Bindi Brook

Structure, function and growth in asthmatic airways

Inflammation, airway hyper-responsiveness and airway remodelling are well-established hallmarks of asthma, but their inter-relationships remain elusive. In order to obtain a better understanding of their inter-dependence, we have developed a number of mechanistic models at, and across, cell- and tissue-scales, accounting for coupled biochemical and mechanical processes. In this talk I will give an overview of these models and our efforts at integrating experimental data from different sources at these different scales. I will highlight both the novel insights gained, as well as the challenges we have faced. Ultimately our aim is to develop powerful predictive models that can be used to develop new therapies; to this end I will also discuss how we intend to progress our work towards informing novel therapies that rely on the emerging field of mechanopharmacology.

Dirk Drasdo

Quantitative single-cell-based modeling reveals predictable response of growing tumor spheroids on external mechanical stress, and how this informs a virtual liver twin

Abstract:

Model simulations show that the response of growing cell populations on mechanical stress follows the same functional relationship and is predictable over different cell lines and growth conditions despite the response curves look largely different. We develop a hybrid model strategy in which cells are represented by coarse-grained individual units calibrated with a high-resolution mathematical cell model and parameterized by measurable biophysical and cell-biological parameters. Cell cycle progression in our model is controlled by volumetric strain, the latter being derived from a bio-mechanical relation between applied pressure and cell compressibility. After parameter calibration from experiments with mouse colon carcinoma cells growing against the resistance of an elastic alginate capsule, the model adequately predicts the growth curve in i) soft and rigid capsules, ii) in different experimental conditions where the mechanical stress is generated by osmosis via a high molecular weight dextran solution, and, after calibration of one model parameter in absence of applied stress, iii) for other cell types with different growth kinetics. We finally integrate the mechanical insight into an agent-based model of liver regeneration after partial hepatectomy and after drug-induced damage, as well as of fibrosis development and bile duct formation, as an important step towards a digital liver twin.

Liesbet Gerit

Title: Connecting Mechanics and Biology in a multiscale model of osteoarthritis

Abstract: Long-term changes in mechanical loading In the knee can lead to destabilization of articular homeostasis and a switch of phenotype, as e.g. observed in osteoarthritis (OA). In this context, multiscale models can be used to capture the translation of mechanical signals

from the joint level down to the cellular level, and subsequently into intracellular biochemical processes.
In our research group, a coupled multiscale model of the human knee joint is being developed to estimate the changes in cell phenotype and activity of the relevant cell secreted factors as a result of (patho)physiological loading at the joint level. The multiscale model incorporates in-silico models at three different length scales: 1) Finite Element (FE) model of the knee joint, 2) FE model of the chondrocyte, and 3) intracellular gene/protein regulatory network for mechanotransduction. Using this multiscale model, the effect of meniscectomy (removal of the meniscus) on the progression of OA was studied. The increased mechanical loading led to a buildup of inflammatory cytokines over time, inducing to a phenotypic switch the chondrocytes. Using the intracellular model, we executed an in-silico screening, complemented by dedicated in-vitro experiments, to identify suitable therapeutic agents to arrest this phenotypic switch in OA.

If it is possible to mention co-authors on the abstract, I would like to mention Satanik Mukherjee (Biomechanic Section, KU Leuven, Belgium) and Raphaelle Lesage (Biomechanics Section, KU Leuven, Belgium). My own affiliations are (1) GIGA in silico medicine, University of Liège, Belgium / Biomechanics Section, KU Leuven, Belgium / Skeletal Biology and Engineering Research center, KU Leuven, Belgium.

A. Movchan
(University of Liverpool)

Eigenvalue problems in the dynamics of fluid-solid biological systems

The talk gives an overview of the recent work focused on the dynamics of biological systems, which include stented blood vessels. The study, published in [1-4], includes dynamics of aneurysms, as well as stented blood vessels affected by stenosis.

A mathematical model is introduced [1] to address the regimes of rapid changes in the blood pressure in the network of stented blood vessels. The focus is on the wave phenomena and, in particular, wave reflection induced by a structured stent.

This study has been advanced further [2, 3] to address different types of three-dimensional stenting structures with repetitive patterns. The analytical modelling has been complemented by the numerical study of the Floquet-Bloch waves under time-harmonic conditions, as well as simulations in the transient regime.

In the paper [4], a model was presented to analyse the nature of forces, acting on a sealed abdominal aortic aneurysm. It was shown that deformations of the aorta and of the EVAS system, induced by static forces and vibrations, lead to irreversible changes in the endovascular sealing structure.
The talk is based on the results of the joint work with L. Argani, D. Bigoni, G. Carta, S. Frecentese, N.V. Movchan, T.K. Papathanasiou, and the team of vascular surgeons R.K. Fisher, R.G. McWilliams, F. Torella, M.L. Wall.

References:

Papathanasiou TK, Movchan AB, Bigoni D., (2017) Wave reflection and transmission in multiply stented blood vessels.
Proc Royal Soc. A, 473(2202):20170015. doi: 10.1098/rspa.2017.0015.
Frecentese S., Argani LP, Movchan AB, Movchan NV, Carta G, Wall ML, (2018) Waves and fluid-solid interaction in stented blood vessels. Proc Royal Soc A, 474 (2209), 20170670, doi: 10.1098/rspa.2017.0670.
Frecentese S, Papathanasiou TK, Movchan AB, Movchan NV., (2019)
Dispersion of waves and transmission-reflection in blood vessels with structured stents.
Proc Royal Soc. A, 475(2223):20180816. doi: 10.1098/rspa.2018.0816.
Argani LP , Torella F, Fisher RK, McWilliams RG, Wall ML, Movchan AB, (2017) Deformation and dynamic response of abdominal aortic aneurysm sealing. Scientific Reports Nature, 7(1):17712. doi: 10.1038/s41598-017-17759-3

R Ocone

From Applications to Fundamentals –the power of multiscale modelling

Engineers often work with macroscopic models that are employed to facilitate the design, the development and the operability of equipment, technologies and processes. Although such models are said to be “predictive”, they often provide answers about trends and qualitative features only. Models that are able to provide quantitative answers with good accuracy are less common, especially when dealing with complex systems and processes. Some examples of causes that hinder the models’ predictability are: inadequate methodologies able to “scale-up” the influence of the physics at the microscopic level; the inability to properly describe the meso-scale; the lack of proper constitutive equations.
In the area of particulate flow, existing models and theories lack the robustness, predictability and flexibility required to handle the totality of phenomena that such flow may exhibit. Some unwanted industrial issues (such as particle agglomeration) and their management still remain largely as an “art”. Current practice is often based mainly on *ad-hoc* models for each specific flow condition and on operator experience.
This talk will focus on the kinetic theory for granular flow (KTGF) which, based on the analogy between solid particles and gas molecules, has been employed to model the macroscopic behaviour of particulate flow with good success. Nevertheless, the KTGF presents limitations that the talk will explore in relation to its challenges. Our current work in the field will be presented and critically.

A.V. Panfilov

Mechano-electric feedback and initiation of cardiac arrhythmias

The heart beat is controlled by electrical excitation waves which propagate through the heart and initiate cardiac contraction. Contraction of the heart also affects the process of wave propagation resulting in a complex global feedback phenomenon known as mechano-electrical feedback (MEF). MEF has been studied in electrophysiology for well over a century and may have both pro-arrhythmic and arrhythmogenic consequences. Some time ago we have developed an approach to study the phenomenon of MEF as coupled reaction-diffusion-mechanics system, which combines the parabolic reaction-diffusion equations with the elliptic equations of finite elasticity. For electrophysiological tissue properties we use models of cardiac tissue either low dimensional of the FitzHugh Nagumo type, or detailed ionic model for human ventricular cells developed in our group. For representation of mechanics we either use a finite element approach, or a discrete mass-lattice framework.

We report on the results on our studies on the various mechanisms of initiation of cardiac arrhythmias due to MEF caused by stretch activated channels, discuss other MEF mechanisms and unsolved questions.