Adhesive forces play key roll in pattern formation and stability in chemotaxing cells

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***Short Abstract* — The slime mold cell *Dictyostelium discoideum* is well studied, serving as both a model for amoeboid motion as well as for g-protein mediated chemotaxis up gradients of cyclic adenosine monophosphate (cAMP). Since cells also secrete cAMP, they end up in heat-to-tail "streams" that help the colony collapse into an aggregate to facilitate sporulation. We investigated the role of cell-cell and cell-surface adhesion on these heat-to-tail patterns. Using cell shape analysis, we found evidence of actin wave transmission across cell neighbors, a phenomena that disappears upon the loss of surface adhesion. Additionally, by tuning external buffer concentrations to diminish cell-cell adhesion, we found that large scale streaming structures were progressively absent from self-aggregation experiments with low adhesion, suggesting a role for mechanical interactions in stabilizing migratory patterns. Using numerical simulations, we demonstrate that adhesion preserves cell-cell contacts over time, which stabilize otherwise transient streams into cohesive structures.**

***Keywords* — Dictyostelium discoideum, chemotaxis, streaming, adhesion, actin, simulations**

I. INTRODUCTION

THE slime mold cell *Dictyostelium discoideum* is well studied, providing a model organism for the study of amoeboid motion as well as for g-protein mediated chemotaxis up gradients of cyclic adenosine monophosphate (cAMP) [1,2]. When in a nutrition poor environment, cells begin to secrete cAMP and migrate, which leads to heat-to-tail "streams" that help the colony collapse into an aggregate to facilitate sporulation. The migration itself is due to preferential polymerization of actin, which has been seen to create protrusion waves that travel down the cell [2].

II. DO MECHANICAL CUES STABILIZE STREAMS?

We focused our attention on investigating possible adhesive cues to stream formation and stability, both due to cell-cell and cell-substrate contact. Ion concentration is known to be able to vary cell-cell adhesion and cell substrate adhesion, because, by screening out the negative charges on cells and some substrates, e,g, glass surfaces, ions reduce the electrostatic repulsion between them [3]. We studied migration of cells in medium with different ion concentrations and found that diluted medium greatly inhibits the formation of cell-cell contact but retains cell-surface contact and cell motility [4]. Cells exhibit significant steaming defect and aggregate through very short streams when cell-cell contact is partially inhibited. With even lower ion concentration, cells remain active motion but do not form multicellular streams or cell-cell contact. Thus, these experiments elucidate that inhibiting cell-cell/substrate contact results in significant collective streaming defect: cells do not align in a head-to-tail fashion without proper adhesions.

To focus only on cell-cell adhesion, we developed a numerical model of chemotactic migration. Treating the center-of-mass motion of each cell as being driven by the relative local cAMP concentration and the resultant motion as a sum over protrusions [2], we compared the stability of cell-cell contacts in ensembles of cells migrating in an external gradient [5]. In particular, we measured the fraction of broken contacts over a period of time, F, which is normalized by the same measure on experiments with secretion inhibited. We demonstrated that this measure properly distinguishes "boundaries" in the pseudo-phase diagram (with respect to density and external concentration) representing regions of steady state individual motion, streaming, and aggregation. By then including cell-cell adhesion, we found that the region of individual motion shrinks in favor of streaming, representing an earlier onset of stream stability.

III. CONCLUSION

We've shown that cell-cell and cell-surface adhesion play a role in stabilizing the local neighborhood allowing for the transmission of actin protrusive waves across cell-cell boundaries as well as preventing loss of neighbor contacts. This in turn allows for easier stream formation and stabilizes those streams that form, leading to faster formed aggregates containing a larger portion of the cell population.

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