Controlling Cell Migration Strategies by External Cues

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In the quickly-evolving, broad scientific field of biochemical signalling networks, which includes eukaryotic chemotaxis, Ca\(^{2+}\)-signalling, embryogenesis, angiogenesis as well as applications for drug delivery and pharmaceutical assays, relevant approaches to introduce large-scale microfluidic cell environments of spatially homogeneous but rapidly time-varied chemical gradients are needed. Earlier approaches in the field of gradient generation, like the pioneering chemotactic micropipette assays, failed to resolve the probabilistic behaviour of cell ensembles. There, exposure to stimuli over extended time periods preclude cellular response characteristics and interplay between different feedback motifs at short time scales. Recent experimental approaches apply a rapid global rise in chemoattractant, thereby preventing the distinction between the leading edge and the signalling involved in the rear contraction.

In our unique setup, we combine continuously tuneable with rapidly switchable gradients, which force cells to invert their polarisation direction [1]. This method thus yields the required statistical data within the timescale of the involved biochemical signalling network. Our novel experimental design makes it possible to access readily the fast time scales of intracellular signalling networks, and allows for massive parallel measurement of cell populations, which opens the way to in-depth statistical analysis.

Proof of principle experiments show cells in a `chemically trapped´ state for switching frequencies extending the response times of intracellular feedback for migrational reorientation. For low frequency gradient switching, corresponding oscillatory runs are observed. Fluorescent measurements, using a Lim-Gfp label that is ideal for observing actin polymerisation, indicates a distinct response delay between the application of a switch in the gradient direction and the reversal of cell polarisation. Furthermore, a down phase of reduced actin polymerisation after the reversal of cellular polarisation is initiated. These results are also promising for identifying spatio-temporal control of cell functions. Further, we expose cells to other external cues and monitor intracellular information transport [2] and cellular response dynamics [3].

References:


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