ASTROCYTE-MEDIATED HIGHER-ORDER CONTROL OF SYNAPTIC PLASTICITY

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Synaptic plasticity has traditionally focused on neuron-driven changes in synaptic efficacy, yet growing evidence highlights the importance of higher-order interactions (HOIs) involving both axo-axonic and tripartite synapses. In tripartite synapses, astrocytes–a type of glial cell–modulate multiple synapses simultaneously [1], effectively implementing link-link interactions and representing a paradigmatic case of HOIs in the brain. Here, we introduce a minimal astrocyte-synapse-neuron short-term plasticity (ASN-STP) model that captures the competition between presynaptic and astrocytic mechanisms in short-term facilitation.

Building on the framework of higher-order topological dynamics [2], our model unifies previous short-term plasticity descriptions [3, 4] under a network formalism where neurons, synapses, and astrocytes correspond to 0-, 1-, and 2-dimensional elements, respectively. Simulations in a simple recurrent motif show that astrocytic modulation can prevent runaway excitation and enhance stimulus responsiveness. This may help explain why tripartite synapses are particularly common in brain regions with highly recurrent circuits, such as the hippocampus [5]. Our results highlight the stabilizing and regulatory role of HOIs in shaping neuronal dynamics.

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