Simulations and Data-Driven Analysis of Dense Monolayers of Motile Bacteria

Supervisors:

- Pierre Illien (HDR, Laboratoire PHENIX, Sorbonne Université)
- Maxime Deforet (Laboratoire Jean Perrin, Sorbonne Université)

Introduction: Bacterial populations are ubiquitous in the living world, and typically display **complex spatial structures**, which govern their ability to colonize their environment. Indeed, the interplay between their biological function (such as intrinsic mobility), their physical or chemical properties, and their interactions, control their **large-scale organization**. Understanding the emergence of these structures from microscopic principles is central to describe the **impact of bacterial populations** in both medical and natural systems, and also raises a number of **fundamental questions**, with applications in the fields of microbiology, nonequilibrium physics, and material science.

In spite of recent progress both in imaging techniques and in the theoretical descriptions of nonequilibrium assemblies, the dynamics of dense bacterial populations is still loosely understood. In particular, ingredients such as bacterial alignment, mitosis and size polydispersity, which are expected to have a **crucial role on large-scale properties**, have not been studied in a thorough and comprehensive way.

Objectives: The objective of this PhD is to develop a **computational model**, built on a deep-learning analysis of experimental data, to simulate the behavior of dense bacterial motile cell populations. The numerical simulations will be designed to measure the impact of alignment and size polydispersity on the collective behavior and pattern formation of these populations.

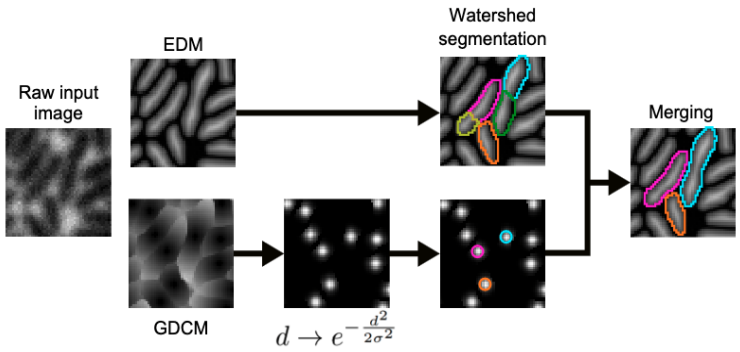

Figure 1. – *Schematic representation of the segmentation method, which will be used to analyze experimental data, and which will be assisted by a deep neural network architecture [1].*

Methodology: We will perform **Brownian dynamics simulations** of a two-dimensional monolayer of bacteria, which will be represented as polydisperse ellipsoids with repulsive interactions. From a computational point of view, we will use the package LAMMPS, which allows efficient and parallel computing. The parameters used in the simulations will be inspired by experiments on bacterial monolayers, using a data-driven approach.

Experimentally Tunable and Measurable Parameters: We will directly control and measure parameters such as cell size distribution and cell density in our experiments. These parameters are adjustable in our

experimental setup at the Laboratoire Jean Perrin through genetic engineering, chemical and physical perturbations. An innovative **deep-learning-based approach** [1] will be used to segment and track a large number of cells (Fig. 1), and statistical analysis will enable extracting the key features. The data obtained from these controlled experiments will serve as input for our simulations, ensuring they are grounded in realistic biological conditions.

Experimentally Measurable but Not Tunable Parameters: Parameters such as cell swimming patterns, including the statistics of swimming direction reversal, cannot be directly manipulated in our experiments but can be accurately measured. These observations will be critical in validating our models and ensuring they reflect the complex behaviors of bacterial motion.

Simulation-Explored Parameters: For parameters that are not directly tunable or measurable in our experimental setup, such as specific interactions between cells that may influence overall monolayer dynamics, we will conduct exploratory analyses within our simulations. This approach allows us to investigate a broader range of theoretical scenarios beyond the limitations of experimental conditions.

Expected Outcomes: The work of the PhD student will result in an improved **understanding of the collective dynamics** of bacterial motile cells, with specific insights into the roles of alignment and size diversity. In addition, we expect our methods to be general and to go beyond the interest for bacterial colonies. We will develop a **robust computational framework**, that combines deep-learning analysis of experimental trajectories and transfer to corresponding molecular simulation, that can be applied to **other nonequilibrium systems** in biological and physical sciences.

Relevance to 'Institut des Sciences du Calcul et des Données': **Deep-learning-based analysis** of biophysical data is an emerging interdisciplinary field of research that raises the interest of physicists, biologists and computer scientists. Moreover, it will be combined here to **particle-based simulations** of systems driven very far from equilibrium: this is one of the central topics of modern computational physics. For these two reasons, we believe that this proposal is completely relevant to ISCD.

Expertise and skills of the supervisors: **Pierre Illien** (chargé de recherche CNRS, HDR defended in 2022), has a strong expertise in theoretical and numerical approaches to nonequilibrium statistical physics, with applications in soft and active matter [2,3]. He will bring support to all the aspects related to Brownian dynamics, and to the statistical analysis of the trajectories generated by numerical simulations. **Maxime Deforet** (chargé de recherche CNRS) is an established specialist of bacterial biofilms, and has been developing many experimental and analysis techniques to study their properties [1,4]. He will be providing support on the deep-learning approach to experimental data.

References:

[1] J. Ollion, M. Maliet, C. Giuglaris, E. Vacher, **M. Deforet**, arXiv:2310.19641, *accepted in PRX Life* (2024).
[2] A. Benois, M. Jardat, V. Dahirel, V. Démery, J. Agudo-Canalejo, R. Golestanian, **P. Illien**, Phys. Rev. E **108**, 054606 (2023).
[3] J. Agudo-Canalejo, **P. Illien**, R. Golestanian, Nano Lett. **18**, 2711 (2018).
[4] **M. Deforet**, Env. Microbiology 25, 1451 (2023).