Cellular Motion: From Waves to Migration

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Short Abstract — *Dictyostelium discoideum* is a model system for the study of cellular migration. Though chemoattractants steer these cells over long time-scales, on short time-scales we found that they do not significantly straighten their paths. Analysis of their dynamic cell shape shows that localized waves of protrusive motion emanate at the front in a zig-zag fashion, suggestive of the robust straightness. As the waves advect backwards, they get closer to the region in which the cell is in contact with the surface. These waves are present even when the majority of a cell is extended over the edge of a cliff.

Keywords* — Cellular Migration, Chemotaxis, *Dictyostelium

I. Purpose

In chemotaxis, cells move in the direction of a chemoattractant. Though the behavior of individual cells varies widely, chemotaxis works remarkably reliably for key processes such as wound healing and development, indicating that the process is well controlled. A standard model of chemotaxis is the "compass" model, in which chemoattractants guide cells by initiating actin polymerization in the direction of highest chemoattractant gradient [1]. Yet recent data, from our group and others, suggests that regardless of the strength of the chemoattractant gradient, and even at uniform chemoattractant concentration, cells move equally persistently at short time scales [1,2]. We sought to better characterize this robust short time-scale motion, using the model system *Dictyostelium discoideum*. These social amoebae sense and secrete chemoattractants, forming 'streams' as they self-aggregate.

II. Results

We compare key metrics of motion -- speed, persistence in direction, and directionality toward a chemical signal - in streaming cells versus mutants unable to stream, and we find that speed and directional persistence on short timescales remain unchanged under all conditions tested. These results point to the presence of an intrinsic motility machinery with inherent persistence and speed that is unaffected by the complicated external signaling environment.

Dynamic cell shape is a highly visible manifestation of the interaction between the internal biochemical state of a cell and its external environment. We developed software to quantitatively analyze dynamic cell shape. Applying a snake algorithm to experimental movies, we extracted cell boundaries in each frame and followed local boundary motion over long time intervals [3]. Using curvature as a local shape measure we found that small peaks in boundary curvature tend to originate at the front of cells and propagate backwards. These waves advect along the surface of the cell at constant speed, indicating that they are governed by intracellular waves. Using a local motion measure that corresponds to protrusive/retractive activity, we also found that protrusions are intermittent and zig-zag. On short time-scales (< 20 seconds) the location of strongest protrusion travels ballistically along the boundary, whereas on longer time-scales the location of protrusions is mostly confined to the front of the cell. When protrusions are first extended, they are usually far from the region of contact. However, by the time curvature waves reach the side of the cell, they are closer to the region of surface contact than nearby areas of the boundary. Due to alternating protrusion waves, cells maintain their direction of motion over several minutes.

In order to explore the coupling of boundary waves to surface adhesion, we used a chemoattractant to direct cells off the edge of cliffs, which were fabricated using multiphoton absorption polymerization [4]. When cells encounter cliffs, they do not fall off, but extend over the edge. Even though the cell is not in contact with a surface and the cell is not actually moving forwards, curvature waves are still generated at the cell fronts.

III. Conclusions

We analyzed the centroid motion and dynamic cell shape of migrating cells. On short-time scales, protrusive motion travels ballistically along the boundary. Also, curvature waves are generated at the cell front in a zig-zag fashion. While apparently coupled to the surface, these waves are seen even in cells that are extended over the edge of a cliff.

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References

[1] King JS, Insall RH (2009) Chemotaxis: finding the way forward with Dictyostelium. *Trends in Cell Biology* **19**, 523-530.

[2] McCann CP, Kriebel PW, Parent CA, Losert W (in press) Cell Speeds, Persistence, and Information Transmission during Signal Relay and Collective Migration. *J Cell Science*.

[3] Xu C, Prince JL (1998) Snakes, Shapes, and Gradient Vector Flow. *IEEE Transactions on Image Processing* **7** 359-369.

[4] Li L, Fourkas JT (2007) Multiphoton Polymerization. *Materials Today* **10**30-37.