EUROPEAN SCIENCE FOUNDATION
SETTING SCIENCE AGENDAS FOR EUROPE

Exploratory Workshops Scheme

Standing Committee for the European Medical Research Councils (EMRC)

ESF Exploratory Workshop on

European Heart Modelling and Supporting Technology

Scientific Report

Oxford, United Kingdom, 15 - 18 May 2007

Convened by:

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EXECUTIVE SUMMARY

The field of heart modelling dates back to 1960 when Professor Denis Noble (Oxford), still a PhD student at the time, showed that mathematical equations could model how the electrical activity of a heart cell is influenced by the movement of sodium and potassium ions in and out, transported by pumps, channels that sit in the cell's membrane. Over more than 40 years, cardiac models have become increasingly sophisticated, mimicking different types of heart cell, and taking into account more of each cell's ion transport systems. Over the years, cardiac modelling research in Oxford has recognised the benefits of collaborative science through working with research groups in Europe, New Zealand, the USA and Asia and more recently through collaborative projects such as the Integrative Biology e-science pilot project. Researchers are currently able to demonstrate computer models founded on millions of mathematical equations that describe the proteins, cells, and tissues of the heart, and this is the product of more than 40 years of research. Research across the globe covers many aspects of this science and the heart modelling community is advanced compared to the cancer modelling community. There still remains, however, many unanswered questions and through leveraging the skills and research of new groups across the globe, we may one day determine a cure for these diseases through utilising the vast compute facilities available to us. The pharmaceutical industry has a keen interest in pursuing research where they could in theory predict the behaviour of the heart when exposed to drugs to prevent a repeat of the withdrawal of the arthritis painkiller Vioxx and the disastrous drug trial in the UK in recent months where 6 volunteers were seriously affected by taking a drug as first human volunteers in a clinical trial. The Integrative Biology project led by Prof. David Gavaghan has developed new partners in the USA and Canada in the area of in-silico heart modelling, recognising the need to work across organisational boundaries to progress science faster.

The ESF workshop on Heart modelling and supporting infrastructure brought together 25 European leaders in the field of Heart Modelling. The participants were invited on the basis of their scientific excellence, potential contribution and reflecting a European dimension. Attendance to the workshop, and participation of all invited speakers was excellent and was key in the success of the workshop.

As can be seen below, the programme of the workshop included two types of sessions: (i) the scientific sessions in which participants presented current work and future perspectives of their research; and (ii) discussion sessions to explore future potential collaborations, in the context of the Seventh Framework Programme, and to determine future needs of the European Heart modelling community. The main conclusions of these two type of sessions are summarized below.

SCIENTIFIC CONTENT OF THE EVENT

The participants at the workshop presented state-of-the-art research on heart modelling and showed the importance and the potential that heart modelling has in understanding cardiovascular function and disease. Mathematical models of different cardiac tissue types including sino-atrial node, ventricles, atria and atrio-ventricular node were presented. The models have been used by the European groups to investigate the mechanisms of ischaemia-related arrhythmias, cardiomyopathy and heart failure, ventricular and atrial fibrillation, and heterogeneity and mutation in the heart. Although the majority of the models presented considered only the electrical function of the heart, mathematical models of electromechanics and cardiovascular hemodynamics have also been developed and were presented at the workshop. In addition, the infrastructure and technologies developed to support cardiac modelling were also covered, including recent advancements in the development of tools and frameworks aiming at personalized heart models and also the challenges posed by the software development to conduct realistic simulations of cardiac function.

ASSESSMENT OF THE RESULTS, CONTRIBUTION TO THE FUTURE DIRECTION OF THE FIELD

The time allocated in the programme for discussions proved to be very productive and welcomed by the participants. The main topics discussed were the needs of the European heart modelling community, the future directions of the fields and the possibility of establishing new collaborations. We agreed that the field was mature and a significant number of models had been developed. Heart modelling was now considered as a legitimate tool to investigate the basis of cardiac function in health and disease. It was agreed that time is now ripe to analyze in detail the applicability and validity of the models under specific circumstances. As the models are also becoming increasingly complicated, scientists discussed the problem that they are at times overcomplicated and thus the need for the complexity of the models to be fully justified by the scientific question to be addressed.

In addition, the large amount of models developed and their complexity call for an infrastructure to be developed to share and maintain them, in order to better support collaborations and the progression of the research field. Participants in the workshop also discussed the need for a standardization of the input and output data format of cardiac models to facilitate collaborations. As the models are becoming increasingly complicated (particularly the whole organ models), the development and maintenance of software has become a priority for most heart modelling groups. However, software development is not strictly a scientific activity for a heart modelling researcher and therefore, it is not a productive activity career wise. The heart modelling community recognizes as a priority the need for support in this aspect of the research. An appropriate form of support suggested was through long-term contract staff specifically dedicated at developing and maintaining the software required for the research. This could be done within each group but also at the community level by building an infrastructure to share models and solvers.

The participants discussed the possibility of collaborating in different proposals within the Virtual Physiological Human theme. In particular, a proposal for network of excellence is being prepared by Prof. David Gavaghan and Dr. Peter Kohl, two of the conveners of the workshop, that will involve a large number of the participants in the workshop. In addition, participants are considering possible partnerships for applications as FP7 opportunities arise, and also applying for visiting fellowships to exchange ideas and establish collaborations.

FINAL PROGRAMME

Tuesday 15 May 2007

Evening *Arrival*

Wednesday 16 May 2007

09.00-10:30 Session 1. Chair: Blanca Rodriguez.

9:00-9:15. Introduction / Welcome / Opening remarks: David Gavaghan

9:15-9:40. Ronald Wilders: "25 years of SA nodal cell modelling"

9:40-10:05. Chema Ferrero and Javier Saiz: "Modelling reentry in ischemia and the effects of antiarrhythmic drugs"

10:05-10:30. Olivier Bernus: "Modelling arrhythmias during ischemia and their visualization using optical mapping"

10:30-11:00 Coffee Break

11:00-12:40 Session 2. Chair: Chema Ferrero.

11:00-11:25. Stefano Severi and Simone Furini: "Ventricular cell modelling: applications to uremic cardiomyopathy and heart failure"

11:25-11:50. Blanca Rodriguez: "Mechanisms of arrhythmias and defibrillation in the heart- Insight from multiscale computer simulations"

11:50-12:15. Nic Smith: "Tightly coupled ventricular cell and tissue models in electromechanics"

12:15-12:40. Tammo Delhaas and Theo Arts: "Non-invasive Determination of Cardiovasular Hemodynamics and Mapping of Depolarization Sequence by Patient-specific Modeling"

12:40-13:45 Lunch / Discussions

13:45-15:00 Session 3. Chair: Nic Smith.

13:45-14:10. Alejandro Frangi: "Statistical modeling of cardiac anatomy: framework and tools"

14:10-14:35. Herve Delingette: "CardioSense3D : Towards a patient specific electro-mechanical model of the heart"

14:35-15:00. David Gavaghan: "Building an IT infrastructure to support in silico physiological experimentation and software development"

15:00-15:30 Tea Break

15:30-17:30 Session 4. Chair: Peter Kohl.

Breakouts/ Discussions/Concluding remarks

19:00 Workshop dinner

Thursday 17 May 2007

09:00-10:40 Session 5. Chair: Sasha Panfilov.

09:00-09:25. Gunnar Seemann: "Electrophysiological heterogeneity and mutation in the human heart"

09:25-09:50. Adriaan van Oosterom: "The Lausanne atrial model; recent applications; new projects"

09:50-10:15. Henggui Zhang: "3D anatomical model of clinical electrophysiology of human atria during atrial fibrillation"

10:15-10:40. Vito Starc: "Mathematical model of global left ventricular function based on cooperativity mechanism"

10:40-11:00 Coffee Break

11:00-12:45	**Session 6. Chair: Gunnar Seemann.**
11:00-11:25.	Vadim Biktashev: "Critical fronts and the problem of initiation of propagating waves in ionic models of excitation."
11:25-11:50.	Richard Clayton: "Computational models of reentry and fibrillation in the heart"
11:50-12:15.	Sasha Panfilov and Kirsten ten Tusscher: 'Modelling cardiac arrhythmias in an anatomically based model of the human ventricles"
12:15-12:40.	Gernot Plank: "Design Challenges posed by structurally and functionally realistic Virtual Heart Simulators"
12:40-13:45	Lunch
13:45-15:30	**Session 7. Chair: Richard Clayton.**
13:45-14:00	Presentation of the European Science Foundation (ESF) Mark Palmer (Standing Committee for the European Medical Reseach Councils)
14:00-15:30	Breakouts / Discussions on possible follow-up activities and/or collaborative actions
15:30-16:00	Tea Break
16:00-17:30	**Session 8. Chair: David Gavaghan.**
	Discussions on possible follow-up activities and/or collaborative actions/ Concluding remarks

Friday 18 May 2007

Morning	Departure

STATISTICAL INFORMATION ON PARTICIPANTS

A total of 25 participants attended the workshop. Of those, 1 came from Austria, 1 from France, 2 from Italy, 1 from Germany, 5 from the Netherlands, 1 from Slovenia, 4 from Spain, 1 from Switzerland, and 9 from the United Kingdom. The approximate composition by age was: 8% below 30 years old, 36% between 30 and 40 years old, 40% between 40 and 50 years old and 16% above 50 years old. 2 of the 25 participants were women.

THE FINAL LIST OF PARTICIPANTS

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