EUROPEAN MECHANICS SOCIETY

Colloquium Final Report

N. 604 – Fluid and solid mechanics for tissue engineering

Dates and location: **23/09/2019 - 25/09/2019, Oxford, UK**

Chairperson **Professor Sarah Waters**

Co-Chairperson **Professor Liesbet Geris**

Conference fees

- Regular registration fee (early bird) **144.0 €**
- Regular registration fee **202.0 €**

What other funding was obtained? **We received funding to support the workshop from "Quantitative Biology Oxford (QBIOX)". QBIOX is an interdisciplinary network, funded by and based at the University of Oxford, that fosters a culture of quantitative research in the biosciences with a focus on applications in developmental biology, cancer and tissue engineering where similar cell- and tissue-level processes are at play and hence have common theoretical methodologies. The aim of QBIOX is to bring together biomedical and physical scientists to exploit synergies between the application areas, and facilitate the formation of large and coherent multidisciplinary consortia of researchers who share a commitment to making biology and medicine quantitative. We received in kind support from the Mathematical Institute, University of Oxford, in the form of access to state of the art lecture room, representing in kind support of £3300. We also received support from Cambridge University Press in the form of the Journal of Fluid Mechanics promotional materials.**

What were the participants offered?
The meeting took place at the Mathematical Institute, University of Oxford, September 23-25 2019.

Delegates arrived for lunch on day 1, and left after lunch on day 3. As part of the Colloquium package, delegates received all lunches, morning and afternoon refreshments, dinner on the evening of day 1 (at a restaurant in central Oxford), and a conference dinner on day 2 (at St Anne's College, Oxford). Delegates had access to WiFi facilities. Administrative enquiries by delegates (both ahead of and during the Colloquium) were expertly handled by Dr Nicola Kirkham, PA to Professor Sarah Waters. All the keynote and invited presentations were held in a state of the art lecture room (provided at no charge by the Mathematical Institute). Posters contributions were exhibited close to the refreshements during breaks and lunches to encourage ongoing interactions. All delegates were provided with a printed Colloquium Program, as well as complementary notebook.

Early bird registration was 174 EUROS, (144 EUROS Members)
Regular registration was 232 EUROS (202 EUROS Members).

40 delegates attended the Colloquium, drawn from the UK (20), Netherlands (3), Israel (1), Germany (1), Singapore (1), Austria (1), Ireland (1), Italy (3), USA (3), South Africa (1), Belgium (4) and Australia (1).

Delegates:

Keynote speakers:

Roger Kamm, Cecil and Ida Green Distinguished Professor of Biological and Mechanical Engineering, MIT

Alicia El Haj, Interdisciplinary Chair of Cell Engineering, Healthcare Technology Institute, University of Birmingham

Invited speakers:

Davide Ambrosi, Politecnico di Torino, Italy

Mojtaba Barzegari, University of Liege, Belgium

Anthony Callanan, University of Edinburgh, UK

Ruth Cameron, University of Cambridge, UK

Sonia Contera, University of Oxford, UK

Linda Cummings, New Jersey Institute of Technology, USA

Mohit Dalwadi, University of Oxford, UK

John Dunlop, University of Salzburg, Austria

Liesbet Geris, University of Liege, Belgium

John King, Nottingham, UK

Nati Korin, Technion, Israel

Catriona Lally, Trinity College Dublin, Ireland

Sandra Loerakker, Eindhoven University of Technology, Netherlands

Scott McCue, Queensland University of Technology, Australia

Pierre-Alexis Mouthuy, University of Oxford, UK

Satanik Mukherjee, KU Leuven, Belgium

Tom Mullin, University of Oxford, UK

Ramin Nasehi, Politecnico di Milano, Italy

Reuben O'Dea, University of Nottingham, UK

James Oliver, University of Oxford, UK

Ioannis Papantoniou, KU Leuven, Belgium

Luigi Preziosi, Politecnico di Torino, Italy

Rebecca Shipley, University College London, UK

Barbara Wagner, Weierstrass Institute for Applied Analysis and Stochastics, Berlin

Sarah Waters, Oxford University, UK

Cathy Ye, Oxford University, UK

Edwina Yeo, Oxford University, UK

Feihu Zhao, Eindhoven University of Technology, Netherlands

Poster presentations:

Ashwin Seetharaman, Singapore

Ridhwaan Suliman, South Africa

Helen Zha, Oxford University, UK

Delegates:

Giulia Celora, Oxford University, UK
Andreas Muench, Oxford University, UK
Amy Kent, Oxford University, UK
Matteo Taffetani, Oxford University, UK
Stefan Llewellyn-Smith, UCSD, USA
Francesco Viola, Netherlands
Sahand Zanjani pour, Oxford University, UK

Number of members of Euromech (reduced registration fee) **15**

Number of non-members of Euromech (full registration fee) **25**

Applicants (members)

- Davide Ambrosi
- Anthony Callanan
- Lally Catriona
- Sonia Contera
- Linda Cummings
- Liesbert Geris
- John King
- Sandra Loerakker
- Ramin Nasehi

- Reuben O'Dea
- Ridhwaan Suliman
- Matteo Taffetani
- Francesco Viola
- Sarah Waters
- Feihu Zhao

Applicants (non members)

- Mojtaba Barzegari
- Ruth Cameron
- Giulia Laura Celora
- Mohit Dalwadi
- John Dunlop
- Alicia El-Haj
- Roger Kamm
- Amy Kent
- Netanel (Nati) Korin
- Stefan Llewellyn Smith
- Scott McCue
- Pierre Mouthuy
- Andreas Muench
- Satanik Mukherjee
- Tom Mullin
- James Oliver
- Ioannis Papantoniou
- Luigi Preziosi
- Ashwin Seetharaman
- Rebecca Shipley
- Barbara Wagner
- Cathy Ye
- Edwina Yeo
- Sahand Zanjani pour
- Helen Zha

Scientific Report

In this colloquium, we presented state-of-the-art theoretical and experimental fluid and solid mechanics for TE, and explored the transformative potential of combined quantitative theoretical and experimental approaches to inform in vitro TE protocols. Delegates were drawn from the theoretical and experimental fluid and solid mechanics communities. To ensure the focus remained applicable to the TE challenges, we invited leading figures from the TE community, which also facilitated new opportunities for interdisciplinary collaboration.

In vitro tissue engineering (TE) aims to create functional tissue and organ samples external to the body to replace damaged or diseased tissues and organs. By using cells (e.g. autologous or allogenic) in combination with natural or synthetic biomaterial scaffolds and biochemical factors, tissue engineered products have many advantages over traditional approaches such as donor tissue and organ transplantation that can elicit an adverse immune response. The development of the growing tissue construct, the combination of scaffold, cells, extracellular matrix (ECM) and biochemical factors, often occurs within a bioreactor that enables precise control of the bio-mechanochemical environment experienced by the cells within the growing construct.

This is particularly important in the development of mechanosensitive tissues, such as bone. Successfully engineering tissues in vitro has required the development of new smart biomaterials, new tissue growth strategies involving defined biological cues, and novel and bespoke bioreactor environments for growing tissue under physiological mechanical conditions. To date, only simple avascular tissues have been successfully generated to a standard where they can be used in a clinical setting, and research into methods for improving tissue viability is essential.

In TE systems, fluid and solid mechanics are used to provide mechanical load (e.g. via fluid shear, elastic deformation) to mechanosensitive tissues such as bone and vasculature, and a key challenge is to recreate the mechanical environment within the bioreactor system that is unique to the tissue under consideration. The fluid flows and solid deformations are intricate, requiring an understanding of novel fluid-structure interactions between the fluid flows, the cells and their ECM, and the (often deformable) biomaterial. Furthermore, successful tissue growth in bioreactor systems relies on appropriate solute delivery to and waste-product removal from the cells in the tissue construct. To promote transport (without recourse to agitation methods that can be damaging to cells in a tissue-engineering setting), fluid flows are exploited to enhance transport by advection.

The Colloquium had 8 sessions organised around themes. Each session stimulated excellent levels of discussion (we ensured the timetable allowed plenty of time for discussion). The sessions were complemented by lively poster sessions, and excellent discussion in all breaks etc. The engagement between the different communities was fantastic.

In the introductory session, El Haj gave an excellent opening keynote by showcasing the ways we grow tissues in vitro and highlighting how multidisciplinary teams with mathematicians, engineers and biologists can combine efforts to address challenges in the field. Waters then showed how mechanistic mathematical modelling can be used to provide insights into the fluid and solid mechanics environments encountered by cells in a tissue engineering setting, considering scales ranging from a scaffold pore to a bioreactor system. O'Dea showed how a multiphase modelling approach together with multi scale homogenisation techniques can be employed to inform scaffold design and functionalisation by understanding how scaffold pore design, nutrient transport and distributions of BMP2 may be tailored to promote osteogenesis and thereby to guide ongoing in vitro experiments.

The focus of the second session was on materials. Callanan demonstrated how experimentation and modelling can be used together to unlock the full potential of biomaterials. Cameron described how ice-templating and electrophoretic deposition technologies can be exploited to create novel, complex and biomimetic 3D environments for the control of tissue growth. The approach is adaptable to a wide range of medical applications, including osteochondral repair, cardiac patches, dermal grafts, breast cancer diagnostics and bioreactors for platelet generation. Mullin presented the results of experimental investigations into the motion of light spheres in a rotating horizontal drum filled with viscous fluid, with applications to biological scaffolds.

In the soft tissue modelling session, Mouthuy spoke about a novel type of dynamic bioreactor
system that makes use of musculoskeletal humanoid robots to apply realistic mechanical stresses to tendon tissue constructs in vitro. Such a system can be used for pre-clinical testing of novel biomaterials, including degradable

biomaterials made of submicron electrospun fibres. Lally spoke about tissue engineering of vascular grafts, showcasing in vitro experiments to quantify the influence of different levels of cyclic tensile strain on the orientation and growth of vascular smooth muscle cells. Loerakker spoke about tissue engineered heart valves and how computationally-inspired changes in valve design can improve the in vivo remodelling of such valves. Finally in this session, Contera talked about the use of atomic force microscopy to quantify viscoelasticity of extracellular matrices/tissue engineering scaffolds across temporal and spatial scales.

The films and fluids session opened with King speaking about multiphase models for tissue growth. Wagner spoke on free boundary problems of active and driven hydrogels. Cummings presented a mathematical model for ischemia-reperfusion injury and postconditioning therapy. The session closed with a talk by Dalwadi on the development and solution of a mathematical framework for the optimisation of freezing protocols in cryopreservation.

The next session focused on bioreactors. Ye discussed the translation of regenerative medicine for human benefit in the context of the associated enabling technology, the bioreactor. The operation and application of bioreactor systems developed from within industry and academia to translate regenerative medicine to patients was delineated. Oliver discussed a mathematical model for a novel class of microfluidic device which can be rapidly fabricated by printing a fluid onto a solid substrate with flows generated passively via surface tension. Zhao presented a computational model to show how fluid flow induced cell stimulation in bone tissue engineering changes due to interstitial tissue formation in vitro. Finally, Papantoniou spoke on developmental engineering of callus organoids as predictively functional micromodules for designed bone organ formation.

In the tissue growth and scaffold design session, Barzegari presented a high-performance simulation of biodegradation behaviour of magnesium based biomaterials. Nasehi showcased how stem cell morphology controls the nuclear import of transcription factors within a bioengineered 3D niche. Mukherjee presented an in silico model of scaffolds for repair of large articular cartilage defects in the human knee joint. Dunlop closed the session demonstrating how surfaces of biomaterial scaffolds can shape and influence tissue form.

In the cell level session, McCue spoke about a morphoelastic model for contraction and expansion of fibroblast populated collagen latices. Yeo presented a mathematical model for magnetically targeted stem cell delivery. Preziosi merged the results of continuum mechanics models and individual cell-based models that take into account cell adhesion mechanics and nucleus mechanical properties to deduce a macroscopic model able describe the motion and growth in dense fibrous environments.

In the closing session, Korin showed how in order to utilize engineering approaches in the design of vascular targeting nano-medicines, various in silico and in vitro microfluidic models can be employed, as well as real size arterial models which emulate both the biological and physical environment relevant to vascular disease conditions. Geris showcased the state of the art in multiphysics and multiscale modelling in skeletal tissue engineering. Finally Kamm closed the meeting with a fascinating keynote talk showcasing vascular networks on chips and their applications.

This was an exciting and stimulating meeting that has already lead to several new research initiatives in fluid and solid mechanics and their applications. We would like to thank everyone who attended and made the event so enjoyable and

successful, and of course to EUROMECH for their excellent support and funding.

Number of participants from each country

Country	Participants
Netherlands	3
United Kingdom	20
Belgium	4
Australia	1
Israel	1
Italy	3
South Africa	1
Austria	1
United States	3
India	1
Germany	1
Ireland	1
Total	**40**

Please send this report in electronic form to the Secretary General of EUROMECH, within one month after your Colloquium.