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Modelling cell motility and pathways that signal to the actin cytoskeleton[1]

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Gradient sensing, polarization, and motility of rapidly moving cells such as neutrophils involves the actin cytoskeleton, and regulatory modules such as membrane bound phosphoinositides (PIs), kinases/phosphatases, and proteins of the Rho family (Rho GTPases). I describe recent work in my group in which we have modeled components of these modules, their interconversions, interactions, and action in the context of protrusive cell motility. By connecting three modules, we find that Rho GTPases work as a spatial switch, and that PIs filter noise, and define the front vs. back. Relatively fast PI diffusion also leads to selection of a unique pattern of Rho distribution from a collection of possible patterns. We use the model to explore the importance of specific hypothesized interactions, to explore mutant phenotypes, and to study the role of actin polymerization in the maintenance of the PI asymmetry. Collaborators on this work include A.T. Dawes, A. Jilkine, and A.F.M. Maree.

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