In June 2009, the Wellcome Trust and the Engineering and Physical Sciences Research Council (EPSRC) announced that they would, in partnership, fund four new Centres of Excellence in Medical Engineering in the UK. The intent was that each centre would provide an environment for mathematics, physical science, engineering and medical research to come together, to encourage exploratory research and the translation of that research into products that can improve healthcare.

Four interdisciplinary research teams – at Imperial College London, King’s College London, the University of Leeds and the University of Oxford – will receive a combined total of £41 million over the next five years. Through the Medical Engineering scheme, the Trust and EPSRC hope to engage engineers, scientists and medics in groundbreaking research, and stimulate collaborations that will continue beyond the five-year lifetime of the funding. The aim is to ensure that cutting-edge technology continues to enter the clinic in an effective and evidence-based manner, to improve the lives of patients in the National Health Service and around the world.

Medical Engineering Solutions in Osteoarthritis Centre of Excellence, Imperial College London

The Imperial College Centre aims to use emerging technologies to revolutionise the management of osteoarthritis. The focus is on the disease, its early detection and monitoring, as well as on interventions for prevention and treatment, and the rehabilitation of patients after intervention. Research at the Centre is interdisciplinary and operates from the molecular to the whole-body level, and includes in vitro, in vivo and in silico approaches. Our Centre has a strong emphasis on producing techniques and products that will be developed by industry, and made available to improve the lives of patients.

Medical Engineering Centre, King’s College London

The King’s College London Medical Engineering Centre aims to break down the barriers between biology, medicine, and the fields of engineering, physics, mathematics, computer science and chemistry. Their work on medical imaging brings together basic scientists and medical researchers in a hospital setting, and they focus on the clinical translation of the underpinning science and technology. As well as moving towards clinical studies that show patient benefit, they aim to facilitate a closer partnership between the University and industry.

WELMEC Centre of Excellence in Medical Engineering, Leeds University

As we age, our musculoskeletal and cardiovascular systems degenerate, impairing our mobility, ability to work and quality of life. Yet our expectations for health, activity and wellbeing in the second 50 years of life are increasing. At the WELMEC Centre, they aim to develop new ways to extend human joint and cardiovascular health, and so improve quality of life, for ‘50 active years after 50’

Centre of Excellence in Personalised Healthcare, Institute of Biomedical Engineering, Department of Engineering Science, University of Oxford

Much of the 20th century was devoted to developing treatments that are broadly effective in most people. However, the management of chronic disease or the treatment of cancer, for example, can be made much more effective if the patient’s response is quantified and used to optimise therapy.

At the Centre of Excellence in Personalised Healthcare they are developing ways to measure precisely an individual’s response to their condition or treatment, so that healthcare can be tuned to the individual’s characteristics. The use of personalised monitoring and treatment, from birth to old age, will lessen the effects of growth restriction in the womb, enable people with chronic diseases to live healthier lives, and improve survival rates for liver cancer.
Osteoarthritis

Around 8.5 million people in the UK have osteoarthritis. It is the most common cause of chronic pain and costs the country an estimated £5.5 billion every year directly and indirectly. It is estimated that there are up to 4 million operations in the world each year as a result of osteoarthritis. Better techniques to diagnose osteoarthritis combined with more tailored interventions could mean a choice of earlier and less intrusive treatments for the most common cause of chronic pain.

Nine initial objectives have been identified as focus areas within the Centre:

- To improve the early detection of osteoarthritis by using improved screening tools based on novel biosensing technologies.
- To develop devices for high-throughput mechanostimulation and screening of tissues and cells.
- To elucidate the role of mechanical factors in the progression of osteoarthritis, identifying novel osteoarthritis biomarkers.
- To provide a validated musculoskeletal computer model to predict local articular loading of the bones and joints of the extremities.
- To provide in vivo and in vitro technologies to optimise implant function post-arthroplasty.
- To engineer minimally invasive implantable material scaffolds and cells to create improved osteochondral constructs.
- To develop a suite of surgical procedures and the supporting technologies to prevent progression and treat joint disease.
- To develop advanced minimally-invasive robotic techniques for osteoarthritis intervention and monitoring.
- To exploit technology to devise, develop and validate treatments for maintaining healthy joints through biodynamic intervention.

Several of these objectives are supported by world-leading technologies in sensing and low-power wireless data transmission.
Early detection of osteoarthritis

Professor Chris Toumazou's research involves development of novel platform technologies aimed at early detection and diagnosis of osteoarthritis. The application is through a novel semiconductor based lab-on-chip technology capable of detecting genetic predisposition to osteoarthritis through real time monitoring of Single-Nucleotide-Polymorphisms (SNP). Sample DNA is extracted and amplified on a single chip, with detection using an ISFET silicon sensor all built into a portable device.

Molecular diagnostics to manage osteoarthritis

The interests of Professor Tony Cass's group lie in the development of point-of-care diagnostics for monitoring the early diagnosis, progression and response to treatment in osteoarthritis. To that end they are using electrochemical sensors (amperometric and potentiometric) combined with specific biomolecular species to detect either genetic predispositions (for early assessment of risk) or biomarkers in blood or urine that report on the status of the joint. The expectation is that by enabling both early assessment and rapid, low cost and decentralised testing there can be improved assessment and hence better targeted treatment of osteoarthritis and that this type of 'personalised diagnostics' will eventually benefit individuals with the condition.

Biosensors

Research activities in Dr Sylvain Ladame’s group focus on the design and synthesis of biocompatible, fluorescent probes and on their applications as responsive biosensors for macromolecules (e.g. nucleic acids) both in vitro and in vivo. Multi-coloured and specific sensing of nucleic acid secondary structures via an oligonucleotide-templated fluorogenic reaction has recently been achieved. Dynamic (i.e. reversible) fluorescent biosensors responsive to external stimuli were also developed. Current projects include the development of fluorescent and fluorogenic chemical tools applied to the diagnosis of osteoarthritis. Typical examples include:

- The use of near-Infrared fluorogenic probes for sensing the viscosity and composition of the synovial fluid;
- The use of Peptide Nucleic Acid probes for detecting single nucleotide polymorphisms within the promoters or 5’-untranslated regions of osteoarthritis-associated genes;
- The development of multi-coloured fluorogenic PNA probes for the high-throughput profiling of circulating miRNAs in the synovial fluid (or plasma) using microfluidic-based devices.

Early detection of osteoarthritis

Professor Chris Toumazou’s research involves development of novel platform technologies aimed at early detection and diagnosis of osteoarthritis. The application is through a novel semiconductor based lab-on-chip technology capable of detecting genetic predisposition to osteoarthritis through real time monitoring of Single-Nucleotide-Polymorphisms (SNP). Sample DNA is extracted and amplified on a single chip, with detection using an ISFET silicon sensor all built into a portable device.
Mechanical factors in osteoarthritis and new biomarkers

The group at the Kennedy Institute of Rheumatology, under the direction of Professor Jeremy Saklatvala, is determining the molecular and cellular events leading to the degeneration of articular cartilage in osteoarthritis. Although the disease occurs spontaneously with age it commonly affects over-used, abused or previously injured joints. The degeneration of cartilage is an active process driven by live cells, not a passive wearing away of the cartilage substance (the extracellular matrix), although it does begin at areas where there is high mechanical stress. The big question is how injury and mechanical factors initiate and sustain degeneration. Because of the connection with joint injury the group is using a model of post-traumatic osteoarthritis in genetically modified mice to identify genes whose expression is altered and contributes to cartilage loss. Understanding the most basic molecular processes will indicate rational ways to intervene in the disease and lead to identification of biochemical markers that can be measured in the circulation to identify individuals developing the disease, and to monitor therapies in the future.

Cell biology and cellular biomechanics

Dr Massimo Marenzana’s research activities focus on dissecting the interplay between local factors (strain at tissue-cell scale) and systemic factors (circulating cytokines) regulating the adaptive response of the skeleton to the mechanical environment. This built-in response is critical to maintaining a functional skeleton, capable of responding to the daily load-bearing demand. Inadequate mechano-adaptive response of bone is implicated in major pathologies ranging from skeletal fragility in osteoporosis at one extreme to osteosclerosis of subchondral bone in osteoarthritis at the other. His studies aim to:

- Determine the spatio-temporal changes in periarticular bone in murine models of experimental osteoarthritis and characterise the mechanical environment of the joint in these models;
- Identify the molecular players involved in the bone-cartilage cross talk during the progression of mechanically-induced osteoarthritis using in vivo and in vitro models of the pathology.

Improved understanding of the relationship between subchondral bone and cartilage remodelling in response to pathogenic mechanical loading has important implications for the development of therapeutic approaches including osteoregulatory drugs and biomechanical interventions. Moreover, the identification of the molecular players involved in the bone-cartilage cross talk at the onset of osteoarthritis might lead to the development of new pharmacological targets and/or the discovery of novel biomarkers for the early diagnosis of osteoarthritis.
Osteochondral tissue engineering

Articular cartilage lesions, which can progress to osteoarthritis, are a particular challenge for regenerative medicine strategies as cartilage function stems from its complex depth-dependent microstructural organisation, mechanical properties, biochemical composition, as well as the underlying bone matrix. Repairing such lesions with engineered constructs containing live cells before they progress to osteoarthritis, therefore, remains an important aim of regenerative medicine strategies. Biodegradable constructs that are functionally graded in terms of organisation, porosity, pore size, and mechanical properties may provide distinct advantages over scaffolds that feature uniform properties and homogeneous compositions. Fibrous scaffolds offer a favourable template for cartilage extracellular matrix production; however, the success of homogeneous scaffolds is limited by their inability to mimic cartilage's zone-specific organisation and properties. To overcome this challenge, Professor Molly Stevens' group is developing a tri-laminar scaffold that mimics the structural organisation and mechanical properties of the collagen fibrillar network in articular cartilage. An additional challenge for this tissue is to recreate the biochemical gradients present in a depth-dependent manner. To recreate these varying biochemical gradients, they are designing peptides to sequester local extracellular matrix molecules in a dual-gradient fashion. The overall goal is to translate tissue-engineered constructs from an in vitro model to in vivo therapy. Professor Stevens' group also has extensive experience in the development of materials for bone repair and will be integrating these with the scaffolds for cartilage repair to enable functional osteochondral tissue engineering.

Polymeric biomaterials

Synthetic polymeric biomaterials with controlled composition and architecture have strong potential applicability in biomedical research. The aim of Dr Jon Weaver's work programme is to translate new synthetic polymer chemistry techniques to address some of the challenges in the treatment of osteoarthritis. In particular, surface functionalisation of synthetic cartilage constructs may provide enhanced joint lubrication; controlled water content and cross-link density of synthetic polymer hydrogels may provide controlled mechanical properties of artificial cartilage; and the use of such scaffolds as templates for site-selective mineralisation may provide controllable synthetic interfaces between the organic and inorganic phases within joints.

Polymeric biomaterials

Synthetic polymeric biomaterials with controlled composition and architecture have strong potential applicability in biomedical research. The aim of Dr Jon Weaver's work programme is to translate new synthetic polymer chemistry techniques to address some of the challenges in the treatment of osteoarthritis. In particular, surface functionalisation of synthetic cartilage constructs may provide enhanced joint lubrication; controlled water content and cross-link density of synthetic polymer hydrogels may provide controlled mechanical properties of artificial cartilage; and the use of such scaffolds as templates for site-selective mineralisation may provide controllable synthetic interfaces between the organic and inorganic phases within joints.
Lower limb musculoskeletal model

Leg movement is produced by large muscle forces that can be up to twenty times bodyweight in magnitude during activities of daily living. These muscle forces serve to rotate the knee, ankle, and hip resulting in large contact and shear stresses on the cartilaginous structures of the joints as well as the ligaments. A small disruption in this normal movement, through ligament sprains, the normal processes of ageing, and events such as falls can result in long-term cartilage damage. Minor adjustments in movement patterns, and optimising rehabilitation protocols and treatment for sprains may delay the onset of osteoarthritis as well as reduce its debilitating effects. This research in musculoskeletal dynamics by Professor Anthony Bull and his research group is developing and using novel engineering measurement and modelling tools to influence these extreme mechanical loads on ligaments and cartilage. The focus of the research is to make this influence count very early on in the degenerative process through the development of a ‘joint biomechanics health check’ that will allow an individual to have a joint analysis conducted and a tailor-made intervention implemented.

Mechanostimulation and screening

The development of living tissues and tissue-engineered constructs is sensitive to mechanics, which influences tissue cellularity, ultrastructure, matrix composition, cell differentiation, and biomechanical properties. Normal tissue development depends critically upon mechanical cues that maintain tissue structure and function, while alteration of these mechanics contributes to cartilage degeneration and osteoarthritis. To uncover the molecular pathways involved in the mechanobiology of osteoarthritis, and ultimately to develop better biomarkers and therapeutic targets, requires improved devices for cell mechanostimulation capable of mimicking the mechanical environment of articular cartilage. The aim of Professor Ross Ethier’s osteoarthritis research group is to develop devices for high throughput mechanical stimulation and preconditioning of engineered bone-cartilage constructs, and rapid throughput screening of changes in cartilage morphology in animal models of osteoarthritis.
Musculoskeletal science

Dr Richie Abel is investigating the causes of osteoarthritis, joint replacement design and healthy ageing of bone. In particular he is interested in finding out whether bone and joint shape, patterns of walking or exercise levels can predispose some people to the disease. By employing new technologies such as computed tomography, also known as CT or CAT scanning, the systems can be used to produce 3-D computer models of bones and joints. These can then be used to understand the shape, composition and structure of bone as well as their behaviour under loading and this information can be used to predict clinical outcomes.

Orthopaedic surgery

Mr Chinmay Gupte is an orthopaedic surgeon and his research interests aspire to improve results and outcomes in patients with sports injuries of the knee, such as ligament and meniscal injuries. To this end, his research is involved in developing keyhole techniques in improving the management of ligament and meniscal injuries, and in prevention and management of early osteoarthritis. Additionally the aim is to develop new operations in cruciate ligament injuries and when patients have had their menisci removed due to injury. In a separate investigation, by analysing MRI scans of patients in a longitudinal study, the hope is to be able to assess the risk of an individual developing osteoarthritis. A further interest lies in simulator training of young surgeons and the use of information technology in improving the surgeon-patient relationship. Specific research projects include:

- In vivo characterisation of articular cartilage in knees using optical identification of damaged tissue and precise tissue sampling. The aim is to allow the delivery to the cartilage disease site of different types of optical probes, as well as surgical instruments and therapeutic techniques;
- Construction of a novel stereo intra-operative system for flexible devices to allow visualisation of the osteoarticular cartilage surfaces;
- Exploration of the precise scanning of the micro-probe tip to allow registration of multimodal imaging data and to develop advanced motion and tracking schemes for optical probe positioning and image mosaicing.
Minimally invasive robotic interventions

The investigation into minimally invasive robotic interventions for osteoarthritis is headed by Professor Guang-Zhong Yang and the aim is to develop a flexible micro-vision-equipped robotic instrument to deliver probes for sensing, imaging, surgery and therapy. The platform will provide significant advantages in endoscopic visualisation and investigation of joint tissues, such as articular cartilage, and in minimally-invasive joint surgery for patients with osteoarthritis. Flexible instruments, that are robotically controlled, will reach target areas more accurately and quickly than might otherwise be accessible. For planning of complex minimally-invasive diagnostic procedures (e.g. arthroscopy), the instrument will allow the target lesion (e.g. the damaged articular surface) to be accessed through an accessible entry point, via an optimised pathway that avoids damaging other tissues. The work is being carried out within the Hamlyn Centre at Imperial College London.

Robot-assisted early surgical interventions in osteoarthritis

Professor Justin Cobb leads the investigation into robot-assisted surgical interventions in osteoarthritis. His team have been working on a software solution to enable them to plan and perform robotic correction of subtle joint deformities that cause pain and disability. The planning software they have created is being used to plan clinical cases and it is expected that the software will be incorporated into robotic platforms in the near future. A protocol that will enable the measurement of exactly how well people walk, both before and after surgery, is also being developed. By measuring the speed and the incline at which pain starts to be a problem, it will be possible to show how well the operation went and what might have gone wrong. A clinical trial of robot-assisted partial joint replacement is planned and novel knee designs have been finalised, and are being mechanically tested prior to the first human trials. Additionally, a robotic trial using conventional prostheses will also be undertaken.
Human joint biomechanics

Hip and knee replacements are the most popular procedures in orthopaedic surgery and have excellent survival rates. However, patient satisfaction is notably different for these two procedures with knee replacement patients having a significantly worse outcome. Implant design plays a major role in determining the post-operative function of the joint, and is considerably more complicated for the knee than the hip. The market leading knee implants were designed over 20 years ago, and a great deal of knowledge has been accumulated on the strengths and weaknesses of these designs. Contemporary imaging methods, e.g. CT and MRI, have led to significant advances in understanding how the knee works, and this information, combined with the knowledge of how implants perform in vivo, is used by Dr Jonathan Jeffers' research group to evolve the current generation of knee designs to improve patient satisfaction.

Technologies to optimise implant function post-arthroplasty

The Medical Engineering group in the Department of Mechanical Engineering under the direction of Professor Andrew Amis works in the areas of biomechanics and mechatronics. The principal areas of orthopaedic interest in biomechanics are the study of the behaviour of human joints and, from that, the design and development of joint replacement prostheses. A number of such devices have been designed and introduced to clinical use in the treatment of osteoarthritis. Allied to this has been extensive work on ligaments, tendons and menisci, both studies of their behaviour in stabilising joints and then development and testing of novel methods of soft tissue reconstruction. These areas of work are undertaken via several approaches: physical testing of joints, both as isolated cadaveric specimens and also in patients at the hospital, and creation of computer models of joints from medical images, and of specific factors such as implant-bone interfaces and fixation. The mechatronics work has led to development of an 'active constraint' robotic surgery system which is in clinical use for joint arthroplasty, and also to a haptic feedback arthroscopy simulator for training surgeons. Current work includes development of a robotic system for testing human joint function and of a novel flexible probe for minimally-invasive access along curvilinear pathways between body structures.
Medical electronics and instrumentation

Research in medical electronics and instrumentation involves the development of intelligent wireless sensing platforms for the monitoring of joint related parameters related to osteoarthritis. Dr Pantelis Georgiou’s aim is to develop smart-clothing that will integrate a number of low power wireless inertia and electromyogram (EMG) sensors for the continuous monitoring of osteoarthritis patients’ joints during activities of daily living. The objective is to facilitate correct rehabilitation of osteoarthritis patients after surgery by ensuring compliance and monitoring the effectiveness of exercise in the home. Additionally this could serve as a tool for multi-parameter analysis of osteoarthritis related factors such as gait symmetry, range of motion and surface EMG of the muscles around the joint, which will allow classification of effective treatment which can then be prescribed. The proposed platform will communicate with a mobile smart-phone allowing ambulatory monitoring in the home.

Rehabilitative and preventative treatments

Osteoarthritis is a chronic condition with a slow insidious onset. Most people only seek advice from their general practitioner when pain becomes unbearable and the ability to perform daily tasks is affected. In the early stages this usually results in a referral to physiotherapy whilst in later stages it results in a referral to a surgeon. The aim of the biodynamics lab under the guidance of Professor Alison McGregor is to try to detect the very early mechanical and physiological changes associated with this degenerative condition, with a view to developing exercise and other interventions that will slow down or prevent further deterioration and allow people to maintain their current levels of activity. This means that researchers need to understand how injuries affect the joint and how an injury to one joint can affect the rest of the limb and indeed body as often if we injure our knees we have to compensate elsewhere in the body so we can continue to function. Thus, this project is exploring the changes that occur to the muscles and the joints in the lower limb as a result of injury and osteoarthritis and will use modelling techniques to use this knowledge to classify patients and to determine important changes. This information will then be used to explore targeted patient-specific treatments, and will be looking at how technological innovations can help to enhance compliance with these new treatments, as well as understand the daily physical limitations of living with osteoarthritis.
Principal Investigator

Prof. C. Ross Ethier
Department of Bioengineering

Named Investigators

Prof. Andrew Amis  
Dept of Mechanical Engineering

Prof. Anthony Bull  
Dept of Bioengineering

Prof. Tony Cass  
Dept of Chemistry

Prof. Justin Cobb  
Dept of Surgery and Cancer

Prof. Alison McGregor  
Dept of Surgery and Cancer

Prof. Jeremy Saklatvala  
Kennedy Institute of Rheumatology

Prof. Molly Stevens  
Depts of Bioengineering and Materials

Prof. Christofer Toumazou  
Dept of Electrical and Electronic Engineering

Prof. Guang-Zhong Yang  
Dept of Computing

Newly Hired Investigators

Dr Richard Abel  
Dept of Surgery and Cancer

Dr Pantelakis Georgiou  
Dept of Electrical and Electronic Engineering

Mr Chinmay Gupte  
Dept of Surgery and Cancer

Dr Jonathan Jeffers  
Dept of Mechanical Engineering

Dr Sylvain Ladame  
Dept of Bioengineering

Dr Massimo Marenzana  
Dept of Bioengineering and Kennedy Institute of Rheumatology

Dr Jonathan Weaver  
Depts of Bioengineering and Materials

Technicians

Mr Dominic Smith
Ms Reva Vaze

Software Developer

Dr Simon Harris

Clinical Trial Coordinator

Ms Yasmin Mowat

Clinical Research Fellow

Dr Anatole Wiik

Additionally, the Centre employs 25 post-doctoral researchers

Programme Manager

Dr Steven J. Heggie
Department of Bioengineering  
Imperial College London  
3.08, Royal School of Mines Building  
South Kensington Campus  
London, UK, SW7 2AZ  
+44 (0)20 7594 6371  
s.heggie@imperial.ac.uk  
http://www3.imperial.ac.uk/osteoarthritis