

# Complexity DTC – Miniproject Proposal

## Modelling Actin/Myosin Dynamics in Cell Polarity Reversals

Till Bretschneider  
Warwick Systems Biology Centre  
[T.Bretschneider@warwick.ac.uk](mailto:T.Bretschneider@warwick.ac.uk)  
<http://go.warwick.ac.uk/bretschneider>

Directed cell motion in response to extracellular signals, for example a source of chemical attractant, electrical fields or mechanical inputs, is key to many fundamental biological processes such as embryogenesis, wound healing, or metastasis. Polarization of cells is a prerequisite for directed cell motion as cells have to form a front that is functionally different from the rear. The front of migrating cells is characterized by a flat membrane protrusion, a so called leading lamella, which is pushed forward by polymerization of the cytoskeletal protein actin into a dense interconnected network of filaments. Contraction of the cell rear mediated by Myosin-II, a motor protein, results in net translocation. Myosin acts as an inhibitor in such that it prevents protrusions to be formed elsewhere than at the front and that extension of the front only sets in when myosin is disassembled there.

*Dictyostelium discoideum*, an eukaryotic microorganism, is a model organism for studying cell motility, because it can be easily genetically modified and the amoeboid form of its movement and the regulation of the latter is very similar to what we find in neutrophil cells of the human immune system. We have studied actin/myosin dynamics in *Dictyostelium* cells undergoing repolarization under mechanical and chemical stimulation (Dalous et al., 2008). An interesting finding is that when the direction of the stimulus is reversed actin at the former front rapidly disassembles before it reassembles at the new cell front. This is contrary to what previous models of cell polarization have suggested, namely fast excitatory kinetics for the activation and self-stimulation of a cell front, and slower inhibition of the cell rear. Our experiments suggest that fast inhibition first destroys any existing actin patterns to make a cell susceptible to stimuli from another direction.

For the miniproject we propose to develop a mathematical model for actin/myosin dynamics that can explain the observed rapid breakdown of actin at an leading edge of a cell in response to a signal input from another direction. We will start with one dimensional generic activator-inhibitor, reaction-diffusion type models using Matlab. These models will be evaluated using existing data. Depending on the student's background there are various options. Either one could develop a more realistic two-dimensional model that tries to mimic the experimentally observed spatio-temporally dynamics of actin and myosin, and/or the model could be implemented in a higher-level systems biology programming environment such as CompuCell 3D.

With regards to a possible PhD project we have developed more refined methods to correlate the motion of the cell boundary with spatio-temporal dynamics of actin/myosin and its regulators (Bosgraaf et al., 2009), which will provide a rich data source for detailed mathematical models in the future.

### References:

- L. Bosgraaf, P.J.M. van Haastert, T. Bretschneider. [Analysis of cell movement by simultaneous quantification of local membrane displacement and fluorescent intensities using Quimp2](#). Cell Motility and the Cytoskeleton, in press, 2009.
- J. Dalous, E. Burghardt, A. Müller-Taubenberger, F. Bruckert, G. Gerisch, T. Bretschneider. [Reversal of cell polarity and actin-myosin cytoskeleton reorganization under mechanical and chemical stimulation](#). Biophys. J., 94(3):1063-1074, 2008.