

The Stochastic Self-Organization of Serotonergic Densities

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Neural networks in adult vertebrate brains are physically embedded in meshworks of thin, functionally active axons (fibers) that originate in the brainstem. As these fibers weave through neural tissue, releasing serotonin (5-HT) with glutamate and other neurotransmitters, they produce a dense matrix macroscopically described by regional fiber densities. This matrix is fundamentally associated with neuroplasticity, with implications for mental disorders and artificial neural networks. We have recently shown that its self-organization strongly depends on the stochastic properties of single fibers and their interaction with the three-dimensional (3D) geometry of the brain. Specifically, the trajectories of individual fibers can be described as paths of reflected fractional Brownian motion (FBM) [1, 2].

We are currently using transgenic, *in vitro* [3], and other experimental approaches to guide further modeling efforts and to motivate the development of the FBM theory itself [4]. In a major extension of our previous studies, we used supercomputing to simulate 960 fibers in a complex, 3D-dimensional shape constructed from serial sections of the late-embryonic mouse brain (at E17.5) [5]. The fibers were modeled as paths of reflected FBM ($H = 0.8$) which interacted with pial and ventricular borders. The simulated densities were compared to the actual regional fiber densities in a recently published comprehensive map. Strong similarities were found in the forebrain and midbrain. This study demonstrates that regional “serotonergic” fiber densities can achieve a substantial degree of self-organization with no biological guiding signals, with implications for neurodevelopment, neuroplasticity, and brain evolution.

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References: [1] Janušonis et al. (2020) *Front. Comput. Neurosci.* 14: 56; [2] Vojta et al. (2020) *Phys. Rev. E* 102: 032108; [3] Hingorani et al. (2022) *Front. Neurosci.* 16: 994735; [4] Wang et al. (2023) *arXiv* 2303.01551; [5] Janušonis et al. (2023) *bioRxiv* 10.1101/2023.03.19.533385.