Proceeding of the Fourth Soft Tissue Modelling Workshop

SofTMech Committee (Eds.)
5–7 June 2019, Glasgow, UK

SOFT TISSUE MODELLING WORKSHOP

June 5-7, 2019

University of Glasgow

The 4th workshop will continue the lively forum on the most recent advances in the field of soft tissue mechanics, with a clear vision of the landscape of multiscale soft tissue modelling and both fundamental and translational research. It will also provide a unique environment for cross-talk, enabling the sharing of novel ideas and expertise necessary for the future advancement of soft tissue modelling. The workshop is supported by the EPSRC centre SofTMech.

Invited Speakers

Gerard Ateshian, USA
Alain Goriely, UK
Gerhard Holzapfel, Austria
Rajagopal Kumbakonam, USA
Alfio Quarteroni, Italy
Paul Steinmann, UK/Germany

Organizing committee:

SofTMech

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EPSRC
Engineering and Physical Sciences Research Council

UNIVERSITY of GLASGOW

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Welcome

One of the greatest challenges of mechanical modelling is to extend its success to fields outside traditional engineering, in particular to physiology, biomedical sciences, and medicine. Following successful Soft Tissue Modelling Workshop in Glasgow during 2012, 2015 and 2017, this fourth workshop will continue the research forum for modelling specialists and medical experts to discuss and exchange ideas on state-of-the-art developments and challenges in the field of soft tissue modelling, with particular applications to tissues in the cardiovascular system and tissues affected by cancer.

Lunches, reception and the workshop dinner:
Presentations will take place in Room 116 (the ground floor), Mathematics and Statistics Building, University of Glasgow, University Avenue, Glasgow G12 8QQ. Tea/coffee/lunches, posters, and the Cheese and Wine Reception will be held in the rooms across from 116. The Workshop dinner will be held at the Hilton Grosvenor,1-9 Grosvenor Terrace, Glasgow G12 0TA, on Thursday 6th June at 7pm. That is 10 minutes walk up the Byres Road from the Mathematics Building.

Funding:
The workshop is organized and sponsored by SofTMech (`www.softmech.org`), an EPSRC-funded Centre for Mathematical Sciences in Healthcare.

Acknowledgements:
The organisers would like to thank the University of Glasgow Conference and Events Team for organizing the workshop and the web team for setting up the website `http://www.softmech.org/events`.

Fourth Soft Tissue Modelling Workshop

Venue: Room 116, Mathematics and Statistics Building, University of Glasgow, University Avenue, Glasgow G12 8QQ

Plenary Talk: 35 mins + 5 mins question **Regular Talk: 15 mins talk + 3 mins question+ 2 mins transition**

PhD presentation with yellow background

Programme

Day 1

Wednesday 5 June 2019

	08:20	09:10	Registration	
	09:10	09:20	Workshop Opening - **Prof. Xiaoyu Luo**	
Morning Session-1 Chair: Prof. Ray Ogden	**09:20**	**10:00**	**Prof. Gerard Ateshian**	*Modeling fatigue failure in soft biological tissues using reactive constrained mixtures*
	10:00	10:20	Prof. Anna Pandolfi	*A microstructural model of crosslink interaction between collagen fibrils in the human cornea*
	10:20	10:40	James Haughton	*A new microstructural strain energy function for the hyperelastic modelling of skin*
	10:40	11:00	Dr. David Nordsletten	*Viscoelastic model of human myocardium*
	11:00	11:30	Coffee break & Registration	
Morning Session-2 Chair: Prof. Alain Goriely	11:30	11:50	Prof. Zishun Liu	*Recent development in mechanics of soft materials and machines – an overview*
	11:50	12:10	Malte Rolf-Pissarczyk	*A continuum approach on modeling the heterogenous distribution of elastin degradation in the aortic wall*
	12:10	12:30	Dr. Will Zhang	*Analyzing the role of viscoelasticity in the residual stress in soft tissues: a case study on human aortas*
	12:30	12:50	Aritra Chatterjee	*Cyclic stretch dependent actin growth and remodelling determines cellular morphoelastic response*
	12:50	13:50	Lunch	
Afternoon Session-1 Chair: Prof. Gerhard Holzapfel	**13:50**	**14:30**	**Prof. Alain Goriely**	*Modelling brain ageing and dementia*
	14:30	14:50	Prof. Xiaoyu Luo	*Growth and Remodelling post myocardial infarction in human left ventricle*
	14:50	15:10	Dr. Kostas Soldatos	*Mass-growth of a finite tube reinforced by a pair of helical fibres*
	15:10	15:30	Dr. Yangkun Du	*Influence of initial residual stress on growth and pattern creation for a layered aorta*
	15:30	16:00	*Coffee Break*	
Afternoon Session-2 Chair: Dr. David Nordsletten	16:00	16:20	Prof. Nick Hill	*Discrete-to-constinuum modelling of cells to tissue*
	16:20	16:40	Adela Capilnasiu	*Nonlinear viscoelastic constitutive model for bovine liver tissue*
	16:40	17:00	Dr. Ankush Aggarwal	*Improved convergence of forward and inverse soft tissue models*
	17:00	17:20	Dr. Igor Karsaj	*Influence of Fiber dispersion on growth and remodeling of abdominal aortic aneurysms*
	17:20	17:40	Mihaela Paun	*Fast uncertainty quantification in a partial differential equation system of the pulmonary circulation*
Poster session Chair: Dr. Hao Gao	17:40	18:10	1-min talk -all posters	
	18:10	19:00	Poster session & Reception	

Day 2

Thursday 6 June

Morning Session-1 Chair: Prof. Xiaoyu Luo				
	09:00	**09:40**	**Prof. Alfio Quarteroni**	*Numerical models of the cardiocirculatory system*
	09:40	10:00	Dr. Melanie Brewis	*Imaging biomarkers in pulmonary hypertension*
	10:00	10:20	Prof. Colin Berry	*Imaging of heart*
	10:20	10:40	Dr. Scott Richardson	*Cardiac poroelasticity modellong using a hybrid immersed boundary framework combined with finite element emthod for the Darcy flow*
	10:40	11:10	*Coffee break*	
Morning Session-2 Chair: Prof. Mark Chaplain				
	11:10	11:30	Prof. Xavier Pelorson	*Physical study of midmembranous lesions of the vocal fold*
	11:30	11:50	Dr. Annemie Van Hirtum	*Study of the influence of water spraying on an ongoing fluid-structure interaction: application to the role of vocal folds surface hydration in phonation*
	11:50	12:10	Gediminas Gaidulis	*Numerical model of mitral valve for transapical repair applications*
	12:10	12:30	Liuyang Feng	*Dynamic modelling of coupled mitral valve and left atrium*
	12:30	12:50	Jay Mackenzie	*A mathematical model of the pulmonary circulatoin with respiration*
	12:50	13:50	Lunch	
Afternoon Session-1 Chair: Prof. Alfio Quarteroni	**13:50**	**14:30**	**Prof. Paul Steinmann**	*Testing of native and biofabricated soft biotissue materials*
	14:30	14:50	Prof. Mark Chaplain	*Mathematical modelling of the metastatic spread of cancer*
	14:50	15:10	Dr. Cicely Macnamara	*Computational modelling and simulation of cancer growth and migration within a 3d heterogeneous tissue*
	15:10	15:30	Peter Mortensen	*Mathematical modelling of coupled myocytes and fibroblasts*

	15:30	16:00	*Coffee break*	
Afternoon Session-2 Chair: Prof. Nick Hill	16:00	16:20	*Dr. Peter Stewart*	*Elastic jumps on networks: predicting retinal haeorrhage*
	16:20	16:40	Marija Smoljkić	*Can we 3D print mechanically realistic arterial replicas?*
	16:40	17:00	Ruoxuan Liu	*Computational study of shape memory polymeter stent*
	17:00	17:20	Guillia Pederzani	*Application of theories of arterial growth, remodelling and damage to understand cerebral vasospasm and its response to treatment*
	17:20	17:40	Mansoor Haider	*Modeling fluid-solid dynamics of cardiovascular networks in the presence of hypertension*
	19:00	22:00	Workshop Dinner	Hilton Glasgow Grosenor

Day 3				
Friday 7 June				
Morning Session-1 Chair: Prof. Zishun Liu	**09:00**	**09:40**	**Prof. Rajagopal Kumbakonam**	*On modelling the growth of soft tissues*
	09:40	10:00	Dr. Hao Gao	*Mathematical modelling acute myocardial infarction using in vivo magnetic resonance imaging*
	10:00	10:20	Dr. Xin Zhuan	*Coupled agent-based and hyperelastic modelling of the left ventricle post-myocardial infarction*
	10:20	10:40	Lynn Laidlaw	*Patient and public involvement in research: reflections from an involved patient*
	10:40	11:10	*Coffee break*	
Morning Session-2 Chair: Prof. Gerard Ateshain	11:10	11:30	Prof. Matthew Dalby	*Nanoscale control of mesenchymal stem cells*
	11:30	11:50	Dr. Lana Virag	*Aneurysm morphology and rupture: computational case study using 3D finite elements*
	11:50	12:10	Prof. Robert Insall	*Self-generated chemotactic gradients to explore the complex environment*
	12:10	12:50	**Prof. Gerhard Holzapfel**	*Biomechanics of fibrous soft tissues: state-of-the-art and challenges ahead*
Open Discussion: Prof. Nick Hill	12:50	13:00	Prize Giving and Workshop Close	
Lunch	13:00	14:00	Lunch	
Social Event	14:00	18:00	After-meeting activities	

Poster Session Programme		
	Sirio Orozco-Fuentes	*Role of noise at cell division on transcription factor heterogeneity in hescs colonies*
	Dr. Andrey Melnik	*Para-universal relations for additively split orthotropic constitutive models*
	Aritra Chatterjee	*Constitutive properties of fiber reinforced elastomers with transverse isotropic symmetry*
	Yalei Yang	*Image segmentation based on myocardial perfusion MRI data*
	Laura Miler	*Effective governing equations for poroelastic composites*
	Alan Lazurus	*Emulation of a biomechanical model of the left venticle*
	Debao Guan	*Effects of myofibre architecture on biventricular biomechanics: a simulation study*
	Dr. Danyang Wang	*The energetics of self-excited oscillations in collapsible channel flow*
	Dr. Fotios Savvopoulos	*The influence of bending on coronary arteries bio-mechanics assessed by fluid-structure interaction modelling*
	Dr. Fotios Savvopoulos	*FSI modelling of an ApoE-/- atherosclerotic murine carotid artery instrumented with a blood flow-modifying cuff*
	Dr. Nan Qi	*A mathematical study to determine the screener size in isolation of exosomes using microfluidic chip*

Abstracts

4th Third Workshop on Soft Tissue Modelling
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SofTMech Commitee (Eds.)

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Modeling fatigue failure in soft biological tissues using reactive constrained mixtures

Prof. Gerard Ateshian
Columbia University

Abstract: Examining fatigue failure of soft biological tissues, such as cartilage and tendon, is essential for understanding degenerative processes that develop slowly with aging. The modeling of fatigue failure is a challenging problem in mechanics and remains an open topic of investigation. This presentation introduces a modeling framework for fatigue failure that accounts for the evolution of intact tissue to fatigued and damaged tissue using reactive kinetics and the axiom of mass balance. The reaction rates are nonlinear functions of the rate of change of a failure measure, such as the von Mises stress in metals or the maximum principal stress in fibrous soft tissues, as well as the state of damage. Model predictions are compared to the limited set of published experimental studies for cartilage and tendon. Further model validation is provided against the more extensive set of results in fatigue failure of metals.

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MODELLING BRAIN AGEING AND DEMENTIA

Prof. Alain Goriely
Mathematical Institute, University of Oxford

Unlike normal ageing, neurodegenerative diseases such as Alzheimer's or Parkinson's are devastating conditions with poorly understood mechanisms and no known cure. Yet a striking feature of these conditions is the characteristic pattern of invasion throughout the brain, leading to well-codified disease stages visible to neuropathology and associated with various cognitive deficits and pathologies. How can we use mathematical modelling to gain insight into this process and, doing so, gain understanding about how the brain works? In this talk, I will show that by linking new mathematical modelling to recent progress in imaging and brain mechanics, we can unravel some of the universal features associated with dementia and, more generally, brain functions.

BIOMECHANICS OF FIBROUS SOFT TISSUES: STATE-OF-THE-ART AND CHALLENGES AHEAD

Gerhard A. Holzapfel[1,2], Kewei Li[1], and Ray W. Ogden[3]

[1]Institute of Biomechanics, Graz University of Technology, Austria {holzapfel|kewei.li}@tugraz.at
[2]Department of Structural Engineering, Norwegian University of Science and Technology (NTNU), Trondheim, Norway gerhard.holzapfel@ntnu.no
[3]School of Mathematics and Statistics, University of Glasgow, Glasgow, Scotland, UK
raymond.ogden@glasgow.ac.uk

Fibrous soft tissues are composed of an extrafibrillar matrix (e.g., proteoglycans and water), collagen, and elastic fibers, whereas the active mechanical contribution is due to cells. For arterial walls the matrix can be considered as an isotropic material while the collagen fibers generate the anisotropy of the tissue. In various soft tissues collagen fibers are not perfectly aligned but are arranged in a rather dispersed structure for which a mean direction can be defined; for a review on microstructural aspects see [1]. Note that the structural arrangements and the associated mechanical properties of the tissue components can be severely damaged or even disrupted by various diseases. For example, in aortic dissections pooling of GAGs/PGs in the medial layer of aortas can lead to significant stress concentrations through intra-lamellar Donnan swelling pressures that disrupt the normal cell-matrix interactions and delaminate the layered micro-structure of the aortic wall. As a consequence, a reduction of the radial elastic properties due to elastic fiber breakage may take place between the elastic laminae before the event of an aortic dissection [2]. For abdominal aortic aneurysms the out-of-plane dispersion of collagen fibers is increased and, consequently, the material and structural parameters change, as shown in [3].

A future challenge is to base material models on a multiscale approach so that the macroscopic mechanical tissue response is linked to the microstructural components. After reviewing morphological aspects of fibrous soft tissues in health and disease we present a recent multiscale model of fiber recruitment and damage with a discrete fiber dispersion method [4]. In particular, the model is based on the triangular discretization of a unit sphere with a finite number of elementary areas. Over each elementary area, we define a representative fiber direction and an elementary fiber density based on the fiber dispersion. In brief, a summation of fiber contributions of all elementary areas yields the resultant fiber strain energy – compressed fibers can easily be excluded. Fiber recruitment, softening and damage are considered. The model was implemented in a finite element program and verified by representative examples.

Finally we discuss challenges ahead, e.g., the cross-linking of collagen fibers has a significant effect on the tissue response within which the fibers are embedded. The number of cross-links increases with age, which is an important factor in the age-related stiffening of arterial walls [5]. Hence, advanced continuum models are needed that take account of information on cross-links at the micro-structure level.

REFERENCES

[1] G.A. Holzapfel and R.W. Ogden. Biomechanical relevance of the microstructure in artery walls with a focus on passive and active components. *Am. J. Physiol. Heart Circ. Physiol.*, 315:H540–H549, 2018.

[2] N.F. MacLean, N.L. Dudek, and M.R. Roach. The role of radial elastic properties in the development of aortic dissections. *J. Vasc. Surg.*, 29:703–710, 1999.

[3] J.A. Niestrawska, Ch. Viertler, P. Regitnig, T.U. Cohnert, G. Sommer, and G.A. Holzapfel. Microstructure and mechanics of healthy and aneurysmatic abdominal aortas: experimental analysis and modeling. *J. R. Soc. Interface*, 13:20160620, 2016.

[4] K. Li and G.A. Holzapfel. Multiscale modeling of fiber recruitment and damage with a discrete fiber dispersion method. *J. Mech. Phys. Solids*, 126:226–244, 2019.

[5] V.M. Barodka, B.L. Joshi, D.E. Berkowitz, C.W. Hogue Jr., and D. Nyhan. Review article: implications of vascular aging. *Anesth. Analg.*, 112:1048–1060, 2011.

ON MODELLING THE GROWTH OF SOFT TISSUES

K. R. Rajagopal
Texas A&M University

In order to describe the growth of soft tissues we need to understand their constitutive structure, namely that they consist in a mixture of an inhomogeneous anisotropic non-linearly elastic solid and a complex "fluid-like body", namely blood, that is in itself a mixture of plasma, erythrocytes, leukocytes, platelets, various lipo-proteins, and numerous ions, etc. This is of course not a feasible task, especially when one recognizes that the erythrocytes themselves are comprise of a thin solid membrane that encapsulates a fluid, etc., and hence one can only try to capture the salient constitutive features. With regard to what one considers as the solid constituent of the tissue, one has to recognize that the solid body has an evolving "natural configuration" that changes during the deformation of the body. The evolution of the natural configuration can be delineated if one can have a sound thermodynamic framework to describe how the body stores energy, dissipates energy, produces entropy, etc., but such a framework is not available for living matter. Thus, at best one can come up with a very crude model for growth. In this talk I will address the various issues that need to be taken into consideration in modeling growth and attempt to develop a framework within which to study the problem.

TESTING OF NATIVE AND BIOFABRICATED SOFT BIOTISSUE MATERIALS

Silvia Budday[1], Aldo Boccaccini[2], Friedrich Paulsen[3], Ben Fabry[4], and Paul Steinmann[5]

[1] Applied Mechanics, Friedrich-Alexander Universität Erlangen-Nürnberg, Germany
[2] Biomaterials, Friedrich-Alexander Universität Erlangen-Nürnberg, Germany
[3] Anatomy, Friedrich-Alexander Universität Erlangen-Nürnberg, Germany
[4] Biophysics, Friedrich-Alexander Universität Erlangen-Nürnberg, Germany
[5] Applied Mechanics, Friedrich-Alexander Universität Erlangen-Nürnberg, Germany
and Glasgow Computational Engineering Centre, University Glasgow, UK

Biological tissues such as blood vessels, skin, cartilage or nervous tissue provide vital functionality to living organisms. Computational simulations of these tissues can provide insights into their biomechanics during injury and disease that go far beyond traditional approaches. This is of ever increasing importance in industrial and medical applications as numerical models will enable early diagnostics of diseases, detailed planning and optimization of surgical procedures, and not least will reduce the necessity of animal and human experimentation. However, the extreme compliance of these, from a mechanical perspective, particular soft tissues stretches conventional modeling and testing approaches to their limits. In this contribution, we will report on our ongoing attempts to experimentally characterise and to model native biological tissues and biofabricated proxy (substitute) materials with similar properties. As a prospect, this will significantly facilitate the choice of appropriate materials for biofabrication of artificial organs, as well as modeling approaches for predictive simulations.

NUMERICAL MODELS OF THE CARDIOCIRCULATORY SYSTEM

Alfio Quarteroni
Ecole Polytechnique Fédérale de Lausanne (EPFL), Switzerland

Mathematical models based on first principles allow the description of the blood motion in the human circulatory system, as well as the interaction between electrical, mechanical and fluid-dynamical processes occurring in the heart. This is a classical environment where multi-physics processes have to be addressed.

Appropriate numerical strategies can be devised to allow an effective description of the fluid in large and medium size arteries, the analysis of physiological and pathological conditions, and the simulation, control and shape optimization of assisted devices or surgical prostheses.

This presentation will address some of these issues and a few representative applications of clinical interest.

Acknowledgment: The work presented in this talk is part of the project iHEART that has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No 740132)

IMPROVED CONVERGENCE OF FORWARD AND INVERSE SOFT TISSUE MODELS

Ankush Aggarwal, Yue Mei, Sanjay Pant
University of Glasgow, Glasgow Computational Engineering Centre

Soft tissues exhibit nonlinear and anisotropic mechanical behavior, which is modeled using exponential function in several constitutive models. In this talk, I will present methods that take into account this exponential nonlinearity to significantly improve the convergence of forward and inverse models.

For the forward model, I will start with a novel formulation that applies a transform on the discretized equations. For an exponential nonlinearity, this transformation is its inverse, i.e. log. This leads to a small modification in the residual vector, which can be implemented in any existing finite element solver and allows us to take 10 to 100 times larger load steps [1].

For the inverse model, I will present two different scenarios – displacement controlled (DC) and force controlled (FC). In DC case, a displacement or strain is applied and force or stress is matched to calculate the elastic parameters. Inversely, in FC case, a force or stress is applied and displacement or strain is matched to calculated the elastic parameters. For the DC case, I will show that using a "log-norm" improves the convergence as well as sensitivity of the solution to data noise. Whereas, for the FC case, a nonlinear parameter transformation with regular L2 norm improves the convergence [2].

Lastly, I will generalize these approaches to computation where the type of nonlinearity is unknown. Thus I will present improved versions of Newton-Raphson and Gauss-Newton methods.

REFERENCES

[1] Mei, Hurtado, Pant, and Aggarwal. CMAME, 337:110-127, 2018 [2] Aggarwal. BMMB, 16(4):1309–1327, Aug 2017.

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IMAGING OF HEART

Prof. Colin Berry
University of Glasgow

Imaging provides information on cardiovascular structure and function with high spatial and temporal resolution. Imaging is harmless, especially if without ionising radiation, meaning the scan can be repeated during longitudinal follow-up. Cardiovascular magnetic resonance imaging (CMR) provides quantitative information on heart structure, function, blood flow and pathology. CT coronary angiography provides similar information but is less informative about tissue pathology. CTCA has higher spatial and temporal resolution than CMR. In this talk, I will describe our work using imaging as applied to patients with stable angina, the symptom that patients experience due to a supply/demand mismatch of blood to the heart. I will also describe recent work in acute myocardial infarction, the condition that is typically caused by transient or sustained coronary artery occlusion. I will describe the applications of mathematical modelling to advance the patient agenda for diagnosis and treatment.

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NONLINEAR VISCOELASTIC CONSTITUTIVE MODEL FOR BOVINE LIVER TISSUE

Adela Capilnasiu[1], Lynne Bilston[2, 3], Ralph Sinkus[1, 4], David Nordsletten[1, 5]
[1]Imaging Sciences & Biomedical Engineering, King's College London, London, United Kingdom
[2]Prince of Wales Clinical School, University of New South Wales, Sydney, Australia
[3]Neuroscience Research Australia, Sydney, Australia
[4]Inserm U1148, LVTS, University Paris Diderot, Paris, France
[5]Department of Biomedical Engineering and Cardiac Surgery, University of Michigan, Ann Arbor, USA

Introduction

Mechanical characterisation of liver tissue is important in the development of implants and devices [1], diagnosis accuracy [2] and transportation safety [3]. Liver tissue damage is one of the most common occurrences in motor vehicle crashes, and biomechanical analysis of safety devices has spurred investigations into liver tissue behaviour. Liver disease is also routinely assessed for inflammation and fibrosis based on tissue properties. Commonly, the liver is assumed to be hyperelastic, with polynomial, exponential and logarithmic laws being used to describe its behaviour in uniaxial deformation or shear. However, employing large cyclic deformations indicates that the liver is a nonlinear viscoelastic strain-rate dependent tissue.

Methods

In this study, the 3D biomechanical behaviour of bovine liver tissue was tested under combined uniaxial compression (1-20%) and rotational shear (1-50%) at 0.5, 1 and 2 Hz [4]. Cylindrical samples of 20 mm diameter were investigated, with torque responses being recorded. Three types of viscoelastic fractional derivative models were proposed, based on polynomial, exponential and Ogden forms.

Data analysis

Fitting the models using the usual L_2 error norm proved to be unsuitable, due to the wide spectrum of deformations employed. With torque readings differing up to two orders of magnitude, the fits were biased by the higher amplitude points. Apart from this, due to the pre-conditioning protocol, the data also exhibited shear-softening. In order to account for this effect, a new error norm was designed, which determined the identification of a unique set of parameters that was then multiplied by scale factors specific to each test. This approach led to an excellent fit of the models to the data.

Conclusions

This study compares the performance of three new models in capturing the nonlinear viscoelastic strain-rate dependent behaviour of liver tissue. This is done by under an error norm that overcomes the strain-softening effect.

[1] J. Marescaux, J. M. Clément, V. Tassetti, C. Koehl, S. Cotin, Y. Russier, D. Mutter, H. Delingette, and N. Ayache, "Virtual reality applied to hepatic surgery simulation: The next revolution," *Ann. Surg.*, vol. 228, no. 5, pp. 627–634, 1998.

[2] R. Sinkus, S. Lambert, K. Z. Abd-Elmoniem, C. Morse, T. Heller, C. Guenthner, A. M. Ghanem, S. Holm, and A. M. Gharib, "Rheological determinants for simultaneous staging of hepatic fibrosis and inflammation in patients with chronic liver disease," *NMR Biomed.*, vol. 31, no. 10, p. e3956, Oct. 2018.

[3] N. Yoganandan, F. A. Pintar, T. A. Gennarelli, and M. R. Maltese, "Patterns of abdominal injuries in frontal and side impacts.," *Annu. proceedings. Assoc. Adv. Automot. Med.*, vol. 44, pp. 17–36, 2000.

[4] K. Tan, S. Cheng, L. Jugé, and L. E. Bilston, "Characterising soft tissues under large amplitude oscillatory shear and combined loading," *J. Biomech.*, vol. 46, no. 6, pp. 1060–1066, Apr. 2013.

Cyclic stretch dependent actin growth and remodelling determines cellular morphoelastic response

Aritra Chatterjee, Paturu Kondaiah,Namrata Gundiah
Indian Institute of Science, Centre for Biosystems Science and Engineering

Mechanical forces are important determinants in development, from molecular assembly of the cell organelles to the constitution of an entire organ. Factors underlying active cytoskeletal remodelling, the individual and combined roles of the cytoskeletal proteins under dynamically stretched conditions, and their links to contractility however remain underexplored. In this study, we provide a novel growth and remodelling framework to study the effect of uniaxial cyclic stretch in fibroblasts using both experimental and theoretical techniques. We show that uniaxial cyclic stretch induces lengthening and realignment in stress fibers along with cortical actin reinforcement which influences the cellular response. Realignment of stress fibers along a uniform angle perpendicular to the direction of applied stretch for prolonged duration also increases the effective elastic cell modulus. Using cytoskeletal disruptors, we further show that microtubules do not influence cell stiffness or reorie ntation changes under cyclic stretch but are important in nuclear reorientation. Based on our experimental observations, we propose a biologically motivated constitutive model to incorporate the effects of amplitude and time duration of uniaxial cyclic stretch on a single cell. The model incorporates novel evolution equations for stress fiber growth and remodelling, which offers predictive capability in generating cellular morphometrics sensitive to a wide range of changes in experimental inputs.

Constitutive properties of fiber reinforced elastomers with transverse isotropic symmetry

Aritra Chatterjee, Paturu Kondaiah, Namrata Gundiah
Indian Institute of Science, Centre for Biosystems Science and Engineering

Fiber reinforced elastomers (FRE) undergo large anisotropic deformations and show immense potential in several engineering applications. Materials like the myocardium are also characterized by transversely isotropic material symmetries which are critical in the overall heart function. Because of challenges in assessing the material properties of natural materials with variable fiber orientations, we developed a novel fiber reinforced elastomer, comprised of low fiber volume fraction polyester fibers in poly dimethyl siloxane (PDMS) substrate using a filament winding technique, and characterized the uniaxial and biaxial stress-strain properties of the FRE using a planar biaxial stretcher. Uniaxial specimens were oriented in 0, 15, 30, 45, 60, 75- and 90-degree orientations to obtain dependence of the fiber orientations on the mechanical responses; biaxial samples were oriented at 45 degree with respect to the stretch direction. We assume a strain energy function, W, assuming incompressibility, based on invariants I1 and I4 to and plotted variations in the partial derivatives of W with respect to I1 and I4 using results from uniaxial experiments. We used results from the 45-degree uniaxial data to assess the form of the functional and tested the sensitivity of the constants in the model for the other fiber orientations. These results showed that the standard reinforcing solid model did not describe the material properties of the FRE well; interactions between the invariants were essential inclusions in the new polynomial form of strain energy function for the FRE. We also tested for the Adkins and Rivlin's constraint for fiber inextensibility in the model and explored the applicability of the model to the biaxial mechanical results. We hope these results will be useful to characterize the large deformations in novel composite materials with directional properties.

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NANOSCALE CONTROLE OF MESENCHYMAL STEM CELLS

Matthew J Dalby
Centre for the Cellular Microenvironment, Institute of Molecular, Cell & Systems Biology, MVLS, Joseph Black Building, University of Glasgow, Glasgow, G12 8QQ.

Skeletal mesenchymal stem cells (MSCs) can be controlled by their physical and mechanical nanoscale environment. Here, we will discuss how nanotopography alone can induce MSC differentiation to osteoblasts through integrin and BMP-2 co-localisation(1). Subsequently, we have developed a nanovibrational bioreactor, the Nanokick, that also induces MSC osteogenesis without use of media supplementation(2). In 2D the nanovibrations drive osteogenesis through focal adhesion-based mechanism, while in 3D, in gels, TRPV1 activation of beta catenin is implicated. These approaches allow us to envisage new orthopaedic biomaterials and also new cell manufacturing routes for orthopaedic indications.

Another focus of the presentation will, however, be on nanoscale control of MSC growth and immunomodulatory phenotype. Out of their marrow niche, skeletal mesenchymal stem cells (MSCs) tend to quickly differentiate into e.g. fibroblasts and their self-renewal is not regulated. This makes it hard to grow large numbers of high-quality stem cells in vitro. It is notable that MSCs are finding use in transplant treatments – not for their regenerative capacity per se, but for their immune-suppressive capacity, for example with islet transplant and in graft vs host disease. This capacity is also lost with time in vitro. Here, the ability of nanotopographies to maintain ex vivo growth and immune-suppressive phenotype of MSCs is discussed(3-5).

Acknowledgements: BBSRC, EPSRC, MRC and Find a Better Way for funding.

References

1. M. J. Dalby, N. Gadegaard, R. Tare, A. Andar, M. O. Riehle, P. Herzyk, C. D. Wilkinson, R. O. Oreffo, The control of human mesenchymal cell differentiation using nanoscale symmetry and disorder. *Nat Mater* **6**, 997-1003 (2007).

2. P. M. Tsimbouri, P. G. Childs, G. D. Pemberton, J. Yang, V. Jayawara, W. Oripiriyakul, K. V. Burgess, C. Gonzales-Garcia, G. Blackburn, D. Thomas, C. Vallejo-Giraldo, M. J. P. Biggs, A. S. G. Curtis, M. Salmeron-Sanchez, S. Reid, M. J. Dalby, Stimulation of 3D osteogenesis by mesenchymal stem cells using a nanovibrational bioreactor. *Nature Biomedical Engineering* **1**, 758-770 (2017).
3. P. M. Tsimbouri, R. J. McMurray, K. V. Burgess, E. V. Alakpa, P. M. Reynolds, K. Murawski, E. Kingham, R. O. Oreffo, N. Gadegaard, M. J. Dalby, Using nanotopography and metabolomics to identify biochemical effectors of multipotency. *ACS Nano* **6**, 10239-10249 (2012).
4. R. J. McMurray, N. Gadegaard, P. M. Tsimbouri, K. V. Burgess, L. E. McNamara, R. Tare, K. Murawski, E. Kingham, R. O. Oreffo, M. J. Dalby, Nanoscale surfaces for the long-term maintenance of mesenchymal stem cell phenotype and multipotency. *Nat Mater* **10**, 637-644 (2011).
5. L. C. Lee, N. Gadegaard, M. C. de Andres, L. A. Turner, K. V. Burgess, S. J. Yarwood, J. Wells, M. Salmeron-Sanchez, D. Meek, R. O. Oreffo, M. J. Dalby, Nanotopography controls cell cycle changes involved with skeletal stem cell self-renewal and multipotency. *Biomaterials* **116**, 10-20 (2017).

INFLUENCE OF INITIAL RESIDUAL STRESS ON GROWTH AND PATTERN CREATION FOR A LAYERED AORTA

Yangkun Du, Chaofeng Lu, Michel Destrade, Weiqiu Chen
NUI Galway, School of Mathematics, Statistics and Applied Mathematics

Residual stress is ubiquitous and indispensable in most biological and artificial materials, where it sustains and optimizes many biological and functional mechanisms. The theory of volume growth is widely used to explain the creation and evolution of growth-induced residual stress and the resulting changes in shape, starting from a stress-free initial state. Furthermore, the theory can also model how growing bio-tissues such as arteries and solid tumours develop a strategy of pattern creation according to geometrical and material parameters, again starting from a stress-free initial stress. This modelling provides promising avenues for designing and directing some appropriate morphology of a given tissue or organ and achieve some targeted biomedical function. In this paper, we rely on a modified, augmented theory to reveal how we can obtain growth-induced residual stress and pattern evolution of a layered artery by starting from an existing, non-zero initial residual stress state. We use experimentally determined residual stress distributions of aged bi-layered human aortas and quantify their influence by a magnitude factor. Our results show that initial residual stress has a most significant impact on residual stress accumulation and the subsequent evolution of patterns. Additionally, we provide an essential explanation for growth-induced patterns driven by differential growth coupled to an initial residual stress. Finally, we show that initial residual stress is a readily available way to control growth-induced pattern creation for tissues and thus, a promising inspiration for biomedical engineering.

DYNAMIC MODELLING OF COUPLED MITRAL VALVE AND LEFT ATRIUM

Liuyang Feng
University of Glasgow, School of Mathematics and Statistics

We develop a coupled left atrium-mitral valve (LA-MV) model that includes physiologically detailed geometry fibre-reinforced hyperelastic materials for both the LA and MV. Fluid-structure interaction is incorporated by using an immersed boundary-finite element framework. The effect of functionality (MV regurtigation and diminished LA contraction due to atrial fibrillation) and geometric variations (uniform vs. non-uniform LA wall thickness, rule-based vs. atlas-based collagen fibre architecture) on the overall LA performance are investigated on two left atrium geometries, respectively. Different flow patterns are found in the case of atrium fibrillation from the normal case, such as the absence of reversal wave in pulmonary venous flow and reduced systolic filling wave in the left atrial appendage. Mitral regurgitation leads to disturbed flow especially during systole where large regurgitant jet can be found with suppressed pulmonary venous flow and high LA pressure. We find rule-based and atlas-based fibre defining methods lead to similar flow fields and structure deformations in the LA, while the changes of wall thickness from non-uniform to uniform can leads to underestimating LA deformation, and the thicker the wall, the lower the strain level. The flow velocity within the left atrial appendage is also increased with a thicker atrium wall. Energy analysis shows that the kinetic and dissipation energies within the left atrium are highly affected by atrial fibrillation and mitral regurgitation.

In summary, we show that mitral regurgitation, LA contractile function and wall thickness approximation can significantly affect the LA dynamics, energy analysis based on FSI modelling could have indicative values in LA function diagnosis.

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NUMERICAL MODEL OF MITRAL VALVE FOR TRANSAPICAL REPAIR APPLICATIONS

Gediminas Gaidulis, Matteo Selmi, Diana ZakarkaitÄ, Audrius Aidietis, Rimantas KaÄianauskas

Vilnius Gediminas Technical University, Department of Biomechanical Engineering

Development and application of the numerical model for the simulation of human heart mitral valve (MV) transapical repair is presented. Transapical repair with neochordae implantation is a novel surgical technique, allowing beating-heart correction of mitral regurgitation caused by chordae tendineae rupture through a minimally-invasive approach. In the present study, the structural finite element (FE) model of the MV decoupled from the blood flow is considered. It comprises two leaflets described by nonlinear thin shell elements and chordae tendineae described by truss elements. Geometry of the model and kinematic boundary conditions for fixed points of MV annulus, papillary muscles, and left ventricle apex are defined by patient-specific data. Decoupled behavior of blood is specified by the time-dependent physiologic transvalvular pressure.

Personalized computational modelling strategy is applied to perform virtual transapical MV repair by positioning neochordae following the real-life surgery procedure executed by surgeons. A dynamic FE analysis in time frame between end-diastole and peak systole is conducted to evaluate post-repair MV function. Computational MV simulation and modelling results provide quantitative information about the neochordae contribution to the MV function improvement and present practical value for the surgical planning of transapical MV repair.

MATHEMATICAL MODELLING ACUTE MYOCARDIAL INFARCTION USING IN VIVO MAGNETIC RESONANCE IMAGING

H. Gao[1], K. Mangion[2], C. Berry[1], and X.Y. Luo[1]

1 School of Mathematics and Statistics, University of Glasgow, UK
2 Institute of Cardiovascular and Medical Science, University of Glasgow, UK

Although death rates from myocardial infarction (MI) are falling, the incidence of heart failure after acute-MI remains persistently high. Left ventricular (LV) dysfunction after MI portends an adverse prognosis, which is responsible for nearly 70% of heart failure cases. However, on an individual basis, risk prediction using LV ejection fraction is limited as majority of patients who die prematurely have a normal or mildly reduced LV ejection fraction. Computational heart modelling has potential to close some of these gaps in risk prediction in individual patients, i.e. myocardial stiffness and contractility [1].

In order to improve patient-specific modelling of myocardial mechanics following an acute-MI, we developed a finite element model of a human left ventricle with MI morphologies derived directly from Late-Gadolinium enhanced (LGE) magnetic resonance (MR) images, as shown in Fig.1(a). The LV geometry is reconstructed from in vivo short-/long-axis cine images of a patient after acute-MI, shown in Fig.1 (b). A linear relationship between LGE intensity and myocardial passive stiffness and contractility is assumed. We assume that the passive myocardium obeys the Holzapfel-Ogden constitutive law with eight unknown material parameters.

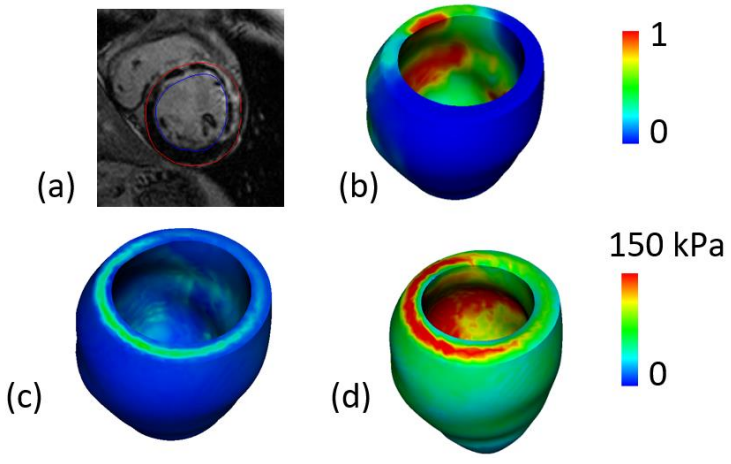

Figure 1: (a) The LGE image, the enhanced region is the MI; (b) Integrated MI information from LGE into a 3D LV model; (c) simulated LV shape at end-diastole, coloured by myofibre stress; (d) simulated LV shape at end-systole.

We inversely determine the eight unknown material parameters by matching the strain measurements estimated from MR images and the LV end-diastolic volume using a multi-step optimisation approach. Finally, the myocardial contractility is inferred by matching the systolic function, including the systolic peak circumferential strain and LV ejection fraction. The myocardial contractility of this patient is around 180.8 kPa from our modelling, which is in the range of previously published human values. Figs.1 (c, d) show the myofibre stress at end-diastole and end-systole. The relatively high stress in and around the MI region, shown in Fig.1 (d), is believed to contribute to the adverse remodelling, in particular adjacent to the MI region.

In summary, our newly developed LV model by integrating MI pathology information directly from LGE MR images for estimating myocardial passive stiffness and contractility will be helpful in management of patients with acute-MI.

References

1. Gao H, et al. Scientific Report. 7:13527 (2017).

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EFFECTS OF MYOFIBRE ARCHITECTURE ON BIVENTRICULAR BIOMECHANICS: A SIMULATION STUDY

DEBAO GUAN, Jiang Yao, Xiaoyu Luo, Hao Gao
University of Glasgow, School of Mathematics and Statistics

Cardiac diseases remain a major public healthy burden, especially the adverse remodelling of cardiac function after acute myocardial infarction (MI). Studies have demonstrated that mechanical stresses and strains in myocardium can have great effects on pathological processes. The three-dimensional (3-D) spatial architecture of myofibres play a very important role in heart function, such as influencing electrical propagation, myocardial expansion in diastole and contraction in systole. To include myofibres into the computational models, two different approaches have been widely used in the literature, one approach is directly mapping myofibres from ex vivo datasets to the computational models, for example the model reconstructed directly from diffusion-tensor magnetic resonance imaging (DT-MRI) datasets or using atlas-based methods to warp the DT-MRI data into the models. The other approach is the rule-based method (RBM) in which myofibres rotate from endocardium to epicardium with pr escribed angles, varied linearly in most of studies. This study develops a 3D neonatal bi-ventricle porcine model to compare ex vivo DT-MRI myofiber architecture based on large deformation diffeomorphic metric mapping (LDDMM) framework with two different simplifications based on a rule-based approach. The first simplification uses AHA17 segments to reconstruct myofibres with different fibre angles at each segment, a further simplification is made by assigning the same fibre rotation angles in the whole ventricle. Different approximations of myofibre architecture are compared in terms of cardiac pump function. Results show that using realistic myofibre architecture can produce better cardiac output, higher ejection fraction and larger apical twist compared to the simplified rule-based myofibres, even though they all are derived from the same DT-MRI dataset. Therefore, it is necessary to incorporate a realistic myofibre architecture if personalized ventricular models are needed.

MODELING FLUID-SOLID DYNAMICS OF CARDIOVASCULAR NETWORKS IN THE PRESENCE OF HYPERTENSION

MA Haider[1], MU Qureshi[1], NA Hill[2] and MS Olufsen[1]
[1]North Carolina State University
[2]University of Glasgow

Pulmonary hypertension (PH) is a rare but deadly cardiovascular disease. Both structural remodeling of the vessel wall constituents and alterations in the vascular network architecture are known to occur as the disease progresses. Model calibration and validation in the context of data from individuals (typically rodents or humans) pose unique challenges in the development of robust mathematical models for coupled fluid-solid biomechanics and remodeling in pulmonary cardiovascular networks. As PH advances, the relative composition of primary vessel wall constituents (collagen, elastin, smooth muscle cells) becomes altered. The ensuing wall stiffening and thickening increases blood pressure which, in turn, can induce further tissue remodeling. Yet, the manner in which these alterations occur is not well understood. We present structural continuum mechanics models that are tailored to incorporating PH-induced wall remodeling into 1D fluids network models of pulmonary cardiovascular dynamics. This modeling approach is used to formulate nonlinear relations between blood pressure and vessel wall cross-sectional area that can capture structural alterations with advancing PH. We also use nonlinear pressure-area relations for investigating cardiovascular flows in pulmonary networks generated directly from CT images of individual mice. This approach enables a more realistic representation of pulmonary vascular network structure via direct segmentation of CT images to obtain an individualized network capturing vessel segment lengths and junction information. We present simulations of pressure, flow and cross-sectional area dynamics on these individualized networks. Challenges in model calibration due to the limited availability of measurements at only a small number of vessel locations will also be discussed.

A NEW MICROSTRUCTURAL STRAIN ENERGY FUNCTION FOR THE HYPERELASTIC MODELLING OF SKIN

James Haughton, Dr Tom Shearer; Prof. William J. Parnell
University of Manchester, School of Mathematics

In the hyperelastic modelling of skin, we construct strain energy functions (SEFs) to model the anisotropic and nonlinear stress-strain behaviour exhibited by skin. Phenomenological models can fit experimental data well, but do not provide information on microstructure-function relationships. Microstructural models, however, contain parameters that are directly connected to the properties and arrangement of skin's constituents and can be used to elucidate how the skin's microstructure influences its macroscopic mechanical behaviour.

We introduce a new model which assumes that collagen fibres are crimped according to a triangular distribution. Furthermore, we postulate that an individual collagen fibre is linearly elastic, but only tautens once straightened. The nonlinear stress-strain behaviour typical of skin is thus caused by the gradual tautening of collagen fibres. All of the new SEF's material parameters can be measured directly via experiments. We fit the new SEF to four uniaxial tensile tests, and compare the quality of fit to that achieved by the commonly used HGO model. We also fit the new SEF simultaneously to tensile tests performed in two, perpendicular directions by accounting for the dispersion of collagen fibres. In particular, we assume that the collagen fibres in skin are oriented with rotational symmetry around a mean fibre direction.

We account for parameter uncertainty in the new SEF by using Approximate Bayesian Computation. In this approach, we propose values for each of the SEF's parameters by sampling from prior distributions determined from experimental data, insert them into the SEF to obtain a simulated data set, and determine if the simulated data satisfies a distance criterion. By repeating this process many times, we obtain posterior distributions for the parameter values that are consistent with the mechanical data.

DISCRETE-TO-CONTINUUM MODELLING OF CELLS TO TISSUE

Nicholas A. Hill, Roxanna G. Barry and Peter S. Stewart
SofTMech, School of Mathematics & Statistics, University of Glasgow, G12 8QQ, U.K.

Living tissues are composed of large numbers of cells packed together within an extracellular matrix. In order to understand the process of growth and remodelling in soft tissues that are subject to internal and external forces and strains, multiscale models that describe the interactions between individual cells and the tissue as a whole are needed. A significant challenge in multiscale modelling of tissues is to produce macroscale continuum models that rationally incorporate the underlying mechanical properties of individual cells, without assuming homogeneity, symmetry or periodicity at the cell level. This challenge is particularly pertinent in modelling cardiac tissue, where the individual cells experience significant mechanical deformation in response to electrical signals. In particular, we are interested in cases where the mechanical properties of the cardiac cells may vary significantly between different regions of the heart, e.g. in disease or following a myocardial infarction.

We consider a single line of nonlinearly hyperelastic cells of finite size, with forces transmitted across the boundaries between neighbours. One or both ends of the line are fixed to represent free expansion or confinement. The dynamics of the array is given by a system of discrete 1D ODE's. Individual cells grow in volume and divide into two identical daughter cells. The parent cell divides its mass equally so that each daughter cell is half the total length of the parent cell, and an extra boundary at the midpoint of the parent cell is introduced. Two examples of resistance to motion are considered. Firstly, we suppose that the cells are binding and unbinding to a fixed substrate, providing a resistive force is proportional to the speed of the cell relative to the substrate (Stokes dissipation). Secondly, we consider a local resistance to motion arising from the motion of a cell boundary relative to its neighbours so that the damping force is proportional to the rate of elongation of the cell (Kelvin dissipation).

Having constructed and solved the discrete model, we then use the methods of discrete-to-continuum upscaling to derive new PDE models using Taylor expansions local to each discrete cell, which requires that the properties of the individual cells

INFLUENCE OF FIBER DISPERSION ON GROWTH AND REMODELING OF ABDOMINAL AORTIC ANEURYSMS

Nino Horvat[1], Gerhard A. Holzapfel[2,3], Igor Karšaj[1]

[1] Faculty of Mechanical Engineering and Naval Architecture, University of Zagreb, Ivana Lučića 5, 10000 Zagreb, Croatia, *nino.horvat;igor.karsaj}@fsb.hr*

[2] Institute of Biomechanics, Graz University of Technology, Stremayrgasse 16/2, 8010 Graz, Austria, *holzapfel@TUGraz.at*

[3] Department of Structural Engineering, Norwegian University of Science and Technology, 7491 Trondheim, Norway, *gerhard.holzapfel@ntnu.no*

Human aortas can be considered as layered fibrous composites with collagen fibers and smooth muscle cells embedded into a ground matrix. Collagen fibers are dispersed within the aortic wall, however, they are typically grouped into two families with mean fiber direction and dispersion around it. Studies have shown that fiber dispersion effect the mechanical response of the aortic wall and it is different in each aortic layer. Furthermore, in diseased aortas microstructure and fiber dispersion significantly alter, effecting in that way mechanical properties of the aortic wall. To the authors' knowledge, none of the numerical studies describing the adaptation of healthy and diseased aortas in response to different stimuli takes fiber dispersions into account. In this study, a non-symmetric fiber dispersion model is implemented into a constrained mixture growth and remodeling model using a generalized structure tensor approach. A finite element software was then used to analyze the influence of various fiber dispersion on abdominal aortic aneurysm growth and on stress distribution inside the aortic wall. Results obtained with a three-layered axisymmetric abdominal aortic aneurysm model have shown that collagen fiber dispersion has a significant influence on aneurysm growth. For example, an increase of fiber dispersion in intima and adventitia leads to a slower growth rate, while the increase of dispersion in adventitia results in a faster growth rate. Furthermore, a simultaneous increase of fiber dispersion in all layers tends to level the circumferential and axial stresses throughout the wall thickness, whereas aligned fibers increase the circumferential stress in the intima and axial stress in the adventitia. Considering the results, we suggest that modeling of the fiber dispersion should not be neglected in future G&R studies of abdominal aortic aneurysms.

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INFLUENCE OF FIBER DISPERSION ON GROWTH AND REMODELING OF ABDOMINAL AORTIC ANEURYSMS

Igor Karsaj, Nino Horvat, Gerhard Holzapfel
University of Zagreb, Faculty of Mechanical Engineering

The human aorta is a multilayered fibrous composite assembled by the ground matrix, smooth muscle cells and collagen fibers. Experimental and imaging studies have shown that collagen fibers are dispersed within the aortic wall and that mechanical responses change with the dispersion. Furthermore, during a disease (e.g., abdominal aortic aneurysms) the microstructure of an aorta may significantly change. In particular, aneurysms have increased out-of-plane dispersion, and decreased mass of elastin and smooth muscle cells. Constrained mixture growth and remodeling (G&R) models are often used in numerical studies that model and analyze aortas in health and disease. However, to the authorsâ€™ knowledge, none of the studies so far have used fiber dispersion models in combination with a constrained mixture G&R model.

Hence, our goal was to implement a non-symmetric fiber dispersion model into the G&R model using a generalized structure tensor approach and to analyze the influence of various fiber dispersions on the abdominal aortic aneurysm growth. Results obtained with an axisymmetric finite element model for abdominal aortic aneurysms have shown that the collagen fiber dispersion has a significant influence on aneurysm growth. For example, an increase of the fiber dispersion in the tangential plane results in a slower growth rate, while an increase of out-of-plane dispersion leads to a faster growth rate and a higher risk of rupture. Thus, we suggest that modeling of the fiber dispersion should not be neglected in future G&R studies of abdominal aortic aneurysms.

EMULATION OF A BIOMECHANICAL MODEL OF THE LEFT VENTRICLE

Alan Lazarus, Dirk Husmeier, Hao Gao, Xiaoyu Luo
University of Glasgow, Mathematics and Statistics

Successful parameter inference in a left ventricle model provides diagnostic abilities, relating to strain on the wall of the LV. Use of these techniques in the clinic require use of emulation, which shifts the computational cost of the simulations to the period before the data arrive. In this talk, I explore the use of bayesian neural networks and Gaussian processes in this context,, as well as the complications in accounting for geometry in the input space of these statistical models.

PATIENT AND PUBLIC INVOLVEMENT IN RESEARCH: REFLECTIONS FROM AN INVOLVED PATIENT

Lynn Laidlaw

NIHR INVOLVE defines Patient and Public Involvement (PPI) in Research as "research" being carried out "with" or "by" members of the public rather than "to", "about" or "for" them. Increasingly funders such as the NIHR and Research Charities expect meaningful PPI as a condition of award for Grants. There are undoubtedly challenges in involving patients meaningfully in research involving basic science, big data, computer and mathematical modelling. I hope that sharing my experiences as a lay reviewer of research grants can offer some insights and stimulate discussion about the value that patient insight can bring to all health research.

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Modelling and Simulation for Expansion of a Shape Memory Polymer Stent

Ruoxuan Liu, Rong Huang and Zishun Liu
Inter. Center for Applied Mechanics, State Key Laboratory for Strength and Vibration of Mechanical Structures, Xi'an Jiaotong University, Xi'an, 710049, China.

As a new kind of smart materials, shape memory polymers (SMPs) possess superior large deformation characteristics, good biocompatibility and biodegradability and so on. They therefore represent a good candidate material to address limitations associated with more traditional materials like metal for vessel stent. This study is concentrated on the feasibility research of shape memory polymer stent by a simulation and computation method. A combined hyperelastic and viscoelastic constitutive model is constructed to allow for large deformations of the SMP stent. The vital expansion performance in a stenosed vessel is analyzed and discussed. The simulation results demonstrate that the SMP stent can obtain a soft and stable expansion performance with the human body, and the expansion properties of SMP stent can be programmed by recovery temperature and time.

KEYWORDS: Shape memory polymer stent (SMP stent), expansion performance, modelling and simulation

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Recent Development in Mechanics of Soft Materials and Machines – An Overview

Zishun Liu
International Center for Applied Mechanics; State Key Laboratory for Strength and Vibration of Mechanical Structures, Xi'an Jiaotong University, China.
zishunliu@mail.xjtu.edu.cn
http://www.zsliu.net or http://gr.xjtu.edu.cn/web/zishun

In this presentation, some of the recent works aligned with the direction of providing a better understanding of soft materials (gels, SMPs etc.) will be reviewed. Then the transient deformation process of polymeric gels and numerical implementation for large deformation kinetics of polymeric gels are studied using the finite element method (FEM). The neutral and environmentally sensitive (such as temperature, pH-value, magnetics and light) hydrogels are investigated. For the SMPs study, we developed different constitutive models which can be used for different SMP materials and can be used for large strain large deformation analyses. To validate the model, simulated and predicted results are compared with our experimental results. Finally, as many issues related to the mechanics of hydrogel and SMPs deformation behaviors remain open, some outlines for plausible future directions in the research of computational mechanics of soft materials/machines will be provided. Furthermore, we will overview the recent development of computational mechanics in the study of soft materials and machines over the worldwide, especially; the advances of computational mechanics for soft materials in different research groups will be discussed.

A MATHEMATICAL MODEL OF THE PULMONARY CIRCULATION WITH RESPIRATION

Jay Aodh Mackenzie, Nick Hill
University of Glasgow, School of Mathematics and Statistics

We present an analytic and computational model for blood flow and pressure in the pulmonary circulatory system that includes external pressure changes due to respiration. Such models are useful as they can aid our understanding of disease mechanisms, such as pulmonary hypertension and microvascular disease.

The 1D model equations for flow and pressure in large vessels are derived from rational approximations to the Navier--Stokes equations.
We use a physiologically realistic, two-sided, large vessel geometry of arteries and veins that allows pulse waves to propagate into the venous side. The sides are matched using an admittance-based boundary condition derived using a structured tree model. A structured tree is an average description of a vascular bed in which all parameters are measurable. The resulting system of equations is solved using a two-step Lax--Wendroff scheme. Flow in the main pulmonary artery is used as the upstream boundary condition and left-atrial pressure as the downstream condition.

Our model includes external pressure changes due to respiration. During inspiration the chest expands outwards and upwards, exerting negative pressure upon the lungs, pulling them open. During expiration, the chest relaxes back to its pre-inhalation state; the lungs decrease in volume. The pulmonary vasculature is also subject to this external pressure change. External (pleural cavity) pressure is measured and available in the literature.

We present simulation results that illustrate the impact of respiration on healthy pulmonary haemodynamics, and that in disease states such microvascular loss or stiffening, and pulmonary hypertension.

COMPUTATIONAL MODELLING AND SIMULATION OF CANCER GROWTH AND MIGRATION WITHIN A 3D HETEROGENEOUS TISSUE

Cicely Macnamara, Alfonso Caiazzo, Ignacio Ramis-Conde, Mark AJ Chaplain

University of St Andrews, School of Mathematics and Statistics

The term cancer covers a multitude of bodily diseases, broadly categorised by having cells which do not behave normally. Since cancer cells can arise from any type of cell in the body, cancers can grow in or around any tissue or organ making the disease highly complex. One of the main Hallmarks of Cancer (Hanahan & Weinberg, 2000; 2011) is tissue invasion and metastasis. Mathematical modelling and simulation can complement traditional biological and experimental approaches to cancer research. Our research is focused on understanding the specific mechanisms that occur in the tumour microenvironment. We are developing a novel model which allows one to simulate the behaviour of and spatio-temporal interactions between cells, blood vessels and other components of the tumour microenvironment. We use a 3D individual-based force-based model, i.e. each element (a single cell, for example) is fully realised within the model and interactions are primarily governed by mechanical forces between elements. In this way we are able to reproduce, in silico, complex features of tumour development such as growth around a blood-vessel network or along the striations of fibrous tissue. As well as the mechanical interactions we also consider chemical interactions. For example, by coupling the code to a finite element solver to model the diffusion of oxygen from blood vessels to cells. In this talk I will present the current state of the art of the model and its capabilities.

PARA-UNIVERSAL RELATIONS FOR ADDITIVELY SPLIT ORTHOTROPIC CONSTITUTIVE MODELS

Andrey V. Melnik[1], Xiaoyu Luo[1], Ray W. Ogden[1]

1 School of Mathematics and Statistics, University of Glasgow, UK

Many soft biological tissues are modelled as composites consisting of isotropic matrix reinforced by anisotropic fibres, e.g., collagen. It is often assumed in homogenised models of such composites, that the total mechanical response is given by the sum of the contributions of the constituents. The general consequences of this additive split assumption are not studied, and the assumption is maintained, as long as the model predictions reflect experimentally observed behaviour. We find that the additive split leads to a relation for the predicted Cauchy stress, which holds universally in a certain class of anisotropic materials [1].

In the theory of nonlinear elasticity, a universal relation is defined is an algebraic relation between stress and deformation that holds for all materials within a certain class, irrespective of the exact form of the material response function and parameter values. The well-known Rivlin's relation for simple shear in isotropic materials $\sigma_{11}-\sigma_{22}=\gamma\sigma_{12}$ [2, 3] and the universal relations established in anisotropic materials [4, 5] apply to stress components produced by one and the same deformation. We propose a family of relations that connect stress components under different deformations, which we call para-universal relations to highlight this difference. The proposed para-universal relations hold for any orthotropic material whose response function is additively decomposed into terms, each of which possesses a symmetry with respect to one of the axes of orthotropy. Like classical universal relations, the proposed para-universal relations hold for all admissible deformations, are linked to material symmetry, and apply to a wide class of materials. These relations can be used to test for the suitability of the additively split strain energy functions. Such a test can be performed on collected experimental data prior to choosing an exact form of the response function and fitting its parameters. We illustrate that using published experimental data for human myocardium and also synthetic data

REFERENCES

[1] A. V. Melnik, X. Y. Luo, and R. W. Ogden, *A para-universal relation for orthotropic materials*, Mechanics Research Communications, 97, 46–51, 2019.

[2] R. S. Rivlin, *Some applications of elasticity theory to rubber engineering*, in *Collected papers of R.S. Rivlin*, 9–16, Springer, 1997.
[3] M. F. Beatty, *A class of universal relations in isotropic elasticity theory*, Journal of Elasticity, 17 (2), 113–121, 1987.
[4] E. Pucci and G. Saccomandi, *On universal relations in continuum mechanics*, Continuum Mechanics and Thermodynamics, 9 (2), 61–72, 1997.
[5] R. Bustamante and R. Ogden, *On nonlinear universal relations in nonlinear elasticity*, Zeitschrift für angewandte Mathematik und Physik ZAMP, 57 (4), 708–721, 2006.

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EFFECTIVE GOVERNING EQUATIONS FOR POROELASTIC COMPOSITES

Laura Miller, Dr Raimondo Penta
University of Glasgow, Mathematics & Statistics

We have derived new effective governing equations for the macroscale behaviour of poroelastic composites using the asymptotic homogenization technique. We consider a linear elastic porous composite with an intrinsically incompressible fluid flowing in the pores. We then have assumed that the size of the pores (microscale) and the size of the whole domain (macroscale) are well separated and we also have assumed a periodic microstructure. The derived model is a system of partial differential equations which describe the effective behaviour of poroelastic composites in terms of the pressure, the average fluid velocity and the elastic displacement. The model reduces to the result of Burridge and Keller in the limit of only one elastic phase and reduces to the case of an elastic composite in the limit of no fluid. We have also been able to prove properties of our new model coefficients which encode precise details on the underlying composite microstructure. This new model has a var iety of applications including biological tissues, artificial constructs for regenerative therapies and soil mechanics. In particular, we discuss relevant applications to biological hard tissues and organs.

MATHEMATICAL MODELLING OF COUPLED MYOCYTES AND FIBROBLASTS WITH MYOCARDIAL INFARCTION SCARS

Peter Mortensen, Dr Radostin Simitev, Dr Hao Gao, Prof Godfrey Smith
University of Glasgow, CoSE, Mathematics and Statistics

The heart beat is controlled by an electrical wave that propagates with a particular pattern. This pattern allows blood to be pumped through the heart with maximum efficiency. However, when a myocardial infarction damages the muscle tissue, this pattern is interrupted, leading to arrhythmia and heart failure. This is due to the changes in the cardiac tissue caused by the damage, specifically the death of myocytes and increase of fibroblasts and collagen, in a process called fibrosis.

Current work couples existing models of myocytes and fibroblasts to create a more comprehensive electrophysiological model of infarcted cardiac tissue. The models being used are for human atrial myocytes (by Courtemanche et al [1]) and for rabbit ventricular myocytes (by Weiss et al [2]). Both models are coupled with a fibroblast electrophysiology model by Morgan et al [3]. By varying the number of fibroblasts and myocytes that are coupled we can begin to create a model of the fibrosis that converts a region of healthy tissue to an myocardial infarction scar. Finite element methods are used to solve this model and explore the numerous effects of the coupling on the propagation of electrical properties in cardiac tissues in 1D strips and 3D slabs.

Currently, the simulations produce contour plots for key properties such as activation times, calcium concentration and action potential duration. We determine the critical ratio of the number of fibroblasts coupled to a myocyte at which action potentials fail to propagate. Future work will involve adapting the fibroblast model to reflect the changes that fibroblasts undergo when they become active to begin the fibrosis process as well as coupling these models with models of muscle contraction.

VISCOELASTIC MODEL OF HUMAN MYOCARDIUM

David Nordsletten[1, 2], Gerhard Sommer[3], Ralph Sinkus[1, 4], Gerhard Holzapfel[3]
[1]Imaging Sciences & Biomedical Engineering, King's College London, London, United Kingdom
[2]Department of Biomedical Engineering and Cardiac Surgery, University of Michigan, Ann Arbor, USA
[3]Institute of Biomechanics, Graz University of Technology, Graz, Austria
[4]Inserm U1148, LVTS, University Paris Diderot, Paris, France

Across species, myocardial tissue has been shown to exhibit viscoelastic behaviour [1,2]. Significant hysteresis at low shear rates, stress relaxation, and frequency dependent stiffness have all been observed experimentally. Despite this long history of experimental evidence, the myocardium is typically modelled as a hyperelastic material [3]. New viscoelastic models have been proposed [4], but these lack the capacity to account for these varying viscoelastic factors that are encountered experimentally.

In this study, we develop a viscoelastic model for human myocardium. The model – based on a nonlinear viscoelastic anisotropic generalized power law – is demonstrated to capture the viscoelastic features of myocardial tissue across shear relaxation, cyclic shear and biaxial experiments. The model is also shown to exhibit behaviours observed in animal studies, including frequency dependent stiffness and transitional nonlinearity.

Integrating the new model into a patient-specific heart model, the behaviors of the hyperelastic and viscoelastic models are compared within the myocardium, focusing specifically on passive inflation and active contraction. Quasi-static and transient cardiac models are considered, demonstrating the impact of these assumptions on the behaviour of biventricular heart models.

Reference

1. Pinto, John G., and Y. C. Fung. "Mechanical properties of the heart muscle in the passive state." Journal of biomechanics6.6 (1973): 597-616.

2. Sommer, Gerhard, et al. "Biomechanical properties and microstructure of human ventricular myocardium." Acta biomaterialia 24 (2015): 172-192.

3. Holzapfel, Gerhard A., and Ray W. Ogden. "Constitutive modelling of passive myocardium: a structurally based framework for material characterization." Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences 367.1902 (2009): 3445-3475.

4. Gültekin, Osman, Gerhard Sommer, and Gerhard A. Holzapfel. "An orthotropic viscoelastic model for the passive myocardium: continuum basis and numerical treatment." Computer methods in biomechanics and biomedical engineering 19.15 (2016): 1647-1664.

ROLE OF NOISE AT CELL DIVISION ON TRANSCRIPTION FACTOR HETEROGENEITY IN HESCS COLONIES

Sirio Orozco-Fuentes, Irina Neganova, Rafael Barrio-Paredes, Laura Wadkin, Nicholas Parker, Andrew Baggaley, Majlinda Lako and Anvar Shukurov
Newcastle University, School of Mathematics, Statistics and Physics

The current scientific viewpoint to describe the relationship between self-renewal and differentiation is established firmly in a regulatory network composed of a core set of pluripotency transcription factors (TFs) expressed to maintain self-renewal or initiate differentiation following signalling cues. The unravelling of the current observed behaviour of each of these components has led to a myriad of experiments in which the behaviour and influence of each TF is dissected and quantified both in space in time, concluding that heterogeneity is an inherent property of pluripotent stem cell populations.
The current paradigm in stem cell biology indicates that the following TFs are necessary to maintain pluripotency: Nanog, Oct4 and Sox2. On top of this, a clonal cell culture is crucial for successful experimental protocols and medical applications of pure populations of cells. In this work, we will model through simulations of tissue mechanics the dynamic behaviour of these TFs within proliferating colonies of hESCs to take into account the role of gene expression noise at cell division and mechanical interactions in the population clonality.

A MICROSTRUCTURAL MODEL OF CROSSLINK INTERACTION BETWEEN COLLAGEN FIBRILS IN THE HUMAN CORNEA

Anna Pandolfi, Alessio Gizzi, Marcello Vasta
Politecnico di Milano, Civil and Environmental Engineering

We propose a simplified micromechanical model of the fibrous reinforcement of the corneal tissue. We restrict our consideration to the structural function of the collagen fibrils located in the stroma and disregard the other all-important components of the cornea.
The reinforcing structure is modelled with two sets of parallel fibrils, connected by transversal bonds within the single fibril family (inter-crosslink) and across the two families (intra-crosslink). The particular design chosen for this ideal structure relies on the fact that its ability to sustain loads is dependent on the degree of the crosslink and, therefore, on the density and stiffness of the bonds.
We analyze the mechanical response of the system according to the type of interlacing and on the stiffness of fibres and bonds. Results show that the weakening of transversal bonds is associated with a marked increase of the deformability of the system. In particular, the deterioration of transversal bonds due to mechanical, chemical, or enzymatic reasons can justify the loss of stiffness of the stromal tissue resulting in localized thinning and bulging typically observed in keratoconus corneas.

FAST MCMC METHODS WITH EMULATION USING GAUSSIAN PROCESSES APPLIED TO A PARTIAL DIFFERENTIAL EQUATION SYSTEM OF PULMONARY CIRCULATION

Mihaela Paun, Dirk Husmeier
University of Glasgow, Mathematics and Statistics

The past few decades have witnessed an explosive synergy between mathematics and the life sciences. In particular, mathematical modelling in medicine and physiology is a topical research area. The present work focuses on a fluid-dynamic description of the pulmonary blood circulation system in terms of coupled partial differential equations (PDEs). This model promises to achieve improved diagnosis of the risk of long-term pulmonary hypertension (increased blood pressure in the lungs), which is a major risk factor fora variety of medical conditions, including coronary artery disease, stroke and heart failure. The practical challenge is the non-invasive estimation of the patient-specific biophysical model parameters. In principle this can be achieved based on a comparison between measured and predicted blood flow and pressure profiles. However, the PDEs have no closed form solution, and repeated numerical integrations as part of an adaptive estimation procedure are computationally exp ensive. In the present article, we demonstrate how fast parameter estimation combined with sound uncertainty quantification can be achieved by a combination of statistical emulation and Markov chain Monte Carlo (MCMC) sampling. We compare a range of state-of-the-art MCMC algorithms and emulation strategies, and assess their performance in terms of their accuracy and computational efficiency. The long-term goal is to develop a method for reliable disease prognostication in real time, and our work is an important step towards an automatic clinical decision support system.

APPLICATION OF THEORIES OF ARTERIAL GROWTH, REMODELLING AND DAMAGE TO UNDERSTAND CEREBRAL VASOSPASM AND ITS RESPONSE TO TREATMENT

Giulia Pederzani, A. Grytsan, P. Bhogal, A.M. Robertson, P.N. Watton
University of Sheffield, Computer Science

Cerebral vasospasm (CVS) is an acute constriction of a cerebral artery which decreases the blood supply to the brain and is the leading cause of death for patients who survive hospitalisation following subarachnoid haemorrhage. Recently, the use of stent-retrievers to resolve the spasm has challenged the understanding of the disease and raised the potential for a shift towards a safer treatment [1]. We apply mathematical models of arterial growth and remodelling to gain insight into the underlying processes.

We model the arterial wall as a nonlinear elastic cylindrical membrane using a constrained mixture approach that explicitly accounts for load bearing, remodelling and damage of individual constituents [2]. Constituents are configured within the tissue in a preferred stretch to achieve optimum mechanical response about the homeostatic configuration. We account for collagen attachment stretch distributions and their remodelling [3], and the passive and active response of VSMCs with remodelling. In addition, we integrate our model [2] into a finite element framework that describes the anisotropic growth of a fibre-reinforced soft tissue [4].

We hypothesize that CVS is driven by VSMCsâ€™ remodelling about the new configuration and stiffening, and that treatment is successful when VSMCs are stretched beyond a failure threshold. This enables us to predict the magnitude of pressure a stent must apply to the wall to treat CVS. We simulate the mechanical behaviour of an artery in health, vasospasm and following constituent damage. Consistently with clinical observations [1], the model predicts that stent-retrievers are generally successful in smaller arteries (<3mm) but fail in the larger ones. However, the pressure necessary is about an order of magnitude smaller than balloon angioplasty, so new stents could be designed which represent a safer treatment option.

REFERENCES

1. Bhogal P. et al., J Neuroint Surg, 9:52-59, 2017 2. Bhogal, Pederzani et al., Clin. Neuroradiol., doi: 10.1007/s00062-019-00776-2, 2019.
3. Aparicio et al, J Biomech 49:2321-30, 2016.
4. Grytsan A. et al., Materials 10(9), 2017.

PHYSICAL STUDY OF MIDMEMBRANOUS LESIONS OF THE VOCAL FOLD

Xavier Pelorson, Annemie Van Hirtum, Anne Bouvet
CNRS, Laboratoire des Ecoulements Geophysiques et industriels

The vocal folds are elastic structures located inside the larynx. In interaction with the airflow coming out of the lungs, the vocal folds can be put into self sustained oscillations. This phenomenon constitutes the primary acoustic source of voiced sounds.
In this study we are interested in vocal folds pathologies altering the vocal folds tissues which can significantly alter or even prevent voicing. This includes the presence of a localised growth at the surface of one, or both, fold (cysts, nodules, polyps) or larger alterations (vocal fold scar, sulcus vocalis). A theoretical model of phonation will first be presented. It consists of a mechanical description of the vocal folds elasticity in a modal approach coupled with a quasi-steady viscous flow model for the airflow and with a linear 1-D description of the acoustics of the vocal tract. This theoretical model will be then modified in order to account for pathological vocal folds in the most plausible physiological way.
The outcomes of the theoretical model are compared with experimental results obtained on a mechanical replica of the larynx and of the vocal tract. The parameters of interest are not only the oscillation threshold pressure, the fundamental frequency but also the stability of the oscillation and the presence of frequency jumps.
It is first shown that, qualitatively, the results obtained by both theory and experiments compare well with what is reported from the literature in laryngology. Quantitatively, it is shown that the departures between the theoretical predictions and the experimental results are likely to be explained by the need for a refinement of the mechanical description of the vocal folds.

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A mathematical study to determine the screener size in isolation of exosomes using microfluidic chip

Nan Qi, Yujin Chu, Yu Zhang, Lin Han
University of Qingdao, China

Exosomes are small membrane vesicles secreted by most cell types and carry a cargo of biomarkers such as proteins and nucleic acids that are of great use for precision medicine. Studies have shown that exosomes from cerebrospinal fluid are involved in central neural system diseases, brain tumour progression and metastasis. To purify/isolate them from body fluid, one of the key procedures in an in-house designed microfluidic chip system is to filtrate the exosomes using a screener. To study this procedure, we modelled exosomes as soft/rigid membrane-like circles, and the size of which is known between 30nm to 150nm. The fluid in microfluidic channel is assumed to be a Poiseuille flow. The screeners selected for the chip design are with typical diameters of 70nm, 90nm and 110nm, so we conducted Monte-Carlo ball throwing simulations accordingly, the results of which are in good comparison. An optimisation algorithm which takes the concentration of filtrated particles as objective function is also explored to determine the optimal physical design of screener. This simple mathematical model could provide a guidance to the chip design and therefore be helpful for non-invasive disease diagnosis and precision treatment.

Cardiac poroelasticity modelling using a hybrid immersed boundary framework combined with finite element method for the Darcy flow

S.I.Heath Richardson, H.Gao, B.E.Griffith, C.Berry, X.Luo
School of Mathematics and Statistics, University of Glasgow, Glasgow

The importance of cardiac perfusion in any model which is aimed at generating an accurate representation of a beating myocardium can not be overstated. Moreover, while simulating the transport of blood within the heart ventricles is in itself a complex and challenging problem it is only after extending this further by, for example, linking to a coronary network tree that a range of significant phenomena can be investigated. Thus, given its importance, it is perhaps surprising that previous studies involving a poroelastic myocardium have neglected the three phase interaction between soft tissue, pore flow and blood flow inside the heart chamber, a crucial consideration for any applicable study. We therefore seek to rectify this through exploring this fluid-structure interaction via numerical simulation of a novel set of equations using a hybrid immersed boundary/finite element approach. Our results are subsequently benchmarked by examining a pair of prototypical poroelastic formations uaing a simple cubic geometry while we thereafter extend and simulate part of a cardiac cycle within a more applicable geometry.

KEYWORDS: Poroelasticity, porous media, finite element, immersed boundary, Darcy flow, fluid-structure interaction,

REFERENCES

1. A poroelastic model valid in large strains with applications to perfusion in cardiac modelling, Chapelle 2010.
2. A computational study of the interaction between coronary blood flow and myocardial mechanics, Smith 2004.
3. A novel porous mechanical framework for modelling the interaction between coronary perfusion and myocardial mechanics, Cookson 2012.

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A continuum approach on modeling the heterogenous distribution of elastin degradation in the aortic wall

Malte ROLF-PISSARCZYK [1], Kewei LI[1] and Gerhard A. HOLZAPFEL[1,2]
1 Institute of Biomechanics, Graz University of Technology,
Streymayrgasse 16-II, 8010 Graz, Austria
e-mail: holzapfel@tugraz.at, web page: https://www.biomech.tugraz.at/
2 Faculty of Engineering Science and Technology,
Norwegian University of Science and Technology (NTNU), 7491 Trondheim, Norway

Aortic dissection is a severe cardiovascular disease. Usually, it initiates as a small tear in the intimal layer of the aortic wall and extends to the medial layer later. Then, it propagates along the longitudinal direction of the medial layer, resulting in a false lumen. It is suggested that the propagation of the dissection is often induced by the degradation of elastin [1], which is an essential part of the aortic wall.

Studying the degradation of elastic fibers in the aortic wall, a possible role is giving to the accumulation of pooled Glycosaminoglycans [1]. They can induce a swelling pressure between the elastic lamellae in the extracellular matrix causing damage of interlamellar elastic fibers which interconnect either with smooth muscle cells or the elastic lamellae. In this study, a constitutive continuum model is proposed to describe the appearing degradation of elastic fibers.

In the constitutive model, we decompose the strain-energy function into three parts: ground substance, collagen fibers and elastin, weighted by the corresponding volume fraction of the constituent. The ground substance is described by the neo-Hookean material model. The discrete fiber dispersion method [2] is used to incorporate the contributions of dispersed collagen and elastic fibers in the aortic wall. The dispersion of the elastic fibers represents the material behavior of all forms of elastin present in the medial layer which includes elastic fibers, struts and lamellae. Furthermore, a degradation parameter is introduced to quantify the degradation of elastic fibers in the radial direction. In consequence of the heterogeneous distribution of Glycosaminoglycans in the aortic wall [3], the degradation parameter is given by a function depending on the transmural location. Representative numerical examples are chosen to demonstrate the performance of the proposed constitutive model with a locally defined degradation parameter.

REFERENCES

[1] J.D. Humphrey: Possible mechanical roles of glycosaminoglycans in thoracic aortic dissection and associations with dysregulated transforming growth factor-beta. J Vasc Res. 2013;50(1):1-10.
[2] K. Li, R.W. Ogden and G.A. Holzapfel: A discrete fibre dispersion method for excluding fibres under compression in the modelling of fibrous tissue. J R Soc Interface. 2018 Jan;15(138). 20170766.

[3] E.U. Azeloglu et al.: Heterogeneous transmural proteoglycan distribution provides a mechanism for regulating residual stresses in the aorta. Am J Physiol Heart Circ Physiol. 2008 Mar;294(3):H1197-205.

CAN WE 3D PRINT MECHANICALLY REALISTIC ARTERIAL REPLICAS

Marija Smoljkić, Josip Živić, Zoran Tomić, Toni Škugor, and Igor Karšaj

Faculty of Mechanical Engineering and Naval Architecture (FSB)
Universitiy of Zagreb
Ivana Lucića 5, 10000 Zagreb, Croatia
e-mail: marija.smoljkic@fsb.hr, web page: https://www.fsb.unizg.hr/

In biomedicine, 3D printing has multiple purposes. Printed replicas are often used for educational purposes and designing, choosing or testing medical devices. However, current 3D printed models provide us with a realistic geometry and unrealistic mechanical behaviour. Our goal is to 3D print geometrically and mechanically realistic arterial replicas. Due to complexity of arterial behaviour, e.g. anisotropy and nonlinearity, this can not be achieved with a single polymer isotropic material. Fortunately, modern 3D printing machines, such as Connex 350 (Stratasys, USA), use multiple materials and enable us to produce geometries with more complex mechanical response.

Common carotid arteries (CCAs) often undergo treatments, e.g. angioplasty and stenting, to prevent stroke [1]. Their mechanical response is known from the experimental studies reported in literature [2]. In this work, the goal is to design an artificial material which will be able to represent mechanical behaviour of CCAs in the *in vivo* pressure range.

Perfectly cylindrical segments representing CCAs are designed in SolidWorks out of two materials. Harder material represents collagen fibres, while softer material represents elastic matrix which mainly consists out of elastin. The materials have been previously tested and characterized with two constitutive material models, Neo-Hookean and Demiray. The geometry of the harder material embedded in the soft matrix has been iteratively changed and compared to the experimental extension-inflation curves reported in [2]. The harder material is designed to have a wavy structure. All the challenges tackled in the design process will be stated and discussed.

The final geometry will be 3D printed and experimentally tested on an extension-inflation setup to confirm simulated mechanical response.

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REFERENCES

[1] Coward LJ, Featherstone RL, "Percutaneous transluminal angioplasty and stenting for carotid artery stenosis (review)," Cochrane Database Syst Rev. 2004:(2):CD000515.

[2] G. Sommer *et al.*, "Mechanical strength of aneurysmatic and dissected human thoracic aortas at different shear loading modes," *J. Biomech.*, vol. 49, no. 12, pp. 2374–2382, 2016.

MASS-GROWTH OF A FINITE TUBE REINFORCED BY A PAIR OF HELICAL FIBRES

Konstantinos Soldatos
University of Nottingham, School of Mathematical Sciences

Several types of tube-like fibre-reinforced tissue are reinforced by a pair of helical fibres wound symmetrically around the tube axis in opposite directions. In many cases, this kind of biological structures grow in an axially symmetric manner that preserves their own shape as well as the direction and shape of their fibres. This study investigates the influence that preservation of fibre direction exerts on pseudo-elastic (elastic-like) mass-growth modelling of the described fibre-reinforced structure. Accordingly, sets of necessary conditions that enable the implied tube mass-growth to take place are initially sought and found, with the scope to provide information which, if combined with standard kinematic relations and equilibrium equations met in hyperelasticity, lead to identification of corresponding admissible classes of strain energy density for growth, W. To a certain extent, the present analysis follows the footsteps of its recent predecessor [J. Eng. Math., 109: 173-210,

2018], which dealt with relevant mass-growth of a tube that preserves the (essentially arbitrary) direction of a single family of embedded fibres. However, a major difficulty met in the case of a pair of fibre families stems from the fact that the classical deformation invariants involved in W are not any more independent. Through successful resolution of this difficulty, the aforementioned necessary conditions enable again development of partial differential equations for W, and, hence, identification of admissible classes of the strain energy for growth that underpin the implied kind of tube mass-growth [Mech. Res. Comm. 95, 71-78 (2019)]. An application is also presented, where the helically reinforced tube grows in an incompressible manner. Namely, in a non-isochoric manner that preserves both fibre directions as well as the material density of the growing fibre-reinforced tube.

ELASTIC JUMPS ON NETWORKS: PREDICTING RETINAL HAEORRHAGE

Peter Stewart, Tamsin Spelman
University of Glasgow, Mathematics and Statistics Department

The blood vessels in the human retina are supplied (drained) by the central retinal artery (vein) which enters (leaves) the eye through the centre of the optic nerve. These blood vessels cross the cerebrospinal fluid in the brain just outside the globe and so constitute a key point of coupling between the eye and the brain. We demonstrate how an acute pressure rise in the brain can induce a large amplitude pressure wave to be transmitted along the central retinal vessels and propagate through the retinal circulation. In some cases this wave steepens to form a shock which then spreads out as it passes bifurcations. We predict the accompanying reduction in amplitude as the pressure wave propagates through the structure and consider the possibility of localised blood vessel bursting in response to the trauma ie a retinal haemorrhage.

STUDY OF THE INFLUENCE OF WATER SPRAYING ON AN ONGOING FLUID-STRUCTURE INTERACTION: APPLICATION TO THE ROLE OF VOCAL FOLDS SURFACE HYDRATION IN PHONATION

Annemie Van Hirtum, Anne Bouvet, Xavier Pelorson
CNRS, Grenoble Alpes University, LEGI

Human voiced sound production or phonation is the result of a fluid-structure instability in the larynx leading to vocal folds auto-oscillation. It is shown that surface hydration affects the fluid-structure instability and resulting auto-oscillation. The physical effects of surface hydration on phonation remain an open research question since most studies consider dry conditions. In this work, water spraying (0 up to 5 mL) is used to quantify the effect on deformable mechanical vocal folds replicas and a flow model is proposed and validated for a rigid vocal folds replica with a motor-driven motion. The pressure upstream from the mechanical vocal fold replica is measured for all replicas. Furthermore, the rigid replica allows measuring the pressure within the glottal constriction as well. For deformable self-oscillating vocal folds replicas changes to the upstream pressure signal are quantified as a function of the sprayed water volume firstly for features commonly assessed in voice research and secondly the complexity or required degrees of freedom for the upstream pressure is sought. For all deformable replicas, it is observed that, for increasing sprayed water volume, the first harmonic decreases, rapid cycle-to-cycle fluctuations increase and a closing-opening asymmetry occurs. Nevertheless, the degree to which these effects are established depends on initial conditions of the replica, i.e. both mechanical and geometrical. From the complexity analysis follows that 1) the ratio of the degree of determinism to the recurrence rate of the phase space and 2) the correlation dimension are suitable parameters to grasp the effect of water spraying on the oscillation pattern and to reflect the influence of initial conditions on the vocal folds replicas. In the case of the motor-driven oscillation (rigid replica) a simplified viscous air-water mixing flow model could be validated. The flow model is suitable for a stability analysis of the fluid-structure interaction.

ANEURYSM MORPHOLOGY AND RUPTURE: COMPUTATIONAL CASE STUDY USING 3D FINITE ELEMENTS

Lana Virag, Nino Horvat, Igor Karsaj
University of Zagreb, Faculty of Mechanical Engineering and Naval Architecture

Abdominal aortic aneurysms (AAAs) are localized dilatations of the infrarenal abdominal aorta. AAAs often remain asymptomatic until rupture, an event with high mortality rate. Current clinical capabilities for predicting rupture remain wanting, and clinical interventions continue to be based primarily on the maximum diameter or expansion rate of the lesion, despite various efforts to find a more reliable rupture criterion, and to increase understanding of the disease. It has been hypothesized that aneurysm morphology are more predictive of rupture risk. Shum et al. (1) defined twenty-five size and shape indices in total, and estimated their importance for aneurysm rupture.

In this contribution, using constrained mixture growth and remodelling model of the arterial wall from [2] implemented into 3D finite elements, we computationally study the importance of aneurysm length and axial features on aneurysm expansion rate and likelihood of rupture. During the growth of axially non-symmetric aneurysm increase in arterial curvature (i.e., tortuosity) due to high axial stresses, and local degradation of elastin was observed. Use of different shapes of spatio-temporal elastin degradation function allows us simulation of effects of possible elastase diffusion directions (e.g., in radial-circumferential plane or perpendicular to aneurysm geometry). Moreover, elastin degradation function determines aneurysm sac shape. We compared numerical results with their clinical findings from [2] showing the effects of morphological features (e.g., length, tortuosity, maximum diameter to length radio, asymmetry factor) on likelihood of aneurysm rupture. Our findings agree excellently with the clinics.

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RERERENCES

1.Shum et al, Ann Biomed Eng, 39(2011).
2.J. D. Humphrey, K.R. Rajagopal, Math Method Appl Sci 12(2002) 407.

THE ENERGETICS OF SELF-EXCITED OSCILLATIONS IN COLLAPSIBLE CHANNEL FLOW

Danyang Wang[1], Peter Stewart[2] , Xiaoyu Luo[2]
[1]Manchester Metropolitan University, School of Engineering
[2]University of Glasgow, School of Mathematics and Statistics

There are many examples of fluid-conveying vessels in the human body. When these vessels are subject to a negative transmural pressure (internal minus external) while conveying a flow, self-excited oscillations can occur. Applications of this phenomenon arise in many physiological examples, such as Korotkoff sound generation during blood pressure measurement. We explore the generation of self-excited oscillations in a two-dimensional channel that consists of rigid and flexible segments conveying a laminar high-Reynolds number flow. In particular, we construct a general framework for analyzing the energy budget of self-excited oscillations about a non-uniform basic state. We then apply this general framework to consider two particular models for the flexible wall, namely a simple membrane model with an external pressure gradient [1] and fluid-beam model [2].

REFERENCES

[1] Stewart P S, Waters S L, Jensen O E. Local instabilities of flow in a flexible channel: asymmetric flutter driven by a weak critical layer. Physics of Fluids, 2010, 22(3): 031902.
[2] Cai Z X, Luo X Y. A fluidâ€“beam model for flow in a collapsible channel. Journal of Fluids and Structures, 2003, 17(1): 125-146.

DYNAMICS OF IRIS IN PHACO PROBE INDUCED FLOW DURING CATARACT SURGERY

Zhaokun Wang[1,*], Chenglei Wang[1], Xiaoyu Luo[2], Hui Tang[1,#]
[1]Department of Mechanical Engineering, The Hong Kong Polytechnic University, Hong Kong SAR, China
[2]School of Mathematics and Statistics, University of Glasgow, Glasgow, UK

Abstract: Cataract is the leading cause of blindness, responsible for 33% of visual impairment worldwide and 51% of world blindness. The most effective treatment for cataracts is phacoemulsification-based cataract surgery, which has become nowadays the standard method to remove cataract[1]. Investigating the interaction between intraocular flow and iris during phacoemulsification-based cataract surgery is important to understand the occurrence of intraoperative floppy iris syndrome (IFIS), which always degrades the surgery outcome. Addressing this problem typically requires the analysis coupling both fluid dynamics and structural mechanics[2]. In the work, we study the dynamics of a simplified iris with the intraocular flow in cataract surgery using a newly developed fluid-structure interaction (FSI) simulation framework, as sketched in Fig. 1. The lattice Boltzmann method (LBM) is used to simulate the intraocular flow driven by a simplified phaco probe. The iris structure with large deformation is solved using the finite element method (FEM) based on the co-rotational formulation method. The immersed boundary (IB) method is used to deal with the fluid-iris interaction. The dynamics of the fluid-iris system is studied in details. Different iris deformation states are identified. In addition, the effects of the iris bending stiffness, mass ratio, and phaco probe position and vibration frequency on these states are examined. The simulation results reveal some physical insights into the dynamics of this intraocular fluid-iris system, which can provide reasonable guidance to clinicians.

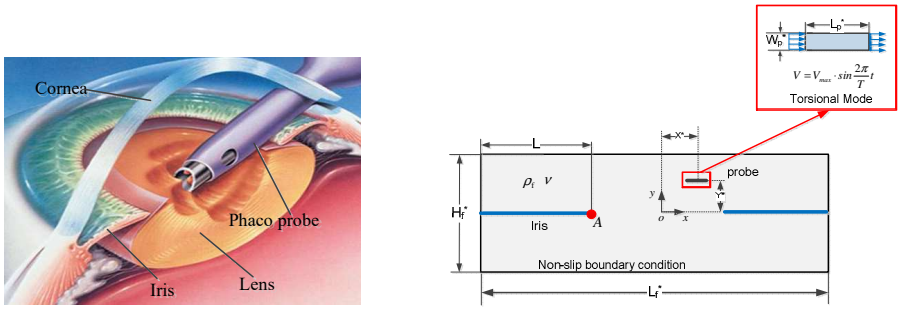

Fig.1. Schematics of (a) cataract surgery (adapted from: http://www.drray.co.uk/cataract-surgery-diagram/) and (b) FSI simulation settings for the probe torsional operation mode.

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REFERENCES

Kelman, C.D. (2018). "Phaco-emulsification and aspiration: a new technique of cataract removal: a preliminary report. " *Am. J. Ophthalmol.* 191, xxx-xl.

Tian, F.-B., H. Luo, L. Zhu, J.C. Liao, and X.-Y. Lu (2011), "An efficient immersed boundary-lattice Boltzmann method for the hydrodynamic interaction of elastic filaments." *J. Comput. Phys.* 230: 7266–7283.

IMAGE SEGMENTATION BASED ON MYOCARDIAL PERFUSION MRI DATA

Yalei Yang, Dirk Husmeier, Aleksandra Radjenovic, Hao Gao
University of Glasgow, School of Mathematics & Statistics

In myocardial perfusion images, there might be some lesions located in the region of interest. The detection of lesions will be vital when the lesions are not easy to be observed by human eyes. The goal can be modeled by a finite mixture model in statistics. There are several algorithms to deal with this case. Basic EM Gaussian Mixture Model can be used but the performance is not good enough. My work is to use some modifications of this algorithm to improve and compare the performance of lesion detection.

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Analyzing the role of viscoelasticity in the residual stress in soft tissues: a case study on human aortas

Will Zhang[1], Gerhard Sommer[2], Gerhard Holzapfel[2], David Nordsletten[1, 3]

[1]Department of Biomedical Engineering and Cardiac Surgery, University of Michigan, Ann Arbor, USA
[2]Institute of Biomechanics, Graz University of Technology, Graz, Austria
[3]Imaging Sciences & Biomedical Engineering, King's College London, London, United Kingdom

Residual stress is a crucial and well-recognized property in understanding the functional mechanical properties of soft tissues. Its existence is crucial in homogenizing the in vivo stresses in tissues and organs, thus also proving its importance in computational studies of biological tissues and organs. The primary example used to study residual stresses is the gradual opening of arterial tissues after being cut longitudinally. However, vast majority of such analyses consider only the elastic component of the tissues, yet the gradual opening of the artery indicates the significant role of viscoelasticity in this time-dependent process. In this study, we built a finite element model using the geometry and data from the study by Holzapfel et al. [1] using the constitutive model and the material parameters for human aorta from Niestrawska et al. [2]. We extended the elastic model for viscoelasticity by embedding the inside a fractional derivative and develop a computationally efficient approach for evaluating the viscoelastic fraction. We determined the degree of viscoelasticity based on the fraction of elastic vs viscoelastic component, and the order of the fractional derivative. These two values were determined by matching the change in opening angle over the course of 18 hours and by simulating the biaxial mechanical testing from Holzapfel et al. [2] and matching the resulting hysteresis. Although the hysteresis exhibited in the physiologic range is small in arterial tissues, matrix of the artery is mostly elastic, approximately 40% of the matrix is viscoelastic. Most of the viscoelastic effects are due to the collagen fiber networks, while the residual strains are in the range of the matrix, below the range where collagen fibers start baring stresses. This suggests that the residual stresses are much smaller than conventional estimates, and that viscoelasticity is important to understand the functional mechanical properties of such soft tissues.

Reference

[1] Holzapfel, G. A.; Sommer, G.; Auer, M.; Regitnig, P. & Ogden, R. W. “Layer-Specific 3D Residual Deformations of Human Aortas with Non-Atherosclerotic Intimal Thickening”. *Annals of Biomedical Engineering, Springer Nature*, 2007, **35**, 530-545

[2] Niestrawska, J. A.; Viertler, C.; Regitnig, P.; Cohnert, T. U.; Sommer, G. & Holzapfel, G. A. “Microstructure and mechanics of healthy and aneurysmatic abdominal aortas: experimental analysis and modelling.” *Journal of The Royal Society Interface*, 2016, **13**, 20160620

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Coupled agent-based and hyperelastic modelling of the left ventricle post-myocardial infarction

Xin Zhuan, Xiaoyu Luo, Hao Gao, Ray Ogden
School of Mathematics and Statistics, University of Glasgow, Glasgow

Understanding the healing and remodelling processes induced by myocardial infarction (MI) of the heart is important and the mechanical properties of the myocardium post-MI can be indicative for effective treatments aimed at avoiding eventual heart failure. MI remodelling is a multiscale feedback process between the mechanical loading and cellular adaptation. In this paper, we use an agent-based model to describe collagen remodelling by fibroblasts regulated by chemical and mechanical cues after acute MI, and upscale into a finite element 3D left ventricular model. We model the dispersed collagen fibre structure using the angular integration method, and have incorporated a collagen fibre tension-compression switch in the LV model. This enables us to study the scar healing (collagen deposition, degradation and reorientation) of a rat heart post-MI. Our results, in terms of collagen accumulation and alignment, compare well with published experimental data. In addition, we show that different shapes of the MI region can affect the collagen remodelling, and in particular, the mechanical cue plays an important role in the healing process.

KEYWORDS:
left ventricular modelling, myocardial infarction, agent-based model, finite element method, fibre orientation

REFERENCES

Zhuan, X., Luo, X., Gao, H. and Ogden, R.W., 2019. Coupled agent-based and hyperelastic modelling of the left ventricle post-myocardial infarction. International journal for numerical methods in biomedical engineering, 35(1), p.e3155

Information for Delegates

4th Soft Tissue Modelling Workshop, 5th to 7th June 2019

Before You Arrive

Insurance

As with all travel, delegates are strongly advised to ensure they have sufficient insurance in place as they will not be covered by the University of Glasgow's insurance or the insurance of any of their associated partners.

European Health Insurance Card

(Please note section is applicable to European Economic Area citizens only)
The European Health Insurance Card (EHIC) replaced the E111 card and allows European Economic Area (EEA) citizens* to access state-provided healthcare in all EEA countries and Switzerland at a reduced cost or free of charge. Applying for the EHIC is free and the cards are valid for up to five years (if you already possess an EHIC it is important to check it is still valid). The EHIC is NOT an alternative to travel insurance. It will not cover any private medical healthcare or the cost of things such as repatriation or lost/stolen property. For these reasons and others, it is important to have both an EHIC and a valid private travel insurance policy.
*exclusions do apply, and you should check your own national guidelines for full information

Wi-Fi and IT

The University of Glasgow has many wi-fi hotspots throughout the campus. We suggest that you access this service using Eduroam: https://www.eduroam.org/. Eduroam is a secure, world-wide roaming access service developed for the international research and education community. This has to be issued in advance at your 'home' institution. At the University of Glasgow it is provided as a broadcast wireless network available wherever there is wireless coverage. A Visitor's guide to Eduroam for the University of Glasgow is available here: http://www.gla.ac.uk/services/it/eduroam/forvisitors/

For those unable to access Eduroam please let us know in advance by emailing Gillian.Brown@glasgow.ac.uk and Hao.Gao@glasgow.ac.uk

Speakers

This is Room 116 where you will be presenting your talk

Lecture Theatre (Rm 116)

We recommend uploading your presentation to the presentation computer and to check the compatibility prior to your session. PowerPoint and PDF presentations are accepted. You can also use your own laptop; however, support is limited. Ideally, we will try and arrange uploading prior to the first talk or during a session break.

Posters

Details for setting up of posters will be given at registration.

Programme

The programme will be available at http://www.softmech.org/events/headline_587639_en.html

Location of the Conference

The conference will take place on the ground floor of the

School of Mathematics & Statistics
The Mathematics and Statistics Building
University of Glasgow
University Place
Glasgow G12 8QQ

Getting Around Glasgow

Please see the University of Glasgow website (http://www.gla.ac.uk/about/maps/howtogethere/) for information on travelling to the University.

Maps

A map of the University campus and surrounding area can be found here
The Mathematics and Statistics Building is C3 on the map.

http://www.gla.ac.uk/media/media_335384_en.pdf

Accessibility maps are available here:
http://www.gla.ac.uk/about/accessibility/physicalaccess-buildingguides/accessibility/

Buses

First Glasgow Bus routes 4 and 4A stop directly outside the Main Building from the city centre. Other routes serve Dumbarton Road, Great Western Road and Byres Road. See First Bus website for timetables and journey planner
http://www.firstgroup.com/ukbus/glasgow/
A seasonal tourist (open top) bus stops at the University (generally departs from George Square in Glasgow city centre).

Subway

This is a very safe method for travelling around Glasgow and is very useful for travelling in and out of the city centre. The nearest subway station to the University is Hillhead Station on Byres Road (approximately 5-minute walk from the University's main building). On exiting Hillhead station, turn left onto Byres Road then take a second left onto University Avenue. Further information (inc. any service disruption) is available from
http://www.spt.co.uk/subway

Local trains

The nearest suburban rail station is Partick, approximately one mile west of the University. It has an interchange with the subway and with bus services on Dumbarton Road. Further information is available from http://www.nationalrail.co.uk/

Taxis

Black Taxis can be flagged on the street or reserved by calling: + 44 (0)141 429 7070 (Glasgow Taxis http://www.glasgowtaxis.co.uk/). Black taxis can also be found outside Hillhead Subway Station. Please note, private hire taxis cannot be flagged on the street and must be booked in advance.

During the Conference

Registration

Registration will take place in Room 110.

Social Events / Excursions

Conference Dinner on Thursday 6th June 7pm: This will be held at the Hilton Grosvenor Hotel, 1-9 Grosvenor Terrace, Glasgow, G12 0TA, United Kingdom. This is a 5-minute walk from the Maths and Statistics Building
https://www3.hilton.com/en/hotels/united-kingdom/hilton-glasgow-grosvenor-GLAGRHN/event/index.html

Afternoon Hike on Friday 7th June: Details to follow; for anyone who would like to take part you will need hiking boots and a waterproof jacket.

Electrical Equipment

Please note there are no power sockets accessible to delegates on campus and as such it is not possible to charge any electrical devices during the conference.

Delegates are also reminded that it is their responsibility to bring any necessary connector cables and/or travel plug adaptors as the organisers and the venue cannot assist in supplying these.

Local Information

The University of Glasgow is situated only a couple of minutes' walk from Byres Road, one of the most famous streets in Glasgow, which has a wide selection of cafes, restaurants and bars alongside well-known high street shops and banks.

ATMs

On campus
McIntyre Building – level one
Fraser Building – level one (next to John Smith Book Shop)

Off campus
Bank of Scotland (174 Byres Street)
Alliance & Leicester (297 – 299 Byres Road)
Royal Bank of Scotland (399 Byres Road)

Pharmacy / Medical Advice

NHS 24 (Helpline):	Freephone 111 (https://www.nhs24.scot/)
On campus:	Barclay Medical Centre, Fraser Building, University of Glasgow
	Hillhead Pharmacy, Fraser Building, University of Glasgow
Off campus:	Boots Pharmacy (277 Byres Road)

Hospital – Emergency Department

Queen Elizabeth University Hospital, Glasgow G51 4SX
http://www.nhsggc.org.uk/patients-and-visitors/main-hospital-sites/queen-elizabeth-university-hospital-campus/

Eating Out

We recommend you register for http://www.5pm.co.uk/restaurant/Glasgow which allows you to
search and book many great value dining options in a huge number of restaurants across Glasgow.

Places to Visit

What's On (https://peoplemakeglasgow.com/whats-on)
The Hunterian (http://www.gla.ac.uk/hunterian/)
Glasgow Museums (http://www.glasgowlife.org.uk/museums/Pages/home.aspx)
Loch Lomond & Trossachs National Park (http://www.lochlomond-trossachs.org/)
King's Theatre, Glasgow (http://www.atgtickets.com/venues/kings-theatre/)
Theatre Royal, Glasgow (http://www.atgtickets.com/8/654/Theatre-Royal)
ABC Glasgow -Club & Live Music Venue (http://www.o2abcglasgow.co.uk/)

Shopping & Leisure

Braehead Shopping & Leisure Centre (https://intu.co.uk/braehead)
Buchanan Galleries (http://www.buchanangalleries.co.uk/)
Princes Square (http://www.princessquare.co.uk/)
The Fort (http://www.glasgowfort.co.uk/)
Silverburn Shopping Centre (http://www.shopsilverburn.com/)
Loch Lomond Shores (http://www.lochlomondshores.com/)

Useful Contacts / Links

Glasgow Tourist Information
0141 204 4400
https://peoplemakeglasgow.com/

Glasgow International Airport
0844 481 5555
http://www.glasgowairport.com

Glasgow Prestwick Airport
0871 223 0700
http://www.glasgowprestwick.com

First ScotRail: Timetables and Tickets
0845 601 5929
http://www.scotrail.co.uk

Virgin Trains: London Euston - Glasgow
08457 222 333
http://www.virgintrains.co.uk

National Rail: Train Times and Tickets
08457 48 49 50
http://www.nationalrail.co.uk/

AA Route Planner
http://www.theaa.com/route-planner/index.jsp

RAC Route Planner
http://www.rac.co.uk/route-planner/

Scotland Public Transport Planner
0871 200 22 33
http://www.travelinescotland.com

Glasgow Bus, Rail and Subway Transport Planner
http://www.travelinescotland.com/lts/#/travelInfo

Glasgow Taxis
0141 429 7070
http://www.glasgowtaxis.co.uk/

Glasgow City Parking
0141 276 1830
http:// www.cityparkingglasgow.co.uk