Stability Analysis of a Model for Collective Migration of Dictyostelium Discoideum

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***Short Abstract* — We developed a persistent random walk model to describe the motion of groups of *Dictyostelium discoideum* cells in response to competing inputs from both an external linear gradient and cell-cell signals. A key parameter is the ratio of amplitude of the cAMP secreted from individual cells versus the external cAMP field. The simulations are compared to experiments for a wide range of different external signal strengths for both cells that secrete cAMP and a mutant which cannot relay cAMP. We carry out a stability analysis to study under which conditions the motion of the cells leads to clustering.**

***Keywords* — Collective motion, gradient sensing, agent-based modeling, stability analysis.**

I. Introduction

Signal relay, a process that transmits information, assists the directional migration of the amoeba *Dictyostelium discoideum* [1]. It is well known that cells are able to migrate towards an external signal (cAMP), a phenomenon also known as chemotaxis. The wild-type strains of *D. discoideum* also relay the signal by emitting additional cAMP which allows information about external signals to be transmitted effectively over long distances, but also attracts cells to their neighbors and leads to the formation of groups of attached cells that move as streams [2]. In contrast, the mutant *aca*$^-$ lacks the inter-cellular communication but still follows an external cAMP signal. Thus, the mutual attraction between neighboring cells and clustering is a hallmark of signal relay. However, the local signal geometry of one commonly used setup for chemotaxis experiments, a needle emitting the chemoattractant cAMP at a constant rate, naturally draws cells toward a point and thus forces cells closer to each other whether they are mutually attracted through signal relay or not.

A linear chemical gradient on the other hand, such as e.g. generated with a taxiscan system [3] has no bias towards a single point. Consequently, experiments show a notable visual distinction between cells that relay signals (they cluster) and cells that do not relay signals. In addition by tuning the linear gradient strength one can tune the relative strength of signal relay and external signal. Our aim is to develop a simple model to capture the clustering instability due to signal relay of migrating cells in a linear gradient.

Acknowledgements: This work was supported by NIH grant R01GM085574.

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II. Model

We use insights from in depth experimental studies of cell migration characteristics to define the following basic parameters: We describe cell motion at time t using the displacement of the cell center position vector $\mathbf{r}_i(t)$ and the orientation $\mathbf{n}_i(t)$. The speed of cells is assumed to be constant, independent of signal strength, in agreement with controlled chemotaxis experiments [4]. The cells are then subjected to the chemoattractant cAMP, which is expressed by a concentration field $C(\mathbf{r},t)$. $\mathbf{n}_i(t)$ depends on the gradient of the chemoattractant. The orientation $\mathbf{n}_i(t)$ is attracted toward the attractor vector $\mathbf{g}_i(t)$, which consists of the gradient of the cAMP calculated at the front of the cell plus a noise term. *D. discoideum* does not require motion to sense directional changes in the concentration [5]. This justifies adding an independent gradient sensing mechanism which affects the motion.

To quantify whether the cells are attracted to each other in a linear gradient chamber, we formulate a phenomenological model: *(i)* Cells are described as soft, penetrable disks, repelling their neighbors based on overlapping area. *(ii)* They move in the direction of their orientation vector, which converges to the gradient of the cAMP. *(iii)* The speed of cells v_0 is constant, as in other agent-based models [6]. *(iv)* We include a simple memory process where cells update $\mathbf{g}$ at a slower rate than the position update rate, which yields a persistence in the orientation of cells, in agreement with experimental observations. We find that the model as anticipated captures both independent motion and the formation of aggregates when cells relay the signal. Finally, we test the stability of the model under different conditions to determine different patterns of aggregation.

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