

# Reflected Fractional Brownian Motion in 3D-Brain Shapes: Insights into the Distribution of Serotonergic Axons

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The immediate neighborhood of virtually every brain neuron contains thin, meandering axons that release serotonin (5-HT). These axons, also referred to as serotonergic fibers, are present in nearly all studied nervous systems (both vertebrate and invertebrate) and appear to be a key component of biological neural networks. In the mammalian brain, they create dense meshworks that are macroscopically described by densities. It is not known how these densities arise from the trajectories of individual fibers, each of which resembles a unique random-walk path. This poses interesting theoretical questions, solving which will advance our understanding of brain plasticity and regeneration. For example, serotonin-associated psychedelics have recently been shown to promote global brain integration in depression [1], and serotonergic fibers are nearly unique in their ability to robustly regenerate in the adult mammalian brain [2].

We have recently introduced a conceptual framework that treats the serotonergic axons as “stochastic axons.” Stochastic axons are different from axons that support point-to-point connectivity (often studied with graph-theoretical methods) and require novel theoretical approaches. We have shown that serotonergic axons can be potentially modeled as paths of fractional Brownian motion (FBM) in the superdiffusive regime (with the Hurst exponent  $H > 0.5$ ). Our supercomputing simulations demonstrate that particles driven by reflected FBM (rFBM) accumulate at the border enclosing the shape [3]. Likewise, serotonergic fibers tend to accumulate at the border of neural tissue, in addition to their general similarity to simulated FBM paths [4].

This work expands our previous simulations in 2D-brain-like shapes by considering the full 3D-geometry of the brain. This transition is not trivial and cannot be reduced to independent 2D-sections because increments of FBM trajectories exhibit long-range correlation. Supercomputing simulations of rFMB ( $H > 0.5$ ) were performed in the reconstructed 3D-geometry of a mouse brain at embryonic day 17 (serotonergic fibers are already well developed at this age and begin to invade the cortical plate). The obtained results were compared to the actual distribution of fibers in the mouse brain. In addition, we obtained preliminary results by simulating rFBM with a region-dependent  $H$ . This next step in complexity presents challenges (e.g., it can be highly sensitive to mathematical specifications), but it is necessary for the predictive modeling of interior fiber densities in heterogenous brain tissue.

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