Dynamic modeling reveals a saturation rule that governs the switch between uni- and multi-polar growth

Jian-geng Chiou[1], Timothy C. Elston[2], Thomas P. Witchelski[3], David G. Schaeffer[3], Daniel J. Lew[1]

1. Department of Pharmacology and Cancer Biology, Duke University
2. Department of Pharmacology, University of North Carolina at Chapel Hill
3. Department of Mathematics, Duke University

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Precisely orchestrated polarization is crucial for the development of complex cell morphology. For example, neuron cells require polarized growth at multiple cortical domain to form dendrites, but robustly switch to uni-polar growth so that only one further elongates and eventually becomes the axon. Results from both experiments and dynamic modeling have shown that the polarization of Rho-GTPases directs polarized growth throughout Eukaryotes, but what determines the number of polarity domain remains elusive.

In previous studies, it has been shown that a two-component partial differential system that models Rho-GTPase dynamics captures the “competition” behavior between multiple transient polarity clusters, which guarantees uni-polarity. Intriguingly, we demonstrated that with appropriate change of parameters, this system switches to multi-polarity. Applying mathematical analyses, we introduced a “Saturation rule”, which formulates the criteria of uni- and multi-polarity, and it can be applied generally to models of similar structures. In the intuitive sense, the saturation rule states that there exists an innate saturation point of Rho-GTPase concentration, and the number of polarity domain that will persist is determined by the number of Rho-GTPase clusters that approach the saturation point.

We then turned to the budding yeast, and showed with fluorescent microscopy that simulations of our model recapitulate the dynamics of polarity clusters *in vivo*. We further showed with cytokinesis defect mutants that the Rho-GTPase machinery of the budding yeast is competent to produce multiple buds. Lastly, we tested the saturation rule by genetically manipulating the Rho-GTPase machinery, and showed that the saturation point and the level of polarity proteins can be engineered to change the number of buds. Confirmed in the budding yeast, this research can be applied to different Rho-GTPase systems in various cell types, where the reason of saturation may differ depending on the specific molecular interactions, but the general rule holds universally.