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**International workshop
Biomathematics and mechanics in
cardiovascular medicine**

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A Novel Patient-Specific Computational Fluid Dynamics Study of the Activation of Primary Collateral Pathways in the Circle of Willis During Vasospasm

The Circle of Willis is a redundant network of blood vessels that perfuses the brain. This manifold mitigates the negative effects of stroke by activating collateral pathways that help maintain physiologically meaningful perfusion. However, the role of collateral pathways during cerebral vasospasm – an involuntary constriction of blood vessels after subarachnoid hemorrhage – is not well-understood. I will present a novel modeling methodology to recreate the hemodynamics in the Circle of Willis before and during vasospasm, using computational fluid dynamics simulations and multimodality medical imaging. Computed tomographic angiography scans are segmented to create the vasculature, and transcranial Doppler ultrasound measurements of blood flow velocity provide patient-specific velocities. Bayesian analysis leverages information about the uncertainty in the measurements of diameters and velocities in multiple vessels to find an optimal model that satisfies all experimental measurements, and is constrained by mass conservation. Virtual angiograms using advection of a passive scalar agree closely with clinical angiography. A sensitivity analysis quantifies the changes in collateral flow rates with respect to changes in the inlet and outlet flow rates. This analysis is being applied to a patient cohort, in an effort to investigate the relationship between the location and severity of vasospasm, the patient's Circle of Willis anatomical variant, and the potential for activation of collateral pathways. The ultimate goal is to predict the location and severity of vasospasm immediately after subarachnoid hemorrhage.

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Simulation of the blood flow in the left atrium appendage (LAA)

The numerical simulations of the blood flow in the LAA are motivated by the problem of patient specific detection of the stagnation zones in the case of LAA fibrillation. The realistic flow rate exhibits in the left atrium high Reynolds numbers, corresponding to the turbulent behavior. The industrial codes often do not converge for naturally modeled boundary conditions (BC), or converge very slowly, for ultra-fine mesh only. They often exhibit instabilities (as the FSI with purely elastic wall). We study several settings: rigid wall and FSI boundary conditions, laminar flow (Navier-Stokes equations) or large eddy simulations (LES), Newtonian and non-Newtonian rheology (Carreau law), combine the inflow and outflow BC. The goal is to approximate complex models by simplified ones in order to accelerate computations and to insure the convergence.

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Multiscale mechanics of Aneurysms: what can biologists and clinicians learn from engineers?

Ascending thoracic aortic aneurysm (ATAA) is a life-threatening cardiovascular disease, leading to weakening of the aortic wall and permanent dilation. ATAA affects approximately 10 out of 100,000 persons per year in the general population, and this disease is associated to high risk of mortality and morbidity. The degeneration of the arterial wall at the basis of ATAA is a complex multifactorial process. Individual genetic, biological or hemodynamic factors are inadequate to explain the heterogeneity of ATAA development/progression mechanisms, thus stimulating the analysis of their complex interplay. We established a methodology to quantify non-invasively local stiffness properties of ATAAs using electrocardiographic-gated computed tomography (ECG-gated CT) scans. We showed strong relationship between the extensional stiffness and the rupture stretch of the aortic tissue, supported by biomechanical explanations. Then we discovered the interrelationship between the obtained local stiffness with other established markers of aortic function such as intravascular flow structures. The observed interrelationship corroborate computational predictions of ATAA progression coupling hemodynamics with mechanobiology after hemodynamic insult. Recently, we eventually related these results to the existence of a specific smooth muscle cell phenotype found in ATAA, exhibiting stronger traction forces and thicker morphologies. We will present all these results during the seminar and show how they open new perspectives for the development of a digital twin of aortic aneurysms.

Cristobal Bertoglio, University of Gröningen, the Netherlands

**Inverse Problems in Coupled Fluid-Solid Cardiovascular Models
from Imaging-based measurements**

We will present results related to the estimation from mechanical properties of arterial and ventricular walls using coupled fluid-solid models and a variety of measurements types, mainly coming from MRI(-like) measurements. We will review algorithms, problems and academic/experimental results in a comprehensive manner.

Machine learning and reduced order modelling for the real-time simulation of flow diverters deployment

Intracranial aneurysms (IAs) are abnormal dilations of cerebral vessels caused by localized weakening of the arterial wall. Their prevalence among the general population is estimated to be around 2-3%. IAs rupture leads to subarachnoid haemorrhage, a life-threatening type of stroke with an incidence of 10/100000 person-years and a mortality up to 50%.

Flow diverters are self-expanding devices used in the IAs endovascular treatment. They are placed in the parent artery covering the aneurysm neck to induce a gradual thrombosis of the sac and prevent coils, if present, from protruding out of the aneurysm space. Given the reduced access, limited visibility, high risk associated to these interventions, 3D images may be insufficient to plan the surgery satisfactorily. Hence, computational models can be a powerful tool to assist practitioners during the planning and interventional stages.

The mechanical behaviour of flow diverter is typically simulated using a finite element (FE) model where beam elements are used to model the wire. However, due to the large amount of degrees of freedom (DOFs) and the necessity to solve the contact with the wall, the computational time required by these traditional techniques is very high.

With the aim of reaching real-time simulations, we propose a machine learning and reduced order modelling framework to predict the stent deployed configuration. This builds up from previous work on optimized finite element simulations of stent deployment, which are here used to build large databases for training. The workflow was validated on an idealised cerebral artery with a saccular aneurysm and we studied the effect of six geometrical and surgical parameters on stent deployment.

During the workshop, we will show the preliminary results of this workflow and present the current efforts to extend our approach to patient-specific geometries.

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Can we reduce the computational burden of coagulation cascade models in cardiovascular simulations?

Thrombosis is a complex process that begins with the coagulation cascade, a series of biochemical reactions involving more than 40 species. Simulating the coagulation cascade requires solving tens of 3D unsteady advection-reaction-diffusion (ADR) equations, which is challenging. In this talk I will discuss a novel approach to drastically reduce the computational burden of these simulations, leveraging the dominance of advection transport over diffusive transport in arteries to simplify the system of PDEs that represent the ADR process to a system of ODEs and a single PDE. I will present a validation test for this methodology in a 2D cavity with a pulsatile flow (representative of an idealized left atrial appendage or aneurism) using a simple coagulation model with three biochemical species (thrombin, factor XIa, and protein Ca). The results show that the reduced model is cost-effective, accurately reproducing the spatio-temporal development of the coagulation cascade. The talk will close with a discussion of applications for this methodology in the Left Atrium, using CFD simulations or medical image data.

Constitutive artificial neural networks and their applications to soft tissue biomechanics

Constitutive modeling remains one of the most important problems in biomechanics. Biological tissues exhibit substantial interindividual differences and also change their properties during aging. Therefore, modeling the constitutive behavior of biological tissues one cannot simply rely on a library of once measured material parameters as it is typically possible for engineering materials. Rather one has to apply constitutive models tailor-made for a specific tissue of a specific patient at a specific age. To tackle the related challenges in constitutive modeling, it is key to understand the relation between the microstructure of biological tissues and their macroscopic mechanical properties.

Here, we introduce a novel machine learning framework that can bridge the gap between the microscale and macroscale. In particular, using data from mechanical tests, histological analyses and advanced imaging, it can predict the nonlinear macroscopic mechanical properties of arterial tissue. The incorporation of substantial prior knowledge from continuum mechanics and materials theory enables our framework to do so even on the basis of a relatively small amount of data and yet with high accuracy. Moreover, using so-called relevance propagation, our framework can quantify the role of different microstructural features for the macroscopic mechanical properties in an automatic, systematic and largely unbiased way opening up a host of new insights into the foundations of soft tissue biomechanics.

The machine learning framework we present bears promise to be transformative for our understanding of soft tissue mechanics and to provide new insights into the changes of soft tissues during aging and various diseases.

Mathematical model of heat transfer through pipe

The standard model for heat transfer between the fluid in the pipe and the exterior medium neglects the effects of the pipe's wall. Our goal is to prove that they are not always negligible. Comparing the ratio between diffusivities of the fluid and the wall (denoted by ε^q with the wall's thickness (denoted by ε), using rigorous asymptotic analysis, we find five different models for effective description of the heat exchange.

In all cases the effective equation remains the same heat conduction equation.

The difference lies in the effective boundary condition (EBC) describing the heat exchange through the pipe's wall S .

Modeling carcinoma activation and impact of surgery

Bleeding due to surgery leads to a pro-coagulant state, and its association with cancer, known since the 19th century and the works of Trousseau, may disrupt treatment. In this presentation, we are interested in the modeling of the regulation of the tumor coagulome. It is estimated that the balance between coagulation and fibrinolysis reactions determines the risk of thrombosis associated with the different types of tumors. Based on statistical analysis of transcriptional profiles of tumors, I will present a new mathematical model describing the interaction between the tumor micro-environment and the coagulome.

Joint works with A. Galmiche, Z. Saidak (Amiens University Hospital), and E. Hingant (LAMFA).

The Darcy-type boundary condition on a porous wall

Porous boundaries appear naturally in many real-life applications, starting from our skin (and other biological tissues), textile, concrete, rocks, sieves and filters that we use in our watering systems, etc. The porosity of the boundary plays an important role in global (and not just local) behavior of the flow. The appropriate boundary condition is not the no-slip condition any more, which can change the flow significantly.

The aim of this talk is to present the derivation of the new effective boundary condition for the fluid flow in a domain with porous boundary. We start from the Stokes system in a domain with an array of small holes on the boundary and on each hole we impose an appropriate dynamic condition, namely the value of the normal stress corresponding to the exterior conditions. The goal is to obtain the effective model by studying the convergence of the homogenization procedure, as the period of the porous boundary tends to zero. As a result, we propose the interface condition in the form of the generalized Darcy law. If no further assumptions are made concerning the isotropy of the geometry of the porous boundary, the obtained result generalizes the Beavers-Joseph condition. In the second part of the talk, we study the roughness-induced effects on the proposed Darcy-type boundary condition.

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Towards virtual aortic valve neocuspization (AVNeo)

We shall present our approach to development of a clinical decision support system which helps to optimize aortic valve neocuspization presurgically. The system combines a personalized mathematical model of the diastolic state of the aortic valve, an optimization procedure for choosing optimal shapes of the valve cusps, and a web interface used by clinicians at the preoperative stage. We compare several hyperelastic models for a reconstructed cusp within several finite element frameworks.

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Fluid–Structure Interaction Modeling of Ascending Thoracic Aortic Aneurysms in Simvascular

Ascending Thoracic Aortic Aneurysm (ATAA) is a cardiovascular disease characterised by a permanent dilatation on the ascending aorta. This pathology is associated with tissue degeneration which may be promoted, among other aspects by aging, disturbed hemodynamics and genetic predisposition. Modelling patient-specific aortic biomechanics using advanced computational techniques may be crucial to provide effective decision-making indices to enhance current clinical practices. In this work, a computational Fluid-Structure Interaction (FSI) framework assisted by Computed Tomography scan (CT) data that considers the in vivo initial stress state is presented. The simulations were implemented in the SimVascular open source software. The implementation of prestress in SimVascular is presented and discussed. The consideration of in vivo initial stress state contributed to reduce the simulation time and accuracy.