Impact of population spatial structure on bacterial evolution
Applications to antibiotic resistance and/or to bacteria evolving in the gut

Advisor: Prof. Anne-Florence Bitbol – anne-florence.bitbol@epfl.ch
https://www.epfl.ch/labs/bitbol-lab/
Location: École Polytechnique Fédérale de Lausanne, Switzerland

Real microbial populations are subdivided between habitats, e.g. among different organs and among different hosts in the case of an infection. This can have major consequences on the way microbial populations evolve [1,2]. Spatially structured populations, with their local competition, have smaller effective population sizes, which can allow the maintenance of larger genetic diversity, due to the increased importance of stochastic fluctuations. Indeed, population size is formally analogous to the inverse temperature in a physical system. Subdivided populations may thus better explore fitness landscapes [1], and specific spatial structures can impact the probability that a mutant takes over the population [2].

We aim to characterize the ability of spatially structured microbial populations to explore rugged fitness landscapes, and to quantify the predictability of their evolution. We are particularly interested in the impact of population spatial structure on the evolution of antibiotic resistance [3], and in understanding the impact of the specific spatial structure of the gut on the evolution of bacteria in the gut [4]. To this end, we employ a combination of analytical calculations and numerical simulations based on statistical physics.

A funded research internship is available on these topics, and it might be continued into a funded PhD thesis. Two internship topics are possible:

- **Studying the impact of population spatial structure on the evolution of antibiotic resistance:**
We will study whether spatial structure can favor or hinder the evolution of antibiotic resistance in a population of bacteria. Subdivision of the population could indeed preserve refugia of resistant bacteria in the absence of antibiotic, despite the fact that their fitness is then lower than that of sensitive bacteria, due to the fitness cost of resistance mutations [3]. We will first consider a minimal model of subdivided population, involving subpopulations of identical size with random migrations between them [1]. We will then move on to more complex structures [2].
- **Modeling evolution of bacteria in the gut**, in collaboration with Claude Loverdo (Sorbonne Université):
The gut contains highly numerous and diverse bacteria, which mutate and evolve within the specific environment of the gut. This intra-host evolution is one of the sources of the genetic diversity of gut bacteria, and happens at timescales relevant to the life of the host. It can have important implications for public health, for instance when gut bacteria evolve antibiotic resistance. The environment of the gut is original, featuring a specific spatial structure, directional hydrodynamic flow and strong gradients of concentrations of food and bacteria, which can affect the evolution of gut bacteria [4]. We aim to characterize adaptation of bacteria in the gut, and to compare it to well-mixed systems.

References:

[1] A.-F. Bitbol and D. J. Schwab. PLoS Comput Biol, 16(4):e1007798 (2014)
[2] L. Marrec, I. Lamberti and A.-F. Bitbol. Phys Rev Lett 127(21):218102 (2021)
[3] L. Marrec and A.-F. Bitbol. PLoS Comput Biol, 10(8):e1003778 (2020)
[4] D. Labavić, C. Loverdo and A.-F. Bitbol. ArXiv:2105.06733 (2021) – in press at Proc Natl Acad Sci USA