Title of the PhD project:

Diversity of evolutionary routes in range expansion

PhD Supervisor

Name, first name : Deforet, Maxime
Email : maxime.deforet@sorbonne-universite.fr
Phone : 01 44 27 22 53
Title/Employer : Chargé de recherche CNRS
Address : LJP, tour 32-33, 5e étage. 4 place Jussieu 75005 Paris
Laboratory : Laboratoire Jean Perrin – UMR 8237
Title of the team : Biophysique des micro-organismes
Team leader (*if different*) : Nelly Henry
Doctoral School : D564 – Physique en Ile de France

Overview of the scientific projects of the team

L'équipe biophysiques des micro-organismes s'intéresse au processus aux processus physiques en jeu dans toutes la diversité qu'offrent les systèmes bactériens, de la cellule unique aux colonies. Nelly Henry s'interesse à la dynamique de population au sein de biofilms multi-espèces. Nicolas Biais rejoindra l'équipe en 2021 avec une thématique sur la mécano-biologie des interactions cellule-cellules, cellule-substrat, et cellule-hôte. Pour ma part, j'étudie la motilité collective chez *Pseudomonas aeruginosa* comme sytème expérimental modèle pour l'étude de la matière active biologique. Nos collaborations se font aussi bien à l'intérieur du laboratoire (modélisations théoriques, mise au point de techniques d'imagerie optique non conventionnelles) qu'à l'extérieur avec des biochimistes et des microbiologistes (Institut Micalis, INRAE).

Main publications since January 1er, 2016

Deforet M., Carmona-Fontaine C., Korolev K. S. and Xavier J. B. (2019). Evolution at the edge of expanding populations. *The American Naturalist*, *194*(3), 291-305.

Estrela S., Libby E., Van Cleve J., Débarre F., **Deforet M.**, Harcombe W. R., Peña J., Brown S. P. and Hochberg M. E. (2019). Environmentally mediated social dilemmas. *Trends in ecology & evolution*, *34*(1), 6-18.

Yan J., **Deforet M.**, Boyle K. E., Rahman R., Liang R., Okegbe C., Dietrich L., Qiu W. and Xavier J. B. (2017). Bow-tie signaling in c-di-GMP: Machine learning in a simple biochemical network. *PLoS computational biology*, *13*(8), e1005677.

Carmona-Fontaine C., **Deforet M.**, Akkari L., Thompson C. B., Joyce J. A. and Xavier J. B. (2017). Metabolic origins of spatial organization in the tumor microenvironment. *Proceedings of the National Academy of Sciences*, *114*(11), 2934-2939.

Boyle K. E., Monaco H. T., **Deforet M.**, Yan J., Wang Z., Rhee K. and Xavier J. B. (2017). Metabolism and the evolution of social behavior. *Molecular biology and evolution*, *34*(9), 2367-2379.

PhD Co-Supervisor

Name, first name : Débarre, Florence
Email : florence.debarre@courriel.upmc.fr
Phone : 01 44 27 56 71
Title/Employer : Chargée de Recherche CNRS
Address : IEES, Bat 34-44, 5e étage. 4 place Jussieu 75005 Paris
Laboratory : Institut d'Ecologie et des Sciences de l'Environnement de Paris
Title of the team : Ecologie et Evolution des Réseaux d'Interactions
Team leader (*if different*) : Elisa Thebault
Doctoral School : ED227-Sciences vie homme : évolution écologie

Overview of the scientific projects of the team

Face aux multiples pressions humaines exercées sur les communautés naturelles, la science Ecologie demeure souvent incapable de livrer des prédictions adéquates. Une cause immédiate est la complexité intrinsèque des écosystèmes. L'équipe EERI s'attache à rendre compte d'une partie de cette complexité en prenant pour objet d'étude les réseaux d'interactions, donc un contexte plurispécifique.
Ces réseaux d'interactions sont souvent restreints aux aspects trophiques.L'équipe s'attache à participer à cette compréhension des réseaux trophiques en privilégiant des approches à l'interface entre différentes disciplines de l'écologie : écologie des communautés, écologie fonctionnelle et écologie évolutive. Les objets d'études sont envisagés par des approches théoriques et expérimentales complémentaires, exercées en collaborations.
Collaborations Florence Débarre :

Main publications since January 1er, 2016

Girardin L., Calvez V. and **Débarre F**. (2019). Catch me if you can: a spatial model for a brake-driven gene drive reversal. *Bulletin of Mathematical Biology*, 81(12), 5054-5088.

Czuppon P., Blanquart F., Uecker H. and **Débarre F**. (2019). The effect of habitat choice on evolutionary rescue in subdivided populations. *bioRxiv*, 738898.

Rode N. O., Estoup A., Bourguet D., Courtier-Orgogozo V. and **Débarre F**. (2019). Population management using gene drive: molecular design, models of spread dynamics and assessment of ecological risks. *Conservation Genetics*, 1-20.

Rego-Costa A., **Debarre F.** and Chevin L. M. (2018). Chaos and the (un) predictability of evolution in a changing environment. *Evolution,* 72(2), 375-385.

Débarre F. and Otto S. P. (2016). Evolutionary dynamics of a quantitative trait in a finite asexual population. *Theoretical population biology*, 108, 75-88.

Doctoral Project

Title: Diversity of evolutionary routes in range expansion

Abstract:
Expanding populations, such as tumors, bacterial colonies, or invasive species, often evolve towards better dispersal. But complex intra-specific interactions can alter this trend. What control the robustness of dispersal evolution? We tested this question with bacterial swarming and saw a diversity of evolutionary outcomes: bacteria's dispersal is sometimes improved and other times impaired. This project combines biophysical and evolutionary approaches to decipher how interactions between bacteria at a microscopic level can lead to changes at the whole colony scale, which will determine the collective spreading ability and ultimately, the individual evolutionary fate.

Context and objective:
Biological invasions and range expansion (population expansion into previously occupied space) is substantially altered by evolution (Hallatschek et al, 2009). There is a large body of experimental work demonstrating that range expansion favours evolution towards faster dispersal (Chuang et al, 2016). Most theoretical models consider cases where a mutant's advantage comes from an improved ability to reach the range margin, where resources are still plentiful, and competition for resources is the only interaction between a mutant and its ancestors. More nuanced scenarios include direct interactions (mechanical or chemical interactions) and can lead to expansion slow-down and complete arrest (Korolev, 2015). But experimental support is still lacking. Here, we propose to explore diversity of evolutionary routes in complex range expansion, by using bacterial swarming as a model system.

Pseudomonas aeruginosa is a bacterium that harbors one flagellum and can swim in water. It cannot move at the surface of an agar gel because of friction. However, when a colony reaches a certain size on the gel, it starts secreting surfactants that spread on the surface, lower the surface tension, and allow the colony to expand dramatically. This behavior is called swarming and generates striking branched-shape colonies. It is an example of range expansion where most of growth takes place near the edge, where the resources are still available.

Experimental evolution performed with this assay leads to two opposite results: an increase of dispersal ability, or a decrease of dispersal ability. The former was described in a previous work as the consequence of a mutation that affects single-cell motility, which translates into improved collective motility (van Ditmarsch et al, 2013; Deforet et al, 2014; Deforet et al, 2019). The latter was overlooked, but was recently obtained in the lab and corresponds to a loss of flagella. The interplays between single-cell motility and collective motility on one side, and between evolution of the collective and selection of the individual on the either side, are the topics of this proposal.

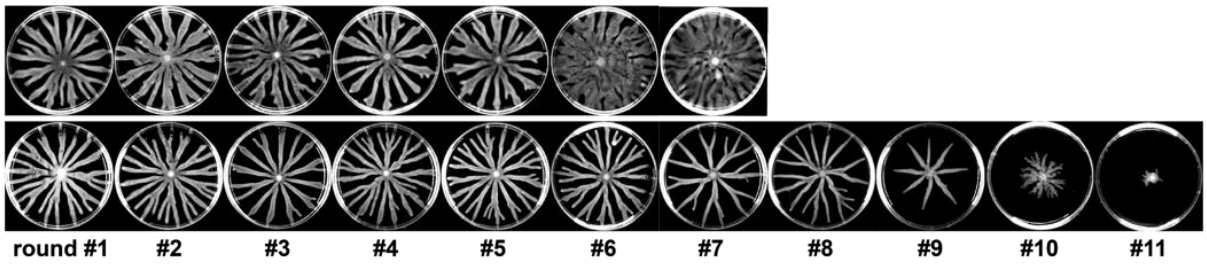

Figure 1 - Two independent replicates of experimental evolution. The upper replicate shows an increase of spreading in 7 rounds. The lower replicate shows a decrease of spreading in 11 rounds. Each plate is 10 cm in diameter.

Such interplay has recently been proposed, but not demonstrated, in a recent experiment where subtle change in single-cell motility let to dramatic change in collective spreading (Meacock et al., 2020). This work focused only on the physical mechanisms involved in motility, and did not explored the evolutionary consequences. Our experimental system is simpler to handle, which enables us to perform experimental evolution in parallel to characterization of the competition at the cellular scale.

We propose to combine evolutionary and physical approaches to decipher the mechanisms leading to the diversity of evolutionary routes in the swarming system, both from experimental and theoretical approaches.

Experimental approach:

- Preliminary experiments led to two outcomes: better spreading and worse spreading. We will explore the contingency scenarios and calculate the frequency of each outcome by replicating the evolutionary experiments at least 50 times, and by varying the experimental conditions (hardness of agar gel, size of the plate)
- In the current protocol, cells inoculated at each subsequent round are randomly sampled from the whole previous plate. In subsequent experiments, we will vary the way the cells are sampled: for instance, we will sample cells from the colony edge only, or we will apply soft selection, not hard selection (a fixed number of cells are used for next round inoculation; Débarre & Gandon, 2011).
- The better spreading advantage comes from better dispersal towards the edge of the colony, where cells have better access to nutrient (see Figure 2). Loss of flagella is likely to affect collective motility and could potentially lead to local jamming of the colonies. This hypothesis remains to be confirmed. These mechanisms hint at a frequency dependence of the evolutionary advantage of each mutation. We will use fluorescently tagged strains to perform competition experiments with various initial ratios. Cells will be collected 24h later and counted, either by flow cytometry or CFU counting.
- To dig deeper into the mechanisms that bring advantages to each mutant, we will use a suite of imaging techniques to observe the spreading dynamics of monoclonal and mixed population colonies. We are equipped to perform live time-lapse imaging at 37°C across spatial scales. The imaging tools range from a whole plate imager down to an inverted microscope, capable of phase-contrast and fluorescence imaging.

Theoretical approach:

- We will develop mathematical models of the experiment to identify the factors leading to one or the other evolutionary outcomes.

- A first set of models will keep the metapopulation structure of the experiment, but will ignore spatial structure within each plate, and will look for conditions under which spiteful strategies like non-swarming can evolve;
- A second set of models will concentrate on within-plate dynamics, and will aim to reproduce the spatial patterns of swarming and non-swarming types observed in the experimental data

- A second set of models will represent different experimental protocols, in particular with soft selection, i.e. with fixed numbers of cells taken from each plate before mixing, rather than mixing them all. We will develop predictions on how this different protocol may affect the results, before testing them experimentally.
- We will develop models to explore the contingency of evolutionary outcomes, in particular the effect of the order of mutations that affect swarming behavior. We will in particular explore what happens when multiple mutants coexist, and which one is more likely to take over the population.

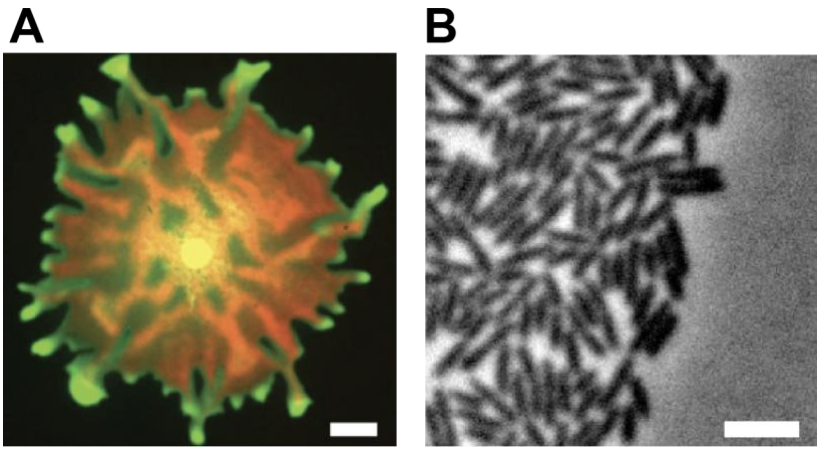

Figure 2 – A: Snapshot of the competition between wild-type *P. aeruginosa* (labeled in red), and its hyperswarmer mutant (label in green). Note how the hyperswarmers self-segregate near the colony edge, thanks to a better dispersal. Scale bar is 1 cm. B: Snapshot of the edge of a colony, where individual cells can be observed, and automatically detected and tracked. Scale bar is 5 µm.

References

- Chuang, A., & Peterson, C. R. (2016). Expanding population edges: theories, traits, and trade- offs. *Global change biology*, 22(2), 494-512.
- **Débarre, F.**, & Gandon, S. (2011). Evolution in heterogeneous environments: between soft and hard selection. *The American Naturalist*, *177*(3), E84-E97.
- **Deforet, M.,** Carmona-Fontaine, C., Korolev, K. S., & Xavier, J. B. (2019). Evolution at the edge of expanding populations. *The American Naturalist*, *194*(3), 291-305.
- **Deforet, M.**, Van Ditmarsch, D., Carmona-Fontaine, C., & Xavier, J. B. (2014). Hyperswarming adaptations in a bacterium improve collective motility without enhancing single cell motility. *Soft matter*, *10*(14), 2405-2413.
- Estrela, S., Libby, E., Van Cleve, J., **Débarre, F**., **Deforet, M.**, Harcombe, W. R., & Hochberg, M. E. (2019). Environmentally mediated social dilemmas. *Trends in ecology & evolution*, *34*(1), 6-18.
- Hallatschek, O., & Nelson, D. R. (2010). Life at the front of an expanding population. *Evolution: International Journal of Organic Evolution*, *64*(1), 193-206.
- Korolev, K. S. (2015). Evolution arrests invasions of cooperative populations. *Physical review letters*, 115(20), 208104.
- Van Ditmarsch, D., Boyle, K. E., Sakhtah, H., Oyler, J. E., Nadell, C. D., Déziel, É., Dietrich, L.E.P and & Xavier, J. B. (2013). Convergent evolution of hyperswarming leads to impaired biofilm formation in pathogenic bacteria. *Cell reports*, *4*(4), 697-708.

Justification of suitability for *i-Bio*:
Both PhD supervisors have been part of a working group on environmentally mediated interactions, which resulted in a synthesis article (Estrela et al. 2019), but they have not closely worked together yet, in spite of their overlapping interests. This project would allow the development of a fruitful collaboration between the two labs, who are interested in similar questions but use complementary and interdisciplinary approaches related to biological questions, in the spirit of the i-Bio initiative.

Role of each supervisor / skills provided:
This proposed project will be carried upon the direction of two PhD advisors:
- Maxime Deforet is a researcher at the Jean Perrin Laboratory, a biophysics lab (Institut Biologie Paris Seine). He is an expert in swarming motility in *Pseudomonas aeruginosa*. Maxime Deforet does not have an HDR yet. Didier Chatenay, from the same lab, will serve as the official PhD advisor until Maxime defends his HDR.
- Florence Débarre is a CNRS researcher at the Institute of Ecology and Environmental Sciences (IEES- Paris). She develops theoretical models in evolutionary ecology, and is particularly interested in how spatial structure affects evolutionary processes. She defended her HDR in 2019 at Sorbonne Université.

Profile of the desired student:
We are looking for a student trained in biology with quantitative approaches, or a student trained in physics and open to biological or evolutionary questions. This project involves experimental (bacteriological culture, imaging and image analysis) and theoretical approaches.