A COMPARATIVE STUDY FOR THE EFFECT OF TISSUE ANISOTROPY ON THE
BEHAVIOR OF A SINGLE CARDIAC PRESSURE CYCLE FOR A SYMMETRIC
TRI-LEAFLET VALVE

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BEHAVIOR OF A SINGLE CARDIAC PRESSURE CYCLE FOR A SYMMETRIC
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Thesis

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ABSTRACT

Several attempts have been made in the past to understand the mechanics and function of the aortic valve and its surrounding geometric structures through finite element analysis, a powerful mathematical tool. As expressed by Thubrikar, there is a need to understand the geometry of the valve in a dynamic state. Sophisticated analysis of the complex interplay between the aortic root and the leaflets, as well as the development of stresses and strains in the leaflet during opening and closing is now possible using powerful computer techniques, which aid in a better understanding of the dynamics of the aortic valve. More importantly, these might prove invaluable in predicting patterns of failure of replacement devices or repair techniques in the work bench setting rather than experiencing it in the clinical situation, with unfortunate consequences. Earlier work on the aortic valve has been well documented along with substantial details of the geometry. Such dimensions have been used in recent studies also. The procedure illustrated by Thubrikar has been used to create the current model. The thickness of the leaflet is assumed to be constant in this model and the orientation was assigned based on the previous work done by Saleeb et al and his team. To check the capability of the material model developed by Saleeb et al and his team, Dokos et al work on the shear properties of passive ventricular myocardium results were compared. Comparative study was performed on the aortic valve model to observe the effect of tissue anisotropy for one
complete cardiac cycle. All results obtained in this study utilized standard ABAQUS [1] FE program and its associated UMATS.
ACKNOWLEDGEMENTS

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1.1 General

Recent developments in the fields of Computer Aided Design (CAD) and Finite Element (FE) technology and the emergence of modern, more powerful computers, have made possible the substitution of real models of products with computer models. This evolution has many advantages in cutting down the cost and the time for a complete design–analysis–creation cycle of a variety of products in a wide range of fields and applications. The construction of finite element models for the purpose of analysis is in itself a laborious task especially for biological objects (e.g. fruits, human body parts etc.) which often have a more complicated geometry than mechanical components. From this point of view the major bottleneck in the complete modeling–analysis cycle is the definition of the geometry of the object under consideration (i.e. modeling part of the cycle). However, emerging technology in image processing techniques allows for the reconstruction of scanned objects (in the form of 3D points on the surface of the object) from image data (photographs, video recordings, CT, NMR etc.). These points could be automatically processed and fitted so that a geometric model of the scanned object is produced. This model could then be supplied to a finite element analysis system for further processing and analysis or be otherwise utilized. There are other alternative
methods to supply a geometric model as an input to FEA system. The computer model developed by Thubrikar et al for the open and closed valve was fully described by only five design parameters, (1) radius of the base $R_b$, (2) Radius of the commissure $R_c$, (3) valve height $H$, (4) height of the commissure $H_s$, and (5) angle of the open leaflet to vertical $\beta$.

The aortic valve is not a static structure in its natural state; it always in motion. Although leaflets are the most dynamic parts of the aortic valve, the motion of other parts also play an important role in the opening and closing of the valve. The true dynamic behavior involves: (1) motion of the commissures, (2) mechanism of opening of the aortic valve, (3) motion of the base, (4) motion of the aortic annulus and aortic sinuses, and change in leaflet length.

The design of aortic valve must be understood in its natural state, which is the functional state in-vivo. Dimensional changes were neglected in our study. The static design can be thought of as the average design parameters over which dimensional changes occurring during a cardiac cycle, are superimposed.

1.2 Objective of Study

The main objective of the present study is to check the capability of the material model developed in order to validate the experimental results, construct a 3D solid model of the aortic valve and compare one complete cardiac cycle using isotropic and anisotropic material properties.
1.3 Outline

The introductory chapter is followed by background and review on literature on aortic valve. Then there would be description of the hyper-visco-elastic-damage model developed by Saleeb et al. The following chapter describes the development of our model. The next chapter checks the capability of the material model developed characterizing experimental results published by Sacks et al & Dokos et al and compares one cardiac cycle using isotropic and anisotropic material properties. Finally conclusions are presented in last chapter.
CHAPTER II
BACKGROUND AND LITERATURE REVIEW

2.1 Background - Biomechanics

In the early fourth century B.C., [2] the works of Aristotle (384-322 B.C.) described the mechanical action of muscles through geometric analysis in producing locomotion of parts. Nearly 2000 years later Leonardo da Vinci (A.D. 1452-1519) in his famous anatomic drawings described the mechanics of standing, walking up and downhill, rising from a setting position and jumping followed by Galileo (A.D. 1564-1643) in his earliest attempts to mathematically analyze physiologic function. William Harvey (A.D. 1578-1657) in his pioneering efforts in defining the anatomic circulation of blood, was credited by many as the father of modern day bio-fluid mechanics, and Alfonso Bernoulli (A.D. 1608-1679) shared the same honor for contemporary bio-solid mechanics due to his efforts to explore the amount of force produced by various muscles. The early work of these pioneers of biomechanics was followed up by Sir Isaac Newton (A.D. 1642-1727), Daniel Bernoulli (A.D. 1700-1782), Jean L.M. Poiseuille (A.D. 1799-1869), Thomas Young (A.D. 1773-1829), Euler (whose work was published in 1862), and others of equal fame.
2.2 Background – Tissues

Biological soft tissues can be characterized as a highly anisotropic material consisting of a complex microstructure. The development of the biomechanics has evolved from mechanics itself. The soft tissues often exhibit characteristic behavior of viscoelasticity i.e., they creep under a constant load and exhibit hysteresis upon cyclic loading. Thus various theories of viscoelasticity which were of differential type (e.g. Maxwell and Voight models) and of integral type (e.g. Boltzmann models) were applied. Because of the inherent nonlinear behavior exhibited by most soft-tissues over finite strains, standard models of linear viscoelasticity are not applicable in general. This led Fung to propose a quasi-linear viscoelasticity theory. The other prominent theory was Thermo mechanics theory. Roy in 1880 had observed the similarities in the thermo elastic behavior of soft tissue and elastomers. Lawton (1954) and Flory (1956) showed that the tissue elasticity is primarily entropic rather than energetic as that of metals. Numerous other structural-based models have been developed. In some of these models the microstructural composition of the tissue is utilized in the formulation allowing for an angular distribution of collagen/elastin fibers and the constitutive response of the fibers was then “assembled”. The planar fibrous connective tissues of the body were composed of a dense extracellular network of collagen and elastin fibers embedded in a ground matrix, and thus can be thought of as biocomposite. Sacks et al [3] used small angle light scattering (SALS) to map the gross fiber orientation of several soft membrane connective tissues. However, the device and analysis methods used in these studies required extensive manual intervention.
2.3 Background and Literature review – Aortic Valve

The aortic valve is one of the four valves (as shown in Fig 2.1 (a) & (b)) which control the blood flow through the heart. It is situated at the outlet of the left ventricle and has three anatomical entities, three leaflets, three sinus cavities and the aortic ring. The area under the free edge is known as the lunula (due to its semi-lunar shape). When the valve is closed, the outlet orifice of the left ventricle is sealed because the lunulae of adjacent leaflets are coincident with each other. The remainder of the leaflet surface, not making contact with adjacent leaflets when the valve is closed, is referred to as the load bearing leaflet portion. The line of attachment of the leaflets to the aortic valve is referred to as the aortic ring (also designated as annulus fibrosus or fibrous coronet). Halfway the free leaflet edge is a thickening called node of arantius. Under normal physiological conditions the closing of the aortic valve starts during the deceleration phase of the aortic volume flow. A small aortic back flow completes the closure of the valve. Both mechanical and kinematical aspects are involved in valve functioning and differ in importance in various phases of cardiac cycle. During one cardiac cycle three main phases can be distinguished in valve performance, the opening and closing phases in systole and diastolic phase during which the valve is closed. Under normal situation valve opening is very fast. The valve is completely open when the peak flow in the ascending aorta has reached 75% of its maximum. Two phases can be distinguished during valve closing. The first is a gradual closing of the valve that starts during the deceleration of aortic flow, resulting in about 80% valve closure at the moment of zero flow in the ascending aorta at end systole, finally a small reverse flow completes closure. The valve
opens and closes approximately 103,000 times each day and approximately 3.7 billion times in its life span. Aortic valve is unique in its accomplishment since no man-made valve, to date, can serve that function with the same efficiency and durability.

Fig 2.1 (a) Anatomy of a human heart

Fig 2.1 (b) Aortic valve in the closed position
C-commissure; F-free edge; L- lunula; N-node of Arantius; S- sinus wall; T-top of a sinus cavity
Based on histological observations, valve leaflet was considered as an elastin meshwork, reinforced with stiff collagen bundles mainly arranged in one particular direction. The sinus valves consist of smooth muscle cells embedded in a grid of elastin fibers showing no definite orientation as shown in fig 2.2. The sinus and aortic tissues appear to be much more compliant than the leaflet tissues. From the results of uniaxial tensile experiments the collagen bundles in the leaflets show a stiffening effect and cause a marked anisotropy. The bundles transmit the pressure load on the membranous parts to the aortic wall. The stress-strain curves of the tissues were slightly sensitive to strain rate. In the leaflets more stress relaxation was found when compared to sinus and aortic valves.

Fig 2.2 SEM micrograph showing the appearance of the subendothelial extracellular matrix. The fibrils are arranged in a network without preferential orientation, x 1300
Literature review reveals that stress analyses have been performed on theoretical valve models. Closed position was considered in all these studies on valve leaflets. Studies ranged from analytical, based upon membrane theory using simple geometry to sophisticated models using finite element methods and detailed geometrical data obtained from stereo-photogrammetric studies. Material properties were assumed, mostly linear-elastic, isotropic and homogenous.

Cataloglu et al [4] in 1977 proposed a method of smoothing the geometrical data obtained from photogrammetric processing of silicon rubber molds of human aortic heart valves under pressure and estimated the magnitude and orientation of stress patterns that are important for both strength and fatigue design requirement. Cataloglu et al performed stress analysis on molds made from freshly excising leaflets in order to accomplish the
Table 2.1: Various efforts in the literature aiming at the computer modeling of the aortic valve

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<tr>
<th>Authors</th>
<th>Year</th>
<th>Element</th>
<th>Valve</th>
<th>Leaflet Material Properties</th>
<th>Experimental Validation</th>
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<tr>
<td>Cataloglu et al [4]</td>
<td>1977</td>
<td>---</td>
<td>Aortic Valve</td>
<td>Linear elastic</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Isotropic</td>
<td></td>
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<tr>
<td>Hamid et al [5]</td>
<td>1986</td>
<td>Membrane</td>
<td>Porcine trileaflet valve</td>
<td>Multistep Linear elastic</td>
<td>No</td>
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<td></td>
<td></td>
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<tr>
<td>Rousseau et al [6]</td>
<td>1988</td>
<td>Membrane</td>
<td>Porcine trileaflet valve, 1/6 valve simulated</td>
<td>Linear elastic matrix embedded with linear elastic truss element as fiber reinforcement</td>
<td>Yes, Commisure &amp; leaflet center displacement were measured cinematographically</td>
</tr>
<tr>
<td>Black et al [8]</td>
<td>1991</td>
<td>Shell</td>
<td>Pericardial bicuspid valve</td>
<td>Non-linear isotropic hyperelastic model</td>
<td>No</td>
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<td>Krucinski et al [9]</td>
<td>1993</td>
<td>Brick Element</td>
<td>Pericardial valve</td>
<td>Non-linear isotropic hyperelastic model</td>
<td>No</td>
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<td>Patterson et al [10]</td>
<td>1996</td>
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<td>Synthetic fiber-reinforced tri-leaflet valve</td>
<td>Fiber-reinforced model, with linear elastic properties for both matrix and fiber</td>
<td>Comparison between images from pulse duplicator and FE</td>
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<td>Li et al [13]</td>
<td>2001</td>
<td>Shell</td>
<td>Porcine aortic valve, ½ leaflet simulated Aortic valve</td>
<td>Transversely isotropic model, use five strain dependent elastic moduli Structural model</td>
<td>No</td>
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best description of the stress distribution. Further improvements in the analysis procedure which enhances the reliability and repeatability of the results were described. Based on the smoothed data which was assumed to be consistent with thin shell theory, a finite element analysis was conducted. Stress patterns consistent with anatomical observations were obtained and stress levels in excess of those previously reported were found. Also, the stress distribution in individual leaflets of the same valves was investigated and the non-coronary leaflet was found to carry the highest maximum stress.

Chong et al [21] worked on stress analysis of the porcine aortic valve leaflets in diastole at 80 mm Hg pressure in-vitro, incorporating local geometrical asymmetry, material inhomogeneity, anisotropy and non-linearity. The stress theory used was a
modified form of thin membrane stress theory for a homogeneous linearly elastic and orthotropic lamina. Modifications were made such that the Hooke’s law constitutive equation of stress can be applied to the inhomogeneous, non-linear elastic and orthotropic thin aortic valve leaflets. Stress calculations were made on the premise that the valve was in pre-transition in circumferential direction and post-transition in the radial direction. The areas of highest stress concentrations were in the areas of mutual leaflet coaptation near the Node of Arantii. Progressive increases of radial stresses from the sinus-annulus edge towards the node were observed.

Hamid et al [5] worked on large-deformation analysis of aortic root leaflets during diastole. The geometry of the leaflet was derived based upon actual configuration of the closed aortic valve leaflets obtained from a cast of the root of the aorta. Variability of the leaflet thickness was incorporated in the finite-element model. The leaflet material was assumed to be isotropic and the three values of Young’s modulus E were used. The first two E values that were used were assumed constant at 300 and 5000 kPa, corresponding to pre-transition and post-transition values, respectively in the stress strain curve. The third E that was used assumed a stress-dependent value according to a tri-linearized approximation of the stress-strain curve. The stress distribution on the leaflet at diastolic aortic pressures of 9.33 and 16.00 kPa were presented and the large-deformation analysis predicted lower maximal principal stresses.

In the year 1985, the anatomy of human aortic valve was studied by SEM in 36 samples [22] without cardiac pathology who died of various accidental causes. Two main types of endothelial cells, elongated and polygonal were detected on the endothelial
surface of the leaflets and possible relationships between endothelial cell morphology and the pattern of the mechanical stress to which the leaflets are subjected was discussed.

As the health and repair of heart valves is of great clinical importance, significant research has been conducted to examine the mechanical behavior of the aortic valve. The motion of the aortic valve has attracted significant attention from experimental as well as theoretical groups. Many methods have been developed to monitor the motion of the aortic valve in the past years. Its small size and rapid motion makes measurements challenging, however imaging technologies have recently demonstrated the acquisition speed and resolution to discern valve motion (Baumert et al. 2005; Boehm et al. 2007). Various constitutive models have been formulated (Biller and Sacks 2000; Holzapfel et al. 2000) and implemented in solid and shell finite elements (Kim et al. 2007; Sun and Sacks 2005; Weinberg and Kaazempur-Mofrad 2005, 2006).

A number of studies have attempted to use computer models of the aortic valve to simulate various aspects of its behavior. In previous numerical simulations of the valve (both static and dynamic), the aortic wall material properties were specified as linear isotropic, meaning that stress is proportional to strain. However, biological soft-tissue such as the aortic root wall is known to be highly anisotropic. This is due to presence of collagen fibers, which at low-strains are coiled up in a non load-bearing state, and at high strains uncoil and bear loads in their stretched configuration. Experimental stress-strain results have been published and the challenge has been to incorporate them into computer models.
Hamid et al [23] developed a finite element model of a bioprosthetic heart valve to determine the influence of the stent height on leaflet stresses under pressure loading conditions after valve closure assuming an elliptic-paraboloid for a relaxed leaflet shape, a rigid stent, isotropic leaflet material property with a Poisson's ratio of 0.45, a uniform leaflet thickness and a stress dependent Young's modulus. A nonlinear solution was used to obtain the stresses in the leaflets for stent heights of 14.6 mm, 19.0 mm and 22.0 mm respectively. Results predicted an increase of stresses on the closed leaflets as the stent height was reduced.

Rousseau et al [6] developed a geometrically non-linear numerical model of a closed Hancock leaflet valve prosthesis (Fig 2.4) in order to obtain mechanical specifications for the design of artificial leaflet valve prosthesis. The fiber reinforcement of the leaflet and the visco-elastic properties of frame and leaflets were incorporated in the model. The calculations were primarily restricted to 1/6th part of the valve and a time varying pressure load was applied. The calculations were verified experimentally by measuring the commissure displacements and leaflet centre displacement of a Hancock valve. Experimentally a difference was found between the three commissure displacements, which was predicted numerically using a simplified asymmetric total valve model. A clear dependency of commissure displacements on frame size was found. Numerically obtained stress distributions revealed that the maximum von Mises intensity in the membranes occurs in the vicinity of the commissure in the free leaflet area (0.2 N/mm²). The maximum fibre stress was found near the aortic ring in the fibers which form
the boundaries of the coaptation area (0.64 N/ mm$^2$). These locations seem to correlate with some common regions of tissue valve failure.

![Hancock Tissue Valve](image)

**Fig 2.4 Hancock Tissue Valve**

Huang et al [7] developed a finite element scheme using Lagrangian techniques for the two-dimensional analysis of bioprosthetic heart valve leaflets undergoing large deformation. A radial and a circumferential slice of a leaflet have been analyzed and the attachment of the slice to the stent was simulated by progressive contact on a circular former and the coaptation of the leaflets in the centre of a heart valve by a straight line of contact. The pressure under which the heart valve closes has been shown to be small in comparison with the normal pressure a heart valve sustains. Heavily stressed regions were subjected to a strong component of bending. The amount was observed to be sensitive to the details of the boundary conditions and to the initial configuration of the valve.

Black et al [8] presented a three dimensional finite element model based on a non-linear elastic representation of the tissue behavior of leaflets of a bicuspid bioprosthetic
heart valve. The geometry of the model was based on measurements from a real valve. Shell elements have been used in the analysis. Results indicated that bending stresses in the leaflets make a significant contribution to their deformation, confirming earlier two-dimensional work which suggested that analyses, where only membrane stresses were modeled, were likely to produce significant errors in the stress states.

Xie et al [24] in his work on the zero stress state of rat veins stated “In examining the function of an organ, one must know the stress distribution. The stress distribution in any organ depends on the zero-stress state of that organ. Stress and strain are measured relative to the zero-stress state so that one can say that stress is zero when strain is zero”. Open position of the valve is assumed to be in zero stress state in our model.

Krucinski et al [9] hypothesized that flexural stresses could be significantly reduced by incorporating a flexible or expansile supporting stent into the valve design. Opening and closing behavior of a trileaflet bovine pericardial valve was simulated using in-house non-linear finite element code (INDAP) and the pre- and post-processor modules of a commercial finite element package (PATRAN). Valve leaflets were assumed to be of uniform thickness with a non-linear elastic behavior adapted from experimentally obtained bending stiffness data. Simulations revealed that during maximal systolic valve opening, sharp curvatures are induced in the leaflets near their commissural attachment to the supporting stent. These areas of sharp flexure were observed to have experienced compressive stresses of similar magnitude to the tensile stresses induced in the leaflets during valve closure. Krucinski et al concluded that high flexural and compressive
stresses existed at sites of sharp leaflet bending causing bioprosthetic valve failure and proper design of the supporting stent can significantly reduce such flexural stresses.

Patterson et al [10] constructed two identical models of the leaflets of a bicuspid bioprosthetic heart valve using finite elements and applied identical boundary conditions to both models. Linear material model has been used in one and a non-linear elastic model in the other. The models contained 2600 Belytschko-Lin-Tsai shell elements which allowed variation of stress through the thickness of the leaflets to be modeled. Pressure difference was applied across the leaflets to model their behavior during a complete cardiac cycle and simulation was performed using a dynamic, explicit, time-stepping, finite element code. Comparing results from two models showed that the nonlinear model was more responsive to the time-varying pressure wave, and deformed into more complex shapes during the opening and closing phases which induced lower compressive but higher tensile stresses in the leaflets.

Grande et al [11] worked on stress variations in the human aortic root and valve discussing the role of anatomic asymmetry which was not considered in previous models. A finite-element model was created from magnetic-resonance images of nine human valve–root specimens, carefully preserving their asymmetry. Regional thicknesses and anisotropic material properties were assigned to higher-order elastic shell elements representing the valve and root. After diastolic pressurization, peak principal stresses were evaluated for the right, left, and non-coronary leaflets and root walls. Valve stresses were highest in the non-coronary leaflet (538 kPa vs right 473 kPa vs left 410 kPa); peak stresses were located at the free margin and belly near the coaptation surfaces (averages
537 and 482 kPa for all leaflets, respectively). Right and non-coronary sinus stresses were 21% and 10% greater than the left sinus. In all sinuses, stresses near the annulus were higher compared to stresses near the sinotubular junction. Stresses vary across the valve and root, likely due to their inherent morphologic asymmetry and stress sharing. These factors may influence bioprosthetic valve durability and the incidence of isolated sinus dilatation.

Burriesci et al [25] constructed a model of the leaflet of a bicuspid valve and assigned orthotropic non-linear elastic material properties and the influence of the natural orthotropy of pericardium on the mechanical behavior of pericardial heart valves during the whole cardiac cycle was studied using the finite element method. Two preferential orthogonal orientations of the tissue were analyzed (axial and circumferential). Results showed that even a small amount of orthotropy can significantly affect the mechanical behavior of the valve, and an appropriate orientation of the fibres can contribute to optimizing the stress distribution in the leaflets.

Moustakides et al [26] in his work on 3D image acquisition and NURBS based geometry modeling of natural objects presented a recently developed Image Acquisition-Geometric Modeling system for the construction of geometric models of natural or artificial objects. Based on the cloud of digitized 3D points, an approximating surface, a geometric model of the object of interest was constructed and coupled with a mesh generation package. The system presented allows for further processing and analysis of the resulting model instead of the real object itself.
Tri-leaflets are currently used only in ventricular assisted devices and artificial hearts as bridges to transplant, as these prostheses were not yet reliable for long-term applications. Failure of bioprosthetic and synthetic valves have been shown in numerous studies to occur for calcification and fatigue failure as a consequence of high stresses in the leaflets during opening and closing (Wiseman et al., 1982; Hilbert et al., 1987; Bernacca et al., 1995). Cacciola et al [12] in his work on 3D mechanical analysis of a stentless fibre reinforced aortic valve prosthesis as shown in Fig 2.5, focused on stress reduction suggesting that combination of a design with minimal stresses and a matrix material showing minimal calcification was considered to be the optimal solution. In the stented prostheses, synthetic or biological, the absence of contraction of the aortic base, due to the rigid stent, causes the leaflets to be subjected to an unphysiological degree of flexure which is related to calcification. It is shown that the absence of the stent, which gives a flexible aortic base and leaflet attachment and leaflet fibre reinforcement results in reduced stresses in the weaker parts of the leaflets in their closed configuration. Results showed that for the stentless models a reduction of stresses up to 75% was obtained with respect to stented models with the same type of reinforcement.

Dokos et al [27] developed a shear-test device for soft biological tissue which is capable of applying simple shear deformations simultaneously in two orthogonal directions while measuring the resulting forces generated in three axes. In order to validate the device, shear characteristics of a sample of rat septal tissue measuring 5×5×2.2 mm with the smallest dimension being the septal thickness was examined. These experiments demonstrated the reproducibility of the apparatus over different
samples and tests, as well as the ability of the device to measure nonlinearities and anisotropies in the material.

Sacks et al [3] developed specialized biaxial testing techniques for the aortic valve cusp, including a method to determine the local structure–strain relationship to assess the effects of boundary tethering forces. Natural and glutaraldehyde (GL) treated cusps were subjected to an extensive biaxial testing protocol in which the ratios of the axial tensions were held at constant values. Results indicated that the local fiber architecture clearly dominated cuspal deformation, and that the tethering effects at the specimen boundaries were negligible. Due to unique aspects of cuspal fiber architecture, the most uniform region of deformation was found at the lower portion as opposed to the center of the cuspal specimen. In general, the circumferential strains were much smaller than the radial
strains, indicating a profound degree of mechanical anisotropy, and that natural cusps were significantly more extensible than the GL treated cusps. Strong mechanical coupling between biaxial stretch axes produced negative circumferential strains under equibiaxial tension. Further, the large radial strains observed could not be explained by uncrimping of the collagen fibers, but may be due to large rotations of the highly aligned, circumferential-oriented collagen fibers in the fibrosa. This study provided new insights into the AV cusp’s structure–function relationship in addition to requisite data for constitutive modeling.

Billiar et al [28] formulated the first constitutive model to describe the measured planar biaxial stress-strain relationship of the native and glutaraldehyde-treated aortic valve cusp using a structurally guided approach. When applied to native, zero-pressure fixed and low pressured fixed cusps, only three parameters were needed to simulate fully the highly anisotropic, and nonlinear in-plane biaxial mechanical behavior. Differences in the behavior of the native, zero and low-pressure fixed cusp were found to be primarily due to change in the effective fiber stress-strain behavior. Knowledge of mechanics of the aortic cusp derived from this model contributed in understanding of fatigue damage in bioprosthetic heart valves and potentially laid the groundwork for the design of tissue-engineered scaffolds for replacing heart valves.

The anisotropic properties of porcine aortic valve leaflet were validated using a finite element model based on the uniaxial experimental data of porcine aortic valve leaflet and properties of nonlinear composite material by Li et al [13]. The anisotropic property of porcine aortic valve leaflet has potentially significant effects on its
mechanical behavior and the failure mechanisms. However, due to its complex nature, testing and modeling the anisotropic porcine aortic valves remains a continuing challenge to date. A finite element code was developed to solve this problem using the 8-node super-parameter nonlinear shells and the updated Lagrangian method. The stress distribution and deformation of the porcine aortic valves with either uniform or non-uniform thicknesses in closed phase and loaded condition were calculated. The results showed significant changes in the stress distributions due to the anisotropic property of the leaflets. Compared with the isotropic valve at the same loading condition, it was found that the site of the peak stress of the anisotropic leaflet was different; the maximum longitudinal normal stress was increased, but the maximum transversal normal stress and in-plane shear stress were reduced. Li et al concluded that it was very important to consider the anisotropic property of the porcine heart valves in order to understand the failure mechanism of such valves in vivo.

Gnyaneshwar et al [14] examined the leaflet/aortic root interaction during the cardiac cycle, including the stresses developed during the interaction. Dynamic finite element analysis was used along with a geometrically accurate model of the aortic valve and the sinuses. Shell elements along with proper contact conditions were used in the model. Pressure patterns during the cardiac cycle were given as an input, and a linear elastic model was assumed for the material. Results showed that aortic root dilation starts before the opening of the leaflet and is substantial by the time leaflet opens. Dilation of the root alone helped in opening the leaflet to about 20%. The equivalent stress pattern showed an instantaneous increase in stress at the coaptation surface during closure.
Stresses increase as the point of attachment is approached from the free surface. The complex interplay of the geometry of the valve system could be effectively analyzed using a sophisticated dynamic finite element model.

Wells et al [29] worked on effects of fixation pressure on the biaxial mechanical behavior of porcine bioprosthetic heart valves with long-term cyclic loading. Zero transvalvular pressure fixation was considered to improve porcine bioprosthetic heart valve durability by preserving the collagen fiber architecture of the native tissue, and thereby native mechanical properties. It was not known if the native mechanical properties were stable during long-term valve operation and thus provided additional durability. They examined the biaxial mechanical properties of porcine BHV fixed at 0 and 4mmHg transvalvular pressure following 0, 1x10^6, 50x10^6, and 200x10^6 in vitro accelerated test cycles. Their observations suggested that the collagen fiber architecture of the 0-mmHg-fixed porcine BHV, although locked in place by chemical fixation, may not be maintained over a sufficient number of cycles to be clinically beneficial. Their study further underscores that chemically treated collagen fibers could undergo conformational changes under long-term cyclic loading not associated with damage.

Dokos et al [30] examined the shear properties of passive ventricular myocardium in six pig hearts. Samples (3x3x3 mm) were cut from adjacent regions of the lateral left ventricular midwall, with sides aligned with the principal material axes. Four cycles of sinusoidal simple shear (maximum shear displacements of 0.1–0.5) were applied separately to each specimen in two orthogonal directions. Resulting forces along the three axes were measured. Three specimens from each heart were tested in different
orientations to cover all six modes of simple shear deformation. Passive myocardium had nonlinear visco-elastic shear properties with reproducible, directionally dependent softening, as strain was increased. Shear properties were clearly anisotropic with respect to the three principal material directions: passive ventricular myocardium was least resistant to simple shear displacements imposed in the plane of the myocardial layers and most resistant to shear deformations that produce extension of the myocyte axis. Comparison of results for the six different shear modes suggested that simple shear deformation was resisted by elastic elements aligned with the microstructural axes of the tissue.

Boerboom et al [15] [31] presented a finite element model of the aortic valve and simulated the effect of collagen remodeling on the mechanical properties of the valve. Collagen remodeling was assumed to be the net result of collagen synthesis and degradation. Limited number of fibers with low initial fiber volume fraction was defined and depending on the loading condition the fibers were either synthesized or degraded. The synthesis and degradation of collagen fibers were both assumed to be functions of individual fiber stretch and fiber volume fraction. Simulations for closed and open configurations were performed and results revealed that the predicted fiber directions for the closed configurations were close to the fiber directions as measured in the native aortic valve.

Utilization of biologically-derived biomaterials in bioprosthetic heart valves required robust constitutive models to predict the mechanical behavior under generalized loading states. Thus, it was necessary to perform rigorous experimentation involving all
functional deformations to obtain both the form and material constants of a strain-energy density function. Sun et al [32] generated a comprehensive experimental biaxial mechanical dataset that included high in-plane shear stresses using glutaraldehyde treated bovine pericardium (GLBP) as the representative BHV biomaterial. To develop an appropriate constitutive model, we utilized an interpolation technique for the pseudo-elastic response to guide modification of the final model form. An eight parameter modified Fung model utilizing additional quartic terms was developed, which fitted the complete dataset well. Model parameters were also constrained to satisfy physical plausibility of the strain energy function. The results of this study underscore the limited predictive ability of current soft tissue models, and the need to collect experimental data for soft tissue simulations over the complete functional range.

Howard et al [16] used an explicit finite element code to study the opening mechanism of aortic valve and examine the time varying displacements of the structure subjected to pressure distributions, which included left ventricular, aortic and thoracic pressures. It was shown that the leaflets of the valve open by a combination of root expansion in a radial direction and leaflet movement in the direction of the blood flow. This was compared to a model in which the aortic root was stiffened significantly, and it was found that this modified valve opened by leaflet folding to give a much smaller orifice. These observations concerning the importance of root expansion were in agreement with earlier experimental observations.

A modified discrete dynamic contour deformable model was implemented by Qui et al [33] to detect the layer boundaries. High-frequency ultrasound techniques were
described for estimating the dimensions of the fibrosa, spongiosa, and ventricularis layers in aortic valve cusp specimens. Top hat and bottom hat transformations are applied to enhance the contrast of the layers in B-mode images. Algorithm was demonstrated via measurements of osmotic swelling of the valve cusp layers produced by submerging the specimens in distilled water. The long-term motivation for this study was to develop a system that can be used to monitor and optimize the preparation of bioprosthetic valves in a manner analogous to the use of ultrasonic nondestructive evaluation in manufacturing industries.

Sripathi et al [17] gave further insights into normal aortic valve function, finding fundamental differences in opening and closing mechanism of a normal aortic valve and a valve with stiff root, using dynamic finite element model with time varying pressure. Shell elements with linear elastic properties for the leaflet and root were used. Results show that a compliant aortic root contributes substantially to the smooth and symmetrical leaflet opening with minimal gradients. In contrast, the leaflet opening inside a stiff root was delayed, asymmetric and wrinkled. However, this wrinkling was not associated with increased leaflet stresses. In compliant roots, the effective valve orifice area could substantially increase because of increased root pressure and transvalvular gradients. In stiff roots this effect is strikingly absent. A compliant aortic root contributes substantially to smooth and symmetrical leaflet opening with minimal gradients. The compliance also contributes much to the ability of the normal aortic valve to increase its effective valve orifice in response to physiologic demands of exercise.
Hart et al [34] investigated the effect of collagen fibers on the mechanics and hemodynamics of a trileaflet aortic valve contained in a rigid aortic root in the systolic phase and demonstrated that collagen fibers reduce stresses substantially in the leaflets both in systolic as well as diastolic phase. Results revealed that collagen reinforcement reduces the fluttering motion (observed in isotropic leaflets) of the leaflets and provide smoother opening and closing.

The ease and robustness with which simulation models can be generated have opened the door to the generation of subject specific models, which can be used to explore a wide range of problems from impacts to the body through vascular flows. Novel techniques have been developed to convert 3D image data, obtained from a range of imaging modalities (MRI, CT, Ultrasound, confocal microscopy), automatically into numerical meshes suitable for Finite Element (FE) and Computational Fluid Dynamic (CFD) analysis. A number of case studies have been carried out in order to test the algorithms developed but these case studies have also been chosen to illustrate unique features of the proposed approach at different stages of the processing pipeline from image to model. The steps involved in the generation and processing of finite element models based on medical imaging data are (1)Scan and image processing, (2)Finite element model generation and (3)Export to FE software.

Ranga et al [35] developed a numerical model of the aortic valve, to validate it with in-vivo data and to computationally evaluate the effect of two types of aortic valve-sparing reconstructions on valve dynamics and hemodynamics. A model of the native aortic valve and two models of the valve after surgical were created. These models were
transferred to finite element analysis software where the interaction between valve structures and blood was taken into account in a dynamic manner. Leaflet and blood dynamics, as well as tissue compliance and stresses were evaluated. Leaflet dynamics and blood velocities were also assessed by magnetic resonance imaging in 15 healthy volunteers. Differences in valve dynamics after surgical reconstruction reported in this computational study, match trends previously reported in other in-vivo studies. Computational results in the native valve model correlated closely with the in-vivo imaging data. Numerical models can serve as increasingly sophisticated tools in the study of aortic valve pathologies and in the optimization of new surgical reconstruction techniques.

As it was not possible to experimentally evaluate the effects of different biaxial test boundary conditions on specimen internal stress distributions, Sun et al [36] conducted numerical simulations to explore these effects. A nonlinear Fung-elastic constitutive model, which fully incorporated the effects of in-plane shear, was used to simulate soft tissue mechanical behavior. Effects of boundary conditions, including varying the number of suture attachments, different gripping methods, specimen shapes, and material axes orientations were examined. Results demonstrated strong boundary effects with the clamped methods, while suture attachment methods demonstrated minimal boundary effects. Suture-based methods appeared to be best suited for biaxial mechanical tests of biological materials. Moreover, the simulations demonstrated that Saint-Venant’s effects depended significantly on the material axes orientation.
The dimensions of the aortic valve components, condition its ability to prevent blood from flowing back into the heart. While the theoretical parameters for best trileaflet valve performance have already been established, an effective approach to describe other less optimal, but functional models has been lacking. Labrosse et al [37] established a method to determine by how much the dimensions of the aortic valve components can vary while still maintaining proper function. Measurements were made on silicone rubber casts of human aortic valves to document the range of dimensional variability encountered in normal adult valves. Analytical equations were written to describe a fully three-dimensional geometric model of a trileaflet valve in both the open and closed positions. A complete set of analytical, numerical and graphical tools was developed to explore a range of component dimensions within functional aortic valves. A list of geometric guidelines was established to ensure safe operation of the valve during the cardiac cycle, with practical safety margins. The geometry-based model presented here, allows determining quickly, if a certain set of valve component dimensions results in a functional valve. This is of great interest to designers of new prosthetic heart valve models, as well as to surgeons involved in valve-sparing surgery.

Replacement of diseased natural heart valves with prosthetic devices has dramatically extended the quality and length of the lives of millions of patients worldwide for over 40 years. Bioprosthetic heart valves (BHV) continued to fail due to structural failure resulting from poor tissue durability and faulty design. An in-depth understanding of the biomechanical behavior of BHV at both the tissue and functional prosthesis levels was essential to improve BHV design and to reduce rates of failure. Sun
et al [38] simulated quasi-static BHV leaflet deformation under 40, 80, and 120 mm Hg quasi-static transvalvular pressures. A Fung-elastic material model was used that incorporated material parameters and axes derived from actual leaflet biaxial tests and measured leaflet collagen fiber structure. Rigorous experimental validation of predicted leaflet strain field was used to validate the model results. An overall maximum discrepancy of 2.36% strain between the finite element (FE) results and experimental measurements was obtained, indicating good agreement between computed and measured major principal strains. Results obtained suggested that the utilization of actual leaflet material properties was essential for accurate BHV FE simulations.

Electrospun poly (ester urethane) ureas (ES-PEUU) are elastomeric and allow for the control of fiber diameter, porosity, and degradation rate. ES-PEUU scaffolds can be fabricated to have a well-aligned fiber network, which is important for applications involving mechanically anisotropic soft tissues. Tissue engineered constructs must exhibit tissue-like functional properties, including mechanical behavior comparable to the native tissues intended to be replaced. The ability to reversibly undergo large strains can help to promote and guide tissue growth. Courtney et al [39] developed ES-PEUU scaffolds under variable speed conditions and modeled the effects of fiber orientation on the macro-mechanical properties of the scaffold. To illustrate the ability to simulate native tissue mechanical behavior, a high velocity spun scaffolds exhibiting highly anisotropic mechanical properties closely resembling the native pulmonary heart valve leaflet was demonstrated. The use of the present fiber-level structural constitutive model
allows for determination of electro-spinning conditions to tailor ES-PEUU scaffolds for specific soft tissue applications.

Ranga et al [40] integrated three key physiologically important features into a realistic structural simulation of the aortic valve: (1) compliance of the aortic root wall, (2) non-linear material properties of the tissues, and (3) dynamic loading. Compliance of the root dramatically changed the opening and closing shape and dynamics of the leaflets, altering the diastolic and systolic geometries and helped reduce stresses in the valve. Their models provided an increasingly accurate tool in investigating valve pathologies, device design and modeling robot-tissue interaction in assisted surgery.

Kim et al [19] developed a finite shell element model in order to achieve a more realistic and accurate computational simulation of native and bioprosthetic heart valve dynamics. Experimentally derived and uncoupled in-plane and bending behaviors were implemented into a fully nonlinear stress resultant shell element. Validation studies compared the planar biaxial extension and three-point bending simulations to the experimental data and demonstrated excellent fidelity. Dynamic simulations of a pericardial bioprosthetic heart valve with the developed shell element model showed significant differences in the deformation characteristics, compared to the simulation with an assumed isotropic bending model. The new finite shell element model developed, also incorporated various types of constitutive models and is expected to help in understanding the complex dynamics of native and bioprosthetic heart valve function in physiological and pathological conditions.
Mathematical models provide valuable information to assess and evaluate the mechanical behavior of tissue-engineered constructs. Driessen et al [41] applied a structural based model to describe and analyze the mechanics of tissue-engineered human heart valve leaflets. Results from two orthogonal uniaxial tensile tests were used to determine the model parameters of the constructs after two, three and four weeks of culturing. Subsequently, finite element analyses were performed to simulate the mechanical response of the engineered leaflets to a pressure load. The stresses in the leaflets induced by the pressure load increased monotonically with culture time due to a decrease in the construct’s thickness. The strains, on the other hand, eventually decreased as a result of an increase in the elastic modulus. When compared to native porcine leaflets, the mechanical response of the engineered tissues after four weeks of culturing was more linear, stiffer and less anisotropic.

Current treatments continue to be challenged, to consistently restore aortic valve function for extended durations despite continued progress in the treatment of aortic valve disease. Improved approaches for aortic valve repair and replacement rests upon the ability to more fully comprehend and simulate aortic valve function. While the elastic behavior of the aortic valve leaflet has been previously investigated, time-dependent behaviors under physiological biaxial loading states have yet to be quantified. Stella et al [42] performed strain rate, creep, and stress-relaxation experiments using porcine aortic valve leaflet under planar biaxial stretch and loaded to physiological levels (60N/m equi-biaxial tension), with strain rates ranging from quasi-static to physiologic. The resulting stress–strain responses were found to be independent of strain rate, as previously
observed low level of hysteresis (~17%). Stress relaxation and creep results indicated that while the aortic valve leaflet exhibited significant stress relaxation, it exhibited negligible creep over the 3 h test duration. Results appear to be unique to valvular tissues, and indicate an ability to withstand loading without time-dependent effects under physiologic loading conditions. The mechanisms underlying this quasi-elastic behavior may be attributed to inter-fibrillar structures unique to valvular tissues. These mechanisms are an important functional aspect of native valvular tissues, and are likely critical to improve our understanding of valvular disease and help guide the development of valvular tissue engineering and surgical repair.

Weinberg et al [18] created a set of multi-scale simulations to examine the dynamic behavior of the human aortic valve at the cell, tissue and organ length scales. Each model is fully three-dimensional and includes appropriate nonlinear, anisotropic material models. The organ-scale model is a dynamic fluid-structure interaction that predicts the motion of the blood, cusps, and aortic root throughout the full cycle of opening and closing. The tissue-scale model simulates the behavior of the aortic valve cusp tissue including the sub-millimeter features of multiple layers and undulated geometry. The cell-scale model predicts cellular deformations of individual cells within the cusps. Each simulation is verified against experimental data. The three simulations linked deformations from the organ-scale model are applied as boundary conditions to the tissue scale model, and the same is done between the tissue and cell scales. This set of simulations was a major advance in the study of the aortic valve as it allowed analysis of
transient, three-dimensional behavior of the aortic valve over the range of length scales from cell to organ.

The aortic valve commonly has three cusps and three sinuses. In 1–2% of the population, however, the aortic valve has two cusps, a condition known as a bicuspid aortic valve (BAV). Patients with bicuspid aortic valve (BAV) are more likely to develop a calcific aortic stenosis (CAS), as well as a number of other ailments, as compared to their cohorts with normal tricuspid aortic valves (TAV). It is currently unknown whether the increase in risk of CAS is caused by the geometric differences between the tricuspid and bicuspid valves or whether the increase in risk is caused by the same underlying factors that produce the geometric difference. Weinberg et al [43] employed multiscale finite-element simulations of the valves, isolating the effect of one geometric factor i.e., the number of cusps, in order to explore its effect on multiscale valve mechanics, particularly in relation to CAS. The BAV and TAV were modeled by a set of simulations describing the cell, tissue, and organ length scales. These simulations were linked across the length scales to create a coherent multiscale model. At each scale, the models were three-dimensional, dynamic, and incorporate accurate nonlinear constitutive models of the valve leaflet tissue. Comparing results between the TAV and BAV at each length scale, at the cell-scale, the region of interest was located where calcification developed; near the aortic-facing surface of the leaflet. Simulations showed the observed differences between the tricuspid and bicuspid valves at the organ scale. The bicuspid valve showed greater flexure in the solid phase and stronger jet formation in the fluid phase relative to the tricuspid. At the cell-scale, however, the region of interest was shielded against strain
by the wrinkling of the fibrosa. Thus, the cellular deformations were not significantly
different between the TAV and BAV in the calcification-prone region. Thus result
supports the assertion that the difference in calcification observed in the BAV versus
TAV may be due, primarily to factors other than the simple geometric difference between
the two valves.

Advances in numerical modeling and in a range of disciplines within
experimental biomechanics, recent models of the heart valves have become increasingly
comprehensive and accurate. Weinberg et al [44] in his work on the multi-scale modeling
of heart valve biomechanics in health and disease first reviewed the fundamentals of
native heart valve physiology, composition and mechanics and then furnished an
overview of the development of theoretical and experimental methods in modeling heart
valve biomechanics over the past three decades, emphasizing the necessity of using
multi-scale modeling approaches in order to provide a comprehensive description of heart
valve biomechanics, which enables to capture general heart valve behavior offering an
outlook for the future of valve multi-scale modeling.
CHAPTER-III
THEORY

The three classes of material models i.e., (i) a model class for large-strain inelastic elastomers (TPV); (ii) a highly anisotropic model for modeling native and treated heart aortic valve tissues, and (iii) a material model capturing softening (due to stiffness degradation and strength reductions) for damage/failure mode localization studies are developed by Saleeb and co workers. Further details of these models can be found in [45], [46], [47], [48], [49], [50] & [51]. Here the outline of one of the anisotropic hyper-elastic visco-elastic plastic damage model developed by Saleeb et al is discussed. In the following chapter we will give a brief overview of the proposed model. The basis of the model is developing governing evolution equations and selecting a set of internal state parameters to handle “nonlinear viscous effects”, “permanent deformation and plastic effects” & “softening and hysteresis effects”. We avoid unnecessary complications for indeterminate multiplicative decomposition in terms of viscous and plastic components (e.g. $F = F_e F_p$). Using only Deformation Gradient at start and end of a time step communicated by global FE code (ABAQUS), with due consideration of the delicate incompressibility constraint. Below is a flow chart describing the model.
In summary, the model outlined above introduces the following material parameters. First, the bulk modulus, $K$ followed by $a_n$ and $\alpha_n$ for a total of $n = 1 \rightarrow N$ hyperelastic terms and $r^{(r)}$ and $\rho^{(r)}$ for $r = 1 \rightarrow m$ viscoelastic mechanisms. For each $\beta = 1 \rightarrow n$ fiber bundles, $c_1^{(\beta)}$ and $c_2^{(\beta)}$ fiber stiffness parameters and $r_{(\beta)}^{(r)}$ and $\rho_{(\beta)}^{(r)}$ for $r = 1 \rightarrow m$ viscoelastic mechanisms. The plastic component of the model requires the material parameters; $\kappa_f$, $n$, $r_P$, $\rho_P$, $\kappa_a$, $H$, $\beta$, $H_r$, $a_P$ and $\alpha_P$. For the damage component, we have; $H_1, H_2, e$ and $b_1, b_2, b_3$. Fig 3.1 represents the model.
CHAPTER IV
DEVELOPMENT OF MODEL GEOMETRY

4.1 Description of model geometry

The mechanical nature of the function of the aortic valve has directed the attention of the anatomists to the study of shape and dimensions of the valve leaflets and to the analysis of the structure and arrangement of the valvular connective tissue components. Detailed information on the dimensions of the valve leaflets of different mammals in relaxed and stressed conditions can be found in the literature. In a computational model of the aortic valve, a number of factors influence the compliance of the valve. They include geometry of the valve, applied loads, boundary conditions, thicknesses of tissues, and material properties. Each must be accurately prescribed in order to achieve reliable, physiologically acceptable results.

Various dimensions of the aortic valve have been measured using different techniques in several mammalian species. The approaches have included measurements of excised hearts, of silicone rubber casts of the valve, and of a functioning valve in vivo. Although the leaflets and sinus wall are not often identical, they are similar enough to permit a general description of a valve having tri-leaflet symmetry (Fig 4.2).

The computer model developed by Thubrikar [52] for the open and closed valve was fully described by only five design parameters: \( R_b, R_c, H, H_s \) and \( \beta \) shown in Fig 4.1.
Fig 4.1 Schematic drawing of the aortic valve showing the design parameters

Fig 4.2 Drawing of a single leaflet, FE—Free edge, C—Line of coaptation, A—Line of attachment, R—redundant (coaptation) surface, L—load-bearing surface, CD—Circumferential direction, RD—Radial direction
This geometric model of the aortic valve was based on characteristics of the valve which would result in optimal functioning. A comparison between the developed optimal valve and the natural aortic valve (notably with Swanson’s studies on excised human valves [53]) indicated that they had similar design parameters. Clearly then, the design of the natural aortic valve is based upon the principles of optimum functioning performance. In line with these conclusions and with the use of Thubrikar’s model by two other finite element analysis studies of the aortic valve, it was decided that the given relationships would be used alternatively, to develop our own models.

4.2 Import and meshing of the geometrical models:

Thus for initial construction [52], our model was constructed with $R_b=10 \text{ mm}$, $R_c=8.3 \text{ mm}$, $H=11.7 \text{ mm}$, $H_s=2.8 \text{ mm}$, and $\beta=5.6^0$ using sketch module in ABAQUS. The model was approximated for our current study by removing the stent portion and then meshed using 1248 linear hexahedral elements of type C3D8H. While it is known that the leaflets have variable thickness, for the simplified models in this work, a thickness of 0.4 mm is assigned to the leaflet elements, these values being within the range of average physiological dimensions.

4.3 Cardiac cycle:

It is important that the function of cardiac anatomy is well understood. Cardiac contraction is initiated by action potentials that are generated by sinal atrial node which is located in the upper posterior wall of right atrium. The depolarization of these cells cause a wave of electrical activity that sweep across the atrium and then down into the
ventricles. This electrical activity causes the muscle cells themselves to depolarize which then initiates contraction. Tissues to undergo depolarization are found in the right and left atrial muscle. So these muscles will contract first within these two chambers. Following a brief time delay, the ventricular muscle itself will undergo contraction. There are two basic phases of the cardiac cycle “Systole” and “Diastole” as shown in Fig 4.3. Systole begins with the actual contraction of the ventricular muscles and shortly after the muscles begins to contract; the ventricles will then be able to eject the blood into the outflow tracks. Towards the end of the phase of contraction and ejection i.e., towards the end of systole, some of these muscles will undergo relaxation and lose the ability to generate force. Once the ejection ceases, the second general phase of the cardiac cycle called diastole, which is the longer of the two phases at normal heart rates. So diastole is initiated with relaxation and once the ventricles relax sufficiently they will then begin to fill with blood from the atrial chambers.

4.4 Orientation, loading and boundary conditions:

Local axes of each element of the leaflet were arranged such that 2-axis of the element is aligned with the circumferential direction of the leaflet and 3-axis is aligned with the radial direction (Fig 4.7). 10 fiber groups were defined accordingly following the Gaussian distribution [3] (Table 4.1). Fully constrained boundary conditions were applied on the surface of attachment of leaflet-stent and inner nodes of the commissures as shown in Fig 4.4 & Fig 4.5. The pressure difference between the aortic and left ventricular pressure (also known as the pressure gradient across the valve) was applied on the leaflets. The initial state of the model in the open configuration was assumed to be stress-
free and loads were gradually applied on this model. One full cardiac cycle was simulated, for a total simulation time of 0.76 seconds shown in Fig 4.6.

Fig 4.3 Profile showing two basic phases of cardiac cycle “Systole” & “Diastole”
AP- Aortic Pressure ; LVP- Left Ventricular Pressure
LV Vol- Left Ventricle Volume; S1,S2,S3&S4- Heart beats
Fig 4.4 Aortic valve model constructed showing boundary conditions and mesh

Fig 4.5 Aortic valve model approximated for our present study showing leaflets only
Fig 4.6 Profile of the pressure difference (MPa) applied on the leaflets for one complete cardiac cycle.

Fig 4.7 One-third of the tri-leaflet valve showing the spatial distribution of local axes for fiber bundles, oriented such that 2-axis is along the C direction and 3-axis is along the R direction.
Table 4.1: Material Parameters:

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Hyperelastic Mechanism (2)

$a_i$'s & $k$ are in MPa.

$\alpha_i$'s & $m$ are non-dimensional

(i) for deviatoric response

(ii) for the hydrostatic / volumetric response.

10 Fiber groups

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5.1 Introduction - Inherent Anisotropic Behavior of Tissues

The material properties exhibited by proteins, cells, tissues, organs and organisms vary over a wide range of incredible spectrum. The biomechanical behavior of the biological cells and tissues is complex and highly nonlinear. The soft tissues exhibit similar characteristic behaviors due to the long-chain, cross-linked polymeric structure of both classes of materials. Most soft tissues exhibit a highly nonlinear, inelastic, heterogeneous and anisotropic behavior. For example tendons and ligaments exhibit transverse isotropy, arteries exhibit cylindrical orthotropy and planar tissues such as skin and pericardium exhibit complex symmetries. To add to the complexities involved, the tissue behavior varies from individual to individual and from time to time. The basic postulates of mechanics such as conservation of mass, momentum and energy are well respected by soft tissues. In summary, tissues exhibit a very complex characteristic behavior. The phenomenological descriptors of the behaviors which are often motivated by only a limited knowledge of the underlying structure are continuing to be relied upon due to the complexity involved in both the microstructure and ultra structure of these materials. In the literature we find more models which have constitutive relations that are
described for the specific conditions of interest rather than the whole material itself. The complexities of the biomechanical behavior of the tissues need to have good classes of experiments which involve all relevant deformations necessary to describe the behavior. The fibers comprising the biological tissues exhibit finite nonlinear stress-strain responses and undergo large strains and rotations, which makes the mechanical behavior highly complex. The careful experimental evaluation and formulation of a good constitutive model makes it inevitable to account for the above aspects of behaviors.

5.2 Numerical Simulation

5.2.1 Uniaxial and Biaxial Extension

To demonstrate the numerical performance of the current model, simulations of selected geometric and load configurations are presented here. The most comprehensive multiaxial test data to date is that given by Billiar and Sacks [3] (2000) which presents data for the Aortic Valve Cusp (treated tissue) for a number of test protocols. Similar test data for fresh tissue was obtained and consisted of seven biaxial test protocols. A 5x5x1 3-dimensional mesh was constructed to model the tissue specimen. Seven biaxial load cases (various Circumferential vs. Radial (C:R) ratios were used for the biaxial membrane stress controlled protocols: 10:60, 30:60, 45:60, 60:60, 60:45, 60:30 and 60:2.5 (N/m)). ABAQUS was utilized in conjunction with optimization routines to determine the material parameters as show in Fig 5.1 (details in [54]). Note, the fiber bundle orientations were determined a priori based upon a Gaussian distribution as
proposed by Billiar and Sacks [3] (2000). Specifically, six different fiber orientations were used to effectively represent the distribution of the fiber bundles (shown in Fig5.2). Also note, usually one of the directions is reinforced by more fibers than the other and will be referred to as the “circumferential” (stronger) direction with the perpendicular direction the “radial” (weaker) direction.

The results of this characterization are shown in Fig 5.3 & Fig 5.4 with the resulting material parameters based on these seven protocols given in Table 5.1 and Table 5.2. Note test protocol 7 produces a compressive strain in the circumferential direction even though a tensile membrane stress was imposed. Such unique behavior demonstrates the effects of the highly anisotropic character present in biological tissues.

![Characterization Procedure Diagram](image-url)
Fig 5.2 Gaussian distribution of Fibers
Table 5.1  Material parameters for characterized Fresh Aortic Valve Cusp for Biaxial Test Data of Billiar and Sacks

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Fig 5.3 Aortic Valve Cusp – native (fresh) tissue characterization
Circumferential:Radial Membrane Stress = C:R

Fig 5.4 Aortic Valve Cusp – native (treated) tissue characterization
Circumferential:Radial Membrane Stress = C:R
Table 5.2 Material parameters for characterized Treated Aortic Valve Cusp for Biaxial Test Data of Billiar and Sacks

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In the above, due to the fiber distribution chosen, the material is symmetric. Thus for demonstration purposes, we have chosen examples in which the material is unsymmetric and consists of fibers aligned in different orientations.

5.2.2 Simple Shear – validating experimental results from Dokos et al

Ventricular myocardium has a laminar structure characterized at any point by identifying axes aligned 1) with the myocyte direction 2) transverse to the myocyte axis within a layer, and 3) normal to the layer (as shown in Fig 5.1). Shear deformation or relative sliding of myocardial layers play an important role in the mechanical function of the heart.

Fig 5.5 Schematic represents transmural base-apex segment cut from lateral left ventricular (LV) free wall.
Shear testing was performed under quasi-static conditions as shown in Fig 5.7a. Sinusoidal tests were carried out first. Four cycles of sinusoidal (30-s period) displacement were imposed separately in X and Y directions (Fig 5.9a). A succession of tests was carried out in which maximum displacement was increased through 10, 20, 30, and 40–50% of specimen thickness (Fig 5.10a). Relaxation test in NF mode was performed and stress as a function of time (300 sec) for a simple shear displacement step of 0.5 is plotted as shown in Fig 5.8a. All the results obtained (in Fig 5.7b, Fig 5.8b, Fig 5.9b, Fig 5.10b) were in good agreement with the experimental results. Material parameters input for our material model to characterize the experimental data is shown in Table 5.3.

Fig 5.6 Six possible modes of simple shear defined with respect to FSN material coordinates.
Fig 5.7 (a): Relationship between stress and displacement during final cycles of sinusoidal simple shear displacement in all 6 modes.\textsuperscript{1}

Fig 5.7 (b) Relationship between shear stress and displacement during final cycles obtained from ABAQUS

\textsuperscript{1} Change in peak-to-peak stress with increasing maximum shear displacement is greatest for $FN$ and $FS$ modes, least for $NF$ and $NS$ modes, and significantly greater for $SF$ and $SN$ modes than for $NF$ and $NS$ modes. However, there was no difference within these pairs. — Dokos et al
Fig 5.8 (a): Stress as a function of time for a simple shear displacement step of 0.5 in NF mode.

Fig 5.8 (b): Stress as a function of time obtained from ABAQUS for a simple shear displacement step of 0.5.
Fig 5.9 (a) Relationship between stress and displacement during 4 cycles of sinusoidal simple shear displacement in NF mode.

Fig 5.9 (b) Relationship between shear stress and displacement during 4 cycles of sinusoidal simple shear displacement obtained from ABAQUS.
Fig 5.10 (a) Relationship between stress and varying displacement (0.1-0.5) during final cycles of sinusoidal simple shear displacement

Fig 5.10 (b) Relationship between stress and varying displacement (0.1-0.5) during final cycles of sinusoidal simple shear displacement obtained from ABAQUS
Fig 5.11 (a) Plot of downward compressive stress arising due to the shear strain in both directions.

Fig 5.11 (b) Plot of downward compressive stress obtained from ABAQUS arising due to the shear strain in both directions.
Table 5.3: Material Parameters input for our material model

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Viscous Mechanism (8)

\( r_i \)'s are non-dimensional.

\( \rho_i \)'s are in seconds

(i) for fractional stored energy mechanism.

(ii) relaxation times for dissipation mechanism.

Hyperelastic Mechanism (2)

\( a_i \)'s & \( k \) are in MPa.

\( \alpha_i \)'s & \( m \) are non-dimensional

(iii) for deviatoric response

(iv) for the hydrostatic / volumetric response

Visco-Plastic Mechanism (1)
$a_i$’s, $k_l$, $k_b$ & $H$ are in MPa.

$\alpha_i$’s, $R_p$, $n$ & $\beta$ are non-dimensional

$\rho_i$’s are in seconds

(v) inelastic energy-storage contribution

(vi) for visco-plastic potential.

   (vi-a) exponent

   (vi-b) viscosity

   (vi-c) yield threshold

(vii) for the non-linear kinematic hardening mechanism.

   (vii-a) hardening threshold

   (vii-b) hardening modulus

   (vii-c) exponent

5.3 Comparison to observe the effect of Anisotropy:

Two different simulations were run: one with a model incorporating linear material properties (Young’s Modulus $E=15$ MPa, Poisson’s ratio $\nu=0.3$), and the other one with our own material model implemented as user routine (Table 4.1). The most striking aspect of these simulations was the dynamic motion evidenced when the deformed shape was animated as a function of time. A snapshot of the closing sequence of the valve is seen in fig 8, with color contour lines denoting displacement values. A number of variables could be tracked over the simulated cardiac cycles. Of particular interest were displacements, velocities, strains and stresses. These results could be plotted as a function of time for any node.
The displacement at the center of the free edge of the leaflet is plotted for the two simulations and observed that the maximal displacements are seen at peak systole, as expected (Fig 5.15). The reinforced leaflet shows a smooth opening and closing behavior, whereas the non-reinforced leaflet flutters in the main stream during mid-systolic phase which is believed to enhance tissue fatigue and ultimately calcification and/or tearing (see Fig 5.15 in the range between time station 0.5 & 0.7 sec).

Stable velocity profile was observed in the anisotropic case with fiber reinforcement as opposed to sharp increase and decrease in the isotropic case measured at the center of the free edge of the leaflet (Fig 5.15).

Considerable stress reduction was noticed during the systolic phase in anisotropic case as observed in normal aortic valve (in literature), opposed to no significant change in the isotropic case (Fig 5.15).

The successive deformed shapes of the tri-leaflet valve during the simulated cardiac pressure cycle for the anisotropic case are shown in Fig 5.14. Initial similarities (Fig 5.13) were observed between the isotropic(middle row) and anisotropic(bottom row) cases at the beginning of the diastolic phase due to “crimped”(inactive) state of the fibers, thus leaving the isotropic ground substance material to be the only active part of the model. However, for the later part of the cycle, marked differences were observed between these predictions, mainly due to the significant amount of progressing stretches in the fiber in the anisotropic case. Similar opening and closing configurations were observed compared to images (top row) of a normal aortic valve (marked in red in Fig 5.13).
Fig 5.12 Photographs of successive frames of the model aortic valve viewed from the aorta, showing single cardiac cycle at time interval of 1/24 sec.
1- Deformed shapes of a normal human aortic valve.

2- Deformed shapes obtained using **Isotropic** material properties.

3- Deformed shapes obtained using **Anisotropic** material properties.

Fig 5.13 Deformed shapes of the tri-leaflet valve during the simulated cardiac pressure cycle.

\[ t = 0.0 \text{ sec} \]
$t = 0.16 \text{ sec}$

$\frac{d}{d \cdot 3} \cdot \text{Step 3}$

$\frac{d}{d \cdot 3} \cdot \text{Increment 42: Step Time = 0.21 sec}$

$\frac{d}{d \cdot 3} \cdot \text{Deformed Var: U Deformation Scale Factor: +1.000e+00}$

$\frac{d}{d \cdot 3} \cdot t = 0.21 \text{ sec}$
$t = 0.27$ sec

$t = 0.33$ sec
t = 0.34 sec

Step: Step-3
Increment: 00: Step Time = 0.3400
Primary Var: U, Magnitude
Deformed Var: U, Deformation Scale Factor: +1.000e+00

Step: Step-3
Increment: 00: Step Time = 0.3500
Primary Var: U, Magnitude
Deformed Var: U, Deformation Scale Factor: +1.000e+00

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$t = 0.36$ sec

$t = 0.38$ sec
$t = 0.44 \text{ sec}$

$t = 0.58 \text{ sec}$
Fig 5.14 Sequence of dynamic cardiac cycle of the valve (t = 0 to 0.76 sec)
Fig 5.15 Representative time histories for important response components of the tri-leaflet valve.
Restricting our scope to the dynamical motion of the leaflets, we present a computational model for a symmetric tri-leaflet valve under a complete cardiac pressure cycle. To this end, we utilized a highly anisotropic material model for the large deformation behavior of the tissue material, for which an experimental validation was provided. We also present detailed results documenting the effect of material anisotropy on deformations, velocity, and stresses in the leaflets.

Parametric studies on our current basic geometry remain to be done in order to expand and investigate other complex “pathological” cases. As well, the incorporation of fluid-structure coupling into our model along with the contact conditions may yield variations in the dynamics of the valve. This model could be used to evaluate the impact of surgical repairs (morphological modifications of the anatomy). It also has the potential to be used as a virtual tool to the study of tissue interaction of the vascular structures with a surgical tool.

In this work, the development of a compliant hyper-elastic model of the aortic valve undergoing dynamic physiological loading was shown. Comparisons with in-vivo image data showed that the dynamics of the valve were reasonably well captured by this
model. The role of tissue anisotropy was emphasized in enabling us to come closer to our final objective of creating a more realistic model of the tri-leaflet aortic valve.

Prior studies with similar objectives were conducted by Kim et al [19] (2007) where they considered the opening sequence from closed to open state of the leaflets. Their results, (see figure 6 in [19]) during the diastolic phase indicated predicted deformations that were much different from the actual images captured (see 1st row in Fig 8). We believe that this is mainly due to the simpler state of anisotropy considered in their work (they treated the tissue as orthotropic material). In comparison, the higher degree of anisotropy we considered here appears to lead to predictions in more conformity in these actual images.

Indeed, our present conclusions regarding the very advantageous role played by the strong anisotropy of the valve tissue is in complete agreement with results reported by other research groups. In particular, Hart et al [55](2004) studied the systolic phase of the cycle and concluded that stresses were reduced and the motion was stabilized due to the presence of fibers. This is in complete agreement with our findings in section 3.

Finally, on the limitations side, we mention here that our study lacks the treatment of a number of very important aspects; i.e, contact effects, motion of such other parts as the commissures, the base, the aortic annulus, aortic sinuses, change in leaflet length, and fluid-valve interaction. These will be considered in our future work.
REFERENCES


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