Stochastic Model of Cell Alignment in Traps

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***Short Abstract* — Experiments with *E. coli* cells growing in open-walled extended microfluidic traps with have shown that cells orient themselves orthogonally to the long side of the trap. We develop a stochastic model of cell dynamics that explains this phenomenon. We find that steady-state cell alignment is a function of the aspect ratio of the trap as well as the cells' ability to sense their position within the trap. In the absence of this sensing, boundary effects dominate and steady-state cell orientation becomes exactly opposite of what is experimentally seen.**

***Keywords* — Cell Alignment, Aspect Ratio, Spatial Moran Model, Mean-Field Approximation, Phase Transition, Transcritical Bifurcation, Synthetic Biology**

EXTENDED ABSTRACT

EMERGENT patterns and structures are ubiquitous in biology: leopards develop spotted patterns on their skin [1], mushrooms form fairy rings, and specialized cells conglomerate to form tissues with specific forms. The question of *how* these structures emerge has been a research focus in recent years from both the biological and mathematical perspectives. Examples include the study of Turing instabilities [2], pattern formation on the skin of several animals [1], and tumor initiation and growth [3,4].

Recently, experimentalists have observed an emergent structure in the synthetic biology laboratory. *E. coli* cells growing in open-walled, extended microfluidic traps as a monolayer align orthogonally to the long side of the trap. In this synthetic setting, cellular movement is driven by the growth of the cells along the major axis of their capsule-like body. Experimental evidence also shows that growth-induced cell movement is preferential toward the nearest boundary in the trap, so as to minimize the number of cells a given cell needs to push in order to grow. That is, cells grow in directions where physical resistance is minimal.

To understand the mechanism behind this emergent behavior, we model the trap as an M x N lattice and treat the cells as oriented (vertical or horizontal) particles growing along their major axis on the lattice according to a spatial Moran process. These are typically used as a modeling framework for tumor initiation and growth [3,4]. One differentiating factor between our Moran process formulation and others' is that the growth rates for cells in our model are space-dependent. This reflects a cell's tendency to grow toward the nearest boundary.

Monte Carlo simulations of this model show steady-state cell alignment orthogonal to the long boundary of the lattice, as in experiments. That is, for $M/N > 1$, cells orient horizontally whereas for $M/N < 1$, cells orient vertically. In the interesting case where $M = N$, the system reaches a quasi-equilibrium wherein cells orient orthogonally to the boundary nearest them; however, cells equidistant from the two boundaries constantly switch between orientations. Specifically, the aspect ratio M/N acts as a bifurcation parameter for a transcritical bifurcation in the system at the critical value $M/N = 1$.

Removing space-dependence from the growth rates yields steady states that have cell alignment *parallel* to the long boundary. This is due to boundary effects. There are more chances for cells oriented orthogonally along the long boundary to exit the trap than the short boundary. Boundary size dichotomy dampens cellular growth orthogonally to the long boundary when growth is space-independent. Cell alignment at steady state is therefore a balance between boundary effects and growth dampening caused by physical resistance from other cells.

We make this balance explicit by characterizing lattice dynamics with Heisenberg equations [5] and invoking a mean field approximation to derive a single effective equation for the dynamics of the fraction of cells in a given orientation. The latter is a logistic equation whose growth term reflects the tug-of-war between boundary effects and physical resistance between cells. In this analytically tractable framework, we show the existence of critical parameter values that dictate a phase transition between bulk cell alignments at steady state.

Steady-state cell alignment in traps is the result of a balance between boundary effects and physical resistance to cellular growth. The latter is crucial for cells to align orthogonally to the long side of the trap, as in experiments. We find that even small differences in growth rate at the level of individual cells can translate to large differences at the population level.

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