INSTITUT NATIONAL DE RECHERCHE EN INFORMATIQUE ET EN AUTOMATIQUE

Team ANUBIS

Tools of automatic control for scientific computing, Models and Methods in Biomathematics

Futurs

THEME BIO

Activity Report

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1. Team

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2. Overall Objectives

The ANUBIS team is joint to INRIA and MAB, UMR CNRS-universités Bordeaux 1-2 5466. It is located in Bordeaux (Bordeaux 1 and Bordeaux 2 universities) and in Pau (université de Pau et des Pays de l'Adour). The team was created in July 2004.

This team is dedicated to developing tools for solving general partial differential equation problems, and more specifically those coming from modelling in Biology. The target is twofold : - provide methods with increased speed and precision to obtain a better interactivity of simulations; -allow the use of more complex and so more realistic models. The proposed way insists on the links with automatic control. We shall study problems naturally formulated in terms of optimal control (optimization, game theory, inverse problems, data assimilation) but also problems where the state equation can be rewritten as an optimal control problem in time or space. The general idea is then to transpose methods and algorithms from automatic control to numerical analysis. We expect numerical methods with properties of stability, robustness and with computing localization from this transposition. The team will investigate biomathematical modelling and simulation more specifically. The biological problems investigated are coming from population dynamics (demography, epidemiology, hematology) and from neuroscience.

3. Scientific Foundations

3.1. Factorization of boundary value problems

We propose a method to solve elliptic boundary value problems inspired by optimal control theory. We use here spatially the technique of invariant embedding which is used in time to compute optimal feedback in control. In the symmetric case we consider the state equation as the optimality system of a control problem, one space variable playing the role of time. The problem is embedded in a family of similar problems defined over subdomains of the initial domain. It allows to decouple the optimality system as for the derivation of the optimal feedback. So one can factorize a second order elliptic boundary value problem in two first order Cauchy problems of parabolic type. These problems are decoupled : one can solve one problem in one space direction ("descent phase") then the other problem in the opposite direction ("climbing phase"). This decoupling technique also works in the nonsymmetric case.

This point of view developed independently, is not completely original as some of the ideas were presented in the book [34], but they seem to have been forgotten since. It is also investigated in the framework of submarine acoustics in [39] (cf infra). Recently M. Gander from Mc Gill university in Montreal has worked on similar ideas and we want to collaborate with him.

At the moment the method has been applied and fully justified in the case of a cylinder [30]. Indeed, the invariant embedding can be done naturally in the direction of the cylinder axis and allowing the factorization of the second order operator in the product of operators of the first order with respect to the coordinate along the cylinder axis. It needs the computation of an operator solution of a Riccati equation. This operator relates two kinds of boundary conditions on the mobile boundary for the same solution (for example the operator relating Neumann and Dirichlet boundary conditions). Furthermore the same method applied to the finite difference discretized problem is nothing but the Gauss block factorization of its matrix. Therefore the method can be seen as the infinite dimensional generalization of the Gauss block factorization.

We look for a generalization of the method to open sets of arbitrary shape and also to families of surfaces sweeping over the domain of arbitrary shape. Two situations are possible : these surfaces have or not an edge. In the second case one can consider for example a family of surfaces starting at the boundary of the domain and shrinking to a point. The difficulty comes from the singularity at that point [29] and to the initialization of the "climbing phase". It is now well understood in the case of a disk. The directions of investigation aim at giving this methodological tool its larger generality:

1. Maria do Céu Soares's PhD at the new university of Lisbon, supervised jointly with B. Louro, aims at implementing the method in the case of a circular domain, swept over by a family of concentric circles. Two possible situations have been dealt with : the family of circles are decreasing from the boundary of the domain or increasing from the origin. In the later case the singularity is met at the initialization of the descent phase. With this formulation one can obtain the Dirichlet-Neumann operator at the boundary which is useful, for example, for domain decomposition methods. More generally we want to deal with the case of star-shaped domains where the subdomains are obtained by homotethy.

2. study of slender domains We aim at studying domains defined by their plane sections evolving smoothly along an axis. Various ways are possible : either by defining an Hilbert basis of the functions on the section, which limits the possible evolutions of this section ; either by using a geometrical transform for each section such that we are lead back to the cylinder case ; either by reasoning in the physical domain. In that later case the difficulty comes from the fact that the spaces of functions defined on sections depend on these sections. We intend to use techniques developed in shape otpimization (velocity method of Sokolowski-Zolesio [42]). The factorization obtained depends on the method used.

3. multiple parameter invariant embedding. It could allow a continuous analogous of the complete Gauss factorization in the discrete case. This needs the study and the factorization of non local kernels linked to operators of the kind previously mentioned (Dirichlet-Neumann, for example);

4. study of other types of equation (parabolic, hyperbolic) with space invariant embedding. It should be noticed the pioneering computation of J.L. Lions [38] for the heat equation on the half infinite domain $\mathbb{R}^+$;

5. obtaining transparent boundary conditions for unbounded domains. This very important problem for the simulation of wave propagation relies on the computation of a Dirichlet-Neumann operator for the neglected part of the domain. Now it can be addressed analogously to the optimal stationary feedback and the algebraic Riccati equation;
6. domain decomposition. The classical presentation of iterative substructuring methods (Schwarz without overlap) uses the Steklov-Poincaré operator at the interface of subdomains [41]. Now it can be directly expressed with the Dirichlet-Neumann operators in each of the neighbouring domains. The Riccati equation furnished by the factorization method allows to let evolve the Steklov-Poincaré operator when the interface is moved. This may be usefull for load balancing in a parallel computation ;
7. study of boundary control problems where the spatial decoupling (as previously explained) can be done jointly with the decoupling of the optimality system ;
8. study of a QR like factorization. As for the Gauss factorization, the QR factorization can be extended to the continuous problem as the product of an orthogonal operator and a Cauchy problem of the same order as the initial problem. One of the interests of this parallel vision of bondary value problems on one side and optimal control problems on the other is that results in one domain can " bounce back" to the other : for example, for linear quadratic control problems, the QR factorization gives rise to an optimal proportional integral feedback;
9. study of non linear problems. If a general approach through a Hamilton-Jacobi equatin seems out of reach, we may think to study a linearized problem within a Newton method. This will lead to quasi-Riccati equation. For quasi-linear systems (which are frequently used in population dynamics) it is possible to iterate without recomputing the solution of the Riccati equation;
10. robust simulation. For ill modelled problems, one can introduce a modelization error as a bounded perturbation which transforms the control problem into a differential game problem. Using a second Riccati equation one can obtain a worst case design simulation.

The goal is to provide Cauchy problems equivalent to boundary value problems in a manner as general as possible. We expect from this an interesting theoretical tool : it has already established a link between certain uniqueness results for the Cauchy problem for the considered operator and backward uniqueness for the parabolic problem in the factorized form. Besides this theoretical tool, giving equivalent formulation to the continuous problem may give rise to new numerical methods based on these formulations.

The method of virtual controls has been set forth by J.-L. Lions and O. Pironneau. It aims at providing methods for domain decomposition, model coupling, and multipyshic model based on optimal control techniques. Yet interactions (between domains or models) are considered as control variables and the problem is solved by minimizing a criterion. This approach suits well with the framework described here and we intend to contribute to it.

3.2. Structured population modelling

3.2.1. Structured populations

Population dynamics aims at describing the evolution of sets of individual of various nature : humans, animals, vegetals, parasites, cells, viruses,.. These descriptions are of interest in various domains : epidemiology, ecology, agriculture, fishing, ... In medicine that kind of models can be used in immmunology, cancer therapy,... First the models are studied qualitatively, particularly in view of the asymptotic behaviour : extinction or persistence of a species, or oscillating behaviour. These topics are also those of automatic control. For example a theoretical tool as Lyapounov functions has long been used in population dynamics. Similarly, the recent trend in automatic control consisting in using families of model giving a finer or coarser representation of the reality can be found in population dynamics : models describing the evolution of interacting populations are quite numerous, ranging from individual centered models to models governed by ordinary or partial differential equations. The choice of the structuring variables is essential to describe the population evolution well. It depends also on the final goal, mathematical analysis or numerical simulation.

For space distributed models, multimodelling techniques could be useful where the model can change from one region to another. The methods presented in section 3.1 could then be used to give interface conditions.

In demography the most significant variable is age for an individual ([43], [37]). This theme, although already intensively studied in our team in the past (see for example [1][8][9][10]) will be central for our future research. Independently of the space variable, other kind of structuration will be considered (size of individuals (fishing), weight,...).

For interacting populations or subpopulations additional structures can be put forth. In the study of disease propagation (microparasites) usually a structure linked to the health status or parasitic state of individuals in the host population is used (models SI, SIS, SIR, SIRS, SEIRS,..); another relevant variable is the age of the disease or the infection age for an individual [8][31]. In the host-macroparasite model of [6], it is the macroparasites that are structured in age.

In previous works, rather strong assumptions are made on demographic and diffusion coefficients (e.g. indentical or independent of age) to obtain qualitative results. In recent works (as [21] J.-M. Naulin's Ph D thesis or works in progress), it becomes possible to weaken these conditions.

3.2.2. Prey-predator models in highly heterogeneous environment

We consider prey-predator models in highly heterogeneous environment allowing certain spatial periodicities at scales that are small compared to the size of the domain. For example this is the case for the dynamics of ladybugs and green flies in orchards with hundreds of trees. The dynamics of the original problem (before going to the limit of small scale) is not known and it is impossible to study the influence of various biological parameters on the system. Nevertheless the limit problem is well posed and allows these studies : [2] [3] and F. Heiser's PhD thesis. We intend to go on investigating this way and determining global dynamics for this kind of problems.

3.2.3. Invasion process in island environment

In a series of joint works with F. Courchamp and G. Sugihara, e.g. [7], we are concerned by invasion models in island environment by species introduced at purpose or by chance, and their control. They highlight singular differential system with unusual dynamics : a finite time extinction may coexist with a Hopf bifurcation. It is important to take into account a space variable as heterogeneities are rather frequent in that environment (e.g. Kerguelen islands). A work has begun jointly with D. Pontier with the PhD thesis of S. Gaucel. In another work we deal with the invasion of a host population by a virus.

3.2.4. Aggregation/fragmentation of groups of individuals in a given population

In this section we are interested by individuals or groups of individuals aggregation/fragmentation phenomena. This question is up to date in works in animal ecology [36], but also in other domains as physiology and medecine.

Phenomena of alignment of fish shoals, of gathering of certain animal species, of cell aggregation are part of this class of problems and we intend to invest in the modelling and simulation of these phenomena which play an important role for understanding the dynamics of the concerned populations. A first work in this direction is [4] where we consider a model structured with respect to a given character (infectiousness, social character,...) diffusing in space and having a non local renewal process. Interactions between individuals are supposed of Boltzman type. For example to model the proliferation of phytoplankton piles we use as structuring variable the size of the piles. Then the research is oriented towards the development of transport-projection numerical techniques. This work is done in the framework of the GDR GRIP.

3.2.5. Space dependent epidemiologic models

With M. Iannelli, we intend to study the impact of the spatial location (developed or underdeveloped country) on the propagation of an infectious disease (tuberculosis, aids...). Then we have to model the way that the infectiveness rate or the recovery rate, which are dependent on the place, influence the dynamics of the infected population. Various ways can be experienced. In a first possibility we could assume that individuals are randomly distributed in space [2][31]. We would obtain a reaction diffusion system whose reaction term would depend on space. In another way, we could define patches where the population dynamics is governed by ordinary differential equation (cf. works by Auger et al.).

3.2.6. Host-parasites systems

This research theme has been present in our team for many years with investigations on virus of carnivorous animals (foxes *Vulpes vulpes*, domestic cats *Felis catus*) [5], or on macroprarasites (*Diplectanum aequens*) infesting of sea-perches (*Dicentrarchus labrax*) populations [6]. It will remain a main theme due to its importance for the biologists with whom we are working and the new opportunity opened after the drastic reduction of simulation time for these problems (cf the PhD of J.-M. Naulin, and joint work with ScalApplix team).

New problems are opened, in particular with the models with indirect transmission through the ground or environment ([5]) or with *interspecific* transmission. Then now we can speak of parameter identification, control,....., and even more with reaction-diffusion systems coupled with ordinary differential systems which arise in [5][25][31], and whose mathematical treatment is not straight forward.

3.2.7. Generating process for blood cells

The process of production of blood elements, called hematopoiesis, is a complex phenomenon, based on self renewal and differentiation of stem cells. For human, it occurs in the bone marrow. Every day billions of cells are produced to face unequal life durations and different renewal rates of blood cells. Mathematical modelling of hematopoiesis is not a new topic. It mainly incorporates models proposed by the team of M.C. Mackey [40][35] and uses partial differential equations structured in age and maturity. Maturity in these models is different from size (classically used for models of mitosis) it is a variable describing the level of development of a cell (quantity of DNA or RNA synthesized, rate of mitochondry,...). There exists cells with maturity as small as one may want in the bone marrow (multipotent primitive stem cells). These cells determine the behaviour of the whole population of blood cells. One can incorporate delays in these equations due to the duration of the cell cycle, nonlinearities due to the piling of cells in the population and stochastic features. Among blood diseases some exhibit oscillations in the production of blood cells. They are called cyclic hematologic diseases. They can affect only one kind of cells (periodic auto-immune hemolytic anemia) or all the kinds of cells. It is the case for periodic chronic myeloid leucemia, where the period can vary between 30 and 100 days which is much longer than the duration of the cell cycle (less than one week). In previous works [16], [17], we have shown the existence of oscillating solutions through Hopf bifurcations for simplified models of hematopoiesis. We intend to go on investigating these questions. Yet the study of these diseases allow a better understanding of regulation phenomena that are acting in hematopoiesis : the periodic nature of these diseases brings evidence of a control on bone marrow proliferation which is still unknown. This question has been investigated by M.C. Mackey's team who developed experiments and numerical approaches for simplified models. Nevertheless this team did not develop the mathematical analysis of these equations sufficiently. Generally speaking the problems arising in hematopoiesis are twofold : differential equation with delay (which may be stochastic) or degenerated hyperbolic partial differential equations. There exists data on maturation velocity or mortality rates which allow the numerical resolution of these equations. Differential equations with delay are solved numerically by adapting Runge-Kutta methods and by using interpolation methods. Solving numerically hyperbolic partial differential equations with delay needs new tools based on one dimensional finite difference or finite element methods or characteristic method or decentered finite volume method more adapted to hyperbolic equations. Implementing these methods needs the use of servers capable of managing heavy computations.

3.2.8. Kinetic models in microbiology

In this work we are interested in developing kinetic models of social behaviour of several cell populations. It consists in a system of several kinetic equations satisfied by the population densities. These equations are coupled by integral source terms expressing the meeting rate of individuals.

3.2.9. Predator-prey models with chemotaxy

We consider predator-prey systems in which we take into account a spatial displacement due to chemotaxy. We assume that predators are chasing their preys by smelling out their scent and reciprocally preys are escaping predators by detecting their approach. So we build nonlinear models of the Keller and Segel type. Displacement velocities are functions of the species density gradient. The main work consists in developing finite volume numerical techniques for these equations.

3.3. Optimal control problems in biomathematics

The controls in population dynamics are of various kinds and generally speaking are due to the action of man on his environment. Prophylaxis, sterilization, vaccination, detecting, quarantine, elimination, re-introduction, capture, hunting, fishing, pesticides are examples of control processes at man's disposal. It is then important to know what is the impact of such actions on the considered population and to distinguish between what is feasible and what is not in terms of optimal management of resources. A rather rich literature exists on this topic ranging from resource management in ecology to applications of Pontryaguin's maximum principle to mathematical biology problems.

One important significant variable is often ignored : the space variable. Its importance is due to space inhomogeneities of the environment and of the control structure which is often localized to small part of the domain. This point is linked to the cost of control and the ability of the controller to access to the individuals.

The other important variable ignored in works on population control is the age of individuals which, in the domains under investigation (demography, ecology, epidemiology, cell growth,....), plays a leading part also. In the framework of this research team-project we will investigate control problems for structured models (size, weight, age, health state, position of individuals, age of the disease,...) from biomathematics. We will use both individual based models and models using densities. The techniques to be used are mainly those from automatic control and the factorization methods described in section 3.1.

3.3.1. Control of fisheries

The problem of management of fish harvesting is very hard from the socio-economical point of view. Determining the quotas depends on the evolution of the stock of fish in the considered area. Most of the models used to determine these quotas are only time dependent although the fishing effort is size dependent due to the techniques of fishing. We intend to use techniques coming from automatic control in order to maximize the income of fishers with bounds on the fishing effort and its derivative. Models will be structured by the age, size and position of the fishes. This last variable is important for migrating fishes and those who spawn at specific areas.

3.3.2. Disease control

Some problems of prevention against disease propagation can be modelled as optimal control problem with control acting on subdomains and/or on certain cohorts. Then several optimization programs can take place depending on the badness of the disease and the cost of the control. The problem consists in minimizing or maximizing an objective function with constraints on the control and on the state.

For some of these problems concerning animal populations the objective consists in finding the smallest domain that can prevent the propagation of the disease : the reduced level of healthy individuals or the absence of any infected prevents the propagation. This is a control problem coupled to a shape optimization problem.

3.3.3. Controlling the size of a population

This is a classical problem in demography. Various kinds of control can be used : control by migration, by elimination (animal populations), by the policy of birth,...Numerical and mathematical difficulties come from the existence of non local terms in the equation due to the mortality and renewal processes of the population. Classical results of automatic control theory cannot be applied directly. Our last results on the topic show that one can control (after a time equivalent to one generation) a population (except the smallest age classes) by acting only on age classes of small size and localized on small domains. These studies could be extended to systems (populations structured by sex, prey-predator systems,..) and to other fields than demography but with similar difficulties (cell growth, epidemiology with sanitary structuration,...).

3.3.4. Age structured population dynamics as a problem of control

For some evolution problems, one can consider that a part of the dynamics comes from a state feedback. This is naturally the case for age structured populations for whose dynamics the birth rate depends on he breakdown of the present population by age. Then one can consider the birth rate as a control. There remains to determine the the criterion and therefore the observation of the system in order that the optimal feedback corresponds exactly to the natural fertility rate. This problem leads to a functional equation which has to be studied and solved numerically. This could allow to transform population evolution problems to an open loop control problem and may be a clue to numerical problems linked to birth rates. Possibly for control problems in population dynamics (fishing, epidemiology,....) such an approach could provide a smooth transition between the phase under optimization and a desired asymptotic behaviour.

3.3.5. Inverse problems : application to parameter identification and data assimilation in biomathematics

A classical way to tackle inverse problems is to set them as optimal control problems. This method has proved to be efficient and is widely used in various fields. Nevertheless we are persuaded that important methodological progresses are still to be done in order to generalize its use. With JP Yvon, we have worked on the numerical stability of these methods, seeking to redefine the mismatch criterion in order to improve the conditioning of the Hessian of the optimization problem. For certain problems the ill-posedness can be related by the factorization method to the ill-posedness of the backward integration of a parabolic equation. Then we can apply the well-known quasi-reversibility method to that case.

An other idea we want to investigate consists in defining a measure of match (positive) and one of mismatch (negative) between the output of the model and the measurements, and to take into account only the positive part in the criterion. This point of view inspired from methods used in genomic sequences comparison (Waterman's algorithm) aims at a better robustness of the method by eliminating from the criterion the effect of unmodelled phenomena. It also leads to free boundary problems (part of the observation taken into account).

The setting in position of programs of vaccination, prophylaxy, detection needs an a priori study of feasibility. This study after a modelling step will go through a step of model tuning to the data. Yet, initial data are badly known or completely unknown, demographic parameters are often unknown and disease transmission mechanisms are subject to discussion between biologists to determine their nature but their exact form and value is unknown. We intend to use parameter estimation techniques for these biomathematics problems.

4. New Results

4.1. Boundary value problem factorization applied to waveguide analysis

Participants: Jacques Henry, Isabelle Champagne.

The method can be used for other linear stationary problems than the Poisson equation. We consider wave propagation in a cylinder waveguide in harmonic regime. The invariant embedding technique is applied along the axis. For the Helmholtz equation the boundary value problem is ill-posed for certain sizes of the domain corresponding to resonances. The related Riccati equation for the Dirichlet to Neumann operator (generalized impedance) has singularities (blow up of solutions) for those domains due to the non positveness of the Helmholtz operator. This difficulty is solved by using representation formulae by homographic transforms well known in control theory. Indeed by this way the Riccati equation is transformed in a linear equation. So the singularities come only from the homographic transforms. This transforms provides a way to numerically integrate the Riccati equation over the singularities. I. Champagne defended her PhD thesis in October [11].

4.2. Space invariant embedding by homothety

Participants: Jacques Henry, Maria do Céu Soares.

In the case of a cylinder the space invariant embedding is done by translation of a section. In more general geometries the family of surfaces sweeping over the domain may be more complicated. We have studied the case of a star shaped domain with a family of surfaces derived by homothety. We derived a new Riccati equation for that case which has been used for the computing zoom [29].

4.3. The computing zoom

Participant: Jacques Henry.

In the framework of boundary value problem factorization we wish to develop and promote the concept of "computing zoom": for a simulation on a given domain, the user defines a region of interest by its center and the magnification ratio. Then to recompute the solution only in the region of interest (with a higher precision), it is a matter of computing boundary conditions providing the behaviour of the solution in the neglected part of the domain. This can be done by integrating a Riccati equation from the boundary of the initial domain to the boundary of the region of interest. So we obtain a relative resolution equal to the one of the original problem if the number of unknowns is kept constant with a cost of computing consequently constant. Therefore the precision (resolution capacity in the optical analogy) is increased locally for any set of data. A toy program in Scilab implementing the principle of the "computing zoom" for a Laplacian in 2D has been developed. The software allows for variation of the center of the region of interest and of the magnification ratio as could be done with a microscope.

4.4. Control problems in population dynamics

Participants: Jacques Henry, Bedr'Eddine Ainseba.

As an application of the technique of localization of computations we began to study the optimal control of fisheries. The fishing area is small compared to the sea. We considered a stationary, linear control problem as a first step. The factorization method provides transparent boundary at the boundary of the fishing area. The control problem can then be solved efficiently by computations done only in the fishing area.

For an observation time sufficiently large we obtained the exact controllability for the age and space population dynamics problem with controls acting on a small space domain and on small age classes (in collaboration with S. Anita) [23][24].

For prey predator and epidemiological reaction diffusion systems we give new conditions for stabilizabilty with positive state constraints (in collaboration with S. Anita) [22].

4.5. Invasion processes

Participants: Bedr'Eddine Ainseba, Michel Langlais, Fabien Marpeau, Cédric Wolf.

This research theme is mostly dedicated to mathematical population dynamics, i.e., predator–prey systems or host–parasite systems in heterogeneous environments. Three main aspects are considered: (1) basic mathematical analysis (global existence and qualitative properties of ODEs or PDEs systems with W.-E. Fitzgibbon, controllability with B. Ainseba), (2) derivation of models and model analysis within a collaborative work with C. Wolf and the team of D. Pontier (feline retroviruses, rodents viruses possibly transmitted to humans), and (3) numerical simulations of complex host–parasite systems within a collaboration with F. Marpeau, H. Malchow (and his group) or with J. Roman (ScalApplix project).

- A new result obtained through numerical simulations shows a specific impact of a parasite on an invasive species: a parasite can slow down and reverse the invasion process of a host population whose dynamic exhibits a Allee effect (bistable dynamics).

- A new result obtained through model analysis and numerical simulations is related to rodent populations experiencing periodic dynamics and a hantavirus: in some circumstances the hantavirus can take advantage of the time periodical dynamics of the reservoir rodent population to invade neighbouring human populations within which it is letal.
- A positive, stable and second order numerical scheme for reaction-diffusion equations arising in population dynamics is being designed to accurately approximate their transient solutions.
- A new result concerning the analysis of an epidemiological age and space population dynamics diffusion system when the demographic functions and the diffusion coefficients are distinct [21].
- A new result (in collaboration with M. Iannelli) concerning the analysis and stability of age dependent epidemiological systems with geographical dependent recover functions.

4.6. The blood production system

Participants: Mostafa Adimy, Fabien Crauste.

This research is devoted to the analysis of mathematical models of blood cells production in the bone marrow (hematopoiesis). In a first work, in collaboration with L. Pujo-Menjouet, we considered a maturity structured model in which the time spent by each cell in the proliferating phase, before mitosis, depends on its maturity. We obtained a system of nonlinear first order partial differential equations, with a time delay depending on the maturity and a retardation of the maturation variable. The maturity in this model is a continuous variable which represents what composes a cell such as proteins or other elements one can measure experimentally. We proved that the stability of this system depends strongly on the behaviour of the immature cell population. In a second work, in collaboration with S.Ruan, we studied a model in which the length of the proliferating phase is distributed on an interval. We showed that instability can occur in this model via a Hopf bifurcation, leading to periodic solutions usually orbitally stable with increasing periods. This was obtained throughout the description of a centre manifold and the subsequently study of the normal form.

4.7. Powdery mildew of grapevine

Participants: Jean-Baptiste Burie, Michel Langlais.

This work is a joint one with A. Calonnec and other phytopathologists from the INRA in Bordeaux. We aim at devising a model that would give a better understanding of the spreading mechanisms of the Powdery Mildew, a fungal disease of the vine whose financial and environmental cost is important. The ultimate goal is to have the ability to predict and control the epidemics. The team involved in this project is a multidisciplinary one which also includes members of Inria Futurs ScalApplix who have their own approach.

On their part, mathematicians involved in this project focus on the important roles of the growth of the vine during the epidemics and of the dual mechanisms of spores dispersal. The models that were devised for this use systems of ODEs (J-M. Naulin at INRA) and reaction-diffusion equations coupled with ODEs (J.-B. Burie).

4.8. Integrated Pest Management in vineyard

Participants: Ahmed Noussair, Bedr'Eddine Ainseba, Jacques Henry.

The prediction of damages caused by the grape moths *Lobesia botrana* and *Eupoecilia ambiguella* is always problematic in the vineyards were these insects occur. The objective of our work is to progress in the risk assessment of this pest by predicting the offspring size of the n generation at the (n-1) generation.*L. botrana* is a species in which the larva is polyphagous. Host plant and grape varieties eaten by the larvae modify the protandry between males and females, the female fecundity, the egg fertility and thus the demography of the offspring, with its consequence on the temporal dynamics of oviposition and thus grape damages. Multistructured models are constructed and describe the distribution of individuals throughout different classes (or stages) based upon individual performance that are important with the regard of individual vital rates and on the basis of a number of physiological characteristics that influence the life history in term of its chance to grow, migrate, reproduce or die. This is a joint work with D. Thierry of INRA (Villenave d'Ornon).

5. Other Grants and Activities

M. Adimy is head for the french part of a UE grant INTERREG III A with Spain on "development of a passive ocean tracer model" for the period 2005-2007. He is also responsible for a Brancusi PAI project with Rumania (polytechnic university of Bucarest) on "stability, bifurcation and control for delay differential equations coming from Biology.

J. Henry has a PAI grant PESSOA with CMAF of the university of Lisbon (B. Louro and L. Trabucho) on "Boundary problems factorization and and application to the elasticity theory and to control".

M. Langlais has a joint grant with C.-H. Bruneau on the "Impact of a contamination by radionucleides on population dynamics" supported by GDR MOMAS from ANDRA, BRGM, CEA, CNRS and EDF.

M. Langlais belongs to a french-japonese PICS program on "Mathematical Understanding of Invasion Processes in Life Sciences" (see section 6.1)

6. Dissemination

6.1. Services to the scientific community, organization of conferences

J. Henry is in charge of International relations for INRIA Futurs unit. J. Henry is vice chairman of IFIP TC7. He is member of INRIA's COST committee for incentive actions.

- J. Henry is vice chairman of the International Program Committee of the 22nd IFIP TC 7 Conference on System Modeling and Optimization Turin, Italy, July 18-22, 2005.
- M. Langlais was a co-organiser and a member of the scientific committee of a French–Japonese workshop "*Mathematical Understanding of Invasion Processes in Life Sciences*" held at CIRM in Marseille on March 15–19 2004 within the framework of a French–Japonese CNRS PICS program.
- M. Langlais was a member of the scientific committee of the conference "*Computational and Mathematical Population Dynamics*" held in Trento, June 21–25 2004, and a co-organiser with W.-E. Fitzgibbon of a minisession on "Complex Diffusive Systems in Mathematical Biology".
- M. Langlais was the chairman of the scientific committee of the 11th meeting of the French speaking Society for Classification (SFC) held in Bordeaux, September 8–10 2004. He co-edited with M. Chavent a special issue of RNTI (Revue des Nouvelles Technologies de l'Information) dedicated to this meeting.
- M. Adimy was the organiser of a conference in memory of O.Arino "Biomathematics" Pau, July 02, 2004.
- M. Adimy was a member of the scientific committee of the 1st international conference of the French Society of Theoretical Biology held in Marrakesh on May 21-25, 2004.
- B.E. Ainseba is member of the scientific committee of the International workshop on differential equations in mathematical biology Le Havre July 11-13, 2005.
- B.E. Ainseba was an organiser of a session dedicated to control in biology at "Computational and Mathematical Population Dynamics" Trento, June 21-25, 2004,

6.2. Academic Teaching

M. Langlais teaches basic deterministic mathematical modelling techniques in Demography and Life Sciences at the Master level in Bordeaux 2 university; 15h per year.

6h lecture by M. Langlais during the Summer School “Mathematical Models in Biology and Population Dynamics", held in Dourdan on July 5–9 2004, organised by CNRS and GRIP GDR.

In the Master 2 MAM (Mathematics and Applications of Mathematics) of the university of Pau, M. Adimy teached in 2004-2005 a course named "Models and methods in populations dynamics" (30 hours).

B.E. Ainseba is teaching a course on Mathematical Control in Biology at the Master level at the university Bordeaux 2.

6.3. Participation to conferences, seminars

J. Henry gave a talk on “the computing zoom” at CANUM’04 (Obernai, May 31, June 4). He gave a presentation on the same subject at the IFIP WG7.2 workshop on “Free and moving boundaries analysis, simulation and control”, HOUSTON, december 2-4. He gave seminars on this technique at CMAF, university of Lisbon and at the university complutense of Madrid. A common paper with J.P. Yvon on “Reduction of Dimension in Control of PDE by a Computing Zoom” was presented at the conference MathGeo 04 honoring Guy Chavent, Rocquencourt, December 9-10.

M. Langlais, B.E. Ainseba, J.B. Burie, J. Henry and C. Wolf attended the “*Computational and Mathematical Population Dynamics*" held in Trento, June 21–25 2004. J. Henry and B.E. Ainseba presented a paper on “Application of the factorization method to the spatially fish harvesting”. B.E. Ainseba made a contributed talk ”Localized population dynamics control problems”. C. Wolf made a contributed talk “Modelling direct and indirect propagation of a hantavirus in spatially structured population”. W. Fitzgibbon and M. Langlais made a contributed talk “Modeling the circulation of a disease between two host populations on non coincident spatial domains”.

Invited lecture by M. Langlais at the “Conference dedicated to the memory of Pr O. Arino", held in Marrakech on January 9-10 2004, organised by H. HBid. At the same conference B.E. Ainseba gave a talk on "Sur la Stabilisation de systèmes épidémiologiques du type SI".

C. Wolf made a contributed talk at the Summer School “Mathematical Models in Biology and Population Dynamics", held in Dourdan on July 5–9 2004.

Invited talks by M. Langlais and by B. Ainseba in the minisession on “biomathematics" within the Canadian–French mathematical Conference held in Toulouse, July 12–15 2004.

M. Langlais was main speaker at the INRA workshop “Biotic interactions within communities: theory and models", held in Villenave d’Ornon December 16–17 2004, organised by A. Franc.

M. Adimy and F. Crauste presented a work on "Stability and Hopf Bifurcation in a Mathematical Model of Pluripotent Stem Cell Dynamics" at the First Joint Canada-France Meeting of the Mathematical Sciences, Toulouse, July 12-15, 2004. They gave a presentation on "A singular transport system describing a proliferating maturity structured cell population" at CMS - CAIMS Summer 2004 Meeting (Halifax, Canada), June 11-15, 2004. They gave a talk on "a nonlinear model of hematopoiesis: extinction and stability" at the 1st international conference of the French Society of Theoretical Biology held in Marrakesh on May 21-25, 2004. They presented a paper on "Stability of a nonlinear model of cell proliferation" at the 33rd Polish National Meeting on Applications of Mathematics, Zakopane (Poland), September 14-20, 2004. They gave a conference on the same subject at the meeting "Computational and Mathematical Population Dynamics" held in Trento, June 21-25, 2004. They gave a presentation at the ESMTB Summer School, Cell Biology and Mathematical Modelling, at Hvar, Croatia, June 7-18, 2004.

J.-B. Burie gave a talk upon the spreading of the powdery mildew in a French–Japanese workshop “*Mathematical Understanding of Invasion Processes in Life Sciences*" held at CIRM in Marseille on March 15–19 2004.

7. Bibliography

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[3] B. AINSEBA, F. HEISER, M. LANGLAIS. *A mathematical analysis of a predator-prey system in a highly heterogeneous environment*, in "Differential and Integral Eqs", vol. 15, 2002, p. 385–404.

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[11] I. CHAMPAGNE. *Méthodes de factorisation des équations aux dérivées partielles*, Ph. D. Thesis, Ecole Polytechnique, October 2004.

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[14] M. ADIMY, F. CRAUSTE. *Existence, positivity and stability for a nonlinear model of cellular proliferation*, in "Nonlinear Analysis - Real World Applications", to appear, 2004.

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