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A PERSONALISED APPROACH TO COMPUTATIONAL HEART MODELLING

Researchers at King's College London, the Medical University of Graz and Oslo University Hospital have applied ARCHER to simulating individual patients' hearts in order to better understand patient physiology, pathology, and treatment outcomes.

Medical University of Graz

Oslo University Hospital

KING'S College LONDON

The heart beats once per second, 24 hours a day, throughout our entire lives. Heart failure affects over half a million people living in the UK and accounts for 2% of the NHS budget.

The heart is a complex organ, with electrical activation and mechanical contraction working together to pump blood around the body. In situations where either of these systems fail or stop working in synchrony, without treatment heart failure can follow.

Understanding how this complex multiphysics and multiscale system works, is regulated, and fails, is crucial to improving patient diagnosis, optimising procedures, and predicting outcomes.

To understand this complexity, researchers have exploited the computational power of ARCHER to develop large computational models that mathematically represent the chemistry, electrics, and mechanics of the heart.

This project has led to the implementation of a novel four-chamber model of the heart that simulates both its electrophysiology and its mechanics.

The heart consists of four chambers, the smaller atria, and the larger ventricles. Blood enters the heart through the atria. The atria act as pump primers, pumping blood to fill the ventricles, which in turn pump blood around the body and to the lungs. During each heartbeat, an electrical activation wave is initiated in the right atrium, then spreading through the left atrium before activating the right and left ventricles. When activated, the muscles contract, and it is this contraction that drives the pumping of blood.

At the whole heart scale, the electrical activation sweeps across the atria and ventricles of the heart. At the cellular level, the mechanical motion of the heart is coupled to the electrical activation via chemical reactions in the cardiac cells. Understanding the interaction between these different physics systems, operating over different spatial and time scales, is crucial to understanding the physiology of the heart, cardiac pathologies, and how to design, optimise, and deliver treatments to maximise patient outcomes.
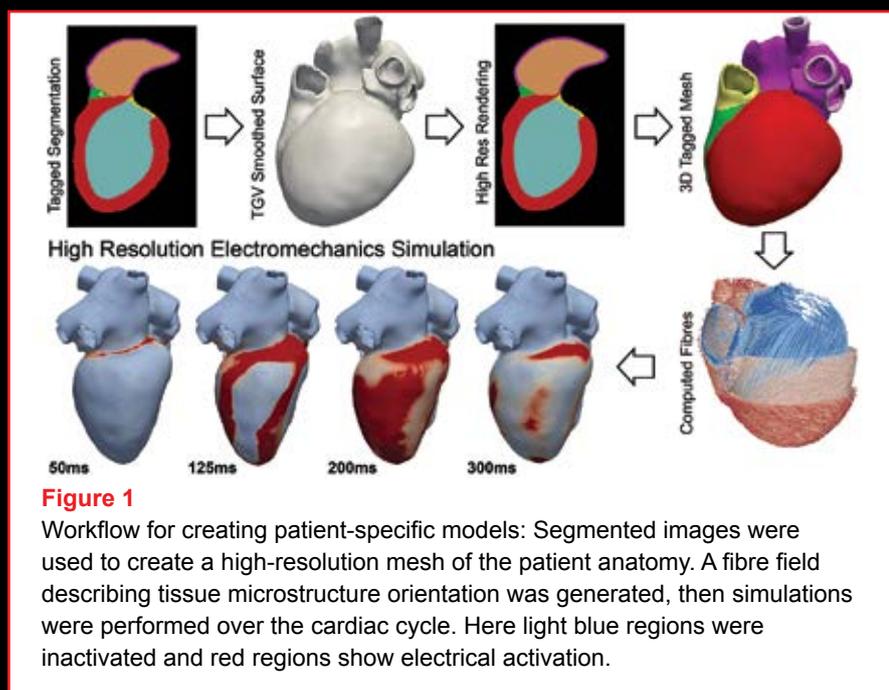
Early cardiac modelling was focused on creating models of small animals to interpret experimental measurements. Recently, the computational power of ARCHER has enabled modelling not only of the human heart in general, but of the hearts of specific individuals. This has led to two clinical studies, described below.

Improving outcomes for Cardiac Resynchronisation Therapy (CRT) patients

CRT involves the permanent attachment of two pacing leads to a patient's heart to augment the electrical activation. It is one of the few effective treatments for patients with moderate to severe heart failure where the electrical activation and hence the contraction of the heart is no longer synchronous. However, 30% of patients selected for this treatment do not improve with CRT. This study used biophysical models to simulate the electrical activation and mechanical contraction of the heart, to identify the best area to electrically stimulate the heart and investigate the effects of changing the pacing.

Personalised biophysical models of the heart were created from patient data. The geometry of the heart was segmented from medical images obtained via computed tomography (CT), magnetic resonance imaging (MRI), or echocardiography. The electrophysiology of the heart was simulated on ARCHER using the Cardiac Arrhythmia Research Package – CARP. The motion of the heart was then simulated based on the spread of the electrical activation in the models. **Figure 1** shows the process of creating patient-specific models from clinical data, and the resulting electrical and mechanical simulations performed on ARCHER.

Figure 1

Workflow for creating patient-specific models: Segmented images were used to create a high-resolution mesh of the patient anatomy. A fibre field describing tissue microstructure orientation was generated, then simulations were performed over the cardiac cycle. Here light blue regions were inactivated and red regions show electrical activation.

Without the practical time constraints of a clinical procedure, all possible options can be comprehensively evaluated in order to identify the optimal pacing lead location and timing for each individual patient. The model can also be analysed to establish what factors determine specific responses, and to identify the patients most likely to benefit from specific pacing protocols.
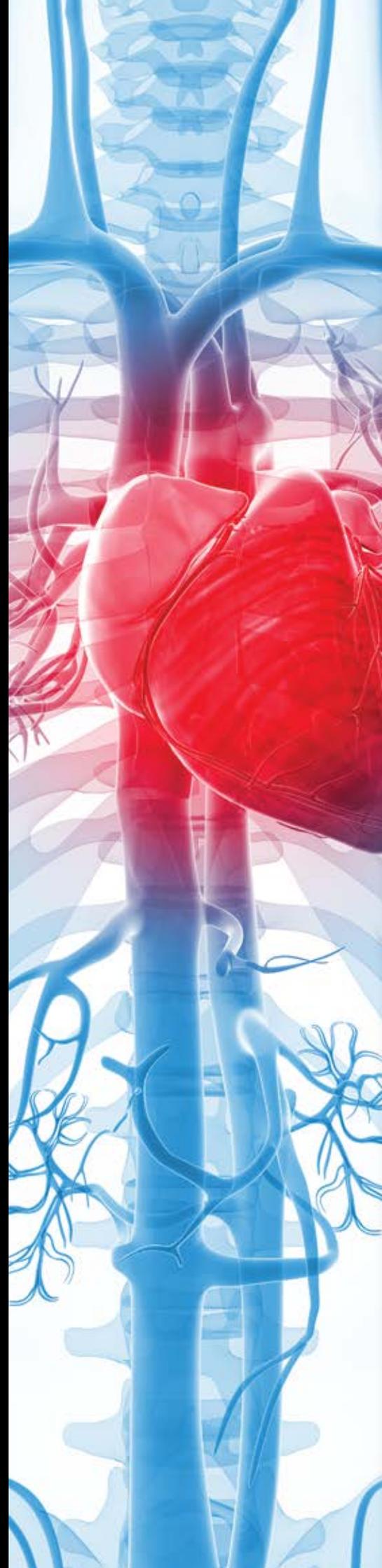
Personalised modelling for patients with Atrial Fibrillation (AF)

AF is an abnormal heart rhythm in which rapid and uncoordinated electrical activation of the atria compromises ventricular filling, resulting in deterioration of the mechanical function of the heart. Personalised models can increase the understanding of the pump mechanisms that trigger and sustain AF, leading to improved disease management.

The atria have a very thin wall with a complex, spatially-varying tissue microstructure. These small length scales and high spatial gradients necessitate high-resolution meshes to simulate the electrical and mechanical properties. The electrical model must be solved with a high frequency to capture the fast spread of the activation wave. Atrial mechanics requires the solution of a system of nonlinear equations, which is computationally expensive. Access to ARCHER has made these simulations computationally tractable.

Personalised computational simulations of atrial electromechanics rely on the consistent generation of high fidelity finite element meshes in the submillimeter scale. Therefore, high-resolution CT data were acquired and analysed **(Figure 2)**.

Figure 2
Smoothed anatomical segmentation of left atrium extracted from high-resolution cardiac CT data.

Statistics-based anatomical image segmentation was performed using tissue-specific thresholds for an accurate identification of the heterogeneous atrial myocardium. The smoothed three-dimensional geometries were tessellated into finite element meshes necessary to solve the mathematical equations governing atrial electrophysiology and mechanics. Anatomical models of the atria and electrophysiological measurements were combined within the modelling framework to simulate physiological and pathological electrical activation in an individual patient's atria **(Figure 3)**.
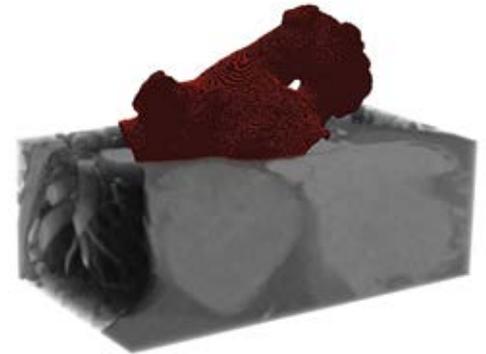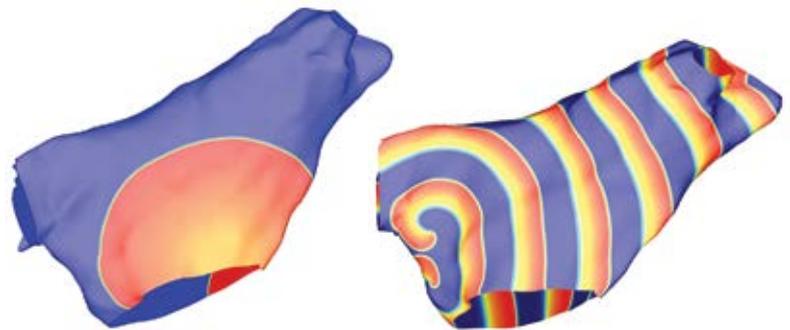

Figure 3
Left panel: Physiological spread of activation across patient-specific model of the left atrium. Right panel: The introduction of an ectopic beat shows how sinus rhythm can break down to a rapidly-initiating spiral wave activation. For both panels blue is low voltage (-90 mV) inactivated tissue and red is high voltage (+20 mV) activated tissue.

ARCHER has supported the development of a personalised left atrial finite element model of atrial electromechanics. This allows a detailed investigation of the causative link between left atrial electrophysiology and mechanics, leading to an increased understanding of the important mechanisms involved in AF.

Personalised modelling provides another step towards personalised medicine in which patient selection and patient treatment will be tailored to individual needs and specific patient conditions.

Key Academics and Collaborators:

King's College London / Cardiac Electromechanics Research Group
Dr Steven Niederer, Dr Angela Lee, Dr Cesare Corrado, Thomas Fastl

King's College London / St Thomas' Hospital Cardiologists
Prof Aldo Rinaldi, Prof Mark O'Neill, Prof Reza Razavi, Dr Ronak Rajani

Medical University of Graz
Prof Gernot Plank

Oslo University Hospital
Dr Espen Remme

Contact:

Dr Steven Niederer
steven.niederer@kcl.ac.uk

www.archer.ac.uk

About ARCHER

ARCHER is the UK National Supercomputing Service. The service is provided to the UK research community by EPSRC, UoE HPCx Ltd and its subcontractors: EPCC and STFC's Daresbury Laboratory, and by Cray Inc. The Computational Science and Engineering (CSE) partners provide expertise to support the UK research community in the use of ARCHER. The ARCHER CSE partners are EPSRC and EPCC at the University of Edinburgh.

The eCSE Programme

The Embedded CSE (eCSE) programme provides funding to the ARCHER user community to develop software in a sustainable manner to run on ARCHER. Funding enables the employment of a researcher or code developer to work specifically on the relevant software to enable new features or improve the performance of the code.

The Case Study Series

This case study has been produced as part of the ARCHER CSE service, supported by EPSRC research grant number EP/N006321/1.