


The Science.....showing here : April 2005

Tulane/Oxford

Scientific Application:

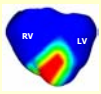
- Obstruction of coronary artery → Ischemia → Sudden Cardiac Death
- Only effective therapy = Defibrillation (application of strong electric shock to the ventricles)
- Ischemia → Defibrillation efficacy ????

Goal: To investigate how ischemic tissue interacts with electric shocks in order to improve defibrillation efficacy in patients with coronary heart disease



Blanca Rodriguez

Heart Modelling on NGS



Heart Modelling Tools

- Memfem
 - Finite element solver
 - Computation of electrical activity of cardiac tissue
 - Bidomain equations (two PDEs coupled by a system of ODEs)
- Mesh
 - Whole ventricles (820 021 tetrahedra)
 - Realistic geometry and fibre orientation
- Visualization
 - Meshalyzer
 - Cool Graphics

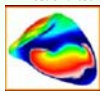
Graz, Austria

Heart Modelling on NGS → HPCx

Computer models for the study of arrhythmogenesis and defibrillation are computationally extremely challenging. Typically, simulations like for instance the computation of a defibrillation shock last at the order of days and memory usage is at the order of Gigabytes. Under these circumstances, studies are usually limited to a reduced number of parameters and models have to be simplified to keep simulations tractable. Services provided by the IB project will allow to overcome most of these limitations.

The Cardiac Arrhythmia Research Package **CARP** consists of several modules:

- bidomain:** The actual simulation software can be compiled to run on both shared memory and distributed memory machines. The distributed memory version is built on top of **MPI** based and uses the **PETSc** library to access different preconditioners and solvers.
- IMP:** This is a ionic model library which is tuned to give excellent performance for parallel large scale simulations.
- Meshalyzer and Flounder:** This is visualization software developed by **Ed Vigmond**. Both were developed using the **Fltk** widget set. **Flounder** is used to visualize 4D data on regular meshes (typically slab setups) whereas **meshalyzer** is used to visualize data on unstructured meshes (typically tetrahedral meshes).


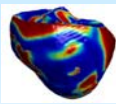


Grainio Plank

Sheffield

Heart Modelling on White Rose Grid

Computational models of action potential propagation in cardiac tissue (cardiac virtual tissue) have an important role to play in understanding the mechanisms of re-entry and it's role in ventricular fibrillation and ventricular tachycardia. During re-entry, electrical activity propagates repetitively along a closed path. In a two dimensional sheet of cardiac tissue re-entry forms a spiral wave rotating around a point of phase singularity. In three dimensional tissue re-entry forms a scroll wave rotating around a linear filament of phase singularity, and the filament acts as an organising centre. Of particular interest are (i) the behaviour of filaments created by a defibrillation shock, which determines whether the shock is successful or not, and (ii) the proliferation of filaments during the early stages of ventricular

It is advantageous to run cardiac virtual tissue on grid resources as this allows many quick and simple models (for example with 3 or 4 state variables on a 2D grid) to be run simultaneously with a range of parameters. The promising results can then be refined with larger and more sophisticated models (for example nonlinear, stiff systems of ODEs with tens of state variables on an anatomically detailed representation of the heart ventricles) run in parallel based on these initial results.


Richard Clayton

To Follow in 2005/6:

Auckland

Extensive research at the University of Auckland had resulted in advanced modelling capability for the heart, in collaboration with selected long term research partners. The Heart Physiome project is a "proof of concept" for the more general Physiome Project, focusing on the heart and in particular on models that link molecular detail at the level of an ion channel - and how this changes with mutations - to the integrated function of the whole heart where disturbances of the normal rhythm - or arrhythmia - can have fatal consequences. Another aim of the project is to develop a framework for handling the hierarchy of computational models, and associated experimental data, which will help integrate knowledge at the genomic and proteomic levels into an understanding of physiological function for individual organisms.

Computationally, the challenges are immense and for this reason, Integrative Biology is working with the team in Auckland and Oxford to enable researchers to access computing services in the **OKM in Integrative Biology Infrastructure**



Peter Hunter/Chris Bradley


Utrecht

Migration to NGS in progress

The model is based on recent human based experimental data for the major ionic currents (the fast sodium, L-type calcium, transient outward, rapid and slow delayed rectifier, and inward rectifier current). The model includes intracellular sodium, potassium and calcium dynamics, allowing for the modeling of calcium transients, frequency dependence of the intracellular sodium concentration, and the positive contraction staircase typical for human ventricular myocardium. The code that will be used describes the process of electrical wave propagation in the human heart to get a better understanding of cardiac arrhythmias. For each heart point 16 to 20 variables need to be solved, this is for a total of 13,000,000 heart points and the equations are stiff, explaining the need for parallel computation.

Open MP and MPI versions exist and are being migrated to NGS, CSAR and ultimately HPCx

Sasha Panfilov/Kerstin Ten Tuschler



Oxford Heart Modelling

Oxford University has extensive experience of heart modelling through Denis Noble's collaboration with the Auckland group over many years. Noble's cellular models merged with detailed models of cardiac anatomy to create the world's first 'virtual organ'.

COR is aimed at providing an environment for cellular and multi-cellular modelling that is built around CellML™. Unlike CellML™, however, COR is not intended to represent many different types of models. Thus biochemical pathway models are not handled by the software, while electrophysiological models are. Despite this limitation, COR offers, through CellML™, an "out of the box" access to a large database of single cell models.

Working with scientists in the University of Oxford, Integrative Biology will endeavour to utilise the UK's grid services and HPCx


Dave Gavaghan/Denis Noble

UCSD

UCSD uses experimental and computational models to investigate the relationships between the cellular and extracellular structure of cardiac muscle and the electrical and mechanical function of the heart during *ventricular remodeling and cardiac arrhythmia*

Computational modelling together with fluorescence optical mapping are used to investigate *excitation-contraction coupling* and the role of *mechanoelectric feedback* in action potential propagation. *In-silico* modelling of signal transduction pathways related to calcium cycling and hypertrophy is a new research area along with the development of new technologies for high-throughput cardiac phenotyping in model organisms.


Andrew McCulloch



Cancer Modelling

The number and variety of mathematical models of solid tumour growth reflect the complexity of the phenomena involved. Most models focus on a single spatial scale of interest (subcellular, cellular or organ), even though there is compelling evidence that behaviour at these scales is closely linked. Equally, the models typically describe generic or idealised tumours rather than specific ones such as breast or lung.

Models of chemotherapy have tended to focus on relatively simple, phenomenological models at the macroscale and neglect factors such as spatial heterogeneity, aspects of the cell cycle and the subcellular mechanisms by which drug-induced cell kill is achieved and drug resistance acquired.



Oxford/Nottingham/Birmingham

.....and new collaborators