Competing Chemical and Topographical Signals in *Dictyostelium discoideum* migration

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***Short Abstract* —We investigate cell motility of a model system, *Dictyostelium discoideum*, in the presence of chemical signals and under more complex inputs. Analytically and in simulations, we investigate signal processing of a single cell. We then experimentally study the operation of groups of cells under chemical signals and, finally, we investigate how individual cells and cell groups operate when chemical signals compete with other input, in particular with surface topography. Our experimental work focuses on characterizing the decision making of cells faced with obstacles in surface topography. Our initial results highlight how surface sensing couples into gradient sensing in motile cells.**

***Keywords* — Cell Migration, Chemotaxis, Dictyostelium, Multiphoton Absorption Polymerization**

I. Introduction

Cellular migration is an important physiological process that is integral to development, metastasis, and wound healing. Cells face a myriad of signals that could affect cellular migration, such as chemical, mechanical and topographical cues. In order to decide in which direction and at what speed to move, cells must interpret these sometimes competing signals.

To study the effects of competing biochemical and topographical signals on cellular migration pathways, we use the model system *Dictyostelium discoideum*. Under certain developmental conditions, the amoeba *D. discoideum* migrates up a cyclic adenosine monophosphate (cAMP) concentration gradient.

In this presentation, we will highlight key features of the gradient sensing pathway of a single cell that we have studied analytically [1] and in simulations [2]. In addition, we will describe experimental observations of the response of cells and cell groups to more realistic cell input, in which chemical and topographical signals compete. In particular, we will focus on grooves and ridges, which polarize the cell in a direction different than the direction of the chemical signal, and on cliffs, which prevent motion of the cell in the direction of the chemical signal.

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II. Methods

We used Multiphoton Absorption Polymerization (MAP) to fabricate micron-scale features out of acrylate polymers. We fabricated variously sized ridges, or wide, short columns, of size a few microns tall and wide, and hundreds of microns long. We also created identically sized grooves. The grooves were created by making a PDMS mold of a set of ridges, and then by further making another PDMS mold of this ridges mold. This mold of a mold allowed us to stamp grooves into surfaces.

III. Results and Conclusions

The response of a single cell to chemical signals is tightly regulated by two positive and one inhibitory feedback loop. Depending on the strength of the feedback loops, the cell can either adapt quickly to changing directions or maintain its orientation in a more stable way. Cell groups cooperate in their response to a signal, though the possible advantages of cooperation are still under investigation. When faced with competing topographical signals, we observe that *D. discoideum* is more affected by ridges than by grooves. When the chemical signal is positioned above and away from the edge of a cliff, cells recognize the abrupt end of a surface and do not fall off the cliff. Instead, cells change their direction of motion, and move along the edge of the cliff structure. How such competing topography influences the intracellular chemotactic signals is currently under investigation by our group.

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References

[1] R. Skupsky, W. Losert, and R. Nossal, "Distinguishing modes of Eucaryotic Gradient Sensing", Biophysical Journal 89, 2806-2823 (2005).

[2] R. Skupsky, C. McCann, R. Nossal, and W. Losert "Bias in the Gradient Sensing Response of Chemotactic Cells" Journal of Theoretical Biology 247, 242-258 (2007).