The important roles of tissue anisotropy and tissue-to-tissue contact on the
 dynamical behavior of a symmetric tri-leaflet valve during multiple cardiac
 pressure cycles

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A B S T R A C T

Restricting our scope to the dynamical motion of the leaflets, we present a computational model for
a symmetric, tri-leaflet, bioprosthetic heart valve (BHV) at the end of five complete cardiac pressure
cycles, reaching the steady state of deformation during both closing and opening phases. 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. The important findings are: (1) material anisotropy
has significant effect on the valve opening/closing; (2) the asymmetric deformations, especially in
the fully closed configuration, justify the use of cyclic symmetry; (3) adopting the fully-open position as
an initial/reference configuration has the advantage of completely bypassing any complications arising
from the need to assume the size and shape of the contact area in the coaptation regions of the leaflets that
is necessary when the alternative, commonly-used, approach of selecting the fully-closed position is used
as a reference; and (4) with proper treatments for both material anisotropy and tissue-to-tissue contact,
the overall BHV model provide realistic results in conformity with the ex vivo/in vitro experiments.

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1. Introduction

During the life cycle, the aortic valve (AV) stiffens due to
calcification, leading to less opening or less closing. Bioprosthetic heart
valves (BHV) are often used to replace the malfunctioning heart
valve in human body. The dynamic response of AV has been studied
extensively over the past few decades to understand the regions
of extreme stress during a cardiac cycle in order to devise an
alternative to a malfunctioning or degenerated valve [1]. Due to their
special three-layered structure (the fibrosa, the spongiosa, and the
ventricularis), the AV leaflets display highly nonlinear stress–strain
behavior, involving large deformations, and stretch (deformation)–
dependent anisotropy [2]. The anisotropic material property of AV
leaflet has significant effects on its mechanical behavior, as well as
the associate failure mechanisms. Although leaflets are the most
dynamic parts of the AV, the opening and closing behaviors of the
valve is governed by the complex interaction between the valve
leaflet, aortic root, blood flow and blood pressures [3]. However,
due to its intrinsic complex nature, the testing and modeling of the
anisotropic AV remains a continuing challenge to date [2,4–8].

Realistically, the anisotropy found in tissues is due to the pres-
ence of collagen and elastin fibers, and is dependent on the amount
of stretch (deformation); i.e., recall marked differences between the
two extreme states of fully stretched (in which the fibers are the
primary load–carrying members) vs. crimped (where the
fibers become completely inactive). A simple illustration of stretch
(deformation)–dependent anisotropy is shown in Fig. 1, where a
mesh of isotropic wires that have negligible bending stiffness rela-
tive to axial stretch stiffness (Fig. 1a) is subjected to a loading that
is not aligned with any of the member wire direction. The orien-
tation of individual members is the source of anisotropy in this
mesh. After deformation, many of these highly flexible wires (es-
pecially in the interior region away from the support constraints) align
themselves in the direction of loading (Fig. 1b), thus increasing the
load carrying capacity of the wire mesh shown in Fig. 1a. In AV
tissue, depending on the loading condition, the fibers are either
synthesized or degraded (i.e., fiber reorientation/collagen remodel-
ing phenomenon to increase the load carrying capacity) [2], that
in turn alters the degree of anisotropy in the tissue material.

Despite the significance effect of deformation-dependent
anisotropy in tissue deformation, many previous works con-
sidered isotropic, linear/non-linear elastic material property to
define the constitutive behavior of tissue [9–13]. However, some
efforts have been made in order to account for the anisotropic
behavior of tissue materials by means of orthotropic or transverse-
anisotropic, hyperelasticity, which are not capable of capturing the
real deformation-dependent anisotropy that exists in tissue materials [2,5,14–18]. For example, in the work reported by Driessen et al. [19], a tissue material model, comprised of an isotropic elastic material matrix, and collagen fibers (one dimensional material) was presented. The amount and distribution of collagen fibers were determined by a normal probability function and a fiber volume fraction, respectively. Although this model was able to give good quantitative agreement with experiment, it lacked several features of tissue material such as orientation of elastin fibers, viscous (or rate-dependent) behavior of tissues, non-linear response of fibers and matrix, etc. Similarly, Fung-elastic material model is often used to model preconditioned soft tissues (see Refs. [8,15,16,20]), which does not account for fiber orientation and deformation-dependent anisotropies.

On the computational modeling side, typically a reduced finite element (FE) model of heart valve, by utilizing mirror/reflective symmetry, is utilized. This, in turn, discards any possibility of asymmetric deformation during non-linear dynamic analysis [21]. The contact conditions on coaptation surfaces on leaflets have typically been idealized either as boundary conditions [10,20,22,23], or contact between a deformable leaflet and an artificial rigid surface [16,24]. Because of their significant effects on the deformation mechanism of BHVVs, very few studies have been conducted while considering the actual contact between two deformable tissues [8,18,25,26], and fluid–structure interaction (FSI) [1,27,28]. A summary of various efforts in the literature aiming at the computer modeling of the AV can be found in Table 1 of Ref. [24].

In summary, despite the significant efforts, most of the works presented to date lack one or the other of the many aspects involved in the actual physics of the valve dynamics (i.e. isotropic vs. anisotropic material, realistic tissue-to-tissue contact vs. rigid constraints, cyclic/repeated symmetry vs. reflective symmetry, etc.). To this end, there is a clear need to further develop realistic material models accounting for higher degrees of anisotropy beyond the simple orthotropic models. In this work, this latter consideration is emphasized. Also, we provide a more realistic FE modeling approach in order to account for asymmetric deformations, and any ensuing buckling/snap-through phenomenon, and to demonstrate the importance of treating deformable tissue-to-tissue contact in significantly affecting the final deformed shape at the valve closing state.

2. Methods

For convenience, the details of the FE modeling approach are subdivided below into four different parts: (1) the anisotropic tissue material model, (2) geometric modeling of the symmetric tri-leaflet valve, (3) loading, boundary conditions, and tissue-to-tissue contact treatment, and (4) material properties of the tri-leaflet AV. Furthermore, for simplicity, we adopt following definitions for stresses in all the subsequent plots:

\[ \sigma = \frac{p}{A}. \]  

(1)

where, \( p \) is the total force normal to original, undeformed area \( A \).

Similarly, we use a dimensionless quantity, stretch ratio \( \lambda \), as a measure of strain. For a uniaxial fiber of initial length \( L_0 \) and deformed length \( L \), the stretch ratio is defined as,

\[ \lambda = \frac{L}{L_0}. \]  

(2)

Furthermore, the stretch ratio is related to the “so called” true/logarithmic strain, \( \varepsilon \), as,

\[ \varepsilon = \ln(\lambda). \]  

(3)

Note that, a stretch greater than unity signifies tension, whereas that lesser than unity represents compression. Furthermore, when generalizing to the three-dimensional (3D) applications, the engineering stress will be replaced by the first Piola–Kirchoff stress tensor, and the stretch ratio, \( \lambda \), will be replaced by three stretch ratios \( (\lambda_1, \lambda_2, \lambda_3) \) obtained as the square roots of the principle values of the Cauchy–Green deformation, \( C_{ij} \) (see Ref. [29] and Fig. 2).

2.1. The anisotropic tissue material model and its experimental validation

For modeling purposes, we adopted specialized form of a non-linear, highly anisotropic, hyper-elasto-visco-plastic material model developed by Saleeb et al. [30–32]. An outline of the governing equations of the model is shown in Fig. 2. Note, in this figure the second Piola–Kirchoff stress tensor, \( S_{ij} \), is built from various contributions accounting for the ground material as well as the different fibers in the fiber bundles representing the material anisotropy (with \( \theta \) defining the orientation angle for a specific fiber direction). A brief description of this material model is presented in Appendix A.

In addition, with reference to Table 1, the material parameters involved in this mode include: \( \kappa \) and \( \mu \) for the bulk/pressure response part, and sets \( (\alpha_i, \alpha_j) \) for a total of \( i = 1, 2, 3 \) hyperelastic terms governing the deviatoric/shear part of the ground substance response. Furthermore, for each \( j \)th fiber in the fiber bundles representing material anisotropy \( j = 1 \rightarrow 10 \) is used here, \( c_{ij}^{(l)} \) and \( d_{ij}^{(l)} \) are fiber stiffness parameters.

To demonstrate the modeling capability of the current non-linear, anisotropic, tissue constitutive model, we present here comparisons of the model predictions vs. experimental measurements under biaxial test protocols (as reported by Billiar and Sacks [6]) on two different types of porcine AV cusp tissues i.e., fresh (natural) and treated. Note that, in the specialized form of the material model utilized here, all time-dependent phenomena are
discarded due to the lack of sufficient experimental data. The pertinent numerical values of the material constants are listed in Table 1. These tests included seven load protocols on a specimen taken from the center of the belly region. They included the following cases for the various ratios (C:R) between circumferential vs. radial loads (in N/m): 60:2.5 (protocol-1), 60:30, 60:45, 60:60, 45:60, 30:60 and 10:60 (protocol-7).

For the purpose of the above characterization, a 3D mesh (1 × 1 × 1 of C3D8H element) of size 5 × 5 × 0.466 mm was constructed to model the tissue specimen under the seven protocols. ABAQUS was utilized in conjunction with optimization routines (see Fig. 3) to determine the material parameters. The whole parameter estimation scheme is organized in the following steps:

1. In the primal analysis step, a set of FE analyses are performed to simulate the experimental data by using a single 3D continuum element.
2. In the second step, material parameter sensitivity is performed using direct differentiation (i.e., exact expression) approach. This is further used to calculate the multi-objective optimization function (involving “error” functions giving the deviations of the model predicted response relative to the experimental measurements in all test protocols), and associated gradients.
3. In the optimization phase, the material parameters (defined as the design variables) are determined by solving the multi-objective optimization problem using the sequential-quadratic-programming technique.

We refer the reader to Refs. [31,32] for further details of the material parameter estimation scheme. The values of these parameters are listed in Table 1. Note, the fiber bundle orientations were selected a priori, based upon a Gaussian distribution as proposed by Billiar and Sacks [4], and they were subsequently kept constant during optimization. Note also that the direction C is the prevailing anisotropy/strong direction in these tissues.

As can be seen from Figs. 4 and 5, there is indeed a very good correlation between the predictions and experimental measurements. In particular, note the marked differences in responses along the C (strong) & R (weak) directions. Note also that the test Protocol-7 produces a “compressive” strain in the C-direction, even though
Table 1
Material parameters for characterized fresh (native) and treated AV cusp (in MPa).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Fresh tissue</th>
<th>Treated tissue</th>
<th>Parameter</th>
<th>Fresh tissue</th>
<th>Treated tissue</th>
</tr>
</thead>
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<td>500</td>
<td>τh</td>
<td>4</td>
<td>4</td>
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</table>

<table>
<thead>
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<th>Fresh tissue</th>
<th>Treated tissue</th>
<th>Parameter</th>
<th>Fresh tissue</th>
<th>Treated tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>a1</td>
<td>1.25 × 10⁻⁸</td>
<td>6.3 × 10⁻⁵</td>
<td>α1</td>
<td>1.1</td>
<td>1.25</td>
</tr>
<tr>
<td>a2</td>
<td>-1.8 × 10⁻⁹</td>
<td>-1.1 × 10⁻⁴</td>
<td>α2</td>
<td>-1.07</td>
<td>-1.35</td>
</tr>
<tr>
<td>a3</td>
<td>1.53 × 10⁻¹⁰</td>
<td>5.5 × 10⁻⁶</td>
<td>α3</td>
<td>2.62</td>
<td>2.84</td>
</tr>
</tbody>
</table>

Fiber groups

c1,2             | 2.425 × 10⁻⁴| 0.4375       | c1,2      | 2.43 × 10⁻⁴ | 0.4375       |
| c1,3             | 6.54         | 5.46         | c1,4      | 1.46 × 10⁻⁶ | 0.09          |
| c2,3             | 1.46 × 10⁻⁶  | 0.09         | c2,4      | 1.46 × 10⁻⁶ | 0.09          |
| θ1                | 6.56         | 6.56         | θ2        | -6.56        | -6.56         |
| θ3                | 4.3133 × 10⁻⁵| 0.006       | θ4        | -18.72       | -18.72        |
| c1,7             | 3.347 × 10⁻⁶| 8.8 × 10⁻⁵   | c1,8      | 3.347 × 10⁻⁶| 8.8 × 10⁻⁵    |
| c2,2             | 6.54         | 5.46         | c2,4      | 6.54         | 5.46          |
| θ5                | 44.59        | 44.59        | θ6        | -44.59       | -44.59        |
| c1,9             | 3.2 × 10⁻⁸   | 2.95 × 10⁻⁷  | c1,10     | 3.2 × 10⁻⁸   | 2.95 × 10⁻⁷   |
| c2,9             | 6.54         | 5.46         | c2,10     | 6.54         | 5.46          |
| θ7                | 90⁻         | 90⁻          | θ10       | -90⁻         | -90⁻          |

Hyperelastic mechanism (3) & 10 fiber groups.

- a_i’s (i = 1, 2, 3) are in MPa.
- a_i’s (i = 1, 2, 3) and c_i (j = 1 → 10) are non-dimensional.
- c_i and a_i for deviatoric response.
- κ and τh for the hydrostatic/volumetric response.

the corresponding tensile membrane stress was imposed. In all the protocols, as the load intensity increases, the fiber groups reorient to further participate in carrying the load. This fiber group reorientation character is directly linked to the physical remodeling of collagen fiber through synthesis and degradation [2]. Such unique deformation-dependent behavior demonstrates the effect of the complex character of anisotropy in biological tissues.

2.2. Geometric modeling of tri-leaflet, BHV

It is well known that the three leaflets of AV are not identical [1,3,18]. However, the geometric construction of FE model becomes simpler by the assumption of having three identical leaflets. Therefore, all the three leaflets were assumed to be identical in geometry as well as material properties, which also has been the common assumption made by many other researchers [12–16].
The transvalvular pressure during the opening phase of the heart valve is much lesser than that during the closing phase, and its gradient changes greatly in different stages of both diastole and systole phases. There is also experimental evidence that the leaflets spend a much longer period during the cardiac cycle at or near to the closed position, with a much rapid transition from the fully-closed to the fully-open position [33]. In addition, several results from FE simulations indicate that, starting from the fully-closed configuration, the complete opening phase was obtained in only 0.09 s corresponding to a change of 4.4 mmHg (0.533 kPa) in the transvalvular pressure [16]. In view of this, we have elected to use the fully-open position corresponding to a zero transvalvular pressure, and a magnitude of 14.41 kPa (108 mmHg) on both of the AV and LV sides (refer to the details of pressure diagram in Section 2.3). There are two arguments in favor of this selection. Firstly, it is consistent with the recommendation made in Ref. [33] (following the experimental evaluation of the dynamics of the aortic leaflets) to adopt an open configuration as a reference with the least values of stretches in both C and R directions. Secondly, the remaining alternative of choosing the closed configuration as a reference will necessarily face the difficult decision as to what constitute the corresponding coaptation area in that case. Note that many of the reported works in the literature have in fact assumed the initially “fully” closed configuration as their reference state with the least magnitude of transvalvular pressure [11,15,16,20,27,34–36]. However, since this implicitly assumes no initial contact area between the leaflets (i.e., no coaptation), we view this alternative choice as non-physical.

We followed the guidelines provided by Thubrikar [3] to prepare the geometric model of AV (see Fig. 6) in ABAQU [37]. The model was constructed with \( R_L = 9.7 \text{ mm}, R_A = 9.7 \text{ mm}, H = 13.2 \text{ mm}, \) and \( \beta = 0^\circ [17] \). By exploiting the repeated/cyclic symmetry [21], only two half portions of adjacent leaflets were modeled (see Fig. 7) for the dynamic analysis in order to reduce the computational cost. Note that this allows for any asymmetry to develop in deformed shapes of the leaflets. Also, by creating a circular pattern about y-axis, the whole BHV model can be visualized (see Fig. 7c). Since tissue materials show nearly incompressible behavior, the model was meshed with 942 (471 in each of the two half leaflets) hexahedral, hybrid continuum 3D elements (C3D8H [37]) in order to account for the more realistic pressure-load treatment on both the aortic and left ventricular sides. While it is known that the leaflets have variable thickness, a thickness of 0.4 mm (within the range of average physiological dimensions) was assigned to the leaflet elements for this simplified model.

Fig. 4. An experimental validation for an AV cusp – native (fresh) tissue.
2.3. Boundary, constraint, and loading conditions

A rigid stent was assumed in modeling. Therefore, fully restrained boundary conditions were applied on the surface of attachment of leaflet–stent interface (nodes along DFB in Fig. 6). Since, the commissures are connected to sinus wall (flexible), the nodes of leaflets in commissures region (edge EF in Fig. 6) are neither fully fixed nor can move/rotate freely. However, lacking the modeling data for commissures, only the inner nodes along edge EF were completely restrained in order to allow free rotation at the edges of leaflets.

As can be seen in Fig. 7c, there exists a cyclic symmetry pattern (with symmetry angle, \( \phi = 120^\circ \)) in the full valve model. This implies, in our model, that the nodes on AB of one leaflet also represent the nodes on CD of the other leaflet. Therefore, all the nodes on AB and CD were constrained by the following equations (cyclic symmetry condition),

\[
U_{AB}^x \cos \phi + U_{AB}^y \sin \phi - U_{CD}^x = 0,
\]

\[
U_{AB}^y - U_{CD}^x = 0,
\]

\[-U_{AB}^x \sin \phi + U_{AB}^y \cos \phi - U_{CD}^y = 0,
\]
where, the symbol $U$ is the displacement component of the nodes on edges ($AB$ and $CD$ in superscript) along the three coordinate axes ($x, y, z$ in subscript). The above equations are necessary in order to satisfy the cyclic symmetry condition. For more information about cyclic symmetric modeling, we refer readers to the Section 10.9 (Repetitive symmetry) in Ref. [21].

In order to account for the coaptation between leaflets during cardiac cycle, contact interaction capabilities of ABAQUS were utilized. The possible contact regions on each of the leaflets are shown in Fig. 7a (shaded surfaces in purple, and blue). A node-to-surface, finite sliding, master-slave contact formulation was used to simulate the contact between two deformable leaflets. In this problem, there is no preference of one surface to act as master over the other. Therefore, symmetric (double pass) contact pairs were defined to exclude any bias; i.e., purple surface as master (and blue surface as slave) in the first contact pair, and vice versa in the second pair. Furthermore, a constant static frictional coefficient of 0.05 [14] was utilized in all the numerical simulations.

The pressure load on the heart valve is the resultant of the blood flow, which leads to spatial variation of pressure. However, very little information regarding such a spatial variation of pressure is available [22]. The correct modeling of spatial pressure variation would require an analysis of FSI. Therefore, a spatially uniform pressure is typically assumed [11,13–17]. The physiological pressure data provided by Kim et al. [16] was considered (see Fig. 8). Here we elected to apply pressures on each side of valve due to the fact that even in presence of equilibrating pressure (i.e., zero transvalvular pressure) in thickness direction, a nearly incompressible tissue will significantly deform in the other two perpendicular directions. Initially, a uniform pressure on the inner (left ventricular side, LV) and the outer (aortic side, AV) leaflet surface was ramped from 0 to 14.41 kPa (or 108 mmHg, initial reading in the physiological data) in a static analysis (Fig. 7d). Subsequently, the time-varying physiological pressures on LV and AV side (Fig. 8a) were applied during the dynamic analysis phase.

Despite the fact that an unloaded organ is in residual stress state, typically a stress free initial state is assumed. During the static analysis step (when pressure was ramped from 0 to the first reading in the physiological pressure data), non-zero stress and strain states were developed. In order to obtain a steady state solution, the above-described pressure loading scheme (Fig. 8a) was repeated to represent five cardiac cycles, each of duration 0.76 s (corresponding to a heart rate of 79 bpm).

2.4. Material properties

Many of the reported FE simulations for leaflet analysis reported in the literature [11,14,16,17,20] have utilized BHV. For the purpose of the analysis reported here, and in order to enable some quantitative comparisons with other works for the stress magnitudes obtained during the opening and closing of the tri-leaflet valve, we utilized some of the typical stress–strain data for healthy BHV presented in [8,24]. An average response under equi-biaxial tension condition for both the strong (C) and the weak (R) directions was matched (see Table 2 for obtained material parameters) by keeping the same degree of anisotropy in the material model of Section 2.1 (through the use of the same 10 fibers indicated earlier in Table 1, see also Fig. 9). Also, to provide for a comparison between an assumed isotropic vs. anisotropic tissue behavior, we selected an intermediate curve to represent the isotropic case, and represented it by a single-term incompressible Ogden hyperelastic model [37] with stiffness coefficient $\mu = 0.725$ MPa, and exponent, $\alpha = −12.814$; thus maintaining the important stiffening character (Fig. 9) of the tissue behavior.

For the anisotropic material, local material axes system for each of the 3D elements of the leaflet were defined such that the 1-material axis was the same as the outward surface normal of the leaflet. The 2-material axis was aligned with the circumferential direction, and the 3-axis was aligned in the radial direction of the
leaflet. This was achieved through the use of user subroutine UORTENT [37] in conjunction with ABAQUAS.

Two sets of dynamic analyses were conducted utilizing the above two models; i.e., (1) with the isotropic, hyperelastic, Ogden material model (BHV-O), and (2) with the highly-anisotropic, tissue material model implemented as user material (BHV-A). In each case, the mass density was taken as 1100 kg m\(^{-3}\). We also included a small amount of mass proportional damping to represent the viscous effect of the surrounding blood in the valve.

3. Results

Firstly, a mesh convergence analysis was carried out by comparing the isotropic-case results from two meshes; i.e., 2004-element (refined) and the 942-elements (coarse) meshes. The solution obtained from the coarse mesh showed very good agreement with that from the refined mesh. This coarse mesh was, therefore, used in all the remaining analyses for both BHV-O and BHV-A. Note that only results from the fifth cardiac cycle will be discussed here \((t = 0\) s denotes the beginning of the fifth cycle). However, it is important to mention that results from the prior cycles indicated (as expected due to the presence of damping) changes in the deformation/stress response before the attainment of the steady state at the end of fourth cycle.

The most striking aspect of these simulations was the dynamics of opening and closing of valve. When the deformed shape was animated as a function of time, significant differences were observed in the predicted responses of BHV-A vs. BHV-O. A snapshot of the

Table 2

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>Ground substance</td>
<td>100</td>
</tr>
<tr>
<td>(m)</td>
<td>4</td>
</tr>
</tbody>
</table>

\[
\begin{array}{lll}
\hline
\text{Parameter} & \text{Value} & \text{Parameter} & \text{Value} \\
\hline
\alpha_{1,2} & -0.0192 & \alpha_{1,2} & -6.4 \\
\hline
\text{Fiber groups} & \text{Value} & \text{Fiber groups} & \text{Value} \\
\hline
\rho_{1, j = 1 \rightarrow 10} & 0.01 & \rho_{2, j = 1 \rightarrow 10} & 7.5 \\
\rho_{3, j = 1 \rightarrow 10} & \pm 0^\circ, \pm 6.56^\circ, \pm 18.72^\circ, \pm 44.59^\circ, \pm 90^\circ \\
\hline
\end{array}
\]
closing and opening sequence of the valve in the fifth cycle is shown in Fig. 10. For example, BHV-A started closing earlier and reached the completely closed, asymmetric configuration by 0.04 s, as compared to the case of BHV-O, in which the closed configuration was delayed to approximately 0.05 s, continuing to 0.061 s, with completely-symmetric deformation mode. Note, however, that this shape for BHV-O later changed to asymmetric deformation by the end of closing phase. It is interesting to observe that the closed configuration was achieved by both models before reaching half of the maximum magnitude of the transvalvular pressure (see Fig. 8b). The closed configuration was maintained by both leaflets until the beginning of opening phase \((t=0.53\,\text{s})\). Similarly, as was the case during the closing phase discussed above, differences in the opening mechanism were also observed for BHV-O and BHV-A cases. However, both of the models reached fully open configuration rather quickly. Note also that the deformation sequence and deformed shape from the analysis presented here show very good resemblance with the experimental observations (Fig. 11), where the opening of valve competed within 0.02 s (see also Fig. 7 in [28], and Fig. 16 in [38]). It is important to mention that the

<table>
<thead>
<tr>
<th>Table 3</th>
<th>A comparison of opening and closing durations from our FE analysis with the experimental observations (porcine AV). Note that approximate time durations are reported here.</th>
</tr>
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<tbody>
<tr>
<td>FE analysis</td>
<td>Experiment</td>
</tr>
<tr>
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<td>Anisotropic</td>
</tr>
<tr>
<td>Opening</td>
<td>0.025 s</td>
</tr>
<tr>
<td>Closing</td>
<td>0.05 s</td>
</tr>
</tbody>
</table>
AV used in the experiment in Ref. [39] was manufactured using polyurethane (Young’s modulus = 15 MPa) with an average thickness of 0.125 mm, and it was tested in a pulse duplicator. These differences in the material and thickness may explain the difference in the opening duration of valve. Also, similar to the experiment (compare the present Fig. 11b, and Fig. 4f in [33]), inflation in the corners of AV was observed at the onset of opening (t = 0.575 s), while the belly remained sunken. Furthermore, a comparison of AV opening and closing durations from our analysis with that from experiments is provided in Table 3.

In Fig. 12, contours of von-Mises stress, maximum and minimum principal true (logarithmic) strain at t = 0.33 s (fully closed condition) are shown. Once again, marked differences between BHV-O and BHV-A can be seen. This is mainly due to the significant amount of stretches in the fibers in the anisotropic case. Also, similar to the observation by De Hart et al. [1], leaflet stresses/strains are mainly concentrated in the fixation region BFD (Fig. 7a). Furthermore, despite the geometric and material symmetry assumed in modeling the two halves of the leaflets, significant asymmetry is observed in both deformations and stress/strain distribution; thus justifying the need for the repeated/cyclic symmetry treatment that we utilized in Section 2.3. This indicates that the common approach [1,11,27,35,36] of modeling one complete leaflet (implying reflective/mirror symmetry) would have misled the analysis, since this would have precluded any such asymmetries in deformation and strain/stress distributions from developing.

The results in Fig. 13 depict the histories of the stretch ratios in three different elements (as shown in Fig. 7a–c). As observed experimentally [33], the stretch history in radial and circumferential directions followed closely the pressure difference profile (shown in Fig. 8b). The stretch magnitude is found to be highest in the commissure region (Fig. 13b), intermediate in the base region (Fig. 13a), and least in the belly region (Fig. 13c). However, note that the stretch histories shown in Fig. 13a and c are different from those obtained experimentally (Figs. 5a and 6 in Ref. [33]). These differences in stretch histories indicate that the

Fig. 12. Comparison of (a) von-Mises stress (in MPa), (b) maximum principal true (logarithmic) strain, and (c) maximum principal true (logarithmic) strain at t = 0.33 s (fully closed configuration) between the Ogden hyperelastic material model (top) and our anisotropic tissue material model (bottom). Note that the contours are plotted on undeformed geometry for better visualization.

Fig. 13. Time histories of stretch in (a) base region, (b) commissure region, and (c) belly region for the anisotropic model (BHV-A). A sample stretch rate history is shown in (d). Note that the output elements for the base, commissure and belly regions are highlighted in Fig. 7.
response quantities are sensitive towards the boundary conditions and the region of interest. Furthermore, the high amplitude oscillations in stretch rate history (Fig. 13d) clearly demonstrate the highly dynamic nature of the deformations in opening and closing of the valve.

Finally, we show the material axis (C- and R-) directions in BHV-A at two instants of time (\(t = 0.33 \, \text{s}\) and \(t = 0.76 \, \text{s}\) corresponding to completely closed and open configurations, respectively) in Fig. 14. For ease in visualization, the rotating material axes at the two different configurations are projected onto the undeformed configuration. The C-direction fibers undergo significant rotation in closed configuration (Fig. 14a) relative to the open configuration (Fig. 14b) in the regions of high stress (see Fig. 12), whereas the R-direction fibers (Fig. 14c and d) remain mostly unaffected. Furthermore, the C-(strong) axis follow the experimentally observed fiber direction (Fig. 10 in Ref. [2]) leading to more pronounced reorientations in the closed configuration. Also, notice the significant differences in the C- and R-direction fiber orientation in the closed configuration (Fig. 14a and c) relative to that in the open configuration (Fig. 14b and d). This further signifies the presence of stretch-dependent anisotropy present in AV tissues.

4. Discussion

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

Contrary to the limitations on the use of the 3D brick element for BHV model mentioned in Ref. [24], the present study confirms that a 3D continuum element can be successfully utilized for the FE dynamic analysis of AV. An important characteristic of BHV dynamics was the appearance of asymmetric deformations. This was in conformity with the experimental observation [39], as well as some other FE results that involved modeling of complete tri-leaflet valves [13,41]. A possible source for this asymmetry is the buckling/snap-through phenomenon of thin shells that is known to be greatly dependent on the system dynamics [42]. This also suggests that the proper treatment of cyclic symmetry and contact conditions would yield more realistic leaflet deformational behavior, whereas the commonly used reflective/mirror symmetry condition (e.g. see Refs. [1,11,27,35,36,40]) would have prevented such asymmetries from developing. Furthermore, modeling in closed configuration requires the prior knowledge of the shape and the area in contact during coaptation. Therefore, we recommend that the coaptation area and its associated deformational behavior should be obtained as a result of realistic contact conditions imposed between two deformable leaflets. Otherwise, if treated artificially through leaflet-to-rigid surface contact, this may completely change the observed behavior and the patterns of any emerging asymmetries in the stress and strain distributions over different parts of the leaflets.

Considering the comparison of our results with those obtained by other researchers, there are both differences and similarities. For example, in prior studies by Kim et al. [16], where they considered the opening sequence from closed to open state of the leaflets, their results (see Fig. 6 in [16]) during the diastolic phase indicated predicted deformations that were much different from the actual images. In particular, starting form a closed configuration (reference/undeformed) a completely open valve configuration was obtained during the first 0.09 s of the pressure history when there was not much variation in the pressure difference. The change from fully open to fully closed configuration was obtained in duration of 0.11 s. This conflicts with the experimental results provided by Yap et al. [33], where the opening phase and the closing phase lasted for 0.03 s and 0.05 s, respectively. In our FE simulations, the closing phase duration was found to be 0.04 s for the anisotropic model, and 0.05 s for the isotropic model. Similarly, the opening phase was completed in approximately 0.025 s and 0.018 s for anisotropic and isotropic models, respectively. Finally, it is noted that in both BHV-O and BHV-A cases, our deformed shapes, and velocity time histories (not shown here) did not show any indication of flutter phenomenon. This is contrary to some of the observations made by others [1], where more significant flutter was observed in an isotropic tissue model compared to the anisotropic case. This is
mainly due to the stiffening nature of the stress–strain curve used in both BHV-O and BHV-A in the present analysis.

On the other hand, several of our present conclusions regarding the effect of anisotropy of the valve tissue are in agreement with results reported by other research groups. For example, we have noted that high tensile stretch regions (i.e., indicating active fiber directions) are distributed as follows (see Figs. 13 and 14): (1) only in the radial direction in the base region (Fig. 13a); (2) only in the circumferential direction in the commissure region (Fig. 13b); and (3) in both radial and circumferential directions in the belly region (Fig. 13c). This is in direct agreement with the experimental and numerical results provided by Boerboom et al. [2] as to the distribution of the principal fiber directions (compare the present Fig. 14a to the Fig. 10 in Ref. [2]). As mentioned in the introduction, the strong fibers align themselves in the direction of deformation in order to increase the load carrying capacity of the tissue structure (recall the simple wire mesh analogy discussed earlier in Fig. 1). The present anisotropic model is able to capture the different degrees of stretch-dependent anisotropy.

On the limitation side, firstly, we neglected the flexibility of the aortic root, and assumed that the commissure region is “infinitely-flexible-against-rotation”. Modeling of commissures and the aortic root with their respective properties will affect the dynamics of leaflets deformation and associated stress/strain distribution [1]. Secondly, there was total disregard of the effect of the aortic wall and sinuses in our modeling. This omission is likely to affect the dynamics of the leaflets when they are pushed towards the sinuses cavity during mid-systole. Furthermore, we discarded any differences among the three individual leaflets in their geometry, material properties, as well as the spatial variation in the fiber distribution within the individual leaflets. Lastly, a more realistic analysis must involve FSI. Due to the fluid motion, a non-uniform (spatially varying) pressure distribution is typically observed, which is not accounted for in this study.

In conclusion, several points are emphasized in connection with the utilization of proper FE modeling approach for the study of AV dynamics. We have shown that the dynamic response of an isotropic material AV differs significantly with that of anisotropic material AV. However, isotropic material model can still be utilized in a preliminary study to obtain overall deformation characteristics, provided that the isotropic material represents an “average” response in equi-biaxial test. Furthermore, artificial treatment of constraints may obscure any emerging asymmetries in the distribution of field quantities, along with buckling/snap-through phenomenon in BHV dynamics. Additionally, we have also highlighted the importance of tissue-to-tissue contacts in significantly affecting the final deformed shape at the valve closing, and the significant advantages in using the fully open position as the initial/reference configuration.

Finally, parametric studies on our current basic geometry remain to be done in order to expand and investigate other complex “pathological” cases in future studies. This, together with the incorporation of fluid–structure coupling, and the utilization of the developed general tissue model to capture different degrees of specially-varying anisotropies in the different parts of the leaflets, will provide a useful tool in evaluating the impact of surgical repairs (morphological modifications of the anatomy).

**Appendix A.**

In this section, we will briefly describe the proposed anisotropic tissue model. Note that we utilize bold face letters (as well as their counterpart matrix/indexial notation) to denote vectorial and tensorial quantities, and “superscript” letters placed between parentheses as indices to identify sets of internal state parameters. Refer also to Fig. 2 for some computational details of this same tissue model.

The stored strain energy, $W$, is assumed to be decomposed into two components: (1) stored energy in ground substance (matrix), $W_{\text{matrix}}$, and (2) that in tissue fibers, $W_{\text{fiber}}$, i.e.,

$$ W = W_{\text{matrix}} + W_{\text{fiber}}. $$

In most general representation, each part of the decomposed energies ($W_{\text{matrix}}$ and $W_{\text{fiber}}$) are further decomposed into elastic (in terms of deformation tensor components) and inelastic (in terms of internal, stress-like, tensorial variables $q$ and $r$ for the matrix and fibers, respectively):

$$ W_{\text{matrix}} = \bar{W}_{\text{matrix}}(\lambda_i) + W_{\text{matrix}}^p(q'^{1}, q'^{2}, \ldots, q'^{m}), $$

$$ W_{\text{fiber}} = \bar{W}_{\text{fiber}}(d^{(1)}, d^{(2)}, \ldots, d^{(n)}) + W_{\text{fiber}}^p(r^{(1)}, r^{(2)}, \ldots, r^{(m)}). $$

where, $\lambda_i$ are the principal stretches, and $d^{(1)}, d^{(2)}, \ldots, d^{(n)}$ are vectors defining the individual fiber bundles. Note that, the first terms on the right hand side of Eqs. (A.2) and (A.3) are purely elastic contribution, whereas the second term represents the dissipative/inelastic contributions (in case time-dependent phenomena are accounted for; see [30]). However, we discard the inelastic terms in the specialized anisotropic model utilized in this study.

The elastic portion of stored energy in ground substance (matrix) is defined as:

$$ \bar{W}_{\text{matrix}}(\lambda_i) = \sum_{n=1}^{N} a_n \left( \lambda_1^{q_{n}} + \lambda_2^{q_{n}} + \lambda_3^{q_{n}} \right), $$

$$ h^p(j) = k' \left( \langle j^{m+1} \rangle / m + 1 \right), $$

where, $a_n, a_n, k, \text{ and } m$ are material constants.

The second Piola–Kirchhoff stress $\mathbf{S}$ can be obtained from above strain energy function as:

$$ \mathbf{S} = \tilde{\mathbf{S}} + \rho \mathbf{C}^{-1} \sum_{r=1}^{m} \mathbf{Q}^{r}_{\mathbf{C}} + \sum_{p=1}^{n} \mathbf{S}^{(p)} + \sum_{p=1}^{n} \left( \sum_{r=1}^{m} (\beta_p \mathbf{R}^{(r)}_{\mathbf{C}}) \right), $$

where, $\tilde{\mathbf{S}}$ and $\rho \mathbf{C}^{-1}$ represent the “shear” and “pressure” (with $p = \langle dh/|d| \rangle$) decomposed parts of the contribution from isotropic matrix, respectively. The tensor $\mathbf{C}$ is the right Cauchy–Green strain tensor, $j$ is the square root of the determinant of $\mathbf{C}$ (or $\mathbf{C}_p$).

Note that in Eq. (A.6), the general form of the stress tensor is the summation of four parts: the first part is associated with the hyperelastic isotropic matrix, the second term is associated with the ‘m’ time-dependent (viscous) mechanisms for the matrix, the third term is the summation of ‘n’ hyperelastic contributions of each ‘p’ fiber bundle, and finally the fourth term represents the additional stress contribution from ‘m’ different viscous mechanisms associated with each ‘p’ fiber bundle in a group of ‘n’ bundles.

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In the present, purely time-dependent, model, the contribution from fiber bundles is defined as,

$$S_{ij} = \sum_{\beta=1}^{n} \frac{\partial W_{\text{fiber}}}{\partial \epsilon_{ij}} = \sum_{\beta=1}^{n} \delta_{ij} \sigma_{\beta}^{(\beta)} \left[ \frac{J^{-2/3}}{2} \left( \epsilon_{\beta}^{(\beta)} - 1 \right) \right] d_{1}^{(\beta)} d_{1}^{(\beta)}, \quad (A.7)$$

$$S_{ij}^{(\beta)} = \frac{\sigma_{\beta}^{(\beta)}}{C_{i}^{\beta} C_{j}^{\beta}}, \quad \sum_{\beta=1}^{n} C_{i}^{\beta} C_{j}^{\beta} = 1, \quad \sum_{\beta=1}^{n} d_{1}^{(\beta)} = 1, \quad \sum_{\beta=1}^{n} \sigma_{\beta}^{(\beta)} = 1, \quad (A.8)$$

where, the scalar function $J$ is defined as $J = \left( J - 1 \right)$ (the symbol $\leftrightarrow$ is the Macaulay bracket, and the invariant $I = d_{1}^{(\beta)} C_{i}^{\beta} d_{1}^{(\beta)}, (A.9)$

and $S_{ij} = \frac{\partial W_{\text{fiber}}}{\partial \epsilon_{ij}}$, and $\sigma_{\beta}^{(\beta)}$ is the fiber stiffness for each $\beta = 1 \rightarrow n$ fiber bundles, and $d_{1}^{(1)}, d_{2}^{(2)}, \ldots, d_{n}^{(n)}$ are the vectors defining the orientation of the individual fiber bundles. We refer the readers to Refs. [30–32] for details of parameter estimation, and implementation of material model in ABAQUS.

Conflict of interest statement

The authors have no conflict of interest regarding the subject matter of this manuscript.

References