

Suncica Canic (canic@math.uh.edu)

Hyperbolic Nets and Networks in Biomedicine

(4 lectures)

This series of lectures will address a timely, and emerging topic of nonlinear hyperbolic nets and networks arising in modeling biomedical applications. In particular, the focus will be on two applications: modeling cardiovascular devices called stents, and modeling the human arterial network (assuming elastic arterial walls). Both applications embody a physical problem that is defined on a multi-component domain in 3D. Understanding the interaction between different components leading to a solution to the global net or network problem represents the main difficulty of the problem. In both examples, the wave interactions between different sub-components form a set of moving boundary problems for a system of nonlinear hyperbolic conservation laws. Existence and uniqueness of a solution to the global problem are still open.

We will cover the biomedical background for the two applications mentioned above, and study the derivation of the modeling equations starting from 3D, and ending with a 1D system of nonlinear hyperbolic conservation laws obtained using dimension reduction. We will define the net/network of hyperbolic conservation laws as a family of 1D problems defined on a domain that forms a graph in 3D, with the 1D hyperbolic conservation laws holding on each sub-component corresponding to the graph's edge. The physics and the geometry of the coupling between the network's sub-components will be described in detail. The resulting global net/network problem will be studied from both the mathematical and numerical point of view. Comparison with the solution of the full 3D problem will be provided for the stent problem, and application of the numerical results to the optimal stent design will be presented.

Céline Grandmont (celine.grandmont@inria.fr)

Theoretical and Numerical Aspects of Fluid-Structure Interaction Problems

(4 lectures)

In these series of lectures we will present some results related to the existence of solution of fluid-structure interaction problems as well as strategies to discretized them in particular in the case of strong added mass effects of the fluid on the structure. After the introduction of the general setting we will detail the proof of existence of a smooth solution in the steady case of the Navier-Stokes system coupled with a Saint Kirchoff elastic media. We will next focus on the existence of weak solutions for the unsteady interaction of viscous, Newtonian fluid with a plate. Finally we will explain the different time discretization strategies that can be used: from the implicit to the staggered ones, and illustrate the added mass effect on a simple exemple and propose and study a semi-implicit scheme stable and efficient.

Alessandro Veneziani (ale@mathcs.emory.edu)

Data Assimilation in Cardiovascular Mathematics

(4 lectures)

The development of new technologies for acquiring measures and images in order to investigate cardiovascular diseases raises new challenges in scientific computing. These data can be in fact merged with the numerical simulations for improving the accuracy and reliability of the computational tools. Accuracy and reliability are increasingly important features in view of the progressive adoption of numerical tools in the design of new therapies and, more in general, in the decision making process of medical doctors. Assimilation of measured data and numerical models is well established in meteorology, whilst it is relatively new in computational hemodynamics. Different approaches are possible for the mathematical setting. The lectures will address the different strategies with particular emphasis to variational methods, based on the minimization of the mismatch between data and numerical results by acting on a suitable set of control variables. Theoretical and numerical aspects of the problem will be considered. Practical examples will cover:

- Merging of velocity data in the simulation of incompressible fluids;
- Merging of images for the fluid structure interaction simulation;
- Image-based patient-specific compliance estimation of the arterial wall.

Matthieu Hillairet (hillairet@ceremade.dauphine.fr)

Close-to-Contact Dynamics of Solids Inside a Viscous Fluid

(3 lectures)

In the mathematical analysis and numerical simulations of fluid-solid interaction systems, a challenging problem is to deal with contacts between several solids or, more generally, to deal with the close-to-contact dynamics of the solids. In this series of lectures, first, we recall classical results on the Cauchy theory for evolution PDEs describing the motion of rigid bodies inside a viscous fluid. Then, we present analytical tools for tackling the contact problem. One of this method is to apply ideas of lubrication theory to fluid-solid models. In the last part, we focus on new justifications for the use of lubrication approximation and present applications to different systems including roughness of the solid particles.

Mária Lukáčová (lukacova@uni-mainz.de)

Fluid-Structure Interaction Problems in Hemodynamics

(2 lectures)

Fluid-structure interaction problems appear in many areas. In the present talk we will concentrate on specific problems

arising in hemodynamics. The aim will be to study the resulting strongly nonlinear coupled system from theoretical as well as numerical point of view. We address the questions of well-posedness and present an efficient and robust numerical scheme in order to simulate blood flow in compliant vessels.

Petr Sváček (Petr.Svacek@fs.cvut.cz)

Mathematical Modelling and Finite Element Approximation of Glottal Flow Induced Vibrations of Human Vocal Folds (joint work with J. Horáček, M. Feistauer)

(1 lecture)

One approach in speech modelling is to model the interaction of the vocal folds using a simplified model based on a simplified description of both fluid and structure dynamics. Even if for these approaches a simplification of the flow problem was used, e.g. potential flow or Bernoulli equation, such simplified models are able to quantify many fundamental physical parameters characterizing the human voice production known in phoniatrics. The reality is much more complex. Human voice is created by passage of airflow between vocal folds, which are located in the upper part of larynx. When air is expired from lungs, the constriction formed by the vocal folds (called glottis) induces acceleration of the flow. Under certain circumstances (subglottal pressure, glottal width, longitudinal tension), fluid-structure interaction between the elastic structure and airflow may invoke vocal fold oscillations. The glottis is almost (or completely) closing during vibrations and the vocal folds collide generating the sound. It is important that the vibration is a passive process – when voicing, no sort of periodic muscle contraction is performed. The modelling of such a complex phenomenon encounters many difficulties as it is a result of coupling complex fluid dynamics and structural behaviour including contact and acoustic problems. A classical approach is to reduce the mechanical part of the problem into a small system of rigid masses, springs and dampers, which is further coupled to a simplified flow model. Although these lumped-parameter models are still widely used and can provide useful and computationally inexpensive data in specific cases, some more complex techniques have also been employed in recent years.

We shall focus on mathematical and numerical modelling of nonlinear coupled problems of fluid-structure interactions. The main attention will be paid to the description of the numerical method. First, the approximation in moving domains and the time discretization will be treated with the aid of Arbitrary Lagrangian-Eulerian method and higher order implicit backward difference formula. The weak formulation of a simplified problem will be introduced. The use of various boundary conditions will be discussed. Further, the weak formulation of the flow problem will be spatially discretized with the aid of a stabilized finite element method. The elastic structure shall be modelled with the aid of Lamé's equations and discretized by finite element method. Moreover, the solution of the nonlinear coupled problem will be treated. The performance of the numerical method will be demonstrated on number of examples.

Miloslav Feistauer (feist@karlin.mff.cuni.cz)

Discontinuous Galerkin Method for the Simulation of Vocal Folds Vibrations Induced by Compressible Flow

(joint work with V. Kučera, J. Prokopová, A. Kosík and J. Horáček)

(1 lecture)

The lecture will be concerned with the simulation of viscous compressible flow in time dependent domains. The motion of the boundary of the domain occupied by the fluid is taken into account with the aid of the ALE (Arbitrary Lagrangian-Eulerian) formulation of the compressible Navier-Stokes equations. This system is coupled with equations describing the behaviour of elastic structures under the action of a moving gas. We consider compressible flow in a channel. The part of its walls is formed by an elastic body whose deformation is described by the dynamical elasticity equations. This model is used for the simulation of airflow in human vocal folds. Compressible flow is discretized by the discontinuous Galerkin finite element method (DGFEM) using piecewise polynomial discontinuous approximations. The time discretization is based on a semi-implicit linearized scheme, which leads to the solution of a linear algebraic system on each time level. The developed technique appears unconditionally stable and robust with respect to the magnitude of Reynolds and Mach numbers. It allows the solution of flows with very low Mach numbers as well as high-speed flow. The solution of dynamical elasticity equations is realized with the aid of conforming finite elements. The fluid-structure interaction is realized via the strong coupling. Some results of numerical tests will be presented.

Giovanni Paolo Galdi (galdi@pitt.edu)

Topics in the Mathematical Theory of Liquid-Solid Interaction

(4 lectures)

Main focus of this short course is the mathematical analysis of some fundamental properties of the motion of the coupled system constituted by a rigid (undeformable) body moving in a viscous liquid that fills the whole space, under the action of prescribed driving mechanisms. Typical examples of interesting physical situations that can be modeled this way are bodies free-falling in a liquid by their own weight, micro-organisms swimming in a liquid by a suitable time-periodic change of part of their bodies in the small scale, etc.

It is readily seen that this type of problems leads, naturally, to as many challenging mathematical questions that find no counterpart in “classical” fluid dynamics. Objective of this course will be to analyze some of these questions, in both steady and unsteady case, and the corresponding strategies that one may use to furnish an appropriate answer. Also a number of significant open problems will be presented.

Antonio Fasano (fasano@math.unifi.it)

Mathematical Models of Blood Clotting

(2 lectures)

Blood coagulation is a familiar process leading to the formation of clots (or thrombi), sealing blood vessels injuries and halting bleeding. Roughly speaking, a clot is a gel-like structure formed by a polymeric network (fibrin) which entraps all blood constituents and adheres rather firmly to the injury site. The growth of a thrombus goes through several stages. It is an incredibly complicated phenomenon, in which blood cells, particularly platelets, play a major role together with a large numbers of proteins involved in a massive chemical cascade. Small injuries occur frequently to blood vessel and they are effectively repaired by coagulation, thus preventing internal bleeding. Any dysfunction in this complex mechanism can have serious consequences. The interplay between the clot formation and the blood flow is very important for several reasons. The machinery triggering blood coagulation is constantly ready and the clot formation, which is rapid, is accompanied by an antagonist, but slower, process eventually leading to its dissolution (fibrinolysis). The biological explanation of the whole process has gone through a long path and it has been reformulated rather recently. New discoveries call for a constant updating of mathematical models. Therefore this is still a fast evolving research field.

In the first of my two lectures on the subject I will summarize the historical path which lead to the modern approach. In the second lecture I will shortly review some of the mathematical models, also emphasizing the need of new ideas.

A useful reference is the survey paper:

A. Fasano, R. Santos, A. Sequeira: Blood coagulation: a puzzle for biologists, a maze for mathematicians. In: *Modelling Physiological Flows* - D. Ambrosi, A. Quarteroni, G. Rozza (Editors), Chapt.3, Springer (2011).

Modeling Liquid and Cells Flow in Tumor Growth

(2 lectures)

Cancer modeling is a huge subject with an impressively large literature, that has taken many different directions. One of the recent trends is to consider a tumor as a mixture, emphasizing the importance of the mechanical behavior of its constituents. Frequently, in the continuum mechanics approach, growth is illustrated as a complex flow, suggesting various constitutive laws for the different components. In this class of models the relative flows of cells and of extracellular liquid, accompanied by mutual mass exchange (due to cell proliferation and death) are the main phenomena driving the evolution of the whole system. The chemical side is also of fundamental importance, with special reference to oxygen and glucose consumption. In particular glucose metabolism, depending of the specific pathway it takes, can increase the level of acidity in the surrounding tissue. Since tumor cells can withstand higher level of acidity than the host tissue, this fact may favor tumor spreading.

We will review some of these aspects with particular reference to mathematical modeling.

Some references:

A. Fasano, A. Gandolfi: The steady state of multicellular tumour spheroids: a modelling challenge. Submitted to "Mathematical Medicine" (AIMS).

A. Fasano, M. A. Herrero, M. Rocha Rodrigo: Slow and fast invasion waves in a model of acid-mediated tumor growth. *Math. Biosci.* 220 (2009) 45-56