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Stochastic Inference of Cell Migration Phenotypes

Cell migration requires precise spatiotemporal regulation of the actin cytoskeleton. Key regulators of cell movement are the Rho family of GTPases. Experimental data and computational models have described the role of the Rho GTPases Rac1, Cdc42 and RhoA in cell polarization and migration.

To investigate the role of RhoG, a Rac-like Rho GTPase, in cell migration, we developed computational tools, based on stochastic modeling, to analyze time series data for the position of randomly migrating cells. Our approach allows parameters that quantitatively characterize cell movement to be efficiently estimated from experimental data. This feature revealed that randomly migrating cells stochastically transition between distinct states of migration characterized by differences in cell speed and persistence.

The predicted states are shown to correlate with differences in the spatiotemporal activity of the Rho family members Rac1 and RhoG. We have also shown that RhoG is actively transported to the leading edge of migrating cells, and this approach has shown that without RhoG the locations of Rac1 activity are less spatiotemporally dynamic leading to an increase in persistence in this case. This leads us to hypothesize that RhoG is required to hasten formation of localized regions of Rac1 activity, and by this mechanism RhoG can regulate turning in randomly migrating cells.