Actin waves as determinants of circular cell trajectories in cell amoeboid migration

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Amoeboid migration is a specific mode of cell movement adopted by leukocytes, such as dendritic cells (DCs) when migrating in restrained spaces. Actin assembles into polar filaments and is directly implied in cell movement by both driving contractile forces and forming membrane protrusions. Theoretical simulations show that in a confined system, independent of adhesion, such as it is the case of amoeboid cell migration, actin filaments can assemble in circular waves [1]. We hypothesize that actin waves determine cell trajectories during amoeboid migration. Experiments were carried out with DCs confined in two-dimensions by adding a well-defined roof on top of the cells [2]. The migration profile was recorded by time-lapse microscopy. Circular actin waves were observed within the cell via TIRF microscopy and were not restricted to the cell front. The speed of these waves were measured. Single 2D trajectories were evaluated according to mean speed, persistence, path length and mean square displacement. Surprisingly, DCs trajectory analysis revealed curved migration trajectories with a preferred radius. These experimental trajectories were compared with trajectories generated from a theoretical model on actin waves. Interestingly, we found a preferred radius of migration within these theoretical trajectories as well as in our experimental data sets. We further investigated the relation between the cell speed and the preferred radius of cells and found a strong correlation, both in the experimental dataset and the theoretical dataset. In the theoretical model, actin waves spontaneously occur only in the presence of a nucleation factor, independent of a motor such as myosin II. To address this question we treated cells with the ROCK inhibitor Y27632. Experimental data shows that molecular motors, like myosin II are dispensable for the generation of cytoskeletal waves and the circular trajectories. We assume that the actin waves inside of living cells might be the reason for the circles in the trajectories we see in amoeboid cells. These results suggest that we can use the actin-wave theoretical model to describe dendritic cell amoeboid migration.

1. Dreher, A., I.S. Aranson, and K. Kruse, *Spiral actin-polymerization waves can generate amoeboidal cell crawling.* New Journal of Physics, 2014. **16**.
2. Le Berre, M., et al., *Methods for two-dimensional cell confinement.* Methods Cell Biol, 2014. **121**: p. 213-29.