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Physical interactions between D1 and NMDA receptors as a possible inhibitory mechanism to avoid excessive NMDA currents

Daniel B Smith, Lawrence C Udeigwe and Jonathan Rubin*

Address: Department of Mathematics, University of Pittsburgh, Pittsburgh, PA, USA

Email: Jonathan Rubin* - rubin@math.pitt.edu

* Corresponding author

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Coactivation of N-methyl-D-aspartate (NMDA) and dopamine (DA) receptors generates a potentially feed-forward system that could lead to excessive NMDA currents [1]. Through second messenger systems, activation of NMDA receptors increases the presence of the D1 subtype of DA receptors in dendritic spines in striatum [2]. Likewise, activation of D1 receptors increases the number of NMDA receptors in synaptic regions in striatum [3,4]. Given the potential contribution of NMDA receptor activation to apoptosis, there must be some mechanism to limit the expression of NMDA currents. This mechanism is not yet currently known, however. Cepeda and Levine [1] have suggested that physical interactions may serve as a limiting mechanism to this positive feedback system. It is known that physical interactions between D1 and NMDA receptors may lead to formation of D1/NMDA complexes and may inhibit NMDA currents [5]. We use both dynamical systems and agent-based modeling techniques to investigate whether such physical interactions are sufficient to generate a stable fixed point for NMDA current levels or, more generally, to bound NMDA currents.

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