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# Bayesian sensitivity analysis of a model of the aortic valve

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ABSTRACT

Understanding the mechanics of the aortic valve has been a focus of attention for many years in the biomechanics literature, with the aim of improving the longevity of prosthetic replacements. Finite element models have been extensively used to investigate stresses and deformations in the valve in considerable detail. However, the effect of uncertainties in loading, material properties and model dimensions has remained uninvestigated. This paper presents a formal statistical consideration of a selected set of uncertainties on a fluid-driven finite element model of the aortic valve and examines the magnitudes of the resulting output uncertainties. Furthermore, the importance of each parameter is investigated by means of a global sensitivity analysis. To reduce computational cost, a Bayesian emulator-based approach is adopted whereby a Gaussian process is fitted to a small set of training data and then used to infer detailed sensitivity analysis information. From the set of uncertain parameters considered, it was found that output standard deviations were as high as 44% of the mean. It was also found that the material properties of the sinus and aorta were considerably more important in determining leaflet stress than the material properties of the leaflets themselves.



## 1. Introduction

The Aortic Valve (AV) has attracted much attention in the biomechanics community due to its remarkable durability—typically experiencing 3.7 billion cycles in its lifetime (Thubrikar, 1990), usually without failure. Prosthetic replacements are necessary when the natural valve becomes diseased, yet both mechanical replacements and bioprosthetics have significant drawbacks (Silberman et al., 2008) and cannot perform with the same reliability as the natural counterpart. Understanding the biomechanics of the natural valve is a key requirement in improving prosthetic design, therefore Finite Element (FE) models have been used extensively to better understand the AV. Recent simulations have been of high complexity, with fluid structure interaction (FSI) included (see e.g. De Hart et al., 2003; Carmody et al., 2006), and encompassing multi-scale approaches (Weinberg and Mofrad, 2007).

A difficulty which is rarely acknowledged however is the problem of dealing with model uncertainties. The AV is typical of a biological system; many model inputs are often quoted over fairly wide ranges—valve dimensions, material properties and loading vary significantly from one individual to the next. To ignore the uncertainty in these parameters can only place the validity of the model in doubt. Some work has been performed (Ranga et al., 2004) to investigate uncertainty in the material properties of the aortic root, although this was not a formal statistical analysis. This paper aims to perform a detailed Uncertainty Analysis (UA) specifically on an AV model, and on a broader scale to highlight the importance (and feasibility) of UA in modelling biological systems in general. A furtherance of UA, known as *Sensitivity Analysis*, measures the sensitivity of the model output to particular (subsets of) inputs. This can provide a deeper insight into the model itself and suggest approaches for reducing the uncertainty in the output. A full discussion of SA is given by Saltelli et al. (2000).

## 2. The finite element model

The FE model was built in LS-Dyna, an explicit solver that has been shown to be capable of modelling the transient behaviour of the AV—some examples include (Howard et al., 2003; Carmody et al., 2006; Weinberg and Mofrad, 2007). A one-sixth section of the full valve (shown in Fig. 1) was created, illustrated in Fig. 2 with appropriate symmetry conditions. The initial geometry of the valve was taken to be in what is assumed to be the unstressed state (as used for example in Weinberg and Mofrad, 2007). All parts of the valve were represented by quadrilateral shell elements. In the leaflet region the thickness of each element was varied to follow the contours detailed in Thubrikar (1990), and

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divided into regions which are later used to examine regional valve stress—see Fig. 3.

FSI effects were also be accounted for since the pressure loading on leaflets is inter-dependent on the position of the valve. Accordingly, an Eulerian fluid mesh was constructed with two pressure sinks at the ventricular and aortic ends that were constrained to follow the pressure variations of the cardiac cycle (Klabunde, 2004). The fluid was modelled by a fluid-like material model and a Gruneisen equation of state (see Hallquist, 2006 for further details) as successfully used by Carmody et al. (2006), amongst others.

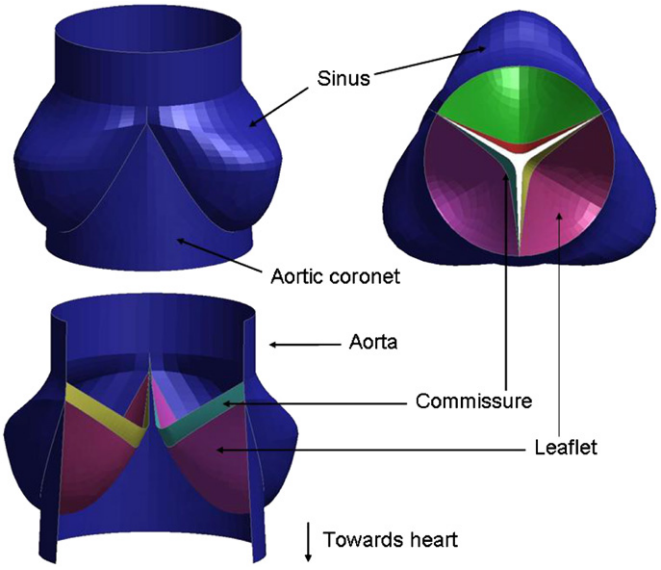


**Fig. 1.** Full representation of the aortic valve with various parts labelled.

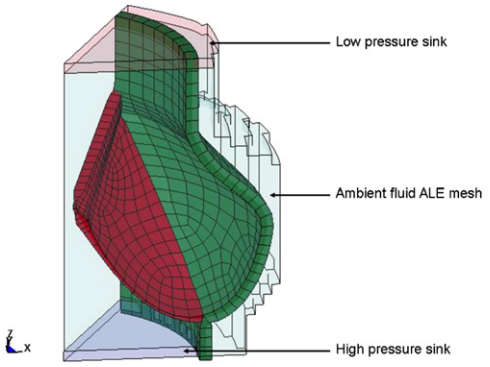


**Fig. 2.** Finite element mesh representing one-sixth of the total valve (shell elements shown with assigned thicknesses).

## 3. Material properties

The material of the AV leaflet is known to be highly nonlinear and anisotropic. Collagen and elastin fibres generally run in the circumferential direction, and are "crimped" in the relaxed state of the valve; as such, at low strains they are not under tension and resistive force is due purely to the connective tissue. However, once the fibres are un-crimped, they provide a strong (and virtually linear-elastic (Billiar and Sacks, 2000)) resistance—this is responsible for the hyperelastic, or roughly bi-modular nature of the material. The leaflet material has also been shown to be largely insensitive to strain rate (Stella et al., 2007), therefore viscoelastic effects were not considered in the model.

In order to model the nonlinearity and anisotropy of the leaflet, a constitutive material model for soft biological tissues is adopted, first proposed by Weiss et al. (1996). This model assumes that the hyperelastic response of the material is due to unidirectional fibres embedded in an isotropic matrix. It has the added advantage of being already implemented in LS-Dyna. The strain energy function is represented in terms of deviatoric and volumetric components,

$$W = F_1\left(\tilde{I}_1,\tilde{I}_2\right) + F_2(\lambda) + \frac{1}{2}K\{\ln(J)\}^2 \tag{1}$$

where $W$ is the strain energy, $\tilde{I}_1$ and $\tilde{I}_2$ are the deviatoric invariants of the right Cauchy deformation tensor, $\lambda$ represents the deviatoric stretch along the fibre direction, $K$ is the effective bulk modulus, and $J$ is the volume ratio (the determinant of the deformation gradient tensor $\mathbf{F}$). The functions $F_1$ and $F_2$ are the (deviatoric) contributions of the isotropic background matrix and the reinforcing fibres, respectively. The last term provides the volumetric component, although heart valve tissue is usually assumed to be incompressible, rendering the term negligible. The background matrix is represented by the Mooney–Rivlin model

$$F_1(\tilde{I}_1,\tilde{I}_2) = C_1(\tilde{I}_1 - 3) + C_2(\tilde{I}_2 - 3) \tag{2}$$

where $C_1$ and $C_2$ are material constants. The fibre term assumes that the fibres provide no resistance in compression, and in tension provide resistance in two stages. Below the critical stretch level $\lambda^*$, stress is described by a scaled exponential function as the fibres "un-crimp", whilst at higher stretches it is a linear function, representing the approximately elastic response of the straightened fibres. This

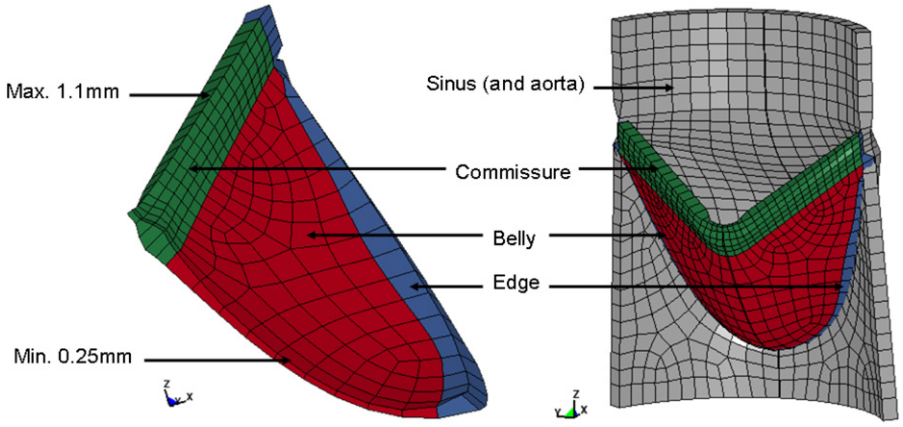


**Fig. 3.** Thickness variations of the AV leaflet (left) and model regions referred to in the stress analysis (right).