Stochastic Modeling of Mechanisms for Cellular Contact Guidance

Can Guven[1], Meghan Driscoll[1], Xiaoyu Sun[2], John Fourkas[2], and Wolfgang Losert[1]

***Short Abstract* — We observe and quantify contact guidance of amoeboid cells. Ridges on the surface are able to guide cells, leading to preferential motion. We analyze the statistics of cell orientations with a model based on a non-linear Langevin equation. The model identifies the surface contact guidance efficiency as the signal to noise strength of the guidance cue. The signal to noise is maximized around 1 µm, the wavelength of actin waves, which drive cell motility. We also characterized the cells as damped harmonic oscillators inspired by observations of traveling actin waves and obtained information about cell mechanics.**

***Keywords* — Langevin equation, stochastic resonance, actin waves, contact guidance, cell motility.**

I. Introduction and Background

DIRECTED cell migration is important in phenomena as diverse as the immune response of higher animals [1], wound healing [2], neuronal patterning [3], and vascular [4] and embryonic [5] development. Cell migration is guided by a number of cues. The best studied are chemical signals that induce migration in a preferred direction.

Cells can also sense the shape of the surface they are migrating on and adjust their migration behavior in response to that shape. This process, called contact guidance, is a well-established, yet not well understood effect. Recent studies have shown that focal adhesion complexes (FACs) [6], structures involving dozens (if not hundreds) of proteins, can organize with a preferred orientation based on the surface nanotopography. However, many fast moving cells migrate in an amoeboid fashion without mature focal adhesion complexes, relying instead on the simpler dynamics of their actomyosin machinery, protrusions and retractions, coupled with non-specific adhesion to surfaces.

In this study, we used stochastic modeling methods to describe the dynamics of surface contact guidance. 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]. We quantified the surface contact guidance efficiency as the ratio of signal strength to noise of the guidance cue. This ratio can be interpreted as a measure of the guidance efficiency. Guidance efficiency peaks at a preferred wavelength of the topography of the surface. To capture the peak we modeled it as a resonance of a driven, damped harmonic oscillator in the presence of external, stochastic or deterministic oscillations. By matching the experimental results with the model, we extracted surface guidance characteristics of the cell in addition to the characteristic features of the stochastic driving force.

II. Dynamics of Contact Guidance

To describe the dynamics underlying contact guidance, we introduced a potential that incorporates the symmetry of the ridges. The Langevin equation is composed of a deterministic torque derived from this potential that drives the cells to orient along the ridges and a stochastic torque that mimics fluctuations. In the large ensemble limit, we calculated the stationary probability distribution from the corresponding Fokker-Planck equation. We observed a peak in guidance efficiency which suggested resonance around the wavelength of actin waves. To further analyze the resonant characteristics, we considered travelling actin waves as the driving force for the cells, which we characterized as damped harmonic oscillators. We fit the power spectrum of stochastic and classical oscillations to the contact guidance efficiency data to extract information about the characteristic time and length scales of the cells. Finally, the asymptotic behavior of the power spectra yields scaling relations, which allows us to assess how contact guidance in our model cell line relates to contact guidance in other cell lines [8].

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[1]Department of Physics, University of Maryland, College Park, MD 20742, USA. E-mail: cguven@umd.edu

[2]Department of Chemistry, University of Maryland, College Park, MD 20742, USA.

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