PhD thesis proposal

Effects of migration on Wolbachia invasion

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1 Context and goal

Dengue fever, zika fever, chikungunya, yellow fever and other arboviruses are transmitted by mosquitoes of genus *Aedes*, now common from the equatorial and tropical regions to the temperate zones. Except for yellow fever, there exist neither treatment nor vaccine for these diseases, and in such conditions, the main method to control them is to focus on the population of mosquitos.

The classical control methods based on insecticides, induce resistance, which reduces their own efficiency, and are detrimental to the environment due to their non-specific action. Among others, the *biological control* methods aiming at reducing the size or the vectorial capacity of the wild population, recently gathered much attention [5, 1]. Sterile Insect Technique is one of them, allowing to reduce or eradicate a wild population, yet with no guarantee against subsequent reintroduction of the latter from the outside of the treated zone. Infection by the bacterium *Wolbachia* constitutes presently another valuable track [8, 9]. This bacterium induces important decrease of the vectorial capacity of the infected mosquitoes, which seems sufficient to suppress dengue fever epidemics [10]. In addition, this approach has the advantage to offer robustness against reinvasion, due to the stability of the fully infected equilibrium [4, 13]. The goal of this project is to study qualitatively and quantitively the effects of migration of wild mosquitoes on the spread and sustainability of *Wolbachia* infection.

The research topic is also motivated by the interest in the **World Mosquito Program** which is helping communities around the world prevent the spread of mosquito-borne diseases by using Wolbachia bacteria. This will lead to various potential collaborations with countries who attend to this program, including Vietnam.

2 Objectives and methods

The subject of this PhD project is to study qualitatively and quantitively the effects of migration of wild mosquitoes on the spread and sustainability of *Wolbachia* infection. The following general issues will be considered, in adequate mathematical settings:

- How to ensure infection by *Wolbachia* (by adequate impulsive release [11, 12] or by feedback [6, 7]) in presence of permanent inflow of non-infected mosquitoes through migration and/or of outflow of infected mosquitoes?
- How to characterize the potentially destabilizing effect of permanent introduction of non-infected mosquitoes from the outside of a domain, or symmetrically of leak of infected mosquitoes towards the exterior of the domain?

These questions, related in spirit to robust control, will be investigated by extending several reaction-diffusion models previously considered in the literature, in order to accommodate inflows of wild mosquitoes. We will generalize the scalar model obtained in [12] as well as study models of larger dimension, e.g. of dimension 2, accounting for the two species; or of dimension 4 in order to integrate (non-diffusing) early aquatic phases in the life cycle of the mosquitoes. These problems are nonlinear parabolic Partial

Differential Equations, typically posed on a bounded domain, and with Neumann boundary condition taking into account the migration terms.

We will seek estimates of the minimal (in adequate sense. . .) migration flows capable of destabilizing the Wolbachia equilibrium, as well as conditions on additional amounts of mosquitoes that we need to release in order to ensure Wolbachia spread in presence of bounded migration rates.

3 Timeline

Recent works mainly focus on the time dynamical systems or consider the spatial dynamics in an unbounded domain (typically the real line). One aim of this work is to study more realistic situations by considering the spatial dynamics in bounded domain.

The tentative timeline of this work is proposed as follows:

- 1st year: Study of a simplified system describing the evolution of the proportion of population infected by Wolbachia in a bounded domain.
- 2nd year: Study of the controllability of this system and numerical simulations.
- 3rd year: Extension to a more general system, numerical investigation, writing of the thesis manuscript.

4 Advisors

The thesis will be co-advised by Luis Almeida (LJLL, Sorbonne University), Pierre-Alexandre Bliman (LJLL, INRIA Paris) and Nicholas Vauchelet (LAGA, University Paris Nord). If the candidate obtains the fellowship, it can be paid by either Sorbonne University, INRIA Paris or Sorbonne Paris Nord.

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