A finite element model of the urinary bladder

Citation for published version (APA):

Document status and date:
Published: 01/01/1997

Document Version:
Publisher’s PDF, also known as Version of Record (includes final page, issue and volume numbers)

Please check the document version of this publication:
• A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
• The final author version and the galley proof are versions of the publication after peer review.
• The final published version features the final layout of the paper including the volume, issue and page numbers.

Link to publication

General rights
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

• Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
• You may not further distribute the material or use it for any profit-making activity or commercial gain
• You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the “Taverne” license above, please follow below link for the End User Agreement:
www.tue.nl/taverne

Take down policy
If you believe that this document breaches copyright please contact us at:
openaccess@tue.nl
providing details and we will investigate your claim.
A finite element model of the urinary bladder

A.J. van Beek

January 30, 1997

WFW 97.012

This project was a part of the post-masters programme in technical design "Computational Mechanics". The project was performed under supervision of P.H.M. Bovendeerd and J.D. Janssen (Dept. of Mechanical Engineering, University of Technology Eindhoven) and J.L. van Leeuwen (Dept. of Physiology, Leiden University).
A.J. van Beek
'A finite element model of the urinary bladder'/
/Beek, A.J. van ;
Ontwerpers opl. Computational Mechanics
Met lit. opg.
ISBN 90-5282-738-9
Trefw.: Biomechanics / Bladder / Modelling
Summary

In the lower urinary tract, the bladder maintains a double function. In the collection phase, it functions as a reservoir for urine. During the micturition phase, the bladder wall contracts, while the urethral sphincter relaxes and urine is expelled from the body.

Modelling is an important tool to gain insight into the functioning of the urinary tract. Therefore, several models of the lower urinary tract have been developed. In all these models, the mechanics of the bladder are greatly simplified. They are based on a spherical shape, assuming a homogeneous distribution of parameters like stress, strain and activation.

Aim of this project is to model the mechanics of the bladder in more detail. To achieve this, the finite element method is used. This method offers the possibility to model bladder geometry in more detail, and to include spatial variation of parameters such as stress, strain, activation and muscle fibre orientation. In this way, it is possible to gain insight into local bladder wall mechanics.

The presented model has the following properties:
The initial geometry is a thick-walled sphere. Initial bladder volume is equal to the wall volume. The passive material behaviour is three-dimensional and it is modelled as a incompressible, isotropic, nonlinearly elastic material. Active behaviour is modelled in the local fibre direction and depends on time (activation), strain and strain rate. Inertial forces and gravity forces are neglected. The urethra is modelled using a impedance consisting of two elements, an inertia and a resistance.

Because there are no quantitative data for fibre direction available, we simulated bladder contraction with three different geometries for the fibre direction of the muscle bundles. In the first case, the fibres were arranged in parallel circles, in the second the fibres ran longitudinally, like meridians, and in the last case they were arranged with a varying fibre direction from inner to outer wall.

From the three simulations we conclude that it is possible to model the large deformations that occur in the bladder with the finite element method. However, many input parameters that are necessary for this method are unknown. With respect to three-dimensional material behaviour and muscle fibre geometry, more experiments are required.

Different fibre geometries were found to result in dissimilar local mechanics, while the urodynamic results are comparable. For that reason, urodynamic measurements are not appropriate to validate the bladder model. A good validation requires experimentally obtained results of local mechanics.
Contents

Summary

1 Introduction
  1.1 General introduction ........................................... 2
  1.1.1 Aim of the project ........................................ 2
  1.1.2 Outline of this report .................................... 3
  1.2 Anatomy and physiology ....................................... 3
  1.2.1 Gross anatomy and physiology ............................. 3
  1.2.2 Musculature ................................................. 4
  1.2.3 Microscopic structure of the bladder: ..................... 5

2 Modelling bladder smooth muscle
  2.1 Equilibrium equations ......................................... 7
  2.2 Constitutive equations for bladder smooth muscle .......... 8
  2.2.1 Passive material behaviour ................................ 8
  2.2.2 Active material behaviour .................................. 11
  2.3 Numerical solution procedure ................................ 14
  2.4 Testing the element ............................................ 16

3 Modelling the bladder and urethra .............................. 18
  3.1 Geometry ....................................................... 18
  3.2 Boundary conditions .......................................... 19
  3.2.1 Kinematic boundary conditions ............................ 19
  3.2.2 Modelling the urethral impedance ......................... 19
  3.2.3 Dynamic boundary conditions .............................. 20

4 Results of the simulations ......................................... 22
  4.1 Simulating the collection phase .............................. 22
  4.2 Simulation of micturition .................................... 22
  4.2.1 Preliminary results ....................................... 22
  4.2.2 Fibres arranged in parallel circles ...................... 23
  4.2.3 Fibres arranged as longitudinal meridians ................ 30
  4.2.4 Fibres arranged with a variable angle .................... 33
Chapter 1

Introduction

1.1 General introduction

Urine incontinence is an extensive problem. In the Netherlands, approximately 0.7 million people of both sexes, suffer from lower urinary tract disorders. Although these problems happen to people of all ages, this number is expected to increase as a result of aging of the population.

Lower urinary tract disorders are not only socially inconvenient. Occasionally, they can even be lethal. For example, for some children, these problems can lead in a short period to irreversible kidney damage.

Urination is a finely tuned, coordinated neuromuscular event. Urinary tract disorders often have a muscular or neurological origin. To understand lower urinary tract functioning, both aspects and their interaction have to be investigated. Although a vast amount of research in urology is concentrated on this subject, it has not been understood completely yet. In many cases, urologists have insufficient means to distinguish between these causes.

Modelling is an important tool to gain insight in the functioning of the urinary tract. Therefore, several models of the lower urinary tract have been developed [13, 22, 23, 34, 37]. In all these models, the mechanics of the bladder are greatly simplified. They are all based on a spherical shape of the bladder, assuming a homogeneous distribution of parameters like stress, strain and activation.

1.1.1 Aim of the project

Aim of this project is to model the mechanics of the bladder in more detail. To achieve this, the finite element method (FEM) is used. This method offers the possibility to model bladder geometry in more detail, and to include spatial variation of parameters such as fibre orientation, stress, strain and activation. Therefore, this method is suitable to gain insight in local bladder wall mechanics.

In future, this mechanical model could be integrated in a neural control model. This combination would form an efficient tool for testing hypotheses of neuromuscular interaction in the bladder. For instance, to investigate the influence of various activation patterns on the bladder wall on the dynamics of micturition. When reliability is proven, such a model could
be useful as a tool to make a correct diagnosis of urinary tract disorders.

1.1.2 Outline of this report

In the following part of this chapter, the anatomy and physiology of the bladder are described. The method used to model bladder wall tissue is demonstrated in chapter 2. In chapter 3, the model containing the bladder and urethra is presented. The results that are obtained with this model are shown in chapter 4. Finally, in chapter 5, the model and the results are discussed. Also the conclusions and recommendations are presented in this chapter.

1.2 Anatomy and physiology

1.2.1 Gross anatomy and physiology

In the field of urodynamics, the urinary tract is divided in an upper and a lower urinary tract. The upper urinary tract is formed by the kidneys and ureters, the lower tract consists of the bladder and urethra. Figure 1.1 shows a diagram of the anatomy of the lower urinary tract. The bladder is situated in the anterior part of the pelvic cavity. The ureters transport urine from the kidneys to the bladder. They enter the bladder at the dorso-caudal side. The bladder outlet, the urethra, originates at the caudal end. The largest part of the bladder wall is formed by the detrusor muscle. A slightly different structure is found in the trigone, the triangle shaped area that lies between the outlets of the ureters and the opening of the urethra. The part of the bladder that forms the entrance to the urethra, is called the bladder neck or base (see figure 1.2). This part is found to be histologically distinct from the detrusor [17].

Figure 1.2 shows that the empty bladder appears to have the form of a tetrahedron with the corners at the left and right ureter outlet, the bladder neck and the apex at the anterior side. When distended, the bladder becomes more spherical, with the base remaining fixed. Contact of the bladder with structures in the pelvis depends on the state of filling of bladder and rectum.
The function of the lower urinary tract is maintaining continence. Two phases are distinguished in which bladder and urethra both have opposite functions. In the collection phase, the bladder functions as a temporary reservoir of urine that is produced in the kidneys continuously. The collected urine is expelled from the body during the micturition phase. The realization of this double function is achieved by the musculature of the bladder and urethra wall, and the urethral sphincter. The detrusor and the internal sphincter, both consist of smooth muscle, while the external urethral sphincter consists of striated muscle.

1.2.2 Musculature

In all muscles, shortening occurs through sliding of thick myosin and thin actin filaments past each other. The filaments are arranged in parallel. Sliding is caused by the formation of cross-bridges between the filaments. These cross-bridges can be considered as mutually independent generators of force and power within the muscle.

In striated muscle fibres, actin and myosin filaments are arranged in a very ordered pattern. They form contractile units that are called sarcomeres. A sarcomere consists of myosin filaments that are surrounded by thin actin filaments. The actin filaments are attached to so-called Z-discs. The sarcomeres are organized in longitudinal series that are called myofibrils. The physiology of striated muscle is described by many authors, e.g. [7, 14, 21, 25]

In smooth muscle cells, the filaments are not arranged as orderly as in striated muscle. Actin filaments are attached on the so-called dense bodies, which are often situated on the cell membrane. Through the dense bodies, contraction force is passed to neighbouring cells. The thick filaments lie in the cytoplasm in parallel with the actin filaments. This is illustrated in figure 1.3. Here is seen that actin filaments form an angle with the longitudinal axis of the cell.

The dimensions of smooth muscle cells vary for the different organs in which they are found. In general, they are smaller than striated muscle cells. In comparison to striated muscle, smooth muscle cells contract slowly. They can generate a force over a large range of their length and are able to maintain the contraction for a long period without stimulation.

In the bladder, smooth muscle cells are arranged in bundles. The individual cells within a
bundle are connected to form a functional syncytium. Nerve terminals run within the bundles, making occasional close connections with the cells, but it is unlikely that every cell receives direct synaptic input. The cells probably interconnect by gap junctions. These are thought to exist of symmetrically arranged protein channels, so that ions and small water-soluble molecules can pass between cells. Gap junctions are present in the guinea pig and rabbit detrusor [10].

1.2.3 Microscopic structure of the bladder:

The bladder wall consists of three layers, the mucosal, muscular and serosal layer. The inner side of the bladder is covered by the mucosa, which is continuous with that of the ureters and urethra.

The mucosa layer consists of an epithelium, which is called the urothelium. It is supported by a layer of loose connective tissue, the lamina propria. The mucosa of the empty bladder is thrown into folds, except in the region of the trigone. In this situation, the urothelium is up to six cells in thickness.

On vesical distension, the mucosal layer gets unfolded. The urothelium becomes thinner, until the layer only consists of three or two cells, which are capable of extreme flattening. The collagen bundles of the lamina propria, protect the epithelium against over-distension. Murakumo et al. [27] subdivided the lamina propria in three portions according to the arrangement of collagen fibres, detected in a scanning electron microscopic study. Elastin fibres are sparse throughout the mucosal layer.
The outer surface of the bladder is called the serosal layer, which consists of a loose network of collagen fibre bundles and mesothelial cells. Elastin fibres form a loose network in the border between the muscular and serosal layer.

The muscular layer consists of numerous smooth muscle cells within muscle fascicles, which are arranged in various directions. Within the muscle fascicle, the cells form a functional, though not a true anatomical syncytium [30].

The muscle bundles form a complex meshwork, which is often said to exist of three layers [24]. The inner and outer layers are said to run mainly longitudinally, and the middle layer circularly. However, discrete layering seems to be a simplification of the complex structure, since the same muscle fibre can be followed up in all three layers [30].

In the trigone, two distinct layers of muscle are distinguished [17]. The deep trigonal muscle should be considered as the posteroinferior portion of the detrusor muscle. The superficial trigonal muscle is composed of muscle bundles with a relatively small diameter.

The smooth muscle bundles in the bladder neck, are also composed of small diameter bundles. In the male, they form a circular collar that extends distally to surround the preprostatic portion of the urethra. In the female, the muscle bundles extend obliquely or longitudinally into the urethra wall.

In this section only a brief description of anatomy and physiology is given. More details can be found in, e.g., [12, 17, 21, 24, 28, 27, 31, 40]
Chapter 2

Modelling bladder smooth muscle

Biological tissues are a compound of cells and connective tissue in a fluid matrix. But the size of the components in the tissue is small compared to the macroscopic scale on which the mechanics are considered. For that reason, the material properties of the tissue are considered to be homogeneous and continuous. Therefore, it is allowed to base the description of bladder deformation on the theory of continuum mechanics.

In section 2.1 the equilibrium equations, that form the basis for this model, are presented. This set of equations has to be completed with constitutive equations that describe the material properties in the model. These equations are derived in section 2.2. In section 2.3 the numerical description is presented, which is used in the finite element calculations.

2.1 Equilibrium equations

In this section the laws, that form the basis for this model are presented. These are the three balance laws: conservation of mass, conservation of momentum and conservation of moment of momentum. More detailed information on the theory of continuum mechanics can for instance be found in Malvern [26].

The deformation of a continuum is governed by the deformation gradient tensor $\mathbf{F}$. This tensor describes the local transformation of an infinitesimal material vector $d\mathbf{x}_0$ from the undeformed reference situation, to a vector $d\mathbf{x}$ in the deformed situation.

$$d\mathbf{x} = \mathbf{F} \cdot d\mathbf{x}_0$$

The deformation gradient tensor is thus defined by:

$$\mathbf{F} = (\nabla_0 \mathbf{x})^c$$

Here $\nabla_0$ is the gradient operator with respect to the reference situation. Bladder tissue is assumed to be incompressible. For an incompressible material, conservation of mass is the same as conservation of volume. Conservation of volume can then be expressed by:

$$\det(\mathbf{F}) = 1$$

When neglecting inertial and gravity effects, conservation of momentum is given by:

$$\nabla \cdot \sigma = 0$$
Conservation of moment of momentum, is equivalent to the condition that the Cauchy stress tensor is symmetric:
\[ \sigma = \sigma^c \] (2.5)

To consider the mechanical behaviour of a continuum, these equations must be solved. However, this set of equations is not complete. It can only be solved if we have additional equations which describe the relation between strain and stress in the material. These are the constitutive equations. In the next section, we describe the constitutive equations for bladder tissue in this model.

Regarding the incompressibility of the tissue it is advantageous to divide the Cauchy stress tensor \( \sigma \) in two parts:
\[ \sigma = \sigma^e - pI \] (2.6)

The hydrostatic pressure term \(-pI\) originates from the incompressibility of the tissue. The effective stress \( \sigma^e \) represents the stress that is generated by deformation of the tissue. In this way, conservation of momentum is given by:
\[ \nabla \cdot \sigma^e - \nabla p = 0 \] (2.7)

### 2.2 Constitutive equations for bladder smooth muscle

For the constitutive model of muscle usually a distinction between passive and active stress is made. Passive stress results purely of deformation and pressure in the tissue, while active stress represents the contractile behaviour, resulting from the interaction between actin and myosin filaments in the muscle cells.

We assume that active stress is generated in the direction of the principal axis of the smooth muscle cell only. For that reason, we define in our model a fibre direction \( \bar{e}_f \), in which active stress \( \sigma_a \) is generated. This fibre direction is dependent on the position in the wall. In this way we write the effective Cauchy stress in two parts:
\[ \sigma^e = \sigma^e_p + \sigma_a \bar{e}_f \bar{e}_f \] (2.8)

The total Cauchy stress \( \sigma \) is accordingly given by:
\[ \sigma = -pI + \sigma^e_p + \sigma_a \bar{e}_f \bar{e}_f \] (2.9)

Consequently, our model requires a description of passive material behaviour in three dimensions, whereas active behaviour is modelled in the muscle fibre direction \( \bar{e}_f \). In sections 2.2.1 and 2.2.2, the constitutive model is described for the passive and active part, respectively.

#### 2.2.1 Passive material behaviour

**Introduction**

To develop a constitutive model, we need results of experiments in which the material is submitted to prescribed loading conditions. These experiments must show if passive material behaviour is dependent on time, whether bladder tissue is anisotropic or not, and how
the tissue behaves under shear loading conditions. For a complete knowledge of material behaviour in three dimensions, experiments in three directions are necessary as well as shear experiments.

The experiments on bladder tissue that we found in literature can be divided in two categories. First we have experiments that are performed on strips that are cut out of the bladder wall. Second, pressure-volume measurements on whole bladders have been carried out.

Experiments on strips have the advantage that the loading condition is known reasonably well. However, the excision and preparation of specimens could cause damage of the material structure, which probably affects the mechanical behaviour of the tissue. Unfortunately, only uni-axial experiments on bladder strips were found in literature.

Damage of the structure occurs less, when experiments are performed on the whole bladder. On the other hand, in this case it is difficult to verify the exact loading condition and deformation that take place. Therefore, also these experiments are not appropriate to verify the constitutive behaviour in three dimensions.

Both experiments on whole bladders and on strips have shown that passive material has time dependent behaviour. As other biological soft tissues, passive bladder wall tissue manifests visco-elastic material behaviour, even if the influence of active properties is reduced. Many investigators have experienced time-relaxation when straining strips, and in whole bladders, a pressure decay is detected after increasing the volume by a step [11, 39].

Nevertheless, trying to keep the model simple at first, we did not take this behaviour into account. For this reason, we selected experiments which are performed slowly, so that time effects have decayed. These results are regarded as if the material behaviour was purely elastic.

We decided to base our constitutive equations on the results of slow-filling cystometry. Slow-filling cystometry means pressure measurement, while filling the bladder quasi-statically. Van Mastrigt et al. [35, 36] performed slow-filling cystometry on bladder of dogs and pigs, in vitro. These experiments demonstrated the influence of active contractions on bladder pressure, even when the bladder is removed from the body. To avoid that this active material behaviour would influence our description of the passive properties, we repeated these experiments on two cat bladders. But in this case, active contraction was constrained by means of medication.

The result of these experiments are described in the next section. At the end of this section, the determination of a mathematical description of the material is presented.

**Pressure measurements in the passive urinary bladder**

Figure 2.1 shows the pressure in the whole volume range of two cat bladders, determined by slow filling cystometry. The curves show a remarkable similarity in slope for high, as well as low volumes. For low volumes, the curve is flat. When the bladder contents are about nine times the wall volume, the pressure starts rising steeply with a continuing inflow.

In both bladders we detected a sudden pressure fall, when reaching a pressure of nearly 9 kPa. This indicates that the bladder wall is damaged. This is demonstrated by recordings made afterwards, that show that even at very large volumes, the pressure remains low.

For more details of the experiments, see appendix A. In the next section, the pressure volume curves of figure 2.1 will be used to derive the material behaviour of the passive bladder.
Figure 2.1: Pressure-volume curve of two cat bladders. Bladder volume $V$ is scaled to the volume of the bladder wall, $V_w$, which was 4.9 ml. for both bladders.

**Mathematical description of passive material behaviour**

Passive bladder tissue is modelled as an incompressible, nonlinearly elastic material. In that case, the relation between stress and strain can be described using a strain energy function:

$$\sigma_p = \frac{1}{\det F} F \cdot \frac{\partial W(E)}{\partial E} \cdot F^c$$  \hspace{1cm} (2.10)

Here, $W$ represents the strain-energy function, and $E$ is the Green Lagrange strain tensor that is defined as:

$$E = \frac{1}{2} (F^c \cdot F - I)$$  \hspace{1cm} (2.11)

The form of $W$ and the value of the parameters in this function have to be derived from experiments.

To describe bladder material we have chosen the following strain-energy function:

$$W(E) = b_1 I_E^2 + b_2 I_E + c [\exp(a_1 I_E^2 + a_2 I_E) - 1]$$  \hspace{1cm} (2.12)

with:

- $I_E = E_{11} + E_{22} + E_{33}$,
- $I_E^2 = E_{11}^2 + E_{22}^2 + E_{33}^2 - E_{12} E_{21} - E_{13} E_{31} - E_{23} E_{32}$.

Initially, this function was chosen to consist only of the exponential part. But it appeared necessary to add the linear part, which describes the linear rise of the pressure at low volumes.

The values of $c$, $a_1$, $a_2$, $b_1$ and $b_2$ are estimated from the results of the whole bladder experiments shown in figure 2.1. For this purpose we used an analytical model in which we considered the bladder as an isotropic thick-walled sphere. In the reference state the pressure is zero, the inner radius is $r_{i,0}$ and the outer radius is $r_{o,0}$. Inflation of the sphere causes an
elongation which depends on the radius:

\[ \lambda_i = \frac{r_i}{r_{i,0}} \]

\[ \lambda_o = \frac{r_o}{r_{o,0}} \]

The cavity pressure which is needed for inflation is given by [29]:

\[ P = \int_{\lambda_i}^{\lambda_o} \frac{\partial W}{\partial \lambda} \frac{1}{\lambda^3 - 1} \, d\lambda \]  

(2.13)

With this analytical model, the pressure volume relation for a given energy function \( W(E) \) is calculated exactly. Figure 2.2 shows the result of a calculation that has a good resemblance with the experimental results. The values of the parameters in that calculation are presented in table 2.1.

Table 2.1: Values of the parameters in the constitutive model of passive bladder tissue.

<table>
<thead>
<tr>
<th>parameter</th>
<th>value</th>
<th>unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>( c )</td>
<td>0.04</td>
<td>kPa</td>
</tr>
<tr>
<td>( a_1 )</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>( a_2 )</td>
<td>1.4</td>
<td></td>
</tr>
<tr>
<td>( b_1 )</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>( b_2 )</td>
<td>0.5</td>
<td></td>
</tr>
</tbody>
</table>

2.2.2 Active material behaviour

Smooth muscle cells in the bladder wall are able to generate active forces, by forming cross-bridges between actin and myosin filaments. Although the contractile units in smooth muscle are difficult to distinguish, the contractile machinery is presumably the same as that for striated muscle [14].

Figure 2.2: Calculated pressure volume relation for the described strain-energy function (dotted curve) compared with the experimental results.
Figure 2.3: The three element model by Hill. It is composed of a parallel elastic element (PE), a series elastic element (SE) and a contractile element (CE).

Striated muscle shows dependence of activation, strain and strain rate. These aspects have also been seen in smooth muscle. The active force is dependent on cell length [33] and contraction velocity [32]. Glerum [15] found length dependence in single smooth muscle cells. Velocity dependence of bladder contraction is presented by Griffiths and Groen [19, 20].

Therefore, we use the same mathematical description as for striated muscle. Contractile behaviour of striated muscle is commonly modelled by a three-element model, developed by Hill. It consists of a passive elastic element (PE), in parallel to a contractile element (CE), which is in series with a second elastic element (SE). This is shown in figure 2.3. The passive elastic element PE represents the stress-strain behaviour of the passive tissue described in the previous section.

The active element consisting of CE and SE, is modelled according to Arts [4] and Bovendeerd [8, 9]. In this case, stress is described by the first Piola-Kirchhoff stress, which is related to the Cauchy stress in the following way:

\[ \sigma = \det(F) F \cdot T \]  \hspace{1cm} (2.14)

The first Piola-Kirchhoff stress in the passive element in series with the active element is described by:

\[ T_a = E_a T \ast (l_s - l_c) \]  \hspace{1cm} (2.15)

where \( l_c \) is the contractile element length and \( l_s \) the sarcomere length for striated muscle which can in this case be regarded as the length of actin filaments between two dense bodies. Here T is given by:

\[ T = T_{max} A_l(l_c)A_t(t) \]  \hspace{1cm} (2.16)

with:

- \( T_{max} \) maximum stress at optimal contraction conditions,
- \( A_l \) definition for length dependence,
- \( A_t \) definition for time dependence.

It includes length dependence of contraction force which is given by the function \( A_l \). Furthermore it includes time dependence of contraction. This function \( A_t \) takes the time response on stimulation into account.
The function $A_t$ is a product of two functions, which describe the ascending and descending parts of the time curve respectively:

$$A_t = A_r \times A_d$$

in which:

$$A_r(t) = 1 - \frac{1}{1 + (t/t_r)^4}$$

and:

$$A_d(t) = \begin{cases} 
  1 - \frac{1}{1+[t_e-t]/t_d}^4 & \text{if } t \leq t_e \\
  0 & \text{if } t > t_e
\end{cases}$$

The time constants $t_r$, $t_d$ and $t_e$ are derived from experiments on single smooth muscle cells of a pig bladder [15, 16]. The time function is shown in figure 2.4a. The contraction reaches its maximum at 6 seconds after activation. After 12 seconds, the contraction is extinguished.

Figure 2.4b shows the length dependence of the active force. This curve is based on the following description:

$$A_l(l_c) = \frac{(l_c - (l_{max} - l_w))(l_c - (l_{max} + l_w))}{l_w^2}$$

where:

- $l_c$ contractile element length,
- $l_{max}$ contractile element length at maximal active force,
- $l_w$ rate for curve width.

The values of $l_{max}$ and $l_w$ are chosen in accordance with existing models [6, 23]. The contractile element length at the maximum active force is 5 $\mu$m. In that case the length of the actin filaments is more than two times the initial length of 2.34 $\mu$m.
The active force-velocity relation for striated muscles during shortening is given by the Hill equation. This equation is also suitable to describe the velocity dependence of the active force of the detrusor [18].

\[
\frac{dl_c}{dt} = \begin{cases} \frac{T_a-T}{T_{a}+T_{0}} * k * v_{max} & \text{if } T_a \leq T \\ \frac{T_a-T}{(13.608+0.8*k)+T} * k * v_{max} & \text{if } T_a > T \end{cases}
\tag{2.19}
\]

The values of the parameters are chosen the same as in the model of Bastiaansen et al. [5, 6]. All parameters of the model for active material behaviour are shown in table 2.2.

<table>
<thead>
<tr>
<th>parameter</th>
<th>value</th>
<th>unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>$E_a$</td>
<td>5.0</td>
<td>$\mu m^{-1}$</td>
</tr>
<tr>
<td>$T_{max}$</td>
<td>400</td>
<td>kPa</td>
</tr>
<tr>
<td>$t_r$</td>
<td>3</td>
<td>s</td>
</tr>
<tr>
<td>$t_d$</td>
<td>3</td>
<td>s</td>
</tr>
<tr>
<td>$t_c$</td>
<td>12</td>
<td>s</td>
</tr>
<tr>
<td>$l_{max}$</td>
<td>5</td>
<td>$\mu m$</td>
</tr>
<tr>
<td>$l_w$</td>
<td>3</td>
<td>$\mu m$</td>
</tr>
<tr>
<td>$v_{max}$</td>
<td>$9.36e-4$</td>
<td>$\mu m/ms$</td>
</tr>
<tr>
<td>$T_0$</td>
<td>200</td>
<td>kPa</td>
</tr>
</tbody>
</table>

### 2.3 Numerical solution procedure

The equilibrium equations form together with the constitutive equations a complete set, which can be solved numerically. The state of stress and strain in the tissue is known, once the position $\vec{x}$, the hydrostatic pressure $p$ and the contractile element length $l_c$ are known in every material point of the tissue.

Because it is not possible to take into account all material points of the tissue, a finite number of material (nodal) points are chosen for calculation of position and contractile element length. In the next paragraph a qualitative description of the discretization is presented, for a detailed description see Bovendeerd [8].

Each material point can be labeled uniquely by a set of three material coordinates $\xi$. In a node, the position vector $\vec{x}$, the pressure $p$ and the contractile element length $l_c$, are denoted by $\vec{x}^I$, $p^I$ and $l_c^I$, respectively. With the use of interpolation functions $\psi$ and $\phi$, the position field, pressure and contractile element length are approximated by:

\[
\vec{x}(\xi) \approx \sum_I \psi^I(\xi) \vec{x}^I
\tag{2.20}
\]

\[
l_c(\xi) \approx \sum_I \psi^I(\xi) l_c^I
\tag{2.21}
\]

\[
p(\xi) \approx \sum_J \phi^J(\xi) p^J
\tag{2.22}
\]

Here $I = 1, \ldots, n_x$ and $J = 1, \ldots, n_p$. 

14
The interpolation functions are dependent on the material coordinates $\xi$ and chosen so that:

\[
\begin{align*}
\psi^j(\xi^K) &= \delta^{jk} \\
\phi^j(\xi^K) &= \delta^{jk}
\end{align*}
\]

(2.23) (2.24)

According to the finite element method the nodes are grouped in elements by choosing the interpolation functions so that the function belonging to a material point $\xi^K$ can be non-zero only in those elements $E$ to which this material point belongs:

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

(2.25)

For the calculation of the deformation, the 20-node brick element, shown in figure 2.5, is used. For interpolation function $\psi$ a quadratic, and for $\phi$ a linear function is chosen. Therefore $\vec{x}$ and $l_\epsilon$ are defined in all twenty nodes of the element, while $p$ is only discretized in the eight corner points. The element contains fourteen integration points.

![Figure 2.5: The 20-node brick element used in the calculations. Graph a: position of the nodal points, $\vec{x}$ and $l_\epsilon$ are defined in all nodal points, $p$ only in the black nodes. Graph b: position of the integration points.](image)

Because we calculate a time varying process, also a discretization in time has to be performed. At the beginning of a new increment, the value of $l_\epsilon$ in each nodal point, is derived from the value of $l_\epsilon$ in that point in previous time steps, with use of equation 2.19. This value is kept constant during the increment.

Also the values of $\vec{x}$ and $p$ at each nodal point have to be estimated. For a first estimation for the new time step, the result of the previous time step is chosen. Because this estimation will contain an error $\delta \vec{x}$ and $\delta p$ for each nodal point, the equilibrium conditions in the nodal points will not be fulfilled. This violation of the equilibrium equations results in force imbalances and deviations from volume conservation in the nodal points. If the deviations from force equilibrium or volume conservation are unacceptably large, a new iteration step is performed. For this, a new estimation for $\vec{x}$ and $p$ in each nodal point is made, with the values of the imbalances, using a Newton-Raphson iteration procedure. This process will be repeated until the solution satisfies the criteria for convergence. The maximum force imbalance must be less than a fraction $\epsilon$ of the loading force. The value of $\epsilon$ was maximally 1%. The criterion for deviation from volume conservation was maximally 0.1%.
2.4 Testing the element

To test the element, an isotonic contraction is performed on a brick consisting of 5 elements. The muscle fibres run in the $e_3$ direction, at every point.

![Figure 2.6: Brick consisting of 5 elements.](image)

Preceding to the contraction, the brick was strained in the fibre direction, until the contractile element length was twice its initial length, which is near its optimum for contraction. Then the applied loading force was maintained during the contraction. This simple case can also be analyzed analytically.

![Figure 2.7: Testing the element: isotonic contraction, comparison of the finite element solution ($dt = 10\,\text{ms}$, dotted curve) with the analytical solution (solid curve). Graph a: active first Piola Kirchhof stress. Graph b: contraction unit length.](image)

Figure 2.7 shows the results of both the analytical and the finite element approach. The time step in the finite element approach was 10 ms. The two different curves in figure 2.7.a and b are hardly distinguishable.

The finite element curve from this figure is also presented in figure 2.8. Here we compare this calculation with others that have different increment steps. From these calculations, it becomes clear, what time step is necessary to have a reliable result. We see that an increment of $dt = 50\,\text{ms}$ gives good results, while those with $dt = 100\,\text{ms}$ are reasonable. A larger increment causes a considerable difference.

The origin of the differences is found in the estimation of $l_c$ for a new increment step. As we described in the previous section, this value is estimated from former increments. The estimation is better for smaller time steps.

For efficiency we start calculating with $dt = 100\,\text{ms}$, but we should realize that this influences the value of $l_c$. 

16
Figure 2.8: Testing the element: isotonic contraction, calculated with different time steps. a: Active first Piola Kirchhoff stress. b: contraction unit length.
Chapter 3

Modelling the bladder and urethra

In this chapter the design of the model is presented. The geometry of the model is shown in section 3.1. In section 3.2, the boundary conditions of the model are presented.

3.1 Geometry

The simulation of bladder mechanics during the micturition cycle starts from the reference state. In this state stresses and strains in the wall are assumed to be zero, while the bladder volume is small compared to the volume at the moment that micturition starts. The shape of the bladder is strongly dependent on loading conditions. For our simulations we have chosen a simple geometry. We modelled the bladder as a thick-walled sphere. In the reference state, the bladder volume, $V$, is chosen equal to the wall volume, $V_w$. This value is estimated from measurements on dog and pig bladders, and is chosen 43 ml in our model.

Because the spherical symmetry of this geometry it was sufficient to calculate with an eighth part of the sphere. To apply the finite element method, this part was divided into three layers of nine elements. This is illustrated in figure 3.1.

Because there are no quantitative data for fibre direction available, we simulated bladder contraction with three different geometries for the fibre direction of the muscle bundles. In the first case the muscle fibres were arranged in circles, parallel to the equator of the sphere.

![Figure 3.1: Mesh used for finite element modelling.](image-url)
Figure 3.2: Geometries for the fibre-direction of the muscle bundles. *left*: parallel circles, *middle*: longitudinal meridians, *right*: variably from $-45^\circ$ at the inner wall to $45^\circ$ at the outer wall.

This is displayed in figure 3.2 on the left graph. In the second case, presented in the middle of figure 3.2, the fibres were arranged like longitudinal meridians. In this case, the angle between the fibres and the equator is $90^\circ$. This geometry is different from the first, as the fibres do not run parallel and cross each other at the poles of the sphere.

In the third case (left graph), the fibres varied in direction as a function of position in the wall. At the inner side, the fibres had an angle of $-45^\circ$ with the equator. At the outer wall this angle was $45^\circ$. The angle had a linear course between the inner and outer wall.

The three simulations will be referred to as *CIRC*, *LONG* and *VAR*, respectively.

### 3.2 Boundary conditions

#### 3.2.1 Kinematic boundary conditions

To perform a finite element analysis of the mechanics of the bladder, rigid body motion must be suppressed. The symmetry is taken into account by boundary conditions on the edges of the eighth part of the sphere.

In simulations *CIRC* and *LONG*, motion of the edges is suppressed in the direction perpendicular to the edges. The edges can only move in radial directions. In simulation *VAR* motion perpendicular on the edge at the equator is suppressed. Also circumferential motion is suppressed at the inner side of the wall at the equator, and there is radial symmetry on the other edges.

#### 3.2.2 Modelling the urethral impedance

To simulate micturition, also the dynamics of the urethra have to be considered. In reality, the dynamics of the urethra depend on the activation of the musculature of the internal and external sphincter. However, this aspect has not been taken into account in this model. Drolet [13], characterized the impedance of the urethra using an engineering approach. It was found that the hydraulic impedance of the urethra can be represented by a pressure threshold in series with a linear impedance. The electronic analogue of the impedance is presented in figure 3.3.
The pressure threshold is implemented in the model by introducing an isovolumetric phase, until that threshold value is reached. In case that the bladder pressure is larger than the threshold value, we have the following relation between bladder pressure and urine flow:

\[ P = L \frac{\partial Q}{\partial t} + RQ \]  

if

\[ P > P_{th} \]

with:

- \( P \): bladder pressure
- \( Q \): urine flow
- \( L \): inertia
- \( R \): urethral resistance

\( P_{th} \) threshold pressure for urethral flow

The values of \( P_{th} \), \( R \) and \( L \) were experimentally obtained on four dogs by Drolet. He also implemented this model in a computer simulation of the bladder control system. The values that he regarded as normal for a female dog, are also presented in table 3.1. In our model, we have chosen the parameters of the same order (see table 3.1).

Table 3.1: Values of \( P, R \) and \( L \). Column 1: Experimentally obtained values, by Drolet [13], mean value and range. Column 2: Values defined as normal in model of Drolet. Column 3: Values used in our model.

<table>
<thead>
<tr>
<th>parameter</th>
<th>experiments</th>
<th>model</th>
<th>this model</th>
<th>unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>( P_{th} )</td>
<td>3.4 (3.0 - 4.5)</td>
<td>1.0</td>
<td>1.0</td>
<td>kPa</td>
</tr>
<tr>
<td>( R )</td>
<td>2.7 (1.7 - 3.5)</td>
<td>3.0</td>
<td>2.0</td>
<td>( 10^8 ) Pa s m(^{-3} )</td>
</tr>
<tr>
<td>( L )</td>
<td>4.0 (2.4 - 6.9)</td>
<td>2.0</td>
<td>1.0</td>
<td>( 10^8 ) Pa s(^2) m(^{-3} )</td>
</tr>
</tbody>
</table>

3.2.3 Dynamic boundary conditions

In the model a uniform pressure is applied to the entire inner wall. On the outer wall of the bladder, the pressure is assumed to be zero during the whole simulation.

During the collection phase of the simulation, only passive material behaviour is present. Time is not relevant in this phase, since the passive material behaviour is independent of time.
Variation of the pressure in time during micturition, is implemented in two phases. As long as the pressure in the bladder is under the threshold value for opening of the urethra, we have an isovolumetric contraction phase. When this threshold value is reached, the voiding phase starts. Emptying of the bladder is simulated, with the impedance describing the urodynamics of the urethra.

Therefore, the dynamic boundary conditions depend on the phase of the simulation:

- During the collection phase, the pressure is prescribed.
- During the isovolumetric phase of contraction, pressure is calculated to balance the passive and active forces in the wall so that the bladder volume is kept constant.
- During the voiding phase, the pressure is determined from the interaction between the contracting bladder and the urodynamic impedance of the urethra.

In the next chapter, the results of the simulations with this model are presented.
Chapter 4

Results of the simulations

4.1 Simulating the collection phase

With the model as described above, the collection phase is simulated. In this phase, only passive material behaviour is included in the model. We compared the results of our model with the analytical approach described in section 2.2.1. This is presented in figure 4.1. In this figure we see the pressure as a function of the relative bladder volume $V/V_w$. We see that if the volume is larger than eight times the initial volume, a small difference is seen. We do not know if the cause of this must be sought in the analytical or the finite element model.

Yet, this difference is small compared to the difference between the analytically solved curve and the experiments, seen in figure 2.2. Furthermore, the physiological normal volumes are found under ten times the initial volumes. And in this range the resemblance is reasonably good.

4.2 Simulation of micturition

In this chapter the simulation of micturition is presented. Before simulating contraction, filling of the passive bladder was simulated. The volume was increased until the pressure in the sphere was 0.5 kPa. In that case, the volume of the contents was 298 ml. This filling phase preceded all the simulations in this section, but only the micturition phase is presented.

Simulation of micturition started with an iso-volumetric phase. Activation caused a rising pressure while bladder volume was kept constant. The flow was not established until the pressure exceeded the threshold value of 1.0 kPa.

4.2.1 Preliminary results

In section 2.2.2, the parameters of the contraction model were given. These values are used in a preliminary calculation on the sphere with the fibres in parallel circles. The calculation demonstrated that the bladder volume did not decrease to its value in the unloaded bladder. The contraction did not last long enough to achieve complete emptying.

For this reason we reconsidered the function that describes the time-dependence of contraction. The form of this function is determined by the value of the parameters $t_r$, $t_d$ and $t_e$. Parameter variation is done to determine the values needed for complete emptying. All
parameters of the time function have been multiplied with a factor two, three and four, respectively. Figure 4.2.a shows the resulting time function $A_0$, in graphs b, c and d, bladder volume, pressure and flow during these calculations are given. We see that the calculation given by the solid line (four times the initial values), results in complete emptying of the bladder. For this reason, we choose the parameters of the time function a factor four larger than the initial values, and also the increment was enlarged with the same factor.

### 4.2.2 Fibres arranged in parallel circles

The first simulation is performed with fibre geometry $CIRC$ (figure 3.2).

#### Urodynamics

In figure 4.3, the urodynamic results of the first simulation are presented. As we can see in graph a of this figure, the starting bladder volume was near 300 ml, and the resulting volume after micturition is approximately 45 ml, which is nearly its initial value in the reference state. The activation time was in this case 48 s. The pressure started to rise after about 7 seconds. After 9 seconds the flow started, reaching its maximum of nearly 21 ml/s., at $t = 15$ s. At this time the pressure was about 4.3 kPa.

#### Deformation

Figure 4.4 shows the deformation of the bladder during micturition. At $t = 0$ s, also the undeformed mesh is displayed.

The figure presents the deformation of the cross-section in the x-z-plane. The x-axis is horizontally, the z-axis is vertically directed (positive part pointing downwards). The y-axis is perpendicular to this page. As the problem is axisymmetrical in respect to all three axes, we can derive the shape of the bladder during contraction from this projection.

As we can see in the figure, the bladder transformed during contraction, from a sphere into an spheroid. The spheroid was prolate, with one long and two short axes. Maximal
elongation of the spheroid was obtained at $t = 18$ s, at this time, the long and short axes were in the proportion of $5 : 2$. The shape became spherical again, at the end of micturition.

At about $t = 16$ s, the wall began to thicken. This process started at the pole of the bladder (lower end in the figure). The following 20 seconds, the wall was at this point thicker than in the rest of the spheroid.

**Local wall mechanics**

In figure 4.5 the value of the active Cauchy stress is shown, for six moments during contraction. The highest values of active stress were over 70 kPa and obtained at $t = 14$ s. These values were found at the equator of the bladder and decrease towards the pole. Furthermore, we see that at the inner side of the wall the values were higher than at the outer side of the wall.

In figure 4.6 the value of $l_s$ is shown for the same points of time. We see that during the micturition, $l_s$ was in the range between 2 and 4 $\mu$m. However, the distribution of $l_s$ over the wall is not clearly visible in this figure.

Therefore, the local mechanics at $t = 14$ s, are presented in figure 4.7. In 4.7.a, the value of active Cauchy stress in the fibre direction is shown. The highest values occurred at the inner wall near the equator. From equator to pole the active stress decreased. In b, the largest value of principal stress of the passive Cauchy stress tensor is displayed. The lowest values were found at the outer side of the wall and near the pole. From outer wall to inner wall, the passive stress increased.

The value of $l_s$ is presented in 4.7.c. We see that the contraction units at the inner wall were longer than those on the outer side. Another important factor in the calculation of active stress is the length of the elastic element in series with the contractile element (see section 2.2.2). The value of this factor, $l_s - l_c$, is presented in d. Here we see that the value decreased from equator to pole. In figure 4.8.a and b, we see the variation of the active and passive Cauchy stress in the fibre direction. These values are mean values over the wall. In c, the mean value of $l_s$ is given. Although we see a smooth curve for $\sigma_a$ and $l_s$, this is not seen for $\sigma_p$. 
Figure 4.2: Parameter variation of the time constants. a: Time function with initial time constants (dotted) and two (dash-dotted), three (dashed) and four (solid) times the initial time constants. b, c and d: Change of bladder volume $V$, pressure $P$ and flow $q$, during micturition, calculated with the time functions of graph a.

Figure 4.3: Urodynamic results of simulation CIRC. Graph a, b and c represent bladder volume, bladder pressure and flow during micturition, respectively.
Figure 4.4: Deformation in simulation \textit{CIRC}.
Figure 4.5: Value of the active Cauchy stress (kPa) in simulation CIRC.
Figure 4.6: Value of the contraction unit length (µm) in simulation CIRC.
Figure 4.7: Local mechanics at $t = 14$ s. 

- a. active Cauchy stress (kPa),
- b. largest value of principal (passive) stress (kPa),
- c. contraction unit length ($l_c$, $\mu$m),
- d. length of series elastic element ($l_s$, $\mu$m).

Figure 4.8: Mean values during simulation of 

- a. active Cauchy stress,
- b. passive Cauchy stress in fibre direction,
- c. contraction unit length.
4.2.3 Fibres arranged as longitudinal meridians

This simulation is performed with fibre geometry LONG (figure 3.2).

![Graphs](image)

Figure 4.9: Urodynamic results of simulation LONG (solid lines) compared with CIRC (dotted lines). Graphs a, b and c represent bladder volume, bladder pressure and flow during micturition, respectively.

**Urodynamics**

In figure 4.9 the results of the simulation with longitudinal meridians are presented together with the previous simulation (dotted curve). In this case, only the first 24 seconds of the micturition were calculated. It was not possible to continue the simulation with the necessary criteria for convergence. However, after 24 seconds, the volume was near the volume in the unloaded passive bladder.

In this simulation, the maximum values of pressure and flow were higher and reached sooner than in the previous calculation. Also the starting time for the flow was somewhat earlier.

**Deformation**

Figure 4.10 shows the deformation of the bladder during this simulation. Also in this case, the bladder turned into a spheroid as micturition was initiated. However, here, the spheroid was oblate, it had one short, and two long axes. At 14s, the spheroid developed its maximum for eccentricity, at that time the long and short axes were in the proportion of 5 : 3. In this simulation, wall-thickening started near the equator of the bladder.

After 10 seconds in the calculation, we detect crumpling of the elements near the pole. This indicates that the results in this area have to be interpreted with care.

**Local wall mechanics**

In figure 4.11 we see that the highest values for active Cauchy stress occurred at the pole of the bladder. From the pole towards the equator, the active stress decreased. There is no visible variation over the wall in radial direction. We see that the largest values are much higher than in the previous calculation.
Figure 4.10: Deformation in simulation \textit{LONG}.
Figure 4.11: Value of the active Cauchy stress (kPa) in simulation \textit{LONG}.
4.2.4 Fibres arranged with a variable angle

The last simulation (VAR), stopped at only one third of the total contraction time. After this, convergence was no longer achieved.

Figure 4.12: Undeformed mesh (a) and deformation at the last converged increment (b), seen from above.

In figure 4.12, the undeformed mesh as well as deformation at the last converged increment is shown. It shows that in this case, torsion of the wall occurred. As a result of this, the elements become so thin that both sides can hardly be distinguished.
Chapter 5

Discussion and conclusions

5.1 Model and method

The underlying method of the model was based on the heart model of Bovendeerd [8]. Constitutive laws of almost the same form as in that model, were considered appropriate to describe bladder material behaviour in the available experiments. For this reason, it was possible to use the numerical solution procedure, which had been proven to work for the heart model. This method appeared to be successful to describe the large deformations that occur in the bladder. Yet, the model was not robust. Sometimes it was necessary to loosen the rules for convergence. But in all calculations, the maximum value of force imbalance was at most 1% of the maximum force. The deviation from volume conservation was always below $10^{-6}$.

As already mentioned in the introduction, the finite element model offers several advantages compared to existing models. Unlike previously used methods, it opens up the possibility of modelling nonuniform distributions of stress and strain and thus simulate bladder wall mechanics in more detail. Since the method is not based on a particular geometry, also other shapes of the bladder could be chosen in the model. However, to make use of the advantages of the method, detailed input for the model is required. Unfortunately, this information is not always present. Therefore, many assumptions had to be done to complete this model. It concerns aspects like geometry, fibre geometry and material behaviour.

Regarding the geometry, an estimation of bladder volume and bladder wall volume in the reference state had to be made. We did not find any values, concerning the human bladder wall volume in literature. However, the pig bladder is commonly assumed to be a representative model for the human bladder [16]. Our chosen value of 43 ml was between volumes of pig and dog bladders found in literature [20, 36].

The initial volume of the unstrained bladder, $V_0$, is difficult to verify. Yet, Van Mastrigt et al. [36] found a high correlation coefficient between this volume and the volume of the bladder wall and indicated that, as the values were almost the same, it was sufficient to measure only one in practice. Consequently, we chose the value of $V_0$ the same as the wall volume.

As we can see in figure 1.1 and 1.2, the shape of the bladder appears to depend strongly on the filling state and the loading conditions. We decided to model the undeformed bladder initially as a sphere.
Another difficulty is fibre geometry. What we found on this subject in literature is descriptive and did not contain quantitative results. Some authors describe a kind of ordered structure, containing three layers [24], while others mention a complex network [10, 17, 30].

The three orientations, used in the present simulations are geometries that were readily generated. We did not expect that the chosen fibre geometries would lead to physiological reliable results. Yet in this way we can gain insight into the possibilities of the model.

With respect to the material behaviour, little is known of smooth muscle. The main problem for defining constitutive equations is the lack of a unique resting state. It is usually assumed that the contractile element offers no resistance to elongation or shortening when the muscle is in the resting state. This leads to the separation of muscle force in a passive and active component, which is also found in the Hill model. Fung [14] already suggested that this assumption might be acceptable for skeletal muscle, is sometimes questionable for the heart and seems doubtful for smooth muscle. However, until now, this approach has always been used to model bladder tissue [5, 13, 34, 37], probably because of the absence of a constitutive model for smooth muscle. Also in this model we follow this approach.

When passive material properties were concerned, many assumptions had to be done. The most obvious simplification is the fact that we did not consider the viscoelastic behaviour. However, as we supposed that active properties would be dominating during micturition, we assumed that this fact would not have a large influence, when simulating the voiding phase.

Since we assumed an ordered geometry for the muscle fibres, it may not seem plausible to combine this with an isotropic behaviour for the passive material. Yet, we did not find any literature that suggested anisotropic behaviour. On the contrary, on measurements in two directions on the same strip, Van Mastrigt [36] did not find a significant difference in material behaviour. Therefore we had no indication that anisotropic passive material behaviour exists.

Also concerning active material properties, many assumptions have been done. Length dependence of active stress is seen in single smooth muscle cells [15]. The actual choice of the parameters describing this length dependence was made according to Bastiaanssen [5, 6]. She based the length dependence on theoretical derivations for striated muscle.

The Hill equation describing velocity dependence of contraction has been proven appropriate for detrusor muscle [19, 20]. It is applied in all the models found in literature [5, 34, 13, 22, 23, 37]. The involved parameters are again chosen according to Bastiaanssen et al. [5, 6], in case of lengthening of the muscle fibre, this curve is based on experimental data of striated muscles.

The initial values for the parameters of the function describing time-dependence were chosen to fit experimental data on single smooth muscle cells that were stimulated for ten seconds. Probably, these data were highly dependent on duration of stimulation. In the simulations, the activation of all muscle cells in the wall was modelled as one simultaneous contraction. Therefore, in that case, the time function of contraction did not represent time dependence of a single muscle fibre, but time dependence of contraction of the entire wall. So it was not very surprising that this function had to be changed to describe the contraction of the entire bladder wall, as found in section 4.2.1.
5.2 Results

In case of simulation LONG, there was a strong indications that the results were not reliable. We detected crumpling of the elements near the pole. Therefore it is not allowed to draw any quantitative conclusions from this simulation.

Urodynamics

The urodynamic results of simulation CIRC are compared to to urodynamic measurements in the next section. Although we have to be careful with the results of simulation LONG, we see in figure 4.9 that in spite of the complete dissimilarity in local mechanics, the urodynamics of this simulation are comparable with those of CIRC.

Deformation

In all three cases, deformation was as expected from the arrangement of the muscle fibres in the model. Contraction occurred in the fibre direction, while perpendicular to this direction the stiffness of the material was low.

In simulation CIRC the sphere transformed into a prolate spheroid, having the short axis in the plane of the fibre circles and the long axis perpendicularly. The thickening of the wall at the pole is explained by the incompressibility of the material. In this region, the fibres ran in concentric circles around the z-axis. Contraction in the x-y-plane had to result in expansion in the z-direction.

In simulation LONG the bladder transformed into an oblate spheroid. Near the equator the fibres are parallel, therefore the stiffness of the material perpendicular to the fibres is low, and in this direction the material is easily strained. At the pole, the fibres run in all directions, and as a result, the material is strained equally in every direction. This results in an oblate spheroid.

In simulation VAR the fibre-direction varied as a function of the location in the wall. As a result of this, shear loading occurred. As the material has low resistance to shear stress, this resulted in such a large deformation of the elements that we cannot expect the results to be mechanically reliable. This explains why the calculation could not be continued.

A finer mesh may solve these numerical problems. However, since we have no quantitative information of fibre arrangement, we do not know if large shear stresses occur in the bladder during normal functioning. As fibres may probably transverse between the different layers [30], shear stresses could be restricted.

If shear stresses do occur during micturition, the material model needs to be improved regarding this aspect. Therefore, information of the material behaviour under shear loading conditions is required. Since we did not find any shear loading experiments on bladder tissue in literature, this means that more experiments are necessary.

Local mechanics

In figure 4.5, and also more clearly in figure 4.8.a, we see that large values for the active stress occurred between \( t = 10\text{--}22 \text{ s} \). This is before reaching the optimum in time-function \( A_t \).

This could be explained as we see that the value of \( l_s \) decreases rapidly in this range. This is shown in figure 4.6 and 4.8.c. From equations 2.15 and 2.19 it can be derived that the difference between \( l_s \) and \( l_c \) has a maximum of \( 1/E_a \), which in this case, is 0.2 \( \mu m \). From
this, we can conclude that also the value of \( l_e \) decreases rapidly in this range. The decrease in \( l_e \) results in lower values for the function \( A_f \) and therefore in a lower value of the active stress.

Figure 4.8.b shows irregularities in the average value of the passive Cauchy stress in the fibre direction. These irregularities occurred when the average of active stress was near its maximum. Apparently, the determination of the passive stress was less accurate when large values for the active stress occurred. The value of the passive stress seems to be proportional to the value of \( l_s \). The error in the estimation of the passive stress is in that case, about 2 kPa. This is about 4% of the sum of active and passive stress. This is a larger value than could be expected from the convergence criteria. No explanation has been found on this point yet.

The local mechanics of simulation \textit{CIRC}, are most clearly displayed in figure 4.7. The distribution of active stress, passive stress, contraction unit length \( l_s \), and the length of the serial passive element \( l_s - l_e \), are displayed.

It can be clearly seen that the value of the active stress was determined by both \( l_s \) and \( l_s - l_e \). The value of \( l_s - l_e \) mainly determined the course of the active stress from equator to pole. The value of \( l_s \) caused the effect of a higher active stress at the inner layer compared to the outer layer.

In figure 4.7.b the maximum principal stress of the passive Cauchy stress is displayed. We see that at the inner wall, near the equator, the passive stress was even larger than the value of the active stress. The direction of the maximum principal stress cannot be seen in the figure. We suppose that the largest values of passive stress were found in the directions perpendicular to the radial direction of the spheroid. As the passive stress decreases in the fibre direction, we expect the maximum principal stress perpendicular to the fibre direction. This is verified for one point at the equator on the inner layer. The maximum principal stress was in the plane of the wall, perpendicular to the fibres. In that case, it meant that the maximum of the passive stress at the equator was in the z-direction. The maximum passive stress in this direction was even larger than the sum of active and passive stress in fibre direction.

In simulation \textit{LONG} we see that the maximum active stress occurred at the pole of the bladder. The values of active stress displayed in figure 4.11 are much larger than in simulation \textit{CIRC}. We can conclude from this simulation that with this fibre geometry, active stress mainly occurs near the pole, and that combination of circular and longitudinal fibres, probably results in a more uniform distribution of active stress.

\section{5.3 Physiological validation of the model}

Because there are no measurements available on the local mechanics of the bladder, the evaluation is restricted to studies of the urodynamics. In the previous section, we saw that local mechanics hardly have any influence on the urodynamic results. Therefore the urodynamic results are not very appropriate to evaluate the local mechanics predicted by the model.

Urodynamic measurements on the normal human bladder are scarce. Most urodynamic studies are on patients with urodynamic complaints and not on healthy people. Therefore Bastiaanssen [5] performed some urodynamic measurements on four presumably healthy females. Appendix B shows a typical result of these measurements. We evaluate the results of
our calculations with these measurements.

Table 5.1 shows the results of the measurements of Bastiaanssen and of calculation CIRC. Standard deviation in the measurements is calculated over all the investigations. The number of investigations for each individual was too small to estimate the inter-individual variation. Clinical parameters are:

- **Voided volume**: total amount of voided liquid after micturition.
- **Peak flow**: maximum of flow.
- **Time to peak flow**: time between start of micturition and the time of the maximum flow.
- **Vesical pressure at peak flow**: pressure registered in the bladder at the time that the flow was maximal.
- **Flow time**: duration of micturition.
- **Average flow**: the voided volume divided by flow time.

To avoid confusion, here micturition time means the time in which flow occurred.

We defined for our calculations the flow time as the time span between the start of flow until the moment that flow decreased to 1% of the maximum flow. Average flow of the calculations is the mean flow during this time span. We compared the vesical pressure during peak flow (peak pressure in table 5.1) with the maximum bladder pressure that occurred during the simulations.

Table 5.1: Comparison of urodynamic results of calculations with measurements (± standard deviation) on healthy females.

<table>
<thead>
<tr>
<th>parameter</th>
<th>Bastiaanssen [5]</th>
<th>CIRC</th>
<th>unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Voided volume</td>
<td>505 ± 123</td>
<td>254</td>
<td>ml</td>
</tr>
<tr>
<td>Peak pressure</td>
<td>5.1 ± 0.5</td>
<td>4.3</td>
<td>kPa</td>
</tr>
<tr>
<td>Peak flow</td>
<td>19 ± 3</td>
<td>21</td>
<td>ml/s</td>
</tr>
<tr>
<td>Time to peak flow</td>
<td>14 ± 5</td>
<td>5.6 ± 0.8</td>
<td>s</td>
</tr>
<tr>
<td>Flow time</td>
<td>45 ± 17</td>
<td>24.0 ± 0.8</td>
<td>s</td>
</tr>
<tr>
<td>Average flow</td>
<td>12 ± 3</td>
<td>7</td>
<td>ml/s</td>
</tr>
</tbody>
</table>

In the measurements, the voided volume is larger than in the simulation. The value of the maximum bladder pressure in the simulation was somewhat lower than the measured vesical pressure during peak flow. The peak flow was nearly equal to the measurements, while the average flow was lower. The time to peak flow is significant lower in the simulation. Flow time was smaller than in the experiments, but if we regard the large standard deviation, this difference is not relevant.

Drolet [13] showed that the parameters in the model of the urethra influence the urodynamic results largely. This is especially true for the threshold pressure $P_{th}$ and resistance $R$. Drolet showed that they have a large influence on the micturition pattern of pressure and
flow, and also on peak pressure and flow. The threshold pressure seemed also have influence on time to peak flow. The value of inertia $L$ had less influence than the factor $L/R$.

In the preliminary calculations in section 4.2.1, we noted that peak pressure and flow are also influenced by the time function. Also the time to peak flow depends slightly on this function. The time function is strongly related to the stimulation of the bladder. Because the voided volume differs in the measurements from the simulation, we might also expect different stimulation time. This aspect of the model deserves more attention.

Dependence of urodynamics on other parameters in the bladder model is not investigated.

5.4 Conclusions

- Simulation CIRC indicates that the method is appropriate to describe the large deformations that occur in the urinary bladder. Although not physiological realistic, the results seem mechanically reliable.

- More experiments are needed to obtain input parameters concerning constitutive equations and fibre geometry.

- Urodynamic results are not appropriate to verify a model that predicts local wall mechanics. For that purpose, measurements on local deformation are required.

5.5 Recommendations

As we concluded, the results of simulation CIRC appear mechanically reliable. Yet, if we regard the other simulations it would be strongly advisable to calculate with a finer mesh.

To improve the model, it is necessary to obtain a more realistic fibre direction, which requires quantitative measurements. If the spatial variation of fibre direction is too large to be correctly defined in the model, it might be better to define active stress in the transversal plane.

If we can expect shear stress from the fibre geometry, it is necessary to improve the constitutive model in this respect. This requires experiments on bladder tissue under shear loading conditions.

Another aspect that did not receive much attention, is the activation pattern of the bladder. Improvement of this aspect can give insight in the influence of activation patterns on urodynamics and local mechanics in the bladder wall.

To evaluate the model with urodynamic measurements it is highly necessary to implement the muscle dynamics of the urethra. This can be combined with another geometry that includes both bladder and urethra.
Bibliography


Appendix A

Pressure measurements in the passive urinary bladder

A.1 Method

The bladders of two cats, mass 2.5 kg, were examined in vitro. The bladders were removed from the body and placed in a saline bath (0.9% NaCl). Saline was infused through a catheter which was connected to the bladder via a needle through the urethra. The proximal urethra was closed around the needle. Filling rate was 2.6 ml per min, established by emptying a 100 ml syringe with a Harvard Infusion/Withdrawal Pump.

Pressure was measured outside the bladder, at the end of the needle, by a Millar catheter tip pressure transducer. The experimental setup is presented in figure A.1. In section A.4 an approximation of the pressure decay over the needle between sensor and bladder is made. From this we can conclude that this pressure difference is small in comparison to other possible errors.

For each bladder, an initial recording of the pressure by a constant filling rate was made. After this recording, active contraction was suppressed by putting the bladder in saline with 10 mg oxybutynine hydrochloride per 100 ml. Then more recordings were made, at which the maximum volume did not exceed 40 ml. Finally the bladder was filled to its maximum. In one case we made some recording afterwards. The bladder volume at the beginning of each measurement was determined by weighing the bladder and its contents.

Figure A.1: Experimental setup.
A.2 Results

Bladder mass was in both cases 4.9 mg. Assuming one mg per ml, bladder tissue volume is estimated as 4.9 ml. Figure A.2 shows the pressure at low volumes for one bladder, with and without suppressing active contraction. Pressure fluctuations are clearly visible in the cystometrogram which was recorded without suppressing active behaviour. Furthermore, the overall pressure is significant higher than in the passive bladder. This indicates that, even when pressure fluctuations are not visible in a cystometrogram, smooth muscle activity is still affecting the material behaviour. So for verification of passive behaviour, contraction has to be constrained by medication.

A.3 Results in chronological order

In figure A.3 and A.4, the results of all measurements are shown. Each succeeding recording is added to the figure.

Figure A.3 shows the pressure-volume curves of the first bladder. Between two recordings the bladder was emptied by pressing on it. Time between following registrations was at least 15 minutes.

Only the first recording of each bladder was made without medication to suppress active contraction. These are shown in figure A.3.a and A.4.a.. All other measurements have no active material behaviour.

In figure A.4.d, the added pressure curve stayed lower than before, this indicates that the bladder material was damaged in the preceding filling.

A.4 Pressure decay over the needle

As can be seen in figure A.1, the pressure is measured outside the bladder. Between the sensor and the bladder, the liquid flows through the needle. As a result of the resistance of the needle, the actual pressure in the bladder is somewhat lower than the measured value.

To estimate the influence of this resistance on the pressure measurement in the experiments, the pressure was recorded during a time interval in which the flow is interrupted. This
is done for the slow filling rate used at the experiments (figure A.5.a) and also for two higher rates (A.5.b).

Figure A.5.b shows that the pressure rise is two times higher for a doubled flow rate. So we conclude that the pressure in the bladder during the experiments is about 25 Pa lower than the recorded pressure.
Figure A.4: Overview of measurements on bladder no. 5522.

Figure A.5: Interrupted pressure registration. The upper figure shows the pressure registration at the filling rate used during the experiments (2.6 ml/min). The lower figure shows the pressure registration at increasing flow rate (2.6, 5.3 and 10.6 ml/min respectively).
Appendix B

A typical urodynamic measurement

In figure B.1 the shape of one of the measurements of Bastiaanssen [5] is presented. The figure shows flow (Qura), urethral pressure and bladder pressure (Pdet) during micturition.

Figure B.1: Registration of micturition of a healthy female (from Bastiaanssen [5]). Qura: outflow of urine; Pmed: urethral pressure; Pdet: detrusor pressure.