Fundamentele Werktuigkunde

Simulation of the mechanical behavior of the left ventricle

P.H.M. Bovendeerd
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<td>$kg$</td>
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<td>$p$</td>
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<td>$Pa$</td>
<td>parameter in contraction model (2.2.4)</td>
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### Symbols (continued)

- \( t_d \)  
  - parameter in contraction model (2.2.4)

- \( t_o \)  
  - parameter in contraction model (2.2.4)

- \( t_i \)  
  - moment of initiation of activation (4.1.2)

- \( t_r \)  
  - parameter in contraction model (2.2.4)

- \((u_x, u_y, u_z)\)  
  - displacements in Cartesian coordinate system (4.1.1)

- \( V_e \)  
  - \( m^3 \)  
  - volume between epi- and endocardial ellipsoid (2.1.1)

- \( V_i \)  
  - \( m^3 \)  
  - volume within endocardial ellipsoid (2.1.1)

- \( V_v \)  
  - \( m^3 \)  
  - volume of left ventricular cavity (2.1.1)

- \( V_p \)  
  - \( m^3 \)  
  - volume of papillary muscles (2.1.1)

- \( V_w \)  
  - \( m^3 \)  
  - volume of left ventricular wall (2.1.1)

- \( V_0 \)  
  - \( m^3 \)  
  - cavity volume at zero transmural pressure (2.1.1)

- \( v_0 \)  
  - \( m \cdot s^{-1} \)  
  - parameter in contraction model (2.2.4)

- \( v_e \)  
  - \( m \cdot s^{-1} \)  
  - parameter in activation model (2.2.5)

- \( W \)  
  - \( Pa \)  
  - strain-energy function (2.2.2)

- \( X \)  
  - column of positions and pressures (3.2)

- \((x, y, z)\)  
  - \( m, m, m \)  
  - Cartesian coordinates (2.1.2)

- \( Z \)  
  - \( m \)  
  - long axis of ellipsoid (2.1.1)

- \( \alpha \)  
  - shear parameter (3.4.4)

- \( \alpha_1 \)  
  - helix fiber angle (2.1.3)

- \( \alpha_{10}, \alpha_{11} \)  
  - parameters in fiber orientation model (2.1.3)

- \( \alpha_{12, en}, \alpha_{13, ep} \)  
  - parameters in fiber orientation model (2.1.3)

- \( \alpha_3 \)  
  - transverse fiber angle (2.1.3)

- \( \alpha_{31}, \alpha_{32} \)  
  - parameters in fiber orientation model (2.1.3)

- \( \Delta \)  
  - difference

- \( \delta \)  
  - convergence criterion (4.1.2)

- \( \delta \)  
  - error in estimate (3.2)

- \( e \)  
  - convergence criterion

- \( e \)  
  - linear strain

- \( \varepsilon_D \)  
  - linear strain of outer ventricular diameter

- \( \varepsilon_h \)  
  - linear strain of equatorial wall thickness

- \( \varepsilon_L \)  
  - linear strain of outer ventricular length

- \( \theta_A \)  
  - parameter in activation model (2.2.5)

- \( \lambda \)  
  - stretch ratio (3.4)

- \((\xi, \theta, \phi)\)  
  - ellipsoid coordinate system (2.1.2)

- \((\tilde{\xi}, \tilde{\theta})\)  
  - local coordinate system (2.1.2)

- \( \xi \)  
  - parameter in fiber orientation model (2.1.3)

- \( \sigma \)  
  - \( Pa \)  
  - Cauchy stress tensor

- \( \phi \)  
  - interpolation function of pressure field (3.2)

- \( \phi_z \)  
  - angle of rotation around long axis

- \( \psi \)  
  - interpolation function of position field (3.2)

- \( I_{II} \)  
  - first strain invariant (2.2.2)

- \( I_{II} \)  
  - second strain invariant (2.2.2)

- \( I_{III} \)  
  - third strain invariant (2.2.2)

- \( I_E \)  
  - scalar combination of strain components (2.2.2)

- \( I_{II_E} \)  
  - scalar combination of strain components (2.2.2)

- \( \nabla \)  
  - gradient operator

- \( \nabla_0 \)  
  - gradient operator with respect to undeformed situation
### Subscripts

<table>
<thead>
<tr>
<th>Subscript</th>
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<td>$a$</td>
<td>active, arterial, aortic</td>
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<tr>
<td>$bd$</td>
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</tr>
<tr>
<td>$be$</td>
<td>beginning of ejection</td>
</tr>
<tr>
<td>$c$</td>
<td>cross-fiber</td>
</tr>
<tr>
<td>$ed$</td>
<td>end of diastole</td>
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<tr>
<td>$ee$</td>
<td>end of ejection</td>
</tr>
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<td>$en$</td>
<td>endocardial</td>
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<td>$f$</td>
<td>fiber</td>
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<tr>
<td>$i$</td>
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<td>$lv$</td>
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### Superscripts

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<tr>
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<td>$\hat{\cdot}$</td>
<td>estimate</td>
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Notation

\[
\begin{align*}
a & \quad \text{scalar} \\
a & \quad \text{vector} \\
||a|| & \quad \text{length of } a \\
g & \quad \text{column, matrix representation of } a \\
g^T & \quad \text{transposed of } g \\
\mathbf{A} & \quad \text{second order tensor} \\
\mathbf{I} & \quad \text{second order unit tensor} \\
\mathbf{A}^{-1} & \quad \text{inverse of } \mathbf{A} \\
\mathbf{A}^c & \quad \text{conjugate of } \mathbf{A} \\
\mathbf{A}^d & \quad \text{deviatoric part of } \mathbf{A} \\
\det(\mathbf{A}) & \quad \text{determinant of } \mathbf{A} \\
\tr(\mathbf{A}) & \quad \text{trace } \mathbf{A} = \mathbf{A} : \mathbf{I} \\
\mathbf{A} & \quad \text{matrix representation of } \mathbf{A} \\
\mathbf{A}^T & \quad \text{transposed of } \mathbf{A} \\
abla & \quad \text{dyadic product of vectors } a \text{ and } b \\
a \cdot b & \quad \text{dot product of vectors } a \text{ and } b \\
\mathbf{A} \cdot \mathbf{b} & \quad \text{dot product of tensor } \mathbf{A} \text{ and vector } \mathbf{b} \\
\mathbf{A} : \mathbf{B} & \quad \text{dot product of tensors } \mathbf{A} \text{ and } \mathbf{B} \\
\mathbf{A} : \mathbf{B} & \quad \text{tr}(\mathbf{A} \cdot \mathbf{B}) \text{ double dot product of tensors } \mathbf{A} \text{ and } \mathbf{B}
\end{align*}
\]
1

Introduction

1.1 The aim of this study

Investigations on the metabolic, electrophysiological and mechanical behavior of the heart under normal and pathological circumstances are major topics in cardiac research. Studies on the mechanical behavior focus mainly on the left ventricle. Important quantities for the description of the mechanics of the left ventricle are ventricular pressure, aortic pressure and aortic flow. These quantities can be determined experimentally using conventional techniques.

The global mechanical performance of the left ventricle is the result of the cooperative action of the muscle cells in the ventricular wall. To understand the mechanical performance of the ventricle as a whole the mechanical behavior of these muscle cells should be known. The mechanical work generated by the cells depends on the local state of stress, deformation and blood supply. For the measurement of deformation several techniques are available. One-dimensional deformation can be determined by measurement of the length of a segment between ultrasonic transducers [7], strain gauges [11] or inductive coils [2]. Two-dimensional deformation can be determined by triangulation, using ultrasonic transducers [13], inductive coils [19] or optical markers [15,12]. Three-dimensional deformation can be assessed by following of radiopaque markers implanted in the wall [6,20]. Dependent on the spatial resolution of these techniques, an indication of the local state of deformation in the myocardial tissue is obtained. Local myocardial perfusion can be measured with the use of radioactive microspheres [4,9,14]. Measurement of the local wall stresses is more difficult. One component of local wall stress is the pressure in the tissue. This intramyocardial pressure can be measured using a micropipette technique [8,16]. Reliable measurement of other stress components in the ventricular wall [5] is difficult, because insertion of a force transducer damages the tissue [10].

The aim of this study is to develop a mathematical model to investigate the spatial distribution of the stresses in the ventricular wall. The model is based on the mechanical behavior of the individual muscle cells and the connective tissue that surrounds the cells. With the model a cardiac cycle can be simulated. The calculated time course of left ventricular pressure, deformation and aortic flow is compared to experimental data. If the values of the calculated and measured parameters agree sufficiently well, it is expected that the calculated wall stresses approximate the stresses in the real ventricle reasonably well.

1.2 Basic anatomy and physiology of the heart

1.2.1 Basic anatomy

The heart is a muscular organ that pumps blood through the vascular system. It consists of two pumps: the right pump maintaining the pulmonary circulation and the left pump maintaining the systemic circulation. Each pump consists of two cavities, the atrium and the ventricle. The actual pumping force is delivered by the right and left ventricles. The right and left atrium collect the blood returning from the systemic and pulmonary circulation, respectively. From the atria the ventricles are filled. The mitral valve separates the left atrium from the left ventricle.
FIGURE 1.1: Basic anatomy of the left ventricle, showing (a) fiber structure of the left ventricular wall, (b) fibers spiralling into the apical vortex, (c) collagen fibers C connecting adjacent myocytes M and (d) sarcomeres with length $l_s$ consisting of thick myosine filaments M, and thin actine filaments A coupled at the Z-lines.

The right atrium is separated from the right ventricle by the tricuspid valve. These valves are supported by fibrous rings, the annuli fibrosi. A third annulus fibrosus supports the aortic valve, between left ventricle and aorta. The annuli fibrosi are connected together tightly, and form the base of the heart. The fourth cardiac valve, the pulmonary valve (between right ventricle and pulmonary artery), lies outside the base. The heart is connected to the surrounding tissue at the base by the large arteries and veins that enter and leave its chambers. The pericardium, a fibrous sac that surrounds the heart, is also connected to these vessels. The space between the pericardium and the outer surface of the heart, the epicardium, is filled with a thin lubricating layer of pericardial fluid.

The geometry of the left ventricle may be considered as a thick-walled truncated ellipsoid [18]. The relatively thin-walled right ventricle is connected to the subepicardial layers of the left ventricle and covers about half of the surface of the left ventricle. The intraventricular septum is the common wall of the ventricles. Anatomically, it belongs to the left ventricle. The epicardial free wall of the left ventricle is smooth. The endocardial wall is irregular, showing many invaginations protruding into the wall up to about 30% of its thickness. This portion of the wall is called the trabecular layer. Beside these trabeculae, a number of papillary muscles originate from the endocardial wall. These papillary muscles support the leaflets of the mitral valve through fine fibers, the chordae tendinae.

The muscle fibers in the ventricular walls are distributed in an ordered pattern [18,1]. The epicardial fibers of the left ventricle run approximately in the axial direction (figure 1.1a). From the base the epicardial fibers spiral down into the apical vortex (figure 1.1b). They emerge again from this vortex in the endocardial layers in which they spiral towards the base. Near the basal plane the fibers cross over from the endocardial wall to the epicardial wall. In the midwall layers
the fibers are oriented more circumferentially. In the basal part of the heart this circumferential layer is most profound, forming the bulbo-spiral muscle. The layers, described here, are not anatomically distinct: the orientation of the muscle fibers changes smoothly from epicardium to endocardium.

In a closer view the myocardial fibers consist of more or less parallely directed cardiac muscle cells (figure 1.1c). Adjacent myocytes are interconnected by numerous bundles of short collagen fibers ('struts' [3]). It is expected that these struts prevent slipping of adjacent cells in both transverse and lateral direction. The collagen fibers also connect myocytes to capillaries. Small groups of myocytes are surrounded by a complex weave of collagen fibers. This weave is tightly connected to the cells it surrounds. Its connections to other weaves are more loose: they are formed by relatively few long collagen fibers. The weave structure could account for the visco-elastic properties of cardiac tissue [3].

The contractile units, the sarcomeres, are located within the myocytes (figure 1.1d). The sarcomeres consist of a parallel three-dimensional array of actine and myosine filaments. Sarcomeres are coupled in series through the Z-discs. These discs are connected to the cell membrane where they form the insertion places for the collagen struts that connect adjacent myocytes [17]. During contraction the actine filaments slide along the myosine filaments, causing shortening of the sarcomere. The details of the contraction process are not fully understood yet. However, it is clear that the force developed by the sarcomeres depends on the time after depolarization of the cell membrane, the length of the sarcomeres, and their velocity of shortening.

1.2.2 Basic physiology: the left ventricular cycle

In a cardiac cycle four phases can be distinguished: the diastolic phase, the isovolumic contraction phase, the ejection phase and the isovolumic relaxation phase. The description of these phases will be focussed upon the left ventricle.

Late in systole and during diastole the left atrium is passively filled from the pulmonary veins. As soon as the pressure in the relaxing left ventricle drops below left atrial pressure, the mitral valve opens and the ventricle is filled rapidly. Towards the end of the diastolic phase atrial contraction is initiated by a depolarization wave originating from the sinoatrial node. This atrial contraction contributes only to a limited extent of the filling of the ventricle. At the end of atrial contraction the depolarization wave has reached the endocardial apical part of the ventricle through a conducting system, the Purkinje network. From here the depolarization wave spreads across the myocardial wall, initiating contraction of the muscle cells. The increasing active stress is reflected by an increase of ventricular pressure that causes closure of the mitral valve.

This moment marks the beginning of the isovolumic contraction phase. During this phase ventricular volume remains constant because both the mitral valve and the aortic valve are closed. Ventricular pressure rises rapidly and as soon as it rises above aortic pressure the aortic valve opens and the ejection phase begins.

The first part of the ejection phase is marked by a rapid increase of aortic flow. After the flow has reached its maximum, it declines slowly. At the end of this phase aortic flow becomes slightly negative, causing complete closure of the aortic valve.

Now once again ventricular volume remains constant. In this isovolumic relaxation phase ventricular pressure falls because of the relaxation of the muscle cells in the ventricular wall. As soon as ventricular pressure drops below atrial pressure the diastolic phase starts again.
1.3 Outline of this report

The design of the model of the left ventricle, starting from experimental physiological data, is described in chapter 2. Ventricular geometry, fiber orientation and boundary conditions are discussed. Constitutive equations are formulated, that describe the mechanical properties of the myocardial tissue, as observed in experiments on excised specimens.

In chapter 3 the constitutive equations are combined with the laws of conservation of mass, momentum, and moment of momentum. The resulting set of equations is transformed into a numerical formulation using the finite element method. A three-dimensional brickshaped element is developed to describe the deformation of a piece of myocardial tissue.

With these elements the geometry of the left ventricle is modelled in chapter 4. Several simulations of a cardiac cycle are performed to investigate the influence of variations in the input parameters. The numerical results are compared with experimental data, derived from literature.

The report concludes with a general discussion on the validity and possible applications of the model.

References


Design of the model of the left ventricle

2.1 Geometry of the model of the left ventricle

2.1.1 Macroscopic geometry

The simulation of the cardiac cycle starts from a reference state, defined as the situation with zero transmural pressure. In this reference state, stresses and strains are assumed to be zero. Thus, existing residual stresses and strains \([12,23]\) are neglected. The finite element method is capable of taking into account the complex geometry of the left ventricle. Because experimental data on this geometry are not complete, in the model the geometry in the reference state is approximated by a set of nested confocal, truncated ellipsoids of revolution, which describes the major part of the real ventricular geometry reasonably well \([32]\).

The ellipsoidal geometry is defined by only 4 parameters: the volume \(V_e\), enclosed between the endocardial and epicardial ellipsoid, the volume \(V_i\) of the enclosed cavity, the height \(h\) above the equator at which the ellipsoids are truncated and the common focal length of the ellipsoids \(C\). To quantify the volumina \(V_e\) and \(V_i\) from experimental data, additional volumina are defined: the left ventricular wall volume \(V_w\) and cavity volume \(V_v\), and the papillary muscle volume \(V_p\). \(V_w\) represents the total volume of the left ventricular wall. \(V_v\) is the volume of part of the ventricular wall lying within the endocardial ellipsoid, and is associated mainly with the papillary muscles. The blood in the ventricular cavity occupies a volume \(V_v\). The volumina are mutually related according to:

\[
V_e = V_v - V_p \tag{2.1}
\]

\[
V_i = V_v + V_p \tag{2.2}
\]

In figure 2.1 the geometry of the left ventricle, as chosen in the model, is illustrated. The choice of the values of the parameters defining the geometry is based upon data presented in literature. Streeter and Hanna \([32]\) used experimental data on the dimensions of the left ventricle, presented by Ross et al. \([27]\), to approximate the geometry by a set of nested, nonconfocal truncated ellipsoids of revolution. Focal length \(C\) and fractional height \(f = h/Z\) above the equator were calculated in 5 hearts fixed at diastole and 5 hearts fixed at systole, for both the endocardial and epicardial ellipsoid. From these 20 values, the following average values were obtained: \(C = 37.5 \pm 1.0\ mm\) and \(f = h/Z = 0.475 \pm 0.029\). The 10 hearts had a left ventricular wall mass \(m_w = 99.0 \pm 4.3\ g\) and a papillary muscle volume \(V_p = 2.6 \pm 0.6\ ml\).

The cavity volume at zero transmural pressure is called the equilibrium volume \(V_0\). Spotnitz et al. \([30]\) measured an equilibrium volume \(V_0 = 12.5 \pm 0.9\ ml\) and a wall mass \(m_w = 96.4 \pm 2.6\ g\ (n = 27)\). Assuming a tissue density of 1.05 g/ml this yields a ratio \(V_0/V_w = 0.14\). Based upon data collected from several studies described in literature, Nikolić et al. \([22]\) obtained the following values: \(m_w = 90 \pm 27\ g\) and \(V_0/m_w = 0.29\ ml.g^{-1}\, (n = 35)\). From these data a ratio \(V_0/V_w = 0.30\) is calculated. McCulloch et al. \([21]\) measured the following values: \(V_0 = 40 \pm 9\ ml, m_w = 145 \pm 19\ g, (n = 6)\), from which a ratio \(V_0/V_m = 0.29\) results.

In the model a value \(V_w = 140\ ml\) is chosen. Assuming papillary muscle volume to be proportional to wall volume, and using the data presented by Streeter \([32]\), a papillary muscle volume \(V_p = 4\ ml\) is found. Using the data from Nikolić et al. \([22]\) and McCulloch et al. \([21]\), the
FIGURE 2.1: Geometry of the model showing inner and outer short axis $R_i$ and $R_o$, inner, midwall and outer long axis $Z_i$, $Z_m$ and $Z_o$, height above the equator $h$, focal length $C$, volume between endo- and epicardial ellipsoid $V_e$, papillary muscle volume $V_p$ and ventricular volume $V_{iv}$.

TABLE 2.1: Values of the parameters describing the geometry of the left ventricle.

<table>
<thead>
<tr>
<th>parameter</th>
<th>value</th>
<th>unit</th>
<th>parameter</th>
<th>value</th>
<th>unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>$V_o$</td>
<td>140.</td>
<td>ml</td>
<td>$R_i$</td>
<td>16.3</td>
<td>mm</td>
</tr>
<tr>
<td>$V_p$</td>
<td>4.</td>
<td>ml</td>
<td>$R_o$</td>
<td>31.3</td>
<td>mm</td>
</tr>
<tr>
<td>$V_0$</td>
<td>40.</td>
<td>ml</td>
<td>$Z_i$</td>
<td>46.0</td>
<td>mm</td>
</tr>
<tr>
<td>$V_o$</td>
<td>40</td>
<td>ml</td>
<td>$Z_o$</td>
<td>53.2</td>
<td>mm</td>
</tr>
<tr>
<td>$C$</td>
<td>43.</td>
<td>mm</td>
<td>$f_m$</td>
<td>0.5</td>
<td>-</td>
</tr>
<tr>
<td>$h$</td>
<td></td>
<td></td>
<td></td>
<td>24.8</td>
<td>mm</td>
</tr>
</tbody>
</table>

$f_m$ represents fractional height $h/Z_m$ of the midwall ellipsoid.

equilibrium volume $V_o$ is chosen to be 40 ml. The ratio $V_o/V_w = 0.14$, obtained by Spotnitz et al. [30], was neglected in this choice: this ratio is very small, as compared to the data obtained in the other studies described above, and might have been caused by ischemic contracture. The values for $C$ and $h$ are based upon above mentioned data obtained by Streeter [32]. Assuming the focal length $C$ to be proportional to $\sqrt{V_w}$, a value $C = 43$ mm is obtained. The fractional height above the equator of the midwall ellipsoid $f_m = h/Z_m$ is assumed to be 0.50. The dimensions of the geometry of the model of the left ventricle are summarized in table 2.1.

2.1.2 Coordinate systems used in the model

In the geometry of the left ventricle three coordinate systems are introduced:

- a global Cartesian coordinate system $(x, y, z)$,
- a global ellipsoid coordinate system $(\xi, \theta, \phi)$, and
- a local normalized coordinate system $(\xi, \theta)$.

The origin of the Cartesian coordinate system $(x, y, z)$ is located in the common center of the nested ellipsoids (figure 2.2a). The positive $z$-axis is directed towards the base along the long axis of the ellipsoids. The positive $x$-axis is directed towards the free wall of the left ventricle, while the negative $x$-axis points at the intraventricular septum. These Cartesian coordinates are used in the finite element program.

The origins of the global Cartesian and ellipsoid coordinate system (figure 2.2b) coincide. The transformation of the ellipsoid coordinates $(\xi, \theta, \phi)$ to the global coordinates $(x, y, z)$ is given
FIGURE 2.2: Coordinate systems used: (a) global cartesian coordinates $(x, y, z)$. (b) global ellipsoid coordinates $(\xi, \theta)$ in a plane of constant $\phi = \arctan(y/x)$; lines of constant $\theta$ (---) are indicated for clarity. (c) local coordinates $(\xi, \bar{\theta})$ in a plane of constant $\phi$.

by:

\[ x = C \sinh(\xi) \sin(\theta) \cos(\phi) \]  
\[ y = C \sinh(\xi) \sin(\theta) \sin(\phi) \]  
\[ z = C \cosh(\xi) \cos(\theta) \]

where $C$ represents the common focal length of the ellipsoids. The circumferential ellipsoid coordinate $\phi$ is equal to $\arctan(y/x)$. The endocardial and epicardial surfaces are surfaces of constant radial ellipsoid coordinate $\xi$: $\xi = \xi_{en}$ and $\xi = \xi_{ep}$, respectively. In the reference geometry, defined in the previous subsection, $\xi_{en} = 0.37$ and $\xi_{ep} = 0.68$. The longitudinal ellipsoid coordinate $\theta$ ranges from 0 on the positive $z$-axis to $\pi$ on the negative $z$-axis. Surfaces of constant $\theta$ intersect surfaces of constant $\xi$ perpendicularly. Ellipsoid coordinates are used in section 2.2.5 to describe the activation pattern of the ventricular wall.

The local normalized coordinates $(\bar{\xi}, \bar{\theta})$ are defined in a plane of constant $\phi$ (figure 2.2c). Like the ellipsoid coordinates, they are chosen to describe the geometry of the ventricle in a simple way. In contrast to the ellipsoid coordinates, the normalized coordinates vary linearly with the actual distances in the ventricular wall. The origin of the normalized coordinate system is located at the equator on the midwall ellipsoid. The normalized radial coordinate $\bar{\xi}$ varies linearly from $\bar{\xi} = -1$ at the endocardial surface to $\bar{\xi} = +1$ at the epicardial surface. The normalized longitudinal coordinate $\bar{\theta}$ varies linearly with the distance from the equatorial plane. This distance is measured along the curve of constant $\phi$ and $\xi$, that passes through the point of interest. $\bar{\theta}$ is defined to vary from $\bar{\theta} = +0.5$ in the basal plane, through $\bar{\theta} = 0$ at the equator until $\bar{\theta} = -1$ at the apex. In the next subsection, muscle fiber orientation will be modeled using the normalized coordinates.

2.1.3 Muscle fiber orientation

In subsection 1.2.1 a qualitative description of the structure of the left ventricular wall has been given. The orientation of muscle fibers in the ventricular wall can be quantified by the
helix fiber angle $\alpha_1$ and the transverse fiber angle $\alpha_3$, as shown in figure 2.3. The helix fiber angle is defined as the angle between the $\phi$-direction and the projection of the fiber path on the $(\theta, \phi)$-plane. The transverse fiber angle is defined as the angle between the $\phi$-direction and the projection of the fiber path on the $(\xi, \phi)$-plane. This way of defining fiber orientation is consistent with Streeter [34]. Since muscle fibers run approximately parallel to the endo- and epicardial surface, measurements of fiber orientation have been focussed almost exclusively upon $\alpha_1$. Some of the results of such measurements are presented in figure 2.4 [13,28,31,34]. A monotonous increase of $\alpha_1$ from epic- to endocardium is measured. In the subepicardial layers $\alpha_1$ ranges from about $-80'$ to $-50'$. In the midwall region fibers run approximately circumferentially. In the subendocardial layers $\alpha_1$ ranges from $+20'$ to $+80'$. The relatively large variation in the endocardial layers is partly caused by the irregular shape of the endocardium, making it difficult to define the endocardial surface. Ross et al. [28] and Streeter [34] use the point of farthest invagination of the endocardium into the wall in their procedure of normalizing the transmural coordinate. With the use of this definition a smaller variation of measured $\alpha_1$-values is found.

The transverse fiber angle $\alpha_3$ describes how the fibers proceed between endocardium and epicardium. This 'cross-over' occurs mainly near the base and the apex [1,36]. Above the equator, $\alpha_3$ has been measured to be positive. Below the equator, $\alpha_3$ ranges from $-30'$ to $0'$, with an average value of $-8.4' \pm 1.0'$ [33]. In another study [34] the value of $\alpha_3$, averaged across the wall thickness, was found to be $-4.6' \pm 0.8'$ near the apex and $-3.5' \pm 0.6'$ halfway between equator and apex.

In the model, the spatial distribution of $\alpha_1$ and $\alpha_3$ is a function of the local coordinates $(\xi, \theta)$ that were defined in subsection 2.1.2. It is assumed that the helix fiber angle $\alpha_1$ is independent of the longitudinal coordinate $\theta$. The transmural variation of $\alpha_1$ is modelled as:

$$\alpha_1(\xi) = \alpha_{10} + \alpha_{11} \xi + \begin{cases} 
\alpha_{12, en} \left(\frac{\xi + \xi_1}{-1 + \xi_1}\right)^2 & \xi \leq -\xi_1 \\
0 & -\xi_1 < \xi < \xi_1 \\
\alpha_{12, ep} \left(\frac{\xi - \xi_1}{1 - \xi_1}\right)^2 & \xi \geq \xi_1 
\end{cases}$$

(2.6)

This transmural course of $\alpha_1$ is illustrated in figure 2.5a.
FIGURE 2.4: Transmural variation of fiber angle $\alpha_1$: (a) Streeter et al. (1969), ten dog hearts; (b) Greenbaum et al. (1981), human heart; (c) Ross et al. (1975), macaque heart; (d) Streeter (1979), eight human hearts. In figures (c) and (d) $\xi^* = 0$ indicates the point of deepest invagination of the endocardium into the wall while at the epicardial surface $\bar{\xi}^*$ equals $+1.0$. Measurements were performed approximately in basal ($\Delta$), equatorial (O), equatorial/apical (□) and apical (▽) region.
Experimental information on the spatial distribution of $\alpha_3$ is limited. Since muscle fibers do not end at the endocardial and epicardial surfaces, $\alpha_3$ was assumed to be zero at these surfaces. The following transmural course of $\alpha_3$ satisfies this condition:

$$\alpha_3(\xi, \theta) = \alpha_3(\theta) \left(1 - \xi^2\right)$$  \hspace{1cm} (2.7)

Since $\alpha_3$ is positive above, and negative below the equator [33] it is assumed that in the equatorial plane $\alpha_3$ equals zero. This condition is satisfied by the following longitudinal course of $\alpha_3$:

$$\alpha_3(\theta) = \begin{cases} 
\alpha_{31} \theta & \text{ if } \theta < 0 \\
\alpha_{31} \theta + \alpha_{32} (2\theta)^2 & \text{ if } \theta \geq 0 
\end{cases}$$  \hspace{1cm} (2.8)

The transmural and longitudinal variation of $\alpha_3$ is illustrated in figure 2.5b and c. Because of the limited experimental information, in the initial calculations $\alpha_3$ is set at 0. In later calculations, the influence of a different choice of $\alpha_3$ will be investigated.

In table 2.2 parameter values determining fiber orientation for both the initial and the later defined (chapter 4) reference calculations are listed.

### Table 2.2: Values of parameters describing muscle fiber orientation in the initial and reference calculations.

<table>
<thead>
<tr>
<th>parameter</th>
<th>$\alpha_{30}$</th>
<th>$\alpha_{11}$</th>
<th>$\alpha_{12,\text{en}}$</th>
<th>$\alpha_{12,\text{ep}}$</th>
<th>$\xi_1$</th>
<th>$\alpha_{31}$</th>
<th>$\alpha_{32}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>initial</td>
<td>$0^\circ$</td>
<td>$-30^\circ$</td>
<td>$30^\circ$</td>
<td>$-30^\circ$</td>
<td>0.5</td>
<td>$0^\circ$</td>
<td>$0^\circ$</td>
</tr>
<tr>
<td>reference</td>
<td>$25^\circ$</td>
<td>$-70^\circ$</td>
<td>$-25^\circ$</td>
<td>$-25^\circ$</td>
<td>0.5</td>
<td>$10^\circ$</td>
<td>$10^\circ$</td>
</tr>
</tbody>
</table>

### 2.1.4 Sarcomere length distribution

Active stress developed by the muscle fibers depends on sarcomere length. In the passive left ventricle, the transmural distribution of sarcomere length has been determined by several investigators, as shown in figure 2.6. According to Spotnitz et al. [30] the longest sarcomeres are...
found in the subendocardial region. This agrees with the results of Yoran et al. [42], as far as the midwall and epicardial region is concerned. At pressures up to 1.6 kPa Yoran et al. found the shortest sarcomeres in the subendocardial layers. This finding agrees with the results of Grimm et al. [14]. However, the latter investigators measured an increase in sarcomere length from the endocardium up to three quarters of the wall thickness. In the subepicardial layers sarcomere length was shorter again.

Because of the large variation observed in these measurements, in the model a homogeneous spatial distribution of sarcomere length is chosen in the reference state. The length is set at 1.85 μm, since passive stress is measured to be zero at this sarcomere length [35].

2.2 The constitutive behavior of myocardial tissue

In subsection 1.2.1 a qualitative description has been given of the constituents of myocardial tissue: connective tissue (mainly collagen fibers), muscle fibers and fluid matrix. Each constituent contributes to the total stress in the tissue in the following way:

\[
\sigma = -pI + \sigma_p + \sigma_a e_3 e_3
\]  

(2.9)

In the fluid matrix only the hydrostatic pressure component \(-pI\) is present. Deformation of the cardiac tissue gives rise to a three-dimensional passive stress \(\sigma_p\) in the collagen fibers. Finally, a uniaxial active stress \(\sigma_a e_3 e_3\) is generated in the muscle fibers, parallel to the fiber direction \(e_3\). In this section experimental results regarding passive and active stress in cardiac tissue will be presented. On the basis of these findings, the mechanical behavior of the tissue is described in terms of constitutive equations.

2.2.1 Passive constitutive behavior: experimental data

The mechanical properties of cardiac tissue in the passive state have been studied by several investigators [25,35,41]. Yin et al. [41] subjected thin (1-2 mm) slices of canine myocardium
FIGURE 2.7: Stress-strain relationship in canine cardiac tissue derived from the strain-energy function proposed by Yin et al. (1987) for the case of equal stretch in fiber and cross-fiber direction in five specimens: (a) second Piola-Kirchhoff fiber stress $S_{ff}$ versus Green-Lagrange fiber strain $E_{ff}$; (b) second Piola-Kirchhoff cross-fiber stress $S_{cc}$ versus Green-Lagrange cross-fiber strain $E_{cc}$. Different specimens are indicated by different line types. Corresponding fiber and cross-fiber data are indicated by the same line type.

to a simultaneous equal stretch in fiber and cross-fiber direction. In both fiber and cross-fiber direction the force, needed to obtain a certain stretch, was measured. Strains were determined in the central part (1 x 1 cm) of the specimen, which measured about 4 x 4 cm. From these strain and force measurements, stress was calculated and plotted as a function of strain. A four-parameter strain-energy function, relating second Piola-Kirchhoff stress to Green-Lagrange strain (see appendix A for stress and strain definitions) was introduced to describe the stress-strain plots mathematically. The parameters in the strain-energy function were determined from a fit to experimental data obtained from five specimens, that were subjected to strains up to about 14 %. Fiber and cross-fiber stresses, calculated from this strain-energy function for the case of an equibiaxial stretch test, are shown in figure 2.7a and b, respectively. In this figure Green-Lagrange strain is used, which is defined as:

$$E = \frac{1}{2} \left( \left( \frac{l}{l_0} \right)^2 - 1 \right)$$  \hspace{1cm} (2.10)

$l$ and $l_0$ denote the actual and reference length of the specimen, respectively\(^1\). In these experiments second Piola-Kirchhoff stress is defined as:

$$S = \left( \frac{l_0}{l} \right)^2 \sigma$$  \hspace{1cm} (2.11)

Cauchy stress $\sigma$ is defined as force divided by actual area\(^2\). The behavior of the five specimens varies significantly: at a Green-Lagrange fiber strain $E_{ff} = 0.15$ the second Piola-Kirchhoff

\(^1\)For small strain values Green-Lagrange strain is approximately equal to linear strain $(l - l_0)/l_0$.

\(^2\)For small strain values second Piola-Kirchhoff stress is approximately equal to Cauchy stress.
FIGURE 2.8: Results of uniaxial stretch experiments in 20 rat trabeculae (Ter Keurs et al., 1980). Passive stress, calculated as applied force $F$ divided by unloaded cross-sectional area $A_0$, is plotted versus sarcomere length $l_s$. Sarcomere length in the unloaded state equals 1.85 μm.

stresses $S_{ff}$ range from 5 kPa to 100 kPa. The cross-fiber stresses $S_{cc}$ were observed to be proportional to the fiber stresses, with a ratio $S_{ff}/S_{cc}$ of 1.10, 1.55, 1.67, 2.67 and 2.95, respectively. The large variations in the observed mechanical behavior may be the result of specimen differences. They can also be caused by variations in the choice of the reference state to which the strains are referred. This reference state, the unloaded state, is not well-defined because of the very compliant behavior of the tissue under conditions of small stress, and because of viscoelastic effects.

In the uniaxial experiments of Ter Keurs et al. both active and passive properties of rat trabeculae were measured [35]. After excision, the trabeculae were submerged in a fluid, that ensured a stable mechanical response during at least 6 hours. Using sarcomere length as a measure of tissue strain, the problems associated with the definition of a reference state were avoided. Stress was calculated by dividing the force, needed to extend the trabeculae, by the cross-sectional area of the unloaded trabeculae. Despite the mechanical stability of the trabeculae and the well-defined measure of strain, large variations in stress-strain behavior are observed in these experiments also, as is apparent from figure 2.8.

At present the data from the experiments, described above, are the most accurate data available. In these experiments, the tissue was subjected to normal stresses. Experiments in which the direction of mechanical loading was neither parallel nor perpendicular to the fiber direction, have not been published yet.

2.2.2 A constitutive law for the passive myocardium

The mechanical behavior of an elastic material may be characterized by a strain-energy function. A suitable form of the strain-energy function can be found using a microstructural or a phenomenological approach.

The microstructural approach was followed by Horowitz et al. [16], who applied a theory proposed by Lanir [20]. In this theory the macroscopic behavior of the tissue is described in terms of the properties of the muscle fibers, the collagen fibers and the fluid matrix. Since the material parameters are associated with microstructural properties, this approach can provide insight into the origin of the observed macroscopic behavior. However, at present not all relevant
material parameters have been evaluated experimentally, and consequently they have to be estimated. Moreover, the mathematical description is complicated.

The advantage of the phenomenological approach is its mathematical simplicity. However, no insight is provided into the mechanisms that are responsible for the macroscopically observed material behavior. Almost all constitutive laws, that have been proposed for the passive myocardium, belong to this category [25,19,41]. The four-parameter strain-energy function proposed by Humphrey and Yin [17] has a phenomenological basis. However, some microstructural information has been included, since the passive tissue is assumed to be transversely isotropic. The values of the parameters in the strain-energy function were determined by minimizing the sum of the squares of the differences between experimental and calculated Cauchy stresses. Experimental results obtained by Yin et al. [41] were used. Different sets of parameter values were found for the same specimen, dependent upon the experimentally applied ratio of fiber to cross-fiber strain [18]. However, with parameters obtained from experiments with equal fiber and cross-fiber strains, the results of other non-equibiaxial stretch experiments could be predicted reasonably well [18]. A major disadvantage of the description by this strain-energy function is the fact that stresses exist in the absence of strain. Application of this function to the model of the left ventricle, as proposed in subsection 2.1.1, would lead to the conclusion that residual stresses exist in the ventricle in the reference configuration. Generally, the ventricle would not be in mechanical equilibrium in this reference state.

To avoid these problems, in the present study a new strain-energy function has been used. This function $W(E)$ relates the second Piola-Kirchhoff stress tensor $S$, based upon the deviatoric Cauchy stress tensor, to the Green-Lagrange strain tensor $E$ according to:

$$ S = \frac{\partial W(E)}{\partial E} $$

(2.12)

The myocardial tissue is assumed to be transversely isotropic with respect to the fiber direction. With respect to an orthonormal coordinate system with direction $e_3$ parallel to the fiber direction, and cross-fiber directions $e_1$ and $e_2$, the strain tensor $E$ is written as the strain matrix $E$ with components $E_{ij}$. According to Ericksen and Rivlin [11], the strain-energy function $W(E)$ for material that is transversely isotropic with respect to $e_3$, can be expressed as a single valued function of the following set of scalars:

$$ I_E = E_{11} + E_{22} + E_{33} $$

(2.13)

$$ II_E = E_{11}^2 + E_{22}^2 + E_{33}^2 - E_{11}E_{22} - E_{22}E_{33} - E_{33}E_{11} $$

(2.14)

$$ III_E = \det(E) $$

(2.15)

$$ I'_{E} = E_{33} $$

(2.16)

$$ II'_{E} = E_{31}^2 + E_{32}^2 $$

(2.17)

The functional form of $W(E)$ is chosen so that (1) stress is an exponential function of strain and (2) no stresses are predicted in the undeformed situation. The following strain-energy function is consistent with these conditions:

$$ W(E) = C \exp[a_1 I_E^2 + a_2 II_E + a_3 E_{33}^2 + a_4 (E_{31}^2 + E_{32}^2)] $$

(2.18)

Because of the additional condition of incompressibility of the cardiac tissue the scalar $III_E$ is left out of this strain-energy function.

The values of the material parameters are estimated from fitting this function to experimentally obtained data. Firstly, according to the experimental findings of Yin et al. [41], the ratio of second Piola-Kirchhoff fiber to cross-fiber stress should equal 2 under conditions of equal fiber and cross-fiber stretch. This condition is satisfied by setting:

$$ a_1 = 2 \ a_2 = a_3 $$

(2.19)
TABLE 2.3: Values of parameters in the strain-energy function describing passive material behavior: \( W(E) = C \exp[a_1 I_E^2 + a_2 II_E + a_3 E_{33}^2 + a_4 (E_{31}^2 + E_{32}^2)] \).

<table>
<thead>
<tr>
<th>parameter</th>
<th>( C )</th>
<th>( a_1 )</th>
<th>( a_2 )</th>
<th>( a_3 )</th>
<th>( a_4 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>value</td>
<td>0.7 [kPa]</td>
<td>5.0</td>
<td>10.0</td>
<td>5.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

FIGURE 2.9: Results of experiments on rat trabeculae at 25°C: (a) twitch force as a function of time \( t \) at constant sarcomere length \( l_s \) of 1.65, 1.75, 1.85, 1.93, 2.11 and 2.28 \( \mu \)m, respectively; (b) relation between active first Piola Kirchhoff stress \( T_a \) (active force divided by cross-sectional area of the trabeculae in the situation with \( l_s = 2.0 \mu \)m) and sarcomere length \( l_s \) for two levels of extracellular calcium concentration: \([Ca^{+2}] = 2.5 \text{ mM} \) (---) and \([Ca^{+2}] = 0.5 \text{ mM} \) (----); (c) velocity of sarcomere shortening versus applied load. 100% load corresponds to zero sarcomere shortening. Data adapted from ter Keurs et al. (1980) (figure b) and van Heuningen et al. (1982) (figures a and c).

Secondly, the uniaxial stress-strain data obtained by Ter Keurs et al. [35] should be described reasonably well. Thirdly, \( a_4 \) is set at zero, because of the lack of experimental data on the mechanical behavior of cardiac tissue under conditions of shear stress. The resulting parameter values are listed in table 2.3.

2.2.3 Contractile constitutive behavior: experimental data

In experiments it has been found that active stress, generated by cardiac muscle cells, depends on time, sarcomere length and velocity of shortening of the sarcomeres [7,26,35,37]. Reviews on these investigations are given by Bergel and Hunter [6] and Fung [12]. As representative example of these investigations, in this subsection the results of experiments performed on rat trabeculae by ter Keurs et al. [35] and van Heuningen et al. [37] are described. In figure 2.9a the time course of active force during a twitch, in which sarcomere length is held constant, is shown. Both maximum active force and duration of contraction increase with increasing sarcomere length. In figure 2.9b active force is shown to increase with increasing extracellular calcium
FIGURE 2.10: Active material behavior according to Arts (1978, 1982): (a) three-element model with parallel elastic element PE, series elastic element SE, contractile element CE, sarcomere length $l_s$ and contractile element length $l_c$; (b) length-dependency of active stress; (c) time dependency of active stress at $l_s = 1.7$, 1.9, 2.1 and 2.3 $\mu$m; (d) force-velocity relationship ($v_c = d(l_c/dt)$).

concentrations as well. Finally, figure 2.9c shows how the velocity of sarcomere shortening decreases with increasing load: a load of 100% corresponds to the isometric contractions shown in figure 2.9a.

2.2.4 A mathematical model describing active material behavior

Commonly, contractile behavior is modeled by a three-element model [15]. This model consists of a passive parallel elastic element, in parallel to a series elastic element in series with a contractile element (figure 2.10a). The passive parallel elastic element represents the stress-strain behavior of the passive tissue, which has been described in the subsections 2.2.1-2.2.2. The active element is modeled according to Arts [2,3]. The first Piola-Kirchhoff stress $T_a$ is used. This measure of stress is easily obtainable in experiments, since it represents generated active force $F_a$ per unit of cross-sectional area $A_0$ in a certain reference situation:

$$T_a = \frac{F_a}{A_0} \quad (2.20)$$

The stress generated by the contractile element is transmitted by the series elastic element. In the unstressed state, the length of this element is zero. In the active state it equals $l_s - l_c$, where
$l_c$ and $l_s$ are the length of the contractile element and the sarcomere, respectively. The stress in the passive element is given by:

$$T_a = E_a T_{max} (l_s - l_c)$$  \hspace{1cm} (2.21)

The stiffness of the passive element is equal to $E_a T_{max}$. $E_a$ is constant. $T_{max}$ depends on $l_s$, $l_c$, and the time $t_s$ that has elapsed since the moment of onset of activation:

$$T_{max} = T_1 A(l_c) B_e(t_s) B_d(t_s, l_s)$$  \hspace{1cm} (2.22)

where $T_1$ is associated with the level of maximum isometric stress. $A(l_c)$ represents the length-dependency of the active stress development (figure 2.10b):

$$A(l_c) = 1 + a_s (l_c - l_s) - \sqrt{(a_s (l_c - l_s))^2 + 0.01}$$  \hspace{1cm} (2.23)

At $l_c > l_s$ the active stress $T_a$ levels off. $a_s$ is associated with the increase of active stress as a function of sarcomere length at small $(1/(2a_s) < l_c < l_s)$ sarcomere lengths. $B_e(t_s)$ describes the rise in time of active stress, while $B_d(t_s, l_s)$ describes its decay (figure 2.10c):

$$B_e(t_s) = 1 - \frac{1}{1 + (t_s/t_e)^4}$$  \hspace{1cm} (2.24)

$$B_d(t_s, l_s) = \begin{cases} 1 - \frac{1}{1 + (t_s - t_e)/t_d}^4 & t_s \leq t_e \\ 0 & t_s > t_e \end{cases}$$  \hspace{1cm} (2.25)

In this equation $t_e$ and $t_d$ are characteristic time intervals for the rise and decay of the active stress, respectively. $t_e$ denotes the total duration of the contraction. This duration depends on $l_s$ according to:

$$t_e = b(l_s - l_d)$$  \hspace{1cm} (2.26)

where $b$ governs the increase of the duration of the activation with increasing sarcomere length, and $l_d$ denotes the extrapolated sarcomere length at which this duration equals zero. The time derivative of $l_c$ is modeled as:

$$\frac{dl_c}{dt} = - \left( \frac{T_a - T_{max}}{T_a + T_0} \right) v_0$$  \hspace{1cm} (2.27) \hspace{1cm} $T_a \leq T_{max}$

$$\frac{dl_c}{dt} = - \left( \frac{T_a - T_{max}}{T_a + T_0} \right) v_0 \exp \left( a_T \left( \frac{T_a}{T_0} \right) \right)$$  \hspace{1cm} (2.28) \hspace{1cm} $T_a > T_{max}$

Equation (2.28) describes a hyperbolic relationship [15] between $dl_c/dt$ and $T_a$ (figure 2.10d), with asymptote velocity $v_0$ and asymptote stress $T_0$. Equation (2.28) represents a modification of Arts’s model: it incorporates the experimentally observed sigmoid shape of the force-velocity curve in the high-force region [37][12, chapter 10].

Table 2.4 lists the values of the parameters in the contraction model. The values of $E_a$, $a_s$, $l_s$, $t_e$, $t_d$, $v_0$ and $b$ were adopted from Arts [3]. Using the experimental data obtained by ter Keurs et al. [35], which are presented in figure 2.9b, $T_1$ was chosen equal to 110 kPa. The ratio $T_1/T_0$ corresponds to the ratio $G_{act}/G_0$ in the model presented by Arts [3], and, according to the latter model, it was set at 2. The choice $a_T = 1.5$ was made, to obtain a force-velocity relation which is similar to the relation obtained by van Heuningen et al. [37]. Choosing $l_d = -0.4 \mu m$, the duration of contraction in the present model and the model presented by Arts [3] is equal. In subsection 3.3.2 the behavior of this model for the description of active stress is illustrated by simulating an experiment in which a trabecula contracts against different loads.
TABLE 2.4: Values of the parameters in the contraction model.

<table>
<thead>
<tr>
<th>parameter</th>
<th>value</th>
<th>unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>$T_1$</td>
<td>110.0</td>
<td>$10^3$ Pa</td>
</tr>
<tr>
<td>$T_0$</td>
<td>55.0</td>
<td>$10^3$ Pa</td>
</tr>
<tr>
<td>$E_a$</td>
<td>20.0</td>
<td>$10^6$ m$^{-1}$</td>
</tr>
<tr>
<td>$a_z$</td>
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<td>$10^6$ m$^{-1}$</td>
</tr>
<tr>
<td>$l_z$</td>
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<td>$10^{-6}$ m</td>
</tr>
<tr>
<td>$l_d$</td>
<td>-0.4</td>
<td>$10^{-6}$ m</td>
</tr>
<tr>
<td>$t_r$</td>
<td>75.0</td>
<td>$10^{-3}$ s</td>
</tr>
<tr>
<td>$t_d$</td>
<td>75.0</td>
<td>$10^{-3}$ s</td>
</tr>
<tr>
<td>$v_0$</td>
<td>7.5</td>
<td>$10^{-6}$ m·s$^{-1}$</td>
</tr>
<tr>
<td>$b$</td>
<td>150.0</td>
<td>$10^3$ s·m$^{-1}$</td>
</tr>
<tr>
<td>$a_T$</td>
<td>1.5</td>
<td>-</td>
</tr>
</tbody>
</table>

FIGURE 2.11: Activation sequence of the left ventricle: (a) assumed path along which a point $P$ in the wall is activated, (b) activation map, indicated by isochrones at intervals of 10 ms.

2.2.5 Activation sequence of the left ventricle

Contraction of the sarcomeres in the myocardium is initiated by a depolarisation wave that spreads across the ventricular wall. A review of the investigations concerning the sequence of activation of the left ventricle is given by Scher [29]. Regularly, activation starts in the endocardial region at the apex. From this region the depolarisation wave travels in radial and longitudinal direction across the wall, until it reaches the epicardial basal region after approximately 50 ms. The interventricular septum is activated slightly earlier than the left ventricular free wall. In the subendocardium, the depolarization wave is conducted relatively fast by the Purkinje fibers. From the endocardium towards the epicardium, the conduction velocity decreases, because gradually less Purkinje fibers are present.

In the model the activation pattern is considered to be rotationally symmetric. The moment of activation of a particular point $P$ in the ventricular wall is assumed to proceed as follows (figure 2.11a):
- activation starts in point $A$ located on the endocardium in the apical region;
- from this point, the depolarisation wave travels along the endocardial surface with a speed $v_e$, until it reaches $B$ after $\Delta t_{AB}$ seconds; $B$ is the point on the endocardial surface located closest to $P$.
TABLE 2.5: Values of the parameters determining the activation sequence of the ventricle.

<table>
<thead>
<tr>
<th>symbol</th>
<th>value</th>
<th>unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>$v_e$</td>
<td>1.5</td>
<td>m/s^-1</td>
</tr>
<tr>
<td>$\theta_A$</td>
<td>$2\pi/3$</td>
<td>—</td>
</tr>
</tbody>
</table>

- from $B$, the depolarisation wave travels into the wall with speed $v_e$, in a period of $\Delta t_{BP}$ seconds.

The delays $\Delta t_{AB}$ and $\Delta t_{BP}$ are calculated using the global ellipsoid coordinates, defined in subsection 2.1.2. It can be shown that:

$$\Delta t_{AB} = \int_{\theta_A}^{\theta_B} \frac{C}{v_e} \sqrt{\sinh^2 \xi_A + \sin^2 \theta} \, d\theta$$

$$\Delta t_{BP} = \int_{\xi_B}^{\xi_P} \frac{C}{v_r(\xi)} \sqrt{\sinh^2 \xi + \sin^2 \theta_B} \, d\xi$$

in which the coordinates of $A$, $B$ and $P$ are given by $(\xi_A, \theta_A)$, $(\xi_B, \theta_B)$ and $(\xi_P, \theta_P)$, respectively. $C$ denotes the focal distance of the ellipsoids. The longitudinal conduction velocity in the subendocardium $v_e$ is assumed to be constant. The radial conduction velocity $v_r$ is assumed to decrease from the endocardium into the wall. In the outer two thirds of the ventricular wall $v_r$ is assumed to be constant. Mathematically, this behavior is written as a function of the linear transmural coordinate $\xi$:

$$v_r(\xi) = \begin{cases} -\frac{\xi}{v_e} & \frac{1}{3} \leq \xi \leq -\frac{1}{3} \\ \frac{1}{3} & -\frac{1}{3} < \xi \leq 1 \end{cases}$$

The values of $v_e$ and $\theta_A$ are listed in table 2.5 [5]. The resulting activation sequence is shown in figure 2.11b.

2.3 Boundary conditions

2.3.1 Kinematic boundary conditions

To perform a finite element analysis of the dynamics of the left ventricle, rigid body motion of the ventricle should be suppressed. In the thorax the left ventricle is restrained by its connections to the right ventricle, the atria, the aorta, the pericardial sac and the lungs. Quantitative information on the kinematic boundary conditions imposed by these structures is not available. In the model the axial motion of the basal plane is suppressed. Circumferential motion of the endocardial ring in the basal plane is suppressed also.

2.3.2 Dynamic boundary conditions

In the real ventricle, the endocardial surface of the ventricular wall is subject to a pressure exerted by the blood in the ventricular cavity. This pressure depends on time and position. The spatial pressure distribution is complicated, and requires knowledge of the hydrodynamics of the blood in the cavity [24]. The epicardial surface of the left ventricle is subject to three types of external loading: (1) a normal stress exerted by the blood in the right ventricle, (2) a stress that is transmitted through the attachment of the right ventricular wall, and (3) a normal stress that is imposed on the left ventricular free wall by the pericardial fluid.
Figure 2.12: Three-element model simulating aortic impedance with characteristic aortic resistance $R_c$, arterial compliance $C_a$ and peripheral resistance $R_p$. $p_{lv}$ represents left ventricular pressure.

For simplicity, in the model a uniform pressure is applied to the entire endocardial surface. Variation of this ventricular pressure with time is implemented differently for different phases in the cardiac cycle (section 4.1):
- during the diastolic filling phase pressure is prescribed,
- during the isovolumic contraction and relaxation phase, pressure is calculated to balance the passive and active forces in the ventricular wall in such a way, that ventricular volume is kept constant,
- during the ejection phase pressure is determined from the interaction between the contracting ventricle and the hemodynamic impedance of the aorta.

Epicardial pressure is assumed to be zero during the whole cardiac cycle.

2.3.3 Hydrodynamic coupling

The left ventricle is coupled to the left atrium by the mitral valve. Although several studies have been dealing with mitral valve dynamics [4,40], in the model the filling phase will be simulated by prescribing ventricular pressure. In our analysis, this simplification is allowed, since we are interested primarily in the active phases of the cardiac cycle.

The hydrodynamic coupling of the left ventricle to the aorta can be described mathematically by a three-element aortic input impedance [38]. This impedance consists of an aortic characteristic resistance $R_c$, placed in series with an arterial compliance $C_a$ which is in parallel to a peripheral resistance $R_p$ (figure 2.12). In experiments, in which a cat left ventricle was loaded with the real arterial system and a three-element model simulating the real system, similar time courses of ventricular and aortic pressure, and aortic flow were measured [10,39]. Burkhoff et al. [8] imposed real and best-fit three-element aortic input impedances on a model of the left ventricle. With the three-element model stroke volume, stroke work, and systolic and diastolic aortic pressures were predicted reasonably well. Peak aortic flow was underestimated by about 15% and the time course of aortic pressure and flow differed slightly from the time course calculated with the real aortic input impedance.

The values of components in the three-element model used in our simulations are based on data reported by Burkhoff et al. [8]. In five dogs with an average body weight of 23 kg, these investigators obtained the following values: $R_c = 3.3 \cdot 10^7$ Pa·s·m$^{-3}$, range $1.8 - 4.7 \cdot 10^7$ Pa·s·m$^{-3}$; $R_p = 6.4 \cdot 10^8$ Pa·s·m$^{-3}$, range $3.0 - 12.1 \cdot 10^8$ Pa·s·m$^{-3}$; $C_a = 3.0 \cdot 10^{-9} \text{m}^3\cdot\text{Pa}^{-1}$, range $1.5 - 6.8 \cdot 10^{-9} \text{m}^3\cdot\text{Pa}^{-1}$. Physiologically, these values are closely related to the size of the left ventricle. Using a ratio of left ventricular weight to body weight of $4.5 \cdot 10^{-3}$ [9], the estimated ventricular weight in Burkhoff's experiments was 104 g. This is about 70% of the ventricular weight used in our model. Assuming a linear relationship between ventricular weight and aortic resistance, peripheral resistance, and the inverse of the arterial compliance, the values listed
TABLE 2.6: Values of the elements in the three-element model used to simulate aortic input impedance.

<table>
<thead>
<tr>
<th>parameter</th>
<th>value</th>
<th>unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>$R_c$</td>
<td>$2.3 \times 10^7$</td>
<td>Pa·s·m$^{-3}$</td>
</tr>
<tr>
<td>$R_p$</td>
<td>$4.8 \times 10^8$</td>
<td>Pa·s·m$^{-3}$</td>
</tr>
<tr>
<td>$C_a$</td>
<td>$4.3 \times 10^{-9}$</td>
<td>m$^3$·Pa$^{-1}$</td>
</tr>
</tbody>
</table>

in table 2.6 are obtained.

References


3

Numerical description of cardiac tissue deformation

3.1 Description of tissue deformation

In this section the equations are presented, that govern the deformation of cardiac tissue. These equations are based on the theory of continuum mechanics, described briefly in appendix A. Application of this theory is possible, because the size of the components forming cardiac tissue, such as muscle cells, collagen fibers, and fluid, is small compared to the macroscopic dimensions of the heart muscle. A more extensive treatment of the theory of continuum mechanics can be found in the textbook by Malvern [5].

Local deformation of a continuum can be described by the deformation gradient tensor $F$. This tensor describes how an infinitesimal material vector $dx_0$ in the undeformed reference situation is transformed into a vector $dx$ in the deformed situation:

$$ dx = F \cdot dx_0 \quad ; \quad F = (\nabla_0 \mathbf{x})^e $$

(3.1)

The local stress state in the material is given by the Cauchy stress tensor $\mathbf{\sigma}$. In an incompressible material only the deviatoric part $\mathbf{\sigma}^d$ of $\mathbf{\sigma}$ is related uniquely to the deformation of the material. In this case it is advantageous to write the Cauchy stress tensor as the sum of its deviatoric part and a hydrostatic pressure $p$:

$$ \mathbf{\sigma} = \mathbf{\sigma}^d - pI $$

(3.2)

The deformation of a continuum is governed by conservation of mass, conservation of momentum and conservation of moment of momentum. As cardiac tissue is assumed to be incompressible, conservation of mass is equivalent to conservation of volume, which is expressed by the relationship:

$$ \det(F) = 1 $$

(3.3)

Conservation of momentum is given by:

$$ \nabla \cdot \mathbf{\sigma} = 0 $$

(3.4)

Inertial and gravity effects are neglected in this equation. Combination of (3.2) and (3.4) yields:

$$ \nabla \cdot \mathbf{\sigma}^d - \nabla p = 0 $$

(3.5)

Conservation of moment of momentum is equivalent to the condition that the Cauchy stress tensor is symmetric:

$$ \mathbf{\sigma} = \mathbf{\sigma}^e $$

(3.6)

The equilibrium equations (3.3) and (3.5) form the basis for the numerical solution procedure.
3.2 Transformation of the equilibrium equations

In this section the equilibrium equations are combined with the constitutive equations, presented in chapter 2, and transformed into a set of matrix equations [7,3,2]. With the resulting set of equations the deformation of the cardiac tissue, as caused by externally applied forces or internally generated active forces, can be calculated.

3.2.1 The weighted residual formulation

The momentum equation (3.5) is equivalent to:

$$\int_V h \cdot (\nabla \cdot \sigma^d - \nabla p) \, dV = 0$$  (3.7)

where \( V \) is the actual volume of the continuum, and \( h \) an arbitrary vector function, defined in \( V \). Equation (3.7) can be transformed into:

$$\int_V [\sigma^d : (\nabla h)^e - p (\nabla \cdot h)] \, dV = \int_A h \cdot (\sigma^d \cdot n - p \, n) \, dA$$  (3.8)

where \( n \) is the normal on \( A \), the surface of \( V \). The term \((\sigma^d \cdot n - p \, n)\) corresponds to the external pressure \(-p_{\text{ext}}\) applied to the surface \( A \):

$$(\sigma^d \cdot n - p \, n) = -p_{\text{ext}}n$$  (3.9)

Transformation to the undeformed configuration yields:

$$\int_{V_0} [\sigma^d : (F^{-\varepsilon} \cdot \nabla_0 h)^e - p (F^{-\varepsilon} \cdot \nabla_0 \cdot h)] \, J \, dV_0 = -\int_{A_0} p_{\text{ext}} h \cdot (F^{-\varepsilon} \cdot n_0) J \, dA_0$$  (3.10)

where \( J = \det(F) \) and \( n_0 \) represents the normal vector on the surface \( A_0 \) of the volume \( V_0 \) in the undeformed configuration. This equation can be written as:

$$\int_{V_0} [(\nabla_0 h)^e : (S \cdot F^{\varepsilon}) - p (\nabla_0 h : F^{-\varepsilon})] \, dV_0 = -\int_{A_0} p_{\text{ext}} h \cdot (F^{-\varepsilon} \cdot n_0) J \, dA_0$$  (3.11)

where \( S \) is the second Piola-Kirchhoff stress tensor related to the deviatoric Cauchy stress:

$$S = \det(F) \cdot F^{-1} \cdot \sigma^d \cdot F^{-\varepsilon}$$  (3.12)

Now suppose that at a certain time estimates are available of (1) the positions \( x \) of all material points of the continuum, (2) the stresses in the continuum and (3) the hydrostatic pressure in the continuum. The estimates are marked by a 'e' and the differences between estimated and the actual situation by '6':

$$x = \hat{x} + \delta x \quad ; \quad p = \hat{p} + \delta p \quad ; \quad S = \hat{S} + \delta S \quad ; \quad F = \hat{F} + \delta F$$  (3.13)

Then, with the use of:

$$\hat{F} = (\nabla_0 \hat{x})^e \quad ; \quad F^{-1} \approx (I - \hat{F}^{-1} \cdot \delta F) \cdot \hat{F}^{-1}$$

$$\delta F = (\nabla_0 \delta x)^e \quad ; \quad \det(F) = \det(\hat{F})(1 + \hat{F}^{-1} : \delta F)$$  (3.14)
and rearranging terms, equation (3.11) is transformed into:

\[
\int_{V_0} (\nabla \phi)^c \cdot (\delta F^c + \delta S \cdot \tilde{F}^c) \, dV_0 + \\
- \int_{V_0} (\nabla \phi)^c \cdot (\delta \tilde{F}^c - \tilde{F}^c \cdot \delta \tilde{F}) \, dV_0 + \\
- \int_{A_0} p_{est} h \cdot (\delta F^c - \delta F) \, dA_0 + \text{higher order terms} = \tag{3.15}
\]

Stresses in cardiac tissue are composed of a passive part \( S_p \) and an active part \( S_a \). The passive component is assumed to be purely elastic (subsection 2.2.2), whereas the active component depends on time, sarcomere length \( l_s \) and the contractile element length \( l_c \) (subsection 2.2.4):

\[
S = S_p(E) + S_a(l_s, l_c, t) \tag{3.16}
\]

The error \( \delta S \) in the estimate of stress can be written as:

\[
\delta S = \frac{\partial S_p}{\partial E} \delta E + \frac{\partial S_a}{\partial l_s} \frac{\partial l_s}{\partial E} \delta l_s + \frac{\partial S_a}{\partial l_c} \frac{\partial l_c}{\partial E} \delta l_c + \frac{\partial S_a}{\partial t} \delta t \tag{3.17}
\]

This expression is substituted in (3.15). Furthermore the lefthandside (LHS) of (3.15) is linearized, and the surface terms in the LHS are neglected. The resulting equation is:

\[
\int_{V_0} (\nabla \phi)^c : \left( \tilde{S}_p \cdot \delta \tilde{F}^c + \left( \frac{\partial S_p}{\partial E} : (\tilde{F}^c \cdot \delta F) \right) \cdot \tilde{F}^c \right) \, dV_0 + \\
\int_{V_0} (\nabla \phi)^c : \left( \tilde{S}_a \cdot \delta \tilde{F}^c + \left( \frac{\partial S_a}{\partial l_s} \frac{\partial l_s}{\partial E} : (\tilde{F}^c \cdot \delta F) \right) \cdot \tilde{F}^c \right) \, dV_0 + \\
\int_{V_0} (\nabla \phi)^c : \left( \left( \frac{\partial S_a}{\partial l_c} \delta l_c + \frac{\partial S_a}{\partial t} \delta t \right) \cdot \tilde{F}^c \right) \, dV_0 + \\
- \int_{V_0} (\nabla \phi)^c : [\delta \tilde{F}^c + \tilde{F}^c \cdot \delta \tilde{F} - \tilde{F}^c \cdot \delta F - \tilde{F}^c \cdot \delta F] \, dV_0 = \\
\int_{V_0} (\nabla \phi)^c : [-\tilde{S}_p \cdot \tilde{F}^c - \tilde{S}_a \cdot \tilde{F}^c + \tilde{F}^c \cdot \delta \tilde{F}] \, dV_0 + \\
- \int_{A_0} p_{est} h \cdot (\tilde{F}^c - n_0) \delta A_0 \tag{3.18}
\]

The righthandside (RHS) of this equation represents the difference between the internal and external forces due to the error in the estimated positions \( \tilde{x} \) and pressures \( \tilde{p} \). This RHS can be used to improve iteratively the estimations \( \tilde{x} \) and \( \tilde{p} \), or equivalently reduce the differences \( \delta \tilde{x} \) and \( \delta \tilde{p} \). It is important to note that no approximations have been made in the RHS of (3.18). Thus, in the procedure of iteratively adapting \( \tilde{x} \) and \( \tilde{p} \), convergence will occur towards the exact solution.
The transformation of the equation describing conservation of volume is analogous to the transformation of the momentum equation. Equation (3.3) is equivalent to:

\[ \int_{V_0} g \, dV = \int_{V_0} g \, dV_0, \quad \int_{V_0} g \left( \det(F) - 1 \right) \, dV_0 = 0 \]  

where \( g \) is an arbitrary scalar function in \( V \) and \( V_0 \). Introduction of an estimation of the deformed situation and linearization yields:

\[ \int_{V_0} g \, \det(\hat{F})(\hat{F}^{-1} : \delta F) \, dV_0 = -\int_{V_0} g \left( \det(\hat{F}) - 1 \right) \, dV_0 \]  

The equations (3.18) and (3.20), which are called the weighted residual equations, are the starting equations for the discretization process, described in the next subsection.

3.2.2 Discretization of the weighted residual equations

The equations (3.18) and (3.20) hold for all points in the continuum. To be able to solve these equations numerically, they have to be reduced to a finite number of linear equations involving a finite number of unknowns. This is accomplished by considering only a finite number of \( n_x \) material (nodal) points where the positions in the deformed configuration will be calculated. The pressure \( p \) will be calculated in \( n_p \) nodal points. From this point on the equations will be presented in an orthonormal coordinate system with unit vectors \( e_1, e_2, e_3 \). With the use of interpolation functions \( \psi \) and \( \phi \) the position field and pressure field are approximated by:

\[
\begin{align*}
\mathbf{x}(t) & \approx \psi^I(\xi) \, \mathbf{x}^I(t) = \psi^I(\xi) \, x^I_i(t) \, e_i \quad I = 1, \ldots, n_x \\
p(t) & \approx \phi^J(\xi) \, p^J(t) \quad J = 1, \ldots, n_p
\end{align*}
\]

where Einstein summation convention is used: a double superscripted capital index denotes summation over the nodal points, whereas a double subscripted index denotes summation over the three coordinate directions. \( x^I_i \) denotes component \( i \) of the position vector \( \mathbf{x}^I \) of node \( I \), and \( p^J \) represents the hydrostatic pressure at node \( J \). The interpolation functions are dependent on the material coordinates \( \xi \) and chosen in such a way that:

\[ \psi^I(\xi^J) = \delta^{IJ} ; \quad \phi^I(\xi^J) = \delta^{IJ} \]  

With the help of the interpolation functions the contractile element length \( l_c \) can also be discretized:

\[ l_c(t) \approx \psi^I(\xi) \, (l_c)^I(t) \quad I = 1, \ldots, n_x \]  

Because of the approximation of \( p \) and \( \mathbf{x} \), the equilibrium equations cannot be fulfilled for all \( g \) and \( h \). Following Galerkin's method, a finite set of weighting functions is chosen, equal to the set of interpolation functions:

\[
\begin{align*}
h & \rightarrow h^I = \psi^I c_i \quad I = 1, \ldots, n_x \\
g & \rightarrow g^J = \phi^J \quad J = 1, \ldots, n_p
\end{align*}
\]

The discrete form of the gradient operator is defined as:

\[ b^I(\xi) = \nabla_0 \psi^I(\xi) \]
from which it follows that:
\[
\nabla_0 \delta x = \left( \nabla_0 \left( \psi^I \delta x^I \right) \right)_{ij} e_i e_j = b^I_0 \delta x^I_{ij} e_i e_j = b^I \delta x^I
\]
\[
\nabla_0 b^I = \left( \nabla_0 \psi^I e_i \right) = (\nabla_0 \psi^I) e_i = b^I e_i
\] (3.26)

After substituting these discrete forms into the equations (3.18) and (3.20) the following matrix equations result:

\[
\sum_{k=1}^{4} k K_{ij}^I \delta x^I_j + \tau K_{ij}^I \delta \psi^I + \delta K^I_{ij} \delta \psi^I = \sum_{k=1}^{4} k R^I_k
\] (3.27)
\[
\tau K_{ij}^I \delta x^I_j = s R^I
\] (3.28)

with:

\[
1 K_{ij}^I = \int \nabla_0 : b^I e_i \cdot b^I e_j \ dV_0 \] (3.29)
\[
2 K_{ij}^I = \int \nabla_0 : b^I e_i \cdot b^I e_j \ dV_0 \] (3.30)
\[
3 K_{ij}^I = \int \left( \hat{\psi}^c \cdot e_i b^I \right) \cdot \frac{\partial S_p}{\partial \psi} \cdot \left( \hat{\psi}^c \cdot e_j b^I \right) \ dV_0 \] (3.31)
\[
4 K_{ij}^I = \int \left( \hat{\psi}^c \cdot e_i b^I \right) \cdot \left( \frac{\partial S_a}{\partial l} \cdot \frac{\partial l}{\partial E} \right) \cdot \left( \hat{\psi}^c \cdot e_j b^I \right) \ dV_0 \] (3.32)
\[
5 K_{ij}^I = \int \left( \hat{\psi}^c \cdot e_i b^I \right) \cdot \left( \hat{\psi}^c \cdot b^I e_j \right) \ n \ dV_0 \] (3.33)
\[
6 K_{ij}^I = \int \left( \hat{\psi}^c \cdot e_i b^I \right) \cdot \left( \hat{\psi}^c \cdot b^I e_j \right) \ n \ dV_0 \] (3.34)
\[
7 K_{ij}^I = \int \hat{\psi}^c \cdot b^I e_i \cdot \phi^J \ n \ dV_0 \] (3.35)
\[
8 K_{ij}^I = \int \left( \hat{\psi}^c \cdot b^I e_i \right) \cdot \left( \hat{\psi}^c \cdot b^I e_j \right) \ n \ dV_0 \] (3.36)
\[
9 K_{ij}^I = \int \left( \hat{\psi}^c \cdot b^I e_i \right) \cdot \left( \hat{\psi}^c \cdot b^I e_j \right) \ n \ dV_0 \] (3.37)
\[
1 R^I_k = \int S_p : \hat{\psi}^c \cdot b^I e_i \ dV_0 \] (3.38)
\[
2 R^I_k = \int S_a : \hat{\psi}^c \cdot b^I e_i \ dV_0 \] (3.39)
\[
3 R^I_k = \int \hat{\psi}^c \cdot b^I e_i \ n \ dV_0 \] (3.40)
\[
4 R^I_k = \int p_{ext} \psi^I e_i : \hat{\psi}^c \cdot n_0 \ dA_0 \] (3.41)
\[ sR^T = \int_{V_0} \psi^T (\mathbf{j} - 1) \, dV_0 \]  

Equation (3.28) can also be written in matrix notation:

\[ \mathbf{X}_K \cdot \delta \mathbf{X} + \mathbf{L} \cdot \delta \mathbf{L} + \mathbf{R}^T \delta t = 0 \]  

where:

\[ \mathbf{X}_K = \begin{bmatrix}
\sum_{i=1}^{6} i K_{11}^{i} & \sum_{i=1}^{6} i K_{12}^{i} & \sum_{i=1}^{6} i K_{13}^{i} & \sum_{i=1}^{6} i K_{14}^{i} & \ldots \\
\sum_{i=1}^{6} i K_{21}^{i} & \sum_{i=1}^{6} i K_{22}^{i} & \sum_{i=1}^{6} i K_{23}^{i} & \sum_{i=1}^{6} i K_{24}^{i} & \ldots \\
\sum_{i=1}^{6} i K_{31}^{i} & \sum_{i=1}^{6} i K_{32}^{i} & \sum_{i=1}^{6} i K_{33}^{i} & \sum_{i=1}^{6} i K_{34}^{i} & \ldots \\
\sum_{i=1}^{6} i K_{41}^{i} & \sum_{i=1}^{6} i K_{42}^{i} & \sum_{i=1}^{6} i K_{43}^{i} & \sum_{i=1}^{6} i K_{44}^{i} & \ldots \\
\sum_{i=1}^{6} i K_{51}^{i} & \sum_{i=1}^{6} i K_{52}^{i} & \sum_{i=1}^{6} i K_{53}^{i} & \sum_{i=1}^{6} i K_{54}^{i} & \ldots \\
\sum_{i=1}^{6} i K_{61}^{i} & \sum_{i=1}^{6} i K_{62}^{i} & \sum_{i=1}^{6} i K_{63}^{i} & \sum_{i=1}^{6} i K_{64}^{i} & \ldots \\
\end{bmatrix} \]

\[ \delta \mathbf{X}^T = \begin{bmatrix}
\delta x_1^1 & \delta x_2^1 & \delta x_3^1 & \delta p_1 & \delta x_1^2 & \ldots \\
\delta x_2^1 & \delta x_2^2 & \delta x_3^2 & \delta p_2 & \delta x_1^3 & \ldots \\
\delta x_3^1 & \delta x_3^2 & \delta x_3^3 & \delta p_3 & \delta x_1^4 & \ldots \\
\delta p_1 & \delta p_2 & \delta p_3 & \delta p_4 & \delta p_5 & \ldots \\
\end{bmatrix} \]

\[ \mathbf{L}^T = \begin{bmatrix}
k_1 & k_2 & k_3 & k_4 & \ldots \\
k_1 & k_2 & k_3 & k_4 & \ldots \\
k_1 & k_2 & k_3 & k_4 & \ldots \\
k_1 & k_2 & k_3 & k_4 & \ldots \\
k_1 & k_2 & k_3 & k_4 & \ldots \\
k_1 & k_2 & k_3 & k_4 & \ldots \\
\end{bmatrix} \]

\[ \mathbf{R}^T = \begin{bmatrix}
\sum_{i=1}^{4} i r_1^1 & \sum_{i=1}^{4} i r_1^2 & \sum_{i=1}^{4} i r_1^3 & \sum_{i=1}^{4} i r_1^4 & \sum_{i=1}^{4} i r_1^5 & \ldots \\
\sum_{i=1}^{4} i r_2^1 & \sum_{i=1}^{4} i r_2^2 & \sum_{i=1}^{4} i r_2^3 & \sum_{i=1}^{4} i r_2^4 & \sum_{i=1}^{4} i r_2^5 & \ldots \\
\sum_{i=1}^{4} i r_3^1 & \sum_{i=1}^{4} i r_3^2 & \sum_{i=1}^{4} i r_3^3 & \sum_{i=1}^{4} i r_3^4 & \sum_{i=1}^{4} i r_3^5 & \ldots \\
\sum_{i=1}^{4} i r_4^1 & \sum_{i=1}^{4} i r_4^2 & \sum_{i=1}^{4} i r_4^3 & \sum_{i=1}^{4} i r_4^4 & \sum_{i=1}^{4} i r_4^5 & \ldots \\
\sum_{i=1}^{4} i r_5^1 & \sum_{i=1}^{4} i r_5^2 & \sum_{i=1}^{4} i r_5^3 & \sum_{i=1}^{4} i r_5^4 & \sum_{i=1}^{4} i r_5^5 & \ldots \\
\sum_{i=1}^{4} i r_6^1 & \sum_{i=1}^{4} i r_6^2 & \sum_{i=1}^{4} i r_6^3 & \sum_{i=1}^{4} i r_6^4 & \sum_{i=1}^{4} i r_6^5 & \ldots \\
\end{bmatrix} \]

Now suppose that at a certain time \( t = t_n \) the deformed configuration of the cardiac tissue is known. The columns \( \mathbf{X} \) and \( \mathbf{L} \) at \( t = t_n \) are written as \( \mathbf{X}_n \) and \( \mathbf{L}_n \), respectively. Furthermore, suppose that an estimation of the nodal positions and pressures at \( t = t_{n+1} \) is available. This estimation is improved iteratively until the column \( \mathbf{R}_{n+1} \), which represents the force imbalances and deviations from volume conservation due to the error in \( \mathbf{X}_{n+1} \), is sufficiently small. The estimation at iteration step \( j \) will be denoted by a superscript \( '^j' \):

\[ t_{n+1} = t_n + \delta t_{n+1} \]

\[ \mathbf{X}_{n+1} = \mathbf{X}_n + \delta \mathbf{X}_{n+1} \]

\[ \mathbf{L}_{n+1} = \mathbf{L}_n + \delta \mathbf{L}_{n+1} \]

As a first estimation of quantities at \( t = t_{n+1} \) the situation at \( t = t_n \) is chosen:

\[ \mathbf{X}^0_{n+1} = \mathbf{X}_n \]

\[ \mathbf{L}^0_{n+1} = \mathbf{L}_n \]

The time steps are prescribed according to:
So it holds that:

\[ \delta t^0_{n+1} = \Delta t_{n+1} \]  
\[ \delta t^j_{n+1} = 0 \text{ for } j > 0 \]  

In the constitutive model for active stress the time derivative of \( l_e \) is given as an explicit function of \( l_e, l_s \) and \( t \):

\[ \frac{\partial l_e}{\partial t} = \frac{\partial l_e}{\partial t}(l_e, l_s, t) \]  

or, equivalently:

\[ \frac{\partial L}{\partial t} = \frac{\partial L}{\partial t}(L, X, t) \]  

It is assumed that \( L_{n+1} \) can be estimated from the situation at \( t = t_n \) with sufficient accuracy:

\[ \delta L^0_{n+1} = \Delta L_{n+1}[L_n, X_n, t_n, \Delta t_{n+1}] \]  
\[ L_{n+1} = L_n + \Delta L_{n+1} \]  

So it holds that:

\[ \delta L^j_{n+1} = 0 \text{ for } j > 0 \]  

Since the differences \( \delta L \) and \( \delta t \) in equation (3.43) are known quantities now, a first estimate \( \delta X^1_{n+1} \) of the error \( \delta X_{n+1} \) can be derived from:

\[ X K^0_{n+1} \cdot \delta X^1_{n+1} = B^0_{n+1} - t B^0_{n+1} \cdot \delta L_{n+1} - t B^0_{n+1} \Delta t_{n+1} \]  

A new estimate \( \hat{X}^1_{n+1} \) is obtained according to:

\[ \hat{X}^1_{n+1} = X^0_{n+1} + \delta X^1_{n+1} \]  

Improvements on this estimate are obtained according to:

\[ X K^j_{n+1} \cdot \delta X^j_{n+1} = B^j_{n+1} \]  

After each iteration a new estimate for \( X_{n+1} \) is calculated:

\[ \hat{X}^{j+1}_{n+1} = \hat{X}^j_{n+1} + \delta X^{j+1}_{n+1} \]  

Using \( \hat{X}^{j+1}_{n+1} \) the error in the momentum and volume balance \( B^{j+1}_{n+1} \) is calculated. If the maximum component of the column \( B^{j+1}_{n+1} \) is larger than a prescribed value \( \epsilon_0 \) the iterative procedure 3.67 through 3.68 is repeated. If the maximum component of the column \( B^{j+1}_{n+1} \) is smaller than \( \epsilon_0 \) it is assumed that the nodal positions and pressures have been estimated sufficiently accurately and a new time step can be performed.
3.3 The 20-node brick element

In the calculation procedure described in the previous section usually a large number of nodes is involved. According to the finite element method these nodes are grouped into elements by choosing the interpolation functions \( \psi \) and \( \phi \) so that an interpolation function belonging to a material point \( \xi^I \) can be non-zero only in those elements \( E \) to which this material point belongs:

\[
\xi^I \notin E \implies \psi^I = \phi^I = 0 \text{ in } E
\]

For the calculation of the deformation of the cardiac tissue the 20-node brick element shown in figure 3.1a is used. Within the element isoparametric coordinates \( \eta \) are defined:

\[
\eta^T = [\eta_1 \eta_2 \eta_3] ; \quad -1 \leq \eta_1, \eta_2, \eta_3 \leq 1
\]

Positions and displacements within the element are interpolations of the positions and displacements of the 20 nodes (3.22). The pressure field within the element is interpolated from the pressures in the eight corner nodes. The interpolation functions \( \phi \) and \( \psi \) (3.12) are defined as a function of the isoparametric coordinates \( \eta \):

\[
\begin{align*}
\phi(\pm 1, \pm 1, \pm 1) & = \frac{1}{8}(1 \pm \eta_1)(1 \pm \eta_2)(1 \pm \eta_3)(\pm \eta_1 \pm \eta_2 \pm \eta_3 - 2) \\
\phi(0, \pm 1, \pm 1) & = \frac{1}{4}(1 - \eta_1^2)(1 \pm \eta_2)(1 \pm \eta_3) \\
\phi(\pm 1, 0, \pm 1) & = \frac{1}{4}(1 - \eta_2^2)(1 \pm \eta_1)(1 \pm \eta_3) \\
\phi(\pm 1, \pm 1, 0) & = \frac{1}{4}(1 - \eta_3^2)(1 \pm \eta_1)(1 \pm \eta_2) \\
\psi(\pm 1, \pm 1, \pm 1) & = \frac{1}{8}(1 \pm \eta_1)(1 \pm \eta_2)(1 \pm \eta_3)
\end{align*}
\]

The stiffness matrix \( K \) and the error column \( R \), that were introduced in the previous section, contain integrals over the volume of the object that is considered. These integrals are calculated as a sum of integrals over the volume of the object \( V_0 \) of the \( n_e \) elements, out of which the object is composed:

\[
\int_{V_0} f(x, y, z, p) dV_0 = \sum_{e=1}^{n_e} \int_{V^e_0} f(x, y, z, p) dV^e_0
\]

After transforming the element integrals to the space of isoparametric coordinates it follows:
The integrals are approximated numerically as a weighted sum over \( n \) integration points:

\[
\int_{V_0} f(x, y, z, p) dV_0 = \int_{-1}^{1} \int_{-1}^{1} \int_{-1}^{1} f(x(\eta), y(\eta), z(\eta), p(\eta)) \det(\frac{\partial x}{\partial \eta}) d\eta_1 d\eta_2 d\eta_3
\]

(3.77)

The integrals are approximated numerically as a weighted sum over \( n \) integration points:

\[
\int_{V_0} f(x, y, z, p) dV_0 \approx \sum_{i=1}^{n_i} w_i g_i
\]

(3.78)

with weighting factor \( w_i \) and function value \( g_i \) at integration point \( i \). Within the element, displacements are approximated by a quadratic function in each of the isoparametric coordinates. Usually, integration of a quadratic function is carried out numerically by a 3 point Gaussian integration rule. So, for the 20-node element usually \( 3 \times 3 \times 3 \) Gaussian integration is applied. However, comparable accuracy can be obtained by a 14-point integration rule [4], which reduces computation time by almost 50%:

\[
\int_{V_0} f(x, y, z, p) dV_0 \approx \sum_{i=1}^{n_i} w_i g_i
\]

(3.79)

with:

\[
A = 0.335180055 \quad a = 0.758786911 \quad B = 0.886426593 \quad b = 0.795822426
\]

(3.80)

The location of the integration points is illustrated in figure 3.1b. Calculation of the surface integrals occurring in previous section, is carried out similarly using \( 3 \times 3 \) Gaussian integration.

### 3.4 Testing the element

#### 3.4.1 Introduction

In this section a number of deformation processes are simulated using the 20-node brick element. The stresses, calculated in the simulations, are compared to the analytical solutions. The material used in the tests is incompressible, nonlinearly elastic and transversely isotropic with respect to the \( e_3 \)-direction. The material behavior is described by the strain-energy function presented in section 2.2.2. Assuming \( \varepsilon_3 = \varepsilon_2 = \varepsilon_3 = 0 \) and \( \varepsilon_4 = 0 \) the following strain-energy function is obtained:

\[
W(\varepsilon) = C \exp \left[ a(\varepsilon_{11}^2 + \varepsilon_{22}^2 + 2\varepsilon_{33}^2) + a(\varepsilon_{12}^2 + \varepsilon_{22}^2 + \varepsilon_{33}^2 + \varepsilon_{33}^2 + \varepsilon_{22}^2 + \varepsilon_{11}^2) \right]
\]

(3.81)

From this strain-energy function the following second Piola-Kirchhoff stress matrix \( S \) can be derived:

\[
S = \begin{bmatrix}
E_{11} & E_{12} & E_{13} \\
E_{21} & E_{22} & E_{23} \\
E_{31} & E_{32} & 2E_{33}
\end{bmatrix} 2aW(\varepsilon)
\]

(3.82)

The material parameter values used in the tests are:

\[
C = 0.5 \text{ kPa} \quad (3.83)
\]

\[
a = 3.0 \quad (3.84)
\]

The test calculations are performed on a solid rectangular block with dimensions \( l_{10} \) in \( e_1 \)-direction, \( l_{20} \) in \( e_2 \)-direction, and \( l_{30} \) in \( e_3 \)-direction. The block is subdivided into 5 elements, as is shown in figure 3.2.
3.4.2 Uniaxial compression and stretch

Consider a uniform compression or extension of the block in figure 3.3 in the e2-direction, that changes its length from \( l_{30} \) to \( l_3 \):

\[
l_3 = \lambda l_{30}
\]

(3.85)

For the matrix representation \( F \) of the deformation gradient tensor \( F \) it holds:

\[
F = \begin{bmatrix}
\frac{1}{\lambda} & 0 & 0 \\
0 & \frac{1}{\lambda} & 0 \\
0 & 0 & \lambda
\end{bmatrix}
\]

(3.86)

The deviatoric Cauchy stress matrix \( \sigma_d \) and the hydrostatic pressure \( p \) are:

\[
\sigma_d = \begin{bmatrix}
S_{11}/\lambda & 0 & 0 \\
0 & S_{22}/\lambda & 0 \\
0 & 0 & \lambda^2 S_{33}
\end{bmatrix}; \quad p = S_{11}/\lambda
\]

(3.87)

Figure 3.3 shows the good agreement between the analytical and the finite element solution.

3.4.3 Equibiaxial stretch

In this case the block in figure 3.2 is subjected to an equibiaxial stretch in \( e_2 \) and \( e_3 \)-direction. The deformation matrix equals:

\[
\hat{F} = \begin{bmatrix}
\frac{1}{\lambda^2} & 0 & 0 \\
0 & \frac{1}{\lambda} & 0 \\
0 & 0 & \frac{1}{\lambda}
\end{bmatrix}
\]

(3.88)

For the deviatoric Cauchy stress matrix \( \sigma_d \) and the hydrostatic pressure \( p \) it can be derived that:

\[
\sigma_d = \begin{bmatrix}
S_{11}/\lambda^4 & 0 & 0 \\
0 & \lambda^2 S_{22} & 0 \\
0 & 0 & \lambda^2 S_{33}
\end{bmatrix}; \quad p = S_{11}/\lambda^4
\]

(3.89)

Analytical and finite element solution are shown in figure 3.4.
FIGURE 3.3: Finite extension and compression in $e_3$-direction of the rectangular block in figure 3.2: analytical (---) and finite element solution: Cauchy stress $\sigma_{33}^{d}$ (O) and pressure $p$ (●) versus stretch ratio $\lambda$.

FIGURE 3.4: Equibiaxial stretch in $e_2$ and $e_3$ direction of the rectangular block in figure 3.2: analytical (---) and finite element solution: Cauchy stresses $\sigma_{22}^{d}$ (◇), $\sigma_{33}^{d}$ (O) and pressure $p$ (●) versus extension ratio $\lambda$. 
3.4.4 Shear

The top surface of the block in figure 3.2 is subjected to a translation \( u_3 \) in the \( e_3 \) direction, while the bottom surface is fixed. The deformation gradient matrix \( \mathcal{F} \) for this process is:

\[
\mathcal{F} = \begin{bmatrix}
1 & 0 & 0 \\
0 & 1 & 0 \\
\alpha & 0 & 1
\end{bmatrix} ; \quad \alpha = (u_3/l_{10}) \quad (3.90)
\]

The components of the deviatoric Cauchy stress matrix \( \sigma^d \) and the hydrostatic pressure \( p \) can be shown to be:

\[
\sigma^d = \begin{bmatrix}
S_{11} & 0 & S_{13} + \alpha S_{11} \\
0 & 0 & 0 \\
S_{31} + \alpha S_{11} & 0 & 2\alpha S_{13} + \alpha^2 S_{11}
\end{bmatrix} ; \quad p = 0 \quad (3.91)
\]

Analytical and finite element solution are shown in figure 3.5.

3.4.5 Inflation of a thickwalled sphere

Consider a thickwalled sphere with inner radius \( r_{i,0} \) and outer radius \( r_{o,0} \). Assume isotropic material behaviour by putting \( a_3 = a_4 = 0 \). Upon inflation this sphere deforms into a sphere with inner radius \( r_i \) and outer radius \( r_o \) according to:

\[
\begin{align*}
    r_i &= \lambda_i r_{i,0} \\
    r_o &= \lambda_o r_{o,0}
\end{align*} \quad (3.92, 3.93)
\]

The cavity pressure \( p_{cav} \) needed for this inflation is given by [6]:

\[
p_{cav} = \frac{\lambda_o}{\lambda_i} \int_{\lambda_i}^{\lambda_o} \frac{\partial W}{\partial \lambda} d\lambda \quad (3.94)
\]

The pressure-volume relationship of a sphere with \( r_{i,0} = 3 \) and \( r_{o,0} = 5 \) is given in figure 3.6.
3.4.6 Simulation of a papillary muscle experiment

Contractile properties of myocardial tissue can be investigated experimentally using papillary muscles. In a typical experiment [1], the papillary muscle is loaded with a preload $T_{pl}$, causing an increase in length of the muscle from $l_0$ to $l_{pl}$. Next, the muscle is stimulated. Muscle length is held constant until the stress, generated by the muscle cells, exceeds a certain level, the afterload $T_{al}$. From this moment on, the muscle is allowed to shorten against a constant afterload. After maximum shortening has occurred, the muscle lengthens again due to the decay of active stress. As soon as the muscle has regained its preload length $l_{pl}$, muscle length is held constant again and active stress decreases to zero.

In figure 3.7 experimentally determined (a) and calculated (b) time course of active stress, sarcomere length, and velocity of shortening are shown. In comparison to the calculations, in the experiment (1) maximum active stress is lower, (2) development of stress in time is slower, (3) amount of shortening is similar, and (consequently) (4) velocity of shortening is lower. The low stress level in the experiment is caused by stretch of the noncontracting ends of the muscle probably. Calculated maximum active stress level agrees with data presented by ter Keurs et al. [8], which were discussed in subsection 2.2.3 and shown in figure 2.9a. The slow response can be attributed to the relatively low temperature (29°C) at which the experiments were performed.

Brutsaert et al. [1] showed that, in a typical experiment, time from stimulus to maximum stress in an isometric contraction decreased from 360 ms at 29°C to 200 ms at 37°C. The calculated response agrees reasonably well with the latter value.

References


FIGURE 3.7: Contraction of papillary muscle against different afterloads: (a) experimental data adapted from Brutsaert et al. (1971); (b) data calculated using the model presented in section 2.2.4: sarcomere length in unloaded and preloaded state equals 1.9 μm and 2.1 μm, respectively. Top panel: time course of active stress expressed as active force $F_a$ divided by undeformed cross-sectional area $A_0$. Middle panel: time course of muscle length $l$ normalized by muscle length at preload level $l_{pl}$. Bottom panel: time course of velocity of shortening normalized by $l_{pl}$. Different line types indicate different afterloads.


4

Simulation of a cardiac cycle

4.1 Introduction

4.1.1 Finite element mesh and boundary conditions

In the model, the initial geometry of the left ventricle is rotationally symmetric with respect to its long axis. In the simulation of the mechanical behavior of the normal left ventricle, no spatial variation of material properties is assumed. As a consequence, rotational symmetry of the ventricle will be maintained during the entire cardiac cycle. Thus it is sufficient to consider only a quarter section of the complete ventricle. This quarter section is composed of 27 elements with a total of 208 nodes, as shown in figure 4.1. The position of a node \( I \) in the reference and deformed situation is given by \( x_0^I \) and \( x^I \), respectively:

\[
x_0^I = x_{10}^I e_1 + x_{20}^I e_2 + x_{30}^I e_3
\]

\[
x^I = x_1^I e_1 + x_2^I e_2 + x_3^I e_3
\]

The displacement \( u^I \) of node \( I \) is given by:

\[
u_1^I = u_1^I e_1 + u_2^I e_2 + u_3^I e_3
\]

\[
x_1^I = x_1^I - x_{10}^I
\]

\[
u_2^I = x_2^I - x_{20}^I
\]

\[
u_3^I = x_3^I - x_{30}^I
\]

To maintain rotational symmetry in the quarter ventricle, displacement and pressure field in both cutting planes must be coupled. Considering two corresponding nodes \( I \) and \( J \) in these planes, with coordinates \((a, 0, b)\) and \((0, a, b)\), respectively, the following conditions are imposed:

\[
u_1^J(0, a, b) = -u_2^J(a, 0, b)
\]

\[
u_2^J(0, a, b) = u_2^J(a, 0, b)
\]

\[
u_3^J(0, a, b) = u_3^J(a, 0, b)
\]

\[
p^J(0, a, b) = p^J(a, 0, b)
\]

Additionally, the boundary conditions, discussed in subsection 2.3.1, are applied:

\[
u_2^J = 0 \quad \text{for all nodes } I \text{ in the basal plane}
\]

\[
u_3^J = 0 \quad \text{for node } A \text{ indicated in figure 4.1}
\]

4.1.2 Phases in the cardiac cycle

In figure 4.2 a flow chart is given of the simulation of a cardiac cycle. A complete cardiac cycle is simulated in a finite number of time increments. Within each increment, two iteration loops are performed. In the inner loop the iterative procedure described in section 3.2 is used to fulfill the conditions of conservation of mass, momentum and moment of momentum. The condition to be fulfilled in the outer loop depends on the actual phase in the cardiac cycle. Most of the quantities in this subsection are a result of the model calculations; the quantities that are prescribed in the model are listed in table 4.1.
The diastolic phase

During the diastolic phase ventricular pressure $p_{iv}$ is prescribed. $p_{iv}$ is raised from 0 kPa at $t = 0$ ms to an end-diastolic pressure $p_{ed}$ at $t = t_i$. At $t = t_i$ the depolarization wave is initiated in the apical endocardial part of the left ventricle (section 2.2.5). From here, it spreads across the ventricular wall. Generation of active stress begins immediately after depolarization. As a consequence of the increase of active stress, the mitral valve closes. This moment, $t = t_{ed}$, marks the end of the diastolic phase.

The isovolumic contraction phase

During the isovolumic contraction phase left ventricular volume equals the end diastolic volume: $V_{iv} = V_{ed}$. The ventricular pressure that balances ventricular wall stress at this volume, has to be calculated in the outer iteration loop indicated in figure 4.2. Assuming pressure and volume are known up to $t = t_n$ a first estimate of the ventricular pressure $p_{n+1}$ at $t = t_{n+1} = t_n + \Delta t_{n+1}$ is made using an explicit two-step Adams-Bashforth integration scheme [10]:

$$p_{n+1}^0 = p_n + \frac{1}{2} \left( 3 \left( \frac{\partial p}{\partial t} \right)_n - \left( \frac{\partial p}{\partial t} \right)_{n-1} \right) \Delta t_{n+1}$$  \hspace{1cm} (4.13)

with:

$$\left( \frac{\partial p}{\partial t} \right)_n = \frac{p_n - p_{n-1}}{\Delta t_n}$$  \hspace{1cm} (4.14)

The superscript '0' denotes iteration 0. At this pressure, in the inner iteration loop the deformed state is calculated. Generally, the ventricular volume $V_{n+1}^0$ in this state will not be equal to $V_{ed}$. The volume error $\Delta V_{n+1}^0$ is given by:

$$\Delta V_{n+1}^0 = V_{n+1}^0 - V_{ed}$$  \hspace{1cm} (4.15)
I read input data
- geometry
- material properties
- boundary conditions

inc ← 0

$\begin{align*}
t &← t + \Delta t \\
\text{read input data}
\text{new increment}
\text{calculate contractile element lengths}\ \bar{l}
\text{impose pressure } p_{lw}
\text{estimate nodal positions and pressures } \bar{X}
\text{calculate nodal force and volume imbalances } \bar{R}
\end{align*}$

$\bar{R} < e_0 \ ?$

$\begin{align*}
y &← \text{write output data} \\
t < t_{ed} \ ? \\
p_{lw} < p_{lw,be,\text{min}} \ ? \\
g_a > 0 \ ? \\
t < t_{cycle} \ ? \\
\|V_{lw} - V_{ed}\| < \delta V \ ? \\
\|q_{lw} - q_{a}\| < \delta_q \ ? \\
\|V_{lw} - V_{ce}\| < \delta V \ ?
\end{align*}$

STOP

FIGURE 4.2: Flow chart of the calculations; the inner iteration loop within the dashed box I has been described in chapter 3; the outer iteration loop, within dashed box II, is explained in section 4.1.2.
TABLE 4.1: Input values of characteristic quantities in the cardiac cycle.

<table>
<thead>
<tr>
<th>parameter</th>
<th>value</th>
<th>unit</th>
<th>meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>$P_{lv, ed}$</td>
<td>1</td>
<td>kPa</td>
<td>end-diastolic left ventricular pressure</td>
</tr>
<tr>
<td>$P_{lv, be, min}$</td>
<td>10</td>
<td>kPa</td>
<td>minimal $P_{lv}$ at beginning of ejection phase</td>
</tr>
<tr>
<td>$t_i$</td>
<td>150</td>
<td>ms</td>
<td>moment of initiation of depolarization wave</td>
</tr>
<tr>
<td>$t_{ed}$</td>
<td>200</td>
<td>ms</td>
<td>end of diastolic phase</td>
</tr>
</tbody>
</table>

Using an estimate of ventricular stiffness $\left(\frac{\partial p}{\partial V}\right)$ a new pressure estimate $p_{n+1}^1$ is made:

$$ p_{n+1}^1 = p_{n+1}^0 + \Delta p_{n+1}^1 \quad (4.16) $$

$$ \Delta p_{n+1}^1 = \left(\frac{\partial p}{\partial V}\right) \Delta V_{n+1}^0 \quad (4.17) $$

With the improved estimate $p_{n+1}^1$ the inner iteration loop is repeated, from which a new ventricular volume results. This iterative procedure is repeated until, in iteration $i$, the volume error $\Delta V_{n+1}^i$ is sufficiently small:

$$ |\Delta V_{n+1}^i| \leq \delta_v \Rightarrow \begin{cases} p_{n+1} = p_{n+1}^i \\ V_{n+1} = V_{n+1}^i \end{cases} \quad (4.18) $$

If, at $t = t_n$, the calculated $p_n$ rises above a preset minimal ventricular pressure at the beginning of the ejection phase $p_{lv, be, min}$, the ejection phase starts:

$$ p_n \geq P_{lv, be, min} \Rightarrow \begin{cases} p_{be} = p_n \\ t_{be} = t_n \end{cases} \quad (4.19) $$

The ejection phase

During the ejection phase the left ventricle pumps out blood into the aorta. The aorta is mathematically described by the three-element Windkessel model (section 2.1.4) shown in figure 4.3. For the aortic flow $q_a$ it holds:

$$ q_a = \frac{p_{lv} - p_a}{R_a} \quad (4.20) $$

$$ = \frac{p_a}{R_p} + C_a \frac{\partial p_a}{\partial t} \quad (4.21) $$

This flow $q_a$ should be equal to the rate of change of left ventricular volume $q_v$:

$$ q_v = -\frac{\partial V_{lv}}{\partial t} \quad (4.22) $$

In the model $q_a$ is calculated as follows. Assuming $q_a$ is known up to $t = t_n$ an initial estimate $q_{a,n+1}^0$ of $q_{a,n+1}$ is made according to:

$$ q_{a,n+1}^0 = q_{a,n} + \frac{1}{2} \left(3 \left(\frac{\partial q_a}{\partial t}\right)_n - \left(\frac{\partial q_a}{\partial t}\right)_{n-1}\right) \Delta t_{n+1} \quad (4.23) $$

with:

$$ \left(\frac{\partial q_a}{\partial t}\right)_n = \frac{q_{a,n} - q_{a,n-1}}{\Delta t_n} \quad (4.24) $$
FIGURE 4.3: Three-element Windkessel model simulating aortic impedance.

$q_{a,n+1}$ represents the mean flow during the interval $t_n \leq t \leq t_{n+1}$. Using a discretized form of equations (4.21) and (4.21) estimates for $p_{lv,n+1}$ and $p_{a,n+1}$ are calculated:

\begin{align*}
    p_{a,n+1}^0 &= \frac{q_{a,n+1}^0 + \left( \frac{C_a}{\Delta t_{n+1}} - \frac{1}{2R_p} \right) p_{a,n}}{2R_p + \frac{C_a}{\Delta t_{n+1}}} \\
    p_{lv,n+1}^0 &= p_{a,n+1}^0 + p_{a,n}^0 - p_{lv,n} + 2R_a q_{a,n+1}^0
\end{align*}  \quad (4.25) \quad (4.26)

With this left ventricular pressure the inner iteration loop is performed, yielding a ventricular volume $V_{0,n+1}$ and a ventricular outflow:

\begin{equation}
    q_{lv,n+1}^0 = -\frac{V_{0,n+1} - V_n}{\Delta t_n} \quad (4.27)
\end{equation}

In general, $q_{lv,n+1}^0$ will not be equal to $q_{a,n+1}^0$. The difference in flow, $\Delta q_{n+1}^0$, is given by:

\begin{equation}
    \Delta q_{n+1}^0 = q_{a,n+1}^0 - q_{lv,n+1}^0 \quad (4.28)
\end{equation}

A new estimate $q_{a,n+1}^1$ for $q_{a,n+1}$ is made according to:

\begin{equation}
    q_{a,n+1}^1 = q_{a,n+1}^0 + \frac{\Delta q_{n+1}^0}{\left( \frac{\partial q_{lv}}{\partial q_a} \right) - 1} \quad (4.29)
\end{equation}

The coefficient $\left( \frac{\partial q_{lv}}{\partial q_a} \right)$ is an estimate of the change in $q_{lv}$ due to a change in $q_a$. The procedure (4.26) through (4.29) is repeated until, at iteration $i$, the difference $\Delta q_{n+1}^i$ is sufficiently small:

\begin{equation}
    |\Delta q_{n+1}^i| \leq \delta q \quad (4.30)
\end{equation}

The end of the ejection phase is reached if the calculated flow becomes negative:

\begin{equation}
    q_{a,n} \leq 0.0 \quad (4.31)
\end{equation}

The isovolumic relaxation phase

The isovolumic relaxation phase is simulated analogously to the isovolumic contraction phase, with ventricular volume kept constant at $V_{ce}$. The calculation is ended at a prescribed moment $t = t_{cycle}$. 

- 4.5 -

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{windkessel.png}
\caption{Three-element Windkessel model simulating aortic impedance.}
\end{figure}
4.2 Preliminary calculations

4.2.1 The diastolic phase

The ventricle, proposed in chapter 2, was passively inflated by increasing ventricular pressure. The resulting pressure-volume relationship is plotted in figure 4.4a. Experimentally obtained $pV$-curves are also presented in figure 4.4a. The data by Spotnitz et al. [8] and McCulloch et al. [3] were obtained in isolated dog hearts. Nikolić et al. [4] determined $pV$-curves in the intact dog heart. From figure 4.4a it is apparent that the model left ventricle is too stiff.

The stiff behavior might be caused by (1) an unrealistic choice of the geometry of the left ventricle, or (2) a too stiff passive material behavior. The representation of the left ventricle by a truncated thickwalled ellipsoid with a smooth endocardial surface can be expected to yield a relatively stiff behavior. In the real ventricle, the endocardial surface shows many invaginations that run approximately in longitudinal direction. Thus, the stiffness in circumferential direction in the endocardial part of the ventricular wall will be lower and the ventricle will be more compliant than in the case of a smooth endocardium. This effect is not considered in the model. The high stiffness of the model left ventricle can also be caused by a too stiff passive constitutive relationship. As described in section 2.2, the passive material parameter values were determined from experimental data obtained in excised cardiac tissue. However, it has been shown that stiffening occurs in excised cardiac tissue. For example, McCulloch et al. determined passive pressure-volume curves in isolated dog hearts. At a ventricular pressure of 3.3 kPa, a decrease in ventricular volume of about 10% ($n = 5$) during a 9-minute interval was noticed. A similar stiffening may have been present in the experiments from which the passive material parameter values were estimated.

To obtain a passive pressure-volume relationship that fits within the range of experimental data, it was decided to adapt passive material properties and to maintain the chosen geometry.
TABLE 4.2: Original and adapted values of parameters in the strain-energy function describing passive material behavior: \( W(E) = C \text{exp} [a_1 I^E_B + a_2 I^E_B + a_3 E^2_B + a_4 (E_{33}^2 + E_{32}^2)] \).

<table>
<thead>
<tr>
<th>parameter</th>
<th>( C )</th>
<th>( a_1 )</th>
<th>( a_2 )</th>
<th>( a_3 )</th>
<th>( a_4 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>original value</td>
<td>0.7</td>
<td>5.0</td>
<td>10.0</td>
<td>5.0</td>
<td>0.0</td>
</tr>
<tr>
<td>adapted value</td>
<td>0.5</td>
<td>3.0</td>
<td>6.0</td>
<td>3.0</td>
<td>0.0</td>
</tr>
<tr>
<td>unit</td>
<td>[kPa]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

of the ventricle. The adapted values of the material parameters are listed in table 4.2. With these parameter values, the calculated \( pV \)-relationship matches the experimentally obtained results by Nikolić et al. [4] reasonably well (figure 4.4a).

The sarcomere length distribution at the equator, calculated for the case of the adapted passive material behavior, is shown in figure 4.4b. Starting from a uniform sarcomere length of 1.85 \( \mu \text{m} \) at \( p_{lw} = 0 \) kPa, endocardial sarcomere length increases to about 2.2 \( \mu \text{m} \) at a ventricular pressure of 1.0 kPa. At this pressure epicardial sarcomere length is still below 2.0 \( \mu \text{m} \).

Comparison with the experimental data in figure 2.6 shows that (1) calculated sarcomere lengths are smaller than experimentally determined sarcomere lengths, and (2) transmural variation of calculated sarcomere length is larger than experimentally measured variation. To bring model calculated length in the range of experimental values, sarcomere length at \( p_{lw} = 0 \) kPa was set at 2.0 \( \mu \text{m} \). Transmural sarcomere length variation will be discussed later.

4.2.2 Initial simulation of a complete cardiac cycle

A first simulation of a complete cardiac cycle was performed using the proposed data describing ventricular geometry (table 2.1), initial muscle fiber orientation (table 2.2), passive material behavior (table 4.2), active material behavior (table 2.4), activation sequence (table 2.5), and aortic impedance (table 2.6). Muscle fiber orientation is shown in figure 4.5.

The global hemodynamical behavior of the ventricle is shown in figure 4.6. During the diastolic phase, ventricular pressure is prescribed to increase from 0.0 kPa to 1.0 kPa. Ventricular volume increases from about 28% to about 54% of the wall volume. This increase is obtained by an increase of both ventricular length and diameter. The depolarization wave is initiated at \( t = 150 \) ms. The mitral valve is assumed to close at \( t = 200 \) ms. During the isovolumic contraction phase, active stress is generated by the muscle fibers in the ventricular wall. The increase of active stress is reflected by an increase of ventricular pressure. Although this phase is isovolumic, a considerable change of shape of the ventricle is calculated: the ventricle becomes longer, while its diameter decreases. At \( t = 268 \) ms ventricular pressure increases above 10 kPa, the aortic valve opens and the ejection phase starts. Peak aortic flow (240 ml/s) is reached after about 40 ms. Peak ventricular pressure is about 19.4 kPa. Ventricular volume decreases to 34% of the wall volume. Ejection fraction, defined as \((V_{cd} - V_{ve})/V_{cd}) \times 100\%\), equals 32%. The diameter of the ventricle decreases monotonously. Ventricular length increases during the first part of the ejection phase, followed by a decrease towards the end of this phase. Ejection stops at \( t = 440 \) ms. During the isovolumic relaxation phase, ventricular pressure declines, and finally the ventricle becomes completely passive again. The global deformation of the ventricle is shown in figure 4.7.

To describe local strain in the ventricular wall, six strain components are needed. From a physiological point of view, strain in the muscle fiber direction is the most important component, since it is an important determinant of the level of active stress that is generated in the muscle cell. Muscle fiber strain can be expressed in terms of sarcomere length. In figure 4.8b the sarcomere length \( l_s \) as a function of time is given at 20 points in the ventricular wall. At the beginning of the cycle, the length of all sarcomeres equals 2.0 \( \mu \text{m} \). During the diastolic phase
FIGURE 4.5: Transmural variation of helix fiber angle $\alpha_1$ as assumed in the initial simulation (---) and measured at the equator approximately; (O) Streeter et al. (1969); (□) Greenbaum et al. (1981); (△) Ross et al. (1975); (○) Streeter (1979). Data from Ross et al. (1975) and Streeter (1979) were plotted assuming that the transmural position $\xi^* = -0.5$ coincides with $\xi = -1.0$ (see also figure 2.4).

FIGURE 4.6: Ventricular pressure $p_{tw}$, ventricular volume divided by wall volume $V_{tw}/V_w$, aortic flow $q_a$, change of outer equatorial diameter $\varepsilon_D = (R_o - R_{o,0})/R_{o,0}$ (---) and change of outer ventricular length $\varepsilon_L = (L_o - L_{o,0})/L_{o,0}$ (— —) as a function of time $t$; the dotted lines indicate the end of the diastolic phase and beginning and end of the ejection phase.
FIGURE 4.7: Global deformation of the ventricle at end diastole (200 ms), begin ejection (268 ms), mid ejection (355 ms) and end ejection (440 ms). Deformed and undeformed geometry are given by a solid and dashed line, respectively.

all sarcomeres lengthen: in the subendocardial layers sarcomere length increases to about 2.3 μm, while the subepicardial sarcomeres are stretched to about 2.15 μm. Early in the isovolumic contraction phase, the sarcomeres in the early activated subendocardial regions near the apex shorten quickly. This shortening levels off towards the end of this phase. In the later activated midwall layers the sarcomeres shorten during the entire isovolumic contraction phase. A slight increase of sarcomere length is found in the late activated subepicardial layers at the base. During the ejection phase, the sarcomeres in the subendocardial layers shorten by a relative small amount. At the end of the ejection phase sarcomere length in these layers is still higher than the sarcomere length at the start of the simulation. In the midwall layers sarcomeres shorten to below their initial length. Towards the end of the ejection phase some lengthening can be observed in these regions. In the late activated subepicardial region at the base, sarcomere shortening continues during the first part of the isovolumic relaxation phase. Finally, during the isovolumic relaxation phase all sarcomere lengths return to a level slightly above 2.0 μm, in agreement with the ventricular volume that is slightly higher than the volume at the beginning of the simulation. To obtain this length, the subendocardial sarcomeres shorten, while the sarcomeres in the other layers lengthen.

Of the six stress components that describe the local stress state in the ventricular wall, the component in the muscle fiber direction is the most important one. Particularly the part of this component, that is actively generated by the muscle cells, is important, since it determines the built-up of ventricular pressure. Active muscle fiber stress is zero during the diastolic phase (figure 4.8c). During the isovolumic contraction phase active fiber stress increases. A relatively strong increase in found in the subendocardial layers. In these layers a maximum stress of about 110 kPa occurs shortly after the beginning of the ejection phase, and during the remaining part of the ejection phase active stress decreases to about 70 kPa. During the ejection phase active fiber stress in the midwall and outer layers is relatively constant, ranging from 25 to 50 kPa. In the apical region, active stress is slightly lower. During the isovolumic relaxation phase, active stress decreases rapidly.

An additional indication of the deformation of the ventricle is given in figure 4.8d. Here, the angle of rotation around the long axis of the ventricle at the 20 points is shown. Rotation of the endocardial point at the base was prohibited. In the remaining points, a rotation in
FIGURE 4.8: Sarcomere length $l_s$ (b), active first Piola-Kirchhoff fiber stress $T_a$ (c) and angle of rotation around long axis of the ventricle $\phi_z$ (d) versus time $t$ at 20 points in the ventricular wall, indicated in (a).
positive circumferential direction is observed during the diastolic phase. During the isovolumic relaxation phase, a strong increase of rotation is found. In the basal region, subepicardial layers rotate further than subendocardial layers. This pattern is reversed in the apical region. Near the equator almost no transmural variation of rotation angle is found. During the ejection phase, a slight increase of rotation is found in the basal region. At the end this phase, the rotation angle of the subepicardial layers with respect to the subendocardial layers is about 40°. In the equatorial region almost no change in rotation is observed during the ejection phase. In the apical region, a rotation in negative circumferential direction is observed during the ejection phase. The transmural difference of rotation angle remains approximately constant, the subendocardial angle being about 20° more positive than the subepicardial angle. During the isovolumic relaxation phase a quick decrease of angle of rotation towards zero is observed.

4.2.3 The hypothesis on homogeneous spatial distribution of active muscle fiber stress

To check the validity of the results of the simulation presented in the previous subsection, two questions must be answered: (1) how do the results depend on the choice of the values of the input parameters and (2) how do the results compare with experimental data?

The values of the input parameters were derived from experimental data that are subject to biological variability and measurement errors. For example, a large variation is found in experimentally determined muscle fiber orientations (figures 2.4 and 4.5). Therefore, the choice of the muscle fiber orientation in the simulation presented in the previous subsection is quite arbitrary. From simulations performed with several distributions of muscle fiber orientation, it was found that the spatial distribution of active muscle fiber stress is very dependent on the particular choice of the muscle fiber orientation. Consequently, the result that subendocardial active fiber stress is two to three times as high as active fiber stress in the other parts of the ventricular wall, holds only for this particular distribution of muscle fiber orientation.

An indication for the correctness of the choice of the muscle fiber orientation can be obtained from a comparison of calculated and experimentally obtained results. Calculated variation with time of ventricular pressure and aortic flow seems to be quite realistic. However, the calculated lengthening of the ventricle during the isovolumic contraction and ejection phase has never been measured. In literature, it has been reported that during those phases both ventricular length and diameter decrease [7,5].

Experimental data on the variation of sarcomere length and muscle fiber stress with time are not available. If the calculated high subendocardial active stresses are realistic, in the subendocardial layers energy requirement should be much higher than in the other layers. However, experimental physiological and biochemical data indicate that no major transmural differences in energy requirements exist under normal circumstances [9]. Moreover, it has been noted that biological tissue adapts to changes in mechanical loading. For example, in the case of a chronic increase of left ventricular pressure, the left ventricular wall becomes thicker, thereby reducing increased wall stress to normal values. This process of adaptation might indicate the existence of a certain level of optimal mechanical loading of the muscle cells. Since no differences between muscle cells in different parts of the ventricular wall have been found, mechanical loading might be homogeneously distributed across the ventricular wall.

The hypothesis that active muscle fiber stress is distributed homogeneously across the ventricular wall was introduced by Arts [1]. Applying this hypothesis to the present model, the transmural distribution of the helix fiber angle $\alpha_1$ was adapted until a homogeneous distribution of active fiber stress was found. The resulting simulation is discussed in the next subsection.
4.2.4 Adaptation of the transmural distribution of the helix fiber angle

In the model, the helix fiber angle distribution was adapted according to the physiological adaptation mechanism described in the previous subsection. Adaptation of the ventricle to the large subendocardial stress levels can be obtained by a thickening of the subendocardial layers. As a consequence, the helix fiber angle distribution shifts towards the epicardium. After performing several simulations, the muscle fiber orientation as shown in figure 4.9 was chosen. It should be noted that this orientation still lies within the range of experimentally determined values. The global hemodynamical behavior of the ventricle, as calculated with the adapted helix angle distribution, is shown in figure 4.10a. Compared to the previous simulation, the ventricle is slightly more compliant: end diastolic ventricular volume equals about 56% of the wall volume. The ejection phase starts earlier \( t = 258 \) ms and lasts longer (up to \( t = 444 \) ms). Peak ventricular pressure \( 20.8 \) kPa and peak aortic flow \( 280 \) ml/s are higher. At the end of the ejection phase, ventricular volume equals 31% of the wall volume, yielding an ejection fraction of 45%. Thus, in this simulation ventricular performance is higher than in the previous simulation. In contrast to the situation in the previous simulation, ventricular diameter and length change more similarly.

In the equatorial region, distribution of active muscle fiber stress across the ventricular wall has become quite homogeneous, as can be observed in figure 4.10c). In the basal region homogeneity is less than in the equatorial region, while in the apical region stress is slightly lower than in the other parts of the wall.

Variation of sarcomere length \( l_s \), shown in figure 4.8b, is also more similar in different parts of the ventricular wall. During the diastolic phase, the stretch of the sarcomeres in the endocardial region is lower, compared to the stretch in the previous simulation. During the ejection phase, sarcomere shortening in the subendocardial region has increased considerably. The reduced level
FIGURE 4.10: Results of the simulation with adapted helix fiber angle distribution: (a) parameters describing global ventricular hemodynamical behavior, (b) sarcomere length \( l_s \), (c) active first Piola-Kirchhoff fiber stress \( T_a \) and (d) rotation angle around long axis of the ventricle \( \phi_z \). See figures 4.6 and 4.8 for additional information.
of active stress in this region is a direct consequence of the lower sarcomere length and greater shortening velocity.

The angle of rotation around the long axis of the ventricle is shown in figure 4.10d. The overall pattern is similar to the pattern found in the previous simulation. The magnitude of rotation has decreased slightly in all parts of the ventricle.

4.2.5 Introduction of the transverse fiber angle

The simulation, presented in the previous subsection, is more realistic than the initial simulation. Firstly, the active fiber stress is distributed rather homogeneously across the ventricular wall. As argued in subsection 4.2.3, this homogeneity may be expected on the basis of experimental data on metabolism in the ventricular wall. Secondly, the global deformation agrees better with experimental observations [7,5].

Experimental data on the rotation of the endocardium and epicardium around the long axis from end diastole to end systole show that rotation increases with increasing distance from the base [2]. In the basal plane, rotation of the endocardial and epicardial surface was measured to be equal. Epicardial rotation angles at the equatorial and apical level were found to be 3.7 ± 0.8° and 11.2 ± 1.3°, respectively. Comparison of calculated and measured angles of rotation shows that (1) calculated angles are higher than measured angles and (2) calculated transmural variation of rotation angle at the basal and apical level is higher than measured transmural variation.

The large transmural differences in rotation are most likely caused by the choice of the muscle fiber direction. In both previous simulations, it was assumed that muscle fibers are located in surfaces parallel to the endocardium and epicardium. Because of the transmural variation of the helix fiber angle, shear stresses act between those parallel surfaces. These shear stresses can only be counteracted by the passive material. The stiffness of the passive material is low compared to the stiffness of the activated muscle fibers. Therefore, the shear stresses induced by the activated muscle fibers are counteracted only at high shear strains, or large transmural differences in angle of rotation. A possible mechanism to prevent these transmural shears, lies in the introduction of a cross-over of the muscle fibers between the subendocardial and subepicardial layers. Experimentally, such a cross-over can be readily observed. However, quantitative data on this cross-over, which can be described by the transverse fiber angle \( \alpha_3 \), are scarce.

In chapter 2, subsection 2.1.3, the transmural course of the transverse fiber angle has been modeled by a quadratic function of the normalized transmural coordinate. Until now, the amplitude of this function has been set at zero. To reduce transmural shear, a number of simulations were performed with non-zero values of \( \alpha_3 \). The aim of these simulations was to determine a combination of helix and transverse fiber angle distribution, at which maximum transmural differences in rotation angle are reduced to approximately 10°. The resulting simulation is presented in the next section.

4.3 The reference cardiac cycle

The simulation of a cardiac cycle presented in this section is expected to approximate the behavior of the real left ventricle reasonably well. It is based upon the data, presented in chapter 2, regarding ventricular geometry (table 2.1), active material behavior (table 2.4), activation sequence (table 2.5) and aortic impedance (table 2.6). For the description of the passive material behavior, the adapted values presented in table 4.2 are used. Muscle fiber orientation is chosen so, that (1) active muscle fiber stress is distributed approximately homogeneously across the left ventricular wall (subsection 4.2.3) and (2) transmural differences in angle of rotation around the long axis of the ventricle are less than 10° (subsection 4.2.5). The boundary conditions at the
base were changed slightly. Each point in the basal plane was assumed to move in a plane defined by the local $\xi$ and $\phi$ direction. This change was made to approximate better the influence of the structures attached to the base, such as the annuli fibrosi and the valves. The muscle fiber orientation, used in this simulation, is shown in figure 4.11. The transmural variation of the helix fiber angle $\alpha_1$ is only slightly different from that in the previous simulation.

The global hemodynamical behavior of the ventricle, shown in figure 4.12a, is very similar to the behavior found in the previous simulation (subsection 4.2.4). The ejection phase strats at $t = 254$ ms and ends at $t = 446$ ms. Ventricular volume at the beginning and end of the ejection phase equals 57% and 31% of the wall volume, respectively. The ejection fraction equals 45%. Peak ventricular pressure equals 21.1 kPa. Peak aortic flow equals 264 ml/s. In comparison to the previous simulation, ventricular stiffness in axial direction has increased. During the isovolumic contraction phase, no change in ventricular diameter and length is calculated. During the ejection phase, ventricular diameter and length decrease similarly. Towards the end of the ejection phase and in the beginning of the isovolumic relaxation phase, a slight oscillation in ventricular length is calculated.

Sarcomere length, shown in figure 4.12b, varies with time rather similarly in all parts of the ventricular wall. During diastole, subepicardial sarcomeres are stretched slightly less than the sarcomeres in the other parts of the wall. During the isovolumic contraction phase, all sarcomeres shorten, except for the sarcomeres in the late activated regions. In the latter regions, in the basal epicardial part of the ventricle, sarcomere length is constant or increases, due to the active stress generated in the early activated regions. During the ejection phase, the sarcomeres in the equatorial and equatorial-basal level shorten to their initial length approximately. In the equatorial-apical and apical region sarcomeres shorten to below their initial length. Towards the end of the ejection phase these sarcomeres lengthen already. In the basal region, no consistent

FIGURE 4.11: (a) Transmural variation of helix fiber angle $\alpha_1$ as assumed in the reference simulation (---) and measured at the equator approximately; (O) Streeter et al. (1969); (□) Greenbaum et al. (1981); (Δ) Ross et al. (1975); (○) Streeter (1979) (see also figure 4.5). Helix angle distribution in the previous simulations is indicated by the dotted line. (b) Transmural variation of transverse fiber angle $\alpha_3$ at the base (- - -) and at the apex (---). At the equator, $\alpha_3$ equals zero.
FIGURE 4.12: Results of the reference simulation: time course of (a) parameters describing global ventricular hemodynamics behavior, (b) sarcomere length $l_s$, (c) active first Piola-Kirchhoff fiber stress $T_a$ and (d) rotation angle around long axis of the ventricle $\phi_z$. See figures 4.6 and 4.8 for additional information.
The pattern of sarcomere shortening is found. During the isovolumic relaxation phase sarcomere length returns to a level slightly above the initial length of 2.0 \( \mu m \).

Active muscle fiber stress as a function of time is plotted in figure 4.12c. At the equatorial level and the levels directly above and below this level active fiber stress is distributed approximately homogeneously across the ventricular wall. In the apical and subendocardial basal region, active stress is slightly lower.

The angle of rotation of the various points around the long axis of the ventricle is plotted in figure 4.12d. In comparison to the previous simulation, the magnitude of rotation has decreased. In the basal plane, rotation has almost disappeared. In the equatorial-basal plane, rotation angle decreases from endocardium to epicardium. In the remaining three planes, almost no transmural differences in angle of rotation are present. The magnitude of rotation in the equatorial and equatorial-basal plane is approximately equal. At the apical level, angles of rotation are higher.

The global deformation pattern of the ventricle is shown in figure 4.13. In contrast to the situation in the previous simulations, no uniform wall thickening is found during the ejection phase.

### 4.4 Variation of input parameter values

In section 4.2 and 4.3 it has been shown that the local mechanical behavior of the left ventricle depends strongly upon the choice of the muscle fiber orientation. In this section the influence will be investigated of a change of other input parameters, such as (1) the activation sequence of the ventricle, (2) the active stress-strain relationship and (3) the afterload of the ventricle.

#### 4.4.1 Simultaneous activation of the ventricle

The ventricle was activated simultaneously by increasing the conduction velocity \( v_c \) (subsection 2.2.5) from 1.5 m/s to 1500 m/s. The moment of initiation of the activation wave, \( t_i \), was shifted from 150 ms to 180 ms. Thus, timing of the global hemodynamical behavior in this simulation and the reference simulation became similar.
FIGURE 4.14: Results of the simulation of a cardiac cycle in which the ventricle is activated simultaneously (——), compared with results from the reference simulation (- -); (a) parameters describing global ventricular hemodynamical behavior; zero levels for change in ventricular diameter $\varepsilon_D$ and length $\varepsilon_L$ have been separated for clarity; (b) sarcomere length $l_s$, (c) active first Piola-Kirchhoff fiber stress $T_a$ and (d) rotation angle around long axis of the ventricle $\phi_z$. See figures 4.6 and 4.8 for additional information.
In figure 4.14a, the hemodynamical behavior is plotted. The slight disturbance around $t = 380$ ms is caused probably by choosing the allowed flow error $\delta q$ too large (subsection 4.1.2). Apart from this disturbance, no significant alterations are introduced by the change in activation pattern. Ventricular length increases during the isovolumic contraction phase, whereas the oscillation at the end of the ejection phase has almost disappeared. Variation of sarcomere length with time has become similar in different parts of the ventricle (figure 4.14b). During the isovolumic contraction phase, the relatively large sarcomere shortening in the early activated regions and the sarcomere stretch in the late activated regions have disappeared. The distribution of active stress is similar to that found in the reference simulation (figure 4.14c). The pattern of rotation has remained unchanged in the basal region and the region directly below it. In the other regions two effects can be observed: (1) the magnitude of rotation has decreased and (2) during the isovolumic relaxation phase, rotation angles decrease to zero monotonously (figure 4.14d).

### 4.4.2 Reduced contractility of the muscle fiber cells

In this simulation the active stress-length relationship was altered by setting $a = 0.85 \cdot 10^6$ m$^{-1}$ and $l_s = 2.2$ $\mu$m. Compared to the original stress-length relationship (figure 2.10b), the increase of active stress with sarcomere length is slower, while active stress levels of at $l_s > 2.2$ $\mu$m. This change simulates the effect of decreased contractility due to a reduced [Ca$^{2+}$] level (figure 2.9b).

The reduced contractility is reflected by a lower global performance of the ventricle: maximum ventricular pressure and ejection fraction decrease (figure 4.15a). The magnitude of sarcomere shortening during the ejection phase has decreased also. However, the pattern of shortening is very similar to the pattern found in the reference simulation (figure 4.15b). A similar change is found in the active muscle fiber stress: maximum stress level has decreased, but the homogeneous distribution of active stress across the ventricular wall has remained (figure 4.15c). Finally, in the pattern of rotation around the long axis of the ventricle only a minor change has occurred: during the isovolumic relaxation phase, no negative rotation angles are found (figure 4.15d).

### 4.4.3 Aortic occlusion

The influence of a change in afterload conditions was investigated by preventing the aortic valve from opening. Thus, an isovolumic cardiac cycle results. Ventricular pressure rises to about 28 kPa. During the active phase, only minor changes in ventricular shape are calculated (figure 4.16a). Sarcomere length is affected after the moment at which ejection starts in the reference cardiac cycle (figure 4.16b). In the period during which the ventricle would eject under normal circumstances, sarcomere length remains constant approximately. Thereafter, sarcomere length returns to the end diastolic level. Like in the previous simulations, active muscle fiber stress is distributed approximately homogeneously across the ventricular wall (figure 4.16c). Maximum stress level is higher, since sarcomeres are longer and sarcomere shortening velocity is lower. The period of generation of active stress is prolonged, because sarcomere length is higher. These changes in active stress are reflected by a change in ventricular pressure. The changes in the pattern of rotation and sarcomere length are similar. Rotation angles are unaffected until the moment at which ejection would start normally. In the period, during which ejection would take place normally, rotation angles remain constant approximately. Finally, rotation angles decrease towards the end diastolic level monotonously (figure 4.16d).
FIGURE 4.15: Results of the simulation of a cardiac cycle in case of reduced contractility of the muscle fibers (–––), compared with results from the reference simulation (––): (a) parameters describing global ventricular hemodynamical behavior; (b) sarcomere length \( l_s \), (c) active first Piola-Kirchhoff fiber stress \( T_a \) and (d) rotation angle around long axis of the ventricle \( \phi_z \).
FIGURE 4.16: Results of the simulation of a cardiac cycle with aortic occlusion (- - -), compared with results from the reference simulation (---); time course of (a) parameters describing global ventricular hemodynamical behavior; (b) sarcomere length $l_s$, (c) active first Piola-Kirchhoff fiber stress $T_a$ and (d) rotation angle around long axis of the ventricle $\phi_z$; see figure 4.14 for additional information.
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FIGURE 4.17: Ventricular pressure $p_v$, aortic flow $q_a$, change of outer equatorial diameter $\varepsilon_D = (R_o - R_{o,ed})/R_{o,ed}$, change of outer ventricular length $\varepsilon_L = (L_o - L_{o,ed})/L_{o,ed}$, and change of equatorial wall thickness $\varepsilon_h = (h - h_{ed})/h_{ed}$ as a function of time $t$; the dotted lines indicate the end of the diastolic phase and beginning and end of the ejection phase; (a) experimental data adapted from Olsen et al., 1981; (b) results from reference simulation.

4.5 Comparison with data derived from literature

To check the validity of the model, in this section calculated and experimentally determined data on global hemodynamical behavior, epicardial fiber strain and rotation angle are compared.

4.5.1 Global hemodynamical behavior

Olsen et al. studied left ventricular minor and major axis diameters and equatorial wall thickness in the conscious dog with chronically implanted pulse-transit ultrasonic dimension transducers [5]. Representative dimension, flow, and pressure data are shown in figure 4.17a. Using a geometric model, presented by Olsen et al., and assuming papillary muscle volume to be 4% of the wall volume (subsection 2.1.1), the following volumina can be calculated from the deformation data: $V_{ed} = 55$ ml, $V_{ve} = 26$ ml, $V_w = 76$ ml. These data indicate that the ventricle is working under high preload conditions (high end diastolic pressure and volume).

The experimental data are compared with the calculated data, presented in figure 4.17b. Relative duration of isovolumic contraction phase and ejection phase is similar for both cases. Magnitudes of ventricular pressure and aortic flow are similar too. In contrast to the simulation, in the experiment maximum ventricular pressure is reached early in the ejection phase. This difference might be caused by a difference in afterload conditions. In agreement with the large ejection fraction in the experiment, measured change of outer ventricular diameter is larger than calculated change. The ventricular lengthening, measured during the isovolumic contraction phase, is not found in the simulations. Moreover, the oscillation in calculated ventricular length towards the end of the ejection phase is not found experimentally. In fact, the time course of ventricular length, as found for the case of simultaneous activation (subsection 4.4.1), agrees better with the experimental data. Finally, calculated change in equatorial wall thickness is
FIGURE 4.18: Epicardial fiber strain: (a) locations A, B, and C where data are presented; (b) experimentally determined epicardial fiber strain $\epsilon_f = (l_f/l_{f,ed}) - 1$ at two locations at the level B (- - -) and two locations at level C (- -); data adapted from Prinzen et al. (1990); (c) experimentally determined epicardial fiber strain at lately (- ----) and early activated (- -); regions; data adapted from Prinzen et al. (1990); (d) calculated epicardial sarcomere length at nodes A (- - -), B (- -) and C (- -). Note that the vertical axis corresponds to 30% fiber strain in all three figures.

relatively high, compared to the measured change. Since equatorial wall thickening increased strongly after introduction of the transverse fiber angle $\alpha_3$ (section 4.3), this might indicate that the value of $\alpha_3$ was chosen too large. On the other hand, the deformation pattern presented in figure 4.13 shows that measured wall thickening may be very dependent on the actual site of measurement.

4.5.2 Epicardial fiber strain

Prinzen et al. measured epicardial fiber strain in the anesthetized open-chest dog using a video technique [6]. Fiber strains were determined on the anterior wall of the left ventricle in a region with a size of 15-20 cm². Representative strain data are shown in figure 4.18b. Under conditions of atrial pacing, fiber strain was found to be distributed homogeneously across this part of the epicardial surface. The homogeneous pattern of fiber strain disappeared under conditions of ventricular pacing (figure 4.18c). In early activated regions, a relatively strong fiber shortening was found during the isovolumic contraction phase, while fiber shortening during the ejection phase was less than during atrial pacing. In late activated regions, fibers were stretched during the isovolumic contraction phase. In the latter regions, fiber shortening during the ejection phase was stronger than during atrial pacing, and shortening continued during the first part of the isovolumic relaxation phase.
In figure 4.18d, variation of sarcomere length with time is shown, as calculated in the model. The difference in variation of sarcomere length with time between points B and C is larger in the model than in the experiments. The calculated pattern of sarcomere length in the lately activated point A is similar to the measured pattern of fiber strain in lately activated regions during ventricular pacing (figure 4.18c). These findings suggest that in the model the activation wave travels across the ventricular wall too slowly. It is also possible, that the description of the early systolic rise of active muscle fiber stress should be adapted, so that early systolic fiber stretch is prevented.

4.5.3 Rotation around the long axis of the ventricle

Buchalter et al. measured rotation of the endocardial and epicardial surface in eight normal humans, using magnetic resonance imaging [2]. Rotation angles were measured at eight locations in circumferential direction, at five longitudinal levels. Differences \( \Delta \phi_z \) between end systolic and end diastolic rotation angles, averaged over the eight subjects and the eight circumferential locations, are plotted in figure 4.19. At the base, no transmural differences in rotation angle were found. \( \Delta \phi_z \) increased with increasing distance from the base, endocardial values being about twice as high as epicardial values.

Calculated endocardial values of \( \Delta \phi_z \) are very different from measured values. The pattern of calculated epicardial \( \Delta \phi_z \) agrees reasonably well with the measured pattern, except for the basal level.

Apparently, the calculated pattern of rotation is not very realistic. Adaptation of the transverse fiber angle distribution might yield results, that agree better with experimental data. As a second possibility, longitudinal variation of the helix angle distribution might be introduced into the model.

References


Conclusions and recommendations

5.1 Conclusions
In this study a mathematical model was developed to simulate mechanical behavior of the left ventricle during a cardiac cycle. Cardiac cycles were simulated with several choices of the model parameter values, resulting into the following conclusions.

- The distribution of active muscle fiber stress across the ventricular wall depends primarily on the transmural distribution of the helix fiber angle $\alpha_1$. Since a large variation is found in experimental data on the spatial distribution of $\alpha_1$, the active stress field in the ventricular wall could not be predicted accurately in a straightforward analysis, starting from anatomical data. Consequently, in the model the spatial distribution of $\alpha_1$ was chosen so, that the spatial distribution of active muscle fiber stress was approximately homogeneous.

- The distribution of the differences in angle of rotation around the long axis of the ventricle depends primarily on the spatial distribution of the transverse fiber angle $\alpha_3$. Anatomical data on the spatial distribution of $\alpha_3$ are scarce and display a large variation. In the model, the spatial distribution of $\alpha_3$ was chosen so, that transmural differences in angle of rotation were smaller than about $10^\circ$.

- The spatial distribution of active muscle fiber stress and angle of rotation around the long axis of the ventricle remained almost unchanged in the case of (1) change of activation sequence of the ventricle, (2) change of active stress-strain relationship and (3) aortic occlusion.

- The present model describes the variation in time of ventricular pressure, ventricular volume and aortic flow quite well.

- The variation in time of ventricular pressure, ventricular volume and aortic flow remained quite unaffected in simulations with significant differences in local mechanical behavior (muscle fiber stress and strain, angle of rotation around long axis).

5.2 Recommendations
In future research, attention should be focussed on the following aspects.

- The calculated pattern of rotation of the ventricle around its long axis does not agree very well with experimental data. Further adaptation of the transverse fiber angle distribution might improve the model in this respect. Variation of the helix fiber angle orientation in longitudinal direction might have to be included into the model also.

- The calculated results were found to agree better with experimentally obtained results, if it was assumed that the ventricle is activated simultaneously. Moreover, preliminary investigations, not included in this report, showed that the distribution of muscle fiber work across the ventricular wall is quite inhomogeneous in the present model. Experimental data on metabolism in the ventricular wall suggest a rather homogeneous spatial distribution of muscle fiber work. In the model, a more homogeneous distribution could be obtained if the ventricle was activated simultaneously. However, the real ventricle is not activated simultaneously. Therefore, these findings suggest that the model for the description of active
muscle fiber stress might have to be adapted. Attention should be focussed especially on the description of the early systolic rise of active muscle fiber stress.

- The present model may be used to simulate the mechanical behavior of the infarcted ventricle and the ventricle in which the activation sequence is disturbed.
Basic continuum mechanics

A.1 Deformation and strain

Consider a three-dimensional body. Every material point of this body can be labeled uniquely by a set of three material coordinates $\xi$:

$$\xi^T = [\xi_1 \ \xi_2 \ \xi_3] \quad (A.1)$$

During deformation the position vector $x$ of a material point changes. In general $x$ will be a function of $\xi$ and $t$:

$$x = x(\xi, t) \quad (A.2)$$

Local deformation of a body can be described by the deformation gradient tensor $F$. This tensor describes how an infinitesimal material vector $dx_0$ in the reference situation is transformed into a vector $dx$ in the deformed situation:

$$dx = F \cdot dx_0; \quad F = (\nabla_0 x)^T$$

$F$ contains information on the change of both orientation and shape of the body. Stresses in the body are related to change in shape, and not to change in orientation. Thus, a measure of strain is defined that describes only the shape change component of the deformation process, the Green-Lagrange strain tensor $E$:

$$E = \frac{1}{2} (F^c \cdot F - I) \quad (A.4)$$

The relative change in length $\lambda(e_0)$ of the material vector $dx_0$ can be expressed as:

$$\lambda(e_0) = \frac{\|dx\|}{\|dx_0\|} = (dx_0 \cdot (2E + I) \cdot dx_0)^{1/2} \quad (A.5)$$

Consider two material vectors $dx_{01}$ and $dx_{02}$, that are transformed into $dx_1$ and $dx_2$, respectively. The angle between the elements equals $\gamma_0$ and $\gamma$ in the undeformed and deformed situation, respectively, with:

$$\gamma_0 = \arccos \left( \frac{dx_{01} \cdot dx_{02}}{\|dx_{01}\| \|dx_{02}\|} \right) \quad (A.6)$$

$$\gamma = \arccos \left( \frac{dx_1 \cdot dx_2}{\|dx_1\| \|dx_2\|} \right) \quad (A.7)$$

$$\gamma = \arccos \left( \frac{dx_{10} \cdot (2E - I) \cdot dx_{20}}{(dx_{01} \cdot (2E - I) \cdot dx_{01})^{1/2} (dx_{02} \cdot (2E - I) \cdot dx_{02})^{1/2}} \right) \quad (A.8)$$

The volumes $dV$ and $dV_0$ of a material element in the deformed and undeformed situation, respectively, are mutually related according to:

$$dV = \det(F) \ dV_0 \quad (A.9)$$
A.2 Stress

Consider an infinitesimal surface with normal vector $n_0$ and area $dA_0$. Upon application of a force $df$, this surface deforms according to a deformation gradient tensor $F$. The deformed surface has a normal vector $n$ and an area $dA$. The local stress state in the material is given by the Cauchy stress tensor $\sigma$. This tensor relates the applied force to the deformed surface:

$$df = \sigma^c \cdot n \, dA$$

(A.10)

In experiments to determine the stress-strain behavior of materials, applied force is related to the undeformed area usually:

$$df = T^c \cdot n_0 dA_0$$

(A.11)

The tensor $T$ is called the first Piola-Kirchhoff stress tensor. $\sigma$ and $T$ are related according to:

$$\sigma = \det(F) \cdot F^{-1} \cdot T$$

(A.12)

The mechanical behavior of an elastic material is described by a constitutive equation, relating some measure of stress to some measure of strain. For the case of large deformations, the Green-Lagrange strain tensor $E$ is an appropriate strain measure. The condition that the constitutive equation must be independent of rigid body motion, leads to the conclusion that in this equation $E$ must be coupled to the second Piola-Kirchhoff stress tensor $P$, which is defined as:

$$P = \det(F) \cdot F^{-1} \cdot (\sigma^d)^c \cdot F^{-e}$$

(A.13)

In an incompressible material only the deviatoric part $\sigma^d$ of $\sigma$ is uniquely related to the deformation of the material. In this case it is advantageous to write the Cauchy stress tensor as the sum of its deviatoric part and a hydrostatic pressure $p$:

$$\sigma = \sigma^d - pI; \quad p = -\frac{1}{3} \text{tr}(\sigma)$$

(A.14)

The second Piola-Kirchhoff stress tensor $S$, related to the deviatoric Cauchy stress tensor, is defined as:

$$S = \det(F) \cdot F^{-1} \cdot (\sigma^d)^c \cdot F^{-e}$$

(A.15)