

A Predictive Model of Serotonergic Fiber Densities Based on Reflected Fractional Brownian Motion

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All vertebrate brains contain a dense matrix of thin axons (fibers) that release serotonin (5-hydroxytryptamine), a neurotransmitter that modulates a wide range of neural, glial, and vascular processes. Altered serotonergic fiber densities have been associated with a number of mental disorders and conditions, such as Autism Spectrum Disorder, Major Depressive Disorder, and exposure to 3,4-methylenedioxymethamphetamine (MDMA, “Ecstasy”). Also, serotonergic fibers can regrow in adulthood and therefore can support the functional recovery of the brain after injury. However, the processes that lead to the self-organization and plasticity of this fiber system remain poorly understood.

Our previous research has shown that the trajectories of serotonergic fibers in terminal fields can be modeled as random walks [1, 2]. We now introduce a computational model that is based on Fractional Brownian Motion (FBM), a continuous stochastic process that generalizes normal Brownian Motion and allows correlations between non-overlapping increments. The model capitalizes on the recently discovered properties of the reflected FBM (rFBM) in one-dimensional domains [3, 4].

FBM is parametrized by the Hurst index (H) that allows subdiffusion ($H < 1/2$) and superdiffusion ($H > 1/2$). We show that in the superdiffusive regime rFBM-walks recapitulate some key features of regional serotonergic fiber densities, on the whole-brain scale. Specifically, by using supercomputing simulations of fibers as FBM-paths in two-dimensional brain-like domains, we demonstrate that the resultant steady-state distributions approximate the fiber distributions in mouse brain sections immunostained for the serotonin transporter (a marker for serotonergic fibers in the adult brain). These results do not sensitively depend on the H -value (for $H > 1/2$), precise estimates of which are currently difficult to obtain experimentally.

This novel framework can support predictive descriptions and manipulations of the serotonergic matrix and it can be further extended to incorporate the detailed physical properties of the fibers and their environment. We also show that this neuroscience-motivated approach can stimulate theoretical investigations of rFBM in two- and three-dimensional domains, with potential applications in other fields of science.

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