DYNAMICS OF OXYGEN-CONTROLLED, SELF-ORGANIZED DICTYOSTELIUM AGGREGATES

LABORATORY : Institut Lumière Matière

LEVEL : M2
TEAM(S) : BIOPHYSIQUE

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SCIENTIFIC CONTEXT :

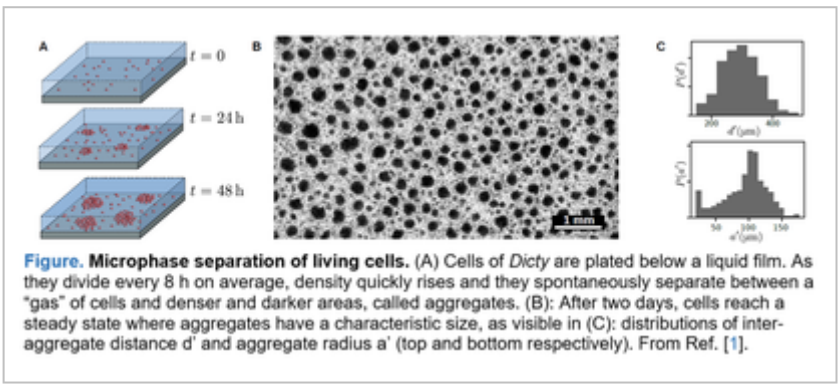

Figure. Microphase separation of living cells. (A) Cells of *Dicty* are plated below a liquid film. As they divide every 8 h on average, density quickly rises and they spontaneously separate between a "gas" of cells and denser and darker areas, called aggregates. (B): After two days, cells reach a steady state where aggregates have a characteristic size, as visible in (C): distributions of inter-aggregate distance d' and aggregate radius a' (top and bottom respectively). From Ref. [1].

Although microphase separation has long been known in inert matter, we have recently discovered that **it also occurs in a population of living cells**. At high density, a dividing population of Dictyostelium discoideum cells, referred to as Dicty, spontaneously separates into **multicellular aggregates with a well-defined size and a collection of single cells** [1]. This characteristic size comes from a compromise between competing interactions. On the one hand, **cell-cell adhesion** acts as a short-range attraction promoting aggregation. On the other, the interplay between **oxygen consumption and aerotaxis** – i.e. the tendency to move towards a preferred oxygen concentration – results in an effective long-range repulsion. Both experiments and simulations support this scenario, very similar to **microphase separation** in physical systems [1].

However, the previous scenario does not consider the 3D structure of aggregates that present, for the larger ones, a dome shape of 50µm height or more, nor the dynamics. Unlike other instances of microphase separation, the cellular aggregates keep moving and never settle into a blocked configuration. Furthermore, preliminary results indicate a complex size dependence of the aggregates' mean squared displacements (MSD): small aggregates diffuse faster than large ones at short time scales while the opposite is true at long time scales.

MISSIONS :

The first goal of this internship will be to run new, better controlled experiments to refine the dynamics analysis as a function of size . The second objective will address the mechanism of locomotion of these aggregates. This will be investigated using single cell tracking in both phases by fluorescence live microscopy in 3D (xy + time) or 4D (xyz + time). Finally, to understand these non-trivial dynamics and collective migration modes, we will perform numerical simulations refining existing Potts models [2]. These will take into account cell division, adhesion, oxygen consumption and aerotaxis [3].

Tasks:

- Improve environmental conditions to get stable microphase separation protocols over longer times. Perform long term, high frame rate videomicroscopy experiments in order to improve aggregate tracking and MSD analysis both at short and long time scales.

- Observe the exchanges between both phases. Experiments will be developped with a small fraction of fluorescent cells. These cells will be imaged with spinning disk microscopy or epifluorescence large field to follow their behavior in both phases.

- Learn to run and analyze simulations of existing Potts models [3].

OUTLOOKS :

Possibility to follow by a PhD funded by ANR.

BIBLIOGRAPHY :

[1]. Carrère et al., *Microphase separation of living cells*. Nat. Commun. 14, 796 (2023).

[2] Granere et al., *Simulation of biological cell sorting using a two-dimensional extended Potts model*. Phys. Rev.Lett. 69, 2013 (1992).

[3] Cochet-Escartin, O. et al., *Hypoxia triggers collective aerotactic migration in dictyostelium discoideum*. eLife 10, 64731 (2021)

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