Contact Guidance of Amoeboid Cells via Nanotopography

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***Short Abstract* — We investigated the shape dynamics of the amoeba *Dictyostelium discoideum* on nano-topographical gratings. Cellular migration parallel to the grating ridges is termed contact guidance. We quantified the cellular velocity, eccentricity, and protrusion dynamics on the gratings. Using a model based on a non-linear Langevin equation, we defined a measure of contact guidance efficiency. Testing various grating spacings, we found that ridges spaced ~1 µm apart had the greatest efficiency, and so best guided cells. We also modeled the cells as damped harmonic oscillators, extracting spatial and temporal scales that could implicate actin waves as a possible mechanism of contact guidance.**

***Keywords* — cellular migration, chemokinesis, contact guidance, resonance, actin waves.**

I. Introduction

THE shape of a surface can guide the way in which cells migrate on that surface, which is a process termed contact guidance [1]. Cells can be guided by surface topographical features that range from the microscopic (*e.g.*, the diameter of collagen fibers) to the nanoscopic (*e.g.*, individual collagen fibrils or molecules). Understanding surface contact mediated guidance is important in understanding how cells migrate through extracellular matrix and in designing substrates for tissue engineering. We studied the contact guidance of the amoeba *Dictyostelium discoideum* on nanotopographical gratings of various spacings.

In the tissue engineering literature, two contact guidance mechanisms have emerged from among many: patterning of focal adhesions, and filopodial sensing [2]. *D. discoideum* do not have focal adhesions, and so, in our case, focal adhesion patterning does not seem to be a plausible contact guidance mechanism. While we cannot rule out filopodial sensing, we would like to propose another possible mechanism for contact guidance. We have previously found that *D. discoidium* have wave-like protrusive dynamics [3,4]. Also, internal waves, such as actin waves, likely play a role in migration dynamics [5]. Since actin waves have been shown to be affected by external objects [6], we hypothesize that contact guidance could be governed by a wave-based mechanism.

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II. Shape Dynamics of Contact Guidance

Even in the absence of focal adhesions, we found that *D. discoideum* preferentially migrate parallel to the ridges in nanotopographical gratings. We quantitatively analyzed the affect of the gratings on the cellular eccentricity, velocity, and protrusion dynamics. We found that the greater the cellular velocity, the more likely the cell is to be moving parallel to the ridges. Similarly, the more eccentric the cell, the more likely the cell is to be oriented parallel to the ridges. Analyzing protrusions and retractions, we found that cells oriented parallel to the ridges extend protrusions and retractions over a more narrow region of their boundary than cells oriented perpendicular to the ridges. Cellular orientation with respect to the ridges does not affect retractions at the front of the cell.

We used two simple models to describe the key physical mechanisms directing amoeboid motility. In the first model, we used a Langevin equation of motion for the cell orientation in the presence of ridges [7]. With this model, we quantified the surface contact guidance efficiency as the ratio of signal strength to noise of the guidance cue. We observed agreement with the experimental observations and a peak which suggested resonance around the wavelength of actin waves.

To capture the resonant characteristic of the cells, we used a driven, damped harmonic oscillator model in the presence of external, stochastic or deterministic oscillations. By matching the experimental results with the model, we extracted mechanical properties of the cell in addition to the characteristic features of the stochastic driving force.

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