Activity Report 2014

# Team MC2

## Modeling, control and computations

RESEARCH CENTER
**Bordeaux - Sud-Ouest**

THEME
**Numerical schemes and simulations**

# Table of contents

## Team MC2

**Keywords:** Scientific Computation, Fluid Dynamics, Fluid-structure Interaction, Multiscale Models, Computational Biology

*In partnership with Université de Bordeaux, Bordeaux INP and the CNRS*
*Located in the Institut de Mathématiques de Bordeaux (IMB)*

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# 2. Overall Objectives

## 2.1. Presentation

The aim of this project is to develop modelling tools for problems involving fluid mechanics in order to explain, to control, to simulate and possibly to predict some complex phenomena coming from physics, chemistry, biology or scientific engineering. The complexity may consist of the model itself, of the coupling phenomena, of the geometry or of non-standard applications. The challenges of the scientific team are to develop stable models and efficient adapted numerical methods in order to recover the main physical features of the considered phenomena. The models will be implemented into numerical codes for practical and industrial applications.
We are interested in both high and low Reynolds number flows, interface and control problems in physics and biology.

Our scientific approach may be described as follows. We first determine some reliable models and then we perform a mathematical analysis (including stability). We then develop the efficient numerical methods, which are implemented for specific applications.

In the next paragraphs, we explain our main goals, we describe our project in terms of development of numerical techniques and we present the team with the competence of the members.

### *2.1.1. The main goals*

#### *2.1.1.1. Modelling*

The first goal of the project consists in modelling some complex phenomena. We combine the term model with the three following adjectives: phenomenological, asymptotical and numerical.
*Phenomenological* : use of ad-hoc models in order to represent some precise phenomena. One example of such modelling process is the construction of nonlinear differential laws for the stress tensor of visco-elastic fluids or for wormlike micelles. Another example is the wall law conditions in microfluidics (fluids in micro-channels) that are often taken heuristically in order to model the slip at the boundary.
In biology, since no fundamental laws are known, the modeling is exclusively phenomenological especially concerning the modeling of tumor growth.
*Asymptotical* : using asymptotic expansions, we derive simpler models containing all the relevant phenomena. Examples of such a process are the penalization method for the simulation of incompressible flows with obstacles or the analysis of riblets in microfluidics that are used to control the mixing of the fluids. Another example is the use of shallow fluid models in order to obtain fast predictions (Hele-Shaw approximation in microfluidics) or the approximation of thin membranes for the modeling of electroporation of cells.

*Numerical* : direct numerical tools are used to simulate the modelized physical phenomena. A precise analysis of the models is performed to find out the most convenient numerical method in terms of stability, accuracy and efficiency. A typical example is the POD (proper orthogonal decomposition) and its use in control theory, or in data assimilation in tumor growth, to obtain fast simulations.

*2.1.1.2. Analysis and computation*

Once the model has been determined, we perform its mathematical analysis. This analysis includes the effect of boundary conditions (slip conditions in microfluidics, conditions at an interface...) as well as stability issues (stability of a jet, of an interface, of coherent structures). The analysis can often be performed on a reduced model. This is the case for an interface between two inviscid fluids that can be described by a Boussinesq-type system. This analysis of the system clearly determines the numerical methods that will be used. Finally, we implement the numerical method in a realistic framework and provide a feedback to our different partners.

*2.1.1.3. Applications*

Our methods are used in four areas of **applications**.

1)*Interface problems and complex fluids*:

This concerns microfluidics, complex fluids (bifluid flows, miscible fluids). The challenges are to obtain reliable models that can be used by our partner Rhodia (for microfluidics).

2)*High Reynolds flows and their analysis*:

We want to develop numerical methods in order to address the complexity of high Reynolds flows. The challenges are to find scale factors for turbulent flow cascades, and to develop modern and reliable methods for computing flows in aeronautics in a realistic configuration.

3) *Control and optimization*: the challenges are the drag reduction of a ground vehicle in order to decrease the fuel consummation, the reduction of turbomachinery noise emissions or the increase of lift-to-drag ratio in airplanes, the control of flow instabilities to alleviate material fatigue for pipe lines or off-shore platforms and the detection of embedded defects in materials with industrial and medical applications.

4) *Tumor growth*: The challenge is to produce patient-specific simulations starting from medical imaging for growth of metastasis to the lung of a distant tumor.

Our main partners on this project will be :

*Industrial:* Renault, IFP, CIRA (Centro italiano ricerche aerospaziali), Airbus France and Boeing for high Reynolds flows, optimization and control and Rhodia (biggest french company of chemistry) for interface problems and complex fluids.

*Academic:* CPMOH (Laboratory of Physics, Bordeaux 1 University) for high Reynolds flows, optimization and control, and Institut Gustave Roussy (Villejuif), University of Alabama at Birmingham and Institut Bergonié (Bordeaux) for tumor growth, optimad (spin-of of the Politecnico de Torino) for simulations of complex flows.

### 2.1.2. The production of numerical codes

We want to handle the whole process from the modelling part until the simulations. One of the key points is to develop numerical codes in order to simulate the models that are studied with our partners and of course we want to be able to have some feed-back toward the experiments.

i)*Multi-fluid flows and interface problems:*

We perform 2D and 3D simulations of multi-fluid flows using level set methods and mixture models. This includes non newtonian flows such as foams or wormlike miscella. The applications are microfluidics, porous media and complex fluids.

ii) *Modeling of tumor growth:*

Tumor growth in our 3D numerical model includes a cell-cycle, diffusion of oxygen, several population of cells, several enzymes, molecular pathways, angiogenesis, extracellular matrices, non-newtonian effects, membrane, effects of treatments, haptotaxy, acidity. We perform data assimilation processes starting from medical imaging.

iii) *2D and 3D simulations at high Reynolds number:*

We develop various computational methods: multi-grid techniques, vortex methods. The possible applications are turbulence, the flow around a vehicle, the stress on a pipe-line (the penalization method is used in order to take into account the obstacles).

iv) *Fluid structure interactions:*
2D and 3D interaction of a mobile rigid body with a fluid thanks penalty methods.

From a technical point of view, our work is organized as follows. We have build a platform (called **eLYSe**) using only cartesian, regular meshes. This is motivated by the following: we want to address interface problems using level set methods and to take into account obstacles by the penalization method. For these interface problems, we will have to compute the curvature of the interface with high precision (in microfluidics, the surface tension is the leading order phenomenon). The level set technology is now very accurate on structured meshes, we therefore made this choice. However, we want to address cases with complex geometry and/or obstacles. We will therefore systematically use the penalization method. The idea is to have an uniform format for the whole team that consists of several boxes:
1) Definition of the geometry and of the penalization zones.
2) Specification of the model (bifluid or not, Newtonian or not, mixing or not, presence of membranes etc...)
3) The boundary conditions that have to be imposed by a penalization operator.
4) The solvers.
5) Graphic interface.
As said before, the interface problems and the interaction with a membrane will be handled by level set methods as well as the shape optimization problem. So this platform will be dedicated to direct numerical simulation as well as to shape optimization and control.

The main effort concerning modelling will concern points 2) and 3) (model and boundary conditions). We do not plan for the moment to make special research effort on the solver part and we will use the solvers available in the literature or already developed by the team.

This platform will have two roles: the first one will be to allow a comprehensive treatment for the simulation of complex fluids with interface, membranes, adapted to the world of physical-chemistry and microfluidics and for solving shape optimization problems. The second role will be to keep a set of numerical modules that will be devoted to more specific applications (for example multi-grid methods or vortex methods for the study of turbulence). We therefore need to have some unified standards for the geometry or the graphic interface but it is of course hopeless to consider 3D turbulence and low-Reynolds flows in a micro-channel with the same code !

# 3. Research Program

## 3.1. Introduction

We are mainly concerned with complex fluid mechanics problems. The complexity consists of the rheological nature of the fluids (non newtonian fluids), of the coupling phenomena (in shape optimization problems), of the geometry (micro-channels) or of multi-scale phenomena arising in turbulence or in tumor growth modeling. Our goal is to understand these phenomena and to simulate and/or to control them. The subject is wide and we will restrict ourselves to three directions: the first one consists in studying low Reynolds number interface problems in multi-fluid flows with applications to complex fluids, microfluidics and biology - the second one deals with numerical simulation of Newtonian fluid flows with emphasis on the coupling of methods to obtain fast solvers.

Even if we deal with several kinds of applications, there is a strong scientific core at each level of our project. Concerning the model, we are mainly concerned with incompressible flows and we work with the classical description of incompressible fluid dynamics. For the numerical methods, we use the penalization method to describe the obstacles or the boundary conditions for high Reynolds flows, for shape optimization, for interface problems in biology or in microfluidics. This allows us to use only cartesian meshes. Moreover, we use the level-set method for interface problems, for shape optimization and for fluid structure interaction. Finally, for the implementation, strong interaction exists between the members of the team and the modules of the numerical codes are used by all the team and we want to build the platform **eLYSe** to systematize this approach.

## 3.2. Multi-fluid flows and application for complex fluids, microfluidics

**Participants:** Angelo Iollo, Charles-Henri Bruneau, Thierry Colin, Mathieu Colin, Kévin Santugini.

Multi-fluid flows,microfluidics

By a complex fluid, we mean a fluid containing some mesoscopic objects, i.e. structures whose size is intermediate between the microscopic size and the macroscopic size of the experiment. The aim is to study complex fluids containing surfactants in large quantities. It modifies the viscosity properties of the fluids and surface-tension phenomena can become predominant.

Microfluidics is the study of fluids in very small quantities, in micro-channels (a micro-channel is typically 1 cm long with a section of 50 $\mu$ m$\times$ 50 $\mu$ m). They are many advantages of using such channels. First, one needs only a small quantity of liquid to analyze the phenomena. Furthermore, very stable flows and quite unusual regimes may be observed, which enables to perfom more accurate measurements. The idea is to couple numerical simulations with experiments to understand the phenomena, to predict the flows and compute some quantities like viscosity coefficients for example. Flows in micro-channels are often at low Reynolds numbers. The hydrodynamical part is therefore stable. However, the main problem is to produce real 3D simulations covering a large range of situations. For example we want to describe diphasic flows with surface tension and sometimes surface viscosity. Surface tension enforces the stability of the flow. The size of the channel implies that one can observe some very stable phenomena. For example, using a "T" junction, a very stable interface between two fluids can be observed. In a cross junction, one can also have formation of droplets that travel along the channel. Some numerical difficulties arise from the surface tension term. With an explicit discretization of this term, a restrictive stability condition appears for very slow flows [77]. Our partner is the LOF, a Rhodia-Bordeaux 1-CNRS laboratory.

One of the main points is the wetting phenomena at the boundary. Note that the boundary conditions are fundamental for the description of the flow since the channels are very shallow. The wetting properties cannot be neglected at all. Indeed, for the case of a two non-miscible fluids system, if one considers no-slip boundary conditions, then since the interface is driven by the velocity of the fluids, it shall not move on the boundary. The experiments shows that this is not true: the interface is moving and in fact all the dynamics start from the boundary and then propagate in the whole volume of fluids. Even with low Reynolds numbers, the wetting effects can induce instabilities and are responsible of hardly predictable flows. Moreover, the fluids that are used are often visco-elastic and exhibit "unusual" slip length. Therefore, we cannot use standard numerical codes and have to adapt the usual numerical methods to our case to take into account the specificities of our situations. In Johana Pinilla's thesis the Cox law has been implemented successfully to allow the interface to move properly between two Newtonian fluids of various viscosity or one Newtonian and one non-Newtonian fluid. Moreover, we want to obtain reliable models and simulations that can be as simple as possible and that can be used by our collaborators. As a summary, the main specific points of the physics are: the multi-fluid simulations at low Reynolds number, the wetting problems and the surface tension that are crucial, the 3D characteristic of the flows, the boundary conditions that are fundamental due to the size of the channels. We need to handle complex fluids. Our collaborators in this lab are H. Bordiguel, J.-B. Salmon, P. Guillot, A. Colin.

The evolution of non-newtonian flows in webs of micro-channels are therefore useful to understand the mixing of oil, water and polymer for enhanced oil recovery for example. Complex fluids arising in cosmetics are also of interest. We also need to handle mixing processes.

## 3.3. Cancer modeling

**Participants:** Sébastien Benzekry, Thierry Colin, Angelo Iollo, Clair Poignard, Olivier Saut, Lisl Weynans.

Tumor growth, cancer, metastasis

As in microfluidics, the growth of a tumor is a low Reynolds number flow. Several kinds of interfaces are present (membranes, several populations of cells,...) The biological nature of the tissues impose the use of different models in order to describe the evolution of tumor growth. The complexity of the geometry, of the rheological properties and the coupling with multi-scale phenomena is high but not far away from those encountered in microfluidics and the models and methods are close.

The challenge is twofold. On one hand, we wish to understand the complexity of the coupling effects between the different levels (cellular, genetic, organs, membranes, molecular). Trying to be exhaustive is of course hopeless, however it is possible numerically to isolate some parts of the evolution in order to better understand the interactions. Another strategy is to test *in silico* some therapeutic innovations. An example of such a test is given in [88] where the efficacy of radiotherapy is studied and in [89] where the effects of anti-invasive agents is investigated. It is therefore useful to model a tumor growth at several stage of evolution. The macroscopic continuous model is based on Darcy's law which seems to be a good approximation to describe the flow of the tumor cells in the extra-cellular matrix [54], [78], [79]. It is therefore possible to develop a two-dimensional model for the evolution of the cell densities. We formulate mathematically the evolution of the cell densities in the tissue as advection equations for a set of unknowns representing the density of cells with position $(x, y)$ at time $t$ in a given cycle phase. Assuming that all cells move with the same velocity given by Darcy's law and applying the principle of mass balance, one obtains the advection equations with a source term given by a cellular automaton. We assume diffusion for the oxygen and the diffusion constant depends on the density of the cells. The source of oxygen corresponds to the spatial location of blood vessels. The available quantities of oxygen interact with the proliferation rate given by the cellular automaton [88].

Another axis of these theoretical investigations is the study of several processes in cancer biology (with a major focus on metastasis) for applications in theoretical and experimental onco-biology as well as preclinical and clinical studies. This axis regroups several projects for which our approach can be decomposed into three steps. First, we base ourselves on a detailed study of the particular biological process, based on the available literature and in close collaboration with biologists and the available data. In a second step, we reduce the biological dynamics to its more essential components and build mathematical models able to simulate the process, to address the particular biological question under investigation and to give nontrivial insights on the overall complex combination of these dynamics. Eventually, the last step consists in confronting the models to the data, using statistical parameter estimation methods, in order to identify theories or hypothesis that could or could not have generated the data and thus improve the biological understanding or identify optimal therapeutic strategies.

A forthcoming investigation in cancer treatment simulation is the influence of the electrochemotherapy [83] on the tumor growth. Electrochemotherapy consists in imposing to the malignant tumor high voltage electric pulses so that the plasma membrane of carcinoma cells is permeabilized. Biologically active molecules such as bleomycin, which usually cannot diffuse through the membrane, may then be internalized. A work in progress (C.Poignard [87] in collaboration with the CNRS lab of physical vectorology at the Institut Gustave Roussy) consists in modelling electromagnetic phenomena at the cell scale. A coupling between the microscopic description of the electroporation of cells and its influence on the global tumor growth at the macroscopic scale is expected. Another key point is the parametrization of the models in order to produce image-based simulations.

The second challenge is more ambitious. Mathematical models of cancer have been extensively developed with the aim of understanding and predicting tumor growth and the effects of treatments. In vivo modeling of tumors is limited by the amount of information available. However, in the last few years there have been dramatic increases in the range and quality of information available from non-invasive imaging methods, so that several potentially valuable imaging measurements are now available to quantitatively measure tumor growth, assess tumor status as well as anatomical or functional details. Using different methods such as the CT scan, magnetic resonance imaging (MRI), or positron emission tomography (PET), it is now possible to evaluate and define tumor status at different levels: physiological, molecular and cellular.

In this context, the present project aims at supporting the decision process of oncologists in the definition of therapeutic protocols via quantitative methods. The idea is to build mathematically and physically sound phenomenological models that can lead to patient-specific full-scale simulations, starting from data collected typically through medical imagery like CT scans, MRIs and PET scans or by quantitative molecular biology for leukemia. Our ambition is to provide medical doctors with patient-specific tumor growth models able to estimate, on the basis of previously collected data and within the limits of phenomenological models, the evolution at subsequent times of the pathology and possibly the response to the therapies.

The final goal is to provide numerical tools in order to help to answer to the crucial questions for a clinician:
When to start a treatment?
When to change a treatment?
When to stop a treatment?
Also we intend to incorporate real-time model information for improving the precision and effectiveness of non-invasive or micro-invasive tumor ablation techniques like acoustic hyperthermia, electroporation, radiofrequency or cryo-ablation.

We will specifically focus on the following pathologies: Lung and liver metastasis of a distant tumor
Low grade and high grade gliomas, meningiomas
Chronic myelogenous leukemia
These pathologies have been chosen because of the existing collaborations between the applied mathematics department of University of Bordeaux and the Institut Bergonié.

Our approach. Our approach is deterministic and spatial: it is based on solving an inverse problem based on imaging data. Models are of partial differential equation (PDE) type. They are coupled with a process of data assimilation based on imaging. We already have undertaken test cases on patients that are followed at Bergonié for lung metastases of thyroid tumors. These patients have a slowly evolving, asymptomatic metastatic disease, monitored by CT scans. On two thoracic images relative to successive times, the volume of the tumor under investigation is extracted by segmentation. To test our method, we chose patients without treatment and for whom we had at least three successive.

## 3.4. Newtonian fluid flows simulations and their analysis

**Participants:** Charles-Henri Bruneau, Angelo Iollo, Iraj Mortazavi, Michel Bergmann, Lisl Weynans.

Simulation, Analysis

It is very exciting to model complex phenomena for high Reynolds flows and to develop methods to compute the corresponding approximate solutions, however a well-understanding of the phenomena is necessary. Classical graphic tools give us the possibility to visualize some aspects of the solution at a given time and to even see in some way their evolution. Nevertheless in many situations it is not sufficient to understand the mechanisms that create such a behavior or to find the real properties of the flow. It is then necessary to carefully analyze the flow, for instance the vortex dynamics or to identify the coherent structures to better understand their impact on the whole flow behavior.
The various numerical methods used or developed to approximate the flows depend on the studied phenomenon. Our goal is to compute the most reliable method for each situation.
The first method, which is affordable in 2D, consists in a directly solving of the genuine Navier-Stokes equations in primitive variables (velocity-pressure) on Cartesian domains [64]. The bodies, around which the flow has to be computed are modeled using the penalization method (also named Brinkman-Navier-Stokes equations). This is an immersed boundary method in which the bodies are considered as porous media with a very small intrinsic permeability [55]. This method is very easy to handle as it consists only in adding a mass term $U/K$ in the momentum equations. The boundary conditions imposed on artificial boundaries of the computational domains avoid any reflections when vortices cross the boundary. To make the approximation efficient enough in terms of CPU time, a multi-grid solver with a cell by cell Gauss-Seidel smoother is used.

The second type of methods is the vortex method. It is a Lagrangian technique that has been proposed as an alternative to more conventional grid-based methods. Its main feature is that the inertial nonlinear term in the flow equations is implicitly accounted for by the transport of particles. The method thus avoids to a large extent the classical stability/accuracy dilemma of finite-difference or finite-volume methods. This has been demonstrated in the context of computations for high Reynolds number laminar flows and for turbulent flows at moderate Reynolds numbers [72]. This method has recently enabled us to obtain new results concerning the three-dimensional dynamics of cylinder wakes.
The third method is to develop reduced order models (ROM) based on a Proper Orthogonal Decomposition (POD) [80]. The POD consists in approximating a given flow field $U(x,t)$ with the decomposition

$$U(x,t) = \sum_i a_i(t)\phi_i(x),$$

where the basis functions are empirical in the sense that they derive from an existing data base given for instance by one of the methods above. Then the approximation of Navier-Stokes equations for instance is reduced to solving a low-order dynamical system that is very cheap in terms of CPU time. Nevertheless the ROM can only restitute what is contained in the basis. Our challenge is to extend its application in order to make it an actual prediction tool.
The fourth method is a finite volume method on cartesian grids to simulate compressible Euler or Navier Stokes Flows in complex domains. An immersed boundary-like technique is developed to take into account boundary conditions around the obstacles with order two accuracy.

## 3.5. Flow control and shape optimization

**Participants:** Charles-Henri Bruneau, Angelo Iollo, Iraj Mortazavi, Michel Bergmann.

Flow Control, Shape Optimization

Flow simulations, optimal design and flow control have been developed these last years in order to solve real industrial problems : vortex trapping cavities with CIRA (Centro Italiano Ricerche Aerospaziali), reduction of vortex induced vibrations on deep sea riser pipes with IFP (Institut Français du Pétrole), drag reduction of a ground vehicle with Renault or in-flight icing with Bombardier and Pratt-Wittney are some examples of possible applications of these researches. Presently the recent creation of the competitiveness cluster on aeronautics, space and embedded systems (AESE) based also in Aquitaine provides the ideal environment to extend our applied researches to the local industrial context. There are two main streams: the first need is to produce direct numerical simulations, the second one is to establish reliable optimization procedures.
In the next subsections we will detail the tools we will base our work on, they can be divided into three points: to find the appropriate devices or actions to control the flow; to determine an effective system identification technique based on the trace of the solution on the boundary; to apply shape optimization and system identification tools to the solution of inverse problems found in object imaging and turbomachinery.

### *3.5.1. Control of flows*

There are mainly two approaches: passive (using passive devices on some specific parts that modify the shear forces) or active (adding locally some energy to change the flow) control.

The passive control consists mainly in adding geometrical devices to modify the flow. One idea is to put a porous material between some parts of an obstacle and the flow in order to modify the shear forces in the boundary layer. This approach may pose remarkable difficulties in terms of numerical simulation since it would be necessary, a priori, to solve two models: one for the fluid, one for the porous medium. However, by using the penalization method it becomes a feasible task [60]. This approach has been now used in several contexts and in particular in the frame of a collaboration with IFP to reduce vortex induced vibrations [61]. Another technique we are interested in is to inject minimal amounts of polymers into hydrodynamic flows in order to stabilize the mechanisms which enhance hydrodynamic drag.

The active approach is addressed to conceive, implement and test automatic flow control and optimization aiming mainly at two applications : the control of unsteadiness and the control and optimization of coupled systems. Implementation of such ideas relies on several tools. The common challenges are infinite dimensional systems, Dirichlet boundary control, nonlinear tracking control, nonlinear partial state observation.

The bottom-line to obtain industrially relevant control devices is the energy budget. The energy required by the actuators should be less than the energy savings resulting from the control application. In this sense our research team has gained a certain experience in testing several control strategies with a doctoral thesis (E. Creusé) devoted to increasing the lift on a dihedral plane. Indeed the extension of these techniques to real world problems may reveal itself very delicate and special care will be devoted to implement numerical methods which permit on-line computing of actual practical applications. For instance the method can be successful to reduce the drag forces around a ground vehicle and a coupling with passive control is under consideration to improve the efficiency of each control strategy.

### *3.5.2. System identification*

We remark that the problem of deriving an accurate estimation of the velocity field in an unsteady complex flow, starting from a limited number of measurements, is of great importance in many engineering applications. For instance, in the design of a feedback control, a knowledge of the velocity field is a fundamental element in deciding the appropriate actuator reaction to different flow conditions. In other applications it may be necessary or advisable to monitor the flow conditions in regions of space which are difficult to access or where probes cannot be fitted without causing interference problems.

The idea is to exploit ideas similar to those at the basis of the Kalman filter. The starting point is again a Galerkin representation of the velocity field in terms of empirical eigenfunctions. For a given flow, the POD modes can be computed once and for all based on Direct Numerical Simulation (DNS) or on highly resolved experimental velocity fields, such as those obtained by particle image velocimetry. An instantaneous velocity field can thus be reconstructed by estimating the coefficients $a_i(t)$ of its Galerkin representation. One simple approach to estimate the POD coefficients is to approximate the flow measurements in a least square sense, as in [76].

A similar procedure is also used in the estimation based on gappy POD, see [92] and [96]. However, these approaches encounter difficulties in giving accurate estimations when three-dimensional flows with complicated unsteady patterns are considered, or when a very limited number of sensors is available. Under these conditions, for instance, the least squares approach cited above (LSQ) rapidly becomes ill-conditioned. This simply reflects the fact that more and more different flow configurations correspond to the same set of measurements.

Our challenge is to propose an approach that combines a linear estimation of the coefficients $a_i(t)$ with an appropriate non-linear low-dimensional flow model, that can be readily implemented for real time applications.

### *3.5.3. Shape optimization and system identification tools applied to inverse problems found in object imaging and turbomachinery*

We will consider two different objectives. The first is strictly linked to the level set methods that are developed for microfluidics. The main idea is to combine different technologies that are developed with our team: penalization methods, level sets, an optimization method that regardless of the model equation will be able to solve inverse or optimization problems in 2D or 3D. For this we have started a project that is detailed in the research program. See also [67] for a preliminary application.

As for shape optimization in aeronautics, the aeroacoustic optimization problem of propeller blades is addressed by means of an inverse problem and its adjoint equations. This problem is divided into three subtasks:

i) formulation of an inverse problem for the design of propeller blades and determination of the design parameters ii) derivation of an aeroacoustic model able to predict noise levels once the blade geometry and the flow field are given iii) development of an optimization procedure in order to minimize the noise emission by controlling the design parameters.

The main challenge in this field is to move from simplified models [81] to actual 3D model. The spirit is to complete the design performed with a simplified tool with a fully three dimensional inverse problem where the load distribution as well as the geometry of the leading edge are those provided by the meridional plane analysis [91]. A 3D code will be based on the compressible Euler equations and an immersed boundary technique over a cartesian mesh. The code will be implicit and parallel, in the same spirit as what was done for the meridional plane. Further development include the extension of the 3D immersed boundary approach to time-dependent phenomena. This step will allow the designer to take into account noise sources that are typical of internal flows. The task will consist in including time dependent forcing on the inlet and/or outlet boundary under the form of Fourier modes and in computing the linearized response of the system. The optimization will then be based on a direct approach, i.e., an approach where the control is the geometry of the boundary. The computation of the gradient is performed by an adjoint method, which will be a simple "byproduct" of the implicit solver. The load distribution as well as the leading edge geometry obtained by the meridional plane approach will be considered as constraints of the optimization, by projection of the gradient on the constraint tangent plane. These challenges will be undertaken in collaboration with Politecnico di Torino and EC Lyon.

# 4. Application Domains

## 4.1. Introduction

We now present our contribution to these above challenges concerning interface problem for complex fluids, direct simulations and analysis, flow control and optimization. From the technical point of view, many productions are common to the different parts of the project. For example, level-set methods, fast-marching procedure are used for shape optimization and for microfluidics, penalization methods are used for high Reynolds flows and for tumor growth. This leads to a strong politic of development of numerical modules.

## 4.2. Multi-fluid flows

- computation of bifluid flows : see the thesis of S. Tancogne ( [90]) and P. Vigneaux ( [93]). Stability of an interface, shape of droplets, formation of a jet. Study of the Plateau-Rayleigh instability. Behaviour of diphasic fluids evolving in square microchannels.
- mixing in micro-channel : see the thesis of J. Dambrine [73]. Passive mixing strategies involving boundary conditions. Enhanced oil recovery (study of mixing oil-water-polymer in a microchannel).
- emulsions and foam : see the thesis of S. Benito [56]. Applications in biology : behaviour of tissues, of tumor,....
- polymer nanotube conglomerate wire : it was the subject of a talk in the following conference "WCCM8-ECCOMAS2008" and of the talk [70].

## 4.3. Cancer modeling

- Specific models : investigation of particular cancers : gliomas (brain tumors), meningioma, colorectal cancers lung and liver metastasis, breast cancer. This is one part of the PhD works of P. Berment, J. Jouganous, G. Lefebvre and post-doc of J. Joie.
- Modelling of electrochemotherapy
- Parameter estimations with the help of low order models : see the PhD of J. Jouganous
- Patient-specific simulations
- Theoretical biology of the metastatic process: dynamics of a population of tumors in mutual interactions, dormancy, pre-metastatic and metastatic niche, quantification of metastatic potential and differential effects of anti-angiogenic therapies on primary tumor and metastases.
- Mathematical models for preclinical cancer research: description and prediction of tumor growth and metastatic development, effect of anti-cancerous therapies

## 4.4. Newtonian fluid flows simulations and their analysis

- Simulation of a synthetic or pulsed jet. This is an ongoing project with Renault and PSA inside a PREDIT project.
- Vortex dynamics : see [75].
- Simulation of compressible flows on cartesian grids : see the thesis of Gabriele Ottino's Thesis [86], who underwent his doctoral studies in conjunction in the MC2 team and at the Politecnico di Torino, and defended in April 2009. He had a grant of the French-Italian university.
- 3D turbulent flows through DESGRIVRE contract with AIRBUS. Thesis of C. Wervaecke [95]. The goal is to use Detached-Eddy Simulation to model turbulent flows around iced bodies.
- Porous media : Numerical study of coupling between Richards and transport-diffusion equations in permeable sediment affected by tidal oscillation. See the thesis of R. Chassagne [68]
- Modeling and numerical simulation of the flow around a real wind turbine. Phd thesis of Xin Jin. This includes reduced order model to design more efficient blades.

## 4.5. Flow control and shape optimization

- passive control : the idea is to put a porous interface between the solid body and the fluid. See the D. Depeyras thesis [74] and Yong-Liang Xiang [97] and CH Bruneau and Iraj Mortazavi) [60]. See also project [65] founded by the Euopean Community.
- active control : see the three PhD thesis: M. Buffoni, J. Weller [94], E. Lombardi and FFAST project funded by EU and iled by the University of Bristol and AIRBUS UK.
- shape optimization for turbo-machines : See [91].
- reduced order models : it consists in designing a non-linear observer that estimates the state of the flow field from a limited number of measurements in the field. The challenge is to reduce as much as possible the information required and to take it from the boundary. See J. Weller [94] and E. Lombardi.
- passive control of flows with porous media : see [62], [59], [58], [85], [63].
- inverse problems in imagery : see [67].

# 5. New Software and Platforms

## 5.1. eLYSe

**Participant:** Olivier Saut.

eLYse is a numerical platform used for our computations in Biology (tumor growth), micro-fluidics and complex Newtonian fluid flows. The platform is divided in two libraries : one is devoted to the modelling equations and the other one includes the numerical solvers. For example, we are able to treat (in 2D and 3D) transport equations, diffusion equations, Navier-Stokes equations, Maxwell system and the interaction fluid-structure by level-set and penalization methods. The solvers are based on finite volume methods on cartesian grids and allow parallel computations. See also the web page http://www.math.u-bordeaux1.fr/~osaut/pages/eLYSe.html.

- Version: 0.7
- ACM: ACM J.2 J.3 G.1.8 G.1.10
- AMS: AMS65Z05 35Q92
- Keywords: Modélization and numerical simulations, Finite volume methods, Level Set approach, Penalization method
- APP: En cours
- Type of human computer interaction: console
- OS/Middelware: Platform developped on Mac OS X architecture.
- Required library or software: Petsc (http://www.mcs.anl.gov/petsc/petsc-as/) Vtk (http://www.vtk.org/) Blitz++ (http://c2.com/cgi/wiki?BlitzPlusPlus) (optionnel) Boost (http://www.boost.org/)
- Programming language: C++
- Documentation: doxygen.

## 5.2. Kesaco

**Participant:** Olivier Saut.

Kesaco is a set of libraries and programs aiming at applications of mathematical modeling in clinical oncology. It features:

- A library of specialized mathematical model describing the growth of different types of cancers (secondary tumors in the lung, gliomas).
- A set of programs useful to validate mathematical models (compute the various behavior they can produce) and to build databases of numerical simulations.
- Segmentation and registration routines to use medical images directly in our numerical codes.
- Calibration methods to recover the parameters of the models using sequences of medical images. Three techniques are implemented (a genetic algorithm, a technique based on reduced order models, a sensitivity technique).

All these routines are adapted to run on a MP architecture. The webpage may be found at http://www.math.u-bordeaux1.fr/~osaut/pages/kesaco.html.

- Version: 0.2
- Keywords: Modélization and numerical simulations
- APP: En cours
- Type of human computer interaction: console
- OS/Middelware: Platform developped on Mac OS X architecture.
- Required library or software: eLYSe, Insight Toolkit (http://www.itk.org)
- Programming language: C++
- Documentation: doxygen.

## 5.3. NaSCar

**Participant:** Michel Bergmann [correspondant].

This code is devoted to solve 3D-flows in around moving and deformable bodies. The incompressible Navier-Stokes equations are solved on fixed grids, and the bodies are taken into account thanks to penalization and/or immersed boundary methods. The interface between the fluid and the bodies is tracked with a level set function or in a Lagrangian way. The numerical code is fully second order (time and space). The numerical method is based on projection schemes of Chorin-Temam's type. The code is written in C language and use Petsc (http://www.mcs.anl.gov/petsc/petsc-as/) library for the resolution of large linear systems in parallel.

NaSCar can be used to simulate both hydrodynamic bio-locomation as fish like swimming and aerodynamic flows such wake generated by a wind turbine.

- Version: 1
- Keywords: numerical analyse, fluid mechanics, langage C, PETSc
- Software benefit : simulate a flow around a deformable obstacle, moving into a fluid.
- APP: En cours
- Patent: non
- Type of human computer interaction: human for the moment
- OS/Middelware: unix, linux, mac os
- Required library or software: PETSc item Programming language: C
- Documentation: in progess

## 5.4. NS-MPI-2D-3D

**Participants:** Charles-Henri Bruneau [correspondant], Khodor Khadra.

The software NS-MPI-2D-3D is a numerical platform devoted to the computation of the incompressible flow around bodies in two or three dimensions modelled by Stokes, Navier-Stokes or Oldroyd-B equations. It is based on finite differences or finite volumes approximations on cartesian grid using the volume penalization method to handle the obstacles. The resolution is achieved by means of the multigrid method. Dirichlet, periodic or artificial boundary conditions are implemented to solve various problems in closed or open domains.

- Version: 3
- Keywords: Numerical simulation of incompressible flows,
- Type of human computer interaction: console
- OS/Middelware: unix, linux, Mac OS X item Programming language: Fortran 95 and MPI
- Documentation: included

## 5.5. Other MC2 codes

- Penalization techniques on cartesian grids to solve incompressible Navier-Stokes equations
  - **Vortex**: sequential, Vortex In-Cell (VIC) scheme : hybrid vortex methods based on the combination of Lagrangian mesh-free schemes and Eulerian grid based schemes on the same flow region.
  - Unstructured body fitted meshes
  - **Richards** : 2D Unstructured finite element code, implicit solver, sequential, to solve the transport-diffusion equations through a porous media including tidal forcing and mechanisms of diagenesis.
  - development inside **FluidBox** software in collaboration with **BACCHUS**. 2D-3D unstructured meshes, Stabilized Finite Elements method (SUPG), RANS turbulence model, parallel: Domain Decomposition and MPI.
- Immersed boundary techniques for:
  - **Compressible flows** : 2D-3D finite volume scheme for compressible Euler equations with solid obstacles on cartesian grids. 3D code parallelized with MPI
  - **Elliptic problems :** 2 2D-3D finite difference scheme for elliptic interface problems, parallelized with PETSc
  - Elmo. C++ Code of Finite Differences on cartesian grid parallelized with PETSC to compute the electropermeabilisation of cells in 2D and 3D.

# 6. New Results

## 6.1. Highlights of the Year

- **Models for gliomas**
  Glioblastoma multiforme (GBM) causes significant neurological morbidity and short survival times. Brain invasion by GBM is associated with poor prognosis. Recent clinical trials of bevacizumab in newly-diagnosed GBM found no beneficial effects on overall survival times; however, the baseline health-related quality of life and performance status were maintained longer in the bevacizumab group and the glucocorticoid requirement was lower. In a recent work in collaboration with UAB, we have constructed a clinical-scale model of GBM whose predictions uncover a new pattern of recurrence in 11/70 bevacizumab-treated patients. The findings support an exception to the Folkman hypothesis: GBM grows in the absence of angiogenesis by a cycle of proliferation and brain invasion that expands necrosis. Furthermore, necrosis is positively correlated with brain invasion in 26 newly-diagnosed GBM. The unintuitive results explain the unusual clinical effects of bevacizumab and suggest new hypotheses on the dynamic clinical effects of migration by active transport, a mechanism of hypoxia-driven brain invasion.

- **Electroporation modeling** (M. Leguebe, C. Poignard)
Based on the new discovery of the team of Vectorolgy and anti-cancerous therapies on the membrane lipid oxidation during the pulse delivery, we have provided a model of cell permeabilization that makes it possible to explain the process of electroporation : pore formation during the pulse and surface diffusion of altered lipids after the pulse. Our model explains the long-term effect of electroporation (the permeable state of the membrane lasts a few minutes after the pulse delivery). A 3D-code in C++ has been implemented during the PhD thesis of M. Leguèbe. The team MC2 is now part of the European Lab EBAM on electroporation modeling. An international workshop on Electroporation and Biophysical Therapies was held in Bordeaux the 15th and 16th December.
- Simulation of **multiphysic fluid-structure impacts in 3D**. See http://www.math.u-bordeaux1.fr/ adebrauer/ for astinishing videos.

## 6.2. Cancer modeling

- **Patient specific simulation for lung metastases**
The calibration process has tremendously improved by a deep study of the model and its parameter space. Work is ongoing to validate the whole process on a retrospective study of 30 patients. A prototype is being built for our collaborators at Institut Bergonié to use in their clinical routine. The same strategy has been applied to meningiomas in the last year of the post-doc of Julie Joie within the IRL MONICA with a retrospectuve study on 10 patients.
- Modelling of the response to targeted therapies for liver metastasis of a gist : 2 clinical cases with a long term longitudinal follow-up with CT-scans. We are able to fit the volume of the lesion but also the the texture of the image, that is the ratio between necrotic tissues and proliferative ones. See [82].
- Tumor growth model for ductal carcinoma: from in situ phase to stroma invasion. See [71].
- Permeable and conducting states of membrane submitted to electric pulse: non-linear PDE model, 2D and 3D code in C++.
- Free boundary value model for invadopodia and migration of cell developed in collaboration with Osaka University and Tokyo University of Sciences.
- Endothelial cell migration on polymers: agent based model. Paper accepted in DCDS-B.
- A. Peretti started her PhD on the modeling of the heterogenity on renal cancer.
- Benjamin Taton started a post-doc on the modeling of the renal function through perfusion MRI. B. Taton is a MD.
- Th. Michel obtained some mathematical properties on the system of PDEs used for the modelling of GIST metastases.
- **Models for preclinical studies**
  - Mathematical **ODE models of tumor volume kinetics in mice** (collaboration with the Center of Cancer and Systems Biology, Boston, USA and J. Ebos, Roswell Park Cancer Institute, Buffalo, USA).
Rational and quantitative evaluation of the predictive and descriptive power of the majority of the classical ODE models for tumor growth against data from two distinct experimental systems [57]. One of the major finding was the huge improvement of the predictive properties when using the population *a priori* information on the distribution of the parameters.

    - Mathematical model for data of **preclinical metastatic burden dynamics** and clinical data of metastatic relapse probability of **breast cancer** (collaboration with J. Ebos, Roswell Park Cancer Institute, Buffalo, USA).
      Validation of the descriptive and predictive ability of a simple and minimally parameterized model. The major finding resulting from the modeling analysis was the quantification of the impact of surgery on survival improvement (highly nonlinear), which suggests a threshold primary tumor size for efficacy of the surgery in terms of preventing metastatic recurrence. A publication is in preparation.
    - Effect of **anti-cancer therapies** in preclinical experiments
        * Evaluation of several models (several already published but also new ones) for the effect of **anti-angiogenic drugs** [1] on tumor growth, based on statistical parameter estimation methods on experimental data (collaboration with J. Ebos, Roswell Park Cancer Institute, Buffalo, USA). The main finding was one model that was able to both describe the effect of the drug (Sunitinib) and predict the effect when changing the scheduling. See [66].
        * Effect of the **sequence of administration between cytotoxic and anti-angiogenic drugs** (collaboration with J. Ciccolini and D. Barbolosi, SMARTc, Inserm, Marseille, Fr). See [84].
- **Theoretical cancer biology**
    - Theories of metastatic initiation (collaboration with A. Bikfalvi, LAMC, Inserm and the RMSB, CNRS in Bordeaux, Fr).
      Confrontation of theories and experimental data challenged the classical view of metastatic establishment and growth and suggested that tumors could merge in initial phases. Quantitative impact of the merging was studied using a dedicated and properly calibrated spatial model.
    - Tumor-tumor distant interactions (collaboration with the Center of Cancer and Systems Biology, Boston, USA).
      Statistical and modeling analysis of experimental data for two tumors implanted in one organism.

## 6.3. Newtonian fluid flows simulations and their analysis

- Development of a high-order (third order in time and space) level-set method which allow to compute consistently the curvature of the interface even for long times (L. Weynans, F. Luddens and M. Bergmann)
- Development of a sharp cartesian method for the simulation of incompressible flows with high density ratios, like air-water interfaces. This method is inspired from the second-order cartesian method for elliptic problems with immersed interfaces developed in Cisternino-Weynans [69]
- Study of the convergence in 1D and 2D of the method developed in Cisternino-Weynans [69]

# 7. Bilateral Contracts and Grants with Industry

## 7.1. Program PREDIT

**Participants:** Charles-Henri Bruneau, Iraj Mortazavi.

Program PREDIT ADEME with Renault and Peugeot. The aim of this program is the work on drag reduction in order to decrease the fuel consumption.

[1] recent anti-cancer drugs that target the tumor vasculature rather than the cancer cells themselves

## 7.2. Renault

**Participants:** Charles-Henri Bruneau, Iraj Mortazavi.

CARAVAJE project with ADEME (PREDIT Véhicules propres et économes) notified october 24th 2008. Collaboration with Renault and Peugeot, two PME and 3 labs to reduce the drag coefficient of a ground vehicle. 95 k euros for 3 years.

## 7.3. Plastic Omnium

**Participant:** Iraj Mortazavi.

The MC2 team works actually with the Plastic Omnium company in order to study the flow behaviour around square back ground vehicles (like buses, camions,...) using LES and DNS techniques. The main target of this collaboration is to identify the structures of velocity fields that generate aerodynamical losses, in order to design drag reduction control strategies using pulsed or synthetic jets. In the framework of this project, we also want to compute accurately instantaneous velocity fields, with high velocities. The computations should be performed on long time for complex geometries. A part of this work is included in the PhD thesis of Yoann Eulalie.

## 7.4. Bilateral Contracts with Industry

Angelo Iollo is consulting with OPTIMAD engineering.

## 7.5. Bilateral Grants with Industry

CIFRE - Conventions Industrielles de Formation par la REcherche - with VALEOL (VALOREM Group)

# 8. Partnerships and Cooperations

## 8.1. Regional Initiatives

Angelo Iollo is belongs to the Aerospace Valley committee IGPC. He is monitoring the project ECOSEA for the fnrae http://www.fnrae.org/.

## 8.2. National Initiatives

### *8.2.1. ANR MEMOVE*

**Participants:** Thierry Colin, Angelo Iollo, Clair Poignard, Olivier Saut, Lisl Weynans.

Part of the team (M.Colin, T.Colin, A.Iollo, C.Poignard, O.Saut and L. Weynans) is involved in the consortium MEMOVE coordinated by MC2 (coordinator C. Poignard), and which begins at the beginning of 2012. This consortium is composed of four partners (the Vectorology and Anticancer therapies team at the IGR, the bioengineering laboratory AMPERE of Lyon and the Department of mathematics of Versailles). It aims at developing electropermeabilization models from the cell scale to the tissue scale. This project focuses on quite long pulses (from micro- to milli-pulses) compared with the ANR consortium INTCELL that has begun in December 2010. The main goal is to provide multi-scale modelling of "classical" eletroporation, in order to obtain numerical tools that can help from one side the biologists to understand the electropermeabilization process when "non standard" pulses are applied, and from the other side it eventually aims at providing tools for the physicians to optimize the pulse delivering when the electrochemotherapy is used.

### 8.2.2. French-German cooperative consortium SmartOnline

**Participants:** Angelo Iollo, Iraj Mortazavi.

- Program: ANR & BMBF
- Project acronym: SmartOnline
- Project title: Online security management toolkit for water distribution networks.
- Duration: 04/2012-04/2015
- Coordinator: Olivier Piller (IRSTEA)
- Other partners: Irstea, Veolia, ENGES, CU Strasbourg, BW Berlin, TZW Dresden, 3S Consult, Franhoefer.
- Abstract: The main objective of the project SMaRT-OnlineWDN is the development of an online security management toolkit for water distribution networks that is based on sensor measurements of water quality as well as water quantity. Its field of application ranges from detection of deliberate contamination, including source identification and decision support for effective countermeasures, to improved operation and control of a WDN under normal and abnormal conditions (dual benefit).

### 8.2.3. Plan Cancer METASTASIS

**Participants:** Sébastien Benzekry, Thierry Colin, Clair Poignard, Olivier Saut.

- Program: Plan Cancer: Systems Biology
- Project acronym: METASTASIS
- Project title: Modeling the Interaction of the (Metastasis) Vascular/Tumor Niche Using a Systems Biology Approach
- Duration: 2013-2015
- Coordinator: A. Bikfalvi (Biologie, Bordeaux University)

### 8.2.4. Plan Cancer MIMOSA

**Participants:** Sébastien Benzekry, Thierry Colin, Clair Poignard, Olivier Saut.

- Program: Plan Cancer: Physique, Mathématiques et Sciences de l'ingénieur appliqués au Cancer
- Project acronym: MIMOSA
- Project title: Mathematical modeling for exploration of the impact of mechanical constraints on tumor growth
- Duration: 2014-2017
- Coordinator: T. Colin

## 8.3. European Initiatives

### 8.3.1. FP7 & H2020 Projects

#### 8.3.1.1. FFAST

Title: FUTURE FAST AEROELASTIC SIMULATION TECHNOLOGIES

Type: COOPERATION (TRANSPORTS)

Instrument: Specific Targeted Research Project (STREP)

Duration: January 2010 - December 2012

Coordinator: University of Bristol (Saint Pierre And Miquelon)

Others partners: University of Bristol, irias, TU Delft, Politecnico di Milano, Numeca, EADS, DLR, Airbus, University of Cap Town, csir, Optimad

See also: http://www.bris.ac.uk/aerodynamics-research/ffast/

Abstract: The FFAST project aims to develop, implement and assess simulation technologies to accelerate future aircraft design. These technologies will demonstrate a step change in the efficiency and accuracy of the dynamic aeroelastic "loads process" using unique critical load identification methods and reduced order modelling. The outcome from the project will contribute to the industrial need to reduce the number of dynamic loads cases analysed, whilst increasing the accuracy and reducing the cost/time for each unsteady aeroelastic analysis performed compared to the current approach. Unsteady loads calculations play an important part across much of the design and development of an aircraft, and have an impact upon the concept and detailed structural design, aerodynamic characteristics, weight

### *8.3.2. Collaborations in European Programs, except FP7 & H2020*

Program: European associated laboratory

Project acronym: EBAM

Project title: Pulsed electric fields applications in biology and medicine

Duration: January 2011 - December 2014

Coordinator: C. Poignard

Other partners: Institut Gustave Roussy (CNRS, Paris), Laboratory of Pharmacology and Structural Biology (CNRS and University of Toulouse, Toulouse), Laboratory XLIM (Limoges), Faculty of Health Sciences (Primorska), Laboratory of Structure and Reactivity of the Complex Molecular Systems (CNRS and University of Lorraine), University of Ljubljana (Ljubljana), Institute of Oncology (Ljubljana)

Abstract: The main aim of the LEA EBAM is to use an interdisciplinary approach, integrating biology, chemistry, physics, biophysics, mathematics, computational modelling and engineering, through the expertise of its members in order to

- Enhance our understanding on the mechanisms of classical electropermeabilization and of the new nanopermeabilization (electropermeabilization using nanosecond electric pulses), as well as on the mechanisms of transmembrane transport of molecules into electroporated cells and tissues on a microscopic and macroscopic scale.
- Contribute to a better and safer implementation of the electropermeabilization-based applications, and to the development of new applications.
- Develop new devices and new equipment for the nanopermeabilisation at cell and tissue levels.
- Develop new approaches like treatment planning in existing applications, such as antitumor electrochemotherapy and in vivo gene transfer for therapeutic purposes.
- Disseminate the knowledge and the applications in the scientific community and in the society, through publications, a one-week course (already implemented) co-directed by the LEA directors, internal and external training, and through other means that the LEA will develop and/or will apply for (to the EC programs for example).

## 8.4. International Initiatives

- Collaboration with Hassan Fathallah, Neuro-oncoly and mathematics, University of Alabama at Birmingham. We work on numerical modeling of brain tumor.
- PHC Sakura on cancer modeling with University of Osaka. (12Keur for 2 years) Collaboration with the University of Osaka on the modeling of the cell migration in cancer.
- Collaboration with IAC, CNR (R. Natalini) and E. Signori on tissue electroporation and DNA transfection.
- Collaboration with John Ebos, Roswell Park Cancer Institute, Buffalo, NY, USA. Quantification of metastatic potential and differential effect of anti-angiogenic therapies on primary tumor and metastasis, in a preclinical setting.

- Collaboration with the Center of Cancer and Systems Biology at Tufts University, Boston, MA, USA. We work together on quantitative modeling of tumor-tumor interactions and their implications on global metastatic dynamics.
- Collaborations with Luca Zannetti, Politecnico di Torino; Simone Camarri, Universita di Pisa; Eyal Arian, Boeing Commercial Airplanes.
- Collaboration with Sinisa Krajnovic, Chalmers University, on the high fidelity simulation and control of ground vehicle flows.
- Collaboration with Spencer Sherwin and Denis Doorly (Imperial College London) on the novel flow diagnostics approaches.

## 8.5. International Research Visitors

### *8.5.1. Visits of International Scientists*

- J. Zubelli (IMPA, Rio de Janeiro, Brazil) from June 30th to July 4th
- V. Pérez-Garcia and A. Martinez (Universidad de Castilla-La Mancha, Ciudad Real, Spain) from November 12th to November 14th
- M. Ohta (Tokyo University of Sciences, Japan) from December 4th to 12th
- L. Wegner (Karlsruhe institute of Technology, Germany) from December 15th to 19th

# 9. Dissemination

## 9.1. Promoting Scientific Activities

### *9.1.1. National structures*

- Thierry Colin is elected as a member of the national committee of the French Universities (CNU). It is a national structure that has in charge a peer review of the carriers of mathematicians in France.
- Olivier Saut is the head of the GDR Metice (Mathématiques appliquées aux espéces, tissus et cellules).
- C. Poignard is elected member of the Evaluation Committee of Inria. He is also Principal Investigator of the European Lab EBAM

### *9.1.2. Scientific events organisation*

#### *9.1.2.1. General chair, Scientific chair*

- Workshop on Electroporation and Biophysical Therapies. (Organisation : C. Poignard, F. Tregan). Website: http://memove2014.sciencesconf.org/

#### *9.1.2.2. Member of the conference program committee*

- S. Benzekry, member of the scientific committee of the MB2 conference (bio-mathematics workshop organized in Besancon, July 7-10, 2015)

### *9.1.3. Journal*

#### *9.1.3.1. Member of the editorial board*

Thierry Colin is a a member of the following scientific boards:

- 2001- : "Mathématiques et Applications", Springer-SMAI, 70 livres parus à ce jour.
- 2011- : Revue CPAA.
- 2012- : Revue Computational Surgery (Springer).
- 2012- : Comité éditorial de SIAM NEWS.
- 2014 - : Revue Mathematical Biosciences and Engineering.

## 9.2. Teaching - Supervision - Juries

### 9.2.1. Teaching

C. Poignard: 80 hours of teaching (Master course and undergraduate)

M. Bergmann: 80 hours of teaching

L. Weynans: teaching in approximation of PDEs and programming (Fortran), exchange operation with high schools, class of mathematics for math minor international engineer students

### 9.2.2. Supervision

HdR: Clair Poignard, A few advances in biological modeling and asymptotic analysis, Universite de Bordeaux, September 2014

HdR: Michel Bergmann, Contributions à la simulation numérique en mécanique des fluides et à la réduction de modèle, Universite de Bordeaux, June 2014

PhD: Michael Leguebe, Modélisation de l'électroperméabilisation à l'échelle cellulaire, Universite de Bordeaux, September 2014, co-supervised by C. Poignard and T. Colin

PhD: Xin Jin, Une chaine d'outils numériques pour la conception aerodynamique de pales d'eoliennes, Universite de Bordeaux, September 2014, co-supervised by M. Bergmann and A. Iollo

PhD: Yoann Eulalie, Etude aérodynamique et contrôle de la traînée sur un corps de Ahmed culot, Jan 2014, co-supervised by I. Mortazavi and C.H. Bruneau.

PhD in progress: F. Cornelis is a medical doctor of the Institut Bergonie´. He is a radiologist practicing CT-Scans, MRI but also local mini-invasive treatments (interventional radiology). He spends one day a week to prepare a PhD on the modelling aspects of his work. started 2010

PhD in progress: F. Bernard, started October 2011

PhD in progress: Etienne Baratchart, Mathematical modeling of the metastatic initiation biology, started December 2012, cosupervised by S. Benzekry, T. Colin and O. Saut

PhD in progress: G. Lefebvre, Image-based modeling of resistance to targeted therapies for metastases from gastro-intestinal tumors, started October 2012, supervised by T. Colin

PhD in progress: J. Jouganous, Prediction of the spatial growth of lung metastatic nodules, started October 2012, supervised by O. Saut

PhD in progress: T. Michel, Modeling of tumor spheroids growth, started October 2013, co-supervised by T. Colin and C. Poignard

PhD in progress: O. Gallinato, Mathematical modeling of invadopodia, started October 2013, in joint supervision with T. Colin, C.Poignard from MC2 and T. Suzuki from Osaka University

PhD in progress: P. Berment, Modeling of PET-scan imaging data of tumor growth, started October 2013, co-supervised by O. Saut and T. Colin

PhD in progress: A. Peretti, Image-based mathematical modeling of kidney cancer, started 2014, co-supervised by T. Colin and O. Saut

PhD in progress: M. Deville, started 2014, in joint supervision by C. Poignard from MC2 and R. Natalini from the CNR and Sapienza University, Rome, Italy.

PhD in progress: M. Jedouaa, Effets collectifs dans l'interaction plasma/globules rouges et la nage de micro-organismes, started 2013, co-supervised by C.H. Bruneau and E. Maître (Grenoble)

### 9.2.3. Juries

Angelo Iollo was in the jury of the following PhDs

- Reviewer: Anna Cattani, Politecnico di Torino, « Multispecies Models to Describe Large Neuronal Networks », Torino, Fev 2014.

- Reviewer: Nicolas Dovetta, LadHX, Ecole Polytechnique, « Data-based models for flow control », Paris, June 2014.
- Reviewer: Ali Al Alaouwi, IMATH, Université de Toulon « Reconstruction 3D des vaisseaux sanguins », Dec 2014.
- Jury: Elisa Schenone, LJLL, UPMC, « Reduced Order Models, Forward and Inverse Problems in Cardiac Electrophysiology », Nov 2014.
- Jury: Guillaume Dechristé, IMB, Université de Bordeaux « Méthodes numériques pour la simulation d'écoulements de gaz raréfiés autour d'obstacles mobiles », Dec 2014.

## 9.3. Popularization

- C. Poignard "Des décharges électriques contre le cancer" (Journée IREM Mai 2014).
- C. Poignard, A. Silve. Différence de potentiel induite par un champ électrique sur la membrane d'une cellule biologique . La Revue 3EI, N°75, Jan 2014.
- O. Saut participates to the "excellence interviews" ( http://www.lesentretiens.org)
- Lisl Weynans and Michel Bergmann held a stand at the "Fete de la science".
- Lisl Weynans is "chargee de mission" from the IMB for relations with high schools and gave talks to students and teachers to introduce scientific calculus.

# 10. Bibliography

## Major publications by the team in recent years


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