VII Soft Tissue Workshop
Politecnico di Milano
11th-13th June, 2025

It is a great pleasure for me to welcome everyone to this Seventh Soft Tissue Workshop. There is a wide-ranging programme of talks highlighting the exciting progress being made in Soft Tissue modelling and simulation, including machine learning, and in the translation of fundamental science and engineering research into clinical applications and healthcare. The number of presentations by talented early career researchers shows the importance of the work and bodes well for the future of the field.

Sadly, two members of our SofTMech Centre have passed away since the previous workshop in Glasgow in 2023. Dr Jakub Köry was a research associate with SofTMech at the University of Glasgow, and died unexpectedly in May, 2024. He was a well-liked and supportive member of our group with a promising career ahead of him. He worked closely with Anna Pandolfi, Peter Stewart, Xiaoyu Luo and me on discrete-to-continuum models of cytoskeletal filament networks and of the cornea. Professor Xiaoyu Luo passed away in February this year after a number of years of living with cancer. She was passionate and enthusiastic about her research, and an inspirational leader who set up and organised the Soft Tissue Workshops. She was also the driving force in winning the funding that established SofTMech, and the Executive Director of the Centre. Both are sorely missed by colleagues, friends and family.

Many thanks are due to the Local Organising Committee of Christian Vergara, Anna Pandolfi, Francesco Migliavacca and Luca Dedé, who have dedicated much time and effort to bring this Workshop to POLIMI. We are all especially indebted to our SofTMech Adminstrator, Dr Gillian Brown, whose hard work, dedication and support in challenging circumstances has enabled us to hold this meeting.

Professor Nick Hill

School of Mathematics & Statistics
University of Glasgow

Director of the SofTMech Centre
www.softmech.org

Predictive Hybrid Digital Twins: Theory, Methods, and Applications.

Linwei Wang
Rochester Institute of Technology

Advances in digital-twin technology within the healthcare sector are confronted with a long-standing challenge: instead of a one-time static construction that fits observed data, a digital twin needs to rapidly adapt to live data and to provide predictive decision support beyond what has been observed. Attaining these breakthroughs face two fundamental hurdles. First, current mechanistic models struggle with rapid adaptation and imperfect knowledge, while data-driven models are limited in interpretability and generalizability. Second, the prevalent twinning strategies based on data-fitting, previously largely tailored for mechanistic models, become the root cause of an un-identifiable data-driven model with limited predictive capabilities. In this talk, we discuss our recent efforts in addressing these challenges towards the ultimate goal of predictive twinning: a what-how & when meta-learning framework for learning to rapidly and continually personalize a latent forecasting function endowed with strong predictive ability owing to its theoretical identifiability, and hybrid neural-mechanistic modeling that combines the generalizable and interpretable mechanistic know-how with flexible data-driven learning to resolve the residual between general knowledge and individuals' data. We will extend these discussions to applications in learning personalized digital twins of the heart.

Physics-informed machine learning for emulation of the systemic blood flow circulation

Dirk Husmeier, William Ryan, Vladislav Vyshemirsky, Mette Olufsen
University of Glasgow, Mathematics & Statistics

Abstract:
There have been impressive advancements in the application of physics to the modelling of complex cardio-physiological systems. In principle this affords opportunities for deeper insight into the nature, cause and best treatment of cardio-physiological diseases. However, the corresponding mathematical models typically don't accommodate closed-form solutions and entirely rely on numerical simulation procedures instead. This becomes problematic in clinical applications, where model calibration and patient specific parameter estimation are indispensable, calling for repeated forward simulations from the model as part of an iterative optimization or sampling procedure at subsantial computational costs. In my talk, I will focus on a fluid dynamics model of the blood flow in a 17-vessel network connected to the human ascending aorta. I will discuss how physics-informed machine learning can be used to build effective and efficient emulators that allow accurate estimation of the physiologica
l parameters at substantially reduced computational costs. In particular, I will focus on physics-informed neural networks (PINN). The key idea is to embed physical laws—such as conservation of mass, energy, momentum, or governing differential equations—into the training process of the neural network. This results in a machine learning surrogate model of the original fluid dynamics model that can make reliable predictions about blood flow and pressure time courses at a fraction of computational time that would be needed for a numerical integration of the original partial differential equations. The blood flow-pressure relation depends on the blood vessel geometry (the so-called vasculature), various boundary conditions and the physiological parameters, which act as inputs to the PINN. I will demonstrate how this provides a framework for compuationally efficient and accurate physiological parameter estimation and uncertainty quantification, which clearly outperforms more traditional methods.

Towards a digital twin for myocardial ischemia: from coronary hemodynamics to cardiac perfusion

Giovanni Montino Pelagi, Andrea Baggiano, Giovanni Valbusa, Gianluca Pontone, Nicholas Hill, Christian Vergara
Politecnico di Milano, Dipartimento di Chimica, Materiali e Ingegneria Chimica "Giulio Natta"

Abstract:
Introduction – Effective management of patients suffering from coronary artery disease greatly benefits from the combined knowledge of coronary hemodynamics and cardiac perfusion at the tissue level. The use of a digital twin to quantify the relevance of coronary lesions would overcome the limitations of the late-stage clinical exams, such as invasiveness or high radiation exposure. We present a framework to address the most critical issues: personalized boundary conditions, 3D multiscale modelling of hemodynamics, and personalized coronary-myocardium association.
Methods – A fully 3D finite-element model of the entire coronary circulation is employed, featuring Navier-Stokes description of the hemodynamics in the epicardial coronaries coupled with a multicompartment Darcy formulation for the microvasculature. The model includes a special formulation accounting for microvessels compliance and cardiac contraction. Personalized boundary conditions are built as hyperemic pressure waveforms starting from routine patients measurement at rest. The geometric coupling between each epicardial coronary and the corresponding perfusion region is implemented through a novel tool, based on ex-vivo detailed morphometric human coronary data, which accounts for the presence of transversal vessels along the main branches. Simulations are run using the Finite Elements software lifex, developed at MOX (DMAT), in cooperation with LaBS (DCMC), PoliMi.
Results – The model successfully reproduces all the characteristic features of coronary hemodynamics, including phasic flow patterns with high diastolic arterial inflow, mostly diastolic perfusion and high systolic venous outflow. Applied to human patients (CT-reconstructed geometries), the model shows high predictive power with respect to the Fractional Flow Reserve (FFR) index and good accordance with stress CT perfusion maps, although precise localization of perfusion defects is challenging. When validated against detailed coronary data, our tool for coronary-myocardium association shows significantly better performances with respect to the previous strategy, allowing for a more precise evaluation of the functional relevance of coronary lesions.

TITLE: Redefining the Fiber Architecture: A Breakthrough in Atrial Digital Twin Modeling

AUTORI: Roberto Piersanti[1,3,*], Ryan Bradley[2,3], Syed Yusuf Ali[3], Alfio Quarteroni[1,5], Luca Dede'[1], Natalia A. Trayanova[3,4]

AFFILIATIONS:

[1] MOX - Laboratory of Modeling and Scientific Computing, Dipartimento di Matematica, Politecnico di Milano, Milano, Italy

[2] Research Computing, Lehigh University, Bethlehem, Pennsylvania, USA

[3] ADVANCE - Alliance for Cardiovascular Diagnostic and Treatment Innovation, Johns Hopkins University, Baltimore, USA

[4] Department of Biomedical Engineering, Johns Hopkins University, Baltimore, USA

[5] Mathematics Institute, École Polytechnique Fédérale de Lausanne, Lausanne, Switzerland (Professor Emeritus)

* presenting author

e-mail:roberto.piersanti@polimi.it

ABSTRACT:

A crucial aspect of developing atrial digital twins (ADT)—virtual models of patients' atria—is the precise assignment of myocardial fibers, which play a key role in tissue characterization. However, reconstructing atrial fibers from medical imaging remains challenging. As a result, mathematical models are commonly employed for fiber generation in ADT. Current methodologies rely on semi-automatic techniques, are designed for specific atrial morphologies, and lack thorough validation against imaging-derived fiber data. In this study, we present a novel atrial rule-based method that enables highly detailed myofiber orientation mapping and robust regional annotation across bi-atrial geometries of varying complexity. We evaluate the method on eight high-resolution bi-atrial geometries reconstructed from a sub-millimeter Diffusion-Tensor-Magnetic-Resonance Imaging (DTMRI) dataset of human atrial fibers. Validation is performed by quantitatively reproducing the fiber architectures observed in DTMRI, with a detailed comparison against ground truth data. Additionally, we analyze electrophysiology (EP) simulations using both rule-based and DTMRI fibers to assess differences in electrical behavior. Our results demonstrate that our method surpasses current state-of-the-art fiber modeling aprroach, highlighting its superior accuracy. This underscores the importance of incorporating highly detailed fiber orientations in EP simulations. This work represents a significant advancement in the development of physics-based atrial digital twins, setting a new standard for fiber prescription in ADT.

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Advanced Statistical Inference of Myocardial Stiffness: A time series Gaussian Process approach of emulating Cardiac Mechanics for real-time clinical decision support

Yuzhang Ge,
University of Glasgow

Abstract:
Our work is primarily motivated to determine the passive stiffness of the myocardium from the measurement of the left ventricle (LV) volume at various time points, which is crucial for diagnosing cardiac physiological conditions. Although there have been significant advancements in cardiac mechanics modelling, the tasks of inference and uncertainty quantification of myocardial stiffness remain challenging, with high computational costs preventing real-time decision support. We adapt Gaussian processes to construct a statistical surrogate model for emulating LV cavity volume during diastolic filling to overcome this challenge. As the LV volumes, obtained at different time points in diastole, constitute a time series, we apply the Kronecker product trick to decompose the complex covariance matrix of the whole system into two separate covariance matrices, one for time and the other for biophysical parameters. To proceed towards personalized health care, we further integrate patient-spec
ific LV geometries into the Gaussian process emulator using principal component analysis (PCA). Utilizing a deep learning neural network for extracting time-series left ventricle volumes from magnetic resonance images, Bayesian inference is applied to determine the posterior probability distribution of critical cardiac mechanics parameters. Tests on real-patient data illustrate the potential for real-time estimation of myocardial properties for clinical decision-making. These advancements constitute a crucial step toward clinical impact, offering valuable insights into posterior uncertainty quantification for complex cardiac mechanics models.

MICROMECHANICAL ANALYSIS OF THE EFFECTIVE STIFFNESS OF POROELASTIC COMPOSITES AND ITS APPLICATION TO MYOCARDIAL INFARCTION

PRESENTER: RAIMONDO PENTA

JOINT WORK WITH LAURA MILLER

Within this work we investigate the role that the microstructure of a poroelastic material has on the resulting elastic parameters.

We are considering the effect that multiple elastic and fluid phases at the same scale [1] have on the estimation of the materials elastic parameters when compared with a standard poroelastic approach [2].

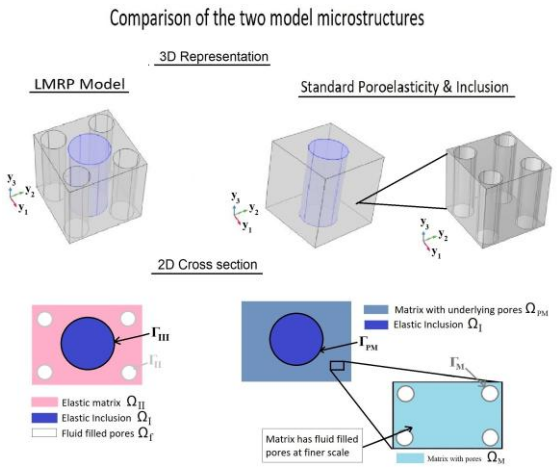

Figure 1: Comparison of the microstructures of both approaches highlighting the direct same scale approach of LMRP and the two-step approach of previous models.

We provide the 3D periodic cell problems with associated boundary loads that are required to be solved to obtain the effective elasticity tensor for both model setups. We then perform a 2D reduction of the cell problems, again presenting the 2D boundary loads that are required to solve the problems numerically.

The results of our numerical simulations show that whenever investigating a poroelastic composite material with porosity exceeding 5% then the model [1] should is better incorporating the structural details in the Young's moduli E_1 and E_3 and the shear C_{44}.

Whenever the porosity exceeds 20% it should also be used to investigate the shear C_{66}. We find that for materials with less than 5% porosity that the voids are so small that a standard poroelastic approach or the model [1] produce the same results.

We investigate how physiologically observed microstructural changes induced by myocardial infarction impact the elastic parameters of the heart [3].

The results of our simulations agree with the physiological observations that can be made post-infarction. That is, the infarcted heart is much stiffer than the healthy heart but with reperfusion of the tissue it begins to soften. We also observe that with the increase in myocyte volume of the non-damaged myocytes the myocardium also begins to soften. With a measurable stiffness parameter the results of our model simulations could predict the range of porosity (reperfusion) that could help return the heart to the healthy stiffness. It would also be possible to predict the volume of the myocytes in the area surrounding the infarct from the overall stiffness measurements.

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Acknowledgements:

RP is partially funded by EPSRC Grants EP/S030875/1 and EP/T017899/1.

Homogenized modelling of the electro-mechanical behaviour of a vascularized poroelastic composite representing the myocardium

Laura Miller, Raimondo Penta
University of Strathclyde, Mathematics and Statistics

Abstract:
We propose a novel model for a vascularized poroelastic composite representing the myocardium which incorporates both mechanical deformations and electrical conductivity. Our structure comprises a vascularized poroelastic extracellular matrix with embedded elastic inclusions (representing the myocytes) and we consider the electrical conductance between these two solid compartments. There is a distinct length scale separation between the scale where we can visibly see the connected fluid compartment separated from the poroelastic matrix and the elastic myocyte and the overall size of the heart muscle. We therefore apply the asymptotic homogenisation technique to derive the new model. The effective governing equations that we obtain describe the behaviour of the myocardium in terms of the zero-th order stresses, current densities, relative fluidâ€"solid velocities, pressures, electric potentials and elastic displacements. It effectively accounts for the fluid filling in the pores of th e poroelastic matrix, flow in the vessels, the transport of fluid between the vessels and the matrix, and the elastic deformation and electrical conductance between the poroelastic matrix and the myocyte. This work paves the way towards a myocardium model that incorporates multiscale deformations and electrical conductivity whilst also considering the effects of the vascularisation and indeed the impact on mechanotransduction.

Title: Model-based learning of local soft tissue contractility from limited kinematic data

Simone Pezzuto
Università di Trento

Abstract: Active solids are a large class of materials, including both living soft tissues and artificial matter, that share the ability to undergo strain even in absence of external loads. While in engineered materials the actuation is typically designed *a priori*, in natural materials it is an unknown of the problem. In such a framework, the identification of inactive regions in active materials is of particular interest. An example of paramount relevance is cardiac mechanics and the assessment of regions of the cardiac muscle with impaired contractility. The impossibility to measure the local active forces directly suggests us to develop a novel methodology exploiting kinematic data from clinical images by a variational approach to reconstruct the local contractility of the cardiac muscle. By finding the stationary points of a suitable cost functional we recover the contractility map of the muscle. Numerical experiments, including severe conditions with added noise to model uncertainties, and data knowledge limited to the boundary, demonstrate the effectiveness of our approach. Unlike other methods, we provide a spatially continuous recovery of the contractility map without compromising the computational efficiency.

Multiscale Modelling of Fluid Flow in a Lymph Node

Alberto Girelli, Giulia Giantesio, Alessandro Musesti, Raimondo Penta
UniversitÃ Cattolica del Sacro Cuore (Brescia), Dipartimento di Matematica e Fisica

Abstract:
Lymph nodes are essential components of the immune system, where lymph fluid, containing immune cells and antigens, is processed. Their structure consists of a porous lymphoid compartment and a surrounding thin subcapsular sinus that allows free fluid flow. In this talk, we present a mathematical model, derived using the asymptotic homogenization technique, to capture the multiscale nature of fluid flow within the lymph node. We employ numerical simulations to investigate flow patterns, pressure distributions, and shear stress in detail. These results provide valuable insights into the mechanical environment of the lymph node, advancing our understanding of its role in immune function and offering a foundation for exploring therapies for lymphatic disorders.

Computational study to assess hemodynamic forces in descending thoracic aortic aneurysm

Francesca Duca, Daniele Bissacco, Luca Crugnola, Chiara Faitini, Maurizio Domanin, Francesco Migliavacca, Santi Trimarchi, Christian Vergara
Politecnico di Milano, LaBS, Department of Chemistry, Materials and Chemical Engineering 'Giulio Natta'

Abstract:
Descending Thoracic Aortic Aneurysm (DTAA) is defined as a localized diameter increase of the descending thoracic aorta. TEVAR is a minimally invasive DTAA treatment based on the deployment of a self-expandable stent-graft. To avoid device migration, it is important to identify the correct Landing Zones (LZs) where to perform the stent-graft sealing. In this context, we propose a Fluid-Structure Interaction (FSI) computational framework with the aim of assessing the DTAA hemodynamics and providing quantitative information, at the pre-operative level, useful to predict TEVAR outcomes.
Our FSI framework includes a turbulence model and two different Young's Moduli for the healthy and the aneurysmatic portion of the aortic wall, considering DTAA stiffer. In our analysis, we propose also a risk index useful to correlate hemodynamic forces with the risk of stent-graft migration associated to each LZ.
We first build nine DTAA ideal scenarios varying the Aortic Arch (AA) type and the aneurysm ubication. Our findings demonstrate that DTAA hemodynamics is profoundly disturbed, with the presence of flow recirculation and transition to turbulence, especially in configurations with a steeper AA. We notice an increase of pressure in configurations with less steep AA and of drag forces for configurations with distal DTAA. In all the configurations, the risk index shows the greatest values in the aneurysm and, for each configuration under study, we try to suggest the most suitable LZs for the device sealing.
Then, we apply our methods to three patient-specific models built by segmenting pre-operative CTA scans of patients who underwent TEVAR. Results in such cases show great affinity with the corresponding ideal scenarios, highlighting that specific morphological feature of DTAA play an important role in hemodynamics and its effects.
Our pre-operative analysis might be a useful tool for clinicians to identify suitable LZs to perform a correct stent-graft sealing.

In silico models of post-dilatation in TAVI patients

Letizia Maria Perri, Benedetta Grossi, Francesco Migliavacca, Gianluigi Condorelli, Giulio Stefanini, Giulia Luraghi
Politecnico di Milano, Department of Chemistry, Materials and Chemical Engineering

Abstract:
Balloon post-dilatation in Transcatheter Aortic Valve Implantation (TAVI) aims to reduce paravalvular leakage (PVL). This study develops a computational model to simulate post-dilatation in patient-specific anatomies, predicting complications and improving clinical outcomes. A post-dilatation balloon model is reconstructed, and simulations of deflation, crimping, and inflation are conducted. The balloon is then integrated into patient-specific anatomical models based on preoperative CT images. Two patients undergoing balloon post-dilatation with implanted self-expandable valves are analyzed using finite-element simulations. Model validation is performed through qualitative and quantitative comparisons with postoperative clinical data, including angiographies and CT images. Additionally, fluid dynamics simulations are conducted to evaluate and predict the PVL with and without post-dilatation. A qualitative match is observed between simulated and in vivo stent configurations. Among all
post-dilation simulations, the maximum and minimum orifice area percentage differences between the simulated and segmented stents are 2.33 Â± 1.32% and 1.14 Â± 0.92%, respectively. Eccentricity errors are 1.7301% (max) and 0.1112% (min). Compared to simulations without post-dilatation, orifice area and eccentricity improvements reach 70% and 75%, respectively. Preliminary fluid dynamics results indicate enhanced PVL prediction and evaluation. The findings confirm that post-dilatation significantly impacts stent configuration, reducing errors in key parameters. Including this phase in simulations enhances computational modeling of TAVI, providing a valuable tool for clinical decision-making and predicting post-implantation complications.

How calcifications can impact TEVAR procedures: insights from computational analyses

Giulia De Campo, Anna Ramella, Sara Barati, Giulia Luraghi, Virginia Fregona, Maurizio Domanin, Robin Heijmen, Santi Trimarchi, Francesco Migliavacca
Politecnico di Milano, Ingegneria Chimica e dei materiale 'Giulio Natta'

Abstract:
Thoracic endovascular aneurism repair (TEVAR) is a mini-invasive technique used to treat the pathological tract of the aorta. TEVAR guidelines discourage the procedure when high calcified aortas are present, in particular in the landing zone regions, due to the possibility of developing endoleak; however, clinicians, sometimes, proceed with the operation off-label despite these recommendations. This study analyzes, in-silico, the effects of the calcification on a patient-specific anatomy after a TEVAR procedure, testing different idealized and patient-specific calcification geometries and mechanical properties.

A patient-specific anatomy without calcification from Professor Hejimen of Radboud University Medical Center, Netherlands, was taken into consideration for this study. Four different idealized calcification models and three different elastic modules of the calcification were tested: 2.75 MPa, 50 MPa and 20 GPa. A total of thirteen simulations of the TEVAR procedure were performed, following the â€˜tracking method.

Comparing the models from a qualitative point of view, the stent-graft apposition looked the same for all the models, suggesting a good stent-graft apposition even in the presence of calcifications. Relevant results were also achieved with the analysis of the von Mises stresses calculated on aorta and calcification: as the Young modulus of the calcification was reduced from 20 GPa to 2.75 MPa, the stresses on the calcification post-TEVAR implant were highly reduced.

From this analysis the calcifications appeared to function as load-bearing structures, reducing stress on the aorta while increasing stress on calcifications. This was a significant finding, as an increase in wall stress on the aorta was associated with a higher risk of aneurysm rupture. In this case, however, calcifications helped reduce the average von Mises stresses on the aorta, potentially lowering the likelihood of aneurysm rupture. This study suggests that TEVAR could still be feasible, at least from the perspectives of stress analysis and qualitative device comparison.

Personalized computational hemodynamics framework to assess the long-term performance of Transcatheter Aortic Valve Implantation

Luca Crugnola, Laura Fusini, Chiara Catalano, Salvatore Pasta, Gianluca Pontone, Christian Vergara
Politecnico di Milano, Chemistry, Material and Chemical Engineering "Giulio Natta"

Abstract:
Transcatheter Aortic Valve Implantation (TAVI) was introduced for treating aortic stenosis in elderly patients at surgical risk and is currently becoming the first-choice therapy even in low-surgical-risk younger patients [1]. In this context, it is particularly relevant to assess the long-term performance of the bioprosthetic valves used for TAVI. This computational retrospective study aims to investigate the relationship between early post-TAVI aortic hemodynamics and Structural Valve Deterioration (SVD), which is the main limiting factor to the durability of TAVI valves. We build on previous findings [2] to propose computational risk scores able to identify a premature onset of SVD.
The study population comprises patients with and without SVD at long-term follow-up exam. We reconstruct pre-operative patient-specific geometries and we create post-TAVI scenarios by virtually inserting a valve model representing the particular bioprosthetic valve implanted in that patient. Computational Fluid Dynamics (CFD) simulations are performed in such virtual scenarios imposing an inflow condition, personalized by considering patient-specific cardiac outputs and velocity temporal evolutions. The numerical results are then post-processed with the aim of discriminating between the SVD and non-SVD groups.
The CFD results showed that the TAVI valve highly influences aortic hemodynamics, characterized by a high velocity jet in the ascending aorta and vortical structures around this jet. Depending on the patient-specific geometry and blood flow features, the evolution of the jet and vortices generates shear stress patterns on the aortic wall and bioprosthetic leaflets that are used to formulate the risk scores.
The results of this study suggest that post-TAVI blood dynamics may have an influence on the development of SVD. Moreover, the proposed risk scores could potentially assist clinicians in a patient-specific planning of follow-up exams, moving toward a personalized care.
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[2] Crugnola et al; CMPB; 259:108517; 2025

The importance of inelasticity when simulating balloon deployment in diseased arteries

Silvia Renon, Sean McGinty, Ankush Aggarwal, Richard Good
University of Glasgow, Biomedical engineering - School of science and engineering

Abstract:
Introduction
Elastic recoil following drug-eluting stent (DES) or drug-coated balloon (DCB) deployment is widely used to assess procedural success. Despite its name, elastic recoil is not a purely elastic displacement, as arteries only partially restore their original shape. This phenomenon is particularly significant in DCB applications. While inelastic arterial models exist, most focus on stents, and simplified plaque models fail to capture the complexity of atherosclerotic plaques. To the best of our knowledge, no existing literature has employed a realistic inelastic plaque model for lesion preparation modelling and drug elution simulations. This computational analysis aims to accurately predict the state of the diseased artery after device deployment, therefore taking into account inelasticity in patient specific plaque geometries and lesion preparation techniques.
Methods
Finite element analysis was used to simulate arterial mechanics. Patient-specific plaque geometries were obtained from literature, and various plasticity models were tested with different plaque compositions. Internal pressure and semi-compliant balloons were deployed, and procedural efficacy was assessed using Elastic Recoil Ratio (ERR) and Lumen Gain Ratio (LGR), along with stress-strain distributions.
Results
Plastic strain and stress distributions were analysed across patient-specific geometries. Geometry 1 was tested with lipidic and calcified plaques, while Geometry 2 was analysed with uniform and mixed plaque compositions. The study compared perfect plasticity and linear hardening models, selecting the latter for further simulations due to its clinical relevance.
Discussion
Plaque composition influenced plastic strain distribution and residual stresses after balloon expansion. These effects contribute to plaque damage and potential morphological changes post-lesion preparation, which may impact drug transport following DCB use. Understanding lesion preparationâ€™s role in plaque morphology is crucial for improving DCB efficacy. This study enhances post-procedure predictions by incorporating realistic inelastic plaque modelling, supporting better lesion preparation strategies and therapeutic outcomes.

Modelling post EVAR vascular adaptations (G&R) and validation

Sathish Kumar Marimuthu, Prof Robert Geelkerken(UofTwente), Dr Robbie Brodie(Terumo Aortic Ltd, UK), Dr Craig Maclean(Terumo Aortic Ltd, UK), Dr Sean McGinty(Uni. o fGlasgow, UK), Prof Nicholas A Hill(Uni.of Glasgow, UK)
University of Glasgow, James Watt School of Engineering

Abstract:
All biological tissues and organs constantly remodel due to stress or changes in the homeostatic conditions. Following endovascular aortic repair, the aorta could grow and remodel over time to reduce the excessive stresses caused by the less compliant and oversized stent grafts (compared to the aorta). The most proximal rings of the Anaconda device (TerumoAortic, UK) are designed with high stiffness and diameter bigger than the aorta to obtain better fixation. These influence the increase in the diameter of the aorta and the reduction in the contact force between the stent graft and the aorta wall. Hence, it is necessary to understand and predict this adaption to minimise complications such as device migration and endoleaks.
This study aimed to understand the growth and remodelling (G&R) following stent graft implantation using a volumetric growth model with growth along the fibre direction. The framework was divided into pre and post-growth phases, and the aorta geometry was assumed to be a simple cylinder with only the medial layer. The modified GOH model was used to model the aortaâ€™s hyperelastic anisotropic behaviour. To validate the framework, finite element simulation results were compared with abdominal aortic aneurysm patient data acquired at pre-operative discharge stages. Then, the growth parameters were estimated using follow-up (up to 2 years) CT scan data. The dilation of the two proximal rings was captured, which closely matches the CT scan data, and the results from this study clearly show the reduction in aorta wall stresses due to vascular adaptation. Also, the peak maximum principal stresses on the Nitinol stent struts were reduced.
This framework could be expanded to using full patient-specific aorta geometries obtained by segmenting the CT scan to design efficient patient-specific stent grafts with reduced unfavourable arterial remodelling and other post-surgery complications.

How does thrombus composition influence the thrombectomy outcome? An in silico study

Virginia Fregona, Giulia Luraghi, Behrooz Fereidoonnezhad, Frank JH Gijsen, Charles BLM Majoie, Jose Felix Rodriguez Matas, Francesco Migliavacca
Politecnico di Milano, Department of Chemistry, Materials and Chemical Engineering "Giulio Natta"

Abstract:
Endovascular thrombectomy (EVT) aims at restoring blood flow in case of acute ischemic stroke by removing the thrombus occluding a large cerebral artery. During the procedure with stent-retriever, the thrombus is captured within the device, which is then retrieved, subjecting the thrombus to several forces, potentially leading to its fragmentation. Histological analysis on retrieved thrombi allowed to associate the thrombus composition (in terms of RBCs and fibrin content) to the outcome of the procedure: fibrin-rich thrombi are more difficult to retrieve, while RBC-rich thrombi are more prone to fragmentation. Moreover, in silico studies, along with mechanical characterisation of thrombi, can enhance our understanding of the EVT, helping the development of new devices and interventional strategies. Our group previously validated a numerical approach to study EVT able to account for thrombus fragmentation in the commercial software LS-DYNA.

In this study, the same methodology was employed to explore the applicability of the chosen failure criterion to EVT simulations and the impact of thrombus composition on the outcome of the in silico procedure. For the first time, human clot analogues experimental data were applied to this methodology. Clot analogues of three different compositions (0% RBCs, 1% RBCs, and 40% RBCs) were tested, and a material model incorporating failure was calibrated, followed by a verification analysis. Finally, the calibrated material model was used to perform EVT simulations, combining the three tested thrombus compositions with three different stent retriever models.

The experimental tests confirmed a compression-tension asymmetry in the stress-strain curves, showing decreasing stiffness with increasing the red blood cell (RBC) content. Applying the resulting material models to EVT simulations demonstrated: (i) the dependency of the failure criterion on the thrombus mesh size, (ii) a greater tendency for RBC-rich thrombi to fragment, and (iii) increased difficulty in retrieving RBC-poor thrombi compared to RBC-rich thrombi.

Title: A model of fiber reorientation in fiber-reinforced biological composite materials

Alessandro Giammarini
Politecnico di Milano

The study of the biological tissues that incorporate fibers among their constituents is an important area of research in Biomechanics and has received considerable attention though the years [1,2,3]. Indeed, quantifying how the fibers affect the mechanical and hydraulic properties of fiber-reinforced tissues answers several biological questions and poses a number of modeling and computational questions.

We consider biological materials that are composed of a soft and porous matrix, saturated with a fluid and reinforced by collagen fibers, and we propose to enrich the framework put forward in [1-5] by studying two remodeling processes that, at different scales, influence the inner structure of the matrix and the reorientation of the fibers embedded in it. One type of remodeling concerns the development of plastic-like distortions [3], while the other addresses the possibility that fibers reorient under stimuli that can be coded as mechanical. We describe the latter form of remodeling as a Langevin-like process [6], from which we can obtain the probability density function describing the probability that a fiber is aligned along a given direction by solving the associated Fokker–Planck equation.

We solve numerically the highly nonlinear system of equations combining, across different scales, the aforementioned processes, and we compare our results with experimental data available in the literature for the articular cartilage.

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Title: A model of fiber reorientation in fiber-reinforced biological composite materials

Alessandro Giammarini
Politecnico di Milano

The study of the biological tissues that incorporate fibers among their constituents is an important area of research in Biomechanics and has received considerable attention though the years [1,2,3]. Indeed, quantifying how the fibers affect the mechanical and hydraulic properties of fiber-reinforced tissues answers several biological questions and poses a number of modeling and computational questions.

We consider biological materials that are composed of a soft and porous matrix, saturated with a fluid and reinforced by collagen fibers, and we propose to enrich the framework put forward in [1-5] by studying two remodeling processes that, at different scales, influence the inner structure of the matrix and the reorientation of the fibers embedded in it. One type of remodeling concerns the development of plastic-like distortions [3], while the other addresses the possibility that fibers reorient under stimuli that can be coded as mechanical. We describe the latter form of remodeling as a Langevin-like process [6], from which we can obtain the probability density function describing the probability that a fiber is aligned along a given direction by solving the associated Fokker–Planck equation.

We solve numerically the highly nonlinear system of equations combining, across different scales, the aforementioned processes, and we compare our results with experimental data available in the literature for the articular cartilage.

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Modelling cerebrovascular pathology and amyloid beta spreading in Alzheimer's disease

Alain Goriely
University of Oxford

Alzheimer's disease (AD) is associated with the accumulation and dissemination of amyloid beta (Aβ) proteins in the brain, a process now known to be intimately linked with vascular dysfunction. Recent evidence demonstrates that Aβ oligomers cause contraction of microvascular mural cells, leading to capillary constriction and elevated flow resistance. In turn, this hypoperfusion enhances Aβ production and impairs its clearance, establishing a pathological positive feedback loop. In this talk, I will introduce a mathematical model that captures the interplay between Aβ dynamics and capillary function, incorporating both the local protein–vascular interactions and the prion-like propagation of Aβ. The model reveals a bistable regime in which both healthy and diseased states coexist stably, with a critical protein seed threshold required to initiate disease onset. We investigate how this bistability influences disease spread across the brain's structural connectome. Finally, we propose a novel mathematical formulation of the two-hit vascular hypothesis, showing how spatially localized perfusion deficits—such as those arising from embolic strokes or leptomeningeal atherosclerosis—can act as initiators of global disease progression.

Numerical Modeling of Protein Spreading and brain atrophy in Neurodegeneration

Mattia Corti[1] P. F. Antonietti[1], V. Pederzoli[1], D. Riccobelli[2]
1. MOX, Dipartimento di Matematica, Politecnico di Milano
2. SISSA, Trieste

Abstract: Neurodegenerative diseases significantly impact the global population, affecting millions of individuals worldwide. Some of these diseases, categorized as proteinopathies (for example, Alzheimer's and Parkinson's diseases), are characterized by the accumulation and propagation of toxic proteins (prion-like hypothesis). Protein agglomerations ultimately lead to the degeneration of neurons and brain atrophy. This talk proposes a novel multiphysics coupled model that describes the interplay between toxic protein dynamics and induced tissue atrophy. We discretize the proposed coupled model using advanced discretization schemes that support agglomerated meshes, enabling efficient high-fidelity numerical simulations while maintaining a high-quality representation of brain sulci and internal interfaces. We present realistic simulations based on patient-specific brain geometries reconstructed from magnetic resonance images to predict the development of the neurodegeneration process.

This research is supported by ERC SyG NEMESIS (Grant Agreement 101115663) funded by the European Union.

A Matrix Differential Equation Approach for Strongly Coupled Arterial Blood Flow and Cerebral Tissue Perfusion Simulations

KUO, JEN-FENG, Lucia Kuo, Alfons Hoekstra, Tamás István Józsa
Universiteit van Amsterdam, Informatics Institute

Computational modelling of blood flow in vascular networks and brain tissue is crucial in understanding organ-scale cerebrovascular conditions like ischaemic stroke. Coupled models predict the impact of arterial blockages on tissue perfusion, but verification, sensitivity analysis, and uncertainty quantification remain challenging due to strongly coupled differential and algebraic equations.

This study presents analytical solutions for a simplified linear problem describing blood flow in a strongly coupled model of large arteries and capillaries within the brain tissue. Both models have been the subject of previous investigations regarding cerebral blood flow in health and disease, e.g., [doi.org/10.1016/j.compbiomed.2023.107543, doi.org/10.1016/j.compbiomed.2021.104802]. The primary variable in the porous continuum model is perfusion pressure coupled with a steady-state arterial network model based on arterial blood pressure. The solution applies boundary and interface conditions to accurately represent blood flow between arterial and tissue domains.

The framework is tested using a single bifurcation including three arteries connected to a tissue column. Analytical results are compared with numerical solutions from finite element (continuum) and direct linear system solvers (network model). The findings provide a rigorous framework for model verification, sensitivity analysis, and uncertainty quantification. The results also highlight the need for sufficiently low tolerance in relation to interface conditions in numerical simulations.
The model is applied to analyse the impact of large artery occlusion on tissue perfusion, supporting future 2D and 3D studies. This analytical framework enhances in silico stroke research which aims to assist in clinical decision-making and digital twin-based healthcare solutions. Potential applications within the GEMINI project (https://eur03.safelinks.protection.outlook.com/?url=https%3A%2F%2Fdth-gemini.eu%2F&data=05%7C02%7CGillian.Brown%40glasgow.ac.uk%7Cb733c26694c74b6d26d908dd4c45aa2c%7C6e725c29763a4f5081f22e254f0133c8%7C1%7C0%7C638750586742537964%7CUnknown%7CTWFpbGZsb3d8eyJFbXB0eU1hcGkiOnRydWUsIlYiOiIwLjAuMDAwMCIsIlAiOiJXaW4zMiIsIkFOIjoiTWFpbCIsIldUIjoyfQ%3D%3D%7C60000%7C%7C%7C&sdata=6aL3HPb%2F09JAdNRalx0MH%2BE%2ByvVtLph6dS296znKtqQ%3D&reserved=0) are discussed to pave the way for advancing stroke treatments through computational modelling. The proposed framework contributes to multi-scale and multi-physics tissue models for medical device and drug development.

Mechanical behavior of hyper-calcified cerebral embolus analogs in acute ischemic stroke

Keefe Manning, Jose L. Monclova, Scott D. Simon, Francesco Costanzo
The Pennsylvania State University, Biomedical Engineering

Abstract:
Stroke is a leading cause of death worldwide, with approximately 20% of surgical interventions resulting in complications. The underlying causes of these complications remain unclear, but calcified emboli are thought to pose a significant risk. This study aims to characterize the nonlinear mechanical behavior of calcified cerebral emboli and fit these data to viscoelastic models.

To create clot analogs, human donor blood was reconstituted and recalcified in a Chandler loop at 37°C for 1 hour. Clots were then incubated in either 0.2M or 2M $CaCl_2$ for 1 or 10 days. Uncalcified clots were aged in cell media, while unaged clots were tested immediately (day 0). Mechanical testing was performed under tension and compression at strain rates of 5%, 10%, and 15% per second, with clots deformed to 80% strain to characterize their rate-dependent behavior.

Clots exhibited strain stiffening in compression and linear behavior in tension. Hypercalcified clots (2M $CaCl_2$) showed a tenfold increase in high-strain stiffness. Day 10 clots exhibited more than twice the peak stress of day 1 clots and nearly quadruple the stresses of clots extracted from patients. The mechanical response of hypercalcified clot analogs was well captured by an Arruda-Boyce viscoelastic model.

Age-dependent calcification significantly increased clot stiffness and fracture risk. Reduced porosity and increased stiffness suggest a clot phenotype that is more resistant to thrombectomy and thrombolytic treatments, highlighting the need for improved therapeutic strategies. This dataset provides a library of mechanical properties that can be integrated into numerical simulations of endovascular thrombectomy (EVT) to improve treatment outcomes.

A multiphase model for fluid dynamics in damaged tissue

Simone Bonfiglio, Ana Carpio, Carmelo Filippo Munafò, Patrizia Rogolino
University of Messina, Department of Mathematical and Computer Sciences, Physical Sciences and Earth Sciences

Abstract:

Tissues are clusters of similar cells that cooperate to perform specific functions within the human body, their internal mechanisms still being intensively researched. Tissues are formed by a mixture of cells, liquid in which chemical substances are dissolved, and an extracellular matrix made of polymer threads that keep the cells bound together. When tissues are damaged due to mechanical or chemical causes, they react by sending a fluid flow to the part involved. Leaving aside this healing role, the uncontrolled concentration of fluid in the involved tissue has an impact on its function and, consequently on human health.
Tissues can be represented as a mixture [3,4] with three fluid components [2] consisting of a biomass phase (cells and polymeric matrix), which is split into two components - alive and dead cells, with volumetric fractions $\phi_{\rm a}(\mathbf{x}, t)$ and $\phi_{\rm d}(\mathbf{x}, t)$ respectively, and a fluid component, $\phi_{\rm f}(\mathbf{x}, t)$, that carries nutrients, waste, and toxicants.

The mixture [1] is governed by the mass and linear momentum balance laws coupled with advection-reaction-diffusion equations for the concentrations of nutrients $ c_{\rm n}(\mathbf{x},t)$ and toxicants $c_{\rm p}(\mathbf{x},t)$.
In our paper we develop and simulate a model, by using a the open acces freeFEM platform [5] that solves systems of partial differential equations through finite element methods. In particular, the action of toxicants and the fluid infiltration caused by toxicants' damage on the tissue are investigated.

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Cardiocirculatory model personalization through data-driven approaches and uncertainty quantification

Andrea Tonini,
Politecnico di Milano, Mathematics

Abstract:
Mathematical cardiocirculatory models provide valuable insights into diagnostics and the impacts of cardiovascular diseases. Many models have been developed to account for the different components of the heart and cardiovascular system, encompassing ionic, electrophysiology, activation, mechanical and circulatory aspects[1].

With such sophisticated tools, the need for model personalization has arised to study the effects of various diseases on the cardiovascular system. Model personalization requires solving inverse problems. The calibration of model parameters is performed using noisy clinical data, which are related to the outputs of the cardiocirculatory models. Due to the high computational cost of solving inverse problems, neural networks efficiently handle these problems.

We investigated the effects of partial anomalous venous return using a 0D cardiovascular model[2]. The model determined the dependance of the shunt fraction (i.e. the fraction of blood bypassing the left atrium) on the pulmonary precapillary resistance. Additionally, we examined the relationship between shunt fraction and pulmonary vascular resistance, right ventricular passive elastance and right ventricular relaxation time for septal defects. The results demonstrated
consistency with clinical knowledge.

We updated the atrial and ventricular ionic models within a 3D-0D electromechanical model[1] to accurately represent the calcium ion transient driving cardiac contraction. The updated model was validated against healthy ranges of clinical quantities.

Finally, we developed a neural network methodology to solve inverse Bayesian problems. This approach enables the efficient computation of the maximum a posteriori parameter estimate and its uncertainty based on noisy observational data.

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A theoretical model for focal adhesion and cytoskeleton formation in non-motile cells

Peter Stewart, Gordon R. McNicol, Matthew J. Dalby
University of Glasgow, Mathematics and Statistics

Abstract:
To function and survive cells need to be able to sense and respond to their local environment through mechanotransduction. Crucially, mechanical and biochemical perturbations initiate cell signalling cascades, which can induce responses such as growth, apoptosis, proliferation and differentiation. At the heart of this process are actomyosin stress fibres (SFs), which form part of the cell cytoskeleton, and focal adhesions (FAs), which bind this cytoskeleton to the extra-cellular matrix (ECM). The formation and maturation of these structures (connected by a positive feedback loop) is pivotal in non-motile cells, where SFs are generally of ventral type, interconnecting FAs and producing isometric tension. In this study we formulate bio-chemo-mechanical continuum models (in both one and two spatial dimensions) to describe the coupled formation and maturation of ventral SFs and FAs. We use a set of reaction–diffusion–advection equations to describe three sets of biochemical events: t
he polymerisation of actin and subsequent bundling into activated SFs; the formation and maturation of cell–substrate adhesions; and the activation of signalling proteins in response to FA and SF formation. The evolution of these key proteins is coupled to a viscoelastic description of the cell cytoplasm and the ECM. We employ this model to understand how cells respond to external and intracellular cues in vitro and are able to reproduce experimentally observed phenomena including non-uniform cell striation and cells forming weaker SFs and FAs on softer substrates.

Multiscale Analysis of Electrically Stimulated Vascularised Tumours: A Patient-Specific Theoretical and Computational Approach

Zita Borbala Fulop, Raimondo Penta
University of Glasgow, Mathematics and Statistics

Abstract:
Electroporation-based therapies such as electrochemotherapy (ECT) hold great promise for improving cancer treatments. While highly effective for superficial tumours, its application for deep-seated malignancies is challenged by complex microstructural properties, and current models often lack a multiscale theoretical framework to capture those phenomena. Here, we develop and solve a novel system of coupled partial differential equations of Darcy-Laplace type obtained by applying the asymptotic homogenisation technique. We study the tumour response stimulated by an electric field, deriving effective macroscale equations for pressure, velocity, and electric potential while incorporating both hydraulic and electric microscale tissue heterogeneities.
Our coupled multiscale approach bridges the gap between the tumour microstructure and macroscale dynamics, offering a more comprehensive understanding of how tumour size, morphology, and hydraulic-electrical interactions influence interstitial flow. Using patient-specific data, we further investigate how the shape of the microscale cell inclusion affects the macroscale domain, specifically the pressure profile and electric field distribution. We present a parametric analysis of the hydraulic conductivity tensor and macroscale numerical simulation results for pressure and velocity fields, highlighting the role of the electric field in modulating fluid flow. Our findings provide meaningful insights toward advancing ECT protocols.

Mariam Almudarra, Ariel Ramirez Torres
University of Glasgow, School of Mathematics & Statistics

Abstract:
This work examines the dynamics of avascular tumour growth, focusing on the inelastic distortions that arise from growth and are introduced through a multiplicative decomposition of the deformation gradient tensor. Building on [1], we derive a governing law for the evolution of growth-induced inelastic distortions by linking generalised forces with kinematic descriptors associated with the growth tensor. This formulation, based on the dissipation inequality, reveals the interactions between inelastic distortions and the source and sink terms in the mass balance equations, highlighting the interplay between mechanical stresses and chemical interactions.

A key aspect of this study is the role of the chemicals' non-local behaviour (in time and/or space), which we identify as a significant factor in the growth process [2]. To represent the non-local properties of these chemicals, assumed to be generated by the tumour's complex and multi-scale microenvironment, we introduce integro-differential operators with power-law-type kernels. We then examine how the anomalous behaviour of these chemicals affects key variables governing the system's evolution and offer new perspectives on the challenges of modelling growth processes in heterogeneous biological systems.

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Electrical impedance spectroscopy-based oral cancer diagnosis using tissue engineering and computational models

Malwina Matella, Rachel Furmidge, Zhicheng Lin, Helen Colley, Craig Murdoch, Zi-Qiang Lang, Dawn Walker
University of Sheffield, School of Computer Science
Abstract:
In 2024, there were 11,000 new cases and almost 4,000 deaths, associated with oral cancer in the UK [1]. The current oral cancer diagnosis involves a visual inspection of the lesion, followed by a biopsy - a painful and expensive procedure, with long turnaround times. Electrical impedance spectroscopy (EIS) is an emerging technology permitting a non-invasive and real-time identification of cancerous changes in various organs (such as cervical epithelium, skin or breast tissue) based on the influence of cellular level tissue structure on the opposition to the flow of an alternating electrical current. Oral tissues are more varied in nature than these other tissue types, which may pose a challenge in the application of EIS to oral cancer detection.
In a pilot study, we aim to explore the feasibility of EIS measurement to enhance the diagnosis of oral cancer. To achieve this, we cultivate tissue-engineered models of healthy and cancerous oral epithelium and measure their electrical impedance using a tetrapolar EIS device. Histology images provide morphological information on the micro- (cell sizes) and macroscale (epithelium layer thicknesses) of these tissues. These are used to develop virtual tissue constructs to simulate the expected EIS measurements using finite element (FE) methods, to further broaden the understanding of the relationship between the tissue structure and their electrical properties in healthy and cancerous tissue.
Comparison of the preliminary in vitro EIS measurements and computed impedance from the virtual tissue constructs revealed a promising agreement, in terms of characteristics of the real and imaginary components of impedance spectra in the healthy and cancerous oral epithelia. In the future work, we plan to validate the FE model to use it to augment the in vitro measured EIS sample size to develop a machine learning algorithm to differentiate between cancerous and non-cancerous tissues, based on EIS measurements.
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A multiscale model of material failure and its applications to soft tissue tearing

Andrew Brown, Nicholas Hill, Raimondo Penta, Steven Roper
University of Glasgow, School of Mathematics and Statistics

Abstract:
Modelling material failure is an open problem in continuum mechanics, with many modelling techniques filling the panorama of damage mechanics. Our research has focused on creating a model that can account for how microscopic changes effect the macroscopic process of material failure. To that end, we have developed a novel multiscale model of the damage phase field method. This was achieved via new analytical methods introduced for the upscaling of the damage phase field. We also introduced new numerical methods for solving a damage phase field model. As a result, we have a rigorous multiscale model of material damage, which can be employed to study a myriad of physical phenomenon. Including processes such as plasticity, cyclic damaging or sudden material failure. This work of course has many applications in the realm of material science, but we are more interested in clinical applications.

Our long-term goal is to apply our modelling methods to biological phenomena of soft tissue tearing. Namely, diseases such as aortic dissections and ACL ruptures. By applying a multiscale model of these diseases, we may potentially understand what microscopic changes in the body are making people more susceptible to these diseases. The clinical applications of these models would include predicting the occurrence of soft tissue tearing and preventing it, or a better understanding of the long-term effects of treatment. This would allow clinicians to make more informed decisions, leading to better patient outcomes.

On inverse elasticity methods for anisotropic hyperelastic materials

Jose Felix Rodriguez Matas
Politecnico di Milano

Biomechanical studies of the cardiovascular system require patient-specific geometries. However, such geometries are typically generated from gated medical images, in which the vascular tissue is under pressure—that is, the imaged tissue is in a prestressed state. Therefore, identifying the zero-pressure geometry allows for a more accurate estimation of device performance and risk assessment.

Iterative methodologies based on solving a sequence of forward problems have been developed, in which the zero-pressure configuration (or reference configuration) is corrected based on the difference between the target geometry and the current deformed configuration. While these methods are straightforward to implement within the classical finite element framework, they may lead to excessive mesh distortion.

A direct methodology based on inverse elastostatics (IE), originally applied to isotropic hyperelastic compressible and quasi-incompressible materials, has been proposed. The theory has since been extended to anisotropic compressible hyperelastic materials. This lecture elaborates on the implementation of the IE framework for quasi-incompressible anisotropic hyperelastic materials, incorporating exact linearization of the governing equations to improve numerical efficiency. The accuracy and convergence properties of the implementation are demonstrated through several examples

Keratoconus Growth Model: : A 10-Year Case Study

Benedetta Fantaci, Alessandra Turra, Jose Felix Rodriguez Matas, Jos Rozema, Begoña Calvo
Universidad de Zaragoza, Department of Mechanics

Abstract:
Keratoconus (KC) is a bilateral disease characterized by asymmetrical steepening and thinning of the cornea, caused by a loss of its mechanical properties. A model capable of reproducing KC progression could be crucial for predicting disease's evolution. In this work, we apply a previously developed KC growth model [1] to evaluate its accuracy against patient-specific data.
Topographical data from a 10-year follow-up of a keratoconic patient were retrieved. A patient-specific finite element corneal model was constructed. An intraocular pressure of 15 mmHg was applied to the posterior surface and the corneal base was fixed. A heterogeneous HGO material model was used.
To model the growth a multiplicative decomposition of the deformation gradient F into a growth component F_g and an elastic component F_e was performed: $F = F_e·F_g$.
To initiate the growth process, the material properties of a localized pathological area progressively degraded over time until reaching 50% of their initial value both in the corneal thickness and radial direction. When strains increase locally, the growth process begins and Fg is updated according to the law:
\begin{equation}
F_g^{(t+1)} = F_g^t + K^+ \left(\frac{F_{g \max} - F_g^t}{F_{g \max} - 1} \right)^\gamma \cdot dt
\end{equation}
where $F_{g max}=1.1$ is a growth limit introduced to avoid unlimited growth, constants $K^+=0.5$ and $γ=1$ module the growth velocity and dt is the time increment. Model's parameters were adjusted to properly reproduce the disease's progression with respect to clinical data.
The KC progression simulated by the model was compared with patient's disease progression in terms of pachymetric thinning (i.e. thickness thinning throughout time). A mean error of 0.3% and a maximum error of 1.1% were obtained with respect to clinical data. In the corneal model at the end of the simulated 10 years, a small bulge is visible, replicating the pathological cornea. The proposed formulation is capable of capturing disease's evolution.

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An Experimental Investigation of the Biomechanical Effects of Epi-On Corneal Collagen Crosslinking in Porcine and Human Models

Anna Pia Bonuomo[1,2], Ibrahim Seven[3], Pat Lopath[3], Paolo Fogagnolo[4], Federica Boschetti[2], Anna Pandolfi[1]

[1] Civil and Environmental Engineering Department, Politecnico di Milano, Milan, Italy,
[2] Chemistry, Materials, and Chemical Engineering Department, Politecnico di Milano, Milan, Italy,
[3] TECLens, Inc. (9 Riverbend Dr S, Stamford, CT 06907, USA),
[4] Eye Clinic, ASST Santi Paolo e Carlo, University of Milan, Health Sciences Department.

Background: Corneal collagen crosslinking (CXL) is an established therapy for halting the progression of corneal ectasia by strengthening the stromal architecture. This study investigated the biomechanical effects of transepithelial (epi-on) CXL through two separate experimental series: one conducted on porcine corneas and the other on human donor tissue. Porcine corneas were primarily used to develop and validate a consistent experimental protocol, due to their accessibility and anatomical similarity to the human cornea. Epi-on CXL offers several clinical advantages over the conventional epi-off approach, such as reduced risk of infection, faster epithelial healing, and improved patient comfort. Although the epithelium presents challenges in riboflavin diffusion and UV-A penetration, advancements in delivery techniques have enhanced its efficacy, making epi-on a promising alternative in corneal crosslinking therapies.

Methods: Fresh porcine corneas were mounted on a custom anterior inflation chamber and preconditioned with cyclic pressurization between 4 and 20 mmHg. Riboflavin was delivered using a reservoir lens for 30 minutes under 15 mmHg pressure, which is considered the physiological intraocular pressure (IOP) in a healthy human eye. The baseline hydration level was carefully controlled by adjusting the NaCl concentration in both the riboflavin and saline solutions at different stages to maintain tissue biomechanics. Epi-on corneal crosslinking (CXL) was then performed with UV-A irradiation at 4 mW/cm² for 10, 20, or 30 minutes. Corneal shape changes were tracked in real time via 3D optical coherence tomography (OCT). A theoretical model based on linearized shell theory was used to estimate the increment of the corneal stiffness. The same experimental workflow was applied to human donor corneas, with adaptations to account for their increased variability. Preconditioning pressures were extended up to 32 mmHg, and hydration control proved more challenging due to post-mortem changes in tissue permeability.

Results and Discussion: The linearized shell theory established a quantitative relationship between corneal stiffness and the UV-A irradiation dose. All experiments showed a significant increase in stiffness post-treatment compared to pre-treatment values, with longer UV-A exposure times resulting in a more pronounced stiffening. In porcine corneas, the most significant stiffening occurred with the longest UV-A exposure. This observation will be verified in human donor corneas in future experiments. The ultimate goal is to develop customized corneal crosslinking (CXL) treatments, tailoring parameters like UV-A exposure time to the biomechanical profiles of individual patients. Future developments will also focus on verifying the influence of the post-UV exposure period on the stiffening process in human corneas, as already observed in porcine corneas.

Keywords: Corneal Collagen Crosslinking (CXL), Transepithelial (Epi-On) CXL, Corneal Stiffening, UV-A Irradiation, Optical Coherence Tomography (OCT).

Stress-relaxation behaviour of the retina characterized through small punch test and computational modelling

Damiano Bertolo, Anna Pandolfi, Federica Boschetti
Politecnico di Milano, Department of Chemistry, Materials and Chemical Engineering "Giulio Natta" (LaBS)

Abstract:
Hereditary retinal diseases are one of the leading causes of blindness among working-age adults, with an incidence of 1:1380 people. The optimal treatment option is genic therapy delivered by subretinal injections. To evaluate the influence of different aspects of the surgery, such as the rate, the site, and the volume of the injection on the rupture of the retina, a material model of the retina is being developed. In the literature, the retina has been characterized mostly through uniaxial tensile testing, a method that does not reproduce the load conditions occurring during the injection, nor the in-vivo physiological state. This study employs a novel approach based on the small punch test to investigate the retinaâ€™s behaviour under a stress-relaxation test. Porcine retinas have been employed due to their similarity to human retinas and their high availability, making them the preferred animal model. The experimental protocol involves three preconditioning cycles at 0.1 mm/s up t o 1 mm, followed by three displacement ramps of 1 mm at the same strain rate, each maintained for 120 s. Preliminary results have demonstrated the efficacy of this protocol in capturing the stress-relaxation behaviour of the retina. To determine the most suitable viscoelastic material model and parameters for the stress-relaxation behaviour of the retina, an axis-symmetrical computational model has been developed in Abaqus/Standard 2022 alongside the experimental test. A response surface methodology is employed to estimate the viscoelastic parameters of the retina by comparing the stress-relaxation curves generated by the model with the experimental ones. The best-fitting parameters are obtained by minimizing the Root Mean Squared Error, selected as the loss function for the comparison.

A coupled multiscale model of the human cornea accounting for the collagenous microstructure and the extracellular matrix

By Christopher Miller, Maria Laura De Bellis, Anna Pandolfi

Abstract

The human cornea is a complex, highly specialized structure necessary for the vision function of the Eye. The cornea, due to its shape and transparency, refracts and transmits the light to the retina. Cornea's mechanical properties, critical for maintaining corneal shape and function under intraocular pressure, arise from the composition of a hydrated proteoglycan-rich extracellular matrix (ECM) reinforced by an intricate network of collagen fibrils organized into lamellae. Despite extensive research, existing biomechanical models often fall short of capturing the coupled interplay between the ECM and collagen reinforcements, especially under physiological and pathological conditions. This work seeks to address this gap by proposing a novel computational model that integrates a continuum representation of the ECM with a discrete collagen-crosslinking network. The continuum approach for the ECM is chosen to represent its viscoelastic behavior and interaction with fluid flow, critical for corneal hydration and load transmission. Conversely, the collagen network is modeled as a discrete, anisotropic reinforcement system, capturing the directional stiffness imparted by the collagen fibrils and their crosslinking. The model is developed in the view to account for the influence of enzymatic degradation, age-related changes, and disease processes such as keratoconus, where alterations in the ECM-collagen coupling are known to drive structural instability.

The innovation of this approach lies in its multiscale integration, bridging the molecular mechanics of collagen crosslinking with macroscopic corneal behavior. By explicitly linking the continuum matrix with a collagen-reinforced network, the model offers some possibility to deepen our understanding of corneal mechanics.

The inclusion of experimentally derived parameters for collagen alignment, crosslink density, and ECM properties, will make the model predictive in the simulation of physiological responses to intraocular pressure and external mechanical perturbations.

Numerical Simulations of Iris Biomechanics: Modeling Active-Passive Muscle Behavior

Kevin Raul, Anna Pandolfi, Luca Dede'
Politecnico di Milano, Civil Engineering

Abstract:
The iris is an adjustable diaphragm located between the cornea and the lens, which surrounds the pupil and separates the anterior segment of the eye into anterior and posterior chambers. The iris behavior is governed by the alternative action of two smooth muscles, the sphincter pupillae, which runs circumferentially around the pupil, and the dilator pupillae, which is disposed radially in the external part of the iris. The two muscles regulate the amount of light entering the pupil, to optimize image sharpness formation on the retina. The aim of this study is to capture by numerical simulations the antagonistic mechanics of the light regulation process, using a finite element model of the iris where the coupled active-passive behavior induced by photo-sensitivity is modelled explicitly. We model the iris as a soft active material, where the passive behavior is governed by the fibrous enriched model by Holzapfel-Ogden model and the active contraction is provided by an active strain a pproach. The numerical simulations are performed using the software LIFEX. The computational framework will allow for understanding the fundamental biomechanics of the iris and its role in vision regulation, as a first step to introduce a more sophisticated model where the effects of the light intensity are assumed to be directly related to active behavior. The model has potential applications in ophthalmology and may provide suggestions for the development of bio-inspired optical systems.

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AN IMAGE-BASED COMPUTATIONAL FLUID DYNAMICS ANALYSIS OF HYPERTROPHIC CARDIOMYOPATHY

Ivan Fumagalli(1), Marco Fedele(1), Piermario Vitullo(1), Giorgia Pase(2), Christian Vergara(3), Luca Dede'(1), Sonia Ippolito(4), Roberto Scrofani(5), Alfio Quarteroni(1,6)

1. MOX – Dipartimento di Matematica, Politecnico di Milano; 2. Bernoulli Instituut, Rijksuniversiteit Groningen; 3. LaBS – Dipartimento di Chimica, Materiali e Ingegneria Chimica, Politecnico di Milano; 4. Radiology Unit, L. Sacco Hospital; 5. Cardiac Surgery Unit, L. Sacco Hospital; 6. Institute of Mathematics, École Polytechnique Fédérale de Lausanne (Professor Emeritus)

Hypertrophic Cardiomyopathy (HCM) is a pathological condition characterized by an abnormal thickening of the myocardium. When it affects the medio-basal portion of the septum, it is named Hypertrophic Obstructive Cardiomyopathy because it induces a flow obstruction in the left ventricle outflow tract, which may compromise the cardiac function and possibly lead to cardiac death. In this talk, we present computational results comparing the hemodynamics of different HCM patients, aiming at quantifying the effects of this pathology on blood flow and thus providing clinical indications that may help diagnosis and the design of surgical treatment (septal myectomy). An image-based computational pipeline was developed for the purpose, integrating CFD simulations with geometrical and functional data from cine-MRI acquisitions [1, 2]. Blood flow is modelled by incompressible Navier-Stokes equations in an Arbitrary Lagrangian-Eulerian framework, and the valve leaflets are accounted for by a resistive method [1, 3]. All simulations were obtained by the life^x library [https://lifex.gitlab.io/lifex].

This project has been funded by the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No 740132, IHEART 2017-2022, P.I. A. Quarteroni).

KEYWORDS: hypertrophic cardiomyopathy, septal myectomy, patient-specific simulations, image-based CFD, cardiac cine-MRI.

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2. Fedele et al, Biomech Model Mechan, 16(5):1779–1803, 2017.
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- Application for a Talk

Mitchel J. Colebank

Department of Mathematics

Department of Biomedical Engineering

University of South Carolina, Columbia, SC, USA

Simulating pulse-wave hemodynamics under the effects of vasoactivity

One-dimensional, pulse-wave propagation models are able to replicate hemodynamic waveforms that are representative of measured data. While these models are a potential tool in the era of digital twins, few models have considered the role of smooth muscle vasoactivity and its effects on blood pressure and flow. This is especially important for understanding cerebrovascular function, especially in diseases like dementia and Alzheimer's, where cerebral vasoactivity is known to be a cause and consequence of altered mechanical stimuli. Thus, there is a need for new computational models that explicitly account for vascular tone during hemodynamic simulation.

Here, we implement a relatively simplistic exponential model of the proximal vasculature pressure-area relationship, given by

$$p(x,t) = p_0\left[e^{\beta_{ECM}\left(\sqrt{\frac{A}{A_0}}-1\right)}+\frac{k}{k_{ref}}e^{\beta_{SMC}\left(\frac{1}{1-k}\sqrt{\frac{A}{A_0}}-1\right)}\right]$$

which incorporates extracellular matrix stiffness, β_{ECM}, vascular smooth muscle cell stiffness, β_{SMC}, the degree of vasomotor tone k in comparison to some reference tone k_{ref}, and the reference pressure, p_0. The strain is measured by the relationship between current and reference area, A and A_0, respectively. We couple this vasoactive large vessel model to the structured tree boundary condition, which represents the microvascular beds. To differentiate between proximal and small vessel vasoconstriction, we also introduce a vasodilation factor in the structured tree that controls microvascular radii. We analyze the model using global sensitivity analysis, and provide insight into the distinct contributions of large and small vessel vasoactivity in an idealized systemic arterial network. Our results show that microvascular vasoconstriction is more impactful that proximal vessel vasotone, but that stress-strain behavior in the large vessels can be modulated divergently depending on the relative magnitudes of ECM and smooth muscle stiffness. This study lays the foundation for future studies investigating the effects of vasoactivity on hemodynamic outcomes.

Shape Instabilities driven by defects with different topological charge in Nematic Polymer Networks

Silvia Paparini, Professor Giulio G. Giusteri, Professor L. Angela Mihai
University of Padova, Department of Mathematics "Tullio Levi-Civita"

Abstract:
Nematic polymer networks (NPNs) are anisotropic rubbers formed by cross-linked polymeric chains with rod-like mesogenic segments, that, in the nematic phase, align along a non-polar director $\textbf{\emph{n}}$. In NPNs the coupling between nematic order and polymer network is strong enough to constrain the director field to follow elastic deformations. Consequently, variations in the degree of orientation of the mesogenic segments, s, can drive the system out of equilibrium, inducing shape changes.
A key characteristic of nematic systems is the existence of singularities in the director field, known as topological defects, which can be classified by their topological charge m. They play a major role in the self-assembly of biological materials, such as plasma membrane, wood, silk, and the insect cuticles. Developing organisms achieve biological organisation by growing persistent protrusions or depleting material to relieve mechanical stresses originating from the presence of topologically required defects.
This talk aims to provide a mathematical framework describing the out-of-plane shape deformations of initially flat NPN sheets subsumed with a central topological defect and resulting director profile spanning the entirety of the film.
We define an energy associated with these deformations,
consisting of two contributions: an elastic energy term accounting for spatial variations in $\textbf{\emph{n}}$, and a strain-energy function describing the elastic response of the polymer network.
The interplay between nematic elasticity, which seeks to minimize distortions in the director field, and mechanical stiffness, which resists deformation, determines the
resulting morphology.
We analyse the transition to instability of the flat configuration, which represents the systemâ€™s ground state in the absence of nematic ordering. We also characterize the nature of the first buckling modes.

A numerical study of the electrophysiological substrate of epilepsy

Caterina Beatrice Leimer Saglio
Politecnico di Milano

Traveling wave phenomena, such as the propagation of electrical impulses in anisotropic neural tissue, are central to many brain processes. In brain electrophysiology, these waves manifest as sharp, rapidly advancing fronts in the transmembrane potential, driven by ionic currents through membrane channels. Traveling wave phenomena, such as the propagation of electrical impulses in anisotropic neural tissue, are central to many brain processes. In brain electrophysiology, these waves manifest as sharp, rapidly advancing fronts in the transmembrane potential, driven by ionic currents through membrane channels. Capturing these dynamics is essential for understanding both healthy brain function and pathological events, such as the initiation and spread of epileptic seizures. The approach solves the monodomain equation coupled with the Barreto-Cressman ionic model, which captures key interactions between excitatory and inhibitory neurons and the dynamics of extracellular potassium-a key factor in seizure-like activity. This model plays a crucial role in capturing the non-linear ionic exchanges responsible for wave initiation and propagation at the cellular level. Numerical simulations of an epileptic event on a two-dimensional heterogeneous context, considering isotropic grey matter and anisotropic white matter.

Effects of Laser Surface Processing on the Biocompatibility of a Potential Biomedical Alloy: High Entropy TiTaHfNbZr Alloy

Sidika Mine Toker, Furkan Bicer, Hadi Jahangiri
Eskisehir Osmangazi University - Turkey, Metallurgical and Materials Engineering

Abstract:
For load-bearing orthopedic applications, biomedical alloys which are advantageous in terms of mechanical properties are widely preferred, however biocompatibility and osseointegration of metallic alloys are still needed to be improved. For this purpose, novel biomedical alloys are being developed and various surface treatment methods are applied to these alloys. Among the new generation alloys, TiTaHfNbZr alloys; which belong to the class of high entropy alloys - an alloy class that has raised attention in recent years in terms of their mechanical properties- are biomedically promising as well, in terms of their elemental content and their potential elastic compatibility with the bone tissue. Among the surface modification methods applied to metal alloys, femtosecond surface treatment methods stand out as an effective method for biomedical applications as they enable formation of controllable patterns and homogeneous topography formation on the surface, while not causing problems su
ch as melting and phase transformation with their short-term interaction with the material. However, in the literature there arenâ€™t any studies focusing on the utility of high entropy alloys for biomedical applications, through modifying their surface with laser processing methods. With this motivation, the current study focuses on obtaining surfaces with different topographic properties by processing the TiTaHfNbZr alloy surfaces with a femtosecond laser and to thoroughly investigate the effect of the obtained surfaces on biocompatibility. Within the scope of the experimental methods, surface of the TiTaHfNbZr alloys were modified by femtosecond laser processing to create surfaces with different topographic properties, surface energy, contact angle and wettability by forming patterns in various shapes and repetition frequencies, and the properties of these surfaces were characterized. Following these processes, biocompatibility of the created surfaces were comprehensively investi
gated via ex situ and in vitro biocompatibility tests, in order to determine the surface pattern with the most promising biocompatibility response.

A Coupled Bi-Ventricle Flow Model With Explicit Arterial Circulation

J. Mackenzie, S. Richardson
University of Glasgow

The development of a comprehensive model of myocardial perfusion is challenging due to the need to incorporate many complex interactions across spatial and temporal scales, and physical domains. Previously, we have presented poro-elastic flow models for the beating left ventricle coupled together with a 1D model for blood flow in the coronary arterial and venous tree that perfuse the myocardium [1].

Here, we present an important extension of this coupled left ventricle model to a poro-elastic bi-ventricle model. In this model, the left ventricle is coupled with the systemic arterial tree including the coronary arterial network and the right ventricle is coupled with the pulmonary circulatory system. We model the large vessels of vascular networks explicitly using imaged data and data from the literature. Feedback between the ventricular models and the arterial flow models on a per time-step basis allow the model to respond to the mechanical stimulus of pressure in a physiologically realistic manner.

We will discuss the separate components of the model, the challenges encountered in coupling the separate parts, and methods used to ascertain that the observed behaviours are reasonable. This coupled myocardial perfusion, and systemic and pulmonary flow model is benchmarked in a healthy heart, and we will present some results for cases of arterial disease.

The development of this model represents a significant step towards the longer-term goal of developing a four-chamber heart model with true feedback loop between the circulatory system and beating heart.

[1]: Richardson, S. H., Mackenzie, J., Thekkethil, N., Feng, L., Lee, J., Berry, C., ... & Gao, H. (2024). Cardiac perfusion coupled with a structured coronary network tree. *Computer Methods in Applied Mechanics and Engineering*, *428*, 117083.

Title: A partitioned solver for Purkinje-muscle coupling in cardiac electrophysiology

Authors: Michele Bucelli*, Samuele Brunati*, Roberto Piersanti*, Luca Dede'*, Christian Vergara^1

* MOX - Laboratory of Modeling and Scientific Computing, Dipartimento di Matematica, Politecnico di Milano, Milano, Italy
1 LABS, Dipartimento di Chimica, Materiali e Ingegneria Chimica, Politecnico di Milano, Milano, Italy

We present a computational methodology for simulating cardiac electrophysiology with an explicit representation of the Purkinje network. The method is based on coupling a three-dimensional eikonal-diffusion model in the myocardium to a one-dimensional eikonal model in the network, and allows to reproduce antidromic muscle-Purkinje reentries by means of iterations between the two solvers, thus leading to a partitioned solver for the 3D-1D coupled problem. The use of the eikonal-diffusion model in this context requires the introduction of a dedicated solver, based on a discrete pseudo-time formulation that can distinguish between active and inactive stimuli in correspondence of the Purkinje-muscle junctions. We present the results of simulations in a realistic model of the human ventricles, under healthy conditions as well as in pathological scenarios including the Wolff-Parkinson-White syndrome, a bundle branch block, and a bundle branch block treated with CRT. These results demonstrate how the proposed framework can correctly reproduce both orthodromic and antidromic propagation, and allow the identification of regions where antidromic reentries occur.

A Physiologically Accurate Active Strain Model for Left Ventricular Contraction

Sarah Donaldson, Hao Gao, Nicholas A. Hill, Xiaoyu Luo
University of Glasgow, Mathematics and Statistics

Abstract:
Modelling the mechanical properties of the myocardium such as the passive and active responses is an essential component of mathematical cardiac models. Often, passive myocardium is considered to be anisotropic and hyperelastic, and its contractile function is usually modelled by an active stress approach. This is where the total stress is obtained by adding the passive and active stress tensors together. Another method to model myocardial contraction is the active strain approach, where the deformation gradient is multiplicatively decomposed into passive and active components to overcome the issues of mathematical convexity arising from the active stress approach. Furthermore, the active stress approach is rather phenomenological, while the active strain approach depends on local distortions that relate to the microstructure of myofilaments, by signifying the sequential order between active distortion and elastic stretch. In this work, we introduce a new active strain model that is
physiologically accurate with parameters that could be calibrated from measured data. By further incorporating a limiting function on the elastic stretch that a living myocyte can experience, the new active strain model can accommodate different levels of active contraction. An existing left ventricular model is then used to simulate realistic left ventricular pump function, which is implemented with an immersed boundary method with finite element extension. We compare the new active strain model with the active stress approach using the same left ventricular model. Results suggest that the new active strain model can simulate left ventricular dynamics as effectively as the active stress model, with subtle differences in fibre stress, despite the two models being fundamentally different. Future studies will apply this new active strain model to patients for personalised modelling.

Patient-Specific Multicompartment Darcy Flow Model: Effect of Heterogeneity and Anisotropy in Porous Parameters

Namshad Thekkethil, Hao Gao, Nicholas A. Hill, Xiaoyu Luo
University of Glasgow, School of Mathematics and Statistics

Abstract:
Myocardial perfusion plays a crucial role in cardiac function, and disruptions in blood flow can contribute to severe cardiovascular diseases. However, modelling perfusion with sufficient physiological detail remains challenging, as traditional homogeneous approaches fail to capture the complex heterogeneity of vascular networks. In this study, we present a novel computational framework for modelling myocardial perfusion using a multi-compartment poroelastic Darcy flow model. This approach incorporates anisotropic and heterogeneous perfusion parameters derived from realistic vascular data.
Through numerical simulations, we compare our proposed framework to conventional homogeneous models and validate it against Poiseuille flow results. Our findings highlight that the heterogeneous anisotropic model significantly improves the accuracy of pore pressure predictions, particularly in capturing spatial variations in permeability from large vessels to microvessels. Additionally, we investigate the impact of compartmentalisation on model accuracy, demonstrating that a three-compartment structure optimally balances computational efficiency and physiological realism.
The model's ability to simulate patient-specific conditions, such as vessel occlusions, further underscores its potential for clinical applications. Our results indicate that under pathological conditions, the discrepancy between homogeneous and heterogeneous models becomes more pronounced, emphasizing the need for detailed vascular reparametrisation in perfusion simulations.
This work represents an advancement in computational modelling for myocardial perfusion, bridging the gap between traditional porous media approaches and high-resolution vascular data. Future extensions of this framework will incorporate unsteady effects, wave dynamics, and external forces to further enhance its applicability in patient-specific simulations.

Modeling the interplay between acute myocardial ischemia and arrhythmogenesis

Alessandra Corda, Stefano Pagani, Christian Vergara
Politecnico di Milano, Dipartimento di Chimica, Materiali e Ingegneria Chimica "Giulio Natta"

Abstract:
Acute Myocardial Ischemia (AMI), especially in early stages, significantly increases the risk of ventricular reentrant arrhythmias. The reduced blood flow distal to a coronary occlusion triggers a cascade of ionic and metabolic effects such as hypoxia (reduced supply of oxygen), hyperkalemia (increased extracellular potassium concentration) and acidosis (reduced intracellular pH). The spatial heterogeneity arising in the myocardial tissue may result in the formation of reentries.

In this context, computational models could simulate the generation of arrhythmias in presence of AMI regions. Since quantitative information about the latter are hardly available from clinics, to date, computational models only integrate imaging data from chronic infarcted ventricles. This may not accurately reflect the acute condition.

In our study we develop an electrophysiological framework based on patient-specific myocardial blood flow maps acquired during a pharmacologically induced acute ischemic event, with the aim to analyze the arrhythmic propensity of the patients under investigation. Specifically, we consider a multiscale model, coupling the monodomain model for macroscopic propagation with the Ten Tusscher-Panfilov model suitably modified to account for the ionic alterations induced by AMI. Additionally, we partition the geometry of the left ventricle using myocardial blood flow maps to identify AMI regions, then assuming a correlation between the least perfused region and ischemic ionic parameters. This inter-individual analysis allows us to examine the impact of the volume of border and ischemic zones on arrhythmogenesis.

Moreover, in order to assess the influence of the dimension of the AMI region on arrhythmogenesis, for one specific patient we build virtual scenarios corresponding to less severe levels of AMI. By performing this intra-patient sensitivity analysis where different levels of AMI are virtually depicted, we can suggest that the distribution of ischemic regions, not just their volume, is critical in assessing the risk of arrhythmia.

A large population of cell-specific action potential models replicating fluorescence recordings of voltage in rabbit ventricular myocytes

Radostin D Simitev, Rebecca J. Gilchrist, Zhechao Yang, Rachel Myles, Francis Burton, Godfrey L. Smith
University of Glasgow, School of Mathematics and Statistics

Abstract:
Recent high-throughput experiments unveil substantial electrophysiological diversity among uncoupled healthy myocytes under identical conditions. To quantify inter-cell variability, the values of a subset of the parameters in a well-regarded mathematical model of the action potential of rabbit ventricular myocytes are estimated from fluorescence voltage measurements of a large number of cells. Statistical inference yields a population of nearly 1200 cell-specific model variants that, on a population-level replicate experimentally measured biomarker ranges and distributions, and in contrast to earlier studies, also match experimental biomarker values on a cell-by-cell basis. This model population may be regarded as a random sample from the phenotype of healthy rabbit ventricular myocytes. Uni-variate and bi-variate joint marginal distributions of the estimated parameters are presented, and the parameter dependencies of several commonly utilised electrophysiological biomarkers are reve
aled. Parameter values are weakly correlated, while summary metrics such as the action potential duration are not strongly dependent on any single electrophysiological characteristic of the myocyte. Our results demonstrate the feasibility of accurately and efficiently fitting entire action potential waveforms at scale.

A first in-silico trial of quantifying the drug effects of SGLT2i in heart failure.

Scott Heath Richardson[a], Matthew Lee[b], Colin Berry[b], Nicholas Hill[a], Dirk Husmeier[a], Hao Gao[a]

[a]*School of Mathematics and Statistics University of Glasgow, Glasgow, UK*
[b]*British Heart Foundation Glasgow Cardiovascular Research Centre, University of Glasgow, Glasgow, UK*

Abstract

Chronic heart failure (HF) is one of the most frequent causes of death worldwide, both in the short and long term, with approximately 50% of patients diagnosed with HF dying within 5 years. This suggests only a moderate success for current existing medical therapies despite intensive research into heart failure. Thus, we aim to supplement this by designing an in-silico trial which uses state-of-art personalized heart models and statistical approaches to quantify the benefit of SGLT2i (used in a drug trial) when added to current standard-of-care in attenuating adverse left ventricle (LV) remodelling in patients with heart failure.

The clinical trial provides the essential data for personalised heart models, developed within the SofTMech Centre, which are scaled up to 100 patients (the test group: 50 with SGLT2i, and the placebo group: 50 on placebo), structural and biomechanical trajectories of heart function will be quantified for each patient, and benefits of SGLT2i will be assessed by analysing key biomechanical biomarkers between the two groups from baseline (before treatment) to 24-36 weeks post treatment. Values of using the predictive in-silico model for the design of clinical trials in heart failure patients will be pursued, i.e. reducing the sample size, early termination. We use the completed data to examine any benefits of this new drug in attenuating adverse remodelling in heart failure patients, with preliminary analysis suggesting a benefit in terms of the biomechanical properties, slowing down adverse remodelling with a less stiff myocardium and required contractility to avoid depleting the contractile reserve completely.

We hope that this work helps establish a cornerstone of translating SofTMech-developed personalized heart models into the clinic, leading to the development of in silico trial platform for drug discovery in heart failure.

An adapted tensorial decomposition for simplifying constitutive modelling of skeletal muscles

Sara Galasso, Giulio G. Giusteri
UniversitÃ degli Studi di Padova, Dept. of Mathematics "Tullio Levi-Civita"

Abstract:
The mechanical response of skeletal muscles is influenced by their microstructural organisation, characterised by fibre arrangements that give rise to anisotropic mechanical properties. Capturing this complex behaviour is essential for biomechanical applications. However, the development of constitutive models for muscular tissue is often obstructed by the numerous material parameters involved, which in most cases lack a clear physical meaning and are hence challenging to determine from standard measurements.

In this talk, we will discuss a general formalism designed to facilitate the experimental identification of material functions for their constitutive characterisation within the context of Cauchy elasticity. Specifically, I will present a theoretical framework for anisotropic nonlinear elasticity based on the decomposition of strain and stress tensors on a tensorial basis adapted to the local microstructure of the material [1]. This decomposition aims at organising the degrees of freedom involved into a mathematically clear and mechanically motivated scheme, which may support theoretical comprehension and experimental investigation.

We will focus on materials which exhibit transversely isotropic behaviour with respect to a reference configuration and discuss the practical advantages of this approach by examining the passive elastic response of skeletal muscles.

Reference:
1. S. Galasso, G. G. Giusteri. "Adapted and objective Voigt representations in anisotropic nonlinear elasticity", submitted to MEMOCS.

Computational modelling of bladder outlet obstruction mechanobiology

Kieran Boniface, Shaghayegh Zamani Ashtiani, Kanako Oda, Naoki Yoshimira, Anne Robertson, Paul Watton
University of Sheffield, School of Computer Science

Abstract:
Bladder outlet obstruction (BOO) is a prevalent condition characterised by increased urethral resistance. BOO gives rise to a myriad of lower urinary tract symptoms (LUTS) including voiding hesitancy, increased voiding frequency and incontinence. Prolonged BOO can lead to irreversible complications, such as kidney failure, that ultimately impact bladder functionality and significantly lowers quality of life.

In an obstructed bladder, smooth muscle cells (SMCs) must generate greater pressures to void. This initiates a biological response that drives the bladder through three stages of remodelling: hypertrophy, compensation, and decompensation. This remodelling process results in structural changes in the bladder wall, but the relationship between increased bladder pressure, remodelling-driven wall changes and bladder functionality is poorly understood.

To better understand these changes, we develop a novel rate-based constrained mixture model of BOO, informed by experimental rat models using an integrative in vivo - in vitro - in silico approach. The bladder wall is modelled as a multi-layered, fibre-reinforced, hyperelastic, constrained mixture in COMSOL Multiphysics. Over a long time scale, constituent growth and remodelling algorithms act to restore bladder function. The active mechanics of voiding are considered over a shorter time scale, with voiding metrics contributing to bladder growth and remodelling.

The model is calibrated to a healthy rat bladder and predictions of evolving structure and function are compared with in vivo/in vitro observations of an obstructed bladder. We investigate the effect of anisotropic, volumetric growth on bladder function. Furthermore, we explore the later stages of bladder remodelling (compensation, decompensation) by coupling a system of ODEs to model biochemical signalling in fibrotic and anti-fibrotic pathways. The model can then be used for in-silico investigations to predict the response of the bladder to obstruction removal and guide the design of pharmacological treatment to maintain bladder functionality.

Intra membrane molecular phototransducers for muscle cell stimulation

Guglielmo Lanzani
Politecnico di Milano

Abstract
Life-machine interfacing holds broad potential in regenerative and therapeutic medicine, robotics, and life-enhancing technologies. Several approaches have been explored to develop functional abiotic/biotic interfaces responsive to external stimuli. In this communication, I present intra-membrane molecular transducers as a promising alternative to both genetic strategies and covalent engineering for cell opto-stimulation. Specifically, I introduce a class of molecular phototransducers based on photochromic molecules and discuss their working mechanisms in detail. Owing to their amphiphilic nature, these molecules exhibit a natural affinity for the plasma membrane, allowing their spontaneous incorporation. Upon light absorption, the phototransducers convert optical energy into an electrical signal, thereby stimulating the host cells. Through chemical engineering, we have developed distinct phototransducers capable of modulating various membrane electrical properties, including capacitance, conductance, and surface charge. Experimental results obtained in muscle cell models will be presented, alongside a simplified mechanistic model. Furthermore, a proof-of-concept actuator based on a quasi-three-dimensional electrospun scaffold seeded with C2C12 skeletal muscle cells will be demonstrated. These findings offer a new design rationale for photo-responsive systems that operate via non-covalent targeting of biological membranes, potentially advancing future life-machine integration technologies.