Modeling the activity spread of Rho GTPases at dendritic spines

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***Short Abstract* — Rho GTPases signaling at dendritic spines is crucial for synaptic plasticity, a cellular correlate for learning and memory. Interestingly the activity of the Rho GTPase Cdc42 localizes persistently at dendritic spines despite it can diffuse rapidly on the membrane. We implemented a computational method that allows us to study GTPase dynamics in dendritic spines by solving PDEs on complex surfaces. Different biochemical mechanisms that could account for Cdc42 localization are evaluated. We explore the role of membrane geometry on signaling confinement.**

***Keywords* — GTPase, dendritic spine, signaling confinement, PDE, closest point method.**

I. Extended Abstract

RHO GTPases signaling is crucial for structural remodeling of dendritic spines during synaptic plasticity associated with learning and memory [1]. Recently it has been possible to image the spatiotemporal dynamics of the activation of the GTPases Cdc42 and RhoA at single spines [2]. Interestingly, the activity of Cdc42 remains localized to the spine despite it can freely diffuse on the membrane. In contrast, the activity of the RhoA diffuses out of the membrane to the dendrite. It is likely that different mechanisms involving the biochemical cycle of the GTPases and the geometry of the spine accounts for such observations. GTPases are activated after the exchange of GDP by GTP induced by guanine nucleotide exchange factors (GEFs) and become deactivated after hydrolysis of GTP promoted by GTPase activating proteins (GAPs). Moreover, active GTPases are found and diffuse at the plasma membrane, and deactivated GTPases are relocated to the cytosol by guanine nucleotide dissociation inhibitors (GDI) [3]. In order to study biochemical mechanisms that may account for the observed spatiotemporal dynamics of GTPase activity at spines, we implemented a computational method to solve reaction diffusion equations on complex geometries. With this method we model the reactions involved in the GTPase biochemical cycle, coupling diffusion on the membrane with diffusion in the cytosol. The method is second order accurate in the grid spacing and is based on an embedding technique known as the closest point method [4,5]. We implement different reaction schemes that predict signaling localization and we focus on how spine geometry may play a role on signaling spatiotemporal dynamics. We observe that membrane curvature can be an important factor to induce signaling compartmentalization by modulating GTPase diffusion.

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