

The Self-Organization of the Brain Serotonergic Matrix: From Stochastic Axon Paths to Regional Densities

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The 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 all vertebrate species (from fish to mammals) and are an essential 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. Solving this problem will advance our understanding of the fundamental structure of neural tissue, including its plasticity and regeneration.

Our interdisciplinary program investigates the stochastic structure of serotonergic fibers, by employing a range of experimental, computational, and theoretical methods. Transgenic mouse models (e.g., Brainbow) and brainstem cell cultures are used with advanced microscopy (3D-confocal imaging, STED super-resolution microscopy, holotomography) to visualize individual serotonergic fibers and their trajectories. Serotonergic fibers are modeled as paths of a superdiffusive stochastic process, with a focus on fractional Brownian motion (FBM). The formation of regional fiber densities is tested with supercomputer modeling in neuroanatomically accurate 2D- and 3D-brain-like shapes. Within the same framework, we are developing the mathematical theory of the reflected, branching, and spatially heterogeneous FBM.