reach the target? The answer is again infinite. However, when three particles all start from $L > 0$,

DOI of original article: <https://doi.org/10.1016/j.plrev.2019.01.001>.

* Corresponding authors.

E-mail addresses: redner@santafe.edu (S. Redner), meerson@mail.huji.ac.il (B. Meerson).

the average first-passage time for the first particle is now finite! That is, the smallest of three first-passage times that are independently drawn from the underlying first-passage distribution (1) has a finite average value.

For N particles that all start at $L > 0$, the probability that one of them first reaches the target at time t is [4,5]

$$f_N(t) = Nf(t)[1 - F(t)]^{N-1} = N \frac{L}{\sqrt{4\pi Dt^3}} e^{-L^2/4Dt} \left[\operatorname{erf}(L/\sqrt{4Dt}) \right]^{N-1} \quad (2)$$

$$\simeq N \frac{L}{\sqrt{4\pi Dt^3}} \left(\frac{L}{\sqrt{\pi Dt}} \right)^{N-1} \quad t \rightarrow \infty. \quad (3)$$

Here $f_N(t)$ is the probability that the shortest first-passage time for N particles equals t . For the target to be reached at time t , $N - 1$ particles must all have their first-passage times longer than t (the error function factor), and one of the N particles must reach the target at time t . Because $f_N(t)$ asymptotically decays as $t^{-(N+2)/2}$, the average first-passage time is divergent for $N = 1$ and $N = 2$, but is finite for $N \geq 3$ [6].

The average time for the first out of $N \gg 1$ particles to reach the target is given by [4]

$$\langle T_N \rangle = \int_0^\infty dt t f_N(t) = \frac{L^2}{2D} \int_0^\infty \frac{dz}{z^3} \operatorname{erf}^N z \simeq \frac{L^2}{2D} \frac{1}{W(2N^2)}. \quad (4)$$

The second equality is obtained by integration by parts, the scaled variable z is $z \equiv L/\sqrt{4Dt}$, and $W(\cdot)$ is the Lambert W -function—the inverse of $f(W) = We^W$. Asymptotically, the first-passage time is [4,7]

$$\langle T_N \rangle \simeq \frac{L^2}{4D} \frac{1}{\ln N}. \quad (5)$$

The salient point is that the first-passage time can be much less than the diffusion time scale, L^2/D , when the number of particles is macroscopic.

This inverse logarithmic dependence on N of the first-passage time is one basic point that was recognized and exploited by the authors of [1]. Section 3 of this article presents a comprehensive review of the first arrival time of N Brownian particles in a range of simple geometries. A general feature that emerges from this section is the reduction in the first-passage time to a specified target by a factor that scales as $1/\ln N$. The nature of optimal paths to reach a target is brought into sharper focus in Section 7, where the authors discuss the more realistic situation of fastest paths to a target in two dimensions. These fastest paths can be described in terms of an effective “geometrical optics” for Brownian motion [8–10]. When there is a direct “line of sight” between the starting point and the target, the paths of the fastest Brownian particles to reach the target are concentrated on this line-of-sight path. When this line-of-sight path is blocked by an obstacle, then the optimal path is merely the shortest geodesic between the source point and the target, subject to the geometrical constraint. This observation should lay the foundations for a quantitative theory of the first-passage time in realistic systems of very many particles. Currently, such a theory does not yet exist. In particular, the heuristic approximation of the path integral (62) of the review to obtain the basic formula immediately following is unjustified.

An important application of the general theme of the focusing onto optimal paths for large N arises in the fertilization of an oocyte by spermatozoa. It is an amazing fact that a human male typically produces of the order of 10^8 sperm cells in a single ejaculation. Once released, each sperm seeks out the unfertilized egg cell and the earliest arriving sperm are the ones that can actually perform the fertilization. The model presented in [4] treated an idealization of this problem in which each sperm cell is mortal and moves by Brownian motion in a purely one-dimensional geometry to reach the egg cell. The main message from this work is that a large number of sperm cells appear to be necessary to counterbalance sperm mortality, so that there is a reasonable chance that fertilization can actually occur. In Section 5 of the review, the authors present an alternative approach, but one that also relies on large N for successful fertilization. In the discussion given in this section, each sperm cell performs ballistic motion in a random direction. Whenever the sperm reaches the wall of the uterus, it experiences a random scattering. While each individual sperm trajectory is stochastic, the trajectories of the sperm cells with the shortest arrival times are geometrically concentrated on rectilinear paths, indicating an emergent “geometrical optics”. The presence of a huge number of sperm cells also leads to a mean arrival time at the egg cell that is a decreasing function of N .

Overall, there is no doubt that the review of Schuss et al. will stimulate further research. One of the possible extensions of the model of $N \gg 1$ searchers is to account for interactions between searchers. Although this problem

is, in general, quite difficult, in some cases the “gas” of interacting particles can be efficiently described in terms of fluctuating hydrodynamics [11] and macroscopic fluctuation theory [12,13].

Acknowledgements

SR acknowledges financial support from NSF grant DMR-1608211. BM acknowledges financial support from the Israel Science Foundation (Grant No. 807/16).

References

- [1] Schuss Z, Basnayake K, Holcman D. *Phys Life Rev* 2019;28:52–79. <https://doi.org/10.1016/j.plrev.2019.01.001> [in this issue].
- [2] Feller W. *An introduction to probability theory and its applications*. New York, NY: J.S. Wiley & Sons; 1968.
- [3] Redner S. *A guide to first-passage processes*. Cambridge: Cambridge University Press; 2001.
- [4] Meerson B, Redner S. *Phys Rev Lett* 2015;114:198101.
- [5] Redner S, Krapivsky PL. *Am J Phys* 1999;67:1277.
- [6] Lindenberg K, Seshadri V, Shuler KE, Weiss GH. *J Stat Phys* 1980;23:11.
- [7] Mejia-Monasterio C, Oshanin G, Schehr G. *J Stat Mech* 2011:P06022.
- [8] Grosberg A, Frisch H. *J Phys A, Math Gen* 2003;36:8955.
- [9] Smith NR, Meerson B. *J Stat Mech* 2019:023205. <https://doi.org/10.1088/1742-5468/ab00e8>.
- [10] Smith NR, Meerson B. *arXiv*:1901.04209.
- [11] Spohn H. *Large-scale dynamics of interacting particles*. New York: Springer-Verlag; 1991.
- [12] Bertini L, De Sole A, Gabrielli D, Jona-Lasinio G, Landim C. *Rev Mod Phys* 2015;87:593.
- [13] Agranov T, Meerson B. *Phys Rev Lett* 2018;120:120601.