

Program of the workshop MOSTICAW 2017

Porquerolles, October 10-15

Schedule of the talks and abstracts

Tuesday, October 10th

9:00-9:45	TU1	MARTIN STRUGAREK
9:45-10:30	TU2	NICOLAS VAUCHELET
10:30-11:00		Pause
11:00-12:00	TU3	PASTOR EMMANUEL PÉREZ-ESTIGARRIBIA

Wednesday, October 11th

9:00-9:45	WE1	MARIO A. NATIELLO & HERNÁN G. SOLARI
9:45-10:30	WE2	DANIEL VILLELA
10:30-11:00		Pause
11:00-12:00	WE3	YVES DUMONT

Thursday, October 12th

9:00-9:45	TH1	ABDERRAHMAN IGGIDR
9:45-10:30	TH2	ALAIN RAPAPORT
10:30-11:00		Pause
11:00-12:00	TH3	DAIVER CARDONA SALGADO

Friday, October 13th

9:00-9:45	FR1	NATALIA E. JIMÉNEZ
9:45-10:30	FR2	CLÁUDIA TORRES CODEÇO
10:30-11:00		Pause
11:00-11:30	FR3	FLÁVIO CODEÇO COELHO
11:30-12:00	FR4	DANIEL VILLELA

- Lunch from 12h15 to 13h15.
- Dinner from 19h15 to 20h15.
- Afternoon pause at 16h15.

• **Tuesday, October 10th**

- **TU1 – Population replacement by means of *Wolbachia* releases: study of an optimal control problem, *Martin Strugarek (AgroParisTech & Université Paris 6, UPMC)***

Under production and release constraints, what are the best releasing strategies of *Wolbachia*-infected mosquitoes in order to get as close as possible to population replacement? In a temporal model, we formulate and study an optimal control problem for a simple system of ordinary differential equations to try and answer this question. In particular, we assume that the sex ratio along with all parameters is kept constant throughout the process. Our main result is that if releases can be sufficiently concentrated (in time) and the maximal number of released mosquitoes is not too high then we can prove qualitative properties of optimal strategies. Namely, the maximal effort needs only be applied at the beginning and at the end of the release program, while "diffuse" releases appear to be optimal in the middle of the process. Numerical simulations confirm and complement these theoretical findings. We will discuss the assumptions, possible extensions and further prospects of this work.

- **TU2 – Mathematical modeling of the spatial spread of *Wolbachia*, *Nicolas Vauchelet (Université Paris 13)***

In this work, we are concerned with the spatial spread of *Wolbachia* infected mosquitoes into a host population. We focus on the two following questions: How the spatial repartition of the releases will influence the spread of the bacteria into the population ? Once the spread is initiated, is it possible that environmental characteristics stop the spread ?

- **TU3 – A Unified Model for joint *Wolbachia* (Maternal) and Mendelian inheritance for resistance to insecticide, *Pastor Enmanuel Pérez-Estigarribia (UNA, Paraguay)***

In the context of the control of arboviroses transmitted by *Aedes aegypti* and *Aedes albopictus* (such as dengue, chikungunya or zika fever), an alternative or a complement to these classical strategies is the genetic control by *Wolbachia* infection, a bacterium that reduces drastically the vectorial capacity of the mosquitoes. However, the release of mosquitoes *Aedes* deliberately infected in laboratory and that are susceptible to insecticides, appears to have a limited effect in practice, due to the widespread use of insecticides in the field. In the first part of this work we introduce some fundamental concepts about control strategies in the field and inheritance mechanisms of attributes related to these strategies. In the second part, to understand further what are the conditions for successful infestation, we build in this work a model describing the interaction of an isolated population composed of several strains of mosquitoes, with inheritable characteristics that involve maternal inheritance for mosquitoes uninfected and infected by the bacterium *Wolbachia*, together with Mendelian autosomal diallelic inheritance for mosquitoes resistant or susceptible to insecticide. The model is comprised of a system of six ordinary differential equations, which represent two homozygous and one heterozygous genotypes for the uninfected mosquitoes, and the same for infected ones. We show, under appropriate assumptions, the existence of various equilibrium points to this system, one of them being the asymptotically stable equilibrium with the whole population being resistant homozygous and infected. Furthermore we demonstrate that sufficient introduction of *Wolbachia*-infected mosquitoes is capable of reaching this equilibrium while departing from a population initially uninfected but resistant to insecticide, even if the introduced strain is susceptible to the insecticide.

Joint work with Pierre-Alexandre Bliman (Inria, France; FGV, Brazil) and Christian Schaerer (UNA, Paraguay)

• Wednesday, October 11th

- **WE1 – Winged promises or biological contamination? Modeling genetic diffusion in the RIDL-SIT technique, Mario A. Natiello (Lund University, Sweden) and Hernán G. Solari (Buenos Aires University, Argentina)**

In 2016 the World Health Organization (WHO) and the Pan-American Health Organization (PAHO) recommend to their constituent countries to test the new technologies proposed to control *Aedes aegypti* populations. Following the endorsement, Argentina endured a mounting pressure by private interests to allow, and economically support, tests on RIDL-SIT technology. Yielding to the requests of public health authorities we developed a model under the general directions of our participation in the MOSTICAW proposal. The model developed is a simple ecological model that implements the genetic-population concept of "reaction norms" as much as it is possible with the information available. It presents a interdependent dynamics of mosquito populations and food in an homogeneous setting. Mosquito populations are described in an stochastic compartmental setup with compartments corresponding to the mosquito developmental stage and mendelian genetics for the autocide gen. Hybridation of the population with the background of the Rockefeller strain of *Aedes aegypti* released is tracked as well. The development of the model allows us to indicate some critical biological knowledge that is missing and could (should) be produced before testing the technology. Using the model we foresee how the releases proposed are likely to increase epidemic risk after they have concluded. Hybridation levels, release numbers of mosquitoes as a function of intervention duration and target are calculated.

- **WE2 – Resource competition among *Aedes* mosquitoes in larval stage and implications for *Wolbachia* dissemination, Daniel Villela (Fiocruz, Rio de Janeiro, Brazil)**

Resource competition among *Aedes* mosquitoes potentially limits population growth given fitness conditions. In particular, the larval stage may impose a significant barrier under resource constraints. We analyze data from experiments of both interspecific and intraspecific competition of *Aedes aegypti*, *Aedes albopictus* and *Aedes aegypti* infected with *Wolbachia*. Experiments were comprised of different combinations of numbers of larvae and food levels. We find that performance of *Ae. albopictus* mosquitoes is highly competitive compared to *Ae. aegypti*. We also observed good fitness of *Ae. aegypti* larvae with *Wolbachia* compared to wild-type *Ae. aegypti* larvae. Whereas *Wolbachia* dissemination clearly depends on the density of *Ae. aegypti* adult mosquitoes, special attention should be given to resource competition, especially an eventual occurrence of *Ae. albopictus* in areas of *Wolbachia* releases.

Joint work with Suellen Oliveira, Fernando Dias, Luciano Moreira, Rafael Maciel-de-Freitas

- **WE3 – Modeling larval interference: some preliminary results, Yves Dumont (CIRAD, Umr AMAP, Montpellier, France & Department of Mathematic and Applied Mathematics, University of Pretoria, South Africa)**

Based on a recent paper [1], we develop a minimalistic generic model of interference between two larval mosquito species. The study took place in french Guyana, where two mosquito species compete: *Ae. aegypti* and *L. durhamii*. The latter is not well known but its living area extends from Mexico to Northern Argentina. Several outdoor experiments have been made using different type of containers (from tank bromeliads to plastic pots) to study the time evolution of both species along the year [2]. In tank bromeliads, in particular, *L. durhamii* outcompetes *A. aegypti* in rural area or in July, after the rainy season. Laboratory experiments have been conducted in order to better understand the interference between larvae [1]. Dry body mass was measured and the experiments showing that interspecific competition leads to an increase of *A. aegypti* dry mass (both male and female) and lifespan. According to the competitive-susceptibility hypothesis, vector competence is inversely correlated to body size: small females develop and transmit viruses more readily than do large ones. In the present study *Ae. aegypti* adult females are larger after larval interference competition with *Li. durhamii*, an interaction that should reduce *Ae. aegypti*'s susceptibility to viral infection. Yet, according to the longevity-susceptibility hypothesis, this interaction might actually increase their longevity and thus indirectly increase their capacity to transmit viruses. Further investigations are needed, but it seems that *Li. Durhamii* might be a good competitor of *Ae. Aegypti*.

- [1] S. Talaga, A. Dejean, C. Mouza, Y. Dumont, C. Leroy, Larval interference competition between the native Neotropical mosquito *Limatus durhamii* and the invasive *Aedes aegypti* improves the fitness of both species. *Insect Science* 2017. Online
- [2] S. Talaga, Ecologie, diversité et évolution des moustiques (Diptera Culicidae) de Guyane française: implications dans l'invasion biologique du moustique *Aedes aegypti* (L.), PhD Thesis, November 2016. Médecine humaine et pathologie. Université de Guyane, France.

• Thursday, October 12th

- **TH1 – On the estimation of susceptible proportions in some epidemic systems, *Abderahman Iggidr (Inria, Metz, France) & Max Souza (UFF, Niterói, Brazil)***

We consider a class of epidemiological models that includes most well-known dynamics for directly transmitted diseases, and some reduced models for indirectly transmitted diseases. We propose a simple observer that can be applied to models in this class. We analyse and implement this observer in two examples: the classical SIR model, and a reduced Bailey-Dietz model for vector-borne diseases. In both cases we obtain arbitrary exponential convergence of the observer. For the latter model, we also apply the observer with real data.

- **TH2 – About the minimal time crisis problem in the prey-predator Lotka-Volterra model, *Alain Rapaport, MISTEA (Inra, Montpellier SupAgro, Univ. Montpellier)***

We consider the classical prey-predator Lotka-Volterra model with a control on the mortality of the predator. We consider that the state of the system is in "crisis" or in danger when the density of the preys is below a given threshold. We first study the viability kernel associated to the constraint to stay above this threshold for any time. We then study the optimal control which consists in minimizing the time spent below the threshold (i.e. minimizing the time crisis) over finite and infinite horizon. We show that the optimal trajectory does not necessarily correspond to the minimal time to reach the viability kernel.

Joined work with Terence Bayen, Univ. Montpellier.

- **TH3 – Optimal control approach for Dengue using *Wolbachia*. Dynamics of female *Aedes aegypti* with Allee effect, *Daiver Cardona Salgado (Universidad Autónoma de Occidente, Cali, Colombia)***

It is proposed SIRS model in order to simplify the Vector-Host Transmission dynamics with *Wolbachia*. Furthermore, it is proposed to apply the optimal control approach to derive the appropriate strategies for the release of *Wolbachia*-infected female mosquitoes into the wild *Aedes aegypti* population. The ultimate goal of control intervention consists in reducing the dengue incidence for human population, replace wild female *Aedes aegypti* population by *Wolbachia*-infected mosquitoes while minimizing the overall time of control intervention together with the total costs related to implementation of the control policy. Under this approach, the control variable stands for the number of *Wolbachia*-infected female mosquitoes to be released daily.

• Friday, October 13th

- **FR1 – Genome-scale models for *Wolbachia*'s mutualism: focusing on what is missing, Natalia E. Jiménez , Ziomara P. Gerdtzen, Álvaro Olivera-Nappa, J. Cristian Salgado, Carlos Conca (Centre for Biotechnology and Bioengineering (CeBiB), University of Chile)**

As a result of their adaptation to depend on other organisms for their survival, *Wolbachia* has developed a reduced genome size. Based on this it is likely that they present a small and rather incomplete metabolic network, as it has been observed previously for other endosymbiotic bacteria. In this work we study the metabolism of two *Wolbachia* strains *wMel* and *wMelPop* (*Drosophila melanogaster*) using genome-scale models. The obtained metabolic reconstructions were validated with experimental data and exhibit known features of both *Wolbachia*'s and *Rickettsia*'s metabolism. This approach provides a new tool for understanding the effect of the absence of specific genes for the survival of *Wolbachia*, and studying its metabolic interaction with its host. It also sets the basis for the study of other endosymbiotic bacteria involved in the spread of arboviral diseases.

- **FR2 – Modeling human behavior and mosquito control: the case of fish farming and the control of anophelines, Antunes F, Aronna MS, Codeço CT**

Fish farming contributes to the burden of malaria in some parts of the Amazon, in particular the Alto Jurua Region, in Acre, and some areas of Peru. Cleaning the border of the ponds is a very effective mosquito control activity but it is time consuming and tiresome, specially because the climate makes it a very short lived action. Here, we present preliminary work on the adaptation of Dumont & Thuilliez's model (2016) to the malaria and fish farming problem. With this model, we seek answers to the following questions: 1) what is the relative contribution of productive and unproductive ponds to the total population of mosquitos? 2) what are the best strategies to control the overall mosquito population while optimizing economic gain? The goal is to study the interactions between individuals and government agents on the containment and resurgence of malaria outbreaks.

- **FR3 – Estimating underobservation and reconstructing the full size of the Zika epidemic in Rio de Janeiro, Flávio Coelho (FGV, Rio de Janeiro, Brazil)**

The 2015-16 Zika epidemic in Rio de Janeiro followed a quick spread of the disease throughout Brazil from north to south. One of the striking features of this epidemic was the much higher incidence in young adult women, due to sexual transmission, and the serious congenital malformations and miscarriages associated to Zika infection in pregnant women. In this paper we use case reporting data along with live-birth records to reconstruct the full size of the Zika epidemic through a Bayesian probabilistic graphical model representing the Zika transmission, probabilities of observation (case reporting) and of birth loss (through miscarriage or abortion). We find that the probability of observing (reporting) a Zika case is different between men and women and ranges between 10 to 13%. From these estimates we reconstruct the full epidemic Zika epidemic size in Rio de Janeiro in 2015-16.

- **FR4 – Analysis of the effect of temperature on estimation of the reproduction number of dengue, Daniel Villela (Fiocruz, Rio de Janeiro, Brazil)**

Certain environmental temperature ranges are known for delaying the extrinsic incubation period of dengue virus in *Aedes aegypti* mosquito. Since temperature varies seasonally in tropical areas and even fluctuates in small timescales, these effects clearly have an impact in the risk of dengue outbreaks. We propose a method to estimate the effective reproduction number of dengue given knowledge of time series of temperature. We analyze some cases of both simulation and real outbreaks and present results obtained using the temperature-dependent method.

Joint work with Cláudia Codeço and Flavio Coelho