# Modeling the spatiotemporal dynamics of Cdc42 activity at dendritic spines accounting for membrane geometry

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***Short Abstract* —Long lasting remodeling of dendritic spines induced by synaptic activity has been associated with learning and memory. Upon synaptic stimulation, the activity of the Rho GTPase Cdc42 localizes to the stimulated dendritic spine in a sustained manner. Long lasting activity localization occurs even though Cdc42 can rapidly diffuse in and out of the spine. Here we describe the spatiotemporal dynamics of Cdc42 activation at dendritic spines as the numerical solution of Reaction-Diffusion equations on spine-like geometries. We propose that positive feedback of activation together with the geometry of the spine can account for long lasting localization of Cdc42 activity.**

***Keywords* — Cdc42, dendritic spine, signaling localization, Reaction-Diffusion equations.**

## I. Introduction

SYNAPTIC activity induces sustained structural remodeling of dendritic spines, the input site of most synapses, in a process associated with learning and memory. This long lasting remodeling is specific to the stimulated spine; neighbor spines not stimulated remain unchanged. The molecular basis of the specificity of sustained spine remodeling has not been fully elucidated, however, upon spine stimulation, the activity of Cdc42, a GTPase known to regulate dendritic spine structure, localizes at the membrane of the stimulated spine in a long lasting manner [1]. Interestingly, sustained localization of active Cdc42 occurs even though Cdc42 itself can rapidly diffuse in and out of the spine.

Cdc42 also localizes in yeast, where it forms a cluster on the membrane that directs budding and mating. In this system a positive feedback of activation that recruits inactive Cdc42 from the cytosol has been shown to be necessary for clustering [2]. Furthermore, it is believed that depletion of a cytosolic substrate of the activation reaction [3, 4], is required to prevent the positive feedback from completely covering the membrane with Cdc42.

Depletion of a cytosolic substrate is not likely to occur in dendritic spines as they are connected to the much larger dendrite. Taking this into consideration we propose a model for sustained localization of Cdc42 activity at dendritic spines that does not require the substrate depletion condition.

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## II. Results

*A.* We describe the spatiotemporal dynamics of Cdc42 activation at the dendritic-spine membrane as the numerical solution of Reaction-Diffusion equations on spine-like geometries. We use a model for positive feedback of Cdc42 activation that describes the spread of Cdc42 activity as a traveling wave front [4]. In this scenario, membrane geometry results in sustained localization of active Cdc42 at dendritic spines without requiring depletion of cytosolic substrates such as inactive Cdc42.

*B.* Our simulations suggest that the width of the spine neck is a critical geometrical parameter that controls sustained localization of activity. Thin spine necks promote activity confinement, whereas thick spine necks result in activity spread. The simulations also show that higher diffusion coefficients of Cdc42 on the membrane promote confinement of activity, which seems counterintuitive.

*C.* The results of our simulations are in qualitative agreement with theoretical predictions of the effect of surface geometry on wave front dynamics. However, we observe quantitative differences between simulations and theory. In particular, the predicted critical values of parameters controlling localization of Cdc42 activity differ between simulations and theory. We investigate the cause of such discrepancy.

## III. CONCLUSION

We propose that positive feedback of activation coupled with the unusual spine geometry can explain the sustained localization of active Cdc42 at dendritic spines upon synaptic activity.

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