

Toward a Predictive Model of Serotonergic Densities: A Supercomputing Simulation of Reflected Fractional Brownian Motion in a 3D-Mouse Brain Shape

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In vertebrate brains, virtually all neural circuits operate inside a dense matrix of axons (fibers) that have a strongly stochastic character. These fibers originate in the brainstem raphe region, produce highly tortuous trajectories, and release serotonin (5-hydroxytryptamine, 5-HT), with other neurotransmitters. They can robustly regenerate in the adult mammalian brain and appear to support neuroplasticity [1], with implications for mental disorders [2] and artificial neural networks [3]. The self-organization of this “serotonergic” matrix remains poorly understood.

In our previous study, we have shown that serotonergic fibers can be modeled as paths of fractional Brownian motion (FBM), a continuous-time stochastic process. FBM is parametrized by the Hurst index, which defines three distinctive regimes: subdiffusion ($H < 0.5$), normal diffusion ($H = 0.5$), and superdiffusion ($H > 0.5$). In two-dimensional (2D) shapes based on the adult mouse brain, simulated FBM-fibers (with $H = 0.8$) have produced regional distributions similar to those of the actual serotonergic fibers [4]. However, increments of superdiffusive FBM trajectories have long-range positive correlations, which implies that a fiber path in one 2D-section depends on its history in other sections. In a major extension of this study, we used a supercomputing simulation to generate 960 fibers in a complex, three-dimensional shape based on the late-embryonic mouse brain (at embryonic day 17.5). The fibers were modeled as paths of reflected FBM with $H = 0.8$. The reflection was caused by natural neuroanatomical borders such as the pia and ventricles. The resultant regional densities were compared to the actual fiber densities in the corresponding neuroanatomically-defined regions, based on a recently published comprehensive map [5]. The relative simulated densities showed strong similarities to the actual densities in the telencephalon, diencephalon, and mesencephalon. The current simulation does not include tissue heterogeneities, but it can be further improved with novel models of multifractional FBM, such as the one introduced by our group [6]. The study demonstrates that serotonergic fiber densities can be strongly influenced by the geometry of the brain, with implications for neurodevelopment, neuroplasticity, and brain evolution.

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