INRIA

INSTITUT NATIONAL DE RECHERCHE EN INFORMATIQUE ET EN AUTOMATIQUE

Project-Team reo

Numerical simulation of biological flows

Rocquencourt

THEME BIO

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1. Team

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2. Overall Objectives

2.1. Overall Objectives

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 the flow of biological fluids, more especially blood in large vessels and air in the respiratory tracts, both in normal and pathological states;
- developing and analyzing efficient, robust and reliable numerical methods for the simulation of such flows;
- developing simulation software to guide medical decision and to design more efficient medical devices.

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 [49] in the frame of combustion. It was later used to develop the Kiva code [41] at the Los Alamos National Laboratory, or the Hesione code [46], for example. It has a wide range of applications, besides the nuclear setting: diesel engines, rocket engines [43], 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 [47]. 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 [44] 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, has been recently developped in the ICEMA project [48]. One of our objectives is to couple artery models with this heart model.

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. Respiratory tract modelling

Work is in progress 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.

5. Software

5.1. LiFE-V library

Keywords: *Finite element library*.

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

LiFE-V[1] 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: C. Grandmont, Y. Maday.

In [38], C. Grandmont, Y. Maday and P. Métier present and analyze a dynamical geometrically nonlinear formulation that models the motion of two-dimensional and three-dimensional elastic structures with large displacements and small strains. The starting point of the formulation is the separation of the rigid body motion from the purely elastic displacements. This is an idea that has been widely used in engineering sciences and has important technological applications. The motivation of the rigid-plus-deformational decomposition is essentially to trace the mean motion of the structure. For this model even if we consider that the stress tensor is given by the Hooke law, the rotations are well described unlike the linearized elasticity model. Thus it can be seen as a model between the linearized elasticity and the standard system of elasticity for a Saint–Venant material for instance. The equations describing the motion of the body has been derived and existence and uniqueness results have been proved.

6.1.2. Numerical methods in fluid-structure interaction

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

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

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

N. Diniz dos Santos, J.-F. Gerbeau and J.-F. Bourgat have proposed a numerical method to simulate the movements of a thin valve immersed in an incompressible viscous fluid [27]. The fluid and structure meshes are not matching: the kinematic continuity is imposed using Lagrange multipliers. The method therefore belongs to the “Fictitious Domain” family. This approach allows very large displacements. A partitioned fluid-structure algorithm is proposed: it keeps the fluid and structure solvers independent and it is able to manage contact without assuming that the structure solvers include contact capabilities. Various numerical tests have been performed. In particular, when the displacement is moderate, the results are in good agreement with Arbitrary Lagrangian Eulerian (ALE) simulations. Futhermore, the proposed approach has been mixed with ALE to tackle problems involving both an elastic valve and an elastic wall.

The standard methods used in fluid-structure interaction problems are generally “nonlinear on subdomains”. M.Á. Fernández, J.-F. Gerbeau, A. Gloria and M. Vidrascu have proposed a new algorithm based on the principle “linearize first, then decompose”. In other words, the domain decomposition techniques classically used in nonlinear elasticity have been extended to fluid-structure problems. This work has been reported in a review paper [33].

M.Á. Fernández and J.-F. Gerbeau have contributed to two chapters of a book in preparation on blood flows simulation, edited by A. Quarteroni, L. Formaggia and A. Veneziani [31], [32].

M.Á. Fernández, J.-F. Gerbeau and C. Grandmont have generalized the stability analysis of the semi-implicit coupling scheme introduced in [17], [35] to the case of projection step performed as a Pressure-Poisson equation. The main idea consists in reformulating the Pressure-Poisson equation as Darcy-like problem with a penalized divergence free condition.

A result on controllability of a 2D fluid-structure interaction problem has been obtained by M. Boulakia in collaboration with A. Osses [29].

During her PhD at Stanford university under the supervision of C. Taylor, I. Vignon-Clementel has been involved in the developpement of a new method, monolithic yet efficient for patient-specific multibranched geometries, to model the fluid-solid interaction of blood flow and vessel wall deformation [18].

6.1.3. Stabilized finite element methods in fluid mechanics

Participants: L. El Alaoui, M.Á. Fernández, J.-F. Gerbeau, V. Martin.

M.Á. Fernández, J.-F. Gerbeau and V. Martin have performed the numerical analysis of stabilized finite element for a problem arising in the modeling of a stent in a terminal aneurysm ([34], see Section 6.3.4). This device acts as a resistance to the flow, and can be thought of as a thin porous medium inserted in the flow domain. The resistive effect is modeled as a surface measure that we add to the the classical Navier-Stokes equations. As a result, the normal stress is discontinuous at the interface and its jump is proportional to the velocity. In particular, the velocity an pressure unknowns are not globally smooth enough to perform a classical convergence finite element analysis. The standard SUPG/PSPG method has been extended to the case of the Navier-Stokes equation with a surface measure. The new stabilizing term is made of two contributions: a standard residual based stabilization giving L^2-control of the stream derivative and the pressure gradient, and a strongly consistent interface term giving L^2-control of the jump of the pressure through the interface, which allows to obtain a mesh-independent inf-sup condition. The convergence properties of the method are analyzed in a simplified configuration (Stokes problem), optimal *a priori* error estimates are established assuming regularity of the solution (only) in each subdomain.

During her PhD at ENPC under the supervision of A. Ern, L. El Alaoui has investigated, with A. Ern and E. Burman, two methods of stabilization for the advection-diffusion equation: the subgrid method [16] and the face penalty method [15].

6.2. Respiration tree modelling

6.2.1. In vitro experiments and validation

Participant: M. Thiriet.

Magnetic resonance gas velocimetry using hyperpolarized 3He gas has been very recently developed to measure the velocity field in sections of phantom pipes and anatomical conduits. Phantom experiments are carried out in order to validate numerical results. In vivo measurements are performed to get computational input data. Magnetic resonance imaging allows acquisition of images of the first, large, visible generations (G0–G7) of the tracheobronchial tree. The 3D reconstruction from the image set leads to a computational mesh and a phantom, using rapid prototyping. Steady laminar inspiratory flow experiments (Reynolds number of 770) have been performed using both methods. Resulting velocity maps have been compared. Streamwise and secondary-flow velocity magnitudes are similar (Fig. 1). Local maximum velocities and velocity-projection vortex centers matched in many explored cross sections.

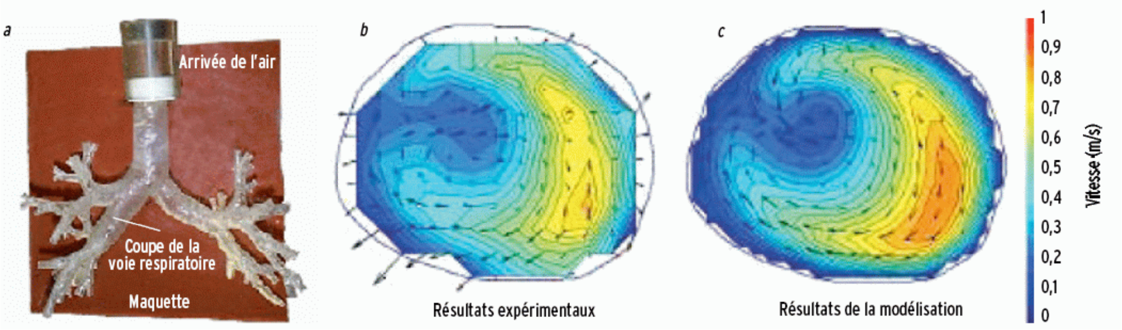

Figure 1. (a) Phantom built by rapid prototyping from the surface mesh of the computational model, with selected cross section for the comparison between measurements (b) and computations (c). The isocontours of the velocity component normal to the plane of the cross section and the velocity vector field of the in-plane component (virtual secondary motion associated with the projection of the velocity vectors in the cross section.

6.2.2. Modelling

Participants: C. Grandmont, Y. Maday, B. Maury.

In [20], B. Maury, N. Meunier (Paris 1) and C. Grandmont elaborate a model to describe some aspects of the human lung considered as a continuous, deformable, medium. To that purpose, they study the asymptotic behaviour of a spring-mass system with dissipation. The key feature of the approach is the nature of this dissipation phenomena, which is related here to the flow of a viscous fluid through a dyadic tree of pipes (the bronches), each exit of which being connected to an air pocket (alveoli) delimited by two successive masses. The first part concentrates on the relation between fluxes and pressures at the outlets of a dyadic tree, assuming the flow within the tree obeys Poiseuille-like laws. In a second part, which contains the main convergence result, the outlets of the tree is intertwined with a spring-mass array. Letting again the number of generations (and therefore the number of masses) go to infinity, the solutions to the finite dimensional problems is shown to converge to the solution of a wave-like partial differential equation with a non-local dissipative term.

Work in progress:

- In order to better understand the nature of the dissipation phenomena 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 the above mentioned dissipative wave equation.
- L. Baffico, C. Grandmont, Y. Maday and A. Osses are working on an homogenized model for an elasticic body filled with gaseous bubbles. This work address the asymptotic behavior of a system modeling a composite material made of an elastic periodically perforated support, with period $\varepsilon > 0$, and a perfect gas placed in each of those perforations, as ε goes to zero.

6.2.3. *Airway flow*

Participants: L. Boudin, C. Grandmont.

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. This model can, then, be coupled with an ODE representing a simple, rather naive, model of the acini. C. Grandmont in collaboration with A. Soulah (PhD student of B. Maury) is studying the wellposedness of the Navier-Stokes equations with those non-standard boundary conditions at the outlets as well as the coupling with the naive acini model (work in progress).

First contacts have been established with J. Castelneau, F. Chometon from the *Conservatoire National des Arts et Mtiers* (CNAM) and surgeons from Hopital Saint-Michel in Paris. 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.

Another work in progress is the implementation of aerosol models within the LiFE-V software in order to investigate a coupling with the Navier-Stokes equations (in a way similar to [42]). 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.

The strategy described above (Section 6.2.1) has also been applied to the blood flow in the carotid artery network. A silicone model of the blood vessels has been built (Fig. 2) and an experimental set-up is under construction 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, caracterized 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. This experimental set could be used in the future to validate numerical simulations.

Figure 2. Phantom built by rapid prototyping from the surface mesh of the computational model of the carotid artery network.

6.3.2. Aortic valve geometry

Participant: M. Thiriet.

A study of the anatomy of the heart, the aortic valve, the ascending aorta, the aortic arch and its branches, and the coronary artery has been carried out (Fig. 3). A simple but representative model of the anatomical area from the left ventricle exit to the descending aorta has been developed, using the computer-aided design software SolidWorks. A computational mesh has been derived from the model with either open or closed leaflets.

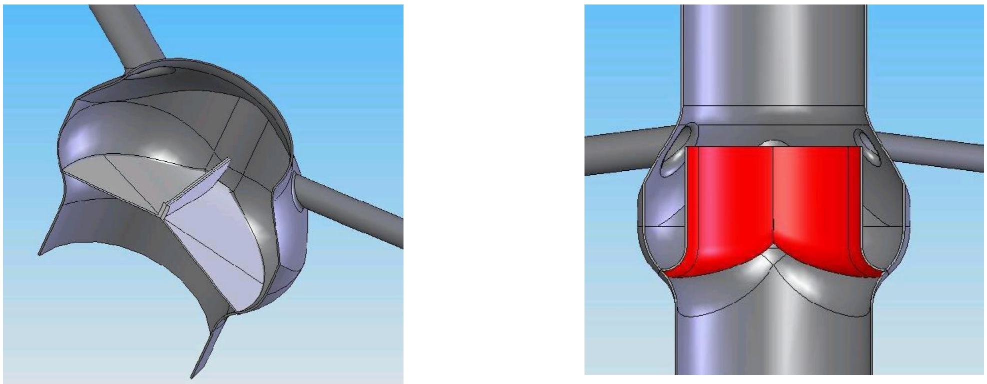

Figure 3. Model of the aortic valve, the aorta, and the coronary artery, with closed (left) and open valve (right).

6.3.3. Design optimization of a coronary stent

Participants: L. Dumas, A. Blouza.

A coronary stent is a permanent metallic implant used to open arteries blocked with atherosclerotic plaques (stenosis). Many types of stents are available which mainly differ from their design. By coupling computational fluid dynamics with optimization, L. Dumas, A. Blouza and I. MBaye [28] have determined the optimal parameters of a simplified stent which could overcome or at least reduce the risk of restenosis in stented segments.

The current results, based on a 2D computational fluid-structure modelling and a multiobjective optimization loop, indicate that there exist some important rules to respect in order to design appropriate stents which may avoid or at least reduce restenosis. The main rule can be summarized by saying that the characteristic ratio "strut spacing over strut height" shall be above the value of 5.7 to ensure a sufficient mean wall shear stress while maintaining a low level of mean flow vorticity. When this ratio is decreased, both performance criteria are degenerating while when it is increased, wall shear stress is increasing but also flow vorticity. Another important observation coming from this work is the relative independence on the design results of some simplificatory hypotheses that can be made during the modelization phase, such as the steady flow hypothesis or the absence of fluid-structure interaction. After this first attempt of automatic optimization on a simplified stent geometry, some future developments will be investigated. Among them is the possibility to study more realistic 3d stent shapes with the same flexible approach of multiobjective optimization.

6.3.4. Numerical simulation of stents for aneurysms

Participants: M.Á. Fernández, J.-F. Gerbeau, V. Martin.

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

In order to reduce the blood flow in a terminal aneurysm, an approach consists in introducing a stent into the artery where the aneurysm develops. This device acts as a resistance to the flow. We have proposed to model this device as a surface measure added to the classical Navier-Stokes equations. The numerical analysis of the model has been performed (see 6.1.3 and [34]). The medical device has been tested on pigs (Cardiatis and M. Bonneau, INRA). The experimental results are qualitatively in good agreements with the numerical simulations.

6.3.5. Parameter estimation for a 1D blood flow models

Participants: L. Dumas, J.-F. Gerbeau, R. Filliat.

Parameter estimation for 1D nonlinear hyperbolic model of blood flow can be tackled by various methods. A first approach with variational methods has been previously done in [45] for determining the compliance parameter, supposed to be constant. This case has been studied again with a new angle of attack, namely by using a hybrid method for the optimization part. Moreover, such method has allowed us to solve more complex cases where the compliance was assumed to be only piecewise continuous.

6.3.6. Blood flow simulations

Participants: M.Á. Fernández, J.-F. Gerbeau, I. Vignon-Clementel.

Heart perfusion is a key factor to understand and model the normal and pathophysiological states of the heart, since it is affected and affects the other components of this complex system. This project, still in progress, is a part of the CardioSense3D action.

During her PhD at Stanford university under the supervision of C. Taylor, I. Vignon-Clementel has investigated multidomain (three-dimensional, one-dimensional and zero-dimensional) methods and outflow boundary condition for blood flows [22], [12] which is particularly relevant for patient-specific multibranched models under various physiological conditions [23], [39].

6.4. Electrophysiology

6.4.1. Electrical activity of the heart

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

This work is a part of the CardioSense3D INRIA project and has been partially supported by the ELA Medical company and a *région Ile de France* grant.

M. Boulakia, M.Á. Fernández, J.-F. Gerbeau and N. Zemzemi have worked on the numerical simulation of electrocardiograms (ECG). The ECG consists in measuring potential differences between fixed positions (derivations) on the thorax surface. The numerical simulation of the ECG requires the coupling of two models describing, respectively, the electrical activity of the heart and the thorax. Within the heart the so-called bidomain model is obtained after homogenization of electrical balances at the cell scale, which are described by a system of ODE equations (the so-called ionic models). Two ionic models have been considered: a phenomenological one (FitzHugh-Nagumo) and a more realistic one which has been recently proposed in the SOSSO2 team by K. Djabella and M. Sorine. The thorax is assumed to be a simple passive conductor. Various organs (lungs, ...) are included in the computation to take into account the heterogeneity. The coupling between the two sub-domains is performed by enforcing the continuity of the potential and the current through the interface. More general coupling conditions have also been tested in order to take into account the presence of the pericardium. The resulting problem is discretized, in space, using finite elements and, in time, using finite differences (BDF formulas). The system of ODE's associated to the ionic model are solved using the CVODE[2] library. The coupling between the heart and the thorax is solved using domain decomposition techniques (Dirichlet-Neumann or Robin-Neumann iterations). This solver has provided first numerical ECG. More deep investigations are still needed to obtain more realistic outcomes. Nevertheless, at this stage, this numerical tool allows to determine the sensitivity of the simulated ECG to cardiac motion, fiber orientation, heart position, heart-thorax coupling conditions, *etc.* It can therefore give insight into the validity of some modelling assumptions.

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[2] http://www.llnl.gov/casc/sundials

The heart-thorax electrical model is a reaction-diffusion degenerate parabolic system. A theoretical studied is in progress to analyze the existence and uniqueness of its solutions. The key ingredient of the proof is a regularization argument which transforms the system into a non-degenerate parabolic problem.

6.4.2. Multisite resynchronisation (work in progress)

Participants: L. Dumas, L. El Alaoui.

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

This study is motivated by the heart resynchronisation via multisite stimulation. The aim would be to determine the optimal positioning of electrodes on a diseased heart in order to help it to recover a normal activity. It can be seen as an inverse type optimization problem that can be solved with the hybrid methods developped in our team by L. Dumas. However, since the placement of electrodes can be done only with a reduced accuracy, a robust optimization is preferable. It consists in finding the best positioning of an unknown number of electrodes leading to a better electrical activity, not only for a given position but also for all the neighborhood. A robust optimization method, including a fast evaluation process for the statistical analysis part, is currently investigated on a simplified geometry.

7. Contracts and Grants with Industry

7.1. Cardiatis

Participants: M.Á. Fernández, J.-F. Gerbeau, V. Martin.

Industrial contracts with the Cardiatis company which is developing a new generation of stents (endoprostheses). Our studies is devoted to the numerical simulation of a stent which aims at excluding cerebral aneurysms. See section 6.3.4 above.

7.2. Alcan

Participant: J.-F. Gerbeau.

Industrial contracts with Ecole Nationale des Ponts et Chausses (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 and Antonin Orriols (ENPC & MicMac project).

A book on magnetohydrodynamics of liquid metal has been published this year [11]. In [25], a numerical study has been proposed to compare linear and nonlinear approaches to model MHD instabilities. In [36], the issue of the moving contact line between a free interface and a wall has been addressed.

8. Other Grants and Activities

8.1. National research program

8.1.1. CARDIOSENSE3D

The REO project is member of the “CardioSense3D project”, an INRIA “Large Initiative Action” aimed at developping an electro-mechanical model of the heart[3].

8.1.2. ACI “le-poumon-vous-dis-je”

This project [4] aims at studying mathematical and numerical issues raised by the modelling of the lungs.

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

[4] http://www.insa-rennes.fr/ACINIMpoumon/

8.1.3. *Other grants*

- The post-doc of Muriel Boulakia has been partially supported by a grant with *Rgion Ile de France*.
- The post-doc of Linda El Alaoui is supported by a grant with *Ple de comptitivit Systematic/IOLS*.
- REO is member of the GDR CNRS *Fluid-structure interaction in blood flows* coordinated by V. Deplano and the GDR CNRS *Fluid-structure interaction* coordinated by Mhamed Souli.

8.2. European research program

8.2.1. *Research Training Network “Haemodel”*

The aim of this project[5] is to investigate the main mathematical and numerical problems related to the simulation of the human cardiovascular system. Participants: INRIA, Universit Paris 6, Politecnico di Milano (Italy), Imperial College (UK), Ecole Polytechnique Fdral de Lausanne (Switzerland), Instituto Superior Tcnico de Lisboa (Portugal), Technische Universität Graz (Austria).

8.2.2. *ERCIM working group “IM2IM”*

The ERCIM Working Group "IM2IM"[6] has been initiated in june 2003 in the context of minimally invasive treatment in medicine and surgery.

9. Dissemination

9.1. Scientific community animation

9.1.1. *Various academic responsibilities*

- L. Boudin
  - Scientific coordinator in Mathematics Departement (DSPT 1) of the *Mission Scientifique, Technique et Pédagogique* (MSTP), of the *Ministère de l’Education Nationale, de l’Enseignement Superieur et de la Recherche*, until August 2006.
  - Co-organizer with C. Grandmont (REO), Y. Maday (Paris 6), B. Maury (Paris 11) et B. Sapoval (Polytechnique) of the workshop *Modelling of the respiratory system: biomechanical, computational and mathematical aspects*, December 11-12, 2006 http://congres.smai.emath.fr/respi/.
- L. Dumas
  - Jury member of *Agrgation de Mathmatiques*.
  - External member of the *Commission de spécialistes* of Paris 13 university.
- M.Á. Fernández
  - Coordination of CardioSense3D (with H. Delingette, Asclepios team).
- J.-F. Gerbeau
  - Editor-in-chief of ESAIM Proceedings (with E. Cancs 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.
  - Jury member of *Agrgation de Mathmatiques*.

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[5] http://mox.polimi.it/it/progetti/haemodel/

[6] http://www-rocq1.inria.fr/Marc.Thiriet/Im2im/

- C. Grandmont
  - member of the *Conseil national des universits* (CNU) section 26 (applied mathematics).
  - external member of the *Commission de spcialistes* of Paris 6 and Besanon universities (section 26)
  - Co-organizer with L. Boudin (REO), Y. Maday (Paris 6), B. Maury (Paris 11) et B. Sapoval (Polytechnique) of the workshop *Modelling of the respiratory system: biomechanical, computational and mathematical aspects*, December 11-12, 2006 http://congres.smai.emath.fr/respi/.
- M. Thiriet
  - Member of the editorial board of *Computer Methods in Biomechanics and Biomedical Engineering*
  - Coordination of working group ERCIM “IM2IM”.
  - Coordination of associated INRIA team “CFT”.
  - Minisymposium "Medical Imaging and Computer-Aided Medicine and Surgery" 7th symposium on Computer Methods in Biomechanics and Biomedical Engineering Juan-Les-Pins, France, March 22-25, 2006
  - Workshop "multiphysics simulation in biomedical applications", Mosbach, Germany, november 21–22, 2006.

9.2. Teaching

- Muriel Boulakia
  - Analysis and numerical methods, Licence, Paris 6 University.
- Laurent Boudin
  - Linear algebra and Hilbert analysis, Licence, Paris 6 University.
- Miguel Á. Fernández
  - “Fluid-structure interaction. Application to blood flows”, Master of numerical analysis, Paris 6 University (with Y. Maday)
  - “Fluid-structure interaction”, Applied Mathematics option, cole Centrale de Paris (with J.-F. Gerbeau)
- Vincent Martin
  - TD de Mathmatiques aux Mines de Paris, 1re anne (Intgrations, Fourier), 16h15.
- Jean-Frédéric Gerbeau
  - Associate professor, Ecole Polytechnique.
  - Analysis and scientific computing courses, Ecole Nationale des Ponts et Chaussées.
  - Master in mathematical engineering, Ecole Polytechnique de Tunisie.
  - “Fluid-structure interaction”, Applied Mathematics option, cole Centrale de Paris (with M.Á. Fernández)
- Marc Thiriet
  - Master 2, Master of Sciences & Technologies, Mention Mathematics & Applications, Programs in Mathematical Modeling.

9.3. Participation in conferences, workshops and seminars

- Laurent Boudin
  - *38 me Congrs National d'Analyse Numrique* (CANUM2006), Guidel, May 29-June 2.
- Muriel Boulakia
  - *38 me Congrs National d'Analyse Numrique* (CANUM2006), Guidel, May 29-June 2.
  - Seminar Université Technologique de Compiègne, March 2006.
- Nuno Diniz dos Santos
  - Contributed talk at ECCOMAS 2006 conference, Egmond aan Zee (The Netherlands), September 4-8.
  - Contributed talk at 3rd International Symposium on Modelling of Physiological Flows, 25-27th September, Bergamo, Italy.
- Laurent Dumas
  - Invited speaker at International seminar on 'Applied Mathematics for Real World Problems', Ryutsu Keizai University, Tokyo (Japan) Sept. 2006.
- Miguel Ángel Fernández
  - Seminar of the Working Group "Mthodes Numriques", Laboratoire Jacques Louis Lions (Universit Paris VI), March 13, 2006.
  - Tenth European Biotech Crossroads EuroBio2006, October 25–27 2006, Paris, France.
  - *XIIme cole Franco-Espagnole Jacques-Louis Lions*, September 18–22 2006, Castro Urdiales, Spain.
  - 7th World Congress on Computational Mechanics WCCM2006, July 16–22, 2006, Los Angeles, USA.
- Jean-Frédéric Gerbeau
  - Invited plenary lecture at *Congrs National d'Analyse Numrique* (CANUM2006), Guidel, May 29-June 2.
  - Invited in a minisymposium at Worl Congress of Biomechanics, Munich (Germany), July 30-Aug 4.
  - Minisymposium organizer at ECCOMAS 2006 conference, Egmond aan Zee (The Netherlands), September 4-8.
  - Contributed talk at the conference of the European Society of Neuroradiology (ESNR06), Geneva (Switzerland), September 14.
  - Invited in a minisymposium at "International Conference on Multifield Problems", Stuttgart (Germany), October 3-6.
  - Invited lecture at *Challenges actuels en mcanique des fluides : modlisation et analyse*, Marseille, October 23-27.
  - Various seminars in french universities.
- Céline Grandmont
  - *38 me Congrs National d'Analyse Numrique* (CANUM2006), Guidel, May 29-June 2.
- Vincent Martin
  - Contributed talk at 3rd International Symposium on Modelling of Physiological Flows, 25-27th September, Bergamo, Italy.
- Marc Thiriet

- Invited lecture at 7th symposium on Computer Methods in Biomechanics and Biomedical Engineering Juan-Les-Pins, France, March 22-25, 2006

10. Bibliography

Major publications by the team in recent years

[1] J.-D. BOISSONNAT, R. CHAINE, P. FREY, G. MALANDAIN, S. SALMON, E. SALTEL, M. THIRIET. *From arteriographies to computational flow in saccular aneurisms: the INRIA experience*, in "Medical Image Analysis (MedIA)", vol. 9, n^{o} 2, 2005, p. 133-143.

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[3] M. BOULAKIA. *Existence of weak solutions for an interaction problem between an elastic structure and a compressible viscous fluid*, in "J. Math. Pures et Appliquées", vol. 84, 2005, p. 1515-1554.

[4] P. CAUSIN, J.-F. GERBEAU, F. NOBILE. *Added-mass effect in the design of partitioned algorithms for fluid-structure problems*, in "Comp. Meth. Appl. Mech. Engng.", vol. 194, n^{o} 42-44, 2005.

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[10] I. VIGNON-CLEMENTEL, C. FIGUEROA, K. JANSEN, C. TAYLOR. *Outflow Boundary Conditions for Three-dimensional Finite Element Modeling of Blood Flow and Pressure in Arteries*, in "Computer Methods in Applied Mechanics and Engineering", vol. 195, 2006, p. 3776-3796.

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Books and Monographs

[11] J.-F. GERBEAU, C. LE BRIS, T. LELIÈVRE. *Mathematical methods for the Magnetohydrodynamics of Liquid Metals*, Oxford Univ. Press, 2006.

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[13] E. BURMAN, M. FERNÁNDEZ, P. HANSBO. *Continuous Interior Penalty Finite Element Method for Oseen's Equations*, in "SIAM Journal on Numerical Analysis", vol. 44, n$^{\mathrm{o}}$ 3, 2006, p. 1248–1274.

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