Contrat Doctoral — ED Galilée

Titre du sujet : Modélisation mathématique et analyse des hétérogénéités dans les techniques de contrôle d'arboviroses

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- Discipline : Mathématiques Appliquées
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- Domaine de recherche : Mathématiques appliquées
- Mots-clés : dynamique des populations, contrôle optimal, systèmes de réaction-diffusion.

1 Context

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 mosquitoes. 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, has recently gathered much attention [1, 4]. Sterile Insect Technique is one of them, allowing to reduce or eradicate a wild population thanks to the release of a large amount of sterilized male mosquitoes. Infection by the bacterium Wolbachia constitutes presently another valuable track [8]. This bacterium induces important decrease of the vectorial capacity of the infected mosquitoes, which seems sufficient to suppress dengue fever epidemics. In addition, this approach has the advantage to offer robustness against reinvasion, due to the stability of the fully infected equilibrium [3, 10].

From a mathematical point of view these two techniques have been widely studied when the environment is assumed to be homogeneous (see e.g. [9, 7] and references therein). However, it is clear that environments are not homogeneous neither in space nor in time. The aim of this project is to investigate the heterogeneous situation. Such a study may have an important impact for practical applications. Indeed, it is well known that the dynamics of the mosquito population depends strongly on the season and on the ressources available in the environment. Therefore the strategy should be adapted and optimized to take into account these variations.

2 Objectives and methods

The subject of this PhD project is to study qualitatively and quantitively the effects of seasonal variations and of spatial heterogeneities into the success of control techniques as population replacement by *Wolbachia* infected mosquitoes or the sterile insect technique. The following general issues will be considered, in adequate mathematical settings :

— Given a seasonal variation, when is it the best period of the year to implement the release of *Wolbachia*-infected mosquitoes or the release of sterilized males ? And how to design these releases with respect to these seasonal variations ?

— How may the spatial heterogeneities influence the success of the replacement strategy and of the sterile insect technique ?

In order to answer to these questions we will base our study on existing mathematical models (for instance the ones built in [9, 7]) and will adapt them to include temporal and spatial heterogeneities. For instance, an already well-established simple model to study the replacement by the *Wolbachia*-infected population is the following model

$$\partial_t n_i - D\Delta n_i = b_i n_i (1 - \frac{n_i + n_u}{K}) - d_i n_i + u$$
$$\partial_t n_u - D\Delta n_u = b_u n_u \frac{n_u}{n_i + n_u} (1 - \frac{n_i + n_u}{K}) - d_u n_u$$

where n_i and n_u denotes respectively the density of infected and uninfected mosquitoes population. The birth and death rates are denoted respectively b_i, b_u, d_i, d_u and K is the carrying capacity. The release function is denoted u. In a homogeneous environment, optimal release strategies for this system (in particular when $D = 0$) have been rigorously studied (see e.g. [2]). To anwser to the first question raised above, we will then consider this system by first assuming that the carrying capacity varies with respect to time $K(t)$ and we will adapt and extend the strategy developped in [2] to this situation. To this aim, we will use techniques from the optimal control theory for differential system and we will need to study reaction-diffusion systems.

3 Timeline

Only few works have started to investigate the temporal and/or spatial heterogeneities in the dynamics, see e.g. [5, 6]. The aim of this project is to extend the already known results in this framework.

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 with a time-varying environmental capacity modeling the seasonal variations. Optimization of the release scenario thanks to tools from optimal control.

— 2nd year : Incorporation of the spatial heterogeneities in the above study. Investigation of the case of the sterile insect technique.

— 3rd year : Extension to a more general system, numerical investigation, writing of the thesis manuscript.

The two PhD advisors are specialists in reaction-diffusion equation, modelization in life sciences, and applications of optimal control theory to these fields. They already successfully collaborated together, with Martin Strugarek [9]. They are involved in a larger informal research group working on reaction-diffusion models in mosquitoes control. The PhD student will benefit from the expertise of the two advisors. He will be based in Paris 13, but the co-advisor (Grégoire Nadin) regularly comes to Paris and could invite the PhD student for short stays in Orléans.

The candidate should have a Master 2 (or equivalent) degree in applied mathematics and should be interested by applications in life sciences, in particular in population dynamics, and by the study of PDE and differential equations. Moreover, this project being interdisciplinary, interactions with entomologists are to be expected.

Références

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