International Advanced Fellowship 2023, Project CNFIS-FDI-2023-F-0214
Prof. Dr. Maria Neuss-Radu (FAU Erlangen-Nürnberg) in collaboration with Centrul de Cercetare Analiza Aplicata al UBB Cluj Napoca

Workshop
"Mathematical Modelling, Analysis and Simulation with Applications to Biomedical Processes"

UBB Cluj Napoca, October 9-10, 2023

Sala Club a Casei Universitarilor (Str. Em. de Martonne, 1)

organized by Prof. Dr. Maria Neuss-Radu and Prof. Dr. Radu Precup

Invited Speakers

Prof. Dr. Drs. h.c. Willi Jäger (IWR, University of Heidelberg)
Dr. Michael Gruber (Clinic of Anesthesiology, Hospital at the University of Regensburg)

Schedule

Time	Monday	Tuesday
9.50-10.00	Opening	
10.00-10.55	Jäger	Precup
10:55-11.20	*coffee break*	*coffee break*
11:20-12.15	Gruber	Knoch
12:15-13:10	Nechita	Neuss-Radu
19:00	*Workshop dinner*	

Abstracts (in the Order of Presentations)

Modelling, analysis and simulations of layers controling transitions between compartments and of epithelial layers in organisms - Challenges and contributions to mathematical, computational and biomedical research

Willi Jäger (IWR, University of Heidelberg)

Gaining an integrative understanding of complex interrelationships in biological and medical systems across all scales is a challenge for interdisciplinary research, especially to mathematics and computational sciences. This became particularly evident in the COVID pandemic, where neither sufficient standard knowledge nor data were available and could be used to fight this disease. Covid in its serious phase can develop into viral sepsis, leading to life-threatening multiple organ dysfunction. Sepsis is defined as a life-threatening multiple organ dysfunction, caused by an inadequate host response to an infection, a disease that can lead to an irreversible collapse of the entire organ system. This lecture will demonstrate with selected examples that mathematical modeling and simulations can qualitatively and quantitatively improve insights into important processes of the infection and the disease, the response of the immune system, the effects on physiological processes on all cellular, tissue and organ level in the body of the host. Our experience is based on research in Sepsis started in 2015. Our research results demonstrate that boundary layers and interfaces are crucial for healthy dynamical processes. The investigation must build on information about the basic structures and functional program of the pathogens and its interactions with the host at the cell and tissue level and at level of the organ system. Of particular importance are the interactions with the immune system, which usually is responding with inflammation as defense against the infection. Disordered responses often occur, especially influenced by a hypoxia, caused by the virus in case of COVID. Since this infection is mainly an air-born, the alveoli in the lungs, which are important for gas exchange, are particularly affected by the virus, which can lead to hypoxia, harmful to the entire body.

A main aim of this lecture is to show with selected examples that mathematical modelling and simulations of the underlying biochemical - biophysical processes, including the mechanics of fluid and solids, may help to understand arising critical disorders better und develop measures to control them. It will also become clear that the upcoming mathematical and computational problems are exciting both in theory and in application and solutions cannot simply be taken off the shelf. The challenges arise in particular from the difficulties in the considered real systems. Reduction of their complexity and

controlling nonlinearities, the arising multi-scales and or randomness, but also the lack of sufficiently good data require new concepts and methods. In particular, the following aspects will be addressed:
- Epithelial and endothelial layers in parts of organisms, controlling transitions and the coupling of processes in different compartments, are highly important for the dynamics of subsystems and finally of the organ system. Effective model equations for the relevant processes can be derived and simulated using mathematical and computational multiscale methods.
- Mitochondrial, epithelial, vascular and further dysfunctions, which seriously endanger the supply with crucial substances and the energy, necessary for the functioning of the system, can be identified by setting up and investigating a model system, based on real data.
- Coupling biomechanics with biochemistry and fluid dynamics, including poro-elastic media, is a hot topic in mathematical and computational research in biosciences and medicine. It is opening up a huge field of future research and transfer to biotechnological and medical applications.

This lecture is based on joint research with Maria Neuss-Radu, Markus Gahn, Jonas Knoch, Gennady Bocharov, Manfred Thiel, Telma Silva, Adelia Sequeira, Yifan Yang, Thomas Richter, Valeria Malieva, Peter Bastian.

Cellular Layers and Neutrophils - A laboratory approximation

Michael Gruber (University of Regensburg)

Cellular layers form the most important barriers in organisms. To elucidate their properties a laboratory model is to be implemented using a porous inorganic support plate and tracer substances as possible basis for diffusion investigations. Human Neutrophil Granulocytes are the first line of defense against intruders. A description of these cells as part of the inborn immune system is given in the second half of the presentation. A possible combination of both parts might be the basis for a new observation model of immune responses.

Ill-posed data assimilation problems: analysis and numerics

Mihai Nechita (UBB Cluj Napoca)

Numerical analysis for partial differential equations (PDEs) traditionally considers problems that are well-posed in the continuum. However, when a part of the boundary is inaccessible for measurements or no information is given on the boundary at all, the problem might be unstable and its numerical approximation more challenging.

In this talk, we discuss ill-posed unique continuation/data assimilation problems in which noisy measurements are given in a subset of the computational domain. We present a framework for stabilized finite element method (FEM) solving such problems based on PDE-constrained optimization with discrete regularization. We consider convection-diffusion equations, for which conditional stability estimates in suitable norms can be used to obtain error estimates in local L^2- and H^1-norms. We also consider fluid-structure interaction (FSI) models with velocity measurements given, where such stabilized FEM can be used in applications related to blood flow and medical imaging data (e.g. 4d-flow MRI data measuring the 3d velocity field of a tissue). Numerical results will be presented and analyzed. Based on joint work with Erik Burman, Miguel Fernndez, Lauri Oksanen.

Control of cell evolution after bone marrow transplantation

Radu Precup (UBB Cluj Napoca)

We focus on a mathematical model of cell evolution after stem cell transplantation. A control problem is formulated to achieve the post-transplant correction of the hematological evolution. To solve the problem, an iterative algorithm based on the idea of lower and upper solution is proposed and used.

Numerical Simulation of Effective Models for Transport Processes in Deformable Porous Media within Mixed Eulerian/Lagrangian Framework

Jonas Knoch (FAU Erlangen-Nürnberg)

We present in this talk an effective model for transport processes in periodically perforated elastic media, taking into account also cyclic elastic deformation as it occurs e.g. in lung tissue due to respiratory movement. The underlying microscopic problem consists of a linear elasticity equation for the displacement within the Lagrangian framework, posed on a fixed domain and a diffusion equation for the concentration within the Eulerian framework, posed on the current deformed domain. After a transformation of the diffusion equation onto the fixed domain, we derive the upscaled model by means of a formal asymptotic expansion. The system is nonlinearly coupled through effective coefficients, which also take into account the periodic microstructure. We develop and study numerical methods for our problem and perform simulations that are inspired by a bioengineered microdevice which is able to reconstitute critical lung functions (Lung-On-A-Chip). The simulations shed light into the sensitivity of the model with respect to several experimental parameters such as frequency or magnitude of the cyclic mechanical strain. This is joint work with Markus Gahn (Heidelberg), Nicolas Neu (Erlangen) and Maria Neuss-Radu (Erlangen).

Derivation of coupled Stokes-Plate-Equations for fluid flow through thin porous elastic layers

Maria Neuss-Radu (FAU Erlangen-Nürnberg)

We consider two fluid-filled bulk domains which are separated by a thin periodically perforated layer consisting of a fluid and an elastic solid part. Thickness and periodicity of the layer are of order ϵ, where ϵ is small compared to the size of the bulk domains. The fluid flow is described by an instationary Stokes equation and the solid via linear elasticity. We perform the rigorous homogenization of the porous structure in the layer and the reduction of the layer to an interface in the limit $\epsilon \to 0$ using two-scale convergence. The effective model consists of the Stokes equation coupled to a time-dependent plate equation on the interface including homogenized elasticity coefficients carrying information about the micro structure of the layer. In the zeroth-order approximation we obtain continuity of the velocities at the interface, where only a vertical movement occurs and the tangential components vanish. The tangential movement in the solid is of order ϵ and given as a Kirchhoff- Love displacement. Additionally, we derive higher-order correctors for the fluid in the thin layer. This is a joint work with Markus Gahn (Heidelberg) and Willi Jger (Heidelberg).