Thursday, July 26th, 14:00 **Room: T.B.A.**

MINISYMPOSIUM

NEW TRENDS IN MODELLING CARDIOVASCULAR DISEASES

Organizer
Nader El Khatib
Lebanese American University
nader.elkhatib@lau.edu.lb

Co-organizer
Adélia Sequeira
IST-ULisboa, Portugal
adelia.sequeira@math.tecnico.ulisboa.pt

Minisymposium Keywords: Cardiovascular diseases, Mathematical Modelling, Blood flow, Atherosclerosis, Numerical Simulations

According to the World Health Organization (WHO), Cardiovascular diseases (CVD) cause more than half of all deaths in Europe (about 46 times the number of deaths and 11 times the disease burden caused by AIDS, tuberculosis and malaria combined). But 80% of premature heart disease and stroke is preventable. The task of modelling cardiovascular diseases involves a variety of mathematical, numerical and computational challenges and leads to deeper understanding with some predictive perspectives.

Multiphysics models are developed in order to describe the dynamics of blood flows in large and micro vessels, the fluid-structure interaction that results in atherosclerotic arteries and aneurysms, dynamics of the immune system, cell population dynamics and many others.

This minisymposium is devoted to the mathematical modelling and numerical simulations of flows in the cardiovascular system and their mechanical and biochemical interactions with the surrounding tissues. It includes but is not limited to the following topics:

- Modelling chronic inflammatory reactions in blood vessels;
- Methods for modelling 3D fluid flows in realistic (patient specific) complex domains like arteries with bifurcations, porous deformable media;
- Modelling the atherosclerotic plaque formation and growth;
- Fluid-structure interaction: blood-plaque and blood-endothelium interactions;
- Cell transport processes: monocytes migration through the vessel wall, red blood cells transportation;
- Blood coagulation in plasma: clot formation and growth and its interaction with the blood flow.

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REACTION-DIFFUSION WAVES OF BLOOD COAGULATION IN QUIESCENT PLASMA AND IN FLOW

Vitaly Volpert

volpert@math.univ-lyon1.fr

Institut Camille Jordan, UMR 5208 CNRS, University Lyon 1, 69622 Villeurbanne, France

Joint work with Anass Bouchnita (Institut Camille Jordan) and Tatiana Galochkina (Institut Camille Jordan)

Keywords: Blood coagulation, Reaction-diffusion equations, Blood flow, Vessel occlusion.

One of the main characteristics of blood coagulation is the speed of clot growth. In the current work we consider a mathematical model of the coagulation cascade and study existence, stability and speed of propagation of the reaction-diffusion waves of blood coagulation [1]. We also develop a simplified one-equation model that reflects the main features of the thrombin wave propagation. For this equation we estimate the wave speed analytically. The resulting formulas provide a good approximation for the speed of wave propagation in a more complex model as well as for the experimental data.

Vessel occlusion is a perturbation of blood flow inside a blood vessel because of the fibrin clot formation. As a result, blood circulation in the vessel can be slowed down or even stopped. This can provoke the risk of cardiovascular events. In order to explore this phenomenon, we used a previously developed mathematical model of blood clotting to describe the concentrations of blood factors with a reaction-diffusion system of equations [2]. The Navier-Stokes equations were used to model blood flow, and we treated the clot as a porous medium. We identify the conditions of partial or complete occlusion in a small vessel depending on various physical and physiological parameters. In particular, we were interested in the conditions on blood flow and diameter of the wounded area. The existence of a critical flow velocity separating the regimes of partial and complete occlusion was demonstrated through the mathematical investigation of a simplified model of thrombin wave propagation in Poiseuille flow.We observed different regimes of vessel occlusion depending on the model parameters both for the numerical simulations and in the theoretical study. Then, we compared the rate of clot growth in flow obtained in the simulations with experimental data. Both of them showed the existence of different regimes of clot growth depending on the velocity of blood flow.

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TOWARDS PATIENT SPECIFIC BLOOD FLOW SIMULATIONS: A VELOCITY TRACKING APPROACH

Jorge Tiago

jftiago@math.tecnico.ulisboa.pt

CEMAT - Center for Computational and Stochastic Mathematics, Instituto Superior Técnico, Universidade de Lisboa

Joint work with Telma Guerra (CEMAT and Instituto Politécnico de Setúbal) and Adélia Sequeira (CEMAT and Dep. of Mathematics, Instituto Superior Técnico, Universidade de Lisboa)

Keywords: Data assimilation, Optimal control, Discretize-then-optimize, Finite element method, Blood flow modeling.

Vascular diseases, such as brain aneurysms and atherosclerosis, are the main cause of death in western countries. Such pathologies are not fully understood and lack precise diagnosis procedures. The mathematical modeling of blood flow in the cardiovascular system, both in normal and pathological conditions, can provide a computational tool to be used for diagnosis, prognosis or training purposes. In this sense, accurate numerical simulations must be achieved, in order to be considered reliable. However, important data needed to close the mathematical model is usually missing. To overcome such difficulty, data assimilation techniques can be used.

In this talk, we will describe a velocity tracking approach that can be applied in several scenarios where individualized simulations are looked for. Such approach is based on the solution of an optimal control problem. Several mathematical and numerical aspects related to these issues will be discussed ([3], [4], [5], [6], [7]).

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PATIENT SPECIFIC 3D NUMERICAL FLUID-STRUCTURE INTERACTION MODEL FOR BLOOD FLOW IN AN ATHEROSCLEROTIC ARTERY

Nader El Khatib

nader.elkhatib@lau.edu.lb

Department of computer science and Mathematics, Lebanese American University, Byblos, Lebanon

Joint work with Jorge Tiago (CEMAT - Center for Computational and Stochastic Mathematics, Instituto Superior Técnico, Universidade de Lisboa), Adélia Sequeira (CEMAT and Dep. of Mathematics, Instituto Superior Técnico, Universidade de Lisboa), Oualid Kafi (Instituto Superior Técnico, Universidade de Lisboa) and Diana Oliveira (Department of Mechanical Engineering, University of Birmingham)

Keywords: Atherosclerosis, Fluid-structure interaction, Blood flow, Wall shear stress.

The inflammatory process of atherosclerosis leads to the formation of an atheromatous plaque in the intima layer of the blood vessel. The plaque changes the geometry of the blood vessel by narrowing its lumen (interior layer). The plaque rupture may result from the interaction between the blood and the plaque. In previous studies [8, 9] we suggested two and three dimensional fluid-structure interaction (FSI) models to study the blood-plaque and blood-vessel wall interactions in an idealized geometry of a carotid artery.

In the current study, a patient specific 3D realistic geometry taken from MRI imaging is considered to study the FSI problem. But since the MRI image provides the 3D geometry only for the lumen of the artery, the endothelium layers should be virtually reconstructed in order to create the whole vessel wall shape. A similar procedure is applied to reconstruct the atherosclerotic plaque inside the artery.

An absorbing boundary condition is imposed directly on the outflow in order to cope with the spurious reflexions due to the truncation of the computational domain. The blood is considered as a non-Newtonian fluid that follows the Carreau-Yasuda model for blood viscosity. We show that the risk of plaque rupture is higher in the case of a moving wall, while in the case of a fixed wall the risk of progression of the atheromatous plaque is more important.

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MATHEMATICAL MODELING OF THE HYDRODYNAMICS OF A FREE-FLOWING LEUKOCYTE TOWARD THE ENDOTHELIAL WALL

Oualid Kafi

oualid.kafi@tecnico.ulisboa.pt

Instituto Superior Técnico, Univ. Lisboa, CEMAT, Lisbon, Portugal and Hassan II University of Casablanca, FSAC. B.P 5366, Maarif, Casablanca, Morocco

Joint work with Adélia Sequeira (Instituto Superior Técnico)

Keywords: Inflammatory response, Oldroyd-B model, Coupled deformation-flow, Numerical simulations.

Leukocyte recruitment is an essential stage of the inflammatory response and although the molecular mechanisms of this process are relatively well known, the influence of the hydrodynamic effects that govern the inflammatory response are still under study. Chronic inflammation may entail atherosclerosis, one of the most devastating cardiovascular diseases. Understanding this mechanism is of crucial importance in immunology and in the development of anti-inflammatory drugs.

In this study we use images and experimental parameters obtained by intravital microscopy in an *in vivo* animal model of inflammation to track the leukocytes trajectories and measure their velocities and diameters [10]. The rate-type Oldroyd-B model is used to capture the viscoelasticity of the leukocyte which is considered as a drop in order to analyze a mathematical model describing the deformation and flow of an individual leukocyte in a microchannel flow. In this model we consider a coupled problem between a simplified Oldroyd-B system and a transport equation which describes the density considered as non constant in the Navier-Stokes equations [11]. Numerical simulations of an individual and of two leukocytes under flow were performed. The results showed that velocity plays an important role in the motion, deformation and attraction of the cells during an inflammatory response. In fact, for higher inlet velocities the cell movement along the endothelial wall is accelerated and the attraction forces break faster. These results highlight the role of the mechanical properties of the blood, namely the ones influenced by the velocity field, in the case of inflammation.

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