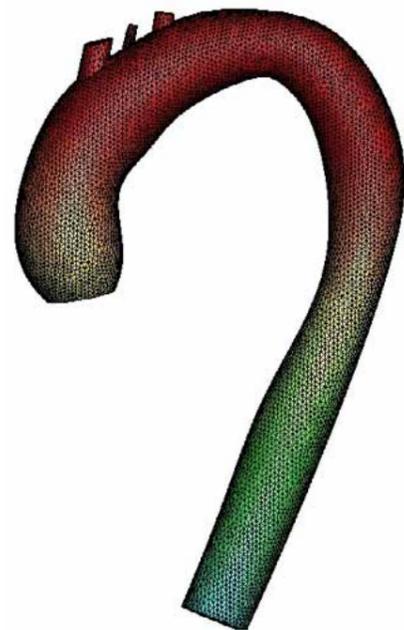


Arterial dissection

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The challenge

An arterial dissection is a tear of the delicate internal lining in the artery. It causes serious damage and is of significant interests to surgeons. When this happens in coronary artery, it leads to myocardial infarction with a high rate of mortality. Although arterial dissection is a frequently occurring phenomenon and a challenging clinical entity the underlying biomechanics remains largely unclear.

How it is solved

In this project, we will address a particular situation of aortic dissection associated with patients with congenitally bicuspid aortic valve. A congenitally bicuspid aortic valve has 2 functional leaflets instead of 3 leaflets. Bicuspid aortic valve is often observed with other left-sided obstructive lesions such as coarctation of the aorta or interrupted aortic arch, and dilated aortic root. This dilatation has some similarities to the dilatation of the aorta seen in Marfan syndrome. The dilatation may involve the ascending aorta (most commonly) but may also involve the aortic root or transverse aortic arch. It is presumably due to the weakened aorta, patients with bicuspid aortic valve is particularly prone to artery dissection.

We will derive analytical solutions for simplified artery dissection models using a novel (cohesive

zone) approach to resolve the crack (dissection) propagation in the arterial wall embedded in fluid (blood). The simplified models will be used to develop more realistic physiological models using numerical methods and MRI, and results will be compared with with Glasgow clinical database of patients with congenitally bicuspid aortic valve. The project will identify the key factors contributing to the higher rate of arterial dissection in this patient group.

Why it is important

Aortic dissection is life threatening. The condition can be managed with surgery if it is done before the aorta ruptures. Less than half of patients with ruptured aorta survive.

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Multi-scale modelling of human heart

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The challenge

Improved approaches are urgently needed to identify the extent of heart muscle injury involved in heart conditions and potentially predict future outcomes, including treatment response. Multi-scale modelling of human heart combined with MRI can be used to develop a clinically-useful framework to combat diseases and to improve our understanding of both physiological and pathological behaviours of human heart.

How it is solved

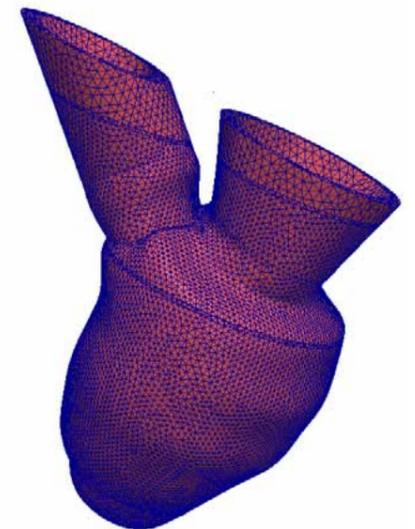
Our work embraces this problem by bringing together imaging, mathematics and medicine. We use novel methods with magnetic resonance imaging (MRI) and mathematics to construct 3D multi-scale modelling of heart, with intention to explore acute myocardial infarction (MI) in experimental animals and humans. The cardiac MRI methods provide information on structure, function and pathology in a single scan. The mathematical methods take the MRI data to recreate geometric models of the heart, include fibre structure, and making use of structure-based constitutive models and bi-domain based active contraction. The parameters of the constitutive models will be identified using an inverse approach from the dynamic strain field measured by the 3D displacement encoding with

stimulated-echos (DENSE) MRI from human subjects at the Glasgow BHF centre. Since MRI is safe and can be repeated, heart models can be developed serially and so evolve in response to changes in the heart post-MI.

For the mechanical modelling of the heart, we use the finite-element immersed boundary method - IBAMR, modelling the 3D finite strain with fluid-structure interaction. IBAMR combines the strength of the conventional IB methods and the finite element methods, and enables both the fluid-structure interaction, and the complicated nonlinear finite strain solid mechanics to be modelled accurately and effectively.

Why it is important

Heart attack is a leading cause of premature ill health and death and places a significant burden on the NHS. Consequently, improved approaches are urgently needed to identify the extent of heart muscle injury and potentially predict future outcomes, including treatment response.



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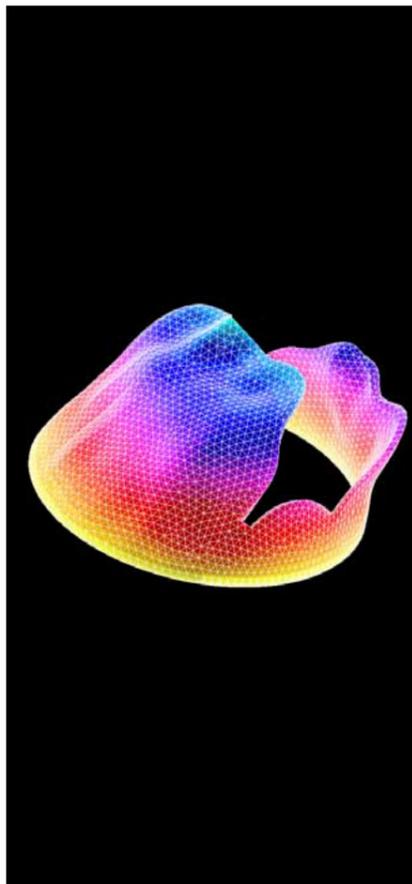
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Dynamic modelling of bioprosthetic and human mitral valves

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The challenge

In human, the mitral valve is a complex anatomical structure consisting of two leaflets, an annulus, chordae tendineae, and papillary muscles. Different to the aortic valve, the leaflets of mitral are asymmetric, and are attached to the left ventricle through a bundle of chordae tendineae, which have a significant effect on its function.

To handle the dynamic modelling, we use the immersed boundary method, modelling the 3D dynamic fluid-structure interactions. The immersed boundary method is a practical and effective way to simulate certain types of fluid-structure interaction (FSI) problems, which uses the elastic fibres to represent the elastic body (heart valve) immersed in a viscous incompressible fluid (blood). Its effective dynamic capability has been used to model blood flow patterns in the heart, and to assist prosthetic valve design.

How it is solved

To investigate the mechanical behaviour of the mitral design under physiological flow conditions without having to model the left ventricle, we make use of in vivo magnetic resonance images of the left ventricle. The relative motion of the mitral annulus and the papillary muscle regions of the ventricle determined from these MRI images is then used as a prescribed boundary condition for the chorded mitral valve in a

dynamic cycle. Results show that without the proper functioning of the papillary muscle, the mitral prosthesis can suffer from an intolerable over-stretch during systole compared with laboratory tests in which the mitral chordae are fixed in space. This turns out to be the key weakness of the current design.

Why it is important

A diseased mitral valve is usually repaired by various surgical means such as to replace or transfer the damaged chordae. When a mitral valve is too severely diseased for repair technique to be effective, it is generally replaced with a mechanical or bioprosthetic valve. Understanding native mitral valve dynamic behaviour is thus highly important for developing more efficient repair techniques, and perhaps even more so for designs of artificial mitral valves. With improved cardiopulmonary bypass, myocardial protection, and surgical techniques, the mortality rate from aortic valve replacement decreased substantially, whereas the mortality rate from mitral valve replacement remains high (around 50% at 10 years), largely because of the low cardiac output syndrome.

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Numerical study of flow in collapsible tubes

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The challenge

Cylindrical tube deforms in a strongly nonlinear fashion when subject to large external pressure, a problem that frequently appear in many biological applications. Engineering approaches to this problem often used linear deformation, which can give very inaccurate predictions.

How it is solved

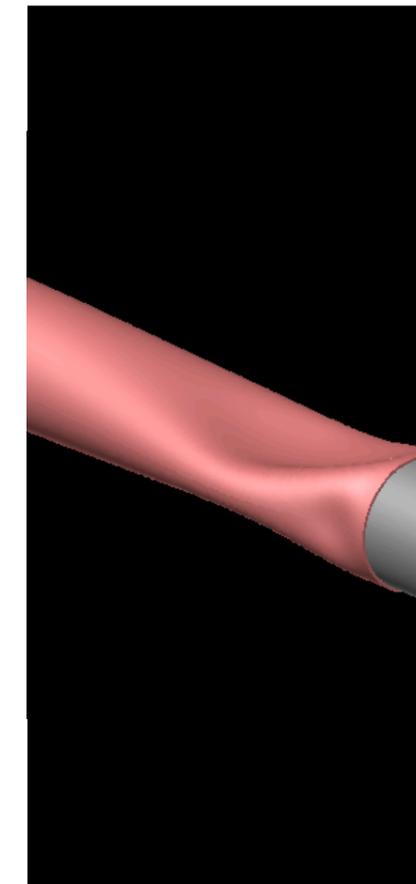
In this project, a totally nonlinear analysis is conducted for axisymmetrically deformed thick-walled cylindrical tube subject to external pressure, and the results are compared to the linear predictions.

For small deformation, both linear and nonlinear models give very similar results. However, cylindrical tubes behaves very differently under large external pressure, and the dominate features are the corner bulging and higher modes. This is the first time that a totally nonlinear analysis is carried out for thick walled tubes, and the results may have significant implications to many physiological applications involving soft vessels undergoing large deformation.

Why it is important

The collapse of compressed elastic tubes conveying a flow occurs in several physiological applications and clinical devices: for example, arteries are collapsed during sphygmomanometry, and large

bronchi collapse during forced expiration. Experiments on such a system have revealed a rich variety of self-excited oscillations that exist in such flows, demonstrating that the system is a nonlinear dynamical system of great complexity. Several one-dimensional and lumped-parameter theoretical models have been proposed, revealing different mechanisms by which oscillations can be generated or maintained. However, due to the crude approximations that have to be used in such models, there is as yet no complete theoretical description of the oscillations in any realizable experimental conditions.



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Mathematical modelling of the cornea

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The challenge

The cornea has a unique shape in that it is steeper centrally than the peripheral cornea. Any change in the curvature of the cornea will affect the refractive status of the eye profoundly. In a diseased condition called keratoconus (KC)

that affects young people, the corneal curvature becomes conical and the central corneal curvature becomes steeper. This results in poor image formation on the retina. This condition requires a corneal transplant. Additionally this corneal transplant is done in a circular in shape and the central 8 mm of the cornea is removed and replaced with a donor cornea. However KC is not always central and it can involve the periphery of the cornea. Current surgical practice still adopt a central corneal graft leaving the peripheral corneal uncorrected.

How it is solved

We will develop a mathematical modelling of the curvature of the cornea in KC, with objectives to design the best fit shape of the graft, which could be extremely useful in surgical planning for diseased eyes, or dealing with eyes that had collapsed due to perforation at the Emergency Department.

Why it is important

Keratoconus is a degenerative condition that affects the front of the

eye causing severe visual impairment. The cases of Keratoconus are not clear but there is a suggestion that the disease might be already in the patient at birth. It is generally diagnosed in young people and although it is not very well known, it is not rare, with an incidence in the general population of 1 to 430/2000.

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Understanding human gallbladder pain

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The challenge

The most common cause of gallbladder disease is the presence of gallstones. However, it is common to have stones in the gallbladder that cause no symptoms. On the other hand, a proportion of people do suffer from severe acalculous (i.e. without gallstones) biliary pain. The decision to surgically remove the gallbladder is made when patients have symptoms (pain), not if they have gallstones.

Of a major concern is that not all patients benefit from the cholecystectomy, and the symptoms continue even though the gallbladder has been removed. The fundamental issue is to understand the underlying mechanisms of gallbladder pain, which remains a challenge.

How it is solved

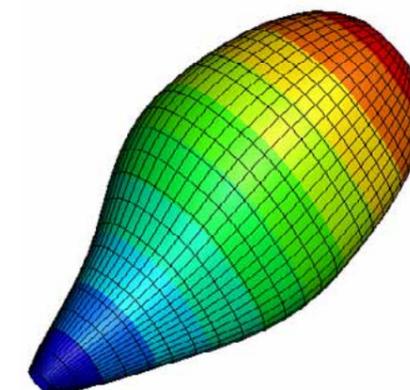
This project aims to develop mechanical models and to identify the mechanisms of gallbladder pain. Initial investigations predicted that the peak total stress in the gallbladder wall has a strong correlation with the pain.

The biliary system consists of pliable tubes and various valves into which bile and pancreatic juices are secreted under pressure. The gallbladder receives dilute bile from the liver, stores and concentrates it during the inter-digestive period and evacuates the more viscous gallbladder bile in response to a meal-stimulated contraction. The bi-directional flow is controlled by the cystic duct,

commonly known as the Heister valve or the spiral valve. Extensive clinical and in vitro studies at the Sheffield Gallstone Centre have strongly suggested that the critical unknown in the normal and pathophysiology of the biliary system is in the filling and evacuation of the gallbladder and the flow through the cystic duct.

Why it is important

Gallstones and other biliary diseases affect about 10% of the adult population of the UK. Up to 60,000 operations to remove the gallbladder are being performed in the UK each year, at a cost of about £40 million to the NHS. Understanding of the pathogenesis of gallstone disease and pain production mechanism is key to improve diagnosis and patient outcome and prevent complications of gallstones such as acute pancreatitis and obstructive jaundice, which can be fatal.



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