MULTISIM: MODELLING OF THE NEUROMUSCULOSKELETAL SYSTEM –
STAKEHOLDER WORKSHOP

MultiSim: Report of **Stakeholder Workshop** Outcomes

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Multiscale Modelling of the Neuromusculoskeletal System
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Executive Summary

The MultiSim programme (sponsored by EPSRC under its Frontier Engineering Awards) held a two-day workshop to discuss the opportunities and technological challenges associated with modelling the neuromusculoskeletal (MSK) system. The workshop was attended by 40 participants from the UK MSK community including leading academics from 15 UK Universities, industrial representatives, key individuals from EPSRC, and several clinicians from Sheffield Teaching Hospitals.

MSK research has made significant progress in the last 5-10 years thanks in particular to the development of new computational modelling techniques and the intensified use of clinical imaging data. This has led to the development of multiscale models that include more and more personalisation about the patient. Such models have enabled for example, much more accurate predictions of the risk of bone fracture in osteoporotic patients and helped surgeons to decide the optimal treatment for lower back pain in a patient-specific manner. In the future, the use of such personalised medicine and multiscale models will intensify to provide more accurate clinical tools and reduce the costs associated with diagnosis, treatment and monitoring of patients.

With the integration of complex biological and physical processes, more transdisciplinarity between engineers, clinicians and biologists is required. This means that more efforts are needed to provide such interdisciplinary training at all levels and to facilitate clinicians to perform research. There is a risk of seeing those scientific and clinical progresses being hindered by the lack of adequate infrastructure that enables testing and validation of our MSK system, and that can handle the integration of large patient data in a seamless manner for the researcher, while preserving the anonymity of the patient. It was recognised that the MSK community needs to have a bigger say at the national level to adequately formulate the importance of MSK disorders within society and highlight the necessity of being included in discussions on the modernisation of the healthcare system. It was concluded that a MSK network within UK should be developed as a result of this workshop. The outcomes from this workshop are well aligned with the research focus and strategic challenges outlined by several key funding bodies.

Findings

The workshop was scheduled on 7 October 2014 at the University of Sheffield and included interactive sessions where participants could provide valuable input on three key topic areas: (i) scientific opportunities in multiscale modelling of the MSK system; (ii) the current technological challenges; and (iii) external constraints associated with the research. This

report presents the outcomes of the workshop, compiled from written and verbal feedback from participants.

(i) Scientific opportunities in multiscale modelling of the MSK system

Within the last 5 years research in the musculoskeletal area has made significant advances, in particular in the ability to use advanced imaging techniques to derive accurate patient-specific computational models. Many computational models are based on *in vivo* and clinical imaging used for pre-clinical and clinical tests. Such advances have enable us to progress towards the use of computational models for clinical practice, with models being used for risk predictions and multiscale modelling being used to identify problems in joint replacement (such as total knee replacement, total hip replacement or treatment of lower back pain). These advancements were helped with the availability of high performance computers for complex simulations and the increased accessibility of open simulation software.

In the next 10 years further effort must be directed towards personalised strategies, in particular identification and prediction of patients at risk, and diagnosing appropriate intervention for that patient. Computational models can be used to improve the reliability of implants and joint replacement, increase their longevity, and improve their efficiency in relieving pain. In addition to efforts towards the improvement of orthopaedic solutions, more patient-specific tissue engineering research is also needed. The diagnosis, treatment and monitoring of MSK disorders (such as osteoporosis, oesto/arthritis, back and neck pain, injuries, obesity, and metabolic syndrome) through the development of patient-specific computational models need to be integrated with sensing technology and clinical support in order to improve patient outcomes, self-management, and exercise. Other areas include improved animal models with more relevant outcomes in humans, biomarkers for targeted intervention, infection control, and improving knowledge about rare bone diseases where the numbers are low, but the impact is high.

In order to reach this 10-year vision a number of capability and skills are needed. First, a greater transdisciplinary approach, with biologists, clinicians and engineering working together at all stages of research in a collaborative environment. There is a requirement for students and researchers to be trained in multiple disciplines to bridge the gap between these three areas. Such multi- and inter-disciplinary approach will ease the integration of software solution to the clinics, providing a tool for the clinicians to treat their patients. As the models rely more and more on personalised data, the community needs to also embrace and participate in the development of big data initiatives where the sensitivity of clinical data makes the infrastructure specific to healthcare. Thus, leadership is needed to help raise the profile and recognition of MSK issues, such as the cost of MSK related disorders. Lessons could be learnt from other systems communities that have effective established networks (such as cardiology). Finally, a centralisation of our key facilities, such as a large animal centre and implant centres, in the UK or Europe, is required for interactions with industry.

There is a skills-gap at undergraduate (UG) level. Key skills missing include coding, linking modelling and experiments, monitoring and testing (with equal competence in each), and software development. The introduction of bioengineering degrees have encouraged more people into the field, but the UG courses do not always provide the depth that is required; masters-level training is therefore necessary to achieve this depth. More specialised courses for UG students could improve this, for example systems engineering in bioengineering, placements, intercalated students, and also projects to bring together undergraduates from bioscience and engineering. The four-year PhD as established in the CDTs is useful to achieve such multidisciplinary training. Focus should be made on enhancing interactions between engineering PhD students and clinicians, as well as modelling and imaging students. It is important to attract the best students, including international PhD students. Such multidisciplinary training should continue at all levels, with disciplinary hoping and longer term fellowships. There is a need for a mixture of super specialised researchers and more generalised coordinators.

(ii) Technological challenges associated to multiscale modelling of the MSK system

The ability to generate complex models for single scales, inverse dynamics and finite element modelling, proper model validation (at least at the organ or body level), and image processing are all strengths within the MSK community. However, there are a number of technological challenges that have been identified, which need to be addressed in order to reach our scientific vision. The main issues are the complexity of the modelling with the inherent multiscale properties, uncertainty and variability of the system. There is opportunity to learn from other fields, where there are similar complexity issues. Examples include consumer goods, self-heating materials, aerospace and the food industry, who are embracing simulations more and more; also software industries such as computer graphics, where they use advanced finite element analysis, and non-invasive tomography techniques used in other fields could be applied to MSK research. Surrogate and uncertainty modelling are a strength in other areas, for example representing exterior load variation and mechanical responses using stochastic finite element models. Although, it would be a challenge to transfer these technologies to the MSK field. Other areas are more effective at continuously monitoring people and coping with the large amount of data generated. Handling a large volume of different data types was identified as a problem, along with the issue of data protection. Obtaining data, and sharing data and databases needs to be improved to make useful data available to the community. A single framework to allow data to be shared between people may be one solution, although there was no universal agreement on this point. There is a lack of awareness of the importance of data for research and ethics/consent. One of the possible solutions to ease the access of data is to enable clinicians to perform more research within the clinical workload. This will also facilitate the collaboration between academics, industry and clinicians to help in the design of devices and improve the patient planning process. Currently there is a gap between basic research and the point where the product is mature enough for industry to invest. This area has a lot of potential, but there has to be a mechanism to fill the gap.

To circumvent these challenges, one of the key infrastructure challenges will be data handling. There is a lack of infrastructure to analyse clinical data and report it back for clinical use, as well as the need for an infrastructure for sharing of data and models across institutions. Attention must be paid on quality control and clear instructions on shared data to prevent a mistrust of data collected by other researchers. Incentives may be important to encourage full release of data and models. In terms of skills, there is a need to have engineers with improved coding skills to create better tools at all levels. Also engineers that have a better understanding of medical approaches, medical methods and numerical methods, with more communication between clinicians, engineers and scientists. One aspect that hinders the sharing of data is also the lack of standardised data formats from different manufacturers' equipment. In terms of infrastructure it was identified that centralisation of large equipment was required, but these can be difficult to setup due to the co-funding requirement and new technologies need to be developed to make the transport of experimental material from one lab to another easier and more reliable. Manufacturers working directly with researchers, in particular to help with regulatory requirements that need to be met for specific devices, and a platform for communication on equipment development would be beneficial.

(iii) External constraints associated to multiscale modelling of the MSK system

There are other external constraints that need to be considered within the 10-year vision. This includes the difficulty in engaging the NHS in research, because in most Trusts the management model is not research oriented with high security, administrative and safety regulations. In Scotland, all clinical data is linked to the GP so there is an integrated clinical traceability. There was a concern that if the privatisation of the NHS continues, it will limit the ability to access information for clinical research. There is a lack of time and national policy for clinicians engaged in research. It is recognised that the MSK community needs to improve its advocacy at the government policy level so that MSK research is given more importance. In relation to this, there is a need to raise public awareness of MSK diseases, as it is not currently seen as a national issue. Also, it is important to participate in the discussion with the public on the benefits of sharing clinical data while at the same time ensuring that adequate firewalls are put into place to ensure privacy and integrity of the personal data. Current ethics limit the use of data to a particular project and prevent the reuse of data. There is a need to work together to get ethical approval to share the data and have continued use. Finally there are not sufficient incentives for home graduates to get into research, which prevent the development of a strong research-led innovation at the academic and industry sectors.

Workshop participants

First Name	Last name	Organisation
Richard	Aspden	University of Aberdeen
Nick	Bishop	University of Sheffield
Darren	Burke	Bose Limited
Sarah	Cartmell	University of Manchester
Martin	Champion	EPSRC
Yuhang	Chen	Heriot-Watt University
Enrico	Dall'Ara	University of Sheffield
Clint	Davis-Taylor	Dassault Systemes Limited
René	De Borst	University of Glasgow
David	Farrar	Smith & Nephew
Richie	Gill	University of Bath
Nicolas	Gruel	University of Sheffield
Lingzhong	Guo	University of Sheffield
Markus	Heller	University of Southampton
Cathy	Holt	Cardiff University
Visakan	Kadirkamanathan	University of Sheffield
Jan	Herman Kuiper	Keele University
Damien	Lacroix	University of Sheffield
Alex	Lennon	Queen's University Belfast
Xinshan	Li	University of Sheffield
Georges	Limbert	University of Southampton
Claudia	Mazzà	University of Sheffield
Sanjeev	Madan	Sheffield Children's NHS Foundation Trust
Victoria	Marlow	EPSRC
Alan	Monk	Nikon Instruments
Rajshree	Mootanah	Anglia Ruskin University
Niamh	Nowlan	Imperial College London
Alex	Pavic	University of Exeter

Cecile	Perrault	University of Sheffield
Andrew	Phillips	Imperial College London
Jeremy	Purches	NVIDIA Limited
Vitomir	Racic	University of Sheffield
Gwen	Reilly	University of Sheffield
Michel	Rochette	Ansys
Julia	Shelton	Queen Mary, University of London
Tim	Simpson	Nikon Instruments
Alison	Traynor	Corin Limited
Marco	Viceconti	University of Sheffield
Jennifer	Walsh	University of Sheffield
Ruth	Wilcox	University of Leeds