Arterial wall mechanics and atherosclerosis

Rutten, M.C.M.

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Arterial wall mechanics
and
atherosclerosis

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Abstract

It is generally assumed that atherosclerosis is related to low and oscillating wall shear forces at the endothelial cells’ surfaces. However, it can be shown that at the locations where atherosclerotic lesions occur, the compressive strains in the wall are high. It is reasonable to assume that the strain distribution in the vessel wall may play an important role in atherogenesis. This strain is induced by the blood pressure and strongly depends on the curvature of the vessel. The means to test this assumption are presented here.

An isotropic and a non-linear anisotropic viscoelastic model mimicking the wave propagation properties of an artery were developed and tested. The anisotropic model shows qualitatively the same wave propagation behaviour as real arteries. This was validated in a wave propagation set-up.

The isotropic vessel model was implemented in a FEM-model. The model incorporates the fluid and the wall motion. The interaction is established using a decoupled approach. First, the pressure inside the vessel is computed using linear wave propagation theory. Next, the wall motion is computed in a geometrically linear FEM-computation. Finally, the fluid motion in the deforming vessel is computed.

The model is validated with an in-vitro experiment. A set-up in which models can be tested was built. The performance of the set-up is tested on an isotropic elastic model of the human thoracic aorta. A physiological flow (Newtonian fluid) is fed into a deformable, straight isotropic model of the human thoracic aorta. The model has approximately the same geometry and mechanical properties as the vessel in the in-vivo situation. At the exit, a physiologically correct terminal impedance is mounted, to ensure a good match between flow and pressure. In the model, the velocity distribution is measured with Laser Doppler anemometry and Ultrasound Doppler. From the velocity profiles, the wall shear rate is determined. The radial motion of the wall is measured using both ultrasound and optical techniques. At the same time and the same position, the pressure inside the model is measured. The behaviour of the experimental model is described well by the numerical model.

The experimental and computational method to perform the analyses to sustain the above postulated assumption were developed. However, in a straight vessel, regions with more or less continuous flow reversals and/or shear rates are not present. Therefore, the formerly described methods should be applied in a more complex geometry such as a curved tube or a bifurcation.

KEYWORDS: Atherosclerosis, Isotropic/Anisotropic models, FEM model, Wave propagation
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<td>( a )</td>
<td>scalar</td>
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<tr>
<td>( \tilde{a} )</td>
<td>complex amplitude of ( a )</td>
</tr>
<tr>
<td>( a' )</td>
<td>dimensionless form of ( a )</td>
</tr>
<tr>
<td>( \mathbf{a} )</td>
<td>vector</td>
</tr>
<tr>
<td>( a^c )</td>
<td>conjugate of ( a )</td>
</tr>
<tr>
<td>( \mathbf{A} )</td>
<td>matrix</td>
</tr>
<tr>
<td>( \mathbf{A}^T )</td>
<td>transpose of ( \mathbf{A} )</td>
</tr>
<tr>
<td>( \mathbf{A}^{-1} )</td>
<td>inverse of ( \mathbf{A} )</td>
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<table>
<thead>
<tr>
<th>Symbol</th>
<th>Property</th>
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<tr>
<td>( A )</td>
<td>cross-sectional area</td>
</tr>
<tr>
<td>( A_0 )</td>
<td>mean cross-sectional area</td>
</tr>
<tr>
<td>( b )</td>
<td>damping of vessel</td>
</tr>
<tr>
<td>( b_p )</td>
<td>damping of peripheral bed</td>
</tr>
<tr>
<td>( c )</td>
<td>wave velocity</td>
</tr>
<tr>
<td>( c_0 )</td>
<td>Moens-Korteweg wave velocity</td>
</tr>
<tr>
<td>( c_1 )</td>
<td>material constant</td>
</tr>
<tr>
<td>( C )</td>
<td>compliance</td>
</tr>
<tr>
<td>( \mathbf{C} )</td>
<td>right Cauchy-Green strain tensor</td>
</tr>
<tr>
<td>( \mathbf{4C} )</td>
<td>fourth-order material tensor</td>
</tr>
<tr>
<td>( D )</td>
<td>distensibility or deformability</td>
</tr>
<tr>
<td>( \mathbf{D} )</td>
<td>matrix representation of ( \mathbf{4C} )</td>
</tr>
<tr>
<td>( \mathbf{D} )</td>
<td>deformation velocity tensor</td>
</tr>
<tr>
<td>( E )</td>
<td>Young's modulus</td>
</tr>
<tr>
<td>( E_i, i = r, \varphi, z )</td>
<td>Young's modulus in direction ( i )</td>
</tr>
<tr>
<td>( E_{ij}, i, j = r, \varphi, z )</td>
<td>( i,j^{th} ) component of Green-Lagrange strain tensor</td>
</tr>
<tr>
<td>( F, \tilde{F} )</td>
<td>force</td>
</tr>
<tr>
<td>( \mathbf{F} )</td>
<td>deformation gradient</td>
</tr>
<tr>
<td>( F_{10} )</td>
<td>Womersley function</td>
</tr>
<tr>
<td>( G(t) )</td>
<td>relaxation function</td>
</tr>
<tr>
<td>( h )</td>
<td>wall thickness</td>
</tr>
<tr>
<td>( I )</td>
<td>( 2^{nd} ) order unit tensor</td>
</tr>
<tr>
<td>( i, j )</td>
<td>complex operator</td>
</tr>
<tr>
<td>( k )</td>
<td>wave number, arterial bed compliance</td>
</tr>
<tr>
<td>Symbol</td>
<td>Property</td>
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<td>--------</td>
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</tr>
<tr>
<td>$L$</td>
<td>transition coordinate, inerance</td>
</tr>
<tr>
<td>$\mathbf{L}$</td>
<td>divergence matrix</td>
</tr>
<tr>
<td>$m$</td>
<td>stiffness ratio, mass</td>
</tr>
<tr>
<td>$M$</td>
<td>mass matrix</td>
</tr>
<tr>
<td>$M_p$</td>
<td>mass matrix for penalty method</td>
</tr>
<tr>
<td>$n$</td>
<td>exponent in power-law model</td>
</tr>
<tr>
<td>$\mathbf{n}$</td>
<td>normal vector</td>
</tr>
<tr>
<td>$\mathbf{N}$</td>
<td>convection matrix</td>
</tr>
<tr>
<td>$p$</td>
<td>pressure</td>
</tr>
<tr>
<td>$p_i, \ (p_r, p_t)$</td>
<td>incident (reflected, transmitted) pressure wave</td>
</tr>
<tr>
<td>$\mathbf{P}$</td>
<td>$2^{nd}$ Piola-Kirchhoff stress tensor</td>
</tr>
<tr>
<td>$Q_1, \ (Q_r, Q_t)$</td>
<td>flow</td>
</tr>
<tr>
<td>$Q_2, \ (Q_r, Q_t)$</td>
<td>incident (reflected, transmitted) flow wave</td>
</tr>
<tr>
<td>$r$</td>
<td>radial coordinate</td>
</tr>
<tr>
<td>$R$</td>
<td>inner tube radius, resistance</td>
</tr>
<tr>
<td>$R_0$</td>
<td>linearized inner tube radius</td>
</tr>
<tr>
<td>$S(\tau)$</td>
<td>relaxation spectrum</td>
</tr>
<tr>
<td>$\mathbf{S}$</td>
<td>stiffness matrix</td>
</tr>
<tr>
<td>$\mathbf{u}$</td>
<td>velocity</td>
</tr>
<tr>
<td>$v_i, i = r, \varphi, z$</td>
<td>velocity in direction $i$</td>
</tr>
<tr>
<td>$t$</td>
<td>time</td>
</tr>
<tr>
<td>$\mathbf{u}$</td>
<td>displacement</td>
</tr>
<tr>
<td>$u_i, i = r, \varphi, z$</td>
<td>displacement in direction $i$</td>
</tr>
<tr>
<td>$V$</td>
<td>mean velocity</td>
</tr>
<tr>
<td>$W$</td>
<td>strain energy density</td>
</tr>
<tr>
<td>$W_k$</td>
<td>strain energy density of component $k$</td>
</tr>
<tr>
<td>$z$</td>
<td>axial coordinate</td>
</tr>
<tr>
<td>$Z$</td>
<td>impedance</td>
</tr>
<tr>
<td>$Z_i, (Z_r, Z_t)$</td>
<td>input (characteristic, terminal) impedance</td>
</tr>
<tr>
<td>$\alpha$</td>
<td>Womersley parameter</td>
</tr>
<tr>
<td>$\Gamma$</td>
<td>gamma function</td>
</tr>
<tr>
<td>$\Gamma_0$</td>
<td>reflection coefficient</td>
</tr>
<tr>
<td>$\varepsilon$</td>
<td>linear strain tensor</td>
</tr>
<tr>
<td>$\varepsilon_0$</td>
<td>strain at $t = 0$</td>
</tr>
<tr>
<td>$\varepsilon_{ij}, i, j = r, \varphi, z$</td>
<td>$i, j^{th}$ component of linear strain tensor</td>
</tr>
<tr>
<td>$\eta$</td>
<td>dynamic viscosity</td>
</tr>
<tr>
<td>$\theta$</td>
<td>time integration parameter</td>
</tr>
<tr>
<td>$\lambda$</td>
<td>wavelength</td>
</tr>
<tr>
<td>$\lambda_i, i = r, \varphi, z$</td>
<td>stretch ratio in direction $i$</td>
</tr>
<tr>
<td>$\mu$</td>
<td>Poisson ratio (isotropic material)</td>
</tr>
<tr>
<td>$\mu_{ij}, i, j = \varphi, \varphi$</td>
<td>Poisson ratio (anisotropic material)</td>
</tr>
<tr>
<td>$\nu$</td>
<td>kinematic viscosity</td>
</tr>
<tr>
<td>$\rho$</td>
<td>specific mass of fluid</td>
</tr>
<tr>
<td>$\rho_0$</td>
<td>specific mass of wall material</td>
</tr>
<tr>
<td>$\sigma$</td>
<td>Cauchy stress tensor</td>
</tr>
<tr>
<td>$\sigma, \sigma_{ij}, i, j = r, \varphi, z$</td>
<td>$i, j^{th}$ component of Cauchy stress tensor</td>
</tr>
<tr>
<td>$\tau_w$</td>
<td>wall shear stress</td>
</tr>
<tr>
<td>$\varphi$</td>
<td>circumferential coordinate</td>
</tr>
<tr>
<td>$\omega$</td>
<td>angular frequency</td>
</tr>
</tbody>
</table>
Chapter 1

Introduction

1.1 Atherosclerosis and arterial wall strains

It is generally agreed upon that the functional behaviour of the vascular endothelium is influenced by local flow phenomena. The presence of shear forces, however small, working on endothelial cells cause these cells to change their shapes and to proliferate (Nerem, 1992; Caro et al., 1971). Furthermore, periodical stretching of endothelium, cultured on a flexible substrate has similar effects (Moore et al., 1993). Thubrikar et al. (1994; 1995) pointed out that atherosclerotic lesions occur at sites that experience high cyclic deformations. Sites with low stresses and low transmural pressures in the coronary arteries (intramyocardial) of animals show less atherosclerotic lesions than epimyocardial vessels of the same subjects. It is therefore reasonable to assume that besides the presence of shear forces, the stresses inside the vessel wall are important as well when endothelial behaviour is concerned.

Consider steady flow in a deformable 180° bend with constrained ends. The fully developed velocity profile is such, that the shear rate at the outer side of the bend is much higher than the shear rate at the inner side. At the same time, due to the pressure, the vessel is deformed in such a way, that the principal stresses at the outer radius are of tensile nature, whereas the same stresses are compressive at the inner radius.

One can therefore postulate the hypothesis that atherosclerosis correlates with low wall shear rates, as well as with low or compressive principal stresses in the vessel wall.

1.2 Mechanical properties of the arterial wall

In the last decades, a vast amount of experimental work has been published concerning the mechanical properties of arteries. In most studies arteries are considered to be orthotropic, thin walled elastic vessels (Carmines et al., 1991; Cox, 1978b; Decraemer et al., 1980a; Fung et al., 1979; Fung, 1993b; Kas’yano, 1974; Vaishnav et al., 1972; Weizsäcker et al., 1983). The mechanical behaviour in terms of strain energy density is mostly described phenomenologically as an exponential function of strain (Fung, 1993b; Kas’yano & Knet-s, 1974) or as a polynomial function of strain (Vaishnav et al., 1972). Microstructural models are hardly reported (Decraemer et al., 1980a).

The viscoelastic properties are reported to a somewhat lesser extent than the elastic properties (Goedhard, n.d.; Tanaka & Fung, 1974; Decraemer et al., 1980b). All models comprise linear viscoelastic behaviour. Although it is not possible to determine the material properties of anisotropic, inhomogeneous tissues with standard (uniaxial) tests (van Ratingen, 1994), most experimental data available today are based on such tests.
1.3 Physical models

In literature, several research groups reported the use of deformable models in cardiovascular flow studies. Most models reported are homogeneous, isotropic casts of some silicone elastomer (Liepsch et al., 1992; Duncan et al., 1990; Friedman et al., 1992) or commercially available latex rubber tubing (Klanchar et al., 1990; Renderink, 1991). Normally, these models behave linearly elastic, but Pythoud (1994) demonstrated, that silicone elastomer (Sylgard 184, Dow Corning) tubes qualitatively show the same mechanical behaviour as the human aorta. Qualitatively, because the compliance of his models is lower overall, which off course has its effect on the wave phenomena in such a model.

Papageorgiou and Jones (1987a; 1987b) manufactured anisotropic models from latex penrose tube, wound under axial and circumferential prestrain with cotton thread. The threads were fixed to the tube while still under prestrain, at three circumferential positions. With the strain released, this yielded non-linear behaviour, induced by the cotton fibres, that participate in the wall-stresses only from a certain circumferential strain-level onwards. According to their report, any stress-strain behaviour could be modeled doing so. Ling and Atabek (1972) used corrugated nylon fibres (from regular nylon stockings) embedded in silicone elastomer for their models. They manufactured models of the descending aorta of a dog, that matched the \textit{in-vivo} situation quite well.

1.4 Computational methods

The coupled solution of the equations of motion (in linearized form) of blood and the arterial wall by Womersley (1957)—although he was not the first to publish it (Witzig, 1914)—initiated much computational effort in this field.

Reuderink (1991) was the first to solve the time-dependent flowfield in a deformable carotid bifurcation numerically. The method was decoupled, which means that the motion of the blood and the artery was computed separately. The motion of the wall was driven by the transmural pressure, computed with wave propagation theory. Perktold (1995) solved essentially the same problem in a weakly coupled manner earlier published by Hilbert (1986): The inlet flow plus the outlet pressure obtained from experiments were prescribed in the solution of the flow problem. The pressure distribution at the vessel wall, obtained after solving the Navier-Stokes equations, was prescribed as boundary condition for the equilibrium equations of the wall after smoothing. The smoothing was necessary to achieve convergence. Steinman (1994) adopted a similar approach as Perktold, but prescribed outlet pressures computed with wave propagation theory rather than experimental data.

1.5 Experimental methods

The experiments performed to get information on arterial behaviour are twofold: The determination of local wall shear stresses related to local flow phenomena is currently a major topic. The other branch is the determination of vascular impedance, including nonlinear effects.

1.5.1 Velocity and shear rate

Friedman (1992) measured the shear rate in a compliant cast of the human aortic bifurcation. The shear rate was determined from near-wall velocity measurements with LDA. The standard deviation on his results was in the same order of magnitude as the shear rate. The high standard deviation is caused by the inadequate spatial resolution of his LDA equipment (Lou...
et al., 1993).

Liepsch (1992) made a silicone elastomer cast of the human aortic arch, which had a physiological compliance comparable to the original vessel. With this model, time dependent flow visualization studies and velocity measurements (LDA) were carried out. The model was perfused with a Newtonian fluid. The velocity profiles in his publication seem to be very noisy, but the error level was not reported. The maximum shear stress that he found was 6-8 Pa.

Klanchar (1990) measured the influence of phase differences between pressure and flow on local wall shear stress. The wall shear rate was measured with a hotfilm anemometer, embedded in a compliant curved model. The model was terminated with a variable hydraulic resistor. Together with the compliance of the tube itself the terminal impedance of the model could be varied. The mean wall shear was measured as function of the phase difference between flow and pressure at the inner- and outer wall of the curve, and remained constant for phase differences between -55 and +50 degrees. At phase differences over 60 degrees, the mean wall shear rate increased to four times the original value in a phase difference interval of only 10 degrees. The terminal impedance therefore seems to have a great influence on the wall shear rate.

1.5.2 Wave propagation

Horsten (1989) and Reuderink (1991) compared linear wave propagation computations with measurements in latex rubber tubes and found great similarity between theory and experiments. Wave propagation experiments on tubes with non-linear behaviour have not yet been reported.

1.6 Outline

In this study, the materials and experimental methods to verify the aforementioned hypothesis will be designed and validated. With the designed set-up, the boundary conditions for in-vitro experiments on endothelial cells may be determined. To study the loads on the arterial wall modelwise, first the mechanical behaviour of the arterial wall in-vivo has to be regarded. Then a physical model, with the most important mechanical characteristics of an artery in-vivo can be manufactured. This model must be anisotropic and viscoelastic. The model will be subjected to wave propagation experiments to test the applicability of linear wave propagation theory to this essentially non-linear model. Further requirements of the model are transparency and controllability of its properties.

At the same time, a hydraulic flow circuit, able to mimick the most important features of the human arterial circulation will be built. In this set-up, flow velocity, wall motion and impedance of compliant models of human arteries will be tested. To control the pressure-flow relations in the set-up adequately, its terminal impedance requires special attention.
Chapter 2

Arteries: morphology and mechanical behaviour

2.1 Morphology

Arteries can be subdivided into several groups with descending diameter: elastic arteries, muscular arteries, arterioles and canules. Because atherosclerotic disease mainly occurs in the larger arteries this study concerns them only. The larger arteries are often called elastic arteries, because of the small amount of vascular smooth muscle in them. The mechanical behaviour, however, is not elastic but viscoelastic. Whenever the arterial wall or arteries are being referred to, only elastic arteries are considered.

The arterial wall consists of three layers:

Tunica Intima: In the aorta of humans the intimal layer consists of endothelium and a subendothelial layer. In other elastic arteries, e.g. a. carotis and a. vertebralis, the subendothelial layer is not present. The endothelium is formed by a single layer of cells, separated from the subendothelial space by a thin basal lamina. The endothelial cells are flat and elongated with their long axis parallel to that of the blood vessel. They have a thickness of ± 0.2 -0.5 μm, except in the area of the nucleus, which protrudes slightly into the vessel. During life, the subendothelial layer of the human aorta develops gradually. In infants it is very thin with a narrow layer of connective tissue fibers. In young adults it increases in thickness and becomes denser and a few cells appear. In middle-aged subjects, the subendothelial layer becomes fibrous and cellular, in an inhomogeneous way. Finally, in senile subjects the layer becomes thick, fibrous and transform partially into a solid glassy matter.

Tunica Media: The media consists of fenestrated elastic laminae (fig. 2.1). In the human aorta 40-60 of these laminae exist. Toward the periphery this number decreases gradually. In small arteries they are rarely present.

The elastic laminae (average thickness 3 μm) are concentric and equidistantly spaced. They are interconnected by a network of elastic fibrils. Thus structured, the media has great strength and elasticity.

The smooth muscle cells are placed within the formerly described network. The cells have an elongated, but irregular shape, with many cellular extensions. The extensions connect the cells to the collagenous bundles in the media.

In the inner part of the media, the muscle cells are oriented both longitudinally and circumferentially (thoracic aorta of the dog). The smooth muscle cells in the rest of the media are oriented helically. The angle between the long axis of the smooth muscle cells

13
and the vessel is 20-40°.
In the pig carotid arteries the smooth muscle cells form a helix. In the rat aorta, the cells were found to be oriented diagonally, with different angles in successive layers (fig. 2.2).

**Tunica Adventitia**: The adventitia of elastic arteries generally comprises only 10% of the vascular wall. The thickness varies considerably in different arteries. The thoracic aorta has a very thin adventitia, but it becomes thicker towards the aortic bifurcation. The adventitia forms a sleeve of interwoven, thick bundles of collagenous fibrils around the media. It gives strength to the vascular wall and limits its deformability.

### 2.2 Mechanical properties of the constituents

The main constituents of vascular tissue, as pointed out in the previous chapter are: 1: Elastin, 2: collagen fibers and 3: smooth muscle cells. The properties of each will be discussed in this section.

#### 2.2.1 Elastin

Elastin is a biological material with an almost linear stress-strain relationship (fig. 2.3). It has a Young's modulus of approx. 0.6 MPa and remains elastic up to stretch ratios of approximately 1.6 (Fung, 1993a). As can be seen from the stress-strain curves the material shows hardly any hysteresis, and fixation in formaline affects the properties only slightly. This is important, because most researchers perform their experiments on tissues in fixated state.
2.2.2 Collagen

Collagen is a basic structural protein in animals. It gives strength and stability to anyone's body, and appears in almost all parts of it. The collagen molecule consists of three helically wound chains of amino-acids. These helices are collected together in micro-fibrils, which in their turn form subfibrils and fibrils. The fibrils have a diameter of 20-40 nm, depending on species and tissue. Bundles of fibrils form fibers, with diameters ranging from 0.2 to 12 µm. The fibers are normally arranged in a wavy form, with typical "wavelengths" of 200 µm (Fung, 1993a). Due to this waviness the stress-strain relationship shows a very low stiffness at small stretch ratios λi (fig. 2.4). The stiffness increases fast once the fibers are deformed to straight lines, the Young's modulus of the material then reaches approx. 1 GPa. At further stretching, the material finally fails at 50-100 MPa longitudinal stress.

2.2.3 Vascular smooth muscle

A constitutive model for vascular smooth muscle is not available from literature. However, Cox (1978b) reported the effect of active vascular muscle on the stress-strain behaviour of vessels as a whole.

2.3 Models

2.3.1 Phenomenological models

Phenomenological models of material behaviour are often nothing more but some function that fits best to experimental data. Because of this, the predictive capacities of a model, for other
Figure 2.3: Stress-strain relationships of elastine from the ligamentum nuchae of cattle. One specimen was fixed for a week in a 10% formalin solution, the other was fresh. (from (Fung, 1993a))

Figure 2.4: Typical stress-strain relationship of collagen from the rabbit limb tendon (from (Fung, 1993a))
loading situations than the experimental one, are often poor. However, as structural data for many tissues are not available, there is often no alternative structural model. The models described in this and the following section are based on the assumption that the reference state of an artery (axially unstretched and no transmural pressure present) is stress-free. Fung and his coworkers (Fung, 1993a; Chuong & Fung, 1986; Han & Fung, 1991) showed that this is not the case. When a piece of artery is cut longitudinally, the original form (a circle) transforms to a (more or less) circular sector. To account for this phenomenon, obviously there were residual stresses present in the uncut specimen. Whether the thus acquired geometry is actually stress-free, however, remains questionable.

**Elastic behaviour**

The simplest model for vascular tissue is isotropic linear elastic behaviour. Isotropic models are not used in literature for the modeling of vascular tissue, but appear in publications when the impedance of a vessel is computed (Westerhof et al., 1969; Milnor, 1989). According to this theory, the Cauchy stress \( \sigma \) in a material is related to the linear strain \( \varepsilon \) by the following equation:

\[
\sigma = 4 \mathbf{C} : \varepsilon
\]  

\( 4\mathbf{C} \) is a constant fourth order tensor, that depends on the Young’s modulus \( E \) and the Poisson ratio \( \mu \) of the material only. Because \( \sigma, 4\mathbf{C} \) and \( \varepsilon \) are symmetric, equation (2.1) may be written in component form as a vector equation:

\[
\sigma = \mathbf{D} \cdot \varepsilon
\]  

with \( \mathbf{D} \) the matrix representation of \( 4\mathbf{C} \). In the axisymmetric case this yields (coordinate system, see fig 2.5):

\[
\begin{bmatrix}
\sigma_{rr} \\
\sigma_{zz} \\
\sigma_{\varphi\varphi} \\
\sigma_{rz}
\end{bmatrix} = \frac{E}{(1+\mu)(1-2\mu)} \begin{bmatrix}
1-\mu & \mu & \mu & 0 \\
\mu & 1-\mu & \mu & 0 \\
\mu & \mu & 1-\mu & 0 \\
0 & 0 & 0 & \frac{1}{2}(1-2\mu)
\end{bmatrix} \begin{bmatrix}
\varepsilon_{rr} \\
\varepsilon_{zz} \\
\varepsilon_{\varphi\varphi} \\
\varepsilon_{rz}
\end{bmatrix}  
\]  

Figure 2.5: Axisymmetric coordinate system: basis vectors

Vascular tissue is anisotropic. Most models describe vascular tissue as an orthotropic material. The linear isotropic model is easily extended to linear orthotropic behaviour by replacement of the matrix \( \mathbf{D} \) in equation (2.3) with the following:

\[
\mathbf{D} = \begin{bmatrix}
\frac{E_r}{1-\mu_r \mu_{\varphi \varphi}} & \frac{\mu_{r \varphi} E_r}{1-\mu_r \mu_{\varphi \varphi}} & \frac{\mu_{r z} E_r}{1-\mu_r \mu_{z z}} & 0 \\
\frac{\mu_{r \varphi} E_r}{1-\mu_r \mu_{\varphi \varphi}} & \frac{E_{\varphi}}{1-\mu_r \mu_{\varphi \varphi}} & \frac{\mu_{r z} E_{\varphi}}{1-\mu_r \mu_{z z}} & 0 \\
\frac{\mu_{r z} E_r}{1-\mu_r \mu_{z z}} & \frac{\mu_{r z} E_{\varphi}}{1-\mu_r \mu_{z z}} & \frac{E_z}{1-\mu_r \mu_{z z}} & 0 \\
0 & 0 & 0 & G_{rz}
\end{bmatrix}
\]  

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$G_{rz}$ is the shear modulus of the material in the $r, z$ plane. For nonlinear, orthotropic behaviour, many models are presented in terms of the strain energy density functions $W$. $W$ is a function of the Green-Lagrange strain tensor $E$. The latter is defined as:

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

(2.5)

with $F$ the deformation gradient and $I$ the second order unit tensor. The term $F^c F$ in equation (2.5) is the right Cauchy-Green strain tensor $C$. The derivative of $W$ with respect to $E$ yields the 2nd Piola-Kirchhoff stress tensor $P$:

$$P = \rho_0 \frac{dW}{dE}$$

(2.6)

with $\rho_0$ the specific mass of the material in undeformed state. This tensor has the following relation with the Cauchy stress tensor:

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

(2.7)

For the modeling of elastic behaviour of vascular tissue, basically, three types of phenomenological models are reported:

- Incremental formulations (Cox, 1975; Cox, 1978a) This type describes the behaviour as linearly elastic, with different Young’s moduli for different stretch ratios of the vessel material.

- Polynomial formulations (Vaishnav et al., 1972). The nonlinear elastic behaviour is described with a polynomial fit. Relationships with 3, 7 and 12 constitutive constants were reported.

- Exponential formulations (Kas’yanov, 1974; Fung et al., 1979; Fung, 1993a; Chuong & Fung, 1983; Carmines et al., 1991; von Maltzahn et al., 1981). In these formulations, the strain energy density function $W$ is written as an exponential function of the components of the Green-Lagrange strain tensor $E$. Fung e.g., postulated this strain energy density function:

$$\rho_0 W = \frac{c}{2} e^q$$

(2.8)

with:

$$q = a_1 E_{\varphi \varphi}^2 + a_2 E_{zz}^2 + 2a_4 E_{\varphi \varphi} E_{zz}$$

(2.9)

and $c$, $a_1$, $a_2$ and $a_4$ material constants. This type is the most used model today.

The parameters in the models usually are determined by uniaxial tensile tests of (mostly) prepared specimens of arterial walls.

An example of an exponential model published by Kas’yanov (1974) is given in fig. 2.6. This model is slightly different from Fung’s model:

$$W = a(e^q - 1) + m(e^r - 1)$$

(2.10)

with:

$$q = b(\lambda_{\varphi} - \lambda_z)^2 + c \left( \lambda_z - \frac{1}{\lambda_{\varphi} \lambda_z} \right)^2 + d \left( \frac{1}{\lambda_{\varphi} \lambda_z} - \lambda_{\varphi} \right)^2$$

$$r = f(\lambda_{\varphi} - \lambda_z)^2 + k \left( \lambda_z - \frac{1}{\lambda_{\varphi} \lambda_z} \right)^2 + l \left( \frac{1}{\lambda_{\varphi} \lambda_z} - \lambda_{\varphi} \right)^2$$

(2.11)

(2.12)

The constants $a, b, c, d, f, k, l$ and $m$ were determined for a human abdominal aorta by uniaxial tensile tests.
Figure 2.6: Typical stress-strain relationship of aortic wall material (from (Kas’yanov & Knet-s, 1974)). Solid curve: Relation between circumferential stretch ratio $\lambda_\phi$ and Cauchy stress $\sigma_{\phi\phi}$. Dashed curve: Relation between axial stretch ratio $\lambda_z$ and Cauchy stress $\sigma_{zz}$. Both curves are fits to experimental data, based on equation (2.10).

Viscoelastic behaviour

All of the abovementioned models describe elastic behaviour. Vascular tissue normally is viscoelastic. The viscoelasticity of the wall has a great influence on the wave propagation properties of the vessel. When a cyclic load is applied to it in an experiment, the load-displacement curve for loading differs from the unloading curve (hysteresis, due to viscoelasticity). Moreover, the curves change after several repetitions of the same loading/unloading cycle. After a certain number of repetitions, the loading-unloading curve doesn’t change anymore, and the loading/unloading curves almost coincide. The state of the specimen then is called preconditioned (Fung et al., 1979; Fung, 1993a). The model is fitted to the loading and the unloading curve separately. For a cyclic process the material behaves in an elastic manner, specific to the process. The material then is called pseudoelastic. How well this state resembles the in-vivo situation is not reported.

A linear viscoelastic constitutive equation for a material can simply be acquired by replacing the real Young’s modulus $E$ in equation (2.3) by a complex one. This results in what is called a power law model. The Cauchy stress $\sigma$ then decreases linearly with a negative power of the time when a step in strain is applied to the material. In the one-dimensional case this model reads:

$$\sigma = E(t)\varepsilon_0 = [c_1 t^{-n}] \varepsilon_0$$

(2.13)

with $\varepsilon_0$ the strain, applied stepwise to the material. The complex modulus $E$ may be determined by Laplace transformation of equation (2.13).

$$\hat{\sigma} = \hat{E} \hat{\varepsilon} = \frac{\hat{E}}{s}\varepsilon_0$$

(2.14)

Together with equation (2.13) this yields for the complex modulus:

$$\hat{E}(s) = c_1 \Gamma(1-n)s^n$$

(2.15)

with $\Gamma$ the gamma function. Equation (2.15) can be rewritten in terms of frequency:

$$\hat{E}(j\omega) = c_1 \Gamma(1-n)\omega^n e^{jn\pi/2}$$

(2.16)
The complex part of $E(j\omega)$ is the loss modulus, the real part the storage modulus. Tanaka and Fung (1974) determined the relaxation curves of arterial tissue experimentally, using uniaxial relaxation tests. They found that the relaxation function of vascular tissue loaded in the physiological range is normalizable.

The time-dependent stress in a specimen can then be written as:

$$\sigma(t, \lambda) = G(t) \sigma^{(e)}(\lambda) \tag{2.17}$$

with $G(t)$ the normalized relaxation function and $\sigma^{(e)}(\lambda)$ the pseudoelastic stress function, related to the stretch ratio $\lambda$.

They fitted the following function to their results:

$$G(t) = \frac{1}{1 + \int_0^\infty S(\tau)e^{-t/\tau}d\tau} \tag{2.18}$$

with $S(\tau)$ the relaxation spectrum. For this spectrum they proposed:

$$S(\tau) = \begin{cases} \frac{\tau}{\tau_1} & \text{for } \tau_1 < \tau < \tau_2 \\ 0 & \text{for } \tau < \tau_1, \tau > \tau_2 \end{cases} \tag{2.19}$$

with $c$ a dimensionless constant.

Typical values for human aorta are: 1: circumferentially: $c = 0.05$, $\tau_1 = 0.2$ s, $\tau_2 = 250$ s and 2: longitudinally: $c = 0.025$, $\tau_1 = 0.1$ s, $\tau_2 = 400$ s.

### 2.3.2 Morphological models

Morphological models are based on the microstructure of the material that these models describe. The great advantage is that parameters in the model directly reflect the properties and orientation of the constituents of the components of the tissue. Generally, the problem is to obtain the microstructural information required to build the model. Because of this, most authors use phenomenological models instead.

A one-dimensional model was used by DeCraemer et al. (1980a; 1980b) to describe the elastic and viscoelastic behaviour of soft tissue. The material was assumed to be thin walled, containing many $(N)$ collagen fibers. The initial length $l_i$ of the fibers was assumed to be normally distributed with mean value $\mu$ and standard deviation $s$. Each fiber has the same transversal cross-section $A$ and Young’s modulus $E$. With increasing strain more and more fibers thus contribute in the load bearing process.

The force $F$ needed to deform a specimen with length $l_0$ to length $l$ then becomes:

$$F(l) = \int_{l_0}^l A E \frac{l - l_i}{l_i} \frac{N}{\sqrt{2\pi s}} e^{-\frac{(l - l_i)^2}{2s^2}} dl_i \tag{2.20}$$

This model was extended to describe viscoelastic behaviour by replacing modulus $E$ with a relaxation function $G(t)$:

$$F(t) = N \int_{-\infty}^t G(t - \tau) \frac{dl(\tau)}{d\tau} \times \int_{l_0}^{l(\tau)} A E \frac{1}{\sqrt{2\pi s}} e^{-\frac{(l - l_i)^2}{2s^2}} dl_i d\tau \tag{2.21}$$

Lanir (1979; 1983) used a microstructural mixture model of the same type to describe the mechanical behaviour of skin tissue. This model is two-dimensional and allows for more than one type of load bearing component of the tissue. Humphrey et al. (1987; 1989) used an almost
identical approach.
The tissue is assumed to consist of fibers, embedded in a matrix. Type $k$ fibers have a uniaxial strain-energy density function $W_k(\lambda)$. The matrix material only provides an hydrostatic pressure $p$. The deformation of matrix and fibers is affine. The total energy of a fraction $k$ fibers then is:

$$W_k = \sum_u S_k \cdot R_k(\vec{u}) \cdot w_k(\lambda) \cdot \Delta \Omega$$

(2.22)

And the total strain energy of the material:

$$W = \sum_k W_k$$

(2.23)

$S_k$ is the volumetric fraction of the fibers, $\vec{u}$ is the direction of the fibers, $R_k(\vec{u})$ is the direction distribution function of fibers of type $k$ and $\Delta \Omega$ is the total undeformed volume. This model is very elegant, as it describes the material behaviour in terms of uniaxial properties of distinct fiber types, with a known spatial distribution. These distribution functions for vascular tissue, however, have not been reported in literature yet.
Chapter 3

Wall and fluid motion

3.1 Introduction

The arterial wall is highly deformable. Due to the pressure waves, generated by the heart, the wall will deform. The radial displacements are in the order of 5-7 \% of the vessel diameter, depending on the type and position of the vessel. In 1957 Womersley derived the coupled harmonic solution for fluid and wall motion in a thin-walled, isotropic, deformable vessel (Womersley, 1957).

In this chapter, his theory will be extended to anisotropic thin-walled tubes. Furthermore, the implications of anisotropy on vessel impedance and wave propagation properties will be highlighted.

More recent, several research groups performed finite element computations on vessel wall motion combined with blood flow (Reuderink, 1991; Perktold & Rappitsch, 1995; Steinman & Ethier, 1994). Their methods to solve the equations of motion of wall and fluid are summarized in fig. 3.1. Reuderinks solution technique comprises the top three blocks of the scheme, whereas the methods presented by Perktold and Steinman comprise the lower three blocks.

In Reuderinks method, the equations of motion for wall and fluid are solved decoupled. The vessel to be modeled is a straight tube with terminal impedance $Z_t$ at axial position $z = L$. The tube itself has a characteristic impedance $Z_c$. With a given entry flow, the pressure wave is computed using linear wave propagation theory. Next, the equilibrium equations for the wall are solved with a standard geometrically linear quasi-static FEM computation (Zienkiewicz & Taylor, 1991), assuming the tube to be homogeneous, isotropic and linearly elastic. The mesh for the fluid motion computation is deformed accordingly. Finally, the fluid motion is computed. Perktold and Steinman solve the equations of motion with a weakly coupled method. At the entry of their models the flow is prescribed, at the end(s) the pressure. Per timestep, the following steps are taken: With the pressure boundary condition, the mesh deformation is computed, and subsequently the fluid velocity and the pressure inside the vessel. With the computed pressure, the wall deformation is computed again. The procedure is repeated until convergence of the pressure is reached.

In this paper, the method proposed by Reuderink will be used in FEM-computations of a human arterial section, terminated with a physiologically relevant terminal impedance.
3.2 Wave propagation

3.2.1 Fluid

The momentum- and continuity equations for a fluid read:

\[ \rho \frac{\partial \mathbf{v}}{\partial t} + \rho \mathbf{v} \cdot \nabla \mathbf{v} = \nabla \cdot \mathbf{\sigma} \]  

(3.1)

\[ \rho \mathbf{v} \cdot \nabla \mathbf{v} = 0 \]  

(3.2)

For a Newtonian fluid, the constitutive equation reads:

\[ \mathbf{\sigma} = -p \mathbf{I} + 2\eta \mathbf{D} \]  

(3.3)

\( \mathbf{D} \) is the deformation gradient tensor:

\[ \mathbf{D} = \frac{1}{2} \left( \nabla \mathbf{v} + (\nabla \mathbf{v})^T \right) \]  

(3.4)

Inserting the constitutive behaviour in equation (3.5) yields the Navier-Stokes equations:

\[ \rho \frac{\partial \mathbf{v}}{\partial t} + \rho \mathbf{v} \cdot \nabla \mathbf{v} = -\nabla p + \eta \nabla^2 \mathbf{v} \]  

(3.5)

\[ \rho \mathbf{v} \cdot \nabla \mathbf{v} = 0 \]  

(3.6)

Applied to an axisymmetric flow through a deformable tube with mean radius \( R_0 \) they transform into (coordinates \( r, \varphi, z \)):

\[ \left[ \frac{\partial v_r}{\partial t} + v_r \frac{\partial v_r}{\partial r} + v_z \frac{\partial v_r}{\partial z} \right] = \frac{1}{\rho} \frac{\partial p}{\partial r} + \nu \left[ \frac{\partial}{\partial r} \left( \frac{1}{r} \frac{\partial (rv_r)}{\partial r} \right) + \frac{\partial^2 v_r}{\partial z^2} \right] \]  

(3.7)
As the velocity plus all derivatives in \(\varphi\)-direction are zero, they are not represented in the equations.

If now only harmonic solutions are permitted with wave number \(k\) and frequency \(\omega\):

\[
\begin{align*}
 v_r &= \hat{v}_r(r) e^{i(\omega t-kz)} \\
 v_z &= \hat{v}_z(r) e^{i(\omega t-kz)} \\
 p &= \hat{p}(r) e^{i(\omega t-kz)}
\end{align*}
\]

Assuming that the wavelength \(\lambda\) is long compared with the length of the tube \((\lambda/z \gg 1)\) and the velocity of the fluid much lower than the wave velocity \(c\): \(v_r/c \ll 1\) and \(v_z/c \ll 1\) the convective terms plus all velocity derivatives in \(z\)-direction may be neglected. The Navier-Stokes equations then reduce to:

\[
\begin{align*}
 \frac{\rho_0}{r} \frac{\partial v_r}{\partial t} + \frac{\partial p}{\partial r} &= \frac{\eta}{r} \frac{\partial^2 v_r}{\partial r^2} + \frac{\partial v_r}{\partial r} - \frac{v_r}{r^2} \\
 \frac{\rho_0}{r} \frac{\partial v_z}{\partial t} + \frac{\partial p}{\partial z} &= \frac{\eta}{r} \frac{\partial^2 v_z}{\partial r^2} + \frac{\partial v_z}{\partial r}
\end{align*}
\]

with boundary conditions:

\[
\begin{align*}
 \vec{v}_{\mid r=R} &= \vec{v}_{\text{wall}} \\
 \frac{\partial \vec{v}}{\partial r} \Big|_{r=0} &= \vec{0}
\end{align*}
\]

These equations can be solved, coupled with the equations of motion for the wall, that will be derived in the next section.

### 3.2.2 Wall

The equation of motion for a solid material with no body forces present reads:

\[
\nabla \cdot \sigma = \overrightarrow{f}
\]

with \(\overrightarrow{f}\) the inertial forces working on the material. The constitutive equation for the wall material that will be used here is equation (2.3), with the material matrix \(D\) of equation (2.4), given in chapter 2. The following extra assumptions are made: 1: The model is thin walled, with radius \(R_0\) and wall thickness \(h\). 2: The loads on the tube are such (no radial stresses), that plane stress theory is applicable. 3: There are no torsional or bending moments in the tube, so shear stresses do not occur.

With \(E_\varphi\) and \(E_z\) the elastic moduli in circumferential and longitudinal direction, and \(\mu_{\varphi z}\) and \(\mu_{\varphi z}\) the corresponding Poisson ratios, the non zero terms in the constitutive equation of the tube reduce to (see equation (2.3) and (2.4)):

\[
\sigma_{\varphi\varphi} = \frac{1}{1-\mu_{\varphi z} \mu_{\varphi \varphi}} \left[ E_\varphi \varepsilon_{\varphi \varphi} + \mu_{\varphi z} E_z \varepsilon_{zz} \right]
\]
with $\varepsilon_{\varphi\varphi}$ and $\varepsilon_{zz}$ the linear strains in circumferential and longitudinal direction:

$$
\varepsilon_{\varphi\varphi} = \frac{(r + u_r) d\varphi - rd\varphi}{rd\varphi} = \frac{u_r}{r} \approx \frac{u_r}{R} \\
\varepsilon_{zz} = \frac{\partial u_z}{\partial z}
$$

Figure 3.2: Infinitesimal wall volume with forces acting on it

The equations of motion of the tube are easily derived by balancing the forces acting upon an infinitesimal part of the wall (sizes $h$, $R d\varphi$ and $dz$, see fig. 3.2).

First of all, the shear force acting in $z$-direction at the inside of the tube is:

$$
\tau_w = -\eta \left[ \frac{\partial v_z}{\partial r} + \frac{\partial v_r}{\partial z} \right]_{r=R_0} \\
$$

This force is counterbalanced by the stress in the wall plus inertial forces:

$$
\rho h \frac{\partial^2 u_z}{\partial t^2} = -\eta \left[ \frac{\partial v_z}{\partial r} + \frac{\partial v_r}{\partial z} \right]_{r=R_0} + h \frac{\partial \sigma_{zz}}{\partial z} \\
$$

In the radial direction the forces are: pressure $p$, which may be a function of the radius $R_0$, inertial forces and circumferential stresses to counterbalance the pressure:

$$
\rho R_0 h \frac{\partial^2 u_r}{\partial t^2} = p(R_0) - \frac{\sigma_{\varphi\varphi} h}{h} \\
$$

### 3.2.3 Wave velocity and -attenuation

Assume that the wall motion is harmonic:

$$
\begin{align*}
    u_r &= \hat{u}_r e^{j(wt-kz)} \\
    u_z &= \hat{u}_z e^{j(wt-kz)}
\end{align*}
$$
with \( \dot{u}_r \) and \( \dot{u}_z \) complex amplitudes of the wall motion. Together with the no-slip condition at the wall:

\[
\begin{align*}
\left. \frac{\partial u_r}{\partial t} \right|_{r=R_0} &= v_r(R_0) \quad (3.27) \\
\left. \frac{\partial u_z}{\partial t} \right|_{r=R_0} &= v_z(R_0) \quad (3.28)
\end{align*}
\]

and the constitutive equations (3.18, 3.19), equations (3.13), (3.14), (3.23) and (3.24) may be solved. The solution determines the wave number \( k \) as a function of the mechanical and geometrical properties of the tube, the density and viscosity of the fluid and the frequency parameter \( \alpha \) (For the derivation of the solution, see appendix A):

\[
k(\omega) = \pm \omega \sqrt{\frac{R_0 \rho_0}{h E_z} \left[ G \pm \sqrt{G^2 - \left( 1 - m \mu_{z\varphi}^2 \right) L} \right]} \quad (3.29)
\]

with:

\[
m = \frac{E_x}{E_z} \quad (3.30)
\]

and

\[
G = \frac{1 + \frac{1}{2} m H(1 - F_{10}) + \left( \frac{1}{4} - \mu_{z\varphi} \right) m F_{10}}{m(1 - F_{10})} \quad (3.31)
\]

\[
L = \frac{F_{10} + 2H}{m(1 - F_{10})} \quad (3.32)
\]

\[
F_{10} = \frac{2 J_1 \left( \alpha j^{3/2} \right)}{\alpha j^{3/2} J_0 \left( \alpha j^{3/2} \right)} \quad (3.33)
\]

The foremost \( \pm \) sign indicates the forward- and backward moving waves. The second \( \pm \) sign indicates two modal solutions. Each solution corresponds to one mode of vibration. When positive, the wavenumber of the shear waves in the tube wall is indicated. In an isotropic tube \((m=1)\), the velocity of the shear waves is much higher than the pressure wave velocity. This enables distinction of the two modes. Otherwise, the pressure wave is indicated. In case of non-reflecting waves, the pressure wave is:

\[
p = \hat{p} e^{-\frac{2 \pi}{L} z} e^{i \omega (t - \frac{z}{c})} \quad (3.34)
\]

The wave velocities \( c \) are:

\[
c = \frac{\omega}{R(k)} = \frac{1}{\sqrt{\frac{R_0 \rho_0}{h E_z} \left[ G \pm \sqrt{G^2 - \left( 1 - m \mu_{z\varphi}^2 \right) L} \right]}} \quad (3.35)
\]

and the attenuation constant \( \gamma \):

\[
\gamma = \frac{-2 \pi \Im(k)}{R(k)} = \frac{-2 \pi \Im \sqrt{\frac{R_0 \rho_0}{h E_z} \left[ G \pm \sqrt{G^2 - \left( 1 - m \mu_{z\varphi}^2 \right) L} \right]}}{\sqrt{\frac{R_0 \rho_0}{h E_z} \left[ G \pm \sqrt{G^2 - \left( 1 - m \mu_{z\varphi}^2 \right) L} \right]}} \quad (3.36)
\]
Equations (3.35) and (3.36) each represent two functions. For physiological purposes, the values of \( c \) and \( \gamma \) with respect to the frequency parameter \( \alpha \) and stiffness ratio \( m \) are interesting. When evaluating \( c \) and \( \gamma \) for constant \( m \) and variable \( \alpha \), the two solutions show remarkable behaviour (see fig. 3.3): At low values of \( \alpha \) (\( \alpha = 1 \)), the pressure (transversal) wave velocity is lower than the longitudinal velocity. For an isotropic tube \( m = 1 \), this remains valid. For anisotropic tubes (\( m > 1 \), e.g., \( m = 10 \)), at some value of \( \alpha \) the two velocity curves intersect (\( \alpha \approx 10 \)), and the pressure wave changes to the second mode of vibration. The intersection can be found in a straightforward manner: The two velocities are the same when the term after the \( \mp \)-sign vanishes:

\[
G^2 - \left(1 - m \mu_{ap}^2\right) L = 0
\]  

(3.37)

The attenuation constant \( \gamma \) is depicted in the right panel of fig. 3.3. At the frequency where the wave velocity curves of the anisotropic tube intersect, the attenuation curves show discontinuity. Why this discontinuity occurs is not yet clear and therefore requires further research.

### 3.2.4 Impedance

Up till now we have considered the wave propagation properties of a homogeneous, cylindrical infinitely long tube, with pressure and shear waves travelling in one direction. To describe the pressure and the flow inside a vessel with finite length, knowledge of the properties of the vessel and the fluid only does no longer suffice. Boundary conditions concerning the pressure-flow relations at the ends of the vessel then play a major role. The relation describing pressure and flow at some position is called impedance. In this section the impedance of a vessel, terminated with some terminal impedance will be discussed. This impedance model will be discretized, to enable simplified modeling for experimental purposes.
Continuous model

In this section we will consider the effect of sudden changes in properties (transitions) on the wave phenomena inside a vessel. The length of the transition is small compared with the wavelength, so there is no difference in pressure and flow proximal and distal from the transition.

Consider a vessel with a transition at axial coordinate $z = L$: The incident pressure and flow are denoted by $\hat{p}_i$ and $\dot{Q}_i$, the reflected pressure and flow by $\hat{p}_r$ and $\dot{Q}_r$ and the transmitted waves by $\hat{p}_t$ and $\dot{Q}_t$. Flow and pressure are continuous so:

$$p_i(\omega, L, t) + p_r(\omega, L, t) = p_t(\omega, L, t)$$

$$Q_i(\omega, L, t) + Q_r(\omega, L, t) = Q_t(\omega, L, t)$$

The characteristic impedance $Z_c$ of a vessel is defined as:

$$Z_c = \frac{\hat{p}_i}{\dot{Q}_i} \quad \text{which is equal to:} \quad \frac{k}{\omega C}$$

The subscript $i$ indicates the forward travelling part of the pressure- and flow waves inside the vessel. The characteristic impedance is the input impedance of an infinitely long vessel, i.e., no reflections occur.

In equation (3.40) $C$ is the dynamic compliance of the vessel. The input impedance of a vessel is similar to the characteristic impedance of the vessel:

$$Z_i = \frac{\hat{p}_i + \hat{p}_r}{\dot{Q}_i + \dot{Q}_r}$$

The pressure- and flow amplitudes now comprise the forward- and backward running waves as well.

The reflection coefficient $\Gamma_0$ is defined as:

$$\Gamma_0 = \frac{\hat{p}_r(\omega, L)}{\hat{p}_i(\omega, L)} = \frac{Z_1 - Z_0}{Z_1 + Z_0}$$

With $Z_1$ the impedance distal and $Z_0$ the impedance proximal from the transition where the reflection occurs. The propagation of a pressure wave $p_i = \hat{p}_i(\omega, 0)e^{i(\omega t - kz)}$ (see also equation (3.34)) in a vessel with a transition at $z = L$ then reads (for $z < L$):

$$p(\omega, z, t) = \hat{p}_i(\omega, z, t) + \hat{p}_r(\omega, z, t)$$

$$= \hat{p}_i(\omega, 0)e^{-ikz} \left[ 1 + \Gamma_0 e^{-2ik(L-z)} \right] e^{i\omega t}$$

(3.43)

The flow is similar:

$$Q(\omega, z, t) = \dot{Q}_i(\omega, z, t) + \dot{Q}_r(\omega, z, t)$$

$$= \dot{Q}_i(\omega, 0)e^{-ikz} \left[ 1 - \Gamma_0 e^{-2ik(L-z)} \right] e^{i\omega t}$$

(3.44)

The input impedance of the system then is:

$$Z_i = \frac{\hat{p}_i(\omega, 0)e^{-ikz} \left[ 1 + \Gamma_0 e^{-2ik(L-z)} \right] e^{i\omega t}}{\dot{Q}_i(\omega, 0)e^{-ikz} \left[ 1 - \Gamma_0 e^{-2ik(L-z)} \right] e^{i\omega t}} = Z_c \left[ 1 + \Gamma_0 e^{-2ik(L-z)} \right] \left[ 1 - \Gamma_0 e^{-2ik(L-z)} \right]$$

(3.45)
Terminal impedance

In this study, the terminal impedance of the experimental set-up will be modeled with a modified windkessel, according to Westerhof. Westerhof and his coworkers reported the use of discrete models for vascular impedance (1969; 1971; 1977; 1979). These models are used because they can be implemented experimentally in an easier fashion than the continuous ones. The discretization is carried out as follows:

Consider a vascular section with length \( l \), compliance \( C \) and cross-sectional area \( A \). A viscous fluid with kinematic viscosity \( \nu \) and density \( \rho \) flow through the section. The vessel is pressurized at one end with a pressure \( p \). The displacement of the fluid is \( u \). The equation of motion in its general form is:

\[
m \frac{\partial^2 u}{\partial t^2} + b \frac{\partial u}{\partial t} + ku = f
\]

For this particular case the equation of motion reads:

\[
\rho A \frac{\partial^2 u}{\partial t^2} + \frac{\pi 8 \nu \rho}{A^2} \frac{\partial u}{\partial t} + \frac{l}{C} u = pA
\]

The damping term is derived from the Poiseuille resistance of a straight tube. This is a rather crude simplification of the actual resistance in oscillatory flow. The flow rate \( q \) inside the vessel is: \( A \partial u / \partial t \). Substituting this in the equation and subsequent division by \( A \) yields:

\[
\frac{\rho A}{A} \frac{\partial q}{\partial t} + \frac{\pi 8 \nu \rho}{A^4} q + \frac{l}{CA^2} \int q dt = p
\]

The impedance \( Z \) is obtained by Laplace transformation of this differential equation:

\[
Z(s) = \frac{Ls^2 + Rs + \frac{1}{C}}{s}
\]

with \( L \) the inerance, \( R \) the resistance and \( C \) the compliance of the section. The model may be refined by assembling several sections into a network.

The advantage of this type of model is that it splits up the impedance into more distinguished parameters: fluid mass, resistance and compliance. This is very useful when building a physical impedance for experimental purposes. Moreover, when the fluid mass and more important, the vessel’s compliance become a function of pressure, this model has the advantage that it gives solutions in the time domain, and can be used in computations easily even when nonlinear behaviour is involved.

### 3.3 Wall motion

The upper three blocks of fig. 3.1 show the computational strategy, as proposed by Reuderink (1991). This strategy incorporates wave phenomena that occur in flows through deformable geometries.

The experiment to be modeled is a straight tube with terminal impedance \( Z_t \) at axial position \( z = L \). The tube itself has a characteristic impedance \( Z_c \). First, the pressure inside the tube is computed using linear wave propagation theory. With a given entry flow, the pressure wave can be computed using equations (3.45) and (3.42).

Next, the equilibrium equations for the wall are solved with a standard geometrically linear quasi-static FEM computation (Zienkiewicz & Taylor, 1991), assuming the tube to be homogeneous, isotropic and linearly elastic. The equilibrium equation (2.3) is discretized with a Galerkin finite element method which yields the classic linear equation:

\[
\mathbf{S} u = f
\]
With $\mathbf{K}$ the stiffness matrix, $\mathbf{u}$ the displacements of the nodal points and $\mathbf{f}$ the loads on the model. The ends of the model are constrained, while the previously computed pressure acts on the inside of the tube. The tube is filled with an elastic material which has a Young’s modulus that is several orders of magnitude lower than the tube material. Furthermore its Poisson ratio is almost zero. In this way, the deformation of the fluid’s mesh is computed together with the wall deformation computation. Tests showed that the presence of the weak core material hardly influences the displacement field of the wall. The maximum differences in displacements were $2 \cdot 10^{-8}$ m in radial direction and $3 \cdot 10^{-9}$ m in axial direction. The mesh consists of 1664 quadratic triangular elements, with a total of 3483 nodal points. 128 Elements form the wall, the rest forms the core material. The properties of the wall material are: Young’s modulus 1MPa, Poisson ratio 0.49, and of the core: Young’s modulus 1 Pa, Poisson ratio: 0.01.

3.4 Fluid motion

The fluid motion is computed after the mesh has been transformed to its deformed state. The Navier-Stokes equations for an incompressible fluid (equations 3.5 and 3.6) are discretized in space using the Galerkin finite element method. The convective term is linearized with one step of a Newton scheme. This yields:

$$
\begin{align*}
\frac{\mathbf{M}}{\Delta t} & \mathbf{v}^{n+1} + \left[ \mathbf{S} + \mathbf{N}(\mathbf{v}) \right] \mathbf{v} - \mathbf{L}^T \mathbf{p} = \mathbf{F} \\
\mathbf{L} \mathbf{v} &= 0
\end{align*}
\quad (3.51, 3.52)
$$

The pressure is eliminated from this set of equations with the following term:

$$
\begin{align*}
\mathbf{L} \mathbf{v} &= \tau \mathbf{M} \mathbf{p}
\end{align*}
\quad (3.53)
$$

Now, the velocity field is no longer divergence-free. This computational method is called the penalty function method. The penalty function parameter $\tau$ is chosen such, that the incompressibility of the fluid is not violated much ($\tau \approx 10^{-6}$).

By applying a finite difference scheme to the discretized equation, time dependent problems can be handled. The spatially discretized equations are discretized in the time domain using a $\theta$-method (Cuvelier et al., 1986):

$$
\begin{align*}
\frac{\mathbf{M}}{\Delta t} & \left[ \mathbf{v}^{n+\theta} - \mathbf{v}^n \right] + \left[ \mathbf{S} + \mathbf{N}(\mathbf{v}) + \frac{1}{\tau} \mathbf{L}^T \mathbf{M}^{-1} \mathbf{L} \right] \mathbf{v}^{n+\theta} = \mathbf{F}(\mathbf{v}^{n+\theta}) \\
\mathbf{v}^{n+1} &= \frac{1}{\theta} \mathbf{v}^{n+\theta} - \frac{1-\theta}{\theta} \mathbf{v}^n, \ 0 \leq \theta \leq 1 \\
t^{n+\theta} &= t^n + \theta \Delta t
\end{align*}
\quad (3.54, 3.55, 3.56)
$$

The computation starts with $\theta = 1$ (Euler implicit) and after a few timesteps $\theta$ changes to 0.5 (Crank-Nicolson). The Euler implicit scheme is less sensitive to errors in the starting values of the computation, while the Crank-Nicolson scheme has the advantage of 2nd order accuracy (Cuvelier et al., 1986). The computation is carried out over two periods, with 256 timesteps per period. After 32 timesteps the time integration scheme swaps from the Euler implicit scheme to the Crank-Nicolson scheme.

The computation is carried out over the entire domain formed by the previously described mesh. This leads to velocities inside the wall, that have no physical meaning. However, the employed FEM-package does not offer the possibility to solve the NS-equations over part of the mesh yet.
Chapter 4

Experiments

4.1 Introduction

To verify the formerly described theory two experiments were designed:

1: Wave propagation experiments on (an)isotropic viscoelastic models. These experiments are similar to the ones carried out by Reuderink (1991). He measured wave velocities and -forms in a straight latex rubber tube. Neither the pressures nor the deformations that he found were in the physiological range, but the experimental results agreed well with his computations. Now, the experiments are performed to test the wave propagation properties of the designed arterial models and to investigate whether the linear wave theory is applicable to them.

2: Wall motion measurements on isotropic tubes and 3: Fluid motion experiments. These experiments are carried out to verify the numerical model, described in chapter 3. The velocities are measured with laser Doppler anometry (LDA) and ultrasound Doppler (USD) to evaluate both methods.

4.2 Materials

Three types of tubes were used in the experiments:

In the velocity measurements, an elastic isotropic tube was used. In the wave propagation experiments, a viscoelastic isotropic tube and a viscoelastic anisotropic tube were tested.

4.2.1 Elastic tube

The elastic tube has a geometry as depicted in fig. 4.1. It is made of silicone elastomer (Sylgard 184, Dow Corning). This is a two-component, room temperature vulcanizing (RTV) silicone rubber which is mixed and subsequently injected into a mould. After one day of curing the tube can be removed from the mould and is ready for use.

Although the tube is made of incompressible material (Poisson ratio \(\mu=0.5\)), in the computations it is modeled as an almost incompressible (\(\mu=0.49\)) linearly elastic material (see equation (2.3), chapter 2) with Young's modulus 0.72 MPa. The modulus was determined by measuring the static pressure-diameter relation of the tube in the set-up.

4.2.2 Viscoelastic isotropic tube

Manufacturing of the model

The isotropic tube consists of EPDM rubber (DSM: Keltan 520). The rubber is dissolved in xylene, and 1% by weight dibenzoylperoxide is added, to enable cross-linking. The solution is
applied in several layers to a teflon-coated mandrel of 20 mm diameter by means of dip-coating until the right wall thickness is reached (0.4 mm). After application of each layer, the mandrel rotates until all the solvent has evaporated. Then the mandrel plus rubber are put in an oven of 120° C for two hours. The cross-linked tube then can easily be removed for further usage.

Properties

Rectangular specimens of $20 \times 5 \times 0.4$ mm length $\times$ width $\times$ thickness were cut from the model to perform tensile- and relaxation tests. The tensile tests were performed with different strain rates, and showed responses that differed accordingly. Therefore the rubber was assumed to be viscoelastic and relaxation tests were performed.

Three specimens were stretched to $\varepsilon_0 = 0.17$, 0.18 and 0.25 respectively. This approximates the physiological strain in the greater arteries from diastolic to peak systolic pressure. The stretch rate was 500 mm/min, which is the maximum velocity of the tensile testing machine. The thus acquired relaxation curves are shown in fig. 4.5, left panel. The curves are normalized with respect to the stress in the first sample taken in the experiment and the relaxation functions published by Tanaka and Fung (1974). The data acquisition is rather slow, therefore it is not possible to get data within approximately 6 seconds after starting the tensile testing machine. For relaxation tests, this is a major drawback.

The stress-strain relation was fitted with the powerlaw model, presented in equation (2.13), chapter 2. Fitting this model to the experimental data, yields: $c_1 = 2.1$ MPa $s^\alpha$ and $n = 0.066$. The dynamic modulus then is (equation (2.16)):

$$E(j\omega) = c_1 \Gamma(1-n)\omega^n e^{j\pi\frac{n}{2}} = 2.19 \omega^{0.066} e^{0.104j} \text{ [MPa]}$$

(4.1)

The pressure-diameter relation of the tube was measured to test the homogeneity of the tube as a whole. Furthermore, this experiment immediately shows the difference between the model and real arteries. The pressure was applied with a watercolumn with variable height. The diameter was measured with a micrometer. The results of six measurements are shown in figure 4.2, left panel. It is clear that the isotropic tube does not behave like a real artery: Its pressure-diameter characteristic shows an increasing slope with increasing pressure, whereas the characteristic of an artery shows a decreasing slope. This is easily verified with the uniaxial elastic behaviour from fig. 2.6.
4.2.3 Anisotropic tube

Manufacturing of the model

The anisotropic models are made in the same way as the isotropic ones. However, after cross-linking, two plies of lycrafibers (DuPont de Nemours: lycra, 78 dtex), wetted with rubber solution, are applied to the model. The fibers are wound at a very small pitch angle, to keep the radial stiffness at zero pressure as low as possible. The fibers are prestrained almost up to their ultimate strength, to gain the greatest non-linearity. After application of the fibers, the model is put in an oven once again, to acquire a firm bond between the fibers and the model. The final result is an orthotropic tube with its material axes approximately coinciding with the geometrical axes.

Properties

The properties of the anisotropic tube depend on the properties of the matrix (EPDM-rubber, see section 4.2.2), the properties of the fibers and their prestrain plus volume fraction and pitch angle.

The lycra fibers are semicrystalline elastomers. When subjected to a tensile force, the entanglement network between the crystals of the material is stretched easily to its maximum stretch ratio and the fiber stiffens dramatically. This is clearly shown by tensile tests, performed on single, untreated fibers, see figure 4.3. The tests revealed no viscoelasticity. The tensile tests were repeated on lycra fibers, that received the same treatment as fibers in the model, after winding (i.e. wetting with EPDM-rubber in solvent, prestraining at \( \lambda \approx 5 \) and a subsequent heat treatment, 120 °C for 30 minutes) and fibers that were heat treated only. The nonlinear stress-strain behaviour then becomes even more pronounced (see fig. 4.4). By prestraining the fibers before the heat treatment, their crystallinity is increased, and therefore the volume of the part of the fiber with high glass temperature increases as well. When the fiber is heated above the glass-temperature, and subsequently cooled down fast (for a thin fiber, even cooling in air is fast) the crystallinity acquired by the prestraining is frozen, and the material has lasting different properties.

The tube consisted of a 0.25 mm layer of EPDM, with 78 dtex fibers on top of it, the volume fraction of the fibers being \( 8.5 \cdot 10^{-3} \). The fibers had a prestrain \( \lambda \) of about 5. The accuracy of
Figure 4.3: Stress-strain behaviour of virgin lycra fibers, experimental data of three different specimens, tested with the same strain rate.

Figure 4.4: Stress-strain behaviour of several lycra fibers, heat treated (solid lines) and wetted with EPDM solution + subsequent heat treatment (dashed lines).
this number is rather poor, as the prestrain was achieved by braking the bobbin on which the fiber was wound. The thus acquired composite underwent relaxation tests, similar to the ones performed on the isotropic model. The measured data could be fitted using the same power-law model as in the isotropic case. The material properties in this case were: $3.9 < c_1 < 4.7 \text{ MPa} \epsilon^n$, $n = 0.05$. Due to the inhomogeneity of the tube, the elasticity of the material varies much. It should be noted that the viscoelastic component of the complex modulus is slightly less than the one of the isotropic model. The results of the relaxation tests are shown in fig. 4.5. For comparison with the isotropic model, the static pressure-diameter relation was measured (fig. 4.2, right panel). The graph shows decreasing compliance with increasing pressure, which is characteristic for arteries. The relaxation curves of the composite and the vascular tissue show the same slope over two decades of $\tau$. The composite material therefore has qualitatively similar viscoelastic properties as the tissue in the in-vitro situation.

4.3 Wave propagation

4.3.1 Methods

Two types of experiments were carried out: First, determination of the wave velocity at different pressures. Second, determination of the shape of the pressure pulse, at physiologically relevant pressures.

Wave velocity

The pressure wave velocity was measured in both models: The models were pressurized stepwise from 7 to 15 kPa, with 1 kPa increments. A single block-shaped pressure pulse of 15 ms duration was released at one end into the vessel and the pressure was measured 100 mm downstream from this point during 0.25 seconds. A second measurement was carried out, with the same pressure pulse, but now the pressure was measured 800 mm downstream. The distance between the two measurement sites, divided by the difference in arrival time of the foot of the pressure wave yields the wave velocity.
Shape of the pressure wave

The shape of the pressure wave was determined in the models, that were pressurized to 10 kPa (75 mmHg). At 8 positions, each 100 mm apart, the pressure was measured during 0.5 seconds. The acquisition time was long enough to see multiple reflections of the pressure wave.

4.3.2 Experimental set-up

The models are mounted on a horizontal bench (F), with an axial prestrain of about 5% (see fig. 4.6). The friction between model and bench is high enough to ensure that there is no axial motion of the model during the experiments. At the inlet, a three-way solenoid valve (C) is mounted. At the opposite end, the model is closed with a tap (N). The solenoid valve is connected to a pressure vessel (D) and a constant head tank (E). When the valve is not engaged, the model is pressurized by the constant head tank. Otherwise, fluid flows from the pressure vessel into the model. Inside the model, a cathetertip manometer (B, Millar, type PC 350) measures the dynamic pressure. The set-up is controlled by a pulse generator/amplifier that operates the solenoid valve. The pulse width and frequency can be varied. Pressure and wall motion signals are sampled using the LabVIEW package plus hardware (National Instruments).

4.4 Wall motion

At three axial positions (106, 231 and 356 mm downstream from the entry of the set-up, the radial wall velocity was measured with LDA and USD. A complete description of this set-up is given in the next section.
Both techniques measure wall velocity rather than displacement, so the displacements had to be computed by time integration of the velocity signals. Therefore, only relative displacements of the wall can be determined.
4.4.1 Method

The wall motion can be measured optically using roughly the same equipment as in LDA-experiments. The Doppler shift is now not achieved by interference of two laser beams (see appendix B), but by interference of one laser beam plus its reflected counterpart. When the beam is reflected by a moving object, the phase between incident and reflected beam on the detector varies. This variation expresses itself in a frequency shift proportional to the velocity of the moving object in the direction of the laserbeam. By measuring the velocities of the moving walls of the artery model and subsequent integration in time, the wall displacement is determined.

The wall velocity measurement with USD is described in appendix B.

4.5 Fluid motion

The blood that flows through an artery exerts two forces on the endothelium of the arterial wall: A normal force—the blood pressure—and a shearing force, the wall shear stress. To measure these forces in-vitro a set-up in which a physiological flow could be generated was built. The pressure can be measured directly, using a catheter tip manometer. The wall shear stress is in the order of 1 Pa, and cannot be measured directly. Therefore an indirect method has to be used. The shear rate near the wall can be determined by computing the spatial derivative of the velocity field $\vec{v}$ perpendicular to the wall. Multiplication of this derivative by the dynamic viscosity $\eta$ of the fluid yields the wall shear stress $\tau_w$:

$$\tau_w = \eta \vec{n} \cdot \nabla \vec{v} \cdot \vec{n} = -\eta \frac{\partial \vec{v}}{\partial r}$$

(4.2)

The problem now has shifted from accurate shear rate measurement to accurate fluid velocity measurement. From the measured velocities the shear rate can be derived using appropriate (polynomial) fitting techniques.

For velocity measurement two methods are feasible: Laser Doppler anemometry (LDA) and Ultrasound Doppler techniques (USD). The advantage of the latter method is that it is also used in clinical practice, and imposes less constraints on the set-up and the fluid. The principles of the two methods are described in appendix B. The accuracy of both methods will be discussed presently.

LDA: Accuracy with respect to shear rates

The measurement accuracy of an LDA-set-up is determined by the size of the probe volume and the type of frequency estimator. In this project a DISA frequency tracker was used. According to the manufacturer, the accuracy of the measured frequency is $\pm 1$ % full scale. This was not checked, because the means to check it were not available in the laboratory.

The size of the probe volume plays an important role in the accuracy of the velocity measurement, especially when high velocity gradients and near-wall flows are involved. The measured velocity is derived from the scatter frequencies emitted by particles inside the probe volume. Consider a 2 dimensional shear flow (fig. 4.7) with the long axis of the probe volume parallel to the velocity gradient. When the velocity distribution over the probe volume is highly inhomogeneous, the frequencyband of the emitted light will be broad. This of course diminishes the accuracy. Furthermore, in parts of the probe volume where the velocity is high, more scattering particles will pass (assuming that the particles are homogeneously distributed in the fluid). This will result in a bias towards higher velocities, as is shown in figure 4.7. The total signal power, generated inside the probe volume is a function of the shape of the volume, the velocity distribution inside it and some weight function over the volume. The shape of this power distribution
Figure 4.7: 2D shear flow, plus LDA probe volume partly inside the wall, and the corresponding weight function

function along the axis perpendicular to the wall of the channel is depicted in the right part of figure 4.7. In this example, the measured velocity $\bar{\bar{v}}_m$ is higher than the actual velocity $\bar{\bar{v}}$ at the centre of gravity of the probe volume.

When part of the probe volume is outside the fluid, another error occurs: The centre of gravity of the part of the probe volume that participates in signal generation then no longer coincides with the centre of gravity of the complete probe volume, but moves over a distance $\Delta x$ from the wall. From these considerations it is obvious that the probe volume should be as small as possible to get a reliable estimate of the wall shear rate.

The size of the probe volume is determined by the wavelength of the used light, the diameter of the laserbeams, the intersection angle of the two beams and the beam expansion ratio (Goldstein, 1983). The set-up used in the experiments has a probe volume with dimensions $330 \times 80 \times 80 \mu m$.

**Ultrasound: accuracy**

The ultrasound equipment is a multi-gate pulsed Doppler system. The flow velocity is estimated from the echo signals with a cross-correlation technique (see appendix B). The accuracy of the estimate is 1-2 % (Hoeks et al., 1993). The spatial resolution is 1 mm, the maximum bandwidth of the velocity signal is 95 Hz.

**4.6 Experimental set-up**

The experimental set-up consists of three major parts: (see fig. 4.8) 1: The flow generation: A stationary gear pump (Verder) plus a computer controlled piston pump (VSI). 2: The measurement section: This part consists of a rectangular PMMA container in which a model vessel is suspended. The space around the model can be filled with a fluid to match the refractive index and/or the specific gravity of the model. The exit of the model is suspended inside part three only. 3: A terminal impedance, that can be adjusted to mimick physiological terminal impedances ranging from the one of the aortic arch to the renal arteries.
Figure 4.8: Experimental set-up for velocity and wall motion measurements

Flow circuit

The fluid (40% glycerol in water, $\rho = 1100 \text{ kg/m}^3, \eta = 3.3 \cdot 10^{-3} \text{ Pa s}$) flows via the stationary pump and an electromagnetic flow probe (EMF) into the measurement section through a glass tube of 2 m length. The instationary flow is superimposed on the stationary one by the piston pump. Both pumps together generate an aortic flow pulse, published by Milnor (1989). The flow probe is used for adjustment of the flow pulse only. Inside the measurement section, the silicone elastomer tube - discussed in section 4.2 of this chapter - is suspended with a prestrain of 12%. The prestrain suppresses lateral motion of the tube during the experiments.

The pressure inside the tube is measured by a catheter-tip manometer (Millar, type PC 350). The manometer can be moved axially, enabling sequential measurement at different positions. For the LDA-measurements, a small amount of scattering particles (drilling oil, 1 ml/kg fluid) is added. These particles do not scatter the ultrasound waves enough to acquire valid data. Therefore, for the ultrasound measurements, small air bubbles (mean diameter 10\(\mu\)m) are injected into the fluid. With the air bubbles in the fluid, the light from the LDA is scattered too much to perform good measurements. The air bubbles gather in the air chamber of the terminal impedance and are thus, after some time, filtered out of the fluid. Then LDA measurements may be carried out again.

Terminal impedance

The terminal impedance is a modified (four element) windkessel according to Westerhof (1979). This windkessel can be modeled with a mass-spring-dashpot model as depicted in fig. 4.9. The mass is modeled physically by a rigid tube with length $l$ and cross-section $A$.

The dashpots represent the viscous dissipation of the impedance. $b$ represents the viscous dissipation of the vessel directly distal from the thoracic aorta. $b_p$ represents the dissipation of the capillary bed. The dashpots are modeled physically by foam (Uxem: Polyurethane foam,
30 pores per inch) filled tube sections. By applying more or less compression to the foam, the damping values \( b \) and \( \dot{b} \) can be adjusted. Because the foam is highly porous (\( > 95\% \) porosity), a great compression ratio can be achieved. Furthermore, the flow inside the foam remains laminar for fairly high Reynolds numbers in the connecting channels.

The spring \( k \) finally represents the compliance of the arterial bed and is modeled by an air chamber (hence the name: windkessel model).

Choosing the velocity of the mass \( m \) as state-space variable, the transfer function or impedance of the model reads:

\[
Z(s) = \frac{(m \dot{b} / k)s^2 + (m + b \dot{b} / k)s + b + \dot{b}}{1 + (\dot{b} / k)s}
\]  

(4.3)

The experiment is designed to model the human thoracic aorta. The input impedance of this vessel is known from Mills et al. (1970), who published input impedances of the human aorta at several positions in terms of pressure and flow velocity. Westerhof (1969) measured the impedances of a major part of the human arterial tree piecewise in terms of compliance, inertance and resistance. The geometry (diameter and length) of each section was reported also. The diameter was used to convert the impedance measured by Mills into the impedance in terms of pressure and flow.

With Westerhof's impedance data of the thoracic aorta, together with the modified input impedance from Mills' data, the terminal impedance of the thoracic aorta can be determined by combining the two impedances. (see fig. 4.10). The thus found terminal impedance is fitted with the above described windkessel model, and the impedance in the set-up is adjusted accordingly.
Figure 4.10: Impedance of the human thoracic aorta: Asterisks: Input impedance according to Mills et al. (Mills et al., 1970), adapted for flow. Dashed line: Input impedance, acquired by fitting Westerhof's data plus a four element windkessel model to the input impedance. Dash-dotted line: Required terminal impedance in the experiment, resulting from the aforementioned fit.
Chapter 5

Results

5.1 Wave propagation

5.1.1 Wave velocity

To compare the experimental data with theoretical ones, first some properties of the models have to be determined. For the wave propagation experiments, the wave velocity as function of transmural pressure was measured. The transmural pressure was varied stepwise with 1 kPa increments from 7 to 15 kPa. The corresponding wave velocity was determined by two subsequent pressure measurements, one 100 mm from the inlet valve and one 700 mm further downstream. The difference in arrival time of the pressure wave after the opening of the valve divided by the distance between the measurement sites gives the wave velocity. The results are plotted in fig. 5.1. The experiment was carried out only once for each pressure increment. As expected, the wave velocity $c_0$ of the isotropic tube slightly drops with increasing pressure, whereas the one for the anisotropic tube increases.

For the reflection experiments, the tubes were excited with a 15 ms pressure pulse and the shape of the pulse was measured every 100 mm for 0.5 seconds. The results are plotted in fig 5.2 for the isotropic tube and in fig. 5.3 for the anisotropic tube. The prepressure ("diastolic pressure") in both experiments was set to 10 kPa.

Figure 5.1: Asterisks: Moens-Korteweg wave velocities of the isotropic tube and the anisotropic tube (circles).
For the simulations, the first 15 ms of the pressure signal, measured at the point nearest to the valve, was decomposed into harmonics by a standard FFT. Using the frequency-dependent complex modulus (from the relaxation experiments), the pressure waveforms inside the tubes were computed (equation (3.43), chapter 3). For both models, the wave number \( k \), see equation (3.29), corresponding to the compliances of the tubes at 10 kPa was used in the computations.

The results are quite clear: The isotropic tube behaves more or less linearly, while the anisotropic one clearly shows nonlinear behaviour. The top of the wave moves faster than its foot, as was expected from the wave velocity measurements. This results in deformation of the shape of the pressure pulse: The rising slope becomes steeper as the pulse moves onward, while the steepness of the falling slope diminishes.

Figure 5.2: Wave propagation and reflection in the isotropic model (solid line), plus simulation based on linear wave theory (dashed line)

Figure 5.3: Wave propagation and reflection in the anisotropic model (solid line), plus simulation based on linear wave theory (dashed line)
5.1.2 Impedance

The terminal impedance was adjusted according to parameters acquired by fitting the input- and terminal impedance of the thoracic aorta to the modified windkessel model. Subsequently, the impedance was measured by application of sinusoidal entry flows with different frequencies. The results are depicted in fig. 5.4. The phase response of the experimental impedance is not bad,

![Graph showing phase response and modulus](image)

**Figure 5.4:** *Dash-dotted line: Required terminal impedance in the experiment, resulting from the aforementioned fit. Circles: Measured impedance, solid line: Fit, based on four element windkessel model*

but the modulus is too high over the entire frequency range. This means that the adjustment of the impedance is not very accurate.

5.2 Wall motion

Describing the model wall as an isotropic linear elastic material, the wall deformation was computed using the computed pressure as boundary condition, assuming geometrical linearity (see chapter 3). Fig. 5.5 shows the results. The measured wall motion is the sum of the time integrals of the measured radial wall velocities (LDA and USD) at one axial position. The LDA-measurement agree well with the computational results, whereas the displacements measured with USD are smaller, especially at the two most downstream positions.

Although the computed pressure at each position is higher (fig. 5.8), the computed wall displacement is smaller than the measured displacement. By assuming geometrical linearity in the computation, the wall thickness in the computation remains the same throughout the flow cycle. This is not the case. When a cylindrical vessel is inflated by an internal pressure, the diameter
Figure 5.5: Measured (dotted lines: LDA, dash-dot: ultrasound) and computed wall motion at three positions (solid lines).
of the vessel rises and the wall becomes thinner. Because of this, to inflate the vessel to greater
diameters, less extra pressure is needed. The compliance of the vessel is therefore greater at
higher pressures. The experiments show this clearly: the mean pressure of the vessel is lower
than in the computations, but the displacement of the vessel wall is larger, due to the increased
compliance.
This does not mean that the inner diameter of the vessel in the experiments is larger than the
one in the computation. The measured wall displacement is added to the vessel diameter at
mean pressure. In the computation, the diameter is computed using the modulus of the material
at mean pressure in the experiments. This yields low estimate of the actual compliance, as we
have seen before. The computed mean diameter therefore is larger.

5.3 Fluid motion

5.3.1 Flow

The velocity profiles measured with LDA were integrated by means of the trapezoid rule for
an axisymmetric coordinate system. This yielded the local flow (fig. 5.6). The flow at each
corresponding site was computed with the FEM-model as well. The numerical model predicts
the local flow quite well.

5.3.2 Velocity

At each axial position, the velocity profiles were measured at 59 points along the horizontal
axis across the tube cross-section. Near the walls, the points were 0.2 mm apart, in the central
region of the tube the points were 0.4 mm apart. The sampling points are fixed in space, so the
moving tube has a velocity with respect to these points.
Because the computed and measured flows are practically the same (fig. 5.6) and the computed
mean diameter of the vessel is greater than the measured diameter (fig. 5.5), naturally the
computed velocities (fig. 5.7) are lower than the measured velocities. The shape of the profiles
qualitatively is the same.
The USD-equipment suffered from signal drop-outs, due to temporarily insufficient scattering
particles in the fluid. This is especially the case in the measurements at the most upstream
position (upper panel in fig. 5.7). Apart from that, the thus obtained results are comparable to
the results of the LDA-experiments.

5.3.3 Pressure

The pressure at each position was measured and compared with the pressure, computed with
linear wave propagation theory (equation (3.43)). For the computation, the measured values of
the terminal impedance (fig. 5.4) were used. The results are depicted in fig. 5.8. The measured
signals are the ensemble averages of 8 flow cycles.

5.3.4 Wall shear rate

The shear rate is derived from the measured velocity profiles (fig. 5.9) by linear interpolation.
For all velocity profiles the corresponding diameter of the tube is determined. The diameter
is determined by the sum of the diameter at mean pressure measured in static experiments
plus the measured wall displacements. With this time-dependent diameter the position of the
velocity sampling points with respect to the wall is computed. The two velocity sampling points
next to the wall are used for the shear rate computation. The velocities at these two points are
subtracted and divided by the distance of the two points (0.2 mm). This yields the shear rate.
Figure 5.6: Measured (dotted lines) and computed flows at three positions. The solid lines represent the flow, computed in the FEM model.
Figure 5.7: Measured (dotted lines: LDA, dashdot: US) and computed axial velocity at three positions (solid lines).
Figure 5.8: Measured (dotted lines) and computed pressure at three positions. (solid lines).
Figure 5.9: Measured (dotted lines: LDA, dashdot: Ultrasound) and computed shear rate at three positions (solid lines).
The same method is applied to the ultrasound measurements. The shear rate measured with LDA is not very smooth. As the near-wall velocity is very low, the measurement accuracy of the LDA-system has to be very good to obtain reliable results on the shear rate (see chapter 4). The probe volume used in the LDA measurements is too big for that (Lou et al., 1993). Furthermore, the computation of the dynamic vessel diameter is based partially on static experiments. When the tube expands, the surrounding fluid in the measurement section must be accelerated. This leads to inertial forces on the tube wall, that counteract the transmural pressure. The diameter estimation from static experiments therefore may be higher than the actual diameter. The velocity samples for the shear rate computation then are taken inside the wall and not inside the flow channel.

However, it is striking that the peak value of the shear rate in the experiment occurs earlier in the flowcycle than in the computations, whereas all other signals (flow, pressure, etc.) of experiment and computation are in phase. In the FEM-models the shear rates are derived in the nodal points that are at the fluid-wall interface. Here the peaks occur because of the wall motion. The fluid velocity is computed disregarding the mesh velocity (Eulerian formulation). This leads to errors in the near-wall velocity (the radial velocity is the highest there), and therefore to errors in the shear rate.
Chapter 6

Discussion & conclusion

An anisotropic model of a human artery, plus the equipment to impose physiologically relevant boundary conditions was manufactured. Furthermore, the experimental method to determine wall motion and shear stresses was tested under physiological conditions.

6.1 Model material

The vessel model has qualitatively good properties, in the sense that it shows nonlinear behaviour in circumferential direction. The nonlinearity is achieved by the stress-strain behaviour of the highly prestrained fibres wound around the model. The nonlinearity is further enhanced by the heat treatment after the winding process. Still, the properties of human arteries are not matched entirely.

The maximum amount of fibres to be applied is determined by the stiffness of the matrix material, the wall thickness and the required wave velocity of the tube. The manufacturing procedure limits the wall thickness at this time to approximately 0.25 mm. Thinner models cannot be removed from the mandrel on which they are made without breaking them.

A volume fraction of less than one percent of fibre already gives the model its required maximum stiffness. A more compliant matrix would allow a higher fraction of fibres, which would enhance the nonlinear behaviour of the model.

Further research therefore should be carried out to find a weaker matrix material and to optimize the fibre properties by prestraining and subsequent heat treatment.

In longitudinal direction, the vessel behaves more or less linearly, whereas in real arteries the nonlinear behaviour in that direction is even more pronounced than in circumferential direction. In the wave propagation experiments carried out so far, this was not a problem, because the vessels were tethered longitudinally. When one wants to use the anisotropic tubes in velocity measurements as described in this report, the longitudinal properties must be matched to the in-vivo situation as well, because then the model can move freely. The required properties may be achieved by applying the fibres at a certain angle to the matrix material.

6.2 Impedance model

As we have seen in the results of the impedance tests, the terminal impedance cannot be adjusted to its required settings straight away. The main problem is the adjustment of the foam resistors. The resistance, acquired by compression of the foams is not very reproducible. The cylindrical foams tend to buckle at the high compression ratios, required for the peripheral resistance.

Furthermore, the porosity of the foams diminishes rapidly under compression. This causes the
fluid passing the resistor to be filtered. Normally, that would not be a problem, but unfortunately LDA- and, more important, ultrasound measurement techniques require a fair amount of particles seeded in the fluid. These particles are filtered out by the compressed foam, disabling the measurements and clogging the resistors.

6.3 Computational methods

The computations match the experiments fairly well. The decoupled method may be considered successful, at least when physically linear wall behaviour is assumed. The numerical model describes the displacement field of the tube adequately. Therefore, the strains inside the wall may be computed with the model, when an experimental method to measure them is not available. The hypothesis, postulated in the introduction (chapter 1) then can be verified with the combination of the numerical and the experimental method.

Nevertheless, a method to measure the local strains in the wall should be developed, because from the experiments on the anisotropic tubes it is clear that the decoupled approach will no longer be valid when nonlinear wall behaviour exists.

The geometrically linear computation describes the wall motion adequately. The course of action for future development should be: First of all, a weakly coupled solution method should be implemented, where the wall motion is driven by the pressure computed in the fluid motion computation. To achieve a good pressure computation, the grid velocity must be accounted for, so an arbitrary Lagrange-Euler formulation for the Navier-Stokes equations must be programmed (Hughes et al., 1981; Szabo & Hassager, 1995).

Then the nonlinear behaviour of the wall can be implemented, and finally geometrically nonlinear behaviour may be added.

6.4 Experimental methods

6.4.1 Wave propagation

The wave velocity was measured in longitudinally tethered models only. To verify the analysis, presented in chapter 3, these experiments should be extended to freely suspended tubes, preferably with different stiffness ratios.

The wave velocity was determined by measuring the time the foot of the wave needs to travel over a certain distance. Because of the viscoelasticity of the models plus their nonlinearity, the wave velocity may vary with the amplitude and the shape of the pulse. This was not checked, because the pulse generator, employed in the experiments, could produce only one pulseshape.

6.4.2 Wall motion

The wall velocity was measured in radial direction only, with both LDA and ultrasound. Both techniques yield agreeable results. The computations show that the axial wall velocity is much higher than the radial velocity. It is therefore essential that in the future wall velocities (or displacements) are measured in at least two dimensions for straight tubes, and in 3D when more complex vessel geometries are involved.

When the complete displacement field of the model can be measured, the strains in the wall can be assessed, and the formerly postulated hypothesis may be verified.
6.4.3 Fluid motion

The velocity measurements with ultrasound and LDA are comparable. The great advantage of ultrasound over LDA is the short acquisition time. To obtain a velocity profile with LDA, many periods of the flow pulse (\( n \approx 500 \)) are required, whereas with ultrasound one period suffices to obtain a complete picture of the velocity field.

To get a good velocity signal, ultrasound techniques require a much greater amount of seeding particles in the fluid than LDA. As we have seen before, this causes clogging of the terminal impedance. Moreover, the seeding concentration for USD is too high to carry out LDA-measurements in the same fluid afterwards. The problem was tackled by injection of small air bubbles (\( \approx 10-20 \ \mu m \)) into the flow. The air bubbles were small enough to pass the first resistor. Subsequently, they gathered in the air chamber of the impedance. After the ultrasound measurement, the bubbles automatically vanished and LDA measurements could be performed.

A major drawback of the seeding with air bubbles is the natural buoyancy of the bubbles. As is clearly visible in the velocity profiles, measured at the most proximal position in the set-up, the bubbles mainly reside in the top half of the flow channel (the lower half of the profiles in the graphs). In the lower part of the tube, the ultrasound probe did not pick up any signal related to fluid velocity.

A new seeding method, preferably applicable for ultrasound and LDA simultaneously, is required.

6.5 Mechanical loads: shear rate and pressure

6.5.1 Pressure

The pressure, as measured, coincides well with the analytically computed pressure. However, in nonlinear vessels, the analytical method breaks down. The numerical method does not yet yield credible solutions for the pressure, because of the motion of the mesh. This problem must be solved in future research.

6.5.2 Shear rate

The wall shear rate is derived from the measured velocity profiles by taking finite differences of the velocities measured at two adjacent points next to the wall. For both LDA and USD, this yields poor results. The reason is twofold: The velocities are not measured during one flow cycle, so small differences in the measured velocities may occur. Near the wall, the velocities are low, which leads to a Doppler frequency that is almost equal to the preshift of the LDA-setup. Then the relative error in the measured velocity is high. The second and more important reason is the poor spatial resolution of the LD-anemometer. The probe volume has dimensions 300 \( \times \) 80 \( \times \) 80 \( \mu m \). According to Lou et al. (1993), this is too big a volume to measure shear rates accurately.

The probe volume dimensions can be adapted simply with a beam expansion unit. The minimally feasible probe volume sizes then would be: 30 \( \times \) 10 \( \times \) 10 \( \mu m \).

Simulation. To study the influence of the LDA probe volume dimensions a relatively simple LDA-experiment was simulated.

Consider a 2D Newtonian, Poiseuille flow in a 20 mm wide channel. The maximum fluid velocity is 0.18 m/s. The long axis of the probe volume is perpendicular to the walls of the channel, as it would be in an experimental situation. The fluid is seeded in such a way, that the mean number of seeding particles inside the probe volume equals 1, at constant fluid velocity. The velocity per sample is averaged over 0.01 s.
The particles move along straight lines, that intersect the symmetry plane of the probe volume, perpendicular to the flow velocity, at random positions. The time at which the particles cross the symmetry plane is random as well. The maximum allowable Doppler frequency is 333 kHz, with a preshift of -200 kHz. This is the range at which a frequency tracker would be set in an experimental situation. The Doppler signal, generated by the passing particles, is computed with four times the maximum frequency as sampling frequency. This signal is filtered by a second order highpass filter, now to simulate the lower range boundary of the tracker. The Doppler frequency is determined by Fourier analysis of the filtered signal. Per point, 8 samples of 0.01 s are computed.

The simulation was carried out with two probe volume sizes: 1: A big probe volume, with the same dimensions as the probe volume of the LDA set-up that is used in the experiments, and 2: a small probe volume, with the smallest feasible dimensions when the existing set-up would be equipped with a beam expansion unit.

The resulting velocities and shear rates, together with the theoretical values are shown in fig. 6.1. Apart from the region near the wall, there are no differences between the big and the small probe volume. At the centre, the performance of the big probe volume is even better. However, when the shear rate is determined by simply taking finite differences of the velocity profiles, the influence of the probe volume size is tremendous.

**Influence of wall velocity** The computations show that the axial wall velocity is not a negligible factor in the determination of wall shear stress, see fig. 6.2. It is highly questionable whether the shear rates, derived from the velocity profiles, have any physical meaning at all when the axial wall velocity is neglected. It is therefore of the utmost importance that the wall velocity is assessed adequately when shear rates are to be computed. Another possibility might be to drop the computation of shear rates from the fluid velocity gradient altogether and look for a way to measure the shear rate more directly.

Figure 6.1: Poiseuille flow: Theoretical profile (left panel, solid line) and shear rate (right panel) plus LDA-measurement simulations, Asterisks: big probe volume, circles: small probe volume
Figure 6.2: Computed axial wall velocity at the three measurement sites (see fig. 4.8). Solid line: 106 mm downstream from the entry, dashed line: 125 mm further downstream, dash-dotted line: another 125 mm further downstream.
References


Appendix A

Derivation of the wavenumber $k$

A.1 Introduction

In 1957 Womersley derived the coupled harmonic solution for fluid and wall motion in a thin-walled, isotropic, deformable vessel (Womersley, 1957). In this appendix, his theory will be extended to anisotropic thin-walled tubes.

A.2 Governing equations

A.2.1 Fluid

The momentum- and continuity equations for a fluid read:

$$\rho \frac{\partial \vec{v}}{\partial t} + \rho \vec{v} \cdot \nabla \vec{v} = \nabla \cdot \sigma$$  \hspace{1cm} (A.1)

$$\rho \nabla \cdot \vec{v} = 0$$  \hspace{1cm} (A.2)

For a Newtonian fluid with dynamic viscosity $\eta$, the constitutive equation reads:

$$\sigma = -pI + 2\eta D$$  \hspace{1cm} (A.3)

$D$ is the deformation gradient tensor:

$$D = \frac{1}{2} \left( \nabla \vec{v} + (\nabla \vec{v})^T \right)$$  \hspace{1cm} (A.4)

Inserting the constitutive behaviour in equation (A.1) yields the Navier-Stokes equations:

$$\rho \frac{\partial \vec{v}}{\partial t} + \rho \vec{v} \cdot \nabla \vec{v} = \nabla p + \eta \nabla^2 \vec{v}$$  \hspace{1cm} (A.5)

$$\rho \nabla \cdot \vec{v} = 0$$  \hspace{1cm} (A.6)

Applied to an axisymmetric flow through a deformable tube with mean radius $R_0$ they transform into (coordinates $r, \varphi, z$):

$$\frac{\partial v_r}{\partial t} + v_r \frac{\partial v_r}{\partial r} + v_z \frac{\partial v_r}{\partial z} = -\frac{1}{\rho} \frac{\partial p}{\partial r} + \nu \left[ \frac{\partial}{\partial r} \left( \frac{1}{r} \frac{\partial}{\partial r} (rv_r) \right) + \frac{\partial^2 v_r}{\partial z^2} \right]$$  \hspace{1cm} (A.7)

$$\frac{\partial v_z}{\partial t} + v_r \frac{\partial v_z}{\partial r} + v_z \frac{\partial v_z}{\partial z} = -\frac{1}{\rho} \frac{\partial p}{\partial z} + \nu \left[ \frac{\partial}{\partial r} \left( \frac{1}{r} \frac{\partial}{\partial r} (v_z) \right) + \frac{\partial^2 v_z}{\partial z^2} \right]$$  \hspace{1cm} (A.8)

$$\frac{1}{r} \frac{\partial}{\partial r} (rv_r) + \frac{\partial v_z}{\partial z} = 0$$  \hspace{1cm} (A.9)
As the velocity plus all derivatives in \( \varphi \)-direction are zero, they are not represented in the equations.

If now only harmonic solutions are permitted with wave number \( k \) and frequency \( \omega \):

\[
\begin{align*}
\dot{v}_r &= \hat{v}_r(r) e^{i(\omega t - kr)} \\
\dot{v}_z &= \hat{v}_z(z) e^{i(\omega t - kz)} \\
p &= \hat{p}(r) e^{i(\omega t - kr)}
\end{align*}
\] (A.10) (A.11) (A.12)

Assuming that the wavelength \( \lambda \) is long compared with the length of the tube \( (\lambda/z \gg 1) \) and the velocity of the fluid much lower than the wave velocity \( c \): \( v_r/c \ll 1 \) and \( v_z/c \ll 1 \) the convective terms plus all velocity derivatives in \( z \)-direction may be neglected. The Navier-Stokes equations then reduce to:

\[
\begin{align*}
\rho_0 \frac{\partial \dot{v}_r}{\partial t} + \frac{\partial \hat{p}}{\partial r} &= - \frac{\partial^2 \dot{v}_r}{\partial r^2} + \frac{\partial \dot{v}_r}{\partial r} - \frac{\dot{v}_r}{r} \\
\rho_0 \frac{\partial \dot{v}_z}{\partial t} + \frac{\partial \hat{p}}{\partial z} &= - \frac{\partial^2 \dot{v}_z}{\partial r^2} + \frac{\partial \dot{v}_r}{\partial r}
\end{align*}
\] (A.13) (A.14)

with boundary conditions:

\[
\begin{align*}
\dot{v} |_{r=R} &= \dot{v}_{\text{wall}} \\
\frac{\partial \dot{v}}{\partial r} |_{r=0} &= 0
\end{align*}
\] (A.15) (A.16)

Substituting the Womersley parameter \( \alpha (\alpha = R_o \sqrt{\omega/\nu}) \) and a dimensionless radial coordinate \( y = r/R_o \) in the equations yields:

\[
\begin{align*}
\frac{\partial^2 \hat{v}_r}{\partial y^2} + \frac{\partial \hat{v}_r}{y \partial y} + j^3 \alpha^2 \hat{v}_r - \hat{v}_r - \frac{R_o}{\rho \nu} \frac{\partial \hat{p}}{\partial y} \\
\frac{\partial^2 \hat{v}_z}{\partial y^2} + \frac{\partial \hat{v}_z}{y \partial y} + j^3 \alpha^2 \hat{v}_z - \hat{v}_r - \frac{R_o}{\rho \nu} \frac{\partial \hat{p}}{\partial y}
\end{align*}
\] (A.17) (A.18)

The continuity equation transforms into:

\[
\frac{1}{y} \frac{\partial}{\partial y} (\dot{v}_r y) = jk R_0 \hat{v}_z
\] (A.19)

If we now follow Womersley (1957) and assume that the pressure \( \hat{p} \) can be written as:

\[
\hat{p} = p_0 J_0(Ay)
\] (A.20)

with \( A \) an unknown constant, integration of (A.17) and (A.18) yields:

\[
\begin{align*}
\hat{v}_r &= C_2 J_1 \left( \alpha \sqrt[3]{2} y \right) - \frac{R_0 A}{\eta} \frac{p_0}{j^3 \alpha^2 - A^2} - J_1(Ay) \\
\hat{v}_z &= C_1 J_0 \left( \alpha \sqrt[3]{2} y \right) - \frac{jk R_0}{\eta} \frac{p_0}{j^3 \alpha^2 - A^2} - J_0(Ay)
\end{align*}
\] (A.21) (A.22)

Substituting these solutions into the continuity equation results in the following solutions for \( A \), \( C_1 \) and \( C_2 \):

\[
\begin{align*}
A &= \frac{jk R_0}{\alpha \sqrt[3]{2}} \\
C_1 &= \frac{jk R_0}{\alpha \sqrt[3]{2}} \\
C_2 &= \frac{jk R_0}{\alpha \sqrt[3]{2}}
\end{align*}
\] (A.23) (A.24)
At this point the following approximations may be introduced:

\[ J_0(Ay) = 1 \] (A.25)

because \(|kR| \ll 1\), and

\[ J_1(Ay) = j \frac{kR_0y}{2} \] (A.26)

See Abramowitz and Stegun (1965). Furthermore, \(j^3 \alpha^2 - A^2\) may be simplified to \(j^3 \alpha^3\), for similar reasons.

With these approximations, the velocity components change into:

\[
\begin{align*}
\dot{v}_r &= j \frac{kR_0y}{2} \left[ C_1 - \frac{2}{\alpha j^{3/2} J_0 \left( \alpha j^{3/2} \right)} \right] + \frac{yA}{2} \frac{k}{\omega p_0} p_0 \\
\dot{v}_z &= C_1 \frac{J_0 \left( \alpha j^{3/2} \right)}{J_0 \left( \alpha j^{3/2} \right)} + \frac{k}{\omega p_0} p_0 J_0(Ay)
\end{align*}
\] (A.27) (A.28)

At the wall of the tube, the velocity components are \((y = 1)\):

\[
\begin{align*}
\dot{v}_r &= j \frac{kR_0}{2} C_1 F_{10}(\alpha) + \frac{1}{2} (k^2 R_0^2) \frac{k}{\omega p_0} p_0 \\
\dot{v}_z &= C_1 + \frac{k}{\omega p_0} p_0
\end{align*}
\] (A.29) (A.30)

with \(F_{10}(\alpha)\) the Womersley function:

\[
F_{10} = \frac{2 J_1 \left( \alpha j^{3/2} \right)}{\alpha j^{3/2} J_0 \left( \alpha j^{3/2} \right)}
\] (A.31)

For the equations of motion of the tube, the wall shear rate is also necessary:

\[
\left. \frac{\partial \dot{v}_z}{\partial y} \right|_{y=1} = - C_1 \frac{j^3 \alpha^2 F_{10}(\alpha) + \frac{1}{2} (k^2 R_0^2) \frac{k}{\omega p_0} p_0}{2}
\] (A.32)

**A.2.2 Wall**

The equation of motion for a solid material with no body forces present reads:

\[
\nabla \cdot \sigma = \bar{f}
\] (A.33)

with \(\bar{f}\) the inertial forces working on the material. The constitutive equation for the wall material that will be used here is equation (2.3), with the material matrix \(D\) of equation (2.4), given in chapter 2. The following extra assumptions are made: 1: The model is thin walled, with radius \(R_0\) and wall thickness \(h\). 2: The loads on the tube are such (no radial stresses), that plane stress theory is applicable. 3: There are no torsional or bending moments in the tube, so shear stresses do not occur.

With \(E_\varphi\) and \(E_z\) the elastic moduli in circumferential and longitudinal direction, and \(\mu_{x\varphi}\) and \(\mu_{xz}\) the corresponding Poisson ratios, the constitutive equation of the tube reduces to:

\[
\sigma_{\varphi\varphi} = \frac{1}{1 - \mu_{x\varphi} \mu_{xz}} \left[ E_\varphi \varepsilon_{\varphi\varphi} + \mu_{xz} E_z \varepsilon_{zz} \right]
\] (A.34)

\[
\sigma_{zz} = \frac{1}{1 - \mu_{x\varphi} \mu_{xz}} \left[ \mu_{x\varphi} E_\varphi \varepsilon_{\varphi\varphi} + E_z \varepsilon_{zz} \right]
\] (A.35)
with $\varepsilon_{\varphi \varphi}$ and $\varepsilon_{zz}$ the linear strains in circumferential and longitudinal direction:

$$
\varepsilon_{\varphi \varphi} = \frac{(r + u_r) d \varphi - r d \varphi}{r d \varphi} = \frac{u_r}{r} \approx \frac{u_r}{R} \tag{A.36}
$$

$$
\varepsilon_{zz} = \frac{\partial u_z}{\partial z} \tag{A.37}
$$

The equations of motion of the tube are easily derived by balancing the forces acting upon an infinitesimal part of the wall (sizes $h$, $d \varphi$ and $dz$, see fig. A.1).

First of all, the shear force acting in $z$-direction at the inside of the tube is:

$$
\tau_w = -\eta \left[ \frac{\partial v_z}{\partial r} + \frac{\partial v_r}{\partial z} \right]_{r=R_0} \tag{A.38}
$$

This force is counterbalanced by the stress in the wall plus inertial forces:

$$
\rho h \frac{\partial^2 u_z}{\partial t^2} = -\eta \left[ \frac{\partial v_z}{\partial r} + \frac{\partial v_r}{\partial z} \right]_{r=R_0} + h \frac{\partial \sigma_{zz}}{\partial z} \tag{A.39}
$$

In the radial direction the forces are: pressure $p$, which may be a function of the radius $R_0$, inertial forces and circumferential stresses to counterbalance the pressure:

$$
\rho R_0 h \frac{\partial^2 u_r}{\partial t^2} = p(R_0) - \frac{\sigma_{\varphi \varphi}}{R_0} \tag{A.40}
$$

Putting equations (A.34) through (A.40) together, with $y = r / R_0$, the equations of motion for the wall are:

$$
\frac{\partial^2 u_r}{\partial t^2} = \frac{p_r}{\rho h} - \frac{1}{\rho(1 - \mu \varphi \mu_{\varphi \varphi})} \left[ \frac{E_{\varphi}}{R_0^2} + \frac{\mu_{\varphi \varphi} E_z}{R_0} \frac{\partial u_z}{\partial z} \right] \tag{A.41}
$$

$$
\frac{\partial^2 u_z}{\partial t^2} = -\frac{\eta}{\rho h R_0} \left[ \frac{\partial v_z}{\partial r} + \frac{\partial v_r}{\partial z} \right]_{y=1} + \frac{1}{\rho(1 - \mu \varphi \mu_{\varphi \varphi})} \left[ \frac{\mu_{\varphi \varphi} E_{\varphi}}{R_0} \frac{\partial u_r}{\partial z} + E_z \frac{\partial^2 u_z}{\partial z^2} \right] \tag{A.42}
$$

With no slip at the wall, the boundary conditions for this set are ($y = 1 + u_r / R_0$):

$$
\frac{\partial u_r}{\partial t} \bigg|_{y=1+u_r/R_0} = v_r(1 + u_r / R_0) \tag{A.43}
$$

$$
\frac{\partial u_z}{\partial t} \bigg|_{y=1+u_r/R_0} = v_z(1 + u_r / R_0) \tag{A.44}
$$
A.3 Wave propagation

Assume that the wall motion is harmonic:

\[ u_r = \hat{u}_r e^{i(\omega t - kz)} \]  
\[ u_z = \hat{u}_z e^{i(\omega t - kz)} \]  

with \( \hat{u}_r \) and \( \hat{u}_z \) complex amplitudes of the wall motion. The no-slip condition at the wall then yields:

\[ \frac{\partial u_r}{\partial t} \bigg|_{y=1} = v_r(1) \rightarrow j\omega \hat{u}_r = \frac{1}{2} (jk R_0) \left[ C_1 F_{10} + \frac{k}{\omega \rho_0} p_0 \right] \]  
\[ \frac{\partial u_z}{\partial t} \bigg|_{y=1} = v_z(1) \rightarrow j\omega \hat{u}_z = C_1 + \frac{k}{\omega \rho_0} p_0 \]  

Inserting equations (A.29), (A.30) and (A.32), equation (A.41) becomes:

\[ -\omega^2 \hat{u}_r = \frac{p_0}{\rho h} - \frac{1}{\rho(1 - \mu_{xz} \mu_{xz})} \left[ -\frac{jk \mu_{xz}}{R_0} E_z \hat{u}_z + E_\infty \hat{u}_r \right] \]  

and equation A.42:

\[ -\omega^2 \hat{u}_z = -\frac{p_0 \nu}{\rho h R_0} \left[ -\frac{j^2 \alpha^2}{2} C_1 + \frac{k}{2 \omega \rho_0} \left( k R_0^2 \right) p_0 \right] - \frac{1}{\rho(1 - \mu_{xz} \mu_{xz})} \left[ (k^2 E_z) \hat{u}_z + \frac{\mu_{xz} E_\infty jk \hat{u}_r} {R_0} \right] \]  

Together with equations (A.47) and (A.48), equations (A.49) and (A.50) form a set of four homogeneous equations in the constants \( p_0 \), \( C_1 \), \( \hat{u}_r \) and \( \hat{u}_z \). These constants may be eliminated by setting the determinant of the system of equations to zero:

\[
\begin{vmatrix}
\frac{k}{\omega \rho_0} & \frac{j k R_0}{2 \omega \rho_0} & \frac{1}{\rho h R_0} & \frac{j \omega}{2} \\
\frac{j k R_0}{2 \omega \rho_0} & \frac{k^2 R_0}{\rho R} & 0 & \frac{j \omega}{2} \\
\frac{1}{\rho h R_0} & 0 & \frac{\omega^2 - E_\infty \beta}{\rho R} & \frac{j F_{10} E_\infty k}{\rho R} \\
\frac{-j k R_0}{2 \omega \rho_0} & \frac{-j k R_0}{2 \omega \rho_0} & \frac{-j B_{Hxz E \infty k}}{\rho R} & \frac{-j B_{Hxz E \infty k}}{\rho R}
\end{vmatrix} = 0
\]  

with

\[ B = \frac{1}{1 - \mu_{xz} \mu_{xz}} \]  

The first step in the solution of this set of equations is to make all elements non-dimensional. Multiplication of the second row by \( 1 \) by \( (jk R_0) \), the third by \( R k / \omega \) and the fourth by \( 1 / (j \omega) \) yields:

\[
\begin{vmatrix}
\frac{k}{\omega \rho_0} & \frac{k}{\omega \rho_0} & \frac{1}{\rho h R_0} & \frac{j \omega}{2} \\
\frac{R k R_0}{2 \omega \rho_0} & 0 & \omega R k & \frac{j k^2 R_0 E_{10} E_\infty k}{\rho \omega} \\
\frac{-j k R_0}{2 \omega \rho_0} & \frac{-k R_0}{2 \omega \rho_0} & \frac{-j B_{Hxz E \infty k}}{\rho R} & \frac{-j B_{Hxz E \infty k}}{\rho R} \\
\frac{-j k R_0}{2 \omega \rho_0} & \frac{-j k R_0}{2 \omega \rho_0} & \frac{-j B_{Hxz E \infty k}}{\rho R} & \frac{-j B_{Hxz E \infty k}}{\rho R}
\end{vmatrix} = 0
\]  

Multiplying the first column by \( p_0 \omega / k \), the third by \( R k / \omega \), the fourth by \( -1 / j \omega \), and substitution of \( \nu \alpha^2 = \omega R^2 \) in the second term of row four gives:

\[
\begin{vmatrix}
\frac{k}{\omega \rho_0} & \frac{1}{\rho h R_0} & \frac{1}{\rho h R_0} & \frac{1}{\rho h R_0} \\
\frac{R k R_0}{2 \omega \rho_0} & 0 & \frac{R^2 k^2 - E_\infty B k^2}{\rho \omega^2} & \frac{k^2 B_{Hxz E \infty B} \rho \omega^2}{\rho \omega^2} \\
\frac{-j k R_0}{2 \omega \rho_0} & \frac{-j k R_0}{2 \omega \rho_0} & \frac{-j B_{Hxz E \infty k}}{\rho R} & \frac{-j B_{Hxz E \infty k}}{\rho R} \\
\frac{-j k R_0}{2 \omega \rho_0} & \frac{-j k R_0}{2 \omega \rho_0} & \frac{-j B_{Hxz E \infty k}}{\rho R} & \frac{-j B_{Hxz E \infty k}}{\rho R}
\end{vmatrix} = 0
\]
At this stage the following approximations may be introduced:
In the third row, the third term $R^2 k^2$ can be neglected in comparison with $E_0 B k^2 / \rho \omega^2$. This is allowed because the order of magnitude of $R^2$ equals $10^{-4}$ and that of $E_0 B k^2 / \rho \omega^2$ is greater than 1.
The first term of the fourth row is of order $k^2 \ 10^{-3}$ and the lowest term in the determinant is of order $k^2 \ 10^3$. This first term therefore may be neglected as well.
Now the following abbreviations are introduced:

$$H = \frac{h \rho}{R \rho_0} \quad (A.55)$$
$$x = \frac{H E_0 B k^2}{\rho \omega^2} \quad (A.56)$$

And the equation transforms into:

$$\begin{vmatrix}
1 & 1 & 0 & 1 \\
\frac{1}{2} E_0^2 & -1 & 0 \\
\frac{1}{2} E_0^2 & -1 & 0 \\
0 - \frac{F_{10}}{H} & -\mu_{z\phi} x & 1 - \frac{x}{H}
\end{vmatrix} = 0 \quad (A.57)$$

The order of the determinant now can be reduced by replacing the second row by row 1 - 2 row 2, the third row by row 1 - H row 3 and the fourth by H row 4:

$$\begin{vmatrix}
1 & 1 & 0 & 1 \\
0 & 1 - F_{10} & -1 & 0 \\
0 & 0 & mx & 1 + \mu_{z\phi} x \\
0 - \frac{F_{10}}{H} & -\mu_{z\phi} mx & H - x
\end{vmatrix} = 0 \quad (A.58)$$

which is equal to:

$$\begin{vmatrix}
1 - F_{10} & -1 & 0 \\
0 & mx & 1 + \mu_{z\phi} x \\
- \frac{F_{10}}{H} & -\mu_{z\phi} mx & H - x
\end{vmatrix} = 0 \quad (A.59)$$

with $m = E_0 / E_z$. Because of the symmetry of the material matrix $D$ (equation (2.4)) we may write:

$$\mu_{z\phi} = \frac{E_0}{E_z} \mu_{z\phi} = m \mu_{z\phi} \quad (A.60)$$

This yields the following quadratic expression in $x$ for the determinant:

$$m(1-F_{10})(1-m\mu_{z\phi}^2)x^2 - \left(2 + mH(1 - F_{10}) + \left(\frac{m}{2} - 2m\mu_{z\phi}\right) F_{10}\right) x + F_{10} + 2H = 0 \quad (A.61)$$

This equation has two roots:

$$x_{1,2} = \frac{1 + \frac{1}{2} m \left[H(1 - F_{10}) + \left(\frac{m}{2} - m\mu_{z\phi}\right) F_{10}\right]}{m(1 - F_{10})(1 - m\mu_{z\phi}^2)} +$$

$$\pm \frac{\left[1 + \frac{1}{2} m \left[H(1 - F_{10}) + \left(\frac{m}{4} - m\mu_{z\phi}\right) F_{10}\right]^2 - m(1 - F_{10})(1 - m\mu_{z\phi}^2) F_{10} + 2H\right]}{m(1 - F_{10})(1 - m\mu_{z\phi}^2)^2}^{\frac{1}{2}} \quad (A.62)$$

Again, some abbreviations may be introduced:

$$G = \frac{1 + \frac{1}{2} m \left[H(1 - F_{10}) + \left(\frac{1}{4} - \mu_{z\phi}\right) m F_{10}\right]}{m(1 - F_{10})} \quad (A.63)$$
and

\[ L = \frac{F_{10} + 2H}{m(1 - F_{10})} \]  

(A.64)

The roots then read:

\[ (1 - m\mu^2_{z\varphi})x = G \pm \sqrt{G^2 - (1 - m\mu^2_{z\varphi})L} \]  

(A.65)

Inserting equations (A.55), (A.64) and (A.65) into the definition of \( x \), equation (A.56) yields the wave number \( k \):

\[ k = \pm \omega \sqrt{\frac{R_\rho_0}{h E_z}} \left[ G \pm \sqrt{G^2 - (1 - m\mu^2_{z\varphi})L} \right] \]  

(A.66)

A.4 Special cases

A.4.1 Inviscid flow

For inviscid flow (which is approximated at high Womersley numbers), the wave velocity equation (3.35) is simplified dramatically: Then the parameters \( G \) and \( L \) are no longer functions of the frequency, and become real:

\[ G_0 = \frac{2 + Hm}{2m} \]  

(A.67)

\[ L_0 = \frac{2H}{m} \]  

(A.68)

The wave velocity \( c_0 \) then reads:

\[ c_0 = \frac{1}{\sqrt{\frac{R_\rho_0}{h E_z}} \left[ G_0 \pm \sqrt{G_0^2 - (1 - m\mu^2_{z\varphi})L_0} \right]} \]  

(A.69)

For an isotropic material, this reduces to the well-known Moens-Korteweg wave velocity:

\[ c_0 = \sqrt{\frac{h E}{2R_\rho_0 \rho_0}} \]  

(A.70)

A.4.2 Longitudinal tethering

When the tube is tethered longitudinally, all terms with \( \dot{u}_z \) become zero, longitudinal shear waves in the wall are suppressed, and the equation for the wave velocity simplifies to:

\[ c = \sqrt{\frac{1}{\Im \sqrt{\frac{2R_\rho_0}{h E_{\varphi}} \frac{1 - m\mu^2_{z\varphi}}{1 - F_{10}}}}} \]  

(A.71)

For the isotropic case, \( m \) is one, and \( E_{\varphi} \) and \( \mu_{z\varphi} \) are \( E \) and \( \mu \), respectively.
Appendix B

Principles of LDA and USD

B.1 LDA

LDA is based on the phenomenon that the observed frequency \( f_0 \) of a source depends on the velocity of the observer with respect to the source. Consider two intersecting laser beams, (beam 1 and 2, figure B.1). A particle P crosses the intersection volume with velocity \( \vec{u} \). The frequency of beam 1 \( (f_0) \), as observed by the particle is:

\[
f_{p1} = f_0 \left[ 1 - \frac{\vec{e}_1 \cdot \vec{u}}{c} \right]
\]  

(B.1)

![Figure B.1: LDA: principle](image)

The light is scattered in all directions. The frequency, as observed by a non-moving observer in direction \( \vec{e}_3 \) is:

\[
f_{o1} = \frac{f_{p1}}{1 - \vec{e}_3 \cdot \vec{u}/c} = f_0 \left[ 1 - \vec{e}_1 \cdot \vec{u}/c \right] / \left[ 1 - \vec{e}_3 \cdot \vec{u}/c \right]
\]  

(B.2)

The observed frequency \( f_{o2} \) of beam 2 is calculated in the same way. Due to interference of the laser beams, the Doppler frequency appears:

\[
f_d = |f_{o1} - f_{o2}| = \frac{f_0}{c} \left| [\vec{e}_1 - \vec{e}_2] \cdot \vec{u} \right|
\]  

(B.3)

This frequency is linearly dependent on the velocity component, perpendicular to the optical axis of the setup.

B.2 Ultrasound Doppler

The ultrasound equipment used in this study was developed by the Department of Biophysics, which participates in the Cardiovascular Research Institute Maastricht (CARIM) at the Rijks-
universiteit Limburg. The acquisition method implemented in their design is what is called multi-gate pulsed Doppler, and is state-of-the-art today.

B.2.1 Acquisition

With a piezoelectric crystal an electric signal is converted into an ultrasound wave. The frequency of this signal usually lies between 2 and 10 MHz and is called the carrier frequency. In the experimental set-up the carrier frequency was 5.0 MHz. The signal is not emitted continuously, but in pulse trains of 2 periods of the carrier signal. The emission is repeated periodically, with frequency $PRF$, the pulse repetition frequency.

The ultrasound signal travels through the material under test (usually a patient) with the speed of sound ($c \approx 1500 m/s$) along a straight line (M-mode Doppler). Because of inhomogeneities in the material, reflection of the ultrasound wave occurs. This reflected radio frequent (RF) signal is sampled with four times the carrier frequency (20.0 MHz). When enough reflective material is present, the RF-signal is a continuous signal.

Theoretically, the maximum measurement depth $d_{th}$ at which one can measure is determined by the $PRF$ and the mean wave velocity $c$ of the material:

$$d_{th} = \frac{c}{2 \cdot PRF} \quad (B.4)$$

The two in the denominator appears because the signal has to travel two times through the material (forward and backward). With a $PRF$ of 4.5 kHz this yields a depth of 167 mm in water. However, within one period of the $PRF$-signal, only 768 samples are acquired. The maximum depth $d_{max}$ due to this limitation is:

$$d_{max} = \frac{768 \cdot c}{2 \cdot f_s} \quad (B.5)$$

With a sampling frequency $f_s$ of 20.0 MHz the maximum depth in water is 29 mm. In that case the distance in space between two adjacent samples is 37.5 μm. The data acquisition is synchronous with the $PRF$, so the temporal distance between two samples is $1/PRF = 222 \mu s$, with a $PRF$ of 4.5 kHz. The samples are stored in what is called an RF-matrix (see fig. B.3). The maximum acquisition time is limited by the size of the memory for data storage and the $PRF$. In the equipment used here, the maximum number of lines to be acquired was 5461. Multiplied by 768 samples in space, of 10 bit each, this requires a memory of 4 Mword (8 Mbyte). The processing of the RF-data is carried out off-line, after acquisition has been completed.

B.2.2 Data processing

Frequency spectrum of the RF-signal

The received RF-signals consist of four major components: 1: reflections induced by stationary or slowly moving material, e.g., the tube wall (high spectral power, narrow bandwidth, low temporal mean frequency); 2: scattering induced by scattering particles (seeding) in the fluid (low spectral power, wide bandwidth, temporal mean frequency depending on flow velocity); 3: reverberations (low spectral power, narrow bandwidth, low temporal mean frequency); 4: noise (low spectral power, uniform spectral distribution). To estimate flow velocity the signal components, induced by reflections or reverberations should be suppressed (Hoeks et al., 1991).

The discrimination between reflections and scattering is based on the difference in temporal properties of these signal components (fig. B.3). The difference in power between reflections and scattering is in the order of 40 dB. In general, ultrasound signal processing for the assessment of mean flow velocity consists of a filter for the discrimination between reflections and scattering,
Figure B.2: Data storage of the acquired RF-signals in a matrix. RF-signals are sampled in depth and time (top to bottom and left to right respectively).

Figure B.3: Spectral power density distribution of a signal from a temporal intersect in an RF-matrix
and a mean frequency estimator for the temporal (Doppler) and spatial (carrier) mean frequency which are directly related to the mean flow velocity by means of the Doppler equation:

$$\hat{v}(t, d) = \frac{c}{2 \cos \alpha} \frac{\hat{f}_t(t, d)}{\hat{f}_c(d)}$$ (B.6)

where $c$ is the speed of sound in the fluid, $\hat{f}_t(t, d)$ the estimated temporal mean frequency of the scattering at a certain time $t$ and depth $d$, $\hat{f}_c(d)$ the estimated mean carrier frequency at depth $d$, and $\alpha$ the angle between the ultrasound beam and the velocity vector. The ultrasound probe must be positioned at an angle $\alpha < \frac{\pi}{2}$ with the expected velocity vector. Equation B.2.2 is called the Doppler equation. $\hat{f}_t(t, d)$ Can be considered as the Doppler shift in the RF-signal, caused by the velocity of the fluid particles.

**Frequency and velocity estimation**

Only recently, frequency estimators in the RF-domain have become available (Bonnefous & Pesque, 1986; Jong et al., 1990). They were developed for accurate estimation of mean frequencies in short time intervals (estimation windows). With an estimation window of 8 to 10 ms the standard deviation of the estimated frequency—and the velocity—is low, while the time dependency of the signal is not compromised much (Hoeks et al., 1993; Brands et al., 1995).

The quality of a temporal mean frequency estimator strongly depends on the model used for the RF-signal (Brands & Hoeks, 1992).

The best estimator of mean frequency in the RF-domain (RF cross-correlation) in a given time and depth window is based on a Gaussian model of the spatial cross-power spectral density distribution of the received ultrasound RF-signals. The RF-domain mean frequency estimator derived from this model is given by the following equation:

$$\hat{f} = \frac{\arctan \left[ \frac{1}{2} \left( \hat{R}(k+1,1) - \hat{R}(k-1,1) \right) \right]}{\arccos \left[ \frac{\hat{R}(k+1,1)}{\hat{R}(k,1)} \right]}$$ (B.7)

where $\hat{R}(k,i)$ is the estimated correlation function from a given estimation window in the RF-matrix and $\hat{f}$ the estimated normalized velocity. The cross-correlation function $\hat{R}(k,i)$ is estimated using the data points within a rectangular estimation window of 8 sample points in depth (spatial estimation window length, in this case $8 \times 37.5 = 300 \mu m$) and 48 sample points in time (temporal estimation window length, in this case $48 \times 222 \mu s = 10.6 ms$). The estimation is carried out on all adjacent 48x8 submatrices of the RF-matrix, plus all 48x8 submatrices with a 24x4 overlap with the matrices from the first set. The estimated normalized velocity is related to velocity as:

$$\hat{v} = \frac{c}{2 \cdot \cos \alpha} \cdot \frac{PRF}{f_s} \cdot \hat{f}$$ (B.8)

**Signal filtering**

Apart from noise, the RF-signal consists of two major components: Reflections, generated by the vessel wall and scattering, generated by the scattering particles in the fluid. These components are clearly recognized from the temporal amplitude spectral distribution of a temporal cross section of the RF-matrix (fig. B.2, left panel). The characteristics of the reflections are:
1: relatively high amplitude; 2: narrow temporal bandwidth; 3: low temporal frequency (maximum wall velocity ≈ 8 mm/s). To estimate the velocity of the fluid the reflections induced by stationary or slowly moving structures should be suppressed. The procedure followed to achieve this suppression is depicted in fig. B.4. Starting with the raw

Figure B.4: Schematic representation of the main processing steps of an adaptive reflection removal filter demonstrated on the temporal spectral density distribution of a temporal intersect in an RF-matrix (a). For further explanation: see text.

data from the RF-matrix (a), the negative frequencies are removed by Hilbert transformation (b). The frequency of the reflections is then estimated using the aforementioned estimation technique (yielding the wall velocity) and the spectrum is shifted towards zero over the reflection’s frequency (c). The reflection’s peak in the spectrum is then removed by a highpass filter with a very low cut-off frequency, to minimize the loss of information in the frequency band, generated by scattering. Finally, the scattering frequency is determined with the same estimation technique (d). The advantage of this adaptive method over a static high-pass filter is the conservation of low-velocity information, especially in near-wall regions (Brands et al., 1995).