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Feedback onto cellular polarization from paxillin, implications for migrating cells.

Cellular polarization plays a critical during cellular differentiation, development, and cellular migration through the establishment of a long-lived cell-front and cell-rear. Although mechanisms of polarization vary across cells types, some common biochemical players have emerged, namely the RhoGTPases Rac and Rho. The low diffusion coefficient of the active form of these molecules combined with their mutual inhibitory interaction dynamics have led to a prototypical pattern formation system that can polarizes cell through a non-Turing pattern formation mechanism termed wave-pinning. We investigate the effects of paxillin, a master regulator of adhesion dynamics, on the Rac-Rho system through a serine phosphorylation-dependent positive feedback loop that amplifies Rac activation. We find that paxillin feedback onto the Rac-Rho system produces cells that (i) self-polarize in the absence of any input signal (i.e., paxllin feedback causes a Turing instability) and (ii) become arrested due to the development of multiple protrusive regions. The former effect is a positive finding, while the latter outcome is likely an artefact of the model. In order to minimize the effects of this artefact to produce cells that can both self-polarize and migrate for extended periods of time, we revisit some of model's parameter values and use lessons from previous models of polarization. After some simple modifcations to the model, our simulations behave very much like these previous models while being significantly simpler yet biochemically detailed. Thus this work yields insights into the biochemical acitivties of paxillin as well as general feedback patterns necessary for effective cellular migration.