PROPOSAL FOR A M2 Internship

Role of contact interaction and secreted factors in the emergence of social behavior in the amoeba Dictyostelium Discoideum

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Dictyostelium is a unicellular amoeba used as simple model organism to investigate coordinated cell movements and emergence of social behavior. As long as nutrients are present, *Dictyostelium* cells multiply as unicellular amoebae (vegetative growth). However, when cells deplete their food source and begin to starve, they enter a developmental cycle : cells become polarized, express new proteins allowing cell to cell adhesion such as to form a motile multicellular organism. It was initially though that vegetative cells were dividing and moving randomly, without interacting much with each other. We have recently showed that the parameters defining cell migration (speed, persistence time, polarization) are regulated by a secreted « quorum sensing factor» (QSF) that accumulates with time [1]. Using PDMS stencils (Figure 1), we analyzed the spreading of circular micro-colonies of various cell densities. We discovered that the initial, colony spreading is too fast to follow a simple diffusion equation with a single diffusion coefficient. By measuring the cells motility parameters, we concluded that cells become temporarily more persistent upon their frequent collisions with each other, a phenomena we termed as **Contact Enhancement of Locomotion** (CEL)[2].

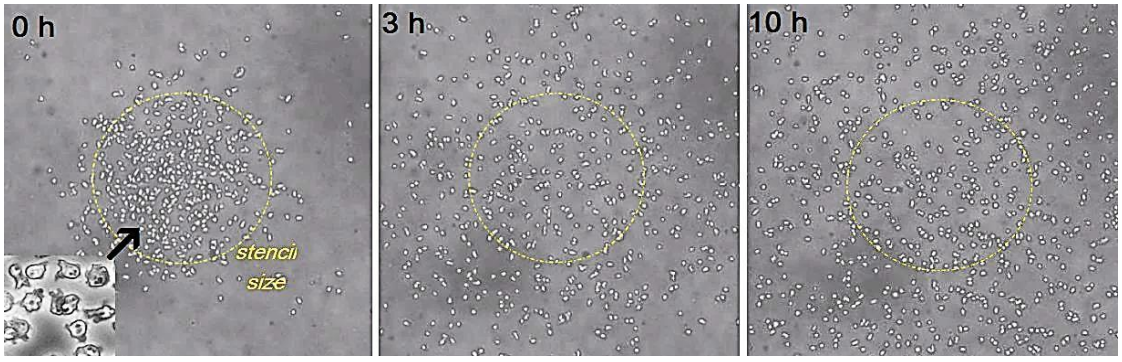

Figure 1. Spreading assay with an initial colony of 320 µm diameter made with a PDMS microstencil (yellow dotted circle) with about 300 *Dictyostelium* cells initially that spread and divide (every 8h)

[1] - L. Golé, C. Rivière, Y. Hayakawa, J.-P. Rieu. A quorum-sensing factor in vegetative Dictyostelium cells revealed by quantitative migration analysis. *PLoS ONE* **6** :(2011) e26901
[2] J. d'Alessandro, A. Solon, Y. Hayakawa, C. Anjard, F. Detcheverry, J.-P. Rieu, C. Rivière. « Contact enhancement of locomotion in spreading cell colonies». Nature Physics, 03 July 2017 and https://arxiv.org/abs/1701.01225

The general objective of the host team is to deduce the rules underlying the cell-cell interactions and their macroscopic outcome in term of collective migration, cell dispersion or self-organization at a population scale. Using, microdevices, we would like to develop during this internship various cell sorters that may help us to understand these rules and to identify later mutants that do not secrete or detect the QSF molecules.

Research plan:

1-Microdevice development. Using the NanoLyon facility (same building as iLM) we will prepare various PDMS-based microdevices to sort fast cells from slow cells or cells more sensitive to group repulsion. In particular, using microstencils, we will produce two cell-sorters: a first one with a linear band geometry (Fig. 2A) and another 3D one with pillars (Fig. 2B).

2. Sorting experiments with Dicty.
We will mix non fluorescent cells with a small amount of fluorescent ones to detect trajectories from timelapse videomicroscopy (phase and fluorescence imaging) even in a crowded environments. We will investigate available *Dicty* mutants with motility defects

- ***2D cell-sorters*** will enable the sorting of cells initially located on rectangular band and to calibrate the sensitivity of the method (time needed to separate a given fast to a slow population). Simulations or modelling with diffusion theory will be used to predict and test the experimental results.
- **3D cell sorters** will enable the collection of the cells after they climb vertical pillars and were collected with inserts.

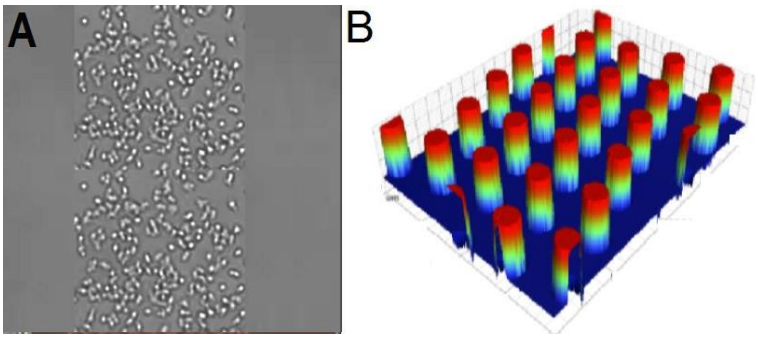

Figure 2. A) Initial colony on a rectangular band (2D cell sorter). **B)** 3d view of the 3D cell sorter (100µm pillars)

Key words: Motility, collective motility, cell signaling, active matter, micro-fabrication**.**