# Investigating the role of structural remodelling in persistent atrial fibrillation

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## Background

Atrial fibrillation (AF) is the most common cardiac arrhythmia. The exact mechanisms behind AF are unclear. Anatomically realistic computer models aid our understanding of mechanisms that initiate and maintain atrial rhythm disturbance. Our group has recently developed an image-based model of normal sheep atrial anatomy incorporating complete structure information of 3D atrial geometry and myofibre organisation, and employed this model to investigate paroxysmal AF[1,2].

### Imaging the atria

Whole sheep atria were fixed, embedded in paraffin wax and serially imaged using extended-volume surface imaging microscopy hosted at Physiology Department with 8μm in-plane resolution and 50μm across-plane (Fig. 1).

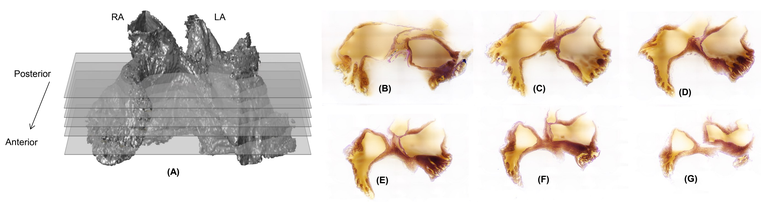



***Fig 1*** *Anatomical structure of normal sheep atria. (**A**) 3D computer reconstruction of the whole atria from anterior view. (**B-G**) Six typical 2D montage atrial images, the locations were indicated in (**A**).*

### Image Processing

3D atrial geometry was reconstructed with a suite of image processing tools. Local fibre orientations were estimated by eigen-analysis of the structure tensor (Fig. 2).

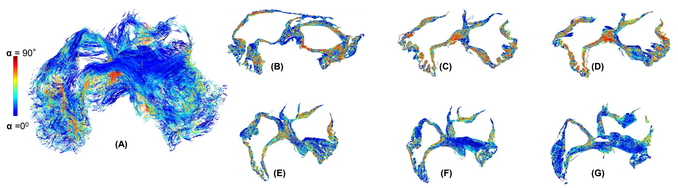



***Fig 2*** *Atria myofibre architecture. (**A**) Anterior view of 3D fibre orientations visualized by fibre tracking. (**B-G**) Inclination angles in the six representative 2D planes in Fig 1.*

### Fibrosis Modelling

There exists compelling evidences that structure remodelling (fibrosis) plays a crucial role in AF[3]. Computer model provides a powerful approach to investigate the effects of fibrosis on electrical instability and formation of rotors.

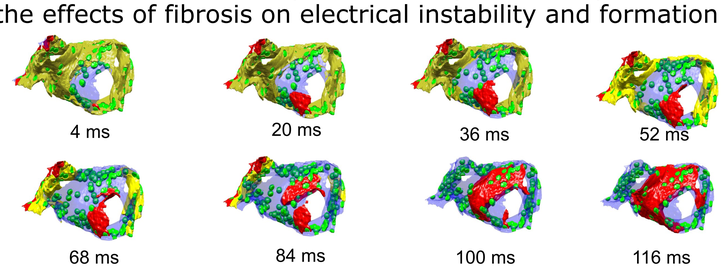



***Fig 3*** *Anisotropy with extensive structure remodelling. The red, yellow and blue indicate regions in activated, ARP and repolarized status. Green colour denotes fibrosis.*

## Diseased atrial models

Patients with persistent atrial fibrillation (PeAF) or permanent AF have very low long term success rate of reversing AF worldwide (<~28%). In my Ph.D. proposal, I seek to develop the first atrial models based on diseased sheep atria and compare with normal atria in order to investigate mechanisms through which atrial structural remodelling increases the risk of (1) PeAF and (2) heart failure (HF).

The sheep models with PeAF and HF will be developed and optically mapped by our overseas collaborators in University of Michigan[4] using their well developed approaches (Fig. 4). The same sheep hearts will be sent back to us, then imaged and reconstructed using the approaches in the left panel. Finally, image-based computer models will be used to evaluate effects of fibrosis and atrial wall thickness during progress of AF.

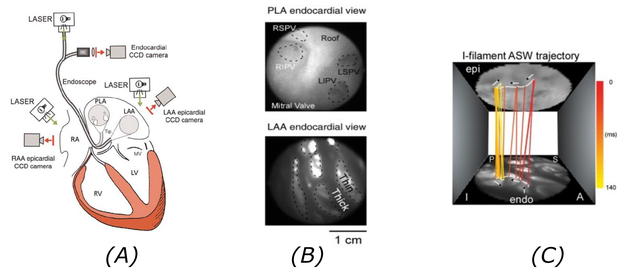
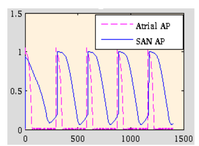



***Fig 4*** *Optical mapping approach developed by the Michigan group. **(A)** Optical mapping experimental setup. **(B)** Background pictures of endocardial anatomy. **(C)** Tracing the I-filament trajectory[4].*

### Numerical Solvers

Beatbox[5] is a finite difference method based cardiac simulation environment for generating fast and scalable simulations in sequential or parallel mode.




This multiscale modelling approach could handle anisotropic and heterogeneous problems on any irregular geometry. Cellular models can be used via CellML.

## Future Work

Since starting my doctoral studies in December 2013, I have been working with MATLAB (image processing) and Beatbox (computer cardiac simulation). Given below is a summary of my proposed work :

- Imaging the sheep atria using confocal microscopy.
- Further develop image processing tools to extract micro-structure information, e.g. fibrosis, from the high resolution images and reconstruct 3D atrial anatomy.
- Develop novel approach to analyse 3D fibrosis distributions across whole atria and compare the differences among the normal, PeAF and HF atria.
- Develop novel method to estimate atrial wall thickness throughout atria and investigate the relationship between atrial wall and AF.
- Image-based atrial models will be used to address more specific hypotheses related to atrial wall thickness and fibrosis.

## References

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5. McFarlane R and Biktasheva I.V., "Beatbox - A Computer Simulation Environment for Computational Biology of the Heart", BCS Inter. Acad. Conf. "Visions of Comp. Science", 2008, London.