

Single serotonergic axons: From a convolutional neural network for trajectory analysis to a neuroscience-inspired dropout in machine learning

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The brain serotonergic axons (fibers) are quintessential “stochastic” axons in the sense that their individual trajectories are best described as sample paths of a spatial stochastic process. These fibers are present in high densities in virtually all regions of vertebrate brains; more generally, they appear to be an obligatory component of all nervous systems on this planet (from the dominating arthropods to such small phyla as the kinorhynchs). In mammals, serotonergic fibers are nearly unique in their ability to robustly regenerate in the adult brain, and they have been strongly associated with neural plasticity. We have recently developed several experimental approaches to trace individual serotonergic fibers in the mouse brain (Mays et al., 2022). To further advance the theoretical analyses of their stochastic properties (e.g., the increment covariance structure), we developed a convolutional neural network (CNN) that performs high-throughput analysis of experimental data collected with sub-micrometer resolution. In contrast to a recently developed mesoscale platform that can separate large-caliber fiber segments from the background on the whole-brain scale (Friedmann et al., 2020), our microscale model prioritizes the accuracy and continuity of individual fiber trajectories, an essential element in downstream stochastic analyses. In particular, it seamlessly integrates information about the physical properties of serotonergic fibers and high-resolution experimental data to achieve reliable, fully-automated tracing of trajectories in brain regions with different fiber densities. This 3D-spatial information supports our current theoretical frameworks based on step-wise random walks (Janusonis & Detering, 2019) and continuous-time processes (Janusonis et al., 2020). In a complementary approach, we also investigated whether the structure of the serotonergic fibers may provide useful information for machine learning architectures. Specifically, we studied whether dropout, a standard regularization technique in artificial neural networks, can be matched or improved by virtual serotonergic fibers moving through CNN layers (endowed with the Euclidean metric) and triggering spatially correlated dropout events.

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