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AMBER

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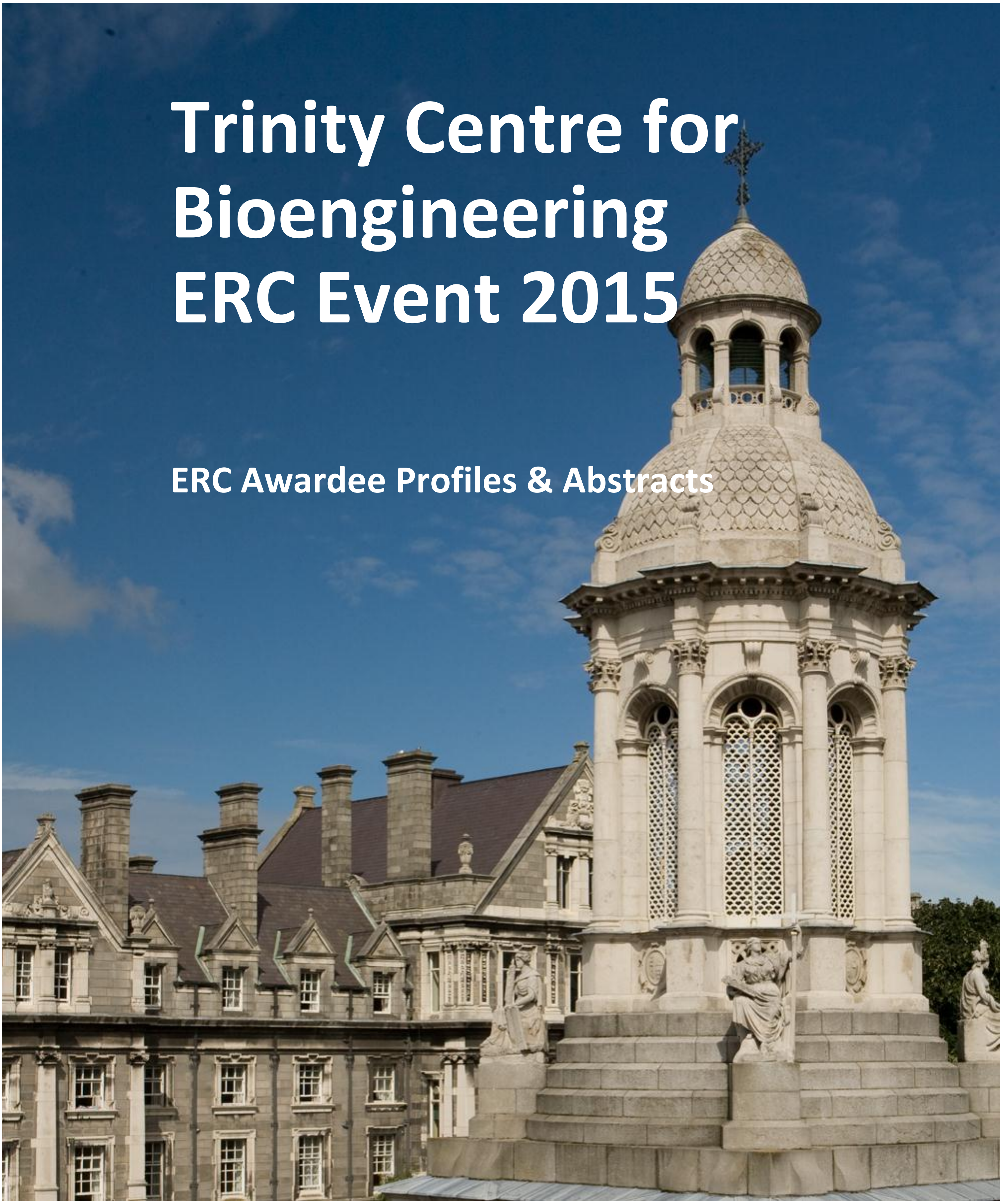
Trinity Centre for Bioengineering ERC Event 2015

ERC Awardee Profiles & Abstracts



Trinity Centre for Bioengineering ERC Event

Friday 25 September 2015

Tercentenary Hall, Trinity Biomedical Sciences Institute, Pearse Street

Celebrating the 10 ERC grants awarded to PIs and/or alumni of the Trinity Centre for Bioengineering

AGENDA

1.30pm – Opening Address

1.40pm – **Laoise McNamara,** Science Foundation Ireland Lecturer in Biomedical Engineering College of Engineering and Informatics, National University of Ireland, Galway

2.05pm – **Fergal O'Brien,** Professor of Bioengineering & Regenerative Medicine, Deputy Director for Research and heads the Tissue Engineering Research Group based in the Royal College of Surgeons in Ireland

2.30pm – **Caitríona Lally,** Professor in Bioengineering, Principal Investigator Trinity Centre for Bioengineering

2.55pm – **Mark Ahearne ,** Senior Research Fellow Trinity College Dublin, Principal Investigator Trinity Centre for Bioengineering

3.20pm – Tea/Coffee

3.50pm – **David Hoey,** Associate Professor in Biomedical Engineering, Trinity College Dublin, Principal Investigator in Trinity Centre for Bioengineering

4.15pm - **Daniel Kelly,** Professor in the School of Engineering Trinity College Dublin and Director of the Trinity Centre for Bioengineering

4.40pm - **Niamh Nowlan,** Senior Lecturer, Faculty of Engineering, Department of Bioengineering, Imperial College London

5.05pm - **Damien Lacroix** Professor of Mechanobiology, Insigneo Institute for in silico medicine, Department of Mechanical Engineering, University of Sheffield, UK

5.30pm – Closing Address & Reception (Knowledge Exchange)

Trinity Centre for Bioengineering   Trinity Biomedical Sciences Institute   Amber Centre

Prof. Daniel Kelly, Trinity Centre for Bioengineering, School of Engineering, Trinity College Dublin

Biography: Dr Daniel Kelly is a Professor in the School of Engineering and Director of the Trinity Centre for Bioengineering. In 2008 he was the recipient of a Science Foundation Ireland President of Ireland Young Researcher Award. In 2009 he received a Fulbright Award to take a position as a Visiting Research Scholar at the Department of Biomedical Engineering in Columbia University, New York. He is the recipient of two European Research Council awards (Starter grant 2010; Consolidator grant 2015) to develop novel strategies for joint regeneration. His research focuses on developing novel approaches to regenerating damaged and diseased musculoskeletal tissues.

Novel tissue engineering strategies for joint regeneration

Abstract: Articular cartilage has a limited capacity for repair. This has lead to increased interest in the development of tissue engineering strategies for cartilage and joint regeneration. This talk will review our attempts to use combinations of novel biomaterials and mesenchymal stem cells (MSCs) to regenerate damaged tissues within synovial joints. I will describe how our lab is using novel approaches to rapidly isolate stromal cells from joint tissues to develop 'single stage' or 'in-theatre' strategies for joint regeneration. I will then demonstrate how it is possible to engineer complex tissues, such as the bone-cartilage interface, by designing tissue engineering strategies that recapitulate aspects of the normal long bone developmental process. The talk will conclude with a demonstration of how we might ultimately scale-up such tissue engineering strategies, through the use of 3D bioprinting, to potentially regenerate entire diseased joints or replace whole bones.

Professor Caitríona Lally

Professor in Bioengineering, PI Trinity Centre for Bioengineering

Biography: Dr. Caitríona Lally received her BEng (Mechanical Engineering) and MEng (Biomedical Engineering) degrees from University of Limerick and later obtained a PhD from Trinity College Dublin in the area of arterial biomechanics and cardiovascular stenting. In March 2004 she took up a lecturing position in the School of Mechanical & Manufacturing Engineering at Dublin City University, and was appointed senior lecturer in 2014. In 2015, she joined the Department of Mechanical & Manufacturing Engineering in Trinity College Dublin as a Professor in Bioengineering where she continues to carry out research focused on arterial tissue mechanics, vascular imaging, vascular mechanobiology and tissue engineering. She has secured considerable research funding from SFI, Enterprise Ireland and the IRC and was awarded an ERC starting grant in 2014.

Abstract: Each year cardiovascular diseases such as atherosclerosis and aneurysms cause 48% of all deaths in Europe. Arteries may be regarded as fibre-reinforced materials, with the stiffer collagen fibres present in the arterial wall bearing most of the load during pressurisation. Degenerative vascular diseases such as atherosclerosis and aneurysms alter the macroscopic mechanical properties of arterial tissue and therefore change the arterial wall composition and the quality and orientation of the underlying fibrous architecture. Information on the complex fibre architecture of arterial tissues is therefore at the core of understanding the aetiology of vascular diseases. The current proposal aims to use a combination of in vivo Diffusion Tensor Magnetic Resonance Imaging, with parallel in silico modelling, to non-invasively identify differences in the fibre architecture of human carotid arteries which can be directly linked with carotid artery disease and hence used to diagnose vulnerable plaque rupture risk.

Knowledge of arterial fibre patterns, and how these fibres alter in response to their mechanical environment, also provides a means of understanding remodelling of tissue engineered vessels. Therefore, in the second phase of this project, this novel imaging framework will be used to determine fibre patterns of decellularised arterial constructs in vitro with a view to directing mesenchymal stem cell growth and differentiation and creating a biologically and mechanically compatible tissue engineered vessel. In silico mechanobiological models will also be used to help identify the optimum loading environment for the vessels to encourage cell repopulation but prevent excessive intimal hyperplasia.

This combination of novel in vivo, in vitro and in silico work has the potential to revolutionise approaches to early diagnosis of vascular diseases and vascular tissue engineering strategies.

Dr. Laoise McNamara

Biomedical Engineering, College of Engineering and Informatics, National University of Ireland, Galway

Biography: Dr. Laoise McNamara was awarded a PhD in Biomedical Engineering from Trinity College Dublin, Ireland in 2004 and conducted a Postdoctoral Fellowship in Bone Cell biology at Mount Sinai School of Medicine, USA. From 2007-2009 she was a lecturer in Mechanobiology and Musculoskeletal Biomechanics at the University of Southampton, UK. She was appointed as a Lecturer in Biomechanics at the National University of Ireland, Galway, in 2009, under the Science Foundation Ireland Stokes program. She has a research group of 8 PhD students and 3 Postdoctoral Researchers, whose research is focused on the development of multidisciplinary approaches to study the role of mechanobiology in bone development and osteoporosis. Dr. McNamara's has published 52 research articles in various high impact factor journals; PNAS, European Cells and Materials, the Journal of the Royal Society Interface, Bone, Tissue Engineering Part A and the Biophysical Journal, among many others. A recent publication was ranked in the top 10% of articles reviewed for the Biophysical Journal and was chosen to be highlighted as "New and Notable". Her research has been recognised by awards from leading international bodies (American Society for Mechanical Engineering, American Society for Bone and Mineral Research, Orthopaedic Research Society, European Society for Biomechanics, MIMICS Innovation Award, Fulbright). She was awarded a European Research Council Starting Independent Researcher Award in 2011 (€1.5 Million), a SFI Investigators Grant in 2015 (€883,219) and has attracted funding of €3,430,167 in total.

Abstract: While previous studies have investigated cell-signalling pathways that facilitate mechanotransduction and have provided a wealth of data, to date, in vivo mechanobiology is not fully understood. Dr. McNamara's research group strives to delineate specific aspects of bone mechanotransduction and deliver significant advances in the understanding of the mechanical regulation of bone remodelling during normal physiology and osteoporosis, and to enhance approaches for regeneration of bone tissue for treatment of bone pathologies. Through the ERC project BONEMECHBIO they have developed novel multiphysics and multiscale computational modelling techniques and have applied these methods to derive an understanding of the mechanical stimuli that bone cells experience in vivo in healthy and osteoporotic bone tissue. They have used experimental techniques to identify the specific mechanosensation and mechanotransduction mechanisms by which bone cells sense mechanical stimuli. These

studies have contributed a novel understanding of changes in bone mechanobiology during osteoporosis. This research has been applied to understand the role of mechanical stimulation in bone regeneration and her research group develop in vitro tissue regeneration strategies to overcome challenges in the field of bone tissue engineering. Dr. McNamara collaborates with the medical device companies Stryker, Boston Scientific and Medtronic Vascular applying her expertise in computational and experimental biomechanics to the pre-clinical assessment of various surgical and minimally invasive devices. In particular her research strives to provide an understanding of the long term performance of transcatheter heart valve technologies for the treatment of aortic valve stenosis. Dr. McNamara's research has been recently awarded a SFI Investigators Grant to investigate the development of a therapeutic approach that targets the mechanobiological responses of bone to provide an effective treatments for osteoporosis.

Professor Fergal O'Brien
Professor of Bioengineering & Regenerative Medicine, Deputy Director for Research and heads the Tissue Engineering Research Group based in the Royal College of Surgeons in Ireland

Biography: Fergal O'Brien is Professor of Bioengineering & Regenerative Medicine, Deputy Director for Research and heads the Tissue Engineering Research Group based in the Royal College of Surgeons in Ireland. He is a graduate in mechanical engineering with a PhD in the area of bone mechanobiology (1997 & 2001 from Trinity College Dublin). He subsequently carried out postdoctoral research in orthopaedic tissue engineering at Massachusetts Institute of Technology and Harvard Medical School. He currently holds an adjunct professorial appointment in bioengineering in TCD and is Chair of the Executive Committee and Principal Investigator in the Trinity Centre for Bioengineering. He is also Deputy Director for Research in RCSI and is a PI and Deputy Director in the €58 million SFI-funded Advanced Materials and Bioengineering Research (AMBER) Centre between RCSI, TCD and UCC and over 20 industry partners. He has served as a reviewer for over 100 scientific journals and a grant reviewer for agencies throughout the world. He is currently a member of the World Council of Biomechanics, EU Council of the Tissue Engineering and Regenerative Medicine International Society, Biomaterials Topic Chair for the Orthopaedic Research Society, a member of Irish Medicines Board Advisory Committee on Medical Devices and President of the Section of Bioengineering of the Royal Academy of Medicine in Ireland. He is also Chairman of the Scientific and Medical Advisory Board of SurgaColl Technologies, a spinout company from his lab which is focussed on the design and manufacture of innovative degradable regenerative technologies. In addition he is an editorial board member of 4 journals, is a Consulting Editor for the *Journal of Biomechanics* and Subject Editor (Tissue Engineering) for the *Journal of the Mechanical Behavior of Biomedical Materials*. He is also Co-chair of the World Congress of Biomechanics which is being held in Ireland in 2018. Since his faculty appointment, he has acquired over €15 million in grant funding as PI, has published over 150 journal articles, book chapters and editorials in peer-reviewed international journals and books, filed 9 patents/disclosures and supervised 22 PhD students to completion. He has a current h-index of 43 (May, 2015) and has been awarded a number of scientific honours including a Fulbright Scholarship (2001), New Investigator Recognition Award by the Orthopaedic Research Society (2002), Science Foundation Ireland, President of Ireland Young Researcher Award (€1.1. million, 2004), Engineers Ireland Chartered Engineer of the Year (2005), European Research Council (ERC) Investigator Award (€2 million, 2009) and Anatomical Society New Fellow of the Year (2014).

Advanced biomaterials & scaffold–based systems for the delivery of therapeutics: new frontiers in regenerating organs & tissues

Abstract: Tissue engineering typically uses a combination of biomaterial scaffolds, cells and signalling mechanisms (such as growth factors or mechanical stimuli) to restore the function of damaged or degenerated tissue. The research carried out in our laboratory investigates each of these three areas with target applications in bone, cartilage, cardiovascular, respiratory, neural and corneal tissues. Recent work has led to the development of a series of porous collagen-based scaffolds with the tailored composition, pore structure and stiffness to promote regeneration of individual tissues. A number of these technologies have been patented resulting in the formation of a spin out company, SurgaColl Technologies, which has brought a number of innovative degradable regenerative technologies for bone and cartilage repair to the market. In the cellular area, we are investigating the therapeutic potential of stem cells in combination with these scaffolds and we have a particular interest in using biophysical stimuli (applied by bioreactors or controlled by scaffold stiffness) to regulate stem cell differentiation. Ongoing research increasingly focuses on the use of these scaffolds as therapeutic bioactive platforms for the controlled delivery of growth factors (eg: [1] Lopez Noriega et al., 2014) or as gene-activated matrices to promote enhanced tissue repair (eg: [2] Curtin et al. 2012). In the former area, we often use microparticle-based approaches to control the release of recombinant proteins [3] while in latter area we focus on the development of non-viral nano-particulate systems for gene delivery. By using tailored specific non-vectors embedded with the scaffolds including PEI [4, 5], chitosan [6] and nano-hydroxyapatite [7, 8], we can achieve a sustained but ultimately transient gene expression profile while still achieving transfection efficiencies in stem cells sufficient to elicit a therapeutic response. These systems have now been applied for delivery of plasmid DNA, microRNA mimics and inhibitors and siRNA nanotherapeutics [9]. This presentation will provide an overview of this ongoing research with particular focus on scaffold-based delivery of therapeutic genes, microRNAs [8] for enhancing bone and cartilage regeneration.

Damien Lacroix
Insigneo Institute for in silico medicine, Department of Mechanical Engineering, University of Sheffield, UK

Biography:
Damien Lacroix is a Professor of Biomedical Engineering in the Department of Mechanical Engineering at the University of Sheffield. His main expertise is on the computational modelling of mechanobiological processes at cell, tissue and organ interfaces and their interactions with biomedical devices. Lacroix has received around £7M in the last 5 years in European and EPSRC funding. He coordinated the only world-wide multi scale patient specific mechanobiological project focused on the lumbar spine (MySpine). He is also the recipient of the European Research Council (ERC) Starting Grant on multi-scale simulations on bone tissue engineering. He is the PI of an ESPRC Frontier Engineering Award on the Individualised Multi-scale Simulation of the Musculoskeletal System. Lacroix has received the 2010 European Society for Biomaterials Jean Leray Award as recognition of his contribution to the field. As past-President of the European Society of Biomechanics (2010- 2012), Lacroix is a leading figure in biomedical engineering.

Modelling the bioreactor environment – a multiscale approach

Abstract:
Tissue engineering has become a new promising field of research with high prospects of

being able to generate any kind of tissues at will. However, after more than ten years of research little is still known on the exact mechanisms of interactions between cells, biomaterials and external stimuli. One of the important processes affecting cell behavior is mechanotransduction, i.e. how the mechanical loading applied on the body is translated onto the cells. In order to better understand this load transfer computational models are being developed. Based on some mechanoregulation laws, the migration, proliferation and differentiation of cells can be predicted. In this study the simulation of cell seeding in a tissue engineering scaffold will be presented. It is shown how the macroscopic external loading applied onto the scaffold is of a different magnitude than the microscopic loading transduced at the scale level. A new methodology to simulate cell seeding enables to predict cell distribution within a scaffold and to optimize cell seeding as a function of cell density, pore shape and pore size. A single cell finite element model will also be presented to show the contribution of each component of the cytosleleton structure. In conclusion computational models are useful to optimize the cell seeding process depending on the type of scaffold chosen and in calculating the local mechanical stimuli affecting cells while it is practically impossible to measure it experimentally. It is believed that such approach will provide in the future a rationale for the consistent design of tissue engineering scaffolds.

Dr Niamh Nowlan
Faculty of Engineering, Department of Bioengineering, Imperial College London

Biography: Dr Niamh Nowlan is a Senior Lecturer in the Department of Bioengineering at Imperial College London. Following an undergraduate degree in Computer Engineering awarded in 2003 and a PhD in Biomechanical Engineering in 2007 (both from Trinity College Dublin), she held IRCSET and Marie Curie postdoctoral fellowships in Ireland and in Spain, and was a Fulbright Scholar in Boston University, USA before joining Imperial in 2011. Dr Nowlan's research employs a multidisciplinary approach to understanding and quantifying the importance of fetal movements for fetal health, with particular emphasis on skeletal development. The two major focusses of her research group are a) the role of fetal movement in joint shape development, with particular relevance to a common postnatal hip abnormality DDH, and b) quantifying normal and abnormal fetal movements as a clinical indicator of fetal wellbeing. Her research is funded by an ERC Starting Grant (2014–2019), and Project Grants from Arthritis Research UK (2014–2017) and The Leverhulme Trust (2015–2018).

Biomechanics and kinematics of fetal movement: Importance for growth and development

Abstract:
Fetal movements have long been of interest to the medical and scientific communities as a possible measure of fetal health. However, the importance of fetal movements for skeletal development has only recently been explored in depth. Of particular interest to my research is joint shape morphogenesis, the process in which joints obtain their distinctive shapes. Several medical conditions involving abnormal joint shape or orientation are related to abnormal prenatal movements, the most common of which is developmental dysplasia of the hip (DDH). We employ a range of approaches in investigating the role of mechanical forces in prenatal skeletal development, including animal embryonic model systems of abnormal prenatal movement (both genetic and pharmacological), *in vitro* culture of limb explants, and computational simulation of growth and development. Translational research is a key priority in the lab, and we are working directly with clinical collaborators, patients and clinical data to develop a greater understanding of human fetal movements through development of a novel

wearable sensor for fetal movements. This sensor will have significant implications for fetal health monitoring. This seminar will give an overview of my group's efforts towards gaining a greater understanding of the biomechanics and kinematics of fetal movement, with particular focus on our *in vivo* and computational modelling approaches.

Dr. David Hoey
Associate Professor in Biomedical Engineering within the Department of Mechanical and Manufacturing Engineering and PI within the Trinity Centre for Bioengineering in Trinity College Dublin (TCD).

Biography: Dr. David Hoey is an Associate Professor in Biomedical Engineering within the Department of Mechanical and Manufacturing Engineering and PI within the Trinity Centre for Bioengineering in Trinity College Dublin (TCD). Dr. Hoey leads a multidisciplinary experimental mechanobiology research group where his goal is to integrate engineering mechanics into the understanding of the molecular basis of physiology and disease. Dr. Hoey's research has discovered novel mechanisms by which bone can sense and respond to a biophysical stimulus. In particular, he is focused on determining indirect and direct biophysical regulation of mesenchymal stem cell contributions to bone formation and repair and how this is altered in disease. These platforms have potential to result in new therapeutics that mimic the beneficial effect of biophysical stimuli and treat orthopaedic diseases such as osteoporosis and osteoarthritis. In 2009 Dr. Hoey received his PhD in Bioengineering from the Trinity Centre for Bioengineering and went on to complete postdoctoral fellowships in Columbia University in the US and the Royal College of Surgeons in Ireland under the Marie-Curie/IRCSET programme. In 2012 he joined the University of Limerick as a Lecturer and was awarded the European Research Council Starting Grant in 2013 to explore the role the primary cilium in stem cell mechanobiology in bone and has recently returned this year to TCD as Associate Professor to continue this work.

Primary Cilium-Mediated Mesenchymal Stem Cell Mechanobiology in Bone
Abstract: Bone is a dynamic tissue which is capable of enhancing formation to meet the demands of its physical environment. Bone formation requires the recruitment, proliferation and osteogenic differentiation of osteoprogenitors cells, yet the mechanisms by which this occurs in response to loading is poorly understood. This talk will explore recent evidence of direct and indirect (i.e. signalling from mechanically stimulated osteocytes) biophysical regulation of MSC contributions to bone formation. Furthermore, how these mechanosensitive cells can sense their local mechanical microenvironment and translate that into a biochemical bone forming response (mechanotransduction) remains equally unknown. Primary cilia (PC) are solitary immotile organelles which project from the cell surface and have been shown to regulate proliferation, migration and differentiation in many cell types. Being approximately 0.2μm in diameter and extending several microns from the cell surface, these organelles represent a distinct cellular microdomain in which receptors, ion channels and signalling molecules specifically localize allowing for key biochemical and biophysical pathways to be activated, amplified and highly regulated. Therefore this seminar will also explore the role of the primary cilium in loading-induced bone formation. Identifying the signalling and mechanotransduction mechanisms responsible for stem cell contributions to bone formation may yield novel therapeutics that mimic the beneficial effect of loading in-vivo, with the ultimate aim of counteracting bone loss in diseases such as osteoporosis.

Dr Mark Ahearne
Senior Research Fellow Trinity College Dublin, Principal Investigator Trinity Centre for Bioengineering

Biography: Mark is currently a senior research fellow and principle investigator at Trinity College Dublin. He received a BEng. in Mechanical Engineering from the University of Limerick in 2001, a MSc. in Cell and Tissue Engineering from Keele University (United Kingdom) in 2003 and a PhD in Biomedical Engineering from Keele University in 2007. His PhD research focused on the development of a novel spherical indentation system to characterise the mechanical behaviour of cell seeded hydrogels. He subsequently worked as a post-doctoral research associate for three years at Keele University where he developed an *in vitro* corneal wound healing model for pharmaceutical screening, in addition to working on other projects. Mark joined the Trinity Centre for Bioengineering (TCBE) as a post-doctoral research fellow in October 2010 to work on developing a growth factor delivery scaffold for articular cartilage repair. In June 2012, he commenced work as an independent research fellow in TCBE in the field of corneal tissue engineering and cornea repair after obtaining a Starting Investigator Research Grant from Science Foundation Ireland (SFI) and the Marie-Curie COFUND. More recently, in December 2014 he was successful in obtaining an ERC starting investigator research grant to develop a scaffold based therapy for corneal regeneration. To date he has 22 journal publications, over 50 conference papers and abstracts and is responsible for over €2 million worth of research funding.

A bioengineering approach towards corneal regeneration

Abstract*:* Corneal blindness resulting from disease, physical injury or chemical burns affects millions worldwide and has a considerable economic and social impact on the lives of many people. Often a corneal transparent may be required to relieve pain and restore vision however there is a shortage of donor tissue suitable for transplantation. For this reason, we have been examining different approaches to develop novel tissue engineering, biomaterial and cell based therapies for corneal repair and regeneration. Our cell based studies have primarily focused on identifying different factors that can modulate corneal cell behaviour and induce stem cell differentiation towards a corneal phenotype. The progress and implications of this research shall be discussed. In addition, several biomaterial based scaffolds currently under development will be explored. These include decellularized corneal scaffolds, corneal extracellular matrix derived hydrogels and electrospun nanofiber scaffolds. While the goal of our research is to regenerate cornea, the techniques developed have the potential to be applied to engineer other tissues.