Gradient sensing by template matching

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Directed motion of animal cells towards external signals, such as mechanical, electrical or chemical cues, plays important roles during development, the immune response and cancer. Gradient sensing is the process whereby external signal gradients are translated into intracellular gradients of specific phospholipids within the cell membrane, specifying an axis of polarity. These patterns are read out by signaling components localising the actin and myosin machinery responsible for pushing the front and pulling the rear of cells. A puzzling question is the enormous sensitivity of cells being capable of detecting differences in concentration of a chemoattractant between cell front and rear of as little as 1-2%, in the case of *Dictyostelium* amoebae. A number of mathematical models for gradient sensing have been proposed which mostly are based on reaction-diffusion Turing-type models. These explain well how minute extracellular gradients can be amplified to give rise to much more strongly graded distributions of intracellular signaling molecules. However, they require that cells have a mechanism to finely adjust the threshold for front activation. The goal of this miniproject is to explore an entirely different mechanism. The idea is based on the observation that components signaling to the actin cytoskeleton and actin itself have been shown to self-organise into dynamic spatial patterns even in the absence of any extracellular signal gradients. Rather than the external gradient promoting front-activation when above a threshold level, we want to explore whether spontaneously generated intracellular patterns could provide a mechanism which works similar to template matching. If an intracellular gradient is perfectly aligned with an external gradient it elicits maximum response, but still results in a partial response in the case of slight mismatches. This corresponds to a convolution of the intracellular and extracellular gradient, a mechanism which essentially would be threshold free.

What the student will do:
Develop ideas for mathematical models for template matching of signal gradients. Couple these models to models for spontaneous intracellular pattern formation and implement these in Matlab.

Avenues for a PhD project:
We have recently started to study reorientation of *Dictyostelium* cells to alternating gradients of shear flow. The theoretical ideas developed in the current miniproject could form the basis for a interdisciplinary project where experiments are designed to rigorously test competing models for gradient sensing.