



IN PARTNERSHIP WITH:
CNRS

Université de Lorraine

Activity Report 2012

Project-Team MASAIE

Tools and models of nonlinear control theory
for epidemiology and immunology

IN COLLABORATION WITH: Laboratoire de mathématiques et applications de Metz (LMAM)

RESEARCH CENTER
Nancy - Grand Est

THEME
**Observation, Modeling, and Control
for Life Sciences**

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Project-Team MASAIE

Keywords: Control Theory, Epidemiology, Estimation, Mathematical Biology

Creation of the Project-Team: January 01, 2008 , Updated into Project-Team: January 01, 2010 .

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2. Overall Objectives

2.1. Overall Objectives

The overall objective of MASAIE is to develop and apply methods and tools of control theory and dynamical systems for the mathematical modeling in epidemiology and immunology. The problem at issue is twofold. The first objective is to obtain a better understanding of epidemiological and immunological systems. The second objective is to mathematically study problems arising naturally when addressing questions in the fields of epidemiology and immunology. In our opinion our two endeavors operate in a synergic way : new problems will appear in control theory and their study will give new tools to epidemiology and immunology.

In this regard the first step is modeling. Modeling has always been a strong activity in control theory, however modeling in epidemiology and immunology has some specificities not encountered in engineering. The systems are naturally complex and have highly nonlinear parts. A second characteristic is the paucity of data. These data, when existing, are often imprecise or corrupted by noise. Finally rigorous laws seldom exists, this is a major difference with engineering. In this situation modeling is a back and forth process between the "mathematician" and the "biologist." When modeling, it is necessary to decide what is important and what can be neglected. This is not an easy task. A term or a structure, that can be discarded by the biologist modeler, turns out to give an unexpected behavior to the system. On the other side the biologist wants the more complete model possible, which can be difficult for the mathematical tractability. In MASAIE a close collaboration with researchers in epidemiology and immunology (IMTSSA, INRA, IRD, Institut Pasteur, University of Tübingen) is essential and will be developed.

Beyond the stage of modeling we have the validation, simulation and mathematical analysis of the models. This is also a part of modeling. For example some models can be rejected for inappropriate behavior while others are accepted for their agreement with data. Once again the role of data and the collaboration with researchers in these fields are certainly crucial, but the mathematical analysis cannot be neglected.

Emerging and reemerging diseases have led to a revived interest in infectious diseases and immunology. Our final objective is to propose and study epidemiological and immunological models for

1. analysis of the spread and control of infectious disease,
2. a better understanding of the dynamics and behavior of epidemics,
3. clarification of hypotheses, variables and parameters,
4. proposition of conceptual results (thresholds, sensitivity analysis ...),
5. simulation as an experimental tool for building and testing theories,
6. effective evaluation of field and outbreak data,
7. planning and evaluation of intervention campaigns.

2.2. Research themes

1. Building models in epidemiology and immunology. Studies of models and their global behavior. We will concentrate primarily on models for disease transmitted by blood-sucking insect vectors (malaria, dengue, chikungunya, yellow fever) but we will also consider some diseases for which we have collaborations and data such as Ebola haemorrhagic fever, Hepatitis B or Meningitis.
2. Modeling and model validation guided by field data.
3. Design of observers (software sensors for biological systems): observers are auxiliary dynamical systems that use the model together with the available measurement data in order to reconstruct the unobservable variables (that are not measured directly) and to estimate some parameters of the system. Observers are related to observability and, therefore, also determine data collection plans.
4. Establishing control strategies for the considered systems that can help to determine some policies in public health and fishery.

In our project, Africa has a special place:

Our research focuses on infectious diseases caused by bacteria, parasites in humans and animals. The populations of less developed countries are specially affected by these diseases. "End users" with whom we work are specialists in tropical diseases. This explains the interest in our project for African collaborations. A strong partnership exists with the network EPIMATH in central Africa. The objective of EPIMATH is to promote collaboration between different communities: Specialists in Health Sciences on the one hand and modelers, mathematicians, computer and automation on the other. Another objective is to encourage mathematicians from Africa to work in the field of mathematical epidemiology. This partner explains the strong set of data we have and also the number of Phd's students coming from sub-Saharan Africa.

2.3. Fields of application

1. Intra-host models for malaria.
2. Metapopulation models considering the dynamics of *Plasmodium falciparum* causing tropical malaria in human populations, and the development of drug resistance.
3. Modeling the dynamics of immunity in human populations in endemic areas. Models describing the intra-host parasite dynamics, considering the development and loss of immunity.
4. Spread of epidemics of arbovirus diseases (dengue, chikungunya ...)
5. Disease leading to structured model to allow to take in account the effect of asymptomatic carriers, differential infectivity or differential susceptibility (HBV, Meningitis ...)

One of the challenge of the project is to ensure the relevance of these models. It is Important to closely involve the “end users” (specialists in the fields, experimenters, observers, physicians, epidemiologists, entomologists, etc.) and “providers” (Mathematicians, numerical, statisticians, computer scientists,...). Users are able to bring a critical evaluation on the quality of results, to validate them or exploit them further. For example we want to understand the genetic diversity and structure of African *Plasmodium falciparum* population. The spread of drug resistance is due to gene flow and the scale of *P. falciparum* population structure. A better understanding of *P. falciparum* population genetics is necessary to adjust control measures. The findings of Rogier et al [18] provide evidence for support structured *P. falciparum* populations in Africa, and suggest that malaria epidemiology in urban areas depends on local transmission, geographic isolation, and parasite flow between the city and the surrounding rural areas. The molecular geneticists use many different statistical measure of distance. (For example F_{st} , Nei’s distance ...). It is important in our modeling process to understand how these measures can be obtained as output of our models. This explains why our team is composed of "control theorist" "applied mathematician" and "statisticians".

2.4. Highlights of the Year

Malaria infection is characterized by the fact that only the peripheral infected red blood cells (young parasites), also called circulating, can be observed (can be seen on peripheral blood smears) and the other ones (sequestered), hidden in some organs like brain and heart, can not be observed. There is no clinical method of measuring those sequestered infected cells. We have developed a simple tool to estimate the sequestered parasites and hence the total parasite burden for *Plasmodium falciparum* malaria patients [14].

3. Scientific Foundations

3.1. Description

Our conceptual framework is that of Control Theory : the system is described by state variables with inputs (actions on the system) and outputs (the available measurements). Our system is either an epidemiological or immunological system or a harvested fish population. The control theory approach begins with the mathematical modeling of the system. When a “satisfying” model is obtained, this model is studied to understand the system. By “satisfying”, an ambiguous word , we mean validation of the model. This depends on the objectives of the design of the model: explicative model, predictive model, comprehension model, checking hypotheses model. Moreover the process of modeling is not sequential. During elaboration of the model, a mathematical analysis is often done in parallel to describe the behavior of the proposed model. By behavior we intend not only asymptotic behavior but also such properties as observability, identifiability, robustness ...

3.2. Structure and modeling

Problems in epidemiology, immunology and virology can be expressed as standard problems in control theory. But interesting new questions do arise. The control theory paradigm, input-output systems built out of simpler components that are interconnected, appears naturally in this context. Decomposing the system into several sub-systems, each of which endowed with certain qualitative properties, allow the behavior of the complete system to be deduced from the behavior of its parts. This paradigm, the toolbox of feedback interconnection of systems, has been used in the so-called theory of large-scale dynamic systems in control theory [33]. Reasons for decomposing are multiple. One reason is conceptual. For example connection of the immune system and the parasitic systems is a natural biological decomposition. Others reasons are for the sake of reducing algorithmic complexities or introducing intended behavior ...In this case subsystems may not have biological interpretation. For example a chain of compartments can be introduced to simulate a continuous delay [27], [29]. Analysis of the structure of epidemiological and immunological systems is vital because of the paucity of data and the dependence of behavior on biological hypotheses. The issue is to identify those parts of models that have most effects on dynamics. The concepts and techniques of interconnection of systems (large-scale systems) will be useful in this regard.

In mathematical modeling in epidemiology and immunology, as in most other areas of mathematical modeling, there is always a trade-off between simple models, that omit details and are designed to highlight general qualitative behavior, and detailed models, usually designed for specific situations, including short-term quantitative predictions. Detailed models are generally difficult to study analytically and hence their usefulness for theoretical purposes is limited, although their strategic value may be high. Simple models can be considered as building blocks of models that include detailed structure. The control theory tools of large-scale systems and interconnections of systems is a mean to conciliate the two approaches, simple models versus detailed systems.

3.3. Dynamic Problems

Many dynamical questions addressed by Systems Theory are precisely what biologist are asking. One fundamental problem is the problem of equilibria and their stability. To quote J.A. Jacquez

A major project in deterministic modeling of heterogeneous populations is to find conditions for local and global stability and to work out the relations among these stability conditions, the threshold for epidemic take-off, and endemicity, and the basic reproduction number

The basic reproduction number \mathcal{R}_0 is an important quantity in the study in epidemics. It is defined as the average number of secondary infections produced when one infected individual is introduced into a host population where everyone is susceptible. The basic reproduction number \mathcal{R}_0 is often considered as the threshold quantity that determines when an infection can invade and persist in a new host population. To the problem of stability is related the problem of robustness, a concept from control theory. In other words how near is the system to an unstable one ? Robustness is also in relation with uncertainty of the systems. This is a key point in epidemiological and immunological systems, since there are many sources of uncertainties in these models. The model is uncertain (parameters, functions, structure in some cases), the inputs also are uncertain and the outputs highly variable. That robustness is a fundamental issue and can be seen by means of an example : if policies in public health are to be taken from modeling, they must be based on robust reasons!

3.4. Observers

The concept of observer originates in control theory. This is particularly pertinent for epidemiological systems. To an input-output system, is associated the problem of reconstruction of the state. Indeed for a given system, not all the states are known or measured, this is particularly true for biological systems. This fact is due to a lot of reasons : this is not feasible without destroying the system, this is too expensive, there are no available sensors, measures are too noisy ...The problem of knowledge of the state at present time is then posed. An observer is another system, whose inputs are the inputs and the outputs of the original system and whose output gives an estimation of the state of the original system at present time. Usually the estimation is required to be exponential. In other words an observer, using the signal information of the original system, reconstructs dynamically the state. More precisely, consider an input-output nonlinear system described by

$$\begin{cases} \dot{x} = f(x, u) \\ y = h(x), \end{cases} \quad (1)$$

where $x(t) \in \mathbb{R}^n$ is the state of the system at time t , $u(t) \in U \subset \mathbb{R}^m$ is the input and $y(t) \in \mathbb{R}^q$ is the measurable output of the system.

An observer for the the system (1) is a dynamical system

$$\dot{\hat{x}}(t) = g(\hat{x}(t), y(t), u(t)), \quad (2)$$

where the map g has to be constructed such that: the solutions $x(t)$ and $\hat{x}(t)$ of (1) and (2) satisfy for any initial conditions $x(0)$ and $\hat{x}(0)$

$$\|x(t) - \hat{x}(t)\| \leq c \|x(0) - \hat{x}(0)\| e^{-at}, \quad \forall t > 0.$$

or at least $\|x(t) - \hat{x}(t)\|$ converges to zero as time goes to infinity.

The problem of observers is completely solved for linear time-invariant systems (LTI). This is a difficult problem for nonlinear systems and is currently an active subject of research. The problem of observation and observers (software sensors) is central in nonlinear control theory. Considerable progress has been made in the last decade, especially by the “French school”, which has given important contributions (J.P. Gauthier, H. Hammouri, E. Busvelle, M. Fliess, L. Praly, J.L. Gouze, O. Bernard, G. Sallet) and is still very active in this area. Now the problem is to identify relevant class of systems for which reasonable and computable observers can be designed. The concept of observer has been ignored by the modeler community in epidemiology, immunology and virology. To our knowledge there is only one case of use of an observer in virology (Velasco-Hernandez J. , Garcia J. and Kirschner D. [38]) in modeling the chemotherapy of HIV, but this observer, based on classical linear theory, is a local observer and does not allow to deal with the nonlinearities.

3.5. Delays

Another crucial issue for biological systems is the question of delays. Delays, in control theory, are traditionally discrete (more exactly, the delays are lags) whereas in biology they usually are continuous and distributed. For example, the entry of a parasite into a cell initiates a cascade of events that ultimately leads to the production of new parasites. Even in a homogeneous population of cells, it is unreasonable to expect that the time to complete all these processes is the same for every cell. If we furthermore consider differences in cell activation state, metabolism, position in the cell cycle, pre-existing stores of nucleotides and other precursors needed for the reproduction of parasites, along with genetic variations in the parasite population, such variations in infection delay times becomes a near certainty. The rationale for studying continuous delays are supported by such considerations. In the literature on dynamical systems, we find a wealth of theorems dealing with delay differential equations. However they are difficult to apply. Control theory approaches (interconnections of systems), is a mean to study the influence of continuous delays on the stability of such systems. We have obtained some results in this direction [5].

4. Application Domains

4.1. Metapopulation models

Heterogeneity plays an important role in many infectious disease processes. For instance, spatial heterogeneity is a strong determinant of host-parasite relationships. In modeling spatial or geographic effects on the spread of a disease, a distinction is usually made between diffusion and dispersal models. In diffusion models, spread is to immediately adjacent zones, hence the phenomenon of traveling waves can appear. These models traditionally use partial differential equations. However, there are some important situations that cannot be modeled by PDE. This is the case when the space considered is discrete. For example, when we have to consider sparsely populated regions, the human population is located in patches. The organization of human-hosts into well-defined social units such as families, villages or cities, are good examples of patches. Another example arises in the study of the human African Trypanosomiasis. The vector is the tse-tse fly, and it is known that flies take fewer blood meals in villages than in coffee plantations where the villagers work during the day. For such situations where human or vectors can travel a long distance in a short period of time, dispersal models are more appropriate. These models consider migration of individuals between patches. The infection does not take place during the migration process. The situation is that of a directed graph, where the vertices represent the patches and the arcs represent the links between patches. Recently, there has been increased interest in these deterministic metapopulation disease models. We have generalized to n patches the Ross-Macdonald model which describes the dynamics of malaria. We incorporate in our model the fact that some patches can be vector free. We assume that the hosts can migrate between patches, but not the vectors.

The susceptible and infectious individuals have the same dispersal rate. We compute the basic reproduction ratio \mathcal{R}_0 . We prove that if $\mathcal{R}_0 \leq 1$, then the disease-free equilibrium is globally asymptotically stable. When $\mathcal{R}_0 > 1$, we prove that there exists a unique endemic equilibrium, which is globally asymptotically stable on the biological domain minus the disease-free equilibrium.

MASAIE is developing, in the framework of the CAPES-COFECUB project (see international program), a metapopulation model for dengue. This model is for the state of Rio and is using the data of foundation FIOCRUZ.

4.2. Estimating total parasite load in falciparum malaria patients

We give a brief review of the biological features of malaria. Malaria in a human begins with an inoculum of *Plasmodium* parasites (sporozoites) from a female *Anopheles* mosquito. The sporozoites enter the liver within minutes. After a period of asexual reproduction in the liver, the parasites (merozoites) are released in the bloodstream where the asexual erythrocyte cycle begins. The merozoites enter red blood cells (RBC), grow and reproduce over a period of approximately 48 hours after which the erythrocyte ruptures releasing daughter parasites that quickly invade a fresh erythrocyte to renew the cycle. This blood cycle can be repeated many times, in the course of which some of the merozoites instead develop in the sexual form of the parasites : gametocytes. Gametocytes are benign for the host and are waiting for the mosquitoes. An important characteristic of *Plasmodium falciparum*, the most virulent malaria parasite, is sequestration. At the half-way point of parasite development, the infected erythrocyte leaves the circulating peripheral blood and binds to the endothelium in the microvasculature of various organs where the cycle is completed. A measurement of *Plasmodium falciparum* parasitaemia taken from a blood smear therefore samples young parasites only. Physician treating malaria use the number of parasites in peripheral blood smears as a measure of infection, this does not give the total parasite burden of the patient. Moreover antimalarial drugs are known to act preferentially on different stages of parasite development. Our work consists in developing tools for estimating the sequestered parasites and hence the total parasite burden of the patient.

5. New Results

5.1. Robustness and \mathcal{R}_0

We have obtained new results about the relation between Robustness and the basic reproduction number \mathcal{R}_0 . It is now well admitted that the basic reproduction ratio \mathcal{R}_0 is a key concept in mathematical epidemiology and the literature devoted to this concept is now quite important, see [20], [40], [19], [22], [23], [24], [26], [28], [30], [34] and references therein.

This number is a threshold parameter for bifurcation of an epidemic system : for a general compartmental disease transmission model, if $\mathcal{R}_0 < 1$, the disease free equilibrium (DFE) is locally asymptotically stable; whereas, if $\mathcal{R}_0 > 1$, the DFE is unstable.

It is said in some papers that \mathcal{R}_0 is a measure to gauge the amount of uniform effort needed to eliminate infection from a population [22], [24], [25], [31], [30].

The concept of robustness, coming from control theory, is associated to uncertainty. Usually the parameters of a system are known within a certain margin. A question is, how some properties, e.g. stability, can be ascertained with uncertainty on the parameters. In control theory “stability margin” is an important concept. Another way to formulate this problem is to analyze the effect of perturbations, unstructured or structured. This problem is also related to the so-called pseudo-spectrum [36], [37], [35].

We found that the basic reproduction number of an epidemic system is not an accurate gauge of the distance from the Jacobian J of this system, computed at the disease free equilibrium, to the set of stable matrices (if J is unstable), respectively to the set of unstable matrices (if J is stable). The same conclusion arises for another indicator, introduced by Heesterbeek et al. [24], [31], [30], the type-reproduction number.

5.2. *Wolbachia* and Dengue

Wolbachia is a genus of bacteria which infects arthropod species, including a high proportion of insects. It is one of the world's most common parasitic microbes and is possibly the most common reproductive parasite in the biosphere. *Wolbachia* is a maternally inherited endosymbiont of a large number of insects and other arthropods that induces various effects on host reproductive biology. Estimated to infect more than 60% of all insect species *Wolbachia* species are present in mature eggs, but not mature sperm. Only infected females pass the infection on to their offspring. Another consequence of infection is cytoplasmic incompatibility, i.e., the inability of *Wolbachia*-infected males to successfully reproduce with uninfected females.

The successful introduction of a life-shortening strain of *Wolbachia* into the dengue vector *Aedes aegypti* that halves adult lifespan has recently been reported.

Mosquitoes carrying this *Wolbachia* strain show around a 50% reduction in adult female lifespan compared to uninfected mosquitoes. It has been reported that wMel and wMelPop-CLA strains block transmission of dengue serotype 2 (DENV-2) in *Aedes aegypti*, forming the basis of a practical approach to dengue suppression. Infection by *Wolbachia* has a triple effect : reduction of recruitment, increasing of mortality for the mosquitoes and reduction of dengue transmission.

With our colleague of Brazil (see International cooperation) we built and study different models for the introduction of *Wolbachia* in a population of *Aedes aegypti*. These models are epidemiological models with vertical transmission only, which is quite new. We found that bistability does exist : three equilibria are present. We show that the coexistence equilibrium is unstable. We show that the equilibrium without infection and the equilibrium with the whole population infected are asymptotically stable. Numerical experimentation shows that the basin of the second equilibrium is appreciable. This indicates that introduction of *Wolbachia* is feasible. The connection of these models with transmission models of dengue is under investigation by the French-Brazilian team.

5.3. Bilharzia

Schistosomiasis or bilharzia is a water-borne parasitic disease that affects 200 million people and poses a treat to 600 million in more than 76 countries [39]. It is caused by blood-dwelling fluke worms of the genus *Schistosoma*. The transmission cycle requires contamination of surface water by excreta, specific freshwater snails as intermediate hosts, and human water contact [21]. Schistosome are transmitted via contact with contaminated water containing cercaria the infective stage of the parasite [39], [32].

In connection with EPLS, a research NGO based in Saint-Louis (Senegal), and Pasteur Institute of Lille, we investigate a spatially deterministic metapopulation model in which infectious agents persist within a network of connected environments. This model accounts for human population age and behavior structure. We completely analyses the asymptotic behavior of this model. We give a formula for computing the basic reproduction ratio \mathcal{R}_0 . If $\mathcal{R}_0 \leq 1$ we prove that the disease free equilibrium is globally asymptotically stable. If $\mathcal{R}_0 > 1$, with an hypothesis on connectedness, we prove that there exists a unique positive endemic equilibrium, which is globally asymptotically stable.

The validation of this model, using data of EPLS, is under investigation and is the subject of a Phd thesis. The defense will occur at the beginning of 2013. We explore the identification of key parameters using different kind of observers.

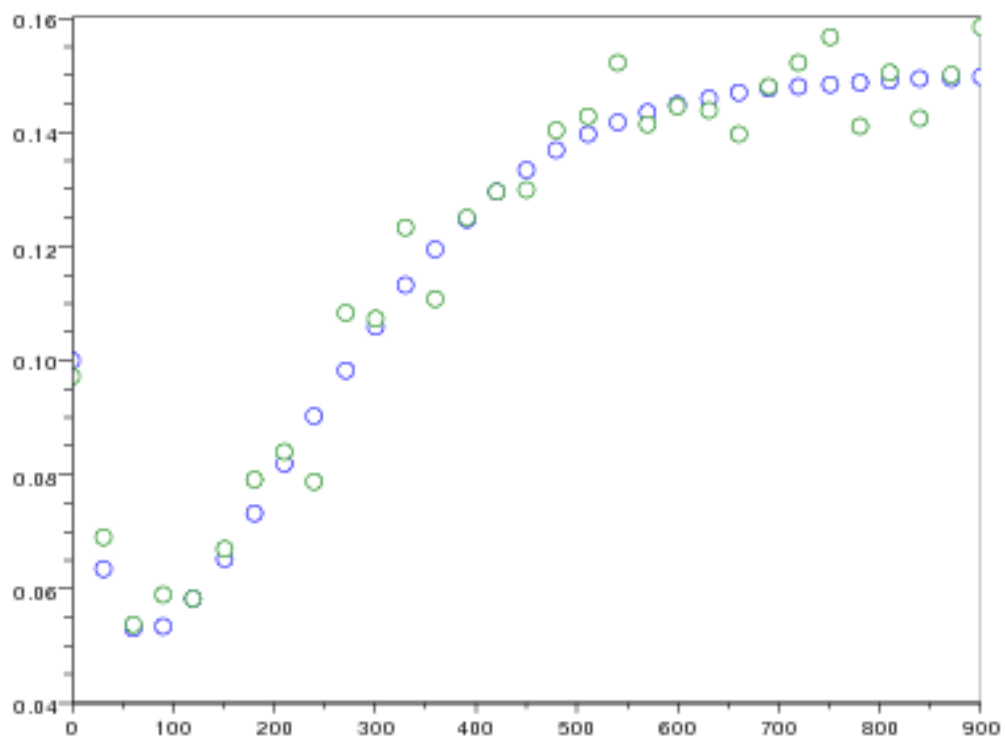


Figure 1. Noisy and discrete measure of host prevalence

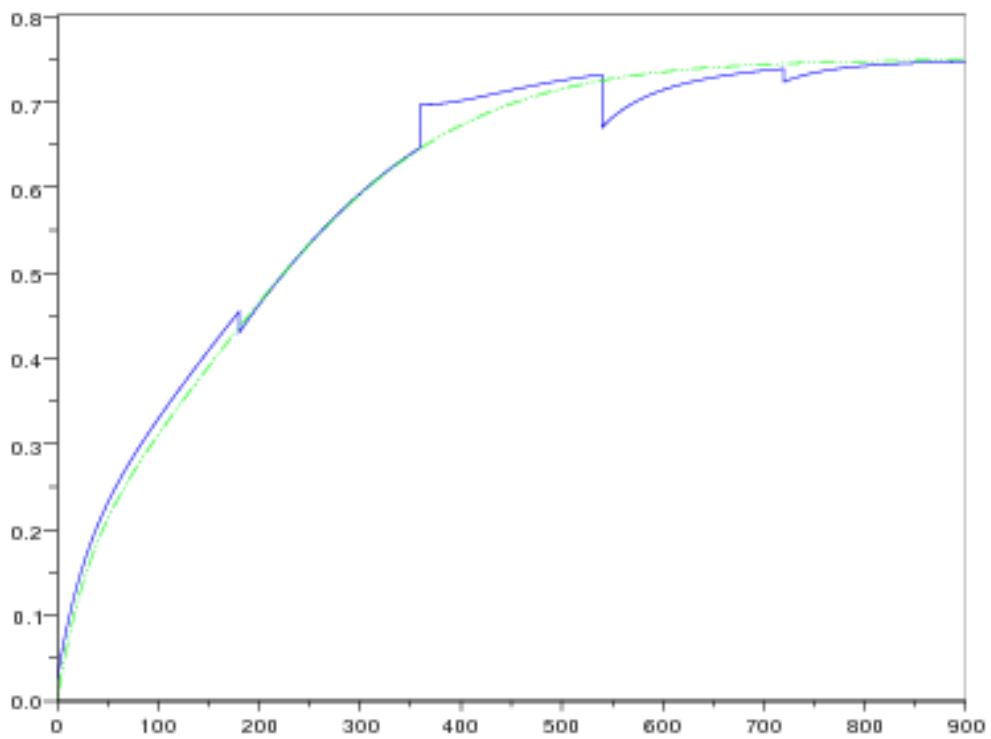


Figure 2. Reconstruction of the snail prevalence from preceding data

6. Bilateral Contracts and Grants with Industry

6.1. Contract with IAEA

Anopheles arabiensis is the target of a sterile insect technique (SIT) program in Sudan. Success will depend in part upon reasonable estimates of the adult population in order to plan the sizes of releases. It is difficult to obtain good estimates of adult population sizes for this mosquito because of the low density of the populations and also because the temporal and spatial distribution of *Anopheles arabiensis* is very dynamic. We have developed a compartmental model capable of predicting the range of adult populations of *Anopheles arabiensis* in two study sites in the North of Sudan. We have provided a software that is “user friendly” and that is able to give an estimate of the whole male and female population for the two geographical areas. A screenshot of the soft user interface is presented in Figure 3. This work is done in collaboration with Yves Dumont (AMAP, CIRAD).

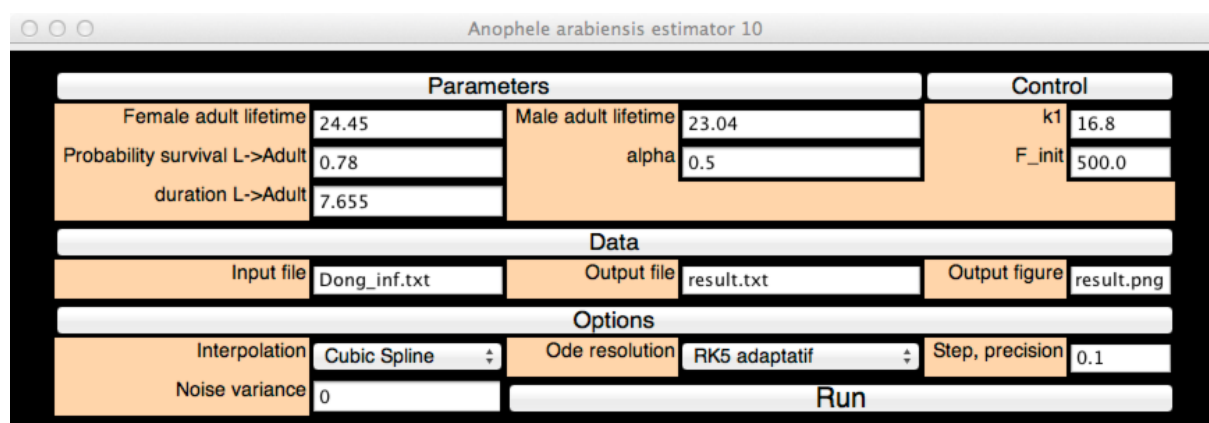


Figure 3. *Anopheles* estimator: screenshot of the soft user interface

7. Partnerships and Cooperations

7.1. Regional Initiatives

MASAIE has obtained a grant from Région Lorraine for a research project : “Dynamique des populations de pathogènes”.

7.2. International Initiatives

7.2.1. Inria International Partners

- University Gaston Berger, St Louis, Senegal.
- University of Ouagadougou and Université Polytechnique de Bobo-Dioulasso, Burkina-Faso.
- University Hassan II, Casablanca, Morocco.
- University of Manitoba, Winnipeg, Canada.

7.2.2. Participation In International Programs

7.2.2.1. CAPES-COFECUB

MASAIE is the french correspondent in a cooperation program with Brazil. This project, funded by CAPES-COFECUB, "new methods in epidemiology and early detection of events" for 4 years, has begun in January 2011.

A Brazilian network has been built in 2011, composed of

- FGV (Fundação Getulio Vargas) Rio de Janeiro. Principal investigator : Jair Koiller
- UFF (Universidade Federal Fluminense) Rio de Janeiro. Principal investigator : Max Oliveira de Souza
- UNICAMP (Universidade Estadual de Campinas) Campinas. Principal investigator :
- Fondation Oswaldo Cruz (Fiocruz, Rio). Principal investigator : Claudia Codeço
- l'université fédérale de l'état de Pernambuco, Recife (<http://www.ufpe.br/ufpenova/>); Principal investigator César Castilho;
- IMPA Rio de Janeiro

We investigate in 2012 the biological control of dengue by *Wolbachia*.

7.2.2.2. PAES-UEMOA

A research project on *Bilharzia* was deposited November 2, 2012, by the universities of Ouagadougou and Gaston Berger of Saint-Louis, in the framework of PAES(projet d'appui à l'enseignement supérieur) of UEMOA (Union Economique et Monétaire de l'Afrique de l'Ouest). MASAIE is an important component of this network. This project has been accepted July, 1, 2012 and funded with 30 000 000 CFA (XOF) (≈ 45 000 euro).

The Phd thesis of Lena Tendeng (MASAIE) is part of this project.

7.3. International Research Visitors

7.3.1. Visits of International Scientists

- Aboudramane GUIRO, Université Polytechnique de Bobo-Dioulasso, Burkina-Faso, March 25 to April 22, 2012.
- Patrick Deleenheer, University of Florida, Gainesville, FL, June 24-28, 2012.
- Diène Ngom, Université de Ziguinchor, Senegal, September 25 to October 18, 2012.
- Blaise Kone (université Ouagadougou) October 26-November 16, 2012.
- Beranrd Bonzi (université Ouagadougou) October 29-November 13,2012.

In the framework of CAPES-COFECUB

- Hyun Mo Yang (UNICAMP) : February 4-February 8, 2012.
- Max Oliveira de Souza (UFF Rio) February 19-March 3, 2012.
- Max Oliveira de Souza (UFF Rio) November 20-December 3, 2012.
- Moacyr Alvim Barbosa da Silva (FGV Rio) November 20-December 3, 2012.

7.3.2. Visits to International Teams

In the framework of CAPES-COFECUB, A. Iggidr and G. Sallet visit FGV and UNICAMP from October 28 to November 19, 2012 (see CAPES-COFECUB).

8. Dissemination

8.1. Scientific Animation

8.1.1. International conferences

8.1.1.1. CIMPA School

A. Iggidr is one of the three scientific directors and organizers of a CIMPA-UNESCO-MESR-MICINN-MOROCCO research School, held in Casablanca, October 1-12 : EpiCasa12 – Introduction to epidemiology: mathematical and statistical models and methods.

G. Sallet was also one of the lecturers.

This research school aims at providing the basic notions in epidemiology and modelling to students, or researchers, in mathematics and statistics, so that they can apply their knowledge to solve practical problems, that is:

- to understand scientific papers describing experiments or data acquisition in epidemiology, or dealing with mathematics applied to epidemiology;
- to perform classical data analyses;
- to model a simple epidemiological problem;
- to participate in research projects in epidemiology together with biologists.

8.1.1.2. Conference Saint-Louis

MASAIE and University of Gaston Berger have organized a conference in honor of Gauthier Sallet in Saint-Louis (Senegal) from December 3 to 7, 2012 (http://www.ugb.sn/?option=com_content&view=article&id=217). This conference was preceded by a school (November 29-30).

The scientific committee was composed of Julien Arino, Pierre Auger, Jean-Michel Coron, Jean-Luc Gouze, Claude Lobry, Mary-Teuw Niane, Michel Langlais, Hamidou Touré. The conference was sponsored by Inria, IRD, UGB, MESR Senegal. More than 50 participants from control theory, population dynamics and epidemiology participated to these events. The journal "Mathematical Control and Related Fields (MCRF)" will offer a special issue in connection to the Conference in honor of G. Sallet.

8.1.2. Expertise, scientific animation

G. Sallet was expert to synthesize all the studies carried out in WorkPackage 3, "Modelling and Simulations", WP leader Dr. Yves Dumont (CIRAD – AMAP). 25th March until 5th April at the CRVOI, La Réunion Island

G. Sallet gives conferences in the network M3D (Mathématiques et Décision pour le Développement Durable) : Structuration dans les modèles épidémiologiques. May 7-10, 2012. Oleron (<http://reseau-m3d.fr/>)

G. Sallet was invited by UMMISCO IRD and GRIMCAPE (LIRIMA) as an expert to participate to "modélisation mathématique des maladies infectieuses en contexte forestier". September 25-29, 2012.

8.2. Teaching - Supervision - Juries

8.2.1. Teaching

Master : G. Sallet, ODE and mathematical epidemiology, 30h, M2, Université Gaston Berger (Saint-Louis), Senegal.

8.2.2. Supervision

Phd Berge Tsanou (MASAIE),

Sandwich these (UPVM-université de Yaoundé I, Cameroun).

Etude de quelques modèles épidémiologiques de métapopulations : application au paludisme et à la tuberculose. Université de Lorraine, Metz, January, 13, 2012.

Phd : Josephine Wairimu Kagunda (MASAIE)

Sandwich these (UPVM-université Nairobi, Kenya).

Mathematical Analysis and Dynamical Systems Modeling of Highland Malaria in Western Kenya. Université de Lorraine, Metz, November, 23, 2012.

Phd : Leontine Nkague Nkamba (MASAIE)

Sandwich these (UPVM-université Gaston Berger Saint-Louis, Senegal).

Robustesse des Seuils en Épidémiologie et Stabilité Asymptotique d'un Modèle à Infectivité et Susceptibilité Différentielle. Université de Lorraine, Metz, November, 23, 2012.

Phd in progress : Derdei Bichara. Application de la théorie des observateurs à l'identification des paramètres de modèles épidémiologiques. Estimated date defence : February 2013

Phd in progress: Lena Tendeng. Modélisation de la bilharziose et validation de modèles. Estimated date defence : March 2013

9. Bibliography

Major publications by the team in recent years

- [1] P. AUGER, E. KOUOKAM, G. SALLET, M. TCHUENTE, B. TSANOU. *The Ross-Macdonald model in a patchy environment*, in "Mathematical Biosciences", 2008, vol. 216, n^o 2, p. 123–131.
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- [4] A. IGGIDR, J.-C. KAMGANG, G. SALLET, J.-J. TEWA. *Global analysis of new malaria intrahost models with a competitive exclusion principle.*, in "SIAM J. Appl. Math.", 2006, vol. 67, n^o 1, p. 260-278.
- [5] A. IGGIDR, J. MBANG, G. SALLET. *Stability analysis of within-host parasite models with delays.*, in "Math. Biosci.", 2007, vol. 209, n^o 1, p. 51-75.
- [6] A. IGGIDR, J. MBANG, G. SALLET, J.-J. TEWA. *Multi-compartment models*, in "Discrete Contin. Dyn. Syst.", 2007, n^o Dynamical Systems and Differential Equations. Proceedings of the 6th AIMS International Conference, suppl., p. 506–519.
- [7] D. NGOM, A. IGGIDR, A. GUIRO, A. OUAHBI. *An Observer for a Nonlinear Age-Structured Model of a Harvested Fish Population*, in "Mathematical Biosciences and Engineering", 2008, vol. 5, n^o 2, p. 337 –354.

Publications of the year

Articles in International Peer-Reviewed Journals

- [8] P. ADDA, D. BICHARA. *Global stability for SIR and SIRS models with differential mortality*, in "International Journal of Pure and Applied Mathematics, IJPAM", October 2012, vol. 80, n^o 3, p. 425-433, <http://hal.inria.fr/hal-00675359>.
- [9] R. ANGUELOV, Y. DUMONT, J. M. S. LUBUMA. *Mathematical modeling of sterile insect technology for control of anopheles mosquito*, in "Computers and Mathematics with Applications", 2012, vol. 64, n^o 3, p. 374-389, <http://www.sciencedirect.com/science/article/pii/S0898122112001939>.

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- [11] Y. DUMONT, J. M. TCHUENCHE. *Mathematical studies on the sterile insect technique for the Chikungunya disease and Aedes albopictus*, in "Journal of Mathematical Biology", 2012, vol. 65, n^o 5, p. 809-854, <http://dx.doi.org/10.1007/s00285-011-0477-6>.
- [12] A. GUIRO, A. IGGIDR, D. NGOM. *On the Stock Estimation for a Harvested Fish Population*, in "Bulletin of Mathematical Biology", 2012, vol. 74, n^o 1, p. 116-142 [DOI : 10.1007/s11538-011-9667-Z], <http://hal.inria.fr/inria-00523963>.
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