INRIA

INSTITUT NATIONAL DE RECHERCHE EN INFORMATIQUE ET EN AUTOMATIQUE

Project-Team reo

Numerical simulation of biological flows

Paris - Rocquencourt

THEME BIO

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1. Team

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2. Overall Objectives

2.1. Introduction

REO is a joint project of the INRIA Research Unit of Rocquencourt and the Jacques-Louis Lions Laboratory (LJLL) of the Pierre and Marie Curie (Paris 6) University. Its research activities are aimed at

- modeling some aspects of the cardiovascular and respiratory systems, both in normal and pathological states;
- developing and analyzing efficient, robust and reliable numerical methods for the simulation of those models;
- developing simulation software to guide medical decision and to design more efficient medical devices.

2.2. Highlights of the year

- REO is one of the four INRIA project-teams members of the Cardiosense3D action which have been awarded by The Apple Research & Technology Support (ARTS) programme for its contribution to the modelling of the electromechanical activity of the heart.
- C. Grandmont has been selected at the first stage of the starting European Research Council (ERC) grant.
- N. Diniz dos Santos and A. Gloria defended their PhD thesis.

3. Scientific Foundations

3.1. Multiphysics modeling

Keywords: *fluid-structure interaction*, *spray modelling*.

In large vessels and in large bronchi, blood and air flows are generally supposed to be governed by the incompressible Navier-Stokes equations. Indeed in large arteries, blood can be supposed to be Newtonian, and at rest air can be modeled as an incompressible fluid. The cornerstone of the simulations is therefore the Navier-Stokes solver. But other physical features have also to be taken into account in simulations of biological flows, in particular fluid-structure interaction in large vessels and transport of sprays, particules or chemical species.

3.1.1. Fluid-structure interaction

Fluid-structure coupling occurs both in the respiratory and in the circulatory systems. We focus mainly on blood flows since our work is more advanced in this field. But the methods developped for blood flows could be also applied to the respiratory system.

Here “fluid-structure interaction” means a coupling between the 3D Navier-Stokes equations and a 3D (possibly thin) structure in large displacements.

The numerical simulations of the interaction between the artery wall and the blood flows raise many issues: (1) the displacement of the wall cannot be supposed to be infinitesimal, geometrical nonlinearities are therefore present in the structure and the fluid problem have to be solved on a moving domain (2) the densities of the artery walls and the blood being close, the coupling is strong and has to be tackled very carefully to avoid numerical instabilities, (3) “naive” boundary conditions on the artificial boundaries induce spurious reflection phenomena.

Simulation of valves, either at the outflow of the cardiac chambers or in veins, is another example of difficult fluid-structure problems arising in blood flows. In addition, we have to deal with very large displacements and changes of topology (contact problems).

Because of the above mentioned difficulties, the interaction between the blood flow and the artery wall has often been neglected in most of the classical studies. The numerical properties of the fuid-structure coupling in blood flows are rather different from other classical fluid-structure problems. In particular, due to stability reasons it seems impossible to succesfully apply the explicit coupling schemes used in aeroelasticity.

As a result, fluid-structure interaction in biological flows raise new challenging issues in scientific computing and numerical analysis : new schemes have to be developped and analyzed.

3.1.2. Aerosol

Complex two-phase fluids can be modeled in many different ways. Eulerian models describe both phases by physical quantities such as the density, velocity or energy of each phase. In the mixed fluid-kinetic models, the diphasic fluid has one dispersed phase, which is constituted by a spray of droplets, with a possibly variable size, and a continuous classical fluid.

This type of model was first introduced by Williams [45] in the frame of combustion. It was later used to develop the Kiva code [36] at the Los Alamos National Laboratory, or the Hesione code [41], for example. It has a wide range of applications, besides the nuclear setting: diesel engines, rocket engines [37], therapeutic sprays, *etc.* One of the interests of such a modeling is that various phenomena on the droplets can be taken into account with an accurate precision: collision, breakups, coagulation, vaporization, chemical reactions, *etc.*, at the level of the droplets.

The model usually consists in coupling a kinetic equation, that describes the spray through a probability density function, and classical fluid equations (typically Navier-Stokes). The numerical solution of this system relies on the coupling of a method for the fluid equations (for instance, a finite volume method) with a method fitted to the spray (particle method, Monte Carlo).

We are mainly interested in modeling therapic sprays either for local or general treatments. The study of the underlying kinetic equations should lead us to a global model of the ambient fluid and the droplets, with some mathematical significance. Well-chosen numerical methods can give some tracks on the solutions behavior and help to fit the physical parameters which appear in the models.

3.2. Multiscale modeling

Multiscale modeling is a necessary step for blood and respiratory flows. In this section, we focus on blood flows. Nevertheless, preliminary investigations are currently carried out in our team on respiratory flows.

3.2.1. Arterial tree modelling

Problems arising in the numerical modeling of the human cardiovascular system often require an accurate description of the flow in a specific sensible subregion (carotid bifurcation, stented artery, *etc.*). The description of such local phenomena is better addressed by means of three-dimensional (3D) simulations, based on the numerical approximation of the incompressible Navier-Stokes equations, possibly accounting for compliant (moving) boundaries. These simulations require the specification of boundary data on artificial boundaries that have to be introduced to delimit the vascular district under study. The definition of such boundary conditions is critical and, in fact, influenced by the global systemic dynamics. Whenever the boundary data is not available from accurate measurements, a proper boundary condition requires a mathematical description of the action of the reminder of the circulatory system on the local district. From the computational point of view, it is not affordable to describe the whole circulatory system keeping the same level of detail. Therefore, this mathematical description relies on simpler models, leading to the concept of *geometrical multiscale* modeling of the circulation [42]. The underlying idea consists in coupling different models (3D, 1D or 0D) with a decreasing level of accuracy, which is compensated by their decreasing level of computational complexity.

The research on this topic aims at providing a correct methodology and a mathematical and numerical framework for the simulation of blood flow in the whole cardiovascular system by means of a geometric multiscale approach. In particular, one of the main issues will be the definition of stable coupling strategies between 3D and 1D models that generalizes the work reported in [38] to general geometries coming from medical imaging.

When modeling the arterial tree, a standard way consists in imposing a pressure or a flow rate at the inlet of the aorta, *i.e.* at the network entry. This strategy does not allow to describe important features as the overload in the heart caused by backward travelling waves. Indeed imposing a boundary condition at the begining of the aorta artificially disturbs physiological pressure waves going from the arterial tree to the heart. The only way to catch this physiological behavior is to couple the arteries with a model of heart, or at least a model of left ventricle.

A constitutive law for the myocardium, controlled by an electrical command, is currently developped in the CardioSense3D project [1]. One of our objectives is to couple artery models with this heart model.

[1] http://www-sop.inria.fr/CardioSense3D/

A long term goal is to achieve 3D simulations of a system including heart and arteries. One of the difficulties of this very challenging task is to simulate the aortic valve. To this purpose, we plan to mix arbitrary Lagrangian Eulerian and fictitious domain approaches.

3.2.2. Heart perfusion modelling

The heart is the organ that regulates, through its periodical contraction, the distribution of oxygenated blood in human vessels in order to nourish the different parts of the body. The heart needs its own supply of blood to work. The coronary arteries are the vessels that accomplish this task. The phenomenon by which blood reaches myocardial heart tissue starting from the blood vessels is called in medicine perfusion. The analysis of heart perfusion is an interesting and challenging problem. Our aim is to perform a three-dimensional dynamical numerical simulation of perfusion in the beating heart, in order to better understand the phenomena linked to perfusion. In particular the role of the ventricle contraction on the perfusion of the heart is investigated as well as the influence of blood on the solid mechanics of the ventricle. Heart perfusion in fact implies the interaction between heart muscle and blood vessels, in a sponge-like material that contracts at every heartbeat via the myocradium fibers.
To perform simulations on this complex system, at the macroscopic scale we will assume that myocardial tissue and small coronary vessels can be approximated as a poroelastic medium. Thus, in this perfusion model, Darcy's law for porous media is coupled to the heart structural model to link the fluid velocity to the fluid pressure gradient. The permeability of the medium takes into account the deformation of the skeleton.

3.2.3. Respiratory tract modelling

We aim to develop a multiscale modelling of the respiratory tract. Intraprenchymal airways distal from generation 7 of the tracheabronchial tree (TBT), which cannot be visualized by common medical imaging techniques, are modelled either by a single simple model or by a model set according to their order in TBT. The single model is based on straight pipe fully developed flow (Poiseuille flow in steady regimes) with given alveolar pressure at the end of each compertment. It will provide boundary conditions at the bronchial ends of 3D TBT reconstructed from imaging data. The model set includes three serial models. The generation down to the pulmonary lobule will be modelled by reduced basis elements. The lobular airways will be represented by a fractal homogenization approach. The alveoli, which are the gas exchange loci between blood and inhaled air, inflating during inspiration and deflating during expiration, will be described by multiphysics homogenization.

4. Application Domains

4.1. Blood flows

Keywords: *blood flows*.

Cardiovascular diseases like atherosclerosis or aneurysms are a major cause of mortality. It is generally admitted that a better knowledge of local flow patterns could improve the treatment of these pathologies (although many other biophysical phenomena obviously take place in the developpement of such diseases). In particular, it has been known for years that the association of low wall shear stress and high oscillatory shear index give relevant indications to localize possible zones of atherosclerosis. It is also known that medical devices (graft or stent) perturbate blood flows and may create local stresses favourable with atherogenesis. Numerical simulations of blood flows can give access to this local quantities and may therefore help to design new medical devices with less negative impacts. In the case of aneurysms, numerical simulations may help to predict possible zones of rupture and could therefore give a guide for treatment planing.

In clinical routine, many indices are used for diagnosis. For example, the size of a stenosis is estimated by a few measures of flow rate around the stenosis and by application of simple fluid mechanics rules. In some situations, for example in the case a sub-valvular stenosis, it is known that such indices often give false estimations. Numerical simulations may give indications to define new indices, simple enough to be used in clinical exams, but more precise than those currently used.

It is well-known that the arterial circulation and the heart (or more specifically the left ventricle) are strongly coupled. Modifications of arterial walls or blood flows may indeed affect the mechanical properties of the left ventricle. Numerical simulations of the arterial tree coupled to the heart model could shed light on this complex relationship.

One of the goals of the REO team is to provide various models and simulation tools of the cardiovascular system. The scaling of these models will be adapted to the application in mind: low resolution for modeling the global circulation, high resolution for modeling a small portion of vessel.

4.2. Respiratory tracts

Keywords: *lungs modelling*, *respiration*.

Breathing, or "external" respiration ("internal" respiration corresponds to cellular respiration) involves gas transport though the respiratory tract with its visible ends, nose and mouth. Air streams then from the pharynx down to the trachea. Food and drink entry into the trachea is usually prevented by the larynx structure (epiglottis). The trachea extends from the neck into the thorax, where it divides into right and left main bronchi, which enter the corresponding lungs (the left being smaller to accommodate the heart). Inhaled air is then convected in the bronchus tree wich ends in alveoli, where gaseous exchange occurs. Surfactant reduces the surface tension on the alveolus wall, allowing them to expand. Gaseous exchange relies on simple diffusion on a large surface area over a short path between the alveolus and the blood capillary under concentration gradients between alveolar air and blood. The lungs are divided into lobes (three on the right, two on the left) supplied by lobar bronchi. Each lobe of the lung is further divided into segments (ten segments of the right lung and eight of the left). Inhaled air contains dust and debris, which must be filtered, if possible, before they reach the alveoli. The tracheobronchial tree is lined by a layer of sticky mucus, secreted by the epithelium. Particles which hit the side wall of the tract are trapped in this mucus. Cilia on the epithelial cells move the mucous continually towards the nose and mouth.

Each lung is enclosed in a space bounded below by the diaphragm and laterally by the chest wall and the mediastinum. The air movement is achieved by alternately increasing and decreasing the chest pressure (and volume). When the airspace transmural pressure rises, air is sucked in. When it decreases, airspaces collapse and air is expelled. Each lung is surrounded by a pleural cavity, except at its hilum where the inner pleura give birth to the outer pleura. The pleural layers slide over each other. The tidal volume is nearly equal to 500 ml.

The lungs may fail to maintain an adequate supply of air. In premature infants surfactant is not yet active. Accidental inhalation of liquid or solid and airway infection may occur. Chronic obstructive lung diseases and lung cancers are frequent pathologies and among the three first death causes in France.

One of the goals of REO team in the ventilation field, in the framework of "R-MOD" (RNTS 2001) and of "le-poumon-vous-dis-je" (ACI Nouvelles Interfaces des Mathématiques, 2003), is to visualize the airways (virtual endoscopy) and simulate flow in image-based 3D models of the upper airways (nose, pharynx, larynx) and the first generations of the tracheobronchial tree (trachea is generation 0), whereas simple models of the small bronchi and alveoli are used (reduced-basis element method, fractal homogenization, multiphysics homogenization, lumped parameter models), in order to provide the flow distribution within the lung segments.

4.3. Electrophysiology of the heart

Keywords: *bidomain equations*, *electrocardiograms*, *heart electrophysiology*.

The numerical simulation of the electrical activity of the heart is a new topic in our team. It is motivated by our participation in the CardioSense3D project and by a collaboration initiated with the ELA Medical company (pacemaker manufacturer).

Our purpose is to simulate the propagation of the action potential in the heart. A lot of works has already been devoted to this topic in the literature (see *e.g.* [40], [44], [43] and the references therein), nevertheless there are only very few studies showing realistic electrocardiograms obtained from partial differential equations models. Our goal is to find a compromise between two opposite requirements: on the one hand, we want to use predictive models, and therefore models based on physiology, on the other hand, we want to use models simple enough to be parametrized (in view of patient-specific simulations). Our strategy is to select the level of complexity with respect to the "numerical electrocardiograms" produced by the model. We are also interested in various clinical and industrial issues related to pacemakers.

5. Software

5.1. LiFE-V library

Keywords: *Finite element library*.

Participants: M. Á. Fernández [correspondant], J.-F. Gerbeau.

LiFE-V[2] is a finite element library providing implementations of state of the art mathematical and numerical methods. It serves both as a research and production library. It has been used already in medical and industrial context to simulate fluid structure interaction and mass transport. LiFE-V is the joint collaboration between three institutions: Ecole Polytechnique Fédérale de Lausanne (CMCS) in Switzerland, Politecnico di Milano (MOX) in Italy and INRIA (REO) in France. It is a free software under LGPL license.

6. New Results

6.1. Mathematical modelling and numerical methods in fluid dynamics

6.1.1. Existence results in fluid-structure interaction

Participants: M. Boulakia, C. Grandmont.

In [32] C. Grandmont considered a three-dimensional viscous incompressible fluid governed by the Navier-Stokes equations, interacting with an elastic plate located on one part of the fluid boundary. The purpose of this work is to study the solutions of this unsteady fluid–structure interaction problem, as the coefficient modeling the viscoelasticity (resp. the rotatory inertia) of the plate tends to zero. As a consequence, the existence of at least one weak solution for the limit problem (Navier–Stokes equation coupled with a plate in flexion) is obtained as long as the structure does not touch the bottom of the fluid cavity.

M. Boulakia has studied with S. Guerrero in [27] the system of equations describing a rigid structure moving inside a Navier-Stokes compressible fluid. A regularity result has been proved for this problem.

6.1.2. Numerical methods in fluid-structure interaction

Participants: M. Astorino, N. Diniz dos Santos, M.Á. Fernández, J.-F. Gerbeau, A. Gloria, C. Grandmont, C. Riccobene, K. Traoré.

This activity on fluid-structure interaction is done in close collaboration with the MACS project-team, in particular with M. Vidrascu and P. Le Tallec.

[2] http://www.lifev.org/

In collaboration with E. Burman (University of Sussex, UK), M. Fernández has proposed a stabilized explicit coupling scheme, based on Nitsche's method, for the efficient solution of fluid-structure interaction problems involving a viscous incompressible fluid. The stability of the method is obtained by the addition of a weakly consistent penalization term of the (time) fluctuations of the fluid load at the interface. They show that the explicit coupling scheme is stable irrespective of the fluid-solid density ratio. The method is flexible with respect to the choice of time stepping schemes for the fluid and the structure and allows for independent meshing of both domains. The main disadvantage of the method is that the consistency of the stabilization term is of order $O(\delta t^{\frac{1}{2}})$, which leads to a scheme that is too dissipative in practice. They have proposed to improve accuracy using a defect-correction approach. Numerical experiences have shown that one correction step allows to recover the accuracy of the underlying fully implicit scheme. Some of the results of this work have been reported, without proof, in [12] as a brief note. The full paper version [28] has been submitted for publication.

Work in progress:

1. In the framework of the ANR PITAC "Parallélisation Incluant le Temps pour Accélérer les Calculs" (parallel in time algorithms), F. Chouly and M. Fernández have carried out a preliminary study, in which the above stabilized explicit coupling scheme is combined with the parareal algorithm. Some stability issues have been found which require deeper investigations.
2. Parallel in time algorithms have been also investigated by C. Riccobene and J.F. Gerbeau for the Navier-Stokes equations, with applications to blood flows through a stent.
3. C. Grandmont and M. Astorino have been working on the detailed numerical analysis of the semi-implicit numerical method, introduced in [16], for fluid-structure interaction problems arising in biological flows for which the fluid added mass acting on the structure is strong. The design of efficient and stable numerical schemes is particularly difficult to face in this context as it happens in haemodynamics for example. They are currently studying the scheme convergence (error estimates, numerical simulations) and have proven that the rate of convergence is at least in $O(\sqrt{\Delta t})$.
4. M. Astorino, K. Traoré and J.F. Gerbeau, in collaboration with O. Pantz (Ecole Polytechnique) are developping methods for managing 3D contacts between several structures immersed in a fluid.

6.1.3. Stabilized finite element methods in fluid mechanics

Participant: M.Á. Fernández.

M. Fernández and E. Burman (University of Sussex, UK) have proved unconditional stability and optimal error estimates, in natural norms, for pressure stabilized finite element approximations of the transient Stokes' problem. They have shown that for small initial time-steps the use of a pressure stabilization dependent Ritz-projection, for the initial data, is essential to avoid pressure instabilities, unless a condition between time and space discretization parameters is satisfied. For the analysis they have considered mainly the backward difference formula of order one, and they indicated how the analysis changes in the case of second order approximations in time. Indeed any $\mathcal{A}$-stable implicit scheme is expected to yield optimal performance. They also illustrated how various pressure stabilization methods enter the framework. From the analysis, they also concluded that a second order scheme (*e.g.* BDF2) can be initialized (without optimality loss) using a first step with BDF1, provided that the Ritz-projection is used for the initial data. It is interesting to note that for low order elements the weakly consistent stabilization operators still yield optimal convergence in time when used with a second order scheme. However, in case SUPG type stabilization is used for the convective term the convergence order in time will be lost unless full consistency is guaranteed in the stabilization term. This is why SUPG type stabilizations prompt space time finite element formulations with discontinuous approximation in time. These results and some numerical experiments have been reported in a INRIA's technical report [24] that has been submitted for publication.

6.2. Respiration tree modelling

6.2.1. Airway flow

Participants: L. Boudin, C. Grandmont, M. Grasseau.

In order to get a better description of the macroscopic mechanical behaviour of the lung tissue, L. Baffico, C. Grandmont, Y. Maday and A. Osses have devised in [25] a macroscopic model for a composite material made of an elastic body filled with gaseous bubbles. In this study, they restrained to the stationary case, and assumed that the number of air molecules in each alveolus remains constant (e.g, roughly speaking, the case of an excised lung filled with air, at a given pressure, and then sealed in order to analyze its mechanical behaviour). Next, they assumed that the air behaves like a perfect compressible gas, and that the parenchyma behaves like a linear elastic material (the deformations are small). Finally, the space repetition of the acini suggests to consider a periodically perforated elastic material. The interaction of the elastic material and the gas leads, after linearization, to a non standard non local boundary condition on the bubble walls. Thanks to a homogenization process (two-scale asymptotic expansion and two-scale convergence methods), a macroscopic model is derived, and the results show that in the case of a soft elastic material (such as living tissues), the absence or presence of gas in the bubbles produces significant variations in the homogenized coefficients, underlying the fact that biomechanical modelling requires special attention. This study is a first step towards the obtention of a viscoelastic model of the parenchyma [25].

If one is only interested in the air flow in the upper airways there is no need to model in detail the air flow in the small airways and in the acini. Nevertheless, representative boundary conditions or simplified models have to be developped to describe it. A way to take into account the air flow in the small air ways (assuming that the flow is described by Poiseuille Law in this region) is to consider natural dissipative boundary conditions. One specificity of this model is that all the outlets of the bronchial tree are coupled and depend on the motion of the diaphragm/parenchyma that is described by a spring equation. Despite its simplicity, this model contains parameters describing the resistances of distal trees and the elastic behaviour of the parenchyma (which is represented by the spring stiffness). By modifying those parameters, one could obtain pathological behaviours such as asthma that increases the resistances, or emphysema that is characterized by a decrease of the spring stiffness. C. Grandmont, B. Maury and A. Soualah have proved that, when the velocity profiles at the outlets are given, the coupled multiscale problem is well-posed [33].

Work in progress

1. C. Grandmont, L. Baffico and B. Maury are currently studying the general problem (well-posedness, discretization and $3D$ numerical simulations).
2. A collaboration is established with F. Chometon from the Conservatoire National des Arts et Métiers (CNAM) and surgeons from Hospital Paris-Sud. The objective is to help the surgeon to decide what surgery is pertinent in order to restore normal air flow for patient with blocked nose. Pertinent simulations rely on the obtention of realistic meshes and M. Grasseau is currently working on such questions.
3. In order to better understand the nature of the dissipation phenomena induced by the airway tree C. Grandmont and C. Vannier (PhD student of B. Maury, Orsay university) investigate the long time behavior as well as the controlability of the solution of a non local dissipative wave equation.

6.2.2. Modelling of the aerosol impact on the human upper airway walls

Participants: L. Boudin, C. Grandmont, A. Moussa, M. Thiriet.

L. Boudin and C. Grandmont supervised the postdoc of L. Weynans in the framework of the “ACI” grant “LePoumonVousDisJe” (March-August 2007). They studied the impact of an aerosol in both the upper airways and an experimental endotracheal tube [26]. They performed a bibliographical study of the impact of droplets on a wall. They then were able to confirm that every single droplet was absorbed by the wall, as observed by some experimental studies led by fellow researchers from Inserm Tours (U618). They also performed 2D numerical simulations in the case of the endotracheal tube, using the Freefem++ software, investigating some modelling questions about the droplets size in the aerosol.

Works in progress:

1. L. Boudin, C. Grandmont, M. Szopos (Toulouse-III), M. Thiriet and L. Weynans are currently studying with the Inserm Tours U618 the effect of the volume fraction of the aerosol on the deposit

locations and quantities. They are mostly involved in numerical studies, whereas U618 is conducting in vitro experiments.

2. Another work in progress which involves L. Boudin, C. Grandmont and A. Moussa (PhD student with L. Desvillettes, ENS Cachan) is the implementation of aerosol models within the LiFE-V software in order to investigate a coupling with the Navier-Stokes equations, as well as the theoretical study of this coupled system. We intend to compare the numerical results with experimental ones, obtained by the Inserm unit U618 in Tours.

6.3. Blood flows

6.3.1. In vitro experiments and numerical simulations

Participant: M. Thiriet.

A silicone model of the carotid artery network has been built (Fig. 1) in order to measure the velocity using particle image velocimetry (PIV). This non-intrusive technique measures the velocities of seeded micron-sized particles illuminated with a light sheet. When neutrally buoyant, the particles follow the fluid paths and PIV thus provides instantaneous velocity vector measurements in a explored sheet of finite thickness through which the laser beam is supposed to have a light intensity with a Gaussian distribution. Stereoscopic arrangement with two cameras is needed in 3D flow, characterized by out-of-sheet motions, to measure the three velocity components. A charge-coupled-device (CCD) camera records separate images that show the positions of the illuminated particles at two different times, t and t + dt. The images are then processed to extract velocities from the displacements of the particles during the time intervals between exposures.

Figure 1. Phantom built by rapid prototyping from the surface mesh of the computational model of the carotide artery network.

Steady flow has been investigated in a carotid artery network (with two successive embranchment, the carotid bifurcation and a branching of the external carotid artery) for various flow distribution. Numerical tests have been carried out using the finite element method. A phantom has been built from the surface mesh. The velocity field has been measured using the particle image velocimetry. Numerical and experimental results are in good agreement (Fig. 2).

6.3.2. Numerical simulation of stents for aneurysms

Participants: M.Á. Fernández, J.-F. Gerbeau, C. Riccobene.

This study is carried on in collaboration with the CARDIATIS company.

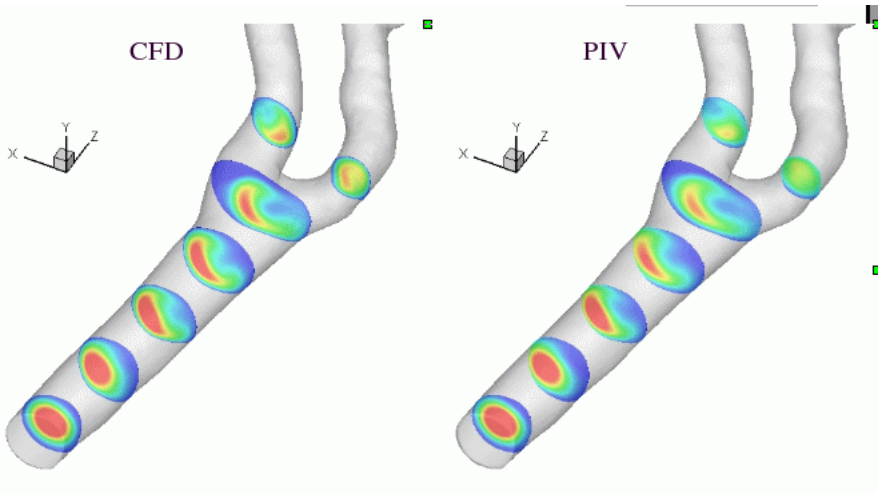

Figure 2. (Left) Numerical steady velocity isocontours in selected cross sections of a carotid artery network. (Right) Velocity field measured in the same loci using PIV. Phantom built by rapid prototyping from the surface mesh of the computational model.

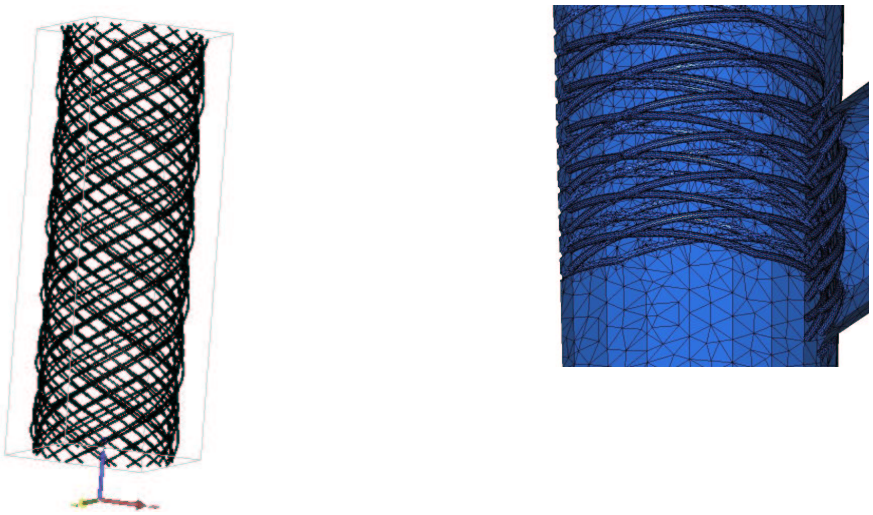

Figure 3. A procedure has been developped to automatically generate a stent mesh from the manufacturer device

Last year a model of stent based on homogenization has been proposed [30]. We investigated this year an alternative way consisting in the direct simulation of the flow through the complex geometry of a stent. A procedure has been developped to generate the finite element mesh directly from the software used by the manufacturer to build the real stent (see Figure 3). Due to the high complexity of the geometry, automatic mesh refinement techniques (developped by the GAMMA project-team) have been used.

6.3.3. Perfusion of the myocardium and blood flows in coronaries

Participants: J.-F. Gerbeau, I. Vignon-Clementel, G. Rossi.

This activity on perfusion is done in close collaboration with the MACS project-team, in particular with D. Chapelle, Ph. Moireau and J. Sainte-Marie, in the framework of the CardioSense3D INRIA project.

Work in progress

1. Coronary perfusion (*i.e.* the delivery of blood flow to the coronary arteries) is an essential component of the heart's performance. Our goal is to develop a numerical model that reproduces its main behavior in terms of its physiologic coupling with the beating myocardium, which is still poorly understood. At each heart beat, the myocardium propels blood into the vascular circulation. As a consequence, it also compresses most coronary arteries, since they are embedded in it, producing a high resistance to flow until the myocardium relaxes. For our purpose, it is thus important to take into account blood flow, pressure together with the displacement of the myocardium. To take advantage of existing codes, a strategy has been developed to couple a Lagrangian nonlinear solid mechanics model to an Eulerian Darcy solver. The latter was first modified to take into account the deformation of the underlying porous media skeleton. The coupling was then sucessfully verified on simple test cases. Simulations have then been run on an analytical "ventricular" geometry with fibers assuming almost physiological conditions and taking into account the displacement of the heart structure. The results obtained in this work are promising and the coupling algorithm seems able to efficiently simulate the fluid structure interaction for the myocardium perfusion. Some physiological aspects can be already represented by these simulations: both ventricular contraction and perfusion pressure affect coronary blood flow. Moreover, the ventricle contraction shows more important effects on perfusion than the symmetric. Nevertheless, not taking into account perfusion for the myocardium stress significantly alters coronary blood flow results. Further developments are however necessary to improve the physiological relevance of the results [35].
2. Perfusion has also been investigated from a macroscopic point of view, that is analyzing blood flow in the first arterial branches. In order to perform this simulation the generation of the computational mesh, starting from biomedical imaging, has been accomplished. This with the help of CAD softwares (3matic) and programs from the GAMMA project-team (yams2 [39] for surface mesh adaptation and ghs3d [3] for the volume mesh). A new coupling algorithm has been performed for this problem, using the MPI software for the exchange of information. The first results have been obtained on the coupling of a few arterial branches with the previously described ventricular geometry. The results show that the porous media acts as a distributed resistance that modifies the distribution of flow in the various coronary branches. These results are very preliminary and further work is needed to model physiological and pathophysiological states.

6.4. Electrophysiology

This work is done in the framework of the CardioSense3D INRIA project. A part of our activity in this field is supported by the ELA Medical company and done in collaboration with Serge Cazeau (Medical Doctor, InParys).

6.4.1. Numerical simulation of the electrical activity of the heart

Participants: M. Boulakia, L. Dumas, G. Ebrard, L. El Alaoui, M.Á. Fernández, J.-F. Gerbeau, E. Phé, N. Zemzemi.

[3] See http://www-c.inria.fr/Eric.Saltel/gamma/ghs3d

M. Boulakia, M.A. Fernández, J.-F. Gerbeau and N. Zemzemi are working on the numerical simulations of electrocardiograms. They have implemented in the Life-V library a model coupling the electrical activity of the heart (the bidomain model complemented with a ionic model) and the electrical activity of the torso. Quite realistic electrocardiograms are now obtained (see Figure 4). The choice of ionic models is determinant and, after different tests, the phenomenological Mitchell-Shaeffer model, which gives realistic action potentials, has been chosen. Many modelling assumptions have been tested to study their influence on electrocardiograms. For instance, the sensitivity of electrocardiograms to physiological properties like the cardiac tissue anisotropy and the cardiac cell heterogeneity have been studied. Different interface coupling conditions (isolated heart, presence of pericardium) and different ionic models have also been compared [20].

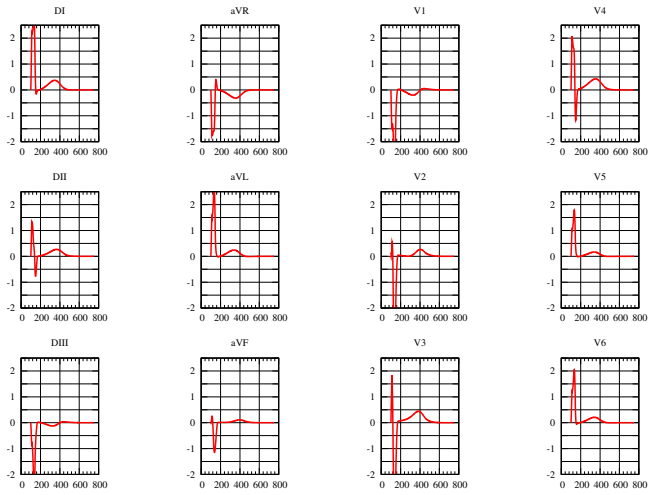

Figure 4. A numerical electrocardiogram obtained by coupling the electrical activity of the heart (bidomain model) and the torso

1. **Multisite resynchronisation**. The heart behaves like a pump where the contraction is induced by an electrical impulse moving across it. In the ventricles, the propagation of the electrical signal is led by the so-called bundle of His causing a wavefront which propagates by a cell-to-cell activation. In each cell, a depolarization phase occurs corresponding to the inflow of sodium ions (causing the electrical activation) followed by a plateau phase, and then by a repolarization phase corresponding to the outflow of potassium ions. The electrical conduction of heart may be defective causing the heartbeat to be too fast, too slow or irregular. Such pathologies can be treated on using an artificial pacemaker, a small device containing a battery and electrode(s) transmitting. In this work, a test case has been studied to show how optimization can improve the placement of the electrodes of a pacemaker. A robust cost function based on the depolarization delay of the disease heart is in particular introduced. The obtained result (presented at GECCO 2007 [21] and EUROGEN 2007 conferences) show how a rather good ECG can be recovered, even with only one electrode, after an optimization of its positioning.

   This work on robust optimization is done within the *Pôle de compétitivité* Systematic/IOLS.

2. **From electrograms to electrocardiograms**. In the framework of a collaboration with ELA Medical, the numerical electrocardiograms produced by our simulation tools are being used by G. Ebrard and N. Zemzemi in order to derive simplified “models” that will allow to reconstruct ECG information from epicardic potential measurements.

6.4.2. Mathematical analysis of the electrical activity of the heart

Participants: M. Boulakia, M.Á. Fernández, J.-F. Gerbeau, N. Zemzemi.

The equations which couple the cardiac potential and the thoracic potential (implemented to obtain numerical electrocardiograms) are reaction-diffusion degenerate parabolic systems. M. Boulakia, M. Fernández, J.F. Gerbeau and N. Zemzemi have proved that this model admits a global weak solution. The result holds for a wide class of ionic models and uniqueness is proved for FitzHugh-Nagumo type ionic models. This work has been submitted for publication in [23].

7. Contracts and Grants with Industry

7.1. Cardiatis

Participants: M.Á. Fernández, J.-F. Gerbeau, C. Riccobene.

Industrial contract. Period: january 2007-december 2007.

Cardiatis is a company which is developing a new generation of stents (endoprostheses). Our studies are devoted to the numerical simulation of a stent which aims at excluding cerebral aneurysms. See section 6.3.2 above.

7.2. ELA Medical

Participants: M.Á. Fernández, J.-F. Gerbeau, G. Ebrard, N. Zemzemi.

Industrial contract. Period: september 2007-august 2008.

ELA Medical is a company producing pacemakers. See section 6.4.1 above.

7.3. Alcan

Participant: J.-F. Gerbeau.

Industrial contract with Ecole Nationale des Ponts et Chaussées (ENPC) in the framework of a collaboration with ALCAN (formerly Aluminium Pechiney) on the mathematical modelling of aluminium electrolysis cells (magnetohydrodynamics in presence of free interfaces). The work is done in collaboration with Claude Le Bris, Tony Lelièvre (ENPC & MicMac project). A book on magnetohydrodynamics of liquid metal has been published [7] in 2006.

8. Other Grants and Activities

8.1. National research program

8.1.1. CARDIOSENSE3D

The REO project is a member of the "CardioSense3D project", an INRIA "Large Initiative Action" aimed at developping an electro-mechanical model of the heart[4].

8.1.2. ACI "le-poumon-vous-dis-je"

This project [5] aims at studying mathematical and numerical issues raised by the modelling of the lungs.

Period: 2003-2007, Participants: L. Boudin, C. Grandmont.

[4] http://www-sop.inria.fr/CardioSense3D/
[5] http://www.insa-rennes.fr/ACINIMpoumon/

8.1.3. ANR Project "PITAC"

This project [6] is funded by the CIS call (High-Performance Computing and Simulation) of the ANR. It aims at developping and studying parallel-in-time numerical methods.

Period: 2007-2011. Participants: F. Chouly, M. Fernández, J.F. Gerbeau.

8.1.4. France-Stanford Center fund

The aim of this projet is to develop computational simulations as a tool to aid in understanding and predicting post-intervention hemodynamics for congenital interventions.

Period: 2007-2008. Participants: I. Vignon-Clementel, J.F. Gerbeau.

8.1.5. Other grants

- The post-doc of Karim Traoré has been supported by a grant with *Région Ile de France* (Paris 6 university) (may 2007-april 2008)
- The post-doc of Linda El Alaoui has been partially supported by the *Pole de compétitivité Systematic/IOLS* (sept. 2006- aug. 2007)
- REO is a member of the following GDR CNRS:
  - *Math-Bio* coordinated by Emmanuel Grenier and Didier Bresch
  - *Fluid-structure interaction in blood flows* coordinated by V. Deplano
  - *Fluid-structure interaction* coordinated by Mhamed Souli

8.2. European research program

8.2.1. ERCIM working group "IM2IM"

The ERCIM Working Group "IM2IM"[7] has been initiated in june 2003 in the context of minimally invasive treatment in medicine and surgery. This group sent a proposal (coordinator: M. Thiriet) to EU FP7 call ICT-2007.5.3: Virtual Physiological Human by a Large-scale integrating project (IP) proposal "Open platform for predictive, patient-specific, multi-physics simulation of pathological alterations of the vascular and respiratory system for diagnosis and outcome" (Acronym: PrognoSIM) gathering 18

participants.

9. Dissemination

9.1. Scientific community animation

9.1.1. Various academic responsibilities

- L. Boudin
  - elected member of Paris-VI "Commission de specialistes" (CSE) and external member of ENS Cachan CSE (26th Section : applied math.)
  - Co-organizer of the "Deuxième journée d'accueil des Maitres de conférence et des Chargés de recherche en mathématiques", with Valentina Busuioc (Univ. Saint-Etienne), Stéphane Cordier (Univ. Orléans), Lucia Di Vizio (CNRS ENS Paris), Pauline Godillon-Lafitte (Univ. Lille-I), Céline Grandmont (INRIA Rocquencourt), Véronique Hédou-Rouillier (Univ. Tech. Compiègne), Frédéric Lagoutière (Univ. Paris-VII), Magali Ribot (Univ. Nice), and co-writer with the same fellow colleagues of the "livret d'accueil" [8]

[6] http://www.ann.jussieu.fr/PITAC/
[7] http://www-rocq1.inria.fr/Marc.Thiriet/Im2im/
[8] see http://postes.smai.emath.fr/accueil/ and http://postes.smai.emath.fr/accueil/livret_final/

- L. Dumas
  - Jury member of *Agrégation de Mathématiques*.
  - External member of the *Commission de spécialistes* of Paris 13 university.
- M.Á. Fernández
  - Coordination of CardioSense3D (with H. Delingette, Asclepios team).
  - Co-organizer of the monthly colloquium of INRIA Paris-Rocquencourt.
- J.-F. Gerbeau
  - Editor-in-chief of *ESAIM Proceedings* (with E. Cancés and P. del Moral).
  - Member of the editorial board of *Mathematical Modelling and Numerical Analysis* (M2AN).
  - Scientific coordinator of the CEA-EDF-INRIA schools organized by INRIA.
  - Contributed in quality of expert to the European research Roadmap for the development of the Virtual Physiological Human [9] and in quality of reviewer to the call FP7 - 5.3 "Virtual Physiological Humal" of the European Commission.
  - PhD thesis committees: Lucie Fréret (president), Paul Vigneaux (reviewer), Dima Abi-Abdallah (reviewer), Antoine Gloria (co-advisor), Aline Lebebvre (member), Libuse Demjancukova (reviewer), Nuno Diniz Dos Santos (co-advisor).
- C. Grandmont
  - member of the former Conseil national des universités (CNU) section 26 (applied mathematics).
  - external member of the Commission de spécialistes of Paris 6, Besançon and Saint-Etienne universities (section 26).
  - Co-organizer of the second "Welcoming Day of the new assisting professors and junior researchers in mathematics" (see L. Boudin)
- M. Thiriet
  - Member of the editorial board of *Computer Methods in Biomechanics and Biomedical Engineering*
  - Coordination of working group ERCIM "IM2IM".
  - Organization IM2IM meeting during Spring ERCIM Days, 2007 meeting May 14-15 in Lausanne at EPFL
  - Coordination of associated INRIA team "CFT" (Centre de Recherche Mathématiques, Canada and SCCS, National Taiwan University)
  - Organization MSH'07 workshop, October 22–25 in Taiwan at the National Taiwan University
- I. Vignon-Clémentel
  - Member of the "Conseil d'orientation scientifique et technologique" (scientific and technologic orientation council) of INRIA, in the subgroup "Actions Incitatives" (incentive action working group) since December 2007.
  - Mediator in case of conflict between PhD students and their supervisors for INRIA Paris-Rocquencourt since October 2007.

[9] On-line 5 July 2007, http://www.europhysiome.org/roadmap

- Participant in an interdisciplinary systems biology group at INRIA to promote research in life sciences modeling. Focus is on collaborations with the medical research institution INSERM.
- Represented INRIA at the "European Research and Innovation Exhibition" (June, 7-9th, 2007). Working with the communication services to prepare adequate media to explain the research done at INRIA on blood flow and the heart. Interviewed by several media such as Les Echos, Canal +, etc., including the newspaper Le Journal Innovation (article appeared July, 12th, 2007)
- Interviewed by the local newspaper Les Nouvelles des Yvelines (article appeared March, 7th, 2007)

9.2. Teaching

- Muriel Boulakia
  - Analysis and numerical methods, Licence, Paris 6 University.
- Laurent Dumas
  - CIMPA School "Numerical methods for PDE", course on "Numerical Optimization and applications in CFD", Ateneo de Manilla, September 2007.
  - Master of Science in Mathematics, course on "Numerical Optimization", UP-Diliman, Manilla, January 2007.
  - Master course "Introduction to Fluent and Gambit", UPMC.
- Miguel Á. Fernández
  - "Fluid-structure interaction. Application to blood flows", Master of numerical analysis, Paris 6 University (with J.F. Gerbeau and Y. Maday)
  - "Inverse problems", Scientific Computing option, Ecole Supérieure d'Ingénieurs Léonard de Vinci
- Jean-Frédéric Gerbeau
  - Associate professor ("professeur chargé de cours", part-time), Ecole Polytechnique.
  - Functional analysis, Ecole Nationale des Ponts et Chaussées.
  - Master in mathematical engineering, Ecole Polytechnique de Tunisie.
  - "Fluid-structure interaction. Application to blood flows", Master of numerical analysis, Paris 6 University (with M.Á. Fernández and Y. Maday)
- Marc Thiriet
  - Master 2, Master of Sciences & Technologies, Mention Mathematics & Applications, Programs in Mathematical Modeling.
- Irene Vignon-Clémentel
  - Blood flow, a graduate level class (15 hours) as part of the "life sciences" section of the applied mathematics major at the Ecole Centrale Paris (Winter 2007).

9.3. Participation in conferences, workshops and seminars

- Matteo Astorino
  - Workshop GDR "MABEM" (Mathematical Modelling in Biology and Medicine), Bordeaux (6-7/12)

- Laurent Boudin
  - 6th International Congress on Industrial and Applied Mathematics ICIAM'07, Zurich, Switzerland, 16-20 July 2007.
- Muriel Boulakia
  - Seminar, European Research Consortium for Informatics and Mathematics working group, EPFL, Lausanne (may)
  - Numerical working group, Orsay (february)
  - Summer school, "EDP, Optimal design and Numerics", Benasque, Spain (august 26-september 07)
  - Analysis and Control of PDE, Pont-à-Mousson, member of the scientific committee (june 25-29)
- Nuno Diniz dos Santos
  - CEMRACS summer school (july-august), Marseille.
- Laurent Dumas
  - Seminar (02/02) at University of Philippines, Baguio, Philippines.
  - Contributed talk (11/06) at EUROGEN 2007, Jyvaskyla, Finlande.
- Linda El Alaoui
  - Seminars in french universities: Pau (18/01), Picardie (12/03), Besançon (13/04), Clermond-Ferrand (07/06)
  - Second European Conference on Computational Optimization (EUCCO 2007).
  - Genetic and Evolutionary Computation Conference (GECCO 2007)
- Miguel Ángel Fernández
  - Seminar, Universidad de Ciudad Real, February 16th, 2007, Cidudad Real, Spain.
  - Seminar, Laboratoire Jacques-Louis-Lions, Université Paris VI, October 29th, 2007, Paris, France.
  - Seminar, MOX, Politecnico di Milano, December 13th, 2007, Milan, Italy
  - Invited to the Mini-Workshop on Variational Multiscale Methods and Stabilized Finite Elements, February 12–13th, 2007, Lausanne, Switzerland.
  - Invited to the 1st NIH-INRIA Biomedical & Life Sciences Computing Workshop, April 16–17th, 2007, Bethesda, USA.
  - Contributed talk at the 4th International Conference on Functional Imaging and Modeling of the Heart, June 7–9th, 2007, Salt Lake City, USA.
  - Invited to a Mini-symposium of the 6th International Congress on Industrial and Applied Mathematics (ICIAM 07), July 16–20th, 2007, Zurich, Switzerland.
  - Keynote lecture of a Mini-symposium of the 9th U.S. National Congress on Computational Mechanics (USNCCM IX), July 23–26th, 2007, San Francisco, USA.
- Jean-Frédéric Gerbeau
  - Keynote lecture of a Mini-symposium of the 9th U.S. National Congress on Computational Mechanics (USNCCM IX), July 23–26th, 2007, San Francisco, USA.
  - Invited in two minisymposia in International Congress of Industrial and Applied Mathematics (ICIAM 2007), Zurich, Switzerland.

  - Invited in the workshop on Blood Modeling, AICES, Aachen university (21-22/09) Germany
  - Invited to the 1st NIH-INRIA Biomedical & Life Sciences Computing Workshop, April 16–17th, 2007, Bethesda, USA.
  - Seminar MOX, Politecnico di Milano, (20/12) Italy.
  - Seminar Optics Valley "Simulation numérique et traitement d'images biomédicales", (18/09), CEA Fontenay-aux-roses.
  - Seminars in french universities: Clermont univ. (11/01), ENS Cachan (11/09), Paris 6 (14/12), Paris 13 (30/11), UTC (12/06)

- Céline Grandmont
  - Seminar of applied mathematics laboratory, UTC, january 2007.
  - Seminar of numerical analysis, Orsay Univ. Dec. 2007.
  - Visiting researcher at University of Santiago de Chile for two weeks in Nov-Dec. 2007. Collaboration with A. Osses on inverse problems. Seminar.

- Chiara Riccobene
  - CEMRACS summer school (july-august), Marseille.

- Giuliana Rossi
  - CEMRACS summer school (july-august), Marseille.

- Marc Thiriet
  - Invited to the 1st NIH-INRIA Biomedical & Life Sciences Computing Workshop, April 16–17th, Bethesda, USA.
  - Invited in Minisymposium "Open Interfaces for Multi-Disciplinary Simulation and Code Coupling", 11th NAFEMS World Congress, May 22-25, Vancouver, Canada.
  - Minisymposium organizer "Modelling and design of complex systems", ICIAM'07, 16 july, Zurich
  - Invited talk, MSH'07 workshop, October 22–25, National Taiwan University.
  - Semainar of Centre de Recherches Mathématiques, Montréal, janvier 2007.
  - Seminar of Dpt of Applied Mathematics, National Taiwan University, october 2007.

- Irène Vignon-Clementel
  - Invited talk at the Euro-Mediterranean Conference on Biomathematics, Cairo, Egypt, June 26-28.
  - Invited in a minisymposium at the United States National Conference on Computational Mechanics, San Francisco, CA, USA, July 22-28.
  - Invited talk at the workshop on Blood Modelling, Aachen, Germany, Sept 20-21.
  - Invited talk at the seminar of the Laboratory "Matière et Systèmes Complexes", Paris 7 Diderot, Paris, France, Sept 24, 2007.

- Nejib Zemzemi
  - Congress SMAI 2007 (Poster award)
  - Young researchers & Life Sciences Meeting, Université Paris 5 (contributed talk)
  - Workshop GDR "MABEM" (Mathematical Modelling in Biology and Medicine), Bordeaux (6-7/12)

– "Cardiac resynchronization therapy, St Georges Hospital London" (participation without presentation)

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[10] M. BELHADJ, E. CANCÈS, J.-F. GERBEAU, A. MIKELIC. *Homogenization approach to filtration through a fibrous medium*, in "Network of Hetorogeneous Media", vol. 2, n^{o} 3, 2007, p. 529-550.

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[28] E. BURMAN, M. FERNÁNDEZ. *Stabilization of explicit coupling in fluid-structure interaction involving fluid incompressibility*, Submitted.

[29] B. DRUEZ, L. DUMAS, N. LECERF. *Adaptive Hybrid Optimization of aircraft engine blades*, to appear in Journal of Computational and Applied Mathematics.

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