Building a universal model for structured microbial populations

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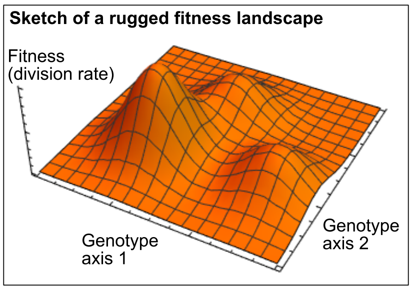
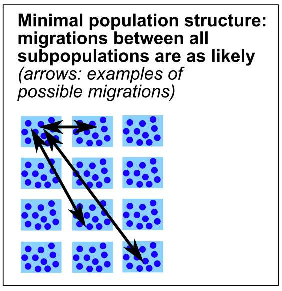
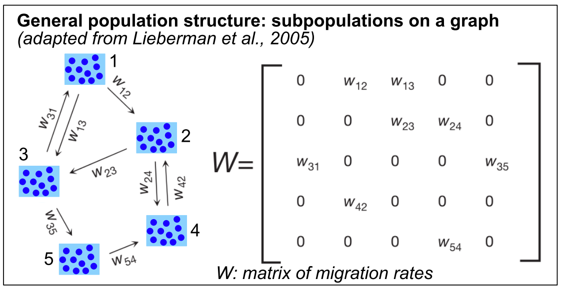
Most studies of microbial populations consider homogeneous, well-mixed populations. However, such a model gives a good description of microbes in a well-agitated liquid suspension in a beaker, but of few natural situations. For instance, during an infection, microbial populations are subdivided between different organs, and between different hosts. Moreover, most microbial populations feature some geographical structure. Even bacteria growing on a Petri dish compete more strongly with their neighbors than with other bacteria.

Population structure can have major consequences on the way microbial populations evolve. Structured populations, with their local competition, have smaller effective population sizes. This 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 also better explore their fitness landscape, which represents fitness (reproduction rate) versus genotype (genetic type), see Figure, left panel. Indeed, the different subpopulations forming a subdivided population perform quasi-independent explorations of the fitness landscape in parallel, and migration can then spread beneficial mutations throughout the population. This could be particularly useful in the exploration of a rugged fitness landscape, featuring multiple optima, like the energy landscape of a glassy system[1] (Figure, left panel). Indeed, our previous work[2] showed that population subdivision within a minimal model (Figure, middle panel) facilitates fitness valley crossing.


Sketch of a rugged fitness landscape


Minimal population structure: migrations between all subpopulations are as likely
(arrows: examples of possible migrations)


General population structure: subpopulations on a graph
(adapted from Lieberman et al., 2005)

W: matrix of migration rates

In this internship, we will develop a universal coarse-grained description of complex subdivided populations on graphs (Figure, right panel). This model can then be used to study what kinds of population structure facilitate the exploration of rugged fitness landscapes. Beyond this general question, the model can be used e.g. to study the impact of population structure on the evolution of antimicrobial resistance, a topic the group is actively working on[3]. Loïc Marrec (PhD student) and Anne-Florence Bitbol are starting to address the impact of structure on the evolution of resistance, within a minimal model (Figure, middle panel).

Structured populations can be described by individuals situated at the nodes of a graph, with probabilities that the offspring of an individual replaces another individual along each edge of the graph[4]. However, in these models, evolutionary outcomes can drastically depend on the details of the dynamics, e.g. whether each birth event precedes a death event or the opposite[5–7]. This lack of universality raises issues for applicability to real microbial populations. We will construct a more realistic coarse-grained model, where each node of the graph contains a well-mixed subpopulation instead of a single individual, and migration rates are specified along the edges (Figure, right panel). We will test the hypothesis that the dependence on the details of the dynamics vanishes in this case. We will study how the limit of small subpopulations relates to previous descriptions.

To study the evolution of such a structured population, we will focus on the process of fixation and spreading of one mutation. We will assume that the fixation of a mutation in each subpopulation is much faster than other processes. This separation of timescales will allow us to represent the evolution of the subdivided population by a coarse-grained Markov process where individual steps are migration events.

The internship will combine numerical simulations and analytical work. Proficiency in programming is a plus. Theoretical approaches will involve Markov chains and graph theory.

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[2] A. F. Bitbol and D. J. Schwab. *PLoS Comput Biol*, 10(8):e1003778 (2014)
[3] L. Marrec and A. F. Bitbol. *J Theor Biol*, 457:190 (2018)
[4] E. Lieberman, C. Hauert, and M. A. Nowak. *Nature*, 433(7023):312 (2005)
[5] K. Kaveh, N. L. Komarova, and M. Kohandel. *R Soc Open Sci*, 2(4):140465 (2015)
[6] L. Hindersin and A. Traulsen. *PLoS Comput Biol*, 11(11):e1004437 (2015)
[7] K. Pattni, M. Broom, et al. *Proc Royal Soc Lond A*, 471(2182) (2015)