

Predatory behaviour of the bacteria *Myxococcus xanthus*: from individual decision-making to collective intelligence

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Abstract (10 lines)*

Myxococcus xanthus is a bacterium that predaes collectively on other microorganisms and serves as a model organism to study microbial cooperation. During predation, *M. xanthus* exhibits different types of motility and collective phases depending on the local environment. Ahead of the group, solitary cells behave as explorers. Upon prey detection, *M. xanthus* forms a 'swarming' phase, with coordinated high-speed streams that invade the prey colony. As prey is being consumed, *M. xanthus* transitions to a 'rippling' phase characterized by coordinated cellular waves. Once prey cells are depleted, the *M. xanthus* cells aggregate to form fruiting bodies. This PhD project aims at explaining the process of collective predation from individual behavioral features. We will develop an agent-based model of *M. xanthus* where agents will interact with each other and with their surroundings, accounting for prey detection, lyse and consumption. The design of the cell dynamics and of these interactions will be directly informed by experiments. We will then use reinforcement learning to determine whether these interactions can emerge as the solution of an optimization process at the population scale, potentially demonstrating that single cell decisions are the building blocks of a form of collective intelligence.

Keywords*

Myxococcus, predation, cooperation, collective behaviour, active complex systems, agent-based model, reinforcement learning

Scientific question and Objectives (10 lines)*

This PhD project aims at understanding how individual response to stimuli shape collective behavior in *M. xanthus* and how individual decision-making results in a form of collective intelligence beneficial for the survival of the population.

The first objective is to understand the emergence of self-organization from cell-cell interactions and the transitions between the various collective phases as prey availability varies in space and time. To this end, we

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will develop an agent-based model where individual cell responses to signals will be obtained from a combination of experimental data and working hypotheses on *M. xanthus*'s sensing capabilities.

The second objective is to determine whether these individual behaviors can arise as a mathematical solution to an optimization problem at the population scale (e.g., maximizing prey intake). To this end, we will model the cell response to stimuli by a parameterized function and use reinforcement learning to determine the optimal response, with the goal of confronting this "theoretical" prediction to experiments.

Proposed approach (experimental / theoretical / computational) and research plan (20 lines)*

During the first year of the PhD, the student will establish the experimental protocol. They will develop the image processing pipeline, based on cell segmentation, prey identification and trajectories reconstruction. This dataset will allow to develop a model of the individual cell dynamics and of its response to prey encounter. This model will then be enriched by adding cell-cell interactions and cell-Extracellular matrix interactions, based on prior studies. Specifically, we will add reversals (inversion of cell polarity) in response to geometrical frustration and alignment of bacteria with self-deposited EPS-trails, which are known to be associated with the rippling and swarming phases, respectively.

During the second year of the PhD, the student will focus on integrating the influence of prey availability on the behavior of myxobacteria. Cell-prey interactions will be added to the model. Prey will have three possible states : alive, lysed, consumed. Upon contact between a cell and its prey, the prey will have a probability of transitioning to the lysed state (obtained from experimental data in the first year). Cells located in the vicinity will then consume the prey at an experimentally-inferred rate. Simulations of the collective behavior of the cells resulting from their motility response (arrest upon prey contact, reversal, change in speed, ...) to the full range of stimuli (prey state, EPS-trail, frustration, ...) will be carried out and confronted to predation experiments to reach the first objective of the PhD.

During the final year of the PhD, we will attempt to give an interpretation of individual cell behavior through the lens of collective intelligence thanks to reinforcement learning. Reinforcement learning is a machine-learning technique allowing to compute the response of agents to sensory cues in such a way that a long-term objective is collectively maximized. The previously established motility response to stimuli will be replaced by an unknown parameterized function, which will be optimized so as to maximize a metric associated to predation efficiency at the collective scale. Comparing the optimal response to the one obtained previously may allow us to hint at the fact that decisions made at the level of single cells generate multicellular intelligence, that manifest as properties that only emerge in cell collectives.

Interdisciplinarity and Implication of the two labs (15 lines)*

(In this section the collaboration of the two laboratories will be explained in details to explain why the project cannot be conducted by one team alone)

The topic of the PhD sits at the biology-physics interface. On one hand, we will rely on concepts and tools from complex systems and active matter physics to provide an explanation to biological functions. On the other hand, we will integrate biological complexity (e.g., cell 'memory' after a change of polarity for a refractory period, multiple modes of motility, two-way coupling between the agents and the environment through the prey field and the self-deposited EPS field) into the model to ensure that predictions can be quantitatively compared to observations.

Therefore, the model will be developed by the PhD student in close collaboration with both T. Mignot (LCB)

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and A. Loisy (IRPHE) to ensure that it is grounded in reality while being as minimalist as possible.

LCB will provide the facilities to perform bacterial culture, microscopy experiments, as well as the tools and the know-how to segment images and extract individual trajectories. T. Mignot will additionally provide his expert knowledge of *M. xanthus*.

IRPHE will provide access to numerical facilities for implementing and simulating the agent-based model as well as access to its internally developed reinforcement learning library. A. Loisy will assist with high-performance programming and provide her experience on agent-based modeling of living organisms in fluctuating environments.

Specify with whom the person recruited will collaborate and on what aspects *

The PhD student will perform experiments at LCB under the guidance of T. Mignot and his team. The numerical implementation of the model and use of reinforcement learning will be undertaken at IRPHE under the guidance of A. Loisy.

PhD student's expected profile*

The PhD student is expected to have a Master in Physics and a specialization in biophysics, complex systems, active matter or related areas. They should be strongly interested in engaging in interdisciplinary research at the biology-physics interface and motivated by the development of computational tools. Practical experience with microscopy/image analysis and advanced programming (e.g., parallel computing) is a plus.

Is this project the continuation of an existing project or an entirely new one?

In the case of an existing project, please explain the links between the two projects (5 lines) *

This is a new project.

Two to five references related to the project*

Dinet, C., Michelot, A., Herrou, J., & Mignot, T. (2021). Linking single-cell decisions to collective behaviours in social bacteria. *Philosophical Transactions of the Royal Society B*, 376(1820), 20190755.

Saulnier, J. B., Romanos, M., Schrohe, J., Cuzin, C., Calvez, V., & Mignot, T. (2024). The mechanism of spatial pattern transition in motile bacterial collectives. *bioRxiv*, 2024-10

Herrou J., My L., Monteil C.L., Bergot M., Jain R., Martinez E., & Mignot T. (2025). Tad pili with adaptable tips mediate contact-dependent killing during bacterial predation. *Nat Commun*16(1):4425. doi: 10.1038/s41467-025-58967-0.

Two main publications from each PI over the last 5 years*

Attia, B., My, L., Castaing, J. P., Dinet, C., Le Guenno, H., Schmidt, V., Espinosa L., Anantharaman V., Aravind L., Sebban-Kreuzer C., Nouailler M., Bornet O., Viollier P., Elantak L. & Mignot, T. (2024). A molecular switch controls assembly of bacterial focal adhesions. *Science Advances* 10(22). doi: 10.1126/sciadv.adn2789

Panigrahi S., Murat D., Le Gall A., Martineau E., Goldlust K., Fiche J.B., Rombouts S., Nöllmann M., Espinosa L., & Mignot T. (2021). Mistic, a general deep learning-based method for the high-throughput cell segmentation of complex bacterial communities. *Elife* 10, 65151. doi: 10.7554/eLife.65151

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Loisy A. & Eloy C. (2022). Searching for a source without gradients: how good is infotaxis and how to beat it. *Proceedings of the Royal Society A: Mathematical, Physical and Engineering Sciences* 478 (2262).

Monthiller R., Loisy A., Koehl M. A. R., Favier B., & Eloy C. (2022). Surfing on Turbulence: A Strategy for Planktonic Navigation. *Physical Review Letters* 129, 064502.

Project's illustrating image

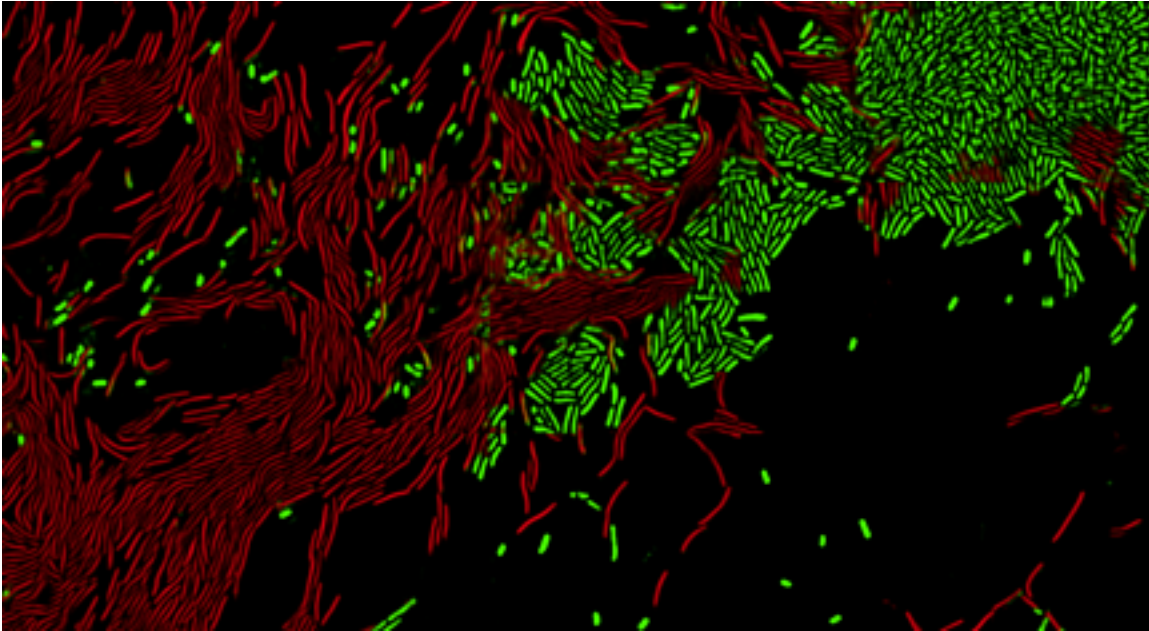


Figure 1: Prey invasion by *M. xanthus*. Myxococcus cells (red) detect *E. coli* Prey cells (green) and signal larger groups, provoking collective invasion and killing of the prey cells

