Imaging Visco-Elastic Properties of Soft Tissue with Ultrasound

by

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We accept this thesis as conforming to the required standard

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Abstract

This thesis describes a system to measure the mechanical properties of soft tissue. The mechanical properties depend on the type of tissue (e.g. fat, muscle, blood) and the presence of disease or pathology. For example, it has been known that many cancers, such as carcinoma of the breast and the prostate, appear as hard nodules. Manual palpation is widely used for detecting these nodules but detection by palpation is restricted to large tumors that reside relatively close to an accessible surface. Current imaging devices such as computed tomography, magnetic resonance imaging and ultrasound are not directly capable of measuring the mechanical properties of tissue.

An emerging research topic, called elastography, aims to produce a new type of image that depicts mechanical properties of tissue. The basic principle is to excite motion in a tissue, record the motion with an imaging device, and then estimate the mechanical properties from the recorded data. This thesis presents a new approach based on this principle where a computer-controlled vibrator induces motion over a range of frequencies simultaneously and the resulting displacement is recorded at multiple locations and time instants with a sequence of ultrasound images. Two methods are proposed for estimating mechanical properties such as stiffness, damping, and mass, from the recorded data. In the first method, the tissue is modeled by using mass elements at different locations connected to each other by springs and dampers. These elements represent the local mass, stiffness, and damping of the tissue. The equation of motion for the proposed one dimensional model is solved to extract these parameters.

The second method performs a transfer function analysis of the tissue motion. According to this method, the tissue dynamics between two locations along the axis of motion is considered as a linear dynamic system. The transfer function between the two locations is obtained by spectral analysis with the recorded motion used as inputs and outputs. The shape of the transfer function can then
be analyzed further. For example, the stiffness of tissue can be estimated from the magnitudes of the transfer function at low-frequencies.

Common to both methods is a new time domain correlation-based tracking algorithm for measuring tissue motion in successive ultrasound images. The algorithm is based on stretching the time domain ultrasound signals according to the local compression applied along the axial direction. The accuracy of the new method is demonstrated to be higher than the standard time domain correlation-based algorithms on a small number of tests on tissue mimicking materials.

Both simulations and experiments have been performed to validate the proposed methods. Simulations show that the parameters can be extracted within 1% error when the measurement noise level is set to 0%, for one dimensional mass-spring-damper models with varying parameters. The simulations are repeated by taking ultrasonic noise and correlation-based motion tracking noise into account. The errors in damping and stiffness values are within 5% at 4 mm resolution, and 12% at 6 mm resolution for mass values, for a simulated one dimensional homogeneous tissue. Initial experimental results from homogeneous and layered tissue mimics are reported which demonstrate the ability of both methods to quantitatively image tissue stiffness. Preliminary results on tissue damping distribution for homogeneous tissue mimics are found to be comparable to the reported damping values for the same type of material in the literature. The shear viscosity values are found to be between 12.5-19.7 Pa·s for a gelatin block with a Young's modulus of 25 kPa. Extraction of mass is still under investigation. Both the simulations and the experimental results show that the new methods are feasible and further investigation is needed to continue development of the ideas.
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Glossary

US  Ultrasound.
Elastography  Techniques for imaging mechanical properties of tissue.
Elastogram  An image obtained by elastography.
1D  One dimensional.
2D  Two dimensional.
3D  Three dimensional.
PSF  Point spread function.
LSM  Least squares method.
IVM  Instrumental variables method.
RF  Radio frequency.
B-mode image  Brightness mode ultrasound image.
B-scan  Brightness mode ultrasound image.
ROI  Region of interest.
SNR  Signal to noise ratio.
L-MSD  Lumped mass spring damper.
MRI  Magnetic resonance imaging.
CT  Computed tomography.
\( \theta \) Parameter vector.

\( \Phi \) Measurement matrix.

\( E(X) \) Expectation of random variable \( X \).

\( \sigma_{ij} \) Stress tensor.

\( \epsilon_{ij} \) Strain tensor.

\( C_{ijkl} \) Tensor of elastic constants.

\( \lambda, \mu \) Lamé constants.

\( \mu \) Shear modulus.

\( \nu \) Poisson’s ratio.

\( E \) Young’s modulus.

\( \rho \) Density.

\( C_l \) Compressional wave speed.

\( a_i(t) \) Acceleration measurement of node \( i \) at time \( t \).

\( v_i(t) \) Velocity measurement of node \( i \) at time \( t \).

\( x_i(t) \) Displacement measurement of node \( i \) at time \( t \).

\( k_i \) Stiffness between nodes \( i \) and \( i + 1 \).

\( b_i \) Damping between nodes \( i \) and \( i + 1 \).

\( m_i \) Mass at node \( i \).

\( F(s) \) Laplace transform of a time domain function.

\( H_i^j(w) \) Transfer function from node \( i \) to node \( j \).

\( P_{x_i x_i}(w) \) Power spectral density of time domain function \( x_i(t) \).

\( P_{x_i x_j}(w) \) Cross spectral density of between time domain functions \( x_i(t) \) and \( x_j(t) \).

\( C_{x_i x_j}(w) \) Coherence function between time domain functions \( x_i(t) \) and \( x_j(t) \).
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Chapter 1

Introduction

1.1 Background

The basis of medical imaging is the measurement of a property of tissue that varies with tissue composition. Medical images are formed by displaying these properties measured at multiple locations in the body. From such images, a depiction of anatomy or pathology is gained. Each different imaging modality in common use, such as X-ray, computed tomography (CT), ultrasound (US) and magnetic resonance imaging (MRI), measures a different property of tissue. None of the properties measured by those modalities describe directly the mechanical properties of tissue. Mechanical properties are properties that describe the deformation of tissue under a static or varying force. Density, compressibility, stiffness, and viscosity are examples of mechanical properties. Creating images from one or more mechanical properties is useful in medical practice, if the variation of the measured property creates sufficient contrast in the image to depict anatomy or pathology.

Table 1.1 lists the variation of density in mammalian tissue. Excluding lung and bone, the density varies between 0.937-1.07 g/cm³.

The compressibility of tissue, also described as Poisson's ratio, is another mechanical parameter of interest, yet there is little information in the literature about the variation of this parameter with tissue composition. Most papers on biomechanical properties of tissue make the assumption that most tissues and tissue-like materials are close to incompressible (Poisson's ratio of 0.5 in [53], 0.495 in [28], and [49]). However, some pathological tissues such as edematous muscle tissues
1.1 Background

<table>
<thead>
<tr>
<th>Tissue type and preparation</th>
<th>Density ( (g/cm^3) )</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole blood, fresh, heparinized</td>
<td>1.055</td>
<td>-</td>
</tr>
<tr>
<td>Bone, skull</td>
<td>1.738</td>
<td>-</td>
</tr>
<tr>
<td>Brain, fresh</td>
<td>1.03</td>
<td>Pathology-free</td>
</tr>
<tr>
<td>Fat, fresh or refrigerated</td>
<td>0.937 (pig)</td>
<td>Measurements at 37(^\circ)C</td>
</tr>
<tr>
<td>Heart muscle (beef)</td>
<td>1.048 ± 0.0036</td>
<td>-</td>
</tr>
<tr>
<td>Kidney (beef)</td>
<td>1.040 (pig)</td>
<td>-</td>
</tr>
<tr>
<td>Liver, fresh</td>
<td>1.064 (pig)</td>
<td>Pathology-free</td>
</tr>
<tr>
<td>Lung, fresh (dog)</td>
<td>0.4</td>
<td>Inflated</td>
</tr>
<tr>
<td>Muscle, striated</td>
<td>1.07 (pig)</td>
<td>-</td>
</tr>
<tr>
<td>Water</td>
<td>1.0</td>
<td>Approx. values</td>
</tr>
</tbody>
</table>

Table 1.1: Typical values of density for selected mammalian tissues (Table is modified from [23]).

were reported to have a Poisson’s ratio lower than 0.5 [30]. The Poisson’s ratio of lung tissue was measured to be 0.3 [30], and adult bovine humeral articular cartilage tissue was reported to be 0.18 [27]. It is mentioned in [30] that due to the relatively small dynamic range of Poisson’s ratio, the image contrast may be limited.

Viscosity of tissue is related to the internal friction caused by the velocity gradient during dynamic tissue deformation. The diagnostic importance of this parameter is not widely investigated in the literature. However, the flow properties of soft tissue may vary significantly with pathology and tissue composition. In vivo values for tissue viscosity are very sparse in the literature. In [45], a theoretical analysis of the behaviour of mechanical vibrations in a visco-elastic medium was made. In particular, the analysis was done for human muscle at vibration frequencies up to 200 kHz. The shear viscosity of muscle was set to 0.15 Pa·s for the calculations. Later in 1971, shear properties of mammalian tissue at 2 - 24 MHz was investigated [17]. According to the experiments on canine liver, kidney and muscle at 25\(^\circ\)C, the range of shear viscosity values were found to be 5-30 centipoise, which converts to 0.005-0.03 Pa·s. At these frequencies, the viscosities are orders of magnitude less than those reported at 0.5-5 kHz in [45]. In [17], this fact was explained by a shift in the level of tissue components controlling the shear properties. It was suggested that at low frequencies the shear acoustic properties are determined to a high degree by the cellular structure, whereas at high frequencies with shorter wavelengths the macromolecular composition of the tissue becomes more important. Later in 2000, shear viscosity values for in vitro porcine liver and kidney tissue specimens were found to be 10.3 Pa·s and 9.2 Pa·s respectively in [34] at low frequencies
(100-500 Hz). The same type of experiments on a gel having a shear stiffness of 9.0 kPa is reported to have a shear viscosity of 15.3 Pa·s [34]. In [6], two elastic gel-based tissue mimics having the same shear modulus (4 kPa) and different viscosity were produced. The viscosity maps for both of these gels were obtained. The mean viscosity of these homogeneous gels were reported to be 0.3 Pa·s and 0.6 Pa·s. The shear waves in [6] were created by focused ultrasound. It was reported that the duration of the applied focused ultrasound was 100 µs, therefore, the minimum frequency of the resultant shear waves were at least 10 kHz. The lower values of the shear viscosities for the gel-based tissue mimics in [6] compared to [34] can be explained by the frequency difference of the mechanical excitations, similar to the discussion above by [17].

The stiffness of tissue, also known as elasticity or its inverse compliance, is well-known as an important measure in diagnostics. In healthy tissue, the stiffness can vary as much as four orders of magnitude [24]. For example, in the bovine kidney, the stiffness contrast between the cortex and the medullary pyramids is approximately a factor of two [46]. The stiffness of tissues is also known to vary with physiological state. The elasticity of muscle is 100 times larger in the contracted state compared to the relaxed state [24].

The presence of disease can also change a tissue’s mechanical properties. For example, the changes can be caused by exudation of fluids from the vascular system into the extra and intra cellular space or by loss of lymphatic systems, as in the case of cancer [24]. It is been known that many cancers, such as carcinoma of the breast and the prostate, appear as hard nodules [46]. In such cases the tumor can be significantly stiffer than surrounding tissue, yet for example tumors of the prostate or the breast could be invisible or barely visible in standard ultrasound images [46]. Tables 1.2, and 1.3 show the variations in stiffness of normal and abnormal breast and prostate tissues. In summary, an imaging device that could depict the elasticity distribution in soft tissue would be a valuable tool for the diagnosis of disease.

Imaging the mechanical properties of tissue has become the subject of increasing interest during the past two decades. The techniques used for imaging these properties of tissue form a new field of study called elastography in the literature. In this thesis, a new imaging technique is described and also labeled elastography, even though it is capable of measuring more than only elasticity. The next section gives a literature review on the status of current elastography approaches.
1.2 Prior Work

All elastography techniques combine mechanical excitation with measurement of the resulting motion. Most measurements are made with conventional imaging systems, such as US, MRI, or CT. Elastography can be categorized by the type of mechanical excitation and the type of imaging method. In this section, elastography is first categorized according to the temporal characteristics of the excitation into two broad categories: static and dynamic. In static elastography, the deformation does not vary with time. The excitation is either static or sufficiently slow to be considered quasi-static (less than 2 Hz). In dynamic elastography some form of oscillating vibration is applied to the tissue and the dynamic response of the tissue is observed.
1.2 Prior Work

1.2.1 Static Methods

In static elastography, only the static properties (such as elasticity or compressibility) of tissue can be observed. The idea of deforming tissue with an external source of static stress to extract the tissue elasticity quantitatively was first proposed by Ophir et al. [48]. An external stress was applied to the skin surface using a wide plate, and two ultrasound images were taken of the deformation. One image was taken during compression of the tissue with a nominal static external force. The second image was taken during compression with a higher static external force. The external force refers to uniform axial pressure (from the flat plate) applied above the region of interest. The basic principle is that stiff tissues will compress less than compliant tissues. Dividing each image into small regions and comparing the movement of these regions between the two images provides a quantitative measurement of the local strain. The elastic modulus is defined as the ratio of stress to strain in a one dimensional (1D) model. Provided that a good estimate of the stress distribution inside the tissue axially is made, the distribution of relative elasticity can be extracted. The underlying assumption is that the strain is linearly related to the stress and that this relationship is modeled as a linear scale factor called the Young's modulus, or simply elasticity. Because of the high correlation between the strain and elasticity in the 1D case, the first elastograms simply displayed the strain distribution of the tissue. These images are often called strain images. The main advantage of strain imaging is simplicity. The disadvantage is the creation of artifacts because the strain is a result of not only tissue motion in the axial direction, but also tissue motion in the lateral and elevational directions and the boundary conditions.

The relationship between strain and elasticity is more complicated in the two dimensional (2D) and three dimensional (3D) cases. Solving the elasticity distribution from the 2D or 3D strain distribution is a challenging inverse problem in the field of elastography. A given strain distribution in a 3D medium can be a result of infinitely many elasticity distribution cases [53]. Therefore, additional information such as boundary conditions and assumptions on tissue mechanical properties is necessary to obtain a unique solution. For example, most of the direct elasticity distribution construction methods are limited to 2D, elastic, isotropic, incompressible media. Sumi et al. (1995) proposed a method to estimate the shear modulus distribution for linear isotropic incompressible 2D elastic media [54]. In his method, linear equation sets were derived with spatial derivatives of shear modulus as unknowns and 2D strain data as the coefficients of the equations. These equa-
tions were solved analytically to obtain the spatial derivatives of the shear modulus distribution in the region of interest (ROI). The elasticity distribution was then found by integration. Scovoroda et al. (1995) proposed a more general approach to the inverse problem [53]. Using a two step procedure, the stress continuity condition was first used to find the discontinuities in the shear modulus distribution. The discontinuities were then used as boundary conditions for solving the partial differential equations. The differential equations described the mechanical equilibrium of a deformed medium under the following conditions: linear elasticity in 3D, incompressibility, and knowledge of the Young’s modulus along the boundary of the ROI. The method was verified in the case of planar strain by experiments on tissue mimicking materials. Barbone (2003) showed in a recent paper [5] that the elasticity distribution can be obtained for 2D isotropic, incompressible media without requiring knowledge of the boundary conditions, or any other prior assumption other than the continuity of the elasticity distribution. It was shown that two displacement fields, one for axial deformation, and one for shear deformation were sufficient to construct the true elasticity distribution in 2D. Such a method is important for in vivo studies where boundary conditions are complicated and usually not known. The direct construction of elasticity distribution from strain data has certain advantages compared to strain imaging. Stiffness images tend to contain fewer artifacts and are easier to interpret. On the other hand spatial resolution depends on the number of mesh nodes in the model. An increase in the number of nodes results in an increase in the number of constitutive relationships to be considered in solving the system of equations. Difficulty in obtaining a unique solution is also another important drawback of the technique. Therefore, these techniques also requires additional a priori information on the tissue under examination such as boundary conditions.

In static elastography, internal biological pressure sources can also be used, instead of external forces. For example, the deformation of arterial walls from oscillating blood pressures can be used for qualitative analyses of the arterial wall elasticity [50]. Yet, internal sources are difficult to measure, so their use is limited to specialized cases.

1.2.2 Dynamic Methods

With recent advances in the frame rate of the modern imaging devices, it has become possible to observe time varying deformations (i.e. the mechanical wave propagation) in tissue. During the
last decade many approaches have been proposed to analyze the mechanical wave propagation in tissue and form elastograms.

In this section dynamic elastography is categorized according to how the mechanical waves are analyzed. Some approaches make direct observations of waves in a region of interest without solving any inverse problem for a predefined model for the tissue. Other approaches solve the inverse problem for wave propagation to obtain the distribution of local dynamic parameters of the tissue.

1.2.2.1 Vibration Doppler Elastography

Measuring the tissue vibration with Doppler ultrasound was first proposed for Elastography by Lerner and Parker et al. 1988 [36]. The basic concept of their method was to propagate low-amplitude, low frequency shear waves (with displacements below 0.1 mm and frequencies typically below 1000 Hz) through deep organs and display the vibration response in real time using Doppler detection techniques. By 1990, their group was using a modified color Doppler instrument to make real-time elastograms, where vibration above a threshold was shown as a saturated red overlay on a traditional ultrasound image. A dark area in the overlay indicates regions that are below a chosen vibration amplitude and indicates the presence of hard nodules, or nulls of the standing wave patterns. The vibration amplitude at each spatial location was found by investigating the spectrum of the Doppler signal. The Doppler spectrum of a scattered ultrasound signal from a vibrating target is similar to that of a pure-tone frequency modulation process if the wave is assumed to propagate as a linear wave. Its Doppler spectrum has symmetric side harmonics around the carrier frequency. The spacing of the harmonics is equal to frequency of the vibrating target, and the amplitudes of the harmonics are given by the successive Bessel functions of the first kind. It was shown that the ratio of the first to the second harmonic is proportional to the vibration amplitude [35, 61]. Later Lin et al. used the vibration Doppler technique to investigate the resonance behavior of the tissue [38]. In a similar manner the tissue was excited with a vibrator at audio frequencies and the tissue response was measured by power Doppler. The difference was that the audio-frequency source swept through sequences of vibrational frequencies to obtain the full frequency spectrum of the tissue at different locations. Various measurements of the shape of the spectrum around the resonance peak were then displayed.
In general, vibration Doppler elastography techniques have the theoretical advantage of being able to image tissue dynamically. However the amplitude images suffer from the presence of standing waves and other aberrations that result from reflections within the tissue. The images presented in [22,35] gives only a rough qualitative estimate of tissue elasticity and lacks the necessary contrast to be medically useful for a wide range of applications. The vibration Doppler elastography techniques also do not take into account any particular dynamic tissue model so a direct extraction of static or dynamic tissue parameters such as elasticity, damping, or density is not possible.

1.2.2.2 Solving the Wave Equations

In continuum mechanics, the wave equations are defined at a point. If the spatial and temporal derivatives of a certain point in tissue are known, the mechanical properties of that point can be extracted if at least one mechanical parameter defined in the wave equations is known. Obtaining the mechanical parameters at a certain point does not require the motion information of the entire tissue. Hence, wave equation techniques have the advantage of being local, and independent of boundary conditions. To obtain the wave propagation parameters of the tissue, the spatial and temporal partial derivative terms must be estimated. A good estimation of the temporal derivatives requires an imaging device with a high frame rate. The estimation of the spatial derivatives on the other hand is limited by the resolution of the imaging device or the wave length of the propagating wave. Increasing the frequency of the vibration decreases the wave length which in turn increases the quality of the spatial derivative estimates for a fixed resolution [52]. But high frequency mechanical waves attenuate faster in tissue, which prevents the imaging of deep organs. There are two approaches for estimating the temporal derivatives. The first approach is increasing the frame rate of the imaging device (for example the ultrasound device imaging at 10,000 frames per seconds in [51]). The second approach is to apply a harmonic excitation and to convert the wave equation into the frequency domain [37,41,52,61].

Yamakoshi et al. developed a Doppler technique to map both the amplitude and phase of a harmonic vibration using Doppler signal detection techniques [61]. It was observed that an inhomogeneity caused a localized disturbance in images of the spatial distribution of vibration phase. Vibration phase images were used to find the wave length of the traveling mechanical waves and the speed of the waves at various spatial locations. The wave speed data was then converted
1.2 Prior Work

to local elasticity by using the fact that elasticity is inversely proportional to the square of wave speed [61]. This approach was later refined to study the visco-elastic properties of human thigh muscles using a plane wave propagation model by Levinson et al. [37]. In this model, the tissue was assumed to be linear, visco-elastic, isotropic, and homogeneous. Only the shear components of the waves were considered. For the harmonic excitation case, the wave equations in the frequency domain related the amplitude and the phase of the vibration to the elasticity and viscosity of the medium with a simple relationship in the complex domain. The amplitude and the phase of the vibrations were obtained by Doppler techniques proposed as before [61]. These elastography methods also suffer from the presence of standing wave patterns.

The shear waves can be analyzed in similar way with MRI. MRI has the advantage of producing higher resolution, higher quality images compared to Doppler ultrasound. The Mayo Clinic has reported visualization of shear waves via a technique where an MRI sequence was phase-locked to the mechanical excitation [41]. The deformation resulting from the external harmonic vibrations were imaged, and a wave pattern was observed. The shear modulus was constructed locally by relating the wave length to wave speed, and wave speed to shear modulus, which is the same approach taken by the previous groups mentioned above. Later, Sinkus et al. used the same method for analyzing the propagation of shear waves using 3D MRI [52]. The wave equations were solved for the harmonic excitation case in the frequency domain using a 3D homogeneous, compressible visco-elastic medium, where tissue anisotropy is assumed for the elasticity distribution. In another MRI elastography work presented in [34], frequency dependency of shear wave speed in a visco-elastic media was exploited to obtain shear viscosity of tissue in vitro. The tissue visco-elastic model was chosen to be a Voigt element. For two types of tissue samples, the shear wave velocity was calculated from 75 to 300 Hz vibration frequencies. The shear viscosity values were obtained for fresh kidney and liver tissue specimens by a nonlinear regression fit to the velocity values. The quality of shear viscosity data highly depends on the nonlinear fit, which may degrade the results. Unfortunately, the MR elastography methods are slow because of the phase-locking technique used. It takes approximately 30 minutes to obtain in vivo results for the breast [52]. Therefore, the images can be affected by patient movement, breathing, or variable blood pressure in the ROI.

Another approach is to solve the inverse problem of calculating the shear modulus from the
wave equation in the time domain assuming a linear, elastic, isotropic 2D medium [51]. Given a
time domain analysis, there is no restriction for the applied excitation. Shear waves are created
either by external vibrations of 50 Hz or focused ultrasound techniques inside the tissue [51]. Robust
stiffness and viscosity images were obtained by using a specially developed 10,000 frames-per-second
ultrasound scanner. The drawback of this approach is the need for specialized ultrasound devices
because conventional ultrasound machines have a frame rate of 100 frames per seconds.

1.2.2.3 Focused Ultrasound Techniques

Another dynamic imaging method excites only a small volume of tissue interior to the body using
high intensity focused ultrasonic waves. In Nightingale et al. [42] a first set of high intensity
ultrasound pushing pulses was used to produce an acoustic radiation force and was measured with
a second set of low-intensity ultrasound images. The high intensity pushing pulses were interleaved
with low intensity imaging pulses to combine excitation and measurement in one device. The
relative local displacements were measured at different locations and displayed. The displacements
were related to the local elasticity. This technique was not modified to capture tissue dynamics.
A drawback of this technique is the use of high-intensity ultrasound because it poses a possible
hazard to the patient. In comparison, conventional medical ultrasound machines use low-intensity
ultrasound and the allowable maximum intensity is carefully regulated.

In a paper by F. Viola and W. Walker, [60], focused ultrasound was used to generate a step
force in a localized region of tissue. The resulting displacement was measured as a function of
time and the relation time constant was used to identify the relative stiffness and relative damping
with which this region is connected to neighboring tissue. This method can be considered to use
local excitation and model-based parameter identification because stiffness and damping are fit to
the relaxation time constant. While this method does measure the dynamic properties of tissue
(eg relative damping), it suffers from a number of drawbacks. First, while focused ultrasound can
produce a step force in a small isolated region, this process must be repeated many times at many
locations to form a complete image. The speed of the repeated measurements is limited by the
need for the tissue to relax from the step force. Viola et al. did not describe a method to speed up
the imaging of a larger region and such method is not obvious. Second, the identification technique
used in Viola et al. to compute relative stiffness and damping relies upon the step response of tissue.
In essence, a fit to an exponentially decaying tissue region displacement must be obtained. It is well known in the field of parameter identification that such an approach produces poor results in the presence of noise [39]. Third, in order to obtain dynamic tissue parameters, Viola et al. fit the actual tissue region response to a model using nonlinear optimization techniques. Many iterations may be required for such an approach to produce a set of parameters. Furthermore, there may be local minima.

The dynamic elastography method proposed by Fatemi et al. used ultrasound radiation force to exert a localized oscillating force at a desired low frequency (in the kHz range) inside the body [13]. The localized oscillating forces create vibrations within the body. The resulting audio range oscillations of the tissue were detected by hydrophones located on the surface of the body. Given a single oscillating frequency, tissues with different visco-elastic properties will produce different amplitudes of emissions. By raster scanning the point source across a region of interest, an image was formed from the magnitude or phase of the measured emissions. The oscillating point force was produced by the intersection of two focused continuous wave ultrasound beams at different frequencies. The interference of the beams at the focal point produced sinusoidal modulation of the ultrasound energy and effectively vibrating the tissue at that point. The use of such systems is called vibro-acoustography. The drawbacks of this approach include the need for specialized equipment for both producing the oscillating point force and measuring the emissions. It also does not measure the underlying properties of the tissue, only the resonance behavior. Moreover, it requires raster scanning of a region of interest, instead of allowing simultaneous measurements. This reduces the speed of forming a complete image.

1.3 Ultrasound Image Formation

In this thesis the tissue motion is measured by a conventional ultrasound imaging system. A brief summary of ultrasound imaging is now given as a way of introducing the terminology used in the next chapters.

An ultrasound imaging system acquires data through the generation of an ultrasound wave directed toward the area to be examined, followed by measurement of the echoes generated by the interaction of the ultrasound wave with the tissue. The system consists of an ultrasound transducer
1.4 Prior Work on Motion Detection in Ultrasound Images

for generating the ultrasound pulses and measurement of the echoes, and a computation system to convert the echo amplitudes into an image. The ultrasound transducer sends out a short burst of ultrasound, followed by a period of silence to listen for the returning echoes. For example, the ultrasound wave transmitted to the body strikes an interface and is partially reflected back to the transducer. The amplitude of the reflected echo depends on the ultrasonic properties of the tissue at the interface. The time between the emitted and the detected echo is used to calculate the depth of the interface assuming the speed of sound is constant throughout the media. The form of the transmitted wave is an amplitude modulated signal with a fixed carrier frequency determined by the probe. The returning echoes are rapidly sampled during the listening interval. The unprocessed samples are known as RF data. A set of RF data collected along one axial line is called an RF line. The set of RF lines (collected on a column-to-column basis) are referred to as RF-images throughout the thesis. Each RF data set is first amplified. The amplification increases as a function of time to compensate for the fact that echoes from deep locations are weaker than echoes from shallow locations. This operation is called time gain compensation and is necessary to compensate for the attenuation of ultrasound in tissue. The next steps are envelope detection of the RF data and conversion to regular spatial coordinates (called scan conversion). An image formed this way is called a B-mode image (or B-scan) because the image pixels have a brightness proportional to each amplitude.

1.4 Prior Work on Motion Detection in Ultrasound Images

Motion tracking in successive ultrasound B-scans or RF data has long been studied by many researchers. Many tracking methods have been proposed based on either analyzing the image data directly or analyzing some sort of transformations of the image data.

In the techniques that analyze the image data directly, a similarity measure is employed for finding the similar feature or region in the next image. According to the particular application different similarity measures have been proposed. One of the similarity measures is the cross-correlation coefficient. The basic idea of cross-correlation-based tracking is to extract a patch of an image (a matrix in 2D or a vector in 1D) and to find the location of the same patch (or segment) in another image by searching for the highest correlation-coefficient in a nearby search space. It
is assumed that the location of the peak correlation-coefficient corresponds to the displacement of the tissue in the patch, from one image to the next.

Correlation-based speckle tracking of successive B-mode images was first proposed in [56] for detecting blood flow. In vivo tracking of blood flow was successfully achieved by using normalized cross correlation operation as a measure of similarity. It was later proposed in [7] that sum of absolute differences (SAD) can also be used in place of the cross-correlation operator. The advantage of SAD as a similarity measure over cross correlation algorithm is its simplicity in implementation. SAD algorithm requires one operation per pixel whereas the normalized cross correlation algorithm requires eight operations per pixel. In [7] it was shown that SAD is as accurate as cross correlation for both RF and B-mode data, in detecting lateral and axial motion within 2 mm.

As mentioned above, the similarity between images can also be detected by first transforming to the frequency domain. An example is a Fourier-based speckle tracking algorithm described in [44]. It was used for tracking arterial wall motion in successive ultrasound images. The technique is based on the idea that a shift in one domain corresponds to a linear phase change in the transform domain. The technique was verified through simulation studies.

For analyzing translational motions as well as deformation analysis, the time domain correlation based tracking techniques [7,56] and Fourier based speckle tracking described in [44] can be used. For deformation analysis direct strain estimators based on the change in the speckle statistics were proposed [32,55,57]. Direct strain estimation techniques are based on the Fourier scaling property. Accordingly, a deformation in tissue will change the density of speckles in an ultrasound image hence the amount of compression or expansion is going to be observed as a shift in the power spectrum of the ultrasound signal. The direct strain estimators have the advantage of being robust under high deformations but have the disadvantage of being less accurate and precise under lower strains [32]. These techniques are not capable of measuring pure translational motion, since translation does not change the frequency of appearances of the speckles in the spatial (image) domain.

1.5 Thesis Objectives

The goal of this work is to describe a new non-invasive method to measure the mechanical properties of tissue including tissue stiffness and damping based on ultrasonic measurements of tissue motion.
under low frequency mechanical vibrations. The specific objectives to be achieved are: (i) providing a method to analyze low frequency tissue vibrations based on a mechanical model to obtain stiffness, density, and damping; (ii) providing a second model-free method to obtain the stiffness distribution in tissue by analyzing the spectrum of tissue motion; (iii) constructing a simulation environment to test the proposed methods; (iv) constructing an experimental set-up to create low frequency mechanical vibrations and measure tissue motion with an ultrasound system; (v) validating the methods by testing tissue mimicking materials with known mechanical properties.

1.6 Thesis Outline

In this chapter, a review of the current elastography approaches and motion tracking methods in successive ultrasound images were given.

Chapter 2 is a review chapter that presents the theory of continuum mechanics in one dimensional visco-elastic media. Firstly, the equations relating stress to strain are given. The basic visco-elastic models are then summarized. Finally, the equations of motion in continuum are given for 1D visco-elastic media.

Chapter 3 starts with the description of a one dimensional discrete visco-elastic tissue model. The equations of motion describing the dynamics of the model are given, followed by a method to solve the inverse problem of estimating the model parameters. An alternative model-free method, which uses spectral analysis of the tissue motion, is also given. A new correlation-based method for tracking motion in successive ultrasound images is proposed. These represent new contributions to the techniques of tissue mechanical parameter identification.

In Chapter 4 computer simulations are used to validate the methods described in Chapter 3. Both parameter identification techniques are tested. It is shown that the first method gives reasonable elasticity and damping values even in the presence of ultrasound noise and decorrelation effects. High resolution high quality elasticity plots are obtained with the second method.

In Chapter 5 tissue mimicking materials are tested to validate the proposed system identification methods. Stiffness and damping plots are obtained.

Chapter 6 presents the conclusions of the research together with suggestions for future work.
Chapter 2

Mechanics of Soft Tissue

This chapter starts with a background on continuum mechanics. The visco-elastic models for soft tissues are then summarized including the popular Voigt model. Next, a derivation is given for the equation of motion in a 1D continuum for a homogeneous and linear visco-elastic material, whose visco-elasticity properties follow the Voigt model. Discretization of the equations of motion in the spatial domain, and derivation of a mass-spring-damper representation for the discrete equation conclude the chapter.

2.1 Continuum Mechanics Background

In this section the concepts of stress and strain, the constitutive equations for elastic solids, and the equation of motion in a 1D continuum are described. More detailed information on the area can be found in “A first course in continuum mechanics” by Y.C. Fung [19]. Throughout this section, the equations are defined in Cartesian coordinates with coordinate axises $x_1$, $x_2$, $x_3$. For simplicity the notation follows the conventions of continuum mechanics [19].

2.1.1 Stress and Strain

Consider a small surface element of area $\Delta S$ inside the body. Let $v$ be a unit vector normal to $\Delta S$. By using the direction of the normal vector, the two sides of this surface can be defined. Let
one side exert a force $\Delta F$, directed along the surface normal, on the other side. The ratio $\Delta F/\Delta S$ tends to a limit as $\Delta S$ goes to zero. This limit depends on the surface orientation and the direction and amplitude of the force. This limiting value is defined as the stress, as shown in Equation (2.1).

$$\frac{v}{T} = \frac{dF}{dS}.$$  \hspace{1cm} (2.1)

Stress is a rank two tensor, whose components are given by $\sigma_{ij}$, where $i$ and $j$ vary from 1 to 3. The stress tensor $\sigma_{ij}$ is related to the stress vector $T$ with components $T_1$, $T_2$, and $T_3$ by Cauchy’s formula as follows:

$$T_i = v_j \sigma_{ji}. \hspace{1cm} (2.2)$$

The deformation of an elastic body can be expressed in terms of the strain. For a 3D continuum, the strain is a rank two symmetric tensor. Cauchy’s infinitesimal strain tensor, $e_{ij}$, can be expressed as

$$e_{ij} = \frac{1}{2} \left[ \frac{\partial u_j}{\partial x_i} + \frac{\partial u_i}{\partial x_j} \right], \hspace{1cm} (2.3)$$

where $u$ is the displacement vector of a particle in the body with components $u_1$, $u_2$, and $u_3$.

### 2.1.2 Constitutive Equations

For a Hookean elastic solid, the relationship between the stress tensor and the strain tensor is linear. The relationship can be expressed by Hooke’s low as

$$\sigma_{ij} = C_{ijkl} e_{kl}, \hspace{1cm} (2.4)$$

where $e_{kl}$ is the strain tensor, and $C_{ijkl}$ is a tensor of elastic constants, or moduli, which are independent of stress and strain. As a tensor, $C_{ijkl}$ has 81 elements, of which 36 are independent. In the case of isotropic material (i.e. when the elastic properties are identical in all directions) the total number of independent elastic constants drops down to two. In other words, two independent elastic parameters are sufficient to characterize an isotropic elastic solid. Hooke’s low for an isotropic
2.1 Continuum Mechanics Background

An elastic solid can be expressed as

$$\sigma_{ij} = \lambda \delta_{ij} + 2\mu \epsilon_{ij},$$  \hspace{1cm} (2.5)$$

where $\mu$ and $\lambda$ are the two elastic constants, also known as the Lamé constants. Young’s modulus (measure of axial deformation to axial stress), Bulk modulus (measure of volume change in the presence of pressure) and Poisson’s ratio (measure of compressibility) are technical derivatives of these two constants.

2.1.3 Equation of Motion in One Dimensions

Consider an elastic string under tension whose motion is restricted along the x axis, as shown in Figure 2.1. Let P and Q be two neighbouring points on the string at $x$ and $x + dx$ at time $t_1$. Assume that at time $t_1$ the spring is at rest so the tension along the string is constant.

![Elastic string figure](image)

Figure 2.1: Two instances of a string during deformation. The string is at rest at $t_1$. At $t_2$ a time varying deformation is present at points P and Q.

When a time varying deformation is present along the string, say at time $t_2$, point P at $x$ is displaced to some point at $x + u$, and point Q at $x + dx$ is displaced to some point at $x + dx + u + \frac{\partial u}{\partial x}$. The forces acting on points P and Q will not be same at time $t_2$ because of the time varying deformation. The tensions at points P and Q are expressed as $T$ and $T + \frac{\partial T}{\partial x} dx$ respectively.

The net vector force that acts on the infinitesimal string element between points P and Q is given by the vector sum of the tensions at P and at Q and is expressed as $\frac{\partial T}{\partial x} dx$. The mass of the infinitesimal string element is $\rho dx$, where $\rho$ denotes the mass per unit length of the string at rest. Applying Newton’s second law gives

$$\frac{\partial T}{\partial x} = \rho \frac{\partial^2 u}{\partial t^2}$$  \hspace{1cm} (2.6)
where $dx$ has been cancelled on both sides of the equation.

In the 1D case, Hooke's law simplifies to $T = E\xi$, where $\xi$ represents the strain. Cauchy's strain tensor simplifies to $\xi = \frac{\partial u}{\partial x}$. Substituting $T$ with $E\xi$, and $\xi$ with $\frac{\partial u}{\partial x}$ in Equation (2.6) results in

$$E \frac{\partial^2 u}{\partial x^2} = \rho \frac{\partial^2 u}{\partial t^2}. \quad (2.7)$$

The above equation describes the time varying deformation of a point on an elastic string in terms of the elasticity constant $E$ and the spatial, and temporal derivatives of displacement at that point. Now the next section derives the above equation for a one dimensional visco-elastic material.

### 2.2 Visco-Elastic Properties of Soft Tissue

#### 2.2.1 Visco-Elastic Models

The visco-elastic behavior of tissue is modeled by combining elements representing ideal elastic, and ideal viscous behavior. A damper (also known as a dashpot) represents ideal viscous behavior, and a spring represents ideal elastic behavior. Different combinations of those elements lead to different models for explaining the visco-elastic behavior of human tissue. The three common mechanical models are the Maxwell model, the Voigt model, and the Kelvin model (also called the standard linear solid) as shown in Figure 2.2. In Figure 2.2 $k$ represents the spring constant of the linear spring and $b$ represents the damping coefficient of the damper.

![Figure 2.2: Three common mechanical models for explaining the visco-elastic behavior of a body.](image-url)
2.3 Discretization of the Equation of Motion in One Dimension

2.2.2 Equation of Motion in Visco-Elastic Media

In our work the Voigt model is used for modeling soft tissue because it is known that the Voigt model represents the dynamic behavior better than the Maxwell model for water-based gels and beef in vitro [8]. The Voigt model is also preferred to standard linear solid because of its simplicity. For the Voigt model, the relationship between the force $F$ and the displacement $u$ at the point of loading is

$$F = k_1 u + b_1 u,$$

(2.8)

where $k_1$ and $b_1$ are the spring and damper constants, and $u$ represents the time derivative of displacement at the point of loading.

For homogeneous, isotropic and linear elastic materials, the constitutive equation in 1D is given as $T = E \varepsilon$. For homogeneous, isotropic and linear visco-elastic elastic materials, whose visco-elasticity is modeled by the Voigt model, the constitutive equation in 1D can be expressed as

$$T = \left( E + B \frac{\partial}{\partial t} \right) \varepsilon,$$

(2.9)

where $B$ is the coefficient of damping. Replacing the elasticity component $E$ with $(E + B \frac{\partial}{\partial t})$ in the equation of motion (Equation (2.7)) results in

$$E \frac{\partial^2 u}{\partial x^2} + B \frac{\partial^2 \dot{u}}{\partial x^2} = \rho \ddot{u}.$$

(2.10)

The above equation is the equation of motion in a 1D continuum for a homogeneous, isotropic and linear visco-elastic material, whose visco-elasticity properties follow the Voigt model.

2.3 Discretization of the Equation of Motion in One Dimension

A visco-elastic body can be approximated by a discrete representation that can be represented by a finite set of parameters. Discretization of the continuum is necessary for simulating, modeling, and characterizing these bodies. Many ways of discretization are proposed in the literature. A summary of these techniques can be found in [10], [11]. The most common models used in the field
of elastography are finite element models and mass-spring models.

2.3.1 Finite Element Models

The finite element method (FEM) is a widely used numerical procedure for analyzing physical phenomenon in continua. The continuous equations that describe the physical behaviour of a solid body are analyzed by dividing the body into a set of discrete sub-domains called elements. Each element is represented by nodes, and each node has the field parameter related to the physical phenomenon under investigation. The physical behaviour can be solved analytically in each element, and combined to estimate the global solution. FEM is based upon continuum mechanics and the physics of materials; therefore it is easy incorporate the results of biomechanical studies. Both static and dynamic tissue behaviour can be modeled and simulated. The models are more accurate compared to mass-spring models. The disadvantages of FEM include more difficult implementation than that for mass-spring models, and computational requirements.

2.3.2 Mass-Spring Models

Mass-spring models consist of a set of mass nodes connected to each other by springs and dampers. Figure 3.1 shows a one dimensional example for the mass-spring models. The main advantage of mass-spring models is their ease of implementation. Both static and dynamic tissue behaviour can be modeled easily by mass-spring models. The main disadvantage of mass-spring models is the sensitivity of the model parameters to topology. Different topologies are possible for modeling two-dimensional and three-dimensional tissue behaviour and the parameter values strictly depend on the topology. Mass-spring models do not rely upon continuum mechanics; therefore their behaviour cannot easily be compared with the results of biomedical studies. Moreover, mass-spring models are not as accurate as FEM in explaining physical phenomena.

In this thesis, a one-dimensional visco-elastic continuum is modeled by a mass-spring model. The problems of mass-spring models related to topology mentioned above does not apply to the one-dimensional case. Relating the biomechanical properties of continua to the parameters of the one-dimensional mass-spring-damper model is easier than in the two-dimensional and three-dimensional cases.
2.3 Discretization of the Equation of Motion in One Dimension

Assume a 1D homogeneous visco-elastic string with elasticity $E$, viscosity $B$, and density $\rho$. Let a section of this string with length $\Delta l$ be modeled with a mass-spring-damper system as shown in Figure 2.3. For this model the equation of motion is given as:

$$k_n (u_{n+1} - 2u_n + u_{n-1}) + b_n (\dot{u}_{n+1} - 2\dot{u}_n + \dot{u}_{n-1}) = m_n \ddot{u},$$

(2.11)

where $m_n$ is the mass, $k_n$ is the stiffness, and $b_n$ is the damping values for the model. The model parameters can be related to the continuous mechanical parameters of the string as $k_n = \frac{E}{\Delta l}$, $b_n = \frac{B}{\Delta l}$, and $\rho \Delta l = m_n$. Substituting these in Equation (2.11) we obtain,

$$\frac{k_n}{\Delta l} (u_{n+1} - 2u_n + u_{n-1}) + \frac{b_n}{\Delta l} (\dot{u}_{n+1} - 2\dot{u}_n + \dot{u}_{n-1}) = \frac{m_n}{\Delta l \rho} \ddot{u}.$$  

(2.12)

A close look at this equation reveals that it is actually the discrete version of Equation (2.10), when the backward rule is used for spatial derivative operations. The discrete approximation of the second derivative with respect to $x$ is defined as

$$\frac{d^2 u}{dx^2} \approx \frac{(u_{n+1} - 2u_n + u_{n-1})}{(\Delta l)^2}.$$  

(2.13)

Substituting Equation (2.13) into Equation (2.12) gives Equation (2.10), which is the wave equation in homogeneous, isotropic, visco-elastic media. Equation (2.11) is the discrete version of Equation (2.10). This equation and the discrete model presented in Figure 2.3 will be used in the
2.4 Conclusion

In this chapter, the wave equation in a one dimensional visco-elastic media is given. The relationship between the wave equations and the equation of motion in a mass-spring model is established. A mass-spring-damper model is derived from the equation of motion. This model is shown in Figure 3.1. The mass, spring, and damper parameters of this model will then be estimated with the elastography technique described in the next chapter.
Chapter 3

Methodology

The chapter starts with the description of a one dimensional visco-elastic tissue model for analyzing the dynamic tissue behaviour. The equations of motion describing the dynamics of the model are then given, followed by several numerical approaches to solve the inverse problem of estimating the model parameters. An alternative model-free method, which uses spectral analysis of the tissue motion is also given. Lastly, a new correlation-based tracking algorithm is proposed that employs iterative signal stretching for more accurate motion estimates.

3.1 Lumped Mass-Spring-Damper Chain as a Tissue Model

A discrete one dimensional visco-elastic model is now proposed. The tissue model is composed of a set of mass elements connected to each other with dampers and springs, as shown in Figure 3.1. The visco-elastic behavior is therefore modeled by Voigt elements. The springs in the model represent the local elasticity of the tissue, and the dampers represent the local damping, and local density is represented by the mass elements at each spatial location.

In the previous chapter, it was shown that if a time varying deformation exists in a 1D isotropic visco-elastic medium, its dynamics can be made discrete in the spatial domain as shown in Figure 2.3. The model shown in Figure 2.3 can be extended to the model shown in Figure 3.1 to describe a 1D heterogeneous visco-elastic medium. This tissue model is labeled a lumped mass spring damper (L-MSD) model throughout the thesis.
According to this model, tissue can be described in 3D space as a bundle of L-MSD chains aligned in the axial direction without any mechanical contact between chains, yet maintaining a constant lateral and elevational separation. The 2D version of this model is shown in Figure 3.2. For the 2D and 3D model to be valid, the following criteria must hold:

- The external force should be uniform laterally and elevationally (the directions orthogonal to the axial direction). In other words, each chain should experience the same amount of
3.1 Lumped Mass-Spring-Damper Chain as a Tissue Model

pressure at the same axial location. The external pressure field and the boundary conditions should be set accordingly.

- The tissue properties should vary only in the axial direction.

- The tissue should not bulge under axial pressure for conserving the volume. The L-MSD chains can only model infinitely compressible media.

This thesis proposes a method to extract the mass, spring, and damper values at each element in an L-MSD chain. These parameters will be considered as the density, stiffness, and damping at each spatial location in the tissue.

The next section formulates the problem by writing the equations of motion for the 1D system.

3.1.1 Solution to the Equations of Motion

Assume a mass element is connected to a static boundary with a spring and a damper, as seen in Figure 3.3. The equation of motion of the mass elements is as follows,

\[ m\ddot{x}(t) + b\dot{x}(t) + kx(t) = F(t). \]  

\[ \text{Figure 3.3: A single mass spring damper system.} \]

For the L-MSD chain shown in Figure 3.1, the same equation can be obtained by writing the equation of motion for each element. For the \(i^{th}\) element, the equation of motion will be extracted by applying Newton's Second Law. The forces acting on the \(i^{th}\) element are shown as \(F_a\) and \(F_b\) in Figure 3.4. The net force effecting the \(i^{th}\) element is \(F_a + F_b\), and it will be equal to \(m_i\ddot{x}\). \(F_a\) originates from the interaction of the element with its right neighbour, and \(F_b\) from its left.
neighbour.

\[
F_a \quad \frac{F_b}{k_{i-1}(x_{i-1} - x_i) + b_{i-1}(\dot{x}_{i-1} - \dot{x}_i) - k_i(x_i - x_{i+1}) - b_i(\dot{x}_i - \dot{x}_{i+1}) = m_i \ddot{x}.}{F_a}
\] (3.2)

When \( k_{i-1} = k_i \) and \( b_{i-1} = b_i \), the above equation reduces to Equation (2.11), which is the discrete version for the equation of motion for a continuum in a 1D isotropic medium.

For the \( n \)-element system of Figure 3.1, \( n \) equations of the form seen in Equation (3.2) are needed to explain the dynamic behavior of the system. These equations can be grouped into one matrix equation as seen in Equation (3.3).

![Figure 3.4: Body diagram for a mass element in an L-MSD system.](image-url)
3.1 Lumped Mass-Spring-Damper Chain as a Tissue Model

$$M \begin{bmatrix} m_1 & 0 & 0 & \cdots & 0 \\ 0 & m_2 & 0 & \cdots & 0 \\ 0 & 0 & m_3 & \cdots & 0 \\ \vdots & \ddots & \ddots & \ddots & \vdots \\ 0 & 0 & 0 & \cdots & m_n \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \\ x_3 \\
(t) \\ \vdots \\ x_n \end{bmatrix} + B \begin{bmatrix} b_1 \\ -b_1 \\ -b_1 \\ \vdots \\ 0 \\ 0 \\ 0 \\ \cdots \\ 0 \end{bmatrix} \begin{bmatrix} \dot{x}_1 \\ \dot{x}_2 \\ \dot{x}_3 \\
(t) \\ \vdots \\ \dot{x}_n \end{bmatrix} + K \begin{bmatrix} k_1 \\ -k_1 \\ -k_1 \\ 0 \\ 0 \\ \vdots \\ 0 \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \\ x_3 \\
(t) \\ \vdots \\ x_n \end{bmatrix} = u(t),$$

(3.3)

or

$$Ma(t) + Bu(t) + K\dot{x}(t) = u(t),$$

(3.4)

where $$m_i$$ is the mass parameter of element $$i$$, $$b_i$$ is the damping parameter between $$m_i$$ and $$m_{i-1}$$, $$k_i$$ is the elasticity parameter between $$m_i$$ and $$m_{i-1}$$, $$x_i(t)$$ is the displacement measurement of the $$i$$th element in the model at time $$t$$, $$v_i(t) = \dot{x}_i(t)$$ is the velocity measurement $$\left( \frac{d\dot{x}_i}{dt} \right)$$ at time $$t$$, $$a_i(t) = \ddot{x}_i(t)$$ is the acceleration measurement $$\left( \frac{d^2x_i}{dt^2} \right)$$ at time $$t$$, and $$f(t)$$ is the force measurement at time $$t$$. The definitions of the matrices $$M$$, $$B$$, $$K$$ and $$x(t)$$, $$\dot{x}(t)$$ and $$\ddot{x}(t)$$ are clear from Equation (3.3).

The above set of equations can be combined and rearranged in a linear form as follows:

$$\varphi^T(t) \theta = u(t)$$

(3.5)
where \( u \) contains the excitation forces, \( \varphi \) contains the measurements of motion of each element (tissue region) at a certain time instant as a response to the applied excitation, and \( \theta \) is a vector of entries of \( M, B \) and \( K \), as follows:

\[
\varphi = \begin{bmatrix}
a_1 & 0 & 0 & \cdots & 0 & 0 \\
0 & a_2 & 0 & \cdots & 0 & 0 \\
0 & 0 & a_3 & \cdots & 0 & 0 \\
\vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\
0 & 0 & 0 & \cdots & a_{n-1} & 0 \\
0 & 0 & 0 & \cdots & 0 & a_n
\end{bmatrix}
\begin{bmatrix}
v_1 - v_2 & v_2 - v_1 & 0 & \cdots & 0 & 0 \\
0 & v_2 - v_3 & v_3 - v_2 & \cdots & 0 & 0 \\
\vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\
0 & 0 & 0 & \cdots & v_{n-1} - v_n & v_n - v_{n-1} \\
0 & 0 & 0 & \cdots & 0 & v_n
\end{bmatrix}
\begin{bmatrix}
x_1 - x_2 & x_2 - x_1 & 0 & \cdots & 0 & 0 \\
0 & x_2 - x_3 & x_3 - x_2 & \cdots & 0 & 0 \\
\vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\
0 & 0 & 0 & \cdots & x_{n-1} - x_n & x_n - x_{n-1} \\
0 & 0 & 0 & \cdots & 0 & x_n
\end{bmatrix}
\]

(3.6)
3.1 Lumped Mass-Spring-Damper Chain as a Tissue Model

\[ \theta = \begin{bmatrix} m_1 \\ m_2 \\ \vdots \\ m_n \\ b_1 \\ b_2 \\ \vdots \\ b_n \\ k_1 \\ k_2 \\ \vdots \\ k_n \end{bmatrix}, \quad \text{and} \quad u(t) = \begin{bmatrix} f(t) \\ 0 \\ 0 \\ \vdots \\ 0 \end{bmatrix}. \quad (3.7) \]

There are \( 3n \) unknowns (\( m_i, b_i, \) and \( k_i, i = 1, \ldots, n \)) in \( \theta \) and \( n \) equations in Equation (3.5). This is insufficient to determine the parameters from a single set of measurements. By measuring the displacement, velocity, and acceleration at \( m \) different time instants \( t_i, i = 1, \ldots, m \) the equation of motion can be expressed multiple times and the problem becomes over-constrained.

The parameters \( \theta \) can then be found by using ordinary least squares [39]. To do this, the system of equations in Equation (3.5) are written for several measurements, and stacked together to produce a set of over-constrained equations as shown below:

\[
\begin{bmatrix} \varphi^T(t_1) \\ \varphi^T(t_2) \\ \vdots \\ \varphi^T(t_m) \end{bmatrix} \theta = \begin{bmatrix} u(t_1) \\ u(t_2) \\ \vdots \\ u(t_m) \end{bmatrix}. \quad (3.8)
\]
3.1 Lumped Mass-Spring-Damper Chain as a Tissue Model

Typically the number of equations \((m \times n)\) is much greater than \(n\) so the system is significantly over-constrained to reduce the effect of measurement noise on the parameter estimation.

The familiar least squares solution that minimizes the Euclidean error \(\|\Phi \theta - u\|_2\) in Equation (3.8) is given by

\[
\theta = (\Phi^T \Phi)^{-1} \Phi^T u, \tag{3.9}
\]

which is valid as long as \((\Phi^T \Phi)\) is invertible. In practice this means that the excitation signal should have at least two frequency components to identify the system to make the equations in the set independent of each other. The excitation signal \(f(wt)\) containing one frequency component \((w)\) is represented in phasor domain as \(F e^{j0}\). Linearity of the system leads to the following phasor domain representation of the displacements of each element:

\[
x_i(t) \rightarrow A_i e^{j\phi_i}, \tag{3.10}
\]

\[
x_i(t) \rightarrow A_i jwe^{j\phi_i},
\]

\[
x_i(t) \rightarrow -A_i w^2 e^{j\phi_i}, \tag{3.11}
\]

where \(A_i\) and \(\phi_i\) are the amplitude and the phase of the sinusoidal vibrations at the specified frequency. In practice, the above phasor domain representations can be obtained by observing the motion of each element to calculate the phase and the amplitude of the vibrations. Substituting the phasor domain representation of the measurements in Equation (3.5) gives:

\[
\varphi^T_{\text{phasor}} \theta = u_{\text{phasor}} \tag{3.12}
\]
3.1 Lumped Mass-Spring-Damper Chain as a Tissue Model

where

\[
\varphi_{\text{phasor}} = \begin{bmatrix}
-A_1w^2e^{j\phi_1} & 0 & \cdots & 0 \\
0 & -A_2w^2e^{j\phi_2} & \cdots & 0 \\
\vdots & \vdots & \ddots & \vdots \\
0 & 0 & \cdots & -A_ne^{j\phi_n}
\end{bmatrix}
\]

and

\[
u_{\text{phasor}}^T = \begin{bmatrix}
Fe^{j\theta} & 0 & \cdots & 0
\end{bmatrix}.
\]

The rank of the matrix \(\varphi_{\text{phasor}}\) is clearly \(n\), so Equation (3.12) has \(n\) linearly independent equations in the complex domain. Both real and imaginary parts of the equations can be used to obtain a solution, which doubles the number of independent equations to \(2n\). In case the excitation signal is composed of two frequencies, two amplitude and two phase measurements can be obtained for each element. This can be used to obtain phasor representations at two different frequencies. Therefore \(4n\) independent equations can be obtained for \(3n\) unknowns. Obviously using more than two frequencies over-constrains the problem, and reduces the effect of measurements noise.

Many alternative approaches for estimating \(\theta\) from Equation (3.8) have been developed in the field of parameter identification.
3.1 Lumped Mass-Spring-Damper Chain as a Tissue Model

For example, an alternative solution to Equation (3.9) uses recursive least squares. In ordinary least squares the multiplication of the two matrices $\Phi^T$ and $\Phi$ can be computationally expensive for large data sets. The recursive least squares approach solves the computation problem by first making an initial guess for $\Phi^T \Phi$, then for each time instant, the estimate is refined until a reasonable solution is obtained [4]. To do this, assume that the matrix $\Phi(t)$ has full rank, that is $\Phi^T(t)\Phi(t)$ is nonsingular for all $t \geq t_0$. Given $\theta(t_0)$ and $P(t_0) = (\Phi^T(t_0)\Phi(t_0))^{-1}$, the least-squares estimate $\theta(t)$ satisfies the recursive equations:

\[
K(t) = P(t - 1)\varphi(t)(I + \varphi^TP(t - 1)\varphi(t))^{-1}
\]

\[
\theta(t) = \theta(t - 1) + K(t)(u(t) - \varphi^T(t)\theta(t - 1))
\]

\[
P(t) = (I - K(t)\varphi^T(t))P(t - 1),
\]

where $\varphi(t)$ is as defined in Equation (3.6), and $\theta$ and $u(t)$ are as defined in Equation (3.7), and $I$ is the identity matrix. In the first iterations of the recursive approach, $P(t)$ is singular. To circumvent this problem, $P(t)$ is initialized to $\alpha I$ where $\alpha$ is a large number. This implies that the gain $K(t)$ in the estimator becomes large and the estimate can be updated with a larger step [4].

3.1.2 Effect of Observation Noise on Least Squares Estimates

The extracted parameters in $\theta$ depend on the displacement, velocity, and acceleration measurements $\Phi$ according to the equation $\theta = (\Phi^T\Phi)^{-1}\Phi^TU$ as given in Equation (3.9). The effect of measurement noise on the extracted parameters is described in [25] as follows.

Let the noisy measurement be $\Phi = A + W$ where $W$ is white noise with zero mean, and $A$ being the measurements without noise. The least squares solution then becomes:

\[
\theta = (\Phi^T\Phi)^{-1}\Phi^TU
\]

\[
= ((A + W)(A + W)^T)^{-1}(A + W)^TU
\]

\[
= (AW^T + AA^T + WW^T + WA^T)^{-1}(A^TU + W^TU)
\]

or

\[
(AW^T + AA^T + WW^T + WA^T)\theta = (A^TU + W^TU).
\]
The expected value of the estimate is calculated by finding the expected value of both sides of Equation (3.15):

\[
\]

which simplifies to

\[
E[\theta'] = (A^T + \Sigma)^{-1}A^TU,
\]

where \(\Sigma = E[WW^T]\) is the covariance of the error \(W\). The expected value of \(W\), \(E[W]\), is zero, hence \(E[W^TY], E[AW^T]\), and \(E[WAT]\) are also zero. On the other hand, the expected value of the unbiased estimate (without measurement noise) is \(E[\theta] = (AT)^{-1}ATU\). Therefore the estimates are lower in magnitude with the presence of noise then their true values.

The problem summarized in this section is common in the area of econometrics, and system identification. The problem arises because of the correlation that occurs in the term of Equation (3.9). In order to solve this problem, instrumental variables are introduced.

3.1.3 Solution to the Bias Problem: Instrumental Variables Method

Starting from Equation (3.8), the following derivation is an alternative solution to the least squares approach.

\[
\Phi\theta = U
\]

\[
Z^T\Phi\theta = Z^TU
\]

\[
\theta = (Z^T\Phi)^{-1}Z^TU,
\]

where \(Z\) is a matrix in which the error-correlated regressors of \(\Phi\) are replaced by other variables (the \textit{instrumental variables}, or simply \textit{instruments}) that are not correlated with the errors in \(\Phi\). For the simulations and experiments presented in the following chapters, the instruments are chosen to be the observations of the same system at different time instants.
3.1 Lumped Mass-Spring-Damper Chain as a Tissue Model

Thus, if \( \Phi = \begin{bmatrix} \varphi^T(t_n) \\ \vdots \\ \varphi^T(t_{n+a}) \end{bmatrix} \), then \( Z = \begin{bmatrix} \varphi^T(t_m) \\ \vdots \\ \varphi^T(t_{m+a}) \end{bmatrix} \), where \( m \neq n \).

The instrumental variables method can also be implemented as a recursive operation similar to the recursive least squares approach.

\[
K(t) = P(t-1)\zeta(t)(I + \varphi^TP(t-1)\zeta(t))^{-1}
\]
\[
\theta(t) = \theta(t-1) + K(t)(u(t) - \varphi^T(t)\theta(t-1))
\]
\[
P(t) = (I - K(t)\varphi^T(t))P(t-1),
\]

where \( \zeta \) contains the instruments.

3.1.4 Parameter Identification from a Subset of Measurements

We now focus on the practical issues of solving the parameter identification problem. It is often the case that only tissue displacements are measured using conventional ultrasound imaging. However, velocities and accelerations can be derived from the displacement measurements so that the same linear Equation (3.5) can still be used. In the Laplace domain Equation (3.4) becomes

\[
Ms^2X(s) + BsX(s) + KX(s) = U(s),
\]

where \( X \) and \( U \) are the Laplace transforms of \( x \) and \( u \).

Applying the filter \( \frac{1}{(s+a)^2} \), to both sides of Equation (3.20) leads to:

\[
M \frac{s^2}{(s+a)^2} X(s) + B \frac{s}{(s+a)^2} X(s) + K \frac{1}{(s+a)^2} X(s) = \frac{1}{(s+a)^2} U(s).
\]

In the above formulation, \( \frac{s^2}{(s+a)^2} X(s) \) approximates the Laplace transform of the vector of accelerations \( \ddot{x}(t) \), \( \frac{s}{(s+a)^2} X(s) \) approximates the Laplace transform of the vector of velocities \( \dot{x}(t) \), with the filters \( \frac{s}{(s+a)^2} \) and \( \frac{s^2}{(s+a)^2} \) approximating a derivative and a double derivative operation.

The positive parameter \( a \) can be interpreted as a cutoff frequency for the derivative filters, in
other words it is the smoothing factor of the low-pass filtered derivative operator. In practice, it can be selected to be around two times larger than the frequency with which the tissue is excited.

If we now change the definitions of \( a \), \( v \), \( x \) and \( u \) from Equation (3.4) and we let \( a(t) \) be the inverse Laplace transform of \( \frac{(s^2 + 2s + 2)}{(s+1)^2} X(s) \), \( v(t) \) be the inverse Laplace transform of \( \frac{s}{(s+1)^2} X(s) \), \( x(t) \) be the inverse Laplace transform of \( \frac{1}{(s+1)^2} X(s) \), and \( u(t) \) be the inverse Laplace transform of \( \frac{1}{(s+1)^2} U(s) \), we obtain again the equation

\[
Ma(t) + Bu(t) + Kx(t) = u,
\]

which can be put in the same linear form as Equation (3.5).

By obtaining the vector sequences \( u(t), x(t), v(t) \) and \( a(t) \) from the filtered tissue displacement and applied force data and using the same definition for \( \theta \) as in Equation (3.5), the solution is exactly the same as before. The only difference is that \( \varphi^T(t) \) and \( u(t) \) have slightly different definitions here than in Equation (3.5) because they are now based on filtered versions of velocity and acceleration.

Alternatively, it is possible that only tissue velocities are measured, and the displacements and accelerations are derived from the velocity measurements. This would occur if the tissue velocity is measured with Doppler ultrasound for example. Again the same form of solution can be found from the equations of motion.

### 3.1.5 Parameter Identification without Force Measurements

There may be applications where the measurement of the applied force is infeasible because of cost or complexity. In such cases, the parameters can still be identified from the same model by reformulating the problem. In particular the force applied to the tissue can be replaced with tissue displacement measurements. To do this, the equation of motion of the system of masses shown in Figure 3.1 (starting from mass \( m_2 \)) is written in the same form as Equation (3.3), except that the force on the right hand side is now dependent on the displacements and velocities between \( m_1 \) and \( m_2 \):
3.1 Lumped Mass-Spring-Damper Chain as a Tissue Model

\[
\begin{pmatrix}
    M' & a(t) \\
    B' & u(t) \\
    K' & x(t)
\end{pmatrix}
\]

where

\[
f = k_1(x_1(t) - x_2(t)) + b_1(\dot{x}_1(t) - \dot{x}_2(t))
\]  

or

\[
M'\ddot{a}(t) + B'\ddot{v}(t) + K'\ddot{x}(t) - b_1(\ddot{x}_1(t) - \ddot{x}_2(t)) = k_1(x_1(t) - x_2(t)).
\]

This equation can be written in a linear form as

\[
\varphi^T(t) \theta' = k_1(x_1(t) - x_2(t))
\]
where \( \phi' \) and \( \theta' \) are slightly changed definitions of \( \phi \) and \( \theta \).

\[
\theta' = \begin{bmatrix}
m_2 \\
\vdots \\
m_n \\
b_2 \\
\vdots \\
b_n \\
k_2 \\
\vdots \\
k_n \\
b_1 
\end{bmatrix}
\] (3.27)

and

\[
\varphi^T = \begin{bmatrix}
\dot{x}_1(t) - \dot{x}_2(t) \\
\vdots \\
0
\end{bmatrix}
\] (3.28)

Since \( x_1(t) \) and \( x_2(t) \) are known, this equation can be used to solve for the tissue parameters relative to the value of \( k_1 \) using the techniques described previously.

The number of unknowns in \( \theta \) is decreased by two because \( m_1 \) and \( k_1 \) are no longer identified. The \( b_1 \) term is retained as the last entry in \( \theta \). The matrix of measurements \( \varphi' \) becomes \((n - 1) \times (3(n - 1) + 1) \) whereas the \( \varphi \) term of Equation (3.5) is \( n \times (3n) \). Here the mass \( m_1 \) and stiffness \( k_1 \) terms are not identified. The solution therefore only provides elasticity, damping and mass values relative to \( k_1 \), but these relative values can still be used to form an image.

Similarly, the removal of the force term can also be applied to the variation of the parameter identification method described in Section 3.1.4 where only a subset of the measurements is available.
3.1.6 Parameter Identification without the Far Field Motion Data

This section presents the solution to the parameter estimation problem for the situation where the motions of the elements far from the excitation are not measured. Consider the case where the measurements of elements with indexes higher than \( i + 1 \) are unknown or unreliable in Figure 3.1. In this case, a solution still can be obtained by removing these far field measurements from Equation (3.3) as shown below:

\[
\begin{bmatrix}
M & a(t)
\end{bmatrix}
\begin{bmatrix}
\ddot{x}_1 \\
\ddot{x}_2 \\
\ddot{x}_3 \\
\vdots \\
\ddot{x}_i \\
0 \\
0 \\
\end{bmatrix}
= \begin{bmatrix}
\begin{bmatrix}
b_1 & -b_1 & 0 & 0 & \cdots & 0 & 0 \\
-b_1 & (b_1 + b_2) & -b_2 & 0 & \cdots & 0 & 0 \\
0 & -b_2 & (b_2 + b_3) & -b_3 & \cdots & 0 & 0 \\
0 & 0 & 0 & \cdots & -b_{i-1} & b_{i-1} + b_i & -b_i \\
0 & 0 & 0 & \cdots & 0 & 0 & 0 \\
0 & 0 & 0 & \cdots & 0 & 0 & 0 \\
\end{bmatrix}
\begin{bmatrix}
x_1 \\
x_2 \\
x_3 \\
\vdots \\
x_i \\
x_{i+1} \\
\end{bmatrix}
\end{bmatrix}
= \begin{bmatrix}
\begin{bmatrix}
k_1 & -k_1 & 0 & 0 & \cdots & 0 & 0 \\
-k_1 & (k_1 + k_2) & -k_2 & 0 & \cdots & 0 & 0 \\
0 & -k_2 & (k_2 + k_3) & -k_3 & \cdots & 0 & 0 \\
0 & 0 & 0 & \cdots & -k_{i-1} & k_i + k_{i-1} & -k_i \\
0 & 0 & 0 & \cdots & 0 & 0 & 0 \\
\end{bmatrix}
\begin{bmatrix}
x_1 \\
x_2 \\
x_3 \\
\vdots \\
x_i \\
x_{i+1} \\
\end{bmatrix}
\end{bmatrix}
\begin{bmatrix}
f \\
0 \\
0 \\
\vdots \\
0 \\
0 \\
\end{bmatrix}
= u(t). \quad (3.29)
\]

With this configuration, the solution takes the same form as Equation (3.9). The only difference is that \( \varphi \) of Equation (3.6) is modified as follows:
With this modification of $\varphi(t)$, the same parameter identification techniques described in sections 3.1.1 to 3.1.6 can still be applied. For example, acceleration and velocity measurements can be obtained by the filtering operation described in Section 3.1.4 from the displacement data, and the force term can be replaced by $k_i(x_i - x_{i+1})$ as described in Section 3.1.5, and by using the instrumental variables method for the over constrained problem, following equation can be rewritten:

$$\theta = (Z^T \Phi)^{-1}Z^T U,$$  \hfill (3.31)

where $\Phi$ and $Z$ is composed of $\varphi$ (as defined above in Equation (3.30)) at different time instances.
3.1.7 Parameter Identification with Prior Knowledge of Tissue Density

In other applications, some tissue density may be known or estimated a priori. Consider the equation of motion for the $i^{th}$ element as defined by Equation (3.2):

\[ k_{i-1}(x_{i-1} - x_i) + b_{i-1}(\dot{x}_{i-1} - \dot{x}_i) + k_i(x_{i+1} - x_i) + b_i(\dot{x}_{i+1} - \dot{x}_i) = m_i \ddot{x}. \]  

(3.32)

Once the mass of element $i$ is known, then Equation (3.32) can be solved for $k_{i-1}$, $b_{i-1}$, $k_i$, and $b_i$ locally by using the displacement information of the neighbouring elements, element $i + 1$ and element $i - 1$. Again Equation (3.32) can be over constrained by obtaining measurements at different time instances, and solved as before.

Using prior information simplifies the problem since the equations become independent of each other and independent of the boundary conditions. Another advantage is that if the measurements are not reliable at certain depths, a solution still can be obtained by local analysis of regions where reliable measurements are obtained.

3.2 Calculating Mechanical Properties from Transfer Functions

This section describes an alternative method for obtaining the elasticity parameters by computing the transfer functions between mass elements. This method has the advantage that no a priori modeling assumptions are required other than linearity. In other words, the L-MSD model of Figure 3.1 need not necessarily apply. According to this method the tissue dynamics between two axial locations is considered as a linear dynamic system, as illustrated in Figure 3.5.

In Figure 3.5, the sequence of tissue displacements at regions $i$ and $j$ are $x_i(t)$ and $x_j(t)$ respectively. These displacements are the inputs and outputs of a linear dynamic system shown as $H_j^i$ in Figure 3.5. The transfer function between element $i$ and element $j$ is calculated with standard techniques [39]. First, the power spectral density $P_{x_i x_i}(\omega)$ of element $x_i(t)$ is computed. Then the cross spectral density $P_{x_i x_j}(\omega)$ between elements $i$ and $j$ is computed. Then the complex transfer function is computed as follows:
3.2 Calculating Mechanical Properties from Transfer Functions

The transfer function is a function of frequency. The quality of the transfer function depends on the quality of the measurements, and the type of tissue excitation. For the transfer function to be meaningful at a given frequency, it is required that the excitation be sufficiently large at that frequency. The excitation should contain many frequency components (e.g. sinusoids at various frequencies or band-limited white noise) within the frequency range of interest for the tissue under examination. For the proposed elastography method in the thesis, the transfer function is used to extract the elasticity properties of tissue, so the frequencies for which the tissue is considered as quasi-static are sufficient for the analysis.

The reliability of the transfer function can be checked by computing the coherence function corresponding to each calculated transfer function. The coherence function between \( x_i \) and \( x_j \) is given by

\[
C_{x_i,x_j}(\omega) = \frac{|P_{x_i,x_j}(\omega)|^2}{(P_{x_i,x_i}(\omega) P_{x_j,x_j}(\omega))},
\]

where \( |P_{x_i,x_j}(\omega)| \) is the magnitude of the cross spectral density between \( x_i \) and \( x_j \), and \( P_{x_i,x_i}(\omega) \) and \( P_{x_j,x_j}(\omega) \) are the power spectral densities of \( x_i \) and \( x_j \). The coherence function gives information about the linearity of the data within the frequency range of the excitations. Its value is between 0 and 1, so a high coherence function indicates that most of the energy in the input signal at a given
3.2 Calculating Mechanical Properties from Transfer Functions

frequency appears at the output as the same frequency. A high coherence function indicates good confidence that the system is linear and the signal to noise ratio is good. Therefore the coherence function can be used as a check to give confidence in the results.

![Figure 3.6: A typical coherence function and transfer function.](image)

It is the combination of measurements at multiple time instances and an excitation that has significant frequency content that leads to the transfer function method providing reliable tissue property estimates in the presence of measurement noise. Typical transfer functions and coherence functions obtained from tissue mimicking gels (tissue mimicking gels will be described in Chapter 5) have the form shown in Figure 3.6. For the system in Figure 3.6, the coherence function drops after 30 Hz, which means that either the system is no longer linear above 30 Hz or there is insufficient data for describing the transfer function above 30 Hz. But the transfer function is still useful below 30 Hz.

After obtaining the transfer function, the stiffness information of the tissue is easily estimated as follows. The magnitude of the transfer function at dc is expected to be a function only of elasticity and not density or damping. In such a case the system can be described simply by springs connected to each other in the axial direction. This simplification is illustrated in Figure 3.7. In such a case the deformation can be explained by the following equation:
3.2 Calculating Mechanical Properties from Transfer Functions

Pressure Field

<table>
<thead>
<tr>
<th>$H_2^2$</th>
<th>$x_1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$H_2^3$</td>
<td>$x_2$</td>
</tr>
<tr>
<td>$H_2^4$</td>
<td>$x_3$</td>
</tr>
<tr>
<td>$\vdots$</td>
<td>$\vdots$</td>
</tr>
<tr>
<td>$H_n$</td>
<td>$x_{n-1}$</td>
</tr>
</tbody>
</table>

At 0 Hz linear dynamic system simplifies to linear spring network

Figure 3.7: Sketch showing the simplification of a linear dynamic system into a static one under excitations of 0 Hz.

\[
\begin{bmatrix}
  k_2 & -k_2 & 0 & 0 & \cdots & 0 \\
  -k_2 & (k_2 + k_3) & -k_3 & 0 & \cdots & 0 \\
  0 & -k_3 & (k_3 + k_4) & -k_4 & \cdots & 0 \\
  \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\
  0 & 0 & 0 & \cdots & -k_{n-1} & k_n + k_{n-1}
\end{bmatrix}
\begin{bmatrix}
  x_2 \\
  x_3 \\
  x_4 \\
  \vdots \\
  x_n
\end{bmatrix}
= 
\begin{bmatrix}
  k_1(x_1 - x_2) \\
  0 \\
  0 \\
  \vdots \\
  0
\end{bmatrix},
\tag{3.35}
\]

where $k_i$ is the stiffness between element $i$ and $i+1$, and $x_i$ represents the displacement at element $i$ from its rest position. The above equation can easily be obtained from Equation (3.23) by setting $\dot{x}_i(t)$ and $\ddot{x}_i(t)$ terms of Equation (3.23) to zero. Let the transfer function from element 1 to element $i$ be shown as $H^i_1(w)$. As noticed, $H^i_1(w)$ is used during the transfer function analysis instead of $H^i_{i+1}(w)$. $H^i_{i+1}(w)$ is only used in Figure 3.7 to show the simplification of a linear
3.2 Calculating Mechanical Properties from Transfer Functions

dynamic system into a spring network. The amplitude of the transfer function from element 1 to element \( i \) at zero frequency is shown as \( H_i^1(0) \). The physical meaning of \( H_i^1(0) \) is the amount of axial deformation that element \( i \) experiences as a response of 1 unit of displacement of element 1. Therefore Equation (3.35) can be written as shown:

\[
\begin{bmatrix}
k_2 & -k_2 & 0 & 0 & \cdots & 0 \\
-k_2 & (k_2 + k_3) & -k_3 & 0 & \cdots & 0 \\
0 & -k_3 & (k_3 + k_4) & -k_4 & \cdots & 0 \\
\vdots & \ddots & \ddots & \ddots & \ddots & \vdots \\
0 & 0 & 0 & \cdots & -k_{n-1} & k_n + k_{n-1}
\end{bmatrix}
\begin{bmatrix}
H_i^1(0) \\
H_i^2(0) \\
H_i^3(0) \\
\vdots \\
H_i^n(0)
\end{bmatrix}
= 
\begin{bmatrix}
k_1(1 - H_i^2(0)) \\
0 \\
0 \\
\vdots \\
0
\end{bmatrix}
\tag{3.36}
\]

Equation (3.35) can be rewritten in a linear form:

\[
\begin{bmatrix}
H_i^2(0) - H_i^2(0) & 0 & \cdots & 0 & 0 \\
H_i^2(0) - H_i^2(0) & H_i^3(0) - H_i^3(0) & \cdots & 0 & 0 \\
\vdots & \vdots & \ddots & \vdots & \vdots \\
0 & 0 & \cdots & H_i^n(0) - H_i^{n-1}(0) & H_i^n(0)
\end{bmatrix}
\begin{bmatrix}
k_2 \\
k_3 \\
\vdots \\
k_n
\end{bmatrix}
= 
\begin{bmatrix}
k_1(1 - H_i^2(0)) \\
0 \\
\vdots \\
0
\end{bmatrix}
\tag{3.37}
\]

where the relative stiffness values are found by inversion:

\[
\begin{bmatrix}
k_2 \\
k_3 \\
\vdots \\
k_n
\end{bmatrix}
\begin{bmatrix}
H_i^2(0) - H_i^2(0) & 0 & \cdots & 0 & 0 \\
H_i^2(0) - H_i^2(0) & H_i^3(0) - H_i^3(0) & \cdots & 0 & 0 \\
\vdots & \vdots & \ddots & \vdots & \vdots \\
0 & 0 & \cdots & H_i^n(0) - H_i^{n-1}(0) & H_i^n(0)
\end{bmatrix}^{-1}
\begin{bmatrix}
k_1(1 - H_i^2(0)) \\
0 \\
\vdots \\
0
\end{bmatrix}
\tag{3.38}
\]

Instead of using the zero-frequency response of the transfer function, it is reasonable to take an average of the magnitude of the transfer function over the range of low frequencies where it is approximately constant. The reason to perform an average is to reduce the influence of measurement error on the estimation of the tissue elasticity. Of course, averaging over a frequency range where the coherence function magnitude is no longer one would introduce additional errors and should be avoided.
3.3 Motion Detection in Ultrasound Images

A time domain cross-correlation based algorithm is proposed to track the tissue motion in successive RF signals. The tracking algorithm uses a non-normalized cross-correlation coefficient shown in Equation (3.39) as the similarity measure.

\[
\text{Correlation Coefficient} = \frac{|A \cdot B|}{\sqrt{|A| \cdot |B|}}, \quad (3.39)
\]

where \(A \cdot B\) represents the dot product of two matrices or vectors and \(|A|\) and \(|B|\) are the magnitudes of these matrices: \(\sqrt{A \cdot A}\) and \(\sqrt{B \cdot B}\).

According to the algorithm, one image is chosen as the reference image and all displacements are measured with respect to this image. The reference image is divided into small regions, called windows, and the displacement of each window from one image to the next is found by finding the maximum correlation coefficient among the candidate regions in the next image. The correlation function can be calculated only in the discrete domain, since the signal is digitized at discrete intervals. Therefore, there is a possibility that the peak cross correlation coefficient falls between the discrete points in its domain. This problem is solved by employing quadratic interpolation algorithms for 1D tracking [12,15]. Accordingly, three values of the correlation coefficients are considered: the highest value and its two neighbours. Quadratic interpolation is applied to the three points, and the location that gives the peak value of the curve is chosen to be the best match. The peak of the curve is determined by finding the point where the derivative is zero. According to Figure 3.8, if \(\lambda\) is the distance of the location of the maximum coefficient to the peak point, then \(\lambda\) is given in [12] as:

\[
\lambda = \frac{c - a}{2 \cdot (-c + 2b - a)}, \quad (3.40)
\]

where \(b\) is the value of the maximum correlation coefficient, and \(a\) and \(c\) are the values of the left and right samples respectively. High accuracy displacement measurements are obtained by this method.
3.3 Motion Detection in Ultrasound Images

3.3.1 Decorrelation Noise

Ultrasound images are formed by the interaction of high frequency sound waves with tissue. Tissue can be considered as a set of small scatterers. The density, distribution, and reflectivity of these scatterers determine the texture formed in the ultrasound image. In elastography, the tissue deformation can be considered as the displacement of the scatterers with respect to each other, which in turn changes the image texture. Tracking a certain location in ultrasound images is challenging because the region in the reference ultrasound image may not appear exactly the same way in the subsequent images. In particular, the speckle pattern of a compressed tissue will appear finer compared to the course speckle pattern of the uncompressed tissue. This means the correlation-coefficient is unlikely to have a value of 1.0 at the peak. Nevertheless most elastography techniques obtain displacement measurements from window matching, also known as speckle tracking. Increasing the level of excitation increases the level of tissue motion and decreases the similarity between the reference region and highly displaced regions. Decreasing the level of excitation on the other hand decreases the signal-to-noise-ratio (SNR) for motion estimates, since white noise becomes dominant in low compression levels. A feasibility analysis showing this trade-off was performed by Verghese et al. [58]. According to their result, at low compression levels white noise is dominant, thus increasing the compression level increases the SNR. As the deformation exceeds a certain level, decorrelation effects become dominant, so the SNR starts to decrease again. For different materials, an optimum compression level exists to obtain the best motion tracking. For our experiments, the maximum compression level is close to 2%.
3.3.2 Adaptive Stretching Algorithm

To decrease the amount of decorrelation noise, stretching the compressed signal was proposed [1, 2]. Stretching a signal $s(t)$ by a factor of $a$ means resampling the signal to obtain $s(t/a)$. For example if the pre-compressed signal is compressed by 1%, then the stretching factor $a$ for the post-compressed signal is 0.99.

When a 1D homogeneous tissue is deformed axially by an external source, the strain values along the tissue will be the same. Therefore, in the compressed signal, the locations of the scatterers will be simply scaled by a constant factor [1]. According to the temporal stretching algorithm described by Alam et al. [1], if the ultrasound signal of the post-compressed tissue is stretched by the same amount, the cross-correlation of pre- and post- compressed signals will approach the auto correlation function of the pre-compressed signal. Since the scaling factor is constant over an entire signal, this method is also called global stretching. In practice, the stretched signal will never exactly match the pre-compressed signal, since stretching also stretches the point spread function (PSF) of the ultrasound system.

Global stretching fails for higher levels of compressions, and large variations in elasticity [46]. In an elastically inhomogeneous tissue, the strains will vary throughout the tissue. As a result, the stretching factor will have to be varied for different parts of the deformed signal. In the adaptive stretching algorithm proposed by Alam et al. [2], the post-compressed RF signal is first divided into overlapping windows. Each window is adaptively stretched until the correlation coefficient between the window segment and the corresponding window segment on the pre-compressed signal is maximized. The stretching factor is then directly related to the strain to form the elastograms. Unfortunately current limitation of their algorithm is its computational complexity due to the iterative process involved in the computations. The time required to produce an elastogram is reported to be one order of magnitude greater than that required for the cross-correlation methods without stretching [2]. Although the algorithm proposed in this thesis is also recursive, it is observed that two iterations is sufficient for obtaining high quality displacement estimates. Therefore, the time required for obtaining the strain measurements is approximately two times than that required for the standard cross-correlation method without stretching.

The flow chart of the new adaptive stretching algorithm is given in Figure 3.9. To understand
the algorithm, consider two RF signals. One is obtained before compression of a heterogeneous tissue (pre-compressed tissue), and the other is obtained after compression (post-compressed) tissue. In the flow chart, two types of blocks are seen, motion estimation block, and adaptive stretching block. The motion estimation block takes two RF signals, separates it into overlapping windows and estimates the motion of each window by using standard correlation-based tracking algorithm [48]. The adaptive stretching block stretches each section of the post-compressed RF signal according to the motion estimates of the motion estimation block, and concatenates to form a new RF signal.
The procedure of the operations can be summarized as follows. The first step is to determine how much each segment of the post-compressed RF signal is deformed. According to the deformation estimates of each section in the signal, the stiffer sections should be stretched less than the softer sections. So the first step is to use the standard correlation algorithm, [48] to provide a first estimate of the motion of each section. According to this first estimate, each section is stretched separately, then the stretched sections are concatenated to form an adaptively stretched post-compressed RF signal. The next step is to use the correlation algorithm between the pre-compressed signal and the adaptively stretched post-compressed signal so that a second estimate of motions is obtained. By using the new estimates, the original post-compressed RF signal (not the previously stretched signal) is adaptively stretched again. The new stretched compressed signal is better than the previous one since the second position estimate is obtained from a roughly-stretched post-compressed RF signal. By iterating this procedure a more accurate estimation of motion is obtained by converging to the optimal solution.

Adaptive stretching algorithm in [2], was proposed mainly for the compressions levels higher than 2%, whereas in our elastography method there are a range of compression levels within 0% to 1.5%. Secondly, in [2], the adaptive stretching algorithm directly outputs the strain values of each window segments, whereas in the standard correlation-based tracking algorithm [48] and the proposed adaptive stretching algorithm output displacements of each windows. The strains are then calculated by taking the spatial derivatives of the displacements. The proposed elastography methods in this thesis require displacement data (not the strain) for calculating the tissue mechanical parameters. Thus, the proposed adaptive stretching algorithm is going to be used in the simulations and experiments in the rest of the thesis.
Chapter 4

Simulation Results

This chapter presents a simulation study of the theory described in the thesis. The chapter starts by validating the methods proposed for identifying the parameters for one-dimensional tissue models. The next sections simulate the effect of measurement noise caused by the ultrasound system and the correlation-based motion tracking. The chapter ends with discussions about the feasibility of the new proposed methods.

4.1 Validation of the Inverse Problem Solution

In this section, various L-MSD chains are simulated to compare the performances of the different parameter estimation methods described in Chapter 3. The overall structure of the simulation is divided into two blocks as shown in Figure 4.1. The first block defines the system and its output for different excitation types. The system properties, such as the number of elements to be used in the L-MSD chain and the coefficients of springs, dampers and masses, are defined in this block. The outputs are the displacements from each element, shown as $X(t)$. Measurement noise is simulated by additive white noise before passing the data to the second block.

The second block solves the parameter identification equation $\Phi \theta = u$ (Equation (3.8)). The displacements $X(t)$ are filtered by the derivative and double derivative filters to obtain approximations for $\dot{X}(t)$ and $\ddot{X}(t)$. The L-MSD parameters $\theta$ are then solved and displayed. The simulation environment is implemented by Simulink and MATLAB.
4.1 Validation of the Inverse Problem Solution

The simulation parameters are chosen to mimic the behaviour of real tissue as closely as possible. The L-MSD chain coefficients are set to the estimated properties a 6 cm long section of human breast fat. The elasticity of human breast fat is given as $20 \, kPa$ in Table 1.2. The density of fat is close to $1000 \, kg/m^3$. The relationship between elasticity $E$, density $\rho$, mass $m_i$, and spring constant $k_i$ is given by Equation (2.12). According to this equation the following relation is derived:

$$\frac{k_i}{m_i} = \frac{E}{\rho} \frac{1}{\Delta l^2}$$

where $\Delta l$ is the distance between two neighbouring elements of the L-MSD chain at rest. If a 20-element L-MSD chain is used to simulate a tissue sample having an axial length of 6 cm, then $\Delta l$ is $3 \, mm$, and $k_i/m_i$ is $2 \cdot 10^6$. The $k_i/b_i$ ratio is set to around 500 which is found experimentally for gelatin gels in Chapter 5, and also reported in [34]. This may not be a realistic value for human tissue but will likely have the correct order of magnitude.

According to these ratios for $m_i$, $b_i$, and $k_i$ presented above, the values shown in Figure 4.2 are assigned for the elements of the L-MSD chain. This L-MSD chain is used in the simulations of Sections 4.1.1 and 4.1.2

The excitation for the simulations is chosen to be white noise band limited to 10 Hz. Another white noise source is used to simulate noise on the measurements of the displacement data $X(t)$ as shown in the simulation setup in Figure 4.1. The amount of noise is given as a percentage value throughout the simulations. It is set with respect to the mean value of the strains given at a time instant of maximum compression. For example, assume an L-MSD chain under vibration. At a
4.1 Validation of the Inverse Problem Solution

certain time instant the elements are displaced the maximum amount from their rest positions. The strain values for that time instant are obtained by subtracting the displacement of each element from the displacement of its neighbouring element. These values are than averaged and a mean strain value is obtained. The mean value is used as a reference for determining the percentage noise. If the measurement noise amount is to be 1 %, then the noise power is set to maximum mean strain multiplied by 0.01. The data is sampled at either 500 Hz or 3000 Hz to show the effect of sampling rate on the identification of parameters. The results obtained by the least squares method and the instrumental variables method at different levels of added white noise are given in Section 4.1.1. The performance of the methods described in Section 3.1.6 by Equation (3.31) and Section 3.1.7 by Equation (3.32) are compared in Section 4.1.2.

4.1.1 Simulation Results for the Solution of Equation (3.31)

Table 4.1 shows the first set of simulation results. The simulated system is a 20-element L-MSD chain with parameters shown in Figure 4.2. The duration of the excitation is 1 second. The obtained displacements are first sampled with a sampling rate of 500 Hz so 500 measurements are used in total. The performances of the least square method (LSM) and the instrumental variables method (IVM) are compared at 0 %, 1 %, and 2 % of added measurement noise. Measurement noise is white noise band-limited to the sampling frequency. The performance of parameter identification for the elements away from the excitation (far field elements) and elements close to the excitation (near field elements) are observed to be different. For any element in the system, the parameter estimates
also differs among the elements mass, stiffness, and damping. To depict these differences in Tables 4.1, 4.2, and 4.3, the errors in \( k \), \( b \), and \( m \) values are shown separately at different columns. The noise performance of far field (elements 11 to 20) and near field elements (elements 1 to 10) are also shown separately. The entries of the tables are the mean values of percentage errors for the specific parameter \((k, b, \text{ or } m)\) for the specific group (far field elements or near field elements). When the same simulation is repeated with 5 seconds of duration at the same sampling rate, there is not a significant improvement in the estimated parameters, as seen in Table 4.2. When the sampling rate is increased to 3000 Hz from 500 Hz, the results are improved considerably, as seen in Table 4.3. It is shown in all three tables that the instrumental variables method has better performance in the presence of white noise in most of the cases, as expected from the discussion in Section 3.1.2.

4.1.2 Simulation Results for the Solution of Equation (3.32)

In Section 3.1.7, an approach depending on prior knowledge on tissue density was presented. The approach formulated in Equation (3.32) has the advantage of being independent of boundary conditions. But the method requires the mass values to be known \textit{a priori}. This may occur for tissue with approximately constant density. For example, many soft tissues have a density close to water. A simulation for comparing the performance of this approach against the method described in Section 3.1.5 by Equation (3.31) is done. The parameters of the L-MSD chain used in the simulation are the same values as the values shown in Figure 4.2. The system is excited with white noise band-limited to 10 Hz for 1 second. The displacements from each element are sampled at 500 Hz.

<table>
<thead>
<tr>
<th>% Mean error for elements 1 to 10</th>
<th>% Mean error for elements 11 to 20</th>
</tr>
</thead>
<tbody>
<tr>
<td>k</td>
<td>b</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>-----------------------------------</td>
</tr>
<tr>
<td>LSM</td>
<td>0.0186</td>
</tr>
<tr>
<td>IVM</td>
<td>0.0177</td>
</tr>
<tr>
<td>LSM</td>
<td>8.10</td>
</tr>
<tr>
<td>IVM</td>
<td>7.67</td>
</tr>
<tr>
<td>LSM</td>
<td>22.6</td>
</tr>
<tr>
<td>IVM</td>
<td>22.8</td>
</tr>
</tbody>
</table>

Table 4.1: Comparison of LSM and IVM. Sampling rate is 500 Hz. The duration of the signal is 1 seconds. The maximum excitation frequency is 10 Hz.
4.1 Validation of the Inverse Problem Solution

<table>
<thead>
<tr>
<th></th>
<th>% Mean error for elements 1 to 10</th>
<th>% Mean error for elements 11 to 20</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>k</td>
<td>b</td>
</tr>
<tr>
<td>0 % noise</td>
<td>LSM</td>
<td>0.0135</td>
</tr>
<tr>
<td></td>
<td>IVM</td>
<td>0.0128</td>
</tr>
<tr>
<td>1 % noise</td>
<td>LSM</td>
<td>7.78</td>
</tr>
<tr>
<td></td>
<td>IVM</td>
<td>7.43</td>
</tr>
<tr>
<td>2 % noise</td>
<td>LSM</td>
<td>21.6</td>
</tr>
<tr>
<td></td>
<td>IVM</td>
<td>23.0</td>
</tr>
</tbody>
</table>

Table 4.2: Comparison of LSM and IVM. Sampling rate is 500 Hz. The duration of the signal is 5 seconds. The maximum excitation frequency is 10 Hz.

<table>
<thead>
<tr>
<th></th>
<th>% Mean error for elements 1 to 10</th>
<th>% Mean error for elements 11 to 20</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>k</td>
<td>b</td>
</tr>
<tr>
<td>0 % noise</td>
<td>LSM</td>
<td>5.15 \cdot 10^{-4}</td>
</tr>
<tr>
<td></td>
<td>IVM</td>
<td>5.10 \cdot 10^{-4}</td>
</tr>
<tr>
<td>1 % noise</td>
<td>LSM</td>
<td>1.54</td>
</tr>
<tr>
<td></td>
<td>IVM</td>
<td>1.54</td>
</tr>
<tr>
<td>2 % noise</td>
<td>LSM</td>
<td>5.29</td>
</tr>
<tr>
<td></td>
<td>IVM</td>
<td>5.19</td>
</tr>
</tbody>
</table>

Table 4.3: Comparison of LSM and IVM. Sampling rate is 3000 Hz. The duration of the signal is 1 seconds. The maximum excitation frequency is 10 Hz.

No observation noise is added to the simulated displacement data. The simulated data is analyzed with both methods, and the comparison of the performances is given in Figure 4.3. For testing the performance at higher sampling rate, the system is again excited with white noise band-limited to 10 Hz for 0.1667 seconds and the displacements are sampled at 3000 Hz. The duration of the excitation signal is lowered six times to have 500 measurements for parameter identification. This way, the same amount of data is used for both 500 and 3000 Hz cases. The results are given in Figure 4.4.

The comparison of methods of Equation (3.31) and Equation (3.32) are also presented in Table 4.4. Accordingly, the method of Equation (3.31) has a better performance then the method of Equation (3.32). Increasing the sampling rate also increases the performance of the method of Equation (3.32) similar to the trend in method of Equation (3.31).
4.1 Validation of the Inverse Problem Solution

Figure 4.3: Estimated parameters using Equation (3.31) and Equation (3.32). 'o' represent the parameters obtained by Equation (3.31), 'x' represent the parameters obtained by Equation (3.32), and the dashed line represents the true values for the parameters. The sampling rate is 500 Hz and the duration of the excitation signal is 1 seconds. No measurement noise is added.

Figure 4.4: Estimated parameters using Equation (3.31) and Equation (3.32). 'o' represent the parameters obtained by Equation (3.31), 'x' represent the parameters obtained by Equation (3.32), and the dashed line represents the true values for the parameters. The sampling rate is 3000 Hz and the duration of the excitation signal is 0.1667 seconds. No measurement noise is added.
4.1 Validation of the Inverse Problem Solution

<table>
<thead>
<tr>
<th></th>
<th>(k)</th>
<th>(b)</th>
<th>(k)</th>
<th>(b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>500 Hz</td>
<td>0.0177</td>
<td>0.4540</td>
<td>0.0357</td>
<td>0.4231</td>
</tr>
<tr>
<td>500 Hz</td>
<td>1.48</td>
<td>2.39</td>
<td>10.8</td>
<td>10.25</td>
</tr>
<tr>
<td>3000 Hz</td>
<td>0.00025</td>
<td>0.08</td>
<td>0.07</td>
<td>3.41</td>
</tr>
<tr>
<td>3000 Hz</td>
<td>1.4544</td>
<td>1.31</td>
<td>2.6</td>
<td>2.564</td>
</tr>
</tbody>
</table>

Table 4.4: Comparison of parameter estimation performances by Equation (3.31) and Equation (3.32) at 500 Hz and 3000 Hz. The duration of the signal at 500 Hz is 1 seconds. The duration of the signal at 3000 Hz is 0.1667 seconds. The maximum excitation frequency is 10 Hz.

4.1.3 Effect of Reducing the Number of Elements of the Lumped Mass-Spring-Damper Chain

In the previous sections, the number of elements in the L-MSD chain is given as prior information. In this section, the effect of changing the number of elements in an L-MSD chain is explored. A simulated 24-element L-MSD chain, with coefficients as shown in Figure 4.5, is excited for 0.5 seconds with white noise band limited to 10 Hz. The displacements of the elements are sampled at 500 Hz giving 250 measurements. For the results presented in Figures 4.6 and 4.7, the white noise level added to the measurements is set to zero. The instrumental variables method given in Equation (3.31) described in Section 3.1.5, is used to obtain the results.

Figure 4.5: The parameters of the 24-element L-MSD chain used for simulating the effect of underestimating the number of elements.

Reducing the number of elements is simulated by using a subset of the displacement data.
obtained from the 24 elements. Figure 4.6 shows the estimated parameters using displacement information of 12 elements. These 12 elements are chosen to be the $1^{st}$, $3^{rd}$, $5^{th}$, ..., $23^{rd}$. Figure 4.7 shows the estimated parameters when the number of elements is chosen to be 8 elements. These 8 elements are chosen to be the $1^{st}$, $4^{th}$, $7^{th}$, ..., $22^{nd}$ elements.

Comparison of Figures 4.6 and 4.7 with Figure 4.5 shows that the relative values of $b$ and $k$ do not change, but $m$ values vary according to the underestimation factor. The $m$ values are found to be around 4 times the original values, when the 24-element L-MSD chain is underestimated as a 12-element chain. For the 8-element case, $m$ values are increased by a factor of 9.

The change in the $m$ values can be explained by Figure 4.8. When two elements are combined, the masses are summed up, and the springs and dampers of the initial two elements are combined
serially to form the spring and the damper of the combined system. For the simple case of Figure 4.8, $k/m$ of the combined system is changed by a factor of 4.

![Figure 4.8: A scheme of the lumping process for L-MSD systems.](image)

Another interesting observation is related to the condition number of the matrices ($Z^T \Phi$ of Equation (3.18)) inverted during parameter identification for different system orders. For 24-element case, the condition number is found to be $7.06 \cdot 10^{12}$, and for 12-element L-MSD case the condition number is $3.99 \cdot 10^{11}$ and for 8-element L-MSD case the condition number is found to be $1.09 \cdot 10^{11}$. The condition number is related to the quality of parameter estimation. It can be seen that the condition number decreases with the decrease in order. Hence, for noisy environments, the parameter identification is expected to give better results at lower orders.

That decreasing the system order improves noise performance can be seen in Figures 4.9 and 4.10 where 2 % white noise is added to the measurements. The condition number for the 24-element L-MSD system in this case is $3.24 \cdot 10^{12}$, and $1.07 \cdot 10^{11}$ for 8-element L-MSD system. In Figure 4.9, the average error in $k$, $b$, and $m$ parameters are over 100 %, whereas in the lumped case shown in Figure 4.10, the average error for the parameters are within 20 % range.

### 4.1.4 Performance of System Identification for Systems with Lower Stiffness

The performance of the system identification algorithm is expected to vary with material type. In this section, soft and hard homogeneous materials are compared in terms of the amount of error in the identified parameters and the condition number of $Z^T \Phi$ of Equation (3.18). For the following simulations, the $k/m$ ratio is varied for the L-MSD chains. Three different L-MSD chains with $k/m$
4.1 Validation of the Inverse Problem Solution

Figure 4.9: Parameters obtained when a 24-element L-MSD chain is used to represent a 24 element chain. 2 % white noise is added to the measurements.

Figure 4.10: Parameters obtained when an 8-element L-MSD chain is used to represent a 24 element chain. 2 % white noise is added to the measurements.

ratios of $2 \cdot 10^6$, $0.4 \cdot 10^6$, $0.2 \cdot 10^6$ and $k/b$ ratio fixed to 500 is simulated. The number of elements in the L-MSD chains is 20. The system is excited for 0.5 seconds with white noise band limited to 10 Hz. The displacements of the elements are sampled at 500 Hz giving 250 measurements. For the results presented in Table 4.5, the level of measurement noise is set to 3 %.

Table 4.5 shows the condition number for the three cases and the total error in the identified parameters. The condition number decreases in softer phantoms, as for the total error in $b$ and $m$ values. There is not a significant trend in the change of the average errors for the $k$ values in the three cases.
4.1 Validation of the Inverse Problem Solution

<table>
<thead>
<tr>
<th>$k/m$</th>
<th>$2 \cdot 10^6$</th>
<th>$0.4 \cdot 10^6$</th>
<th>$0.2 \cdot 10^6$</th>
<th>Condition number</th>
<th>% error in $m$</th>
<th>% error in $b$</th>
<th>% error in $k$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$0.4 \cdot 10^6$</td>
<td>1.63 $\cdot 10^{12}$</td>
<td>9.00 $\cdot 10^{11}$</td>
<td>2.76 $\cdot 10^{11}$</td>
<td>111</td>
<td>80.0</td>
<td>36.9</td>
<td>44.5</td>
</tr>
<tr>
<td>$0.2 \cdot 10^6$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4.5: Average percentage errors in the identified parameters, and the condition numbers for the three homogeneous L-MSD chains with varying $k/m$ ratios. The measurement noise level is set to 3%.

4.1.5 Homogeneous Phantom Versus Layered Phantom to System Identification

The performance of the system identification algorithm is expected to vary with the homogeneity of the material. In this section, homogeneous and layered materials are compared in terms of the amount of error in the identified parameters and the condition number of $Z^T \Phi$ of Equation (3.18).

Figure 4.11: The parameters of the 24-element heterogeneous L-MSD chain used as a comparison to a 24-element homogeneous L-MSD chain.

The elements of the homogeneous L-MSD chain used in the simulation have a $k/m$ ratio of $2 \cdot 10^6$ and a $k/b$ ratio of 500. The layered L-MSD chain has the element properties as shown in Figure 4.11. The systems are excited for 0.5 seconds with white noise band limited to 10 Hz. The displacements of the elements are sampled at 500 Hz giving 250 measurements. For the results presented in Table 4.6, the measurement noise level is set to 1%.

According to Table 4.6, for all the parameters the performance of the parameter identification is better in homogeneous L-MSD chain.
4.2 Simulation of a Lumped Mass-Spring-Damper System with Ultrasound-Based Displacement Sensing

In parameter identification, the quality of the input data is crucial. There are two major sources affecting the quality of displacement data: the imaging system and the method in which the displacement is measured in the images. This section simulates the effect of these two sources of potential error.

Figure 4.12 shows the overall block diagram for the simulation. The simulation is an extended version of the system given in Figure 4.1 with Block 1 and Block 2 of Figure 4.1 repeated here. The additive white noise in Figure 4.1 is replaced by a block for moving the scatterers according to an underlying dynamic model of the tissue, an ultrasound simulator, and a block for speckle tracking. These three blocks are described in the following sections.

4.2.1 One Dimensional Ultrasound Simulator

The output of an ultrasound system can be modeled by the following equation [59]:

Table 4.6: Average percentage errors in the identified parameters, and the condition numbers for the homogeneous and layered L-MSD. The measurement noise level is set to 1 %.

<table>
<thead>
<tr>
<th></th>
<th>Homogeneous</th>
<th>Layered</th>
</tr>
</thead>
<tbody>
<tr>
<td>condition number</td>
<td>3.20 $\cdot$ 10^{12}</td>
<td>6.09 $\cdot$ 10^{12}</td>
</tr>
<tr>
<td>% error in $m$</td>
<td>33.2</td>
<td>63.4</td>
</tr>
<tr>
<td>% error in $b$</td>
<td>1.86</td>
<td>14.8</td>
</tr>
<tr>
<td>% error in $k$</td>
<td>7.75</td>
<td>23.8</td>
</tr>
</tbody>
</table>
4.2 Simulation of a Lumped Mass-Spring-Damper System with Ultrasound-Based Displacement Sensing

\[ y(x) = h(x) \ast s(x) + n(x), \]  
\[ (4.2) \]

where \( h(x) \) is the point spread function of the ultrasound system, \( n(x) \) is uncorrelated random noise, \( \ast \) denotes the convolution operation, and \( s(x) \) is the scattering function that depends on the position and reflectivity of the scatterers. The output, \( y(x) \) is the measured RF signal.

The PSF of the ultrasound system is given as a Gaussian modulated sine wave at the ultrasound working frequency [43]. The width of the Gaussian signal is two cycles of the carrier frequency. The left plot of Figure 4.13 shows the shape of the point spread function. The frequency of the ultrasound wave is set to 5 MHz and the propagation speed is set to 1540 m/s. The resultant RF lines are sampled at 40 MHz. These parameters are chosen to simulate the real ultrasound system as closely as possible.

The scattering function, \( s(x) \), is described as follows. The scatterers are randomly positioned along a single line. The density of scatterers is suggested to be 40 scatterers per wave length [43]. For the simulations in this chapter, 3 scatterers are given for every 2 wavelengths to increase the speed of the simulation. The reflectivity of each scatterer is assigned a random value from a uniform distribution with zero mean and standard deviation of one. 400 scatterers are used in total over a length of 5 cm. The same scatterer distribution and ultrasonic system properties are used in all simulations.

4.2.2 Scatterer Position Realignment

As described earlier, the first block of Figure 4.1 defines the system that produces outputs \( X(t) \) for a given excitation. Then each mass element is mapped to the 5 cm section of scatterers simulated in the previous section. The motion of each scatterer is estimated according to its location with respect to the mass elements. If a scatterer lies between two elements the assigned motion of the scatterer is determined by linearly interpolating the motion of the two neighbouring elements. By following this procedure, multiple sets of 1D scatterer distributions are obtained to represent deformed versions of a starting scatterer distribution at different instances in time. The next step is to obtain the RF signals at each time instants according to Equation (4.2).
4.2 Simulation of a Lumped Mass-Spring-Damper System with Ultrasound-Based Displacement Sensing

Figure 4.13: The left plot shows the point spread function of the one dimensional ultrasound simulator. The signal is an amplitude modulated Gaussian function. The duration of the signal is approximately two periods of the carrier signal. The right plot shows a sample RF signal obtained by the ultrasound simulator.

4.2.3 Speckle Tracking Block

According to the simulation set-up shown in Figure 4.12, the inputs to this block are successive RF signals. The output is the motion information from different locations of the RF signals. The motion is estimated by the proposed time domain correlation-based speckle tracking algorithm with adaptive stretching described in Section 3.3.2. A comparison of this method with the standard correlation-based tracking [48] and the adaptive stretching algorithm of [2] will be done in Chapter 5.

For the simulations presented in the next section, the length of the tissue is set 50 mm, the resulting RF line length is 64 \( \mu \text{sec} \). The RF signals are divided into 47 windows of size 2.5 \( \mu \text{sec} \). The distance between the centers of the two successive windows is called window separation. The neighbouring windows may overlap each other. This overlap is described in terms of percentage. For the following simulation, the window separations are half of the window size. Therefore, the window overlap is 50 %. For the simulation results presented in Section 4.2.4, the motion tracking is performed by using the proposed adaptive stretching algorithm described in Section 3.3.2.
4.2.4 Simulation Results

In this section, the mechanical properties of the tissue are simulated by a 24-element L-MSD chain. In all simulations the ultrasonic properties of the tissue defined by $s(x)$ of Equation (4.2) remain fixed, and the length of the tissue is set to 50 mm. The underlying mechanical properties are varied to simulate different types of tissue by changing the L-MSD chain parameters.

4.2.4.1 Homogeneous Tissue

The first simulated 1D tissue is homogeneous in mass, stiffness and damping along its length. The $k_i/b_i$ ratio is set to 500 and the $k_i/m_i$ ratio is set to $5 \cdot 10^6$ to simulate a tissue with elasticity of 20 kPa and density of $1000 \text{ kg/m}^3$.

The system is excited for 1 second with white noise band limited to 10 Hz. The displacements of the elements are sampled at 500 Hz giving 500 measurements. The equation of motion is solved according to Equation (3.31) explained in Section 3.1.5.

Figure 4.14 shows the results obtained by underestimating the number of elements of the L-MSD chain to be 11. Starting from the first window, the measurements from every forth window of the 47 windows are used. Figure 4.15 shows the results obtained by underestimating the number of elements of the L-MSD chain to be 6. Starting from the first window, the measurements from every sixth window are used. Using fewer elements decreases the errors in the identified mass parameters of the L-MSD chain considerably as indicated in Table 4.7. The condition numbers for $Z^T\Phi$ of Equation (3.18) also decreases with decreasing the number of elements (Table 4.7). There are two main reasons to explain this somewhat counter intuitive result. Firstly, there are fewer parameters to be identified. Secondly, the errors in displacements cause less effect on the spatial difference terms of Equation (3.6) when fewer elements are used. As the tracked locations get spatially closer, the spatial difference terms (strains, strain rates) get smaller in absolute value, whereas the measurement error stay the same.
4.2 Simulation of a Lumped Mass-Spring-Damper System with Ultrasound-Based Displacement Sensing

Figure 4.14: A 11-element L-MSD chain is used to obtain the $k$, $b$, and $m$ values. The continuous line shows the true values.

Figure 4.15: A 6-element L-MSD chain is used to obtain the $k$, $b$, and $m$ values. The continuous line shows the true values.

### 4.2.4.2 Layered Tissue

The second phantom is homogeneous in mass, and varies in stiffness, and damping along its length. The stiffness values are chosen to create a stiff layer between two soft layers with a ratio of four

<table>
<thead>
<tr>
<th></th>
<th>11 element L-MSD</th>
<th>7 element L-MSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>condition number</td>
<td>$2.33 \cdot 10^{10}$</td>
<td>$3.26 \cdot 10^9$</td>
</tr>
<tr>
<td>% error in $m$</td>
<td>45.6</td>
<td>11.9160</td>
</tr>
<tr>
<td>% error in $b$</td>
<td>1.44</td>
<td>4.7594</td>
</tr>
<tr>
<td>% error in $k$</td>
<td>1.81</td>
<td>0.4426</td>
</tr>
</tbody>
</table>

Table 4.7: The effect of lumping to the average percentage errors in the identified parameters, and to the condition numbers for the homogeneous L-MSD chain.
4.2 Simulation of a Lumped Mass-Spring-Damper System with Ultrasound-Based Displacement Sensing

to one. The damping value for the stiff layer is chosen to be 2 times higher than the soft layers. Hence, for the softer layers the \( \frac{k_i}{b_i} \) ratio is 500 and the \( \frac{k_i}{m_i} \) ratio is to \( 5 \cdot 10^6 \). All of the excitation, and acquisition parameters remain unchanged.

![Stiffness Values](image1)
![Damping Values](image2)
![Mass Values](image3)

Figure 4.16: A 11-element L-MSD chain is used to obtain the \( k \), \( b \), and \( m \) values. The continuous line shows the expected values.

![Stiffness Values](image4)
![Damping Values](image5)
![Mass Values](image6)

Figure 4.17: A 6-element L-MSD chain is used to obtain the \( k \), \( b \), and \( m \) values. The continuous line shows the expected values.

Figures 4.16 and 4.17 show the results obtained by underestimating the number of elements of the L-MSD chain to be 11 and 6 respectively. For 11-element case the condition number of \( Z^T \Phi \) of Equation (3.18) is \( 5.34 \cdot 10^{10} \), and for 6-element case the condition number is \( 9.09 \cdot 10^9 \). For both cases, mass values have the maximum error and the stiffness values are the most reliable identified parameters. The performance of parameter identification for the homogeneous L-MSD chain of Section 4.2.4.1 is better than the layered L-MSD chain. The results also support the discussion in Section 4.1.5.
4.2 Simulation of a Lumped Mass-Spring-Damper System with Ultrasound-Based Displacement Sensing

4.2.4.3 Transfer Function Analysis Simulation

The layered tissue of Section 4.2.4.2 is used in this simulation. Again, all of the excitation and acquisition parameters remain unchanged. The transfer function analysis method, described in Section 3.2, is used with 47 marker points. The power spectral and cross-spectral densities are calculated by the pre-defined MATLAB functions `psd` and `csd`. The spectral information is used to calculate the transfer functions and the coherence functions by Equation (3.33) and Equation (3.34) in Chapter 3.

![Transfer Function and Coherence Function](image)

Figure 4.18: A typical transfer function (solid line) and coherence function (dashed line) used in the transfer function analysis.

In Figure 4.18 the left plot shows the transfer function and the coherence function obtained by using the motion data of the first and 22\textsuperscript{th} markers. The spectral information of the motion data of the first and 22\textsuperscript{th} window is first extracted, then transfer and coherence functions are found as described. In the same plot the shaded area indicates the frequencies used for averaging the stiffness data. Accordingly, frequencies up to 10 Hz are used to average the stiffness data. In Figure 4.18, it should also be noted that the coherence function is above 0.95 up to 30 Hz, although the excitation signal is band-limited to 10 Hz. It is not expected to see frequencies that are not present in the input signal, since the system is linear. However, the input noise is filtered by a sixth order Butterworth filter with a cutoff frequency of 10 Hz. So the higher frequencies are often attenuated but still present. For example, the signal at 20 Hz is 15 dB lower and 30 Hz is 19 dB lower than
the signal amplitude at 10 Hz. These higher frequencies are closer to the natural frequency of the system so they are amplified in the system response. Therefore, frequencies higher than 10 Hz are observed in the system output.

The transfer functions from the first marker to all other 46 markers are used for the transfer function analysis. The left plot in Figure 5.21 shows the low frequency values of the transfer functions for all the markers. The stiff and soft regions can be visually identified by the density of the transfer functions at low frequencies. The right plot in Figure 5.21 shows the stiffness values obtained by this method. This method is more stable for high resolution analysis compared to the above approaches presented in the simulations of Sections 4.2.4.1 and 4.2.4.2.

Figure 4.19: The left plot shows the low frequency values of the transfer functions for all the markers used in the transfer function analysis. The right plot is the relative stiffness plot obtained by using averaged transfer function method. The continuous line in the right plot shows the expected parameter values.
4.3 Discussions

- It is shown in Tables 4.1, 4.2, and 4.3 in Section 4.1.1 that the instrumental variables method gives better results than the least squares method for most of the cases. These results also support the discussion given for the advantages of instrumental variables method to least squares method in Section 3.1.3.

- In Table 4.4, it is shown that the solution to Equation (3.31) has better performance than the solution to Equation (3.32). The results presented in Table 4.4 are obtained with 0 % noise added to the measurements. In the presence of 0.5 % measurement noise, the errors in $b$ and $k$ values exceed 50 % when Equation (3.32) is solved at 500 Hz, while the errors are below 5 % when Equation (3.31) is solved at 500 Hz. One reason for the stability of solving Equation (3.31) is that the solution gets more stable by the regularizing effect of the other equations in the linear set of equations.

- Table 4.4 also shows that the performances of both Equation (3.31) and Equation (3.32) increase with the increase in the frame rate at which the displacement data is sampled. In the inverse problem solution the quality of the time derivative and double derivative estimates increases by the increase in sampling rate. This affects the quality of the identified parameters in both approaches.

- In system identification theory, estimating the order of the system is crucial. The simulation analysis in Section 4.1.3 shows that underestimating the number of elements in an L-MSD chain still gives reasonable results. The effect of underestimation is seen in the change of the ratios of mass versus stiffness and mass versus damping values. This phenomenon is explained by the sketch in Figure 4.8. It is also observed in Figures 4.9 and 4.9 that the quality and reliability of the estimated parameters increases with a decrease of the system order. In an underestimated model, the inertial terms become more effective in determining the system response. This effect and the decrease in the number of identified parameters highly decrease the condition number of the system.

- The performance of parameter identification is better in an homogeneous L-MSD chain than a layered L-MSD chain, as shown in Table 4.6. The condition number for the layered case is around 3 times higher than the homogeneous case. The errors in the identified mass,
damping, and stiffness values are considerably higher in the layered case. Similar simulation results are also obtained in the simulations of Section 4.2. The comparison of Figures 4.15 and 4.17 shows that especially the errors in mass and damping values are much less in the homogeneous case than in the layered case.

- The performance of parameter identification also depends on the ratio of stiffness and mass values of the L-MSD chains used in the simulations. A simulation study is done to observe the performances of parameter identification for three homogeneous L-MSD chains with varying stiffness to density ratio. According to the results presented in Table 4.5, the condition number and the total error in $b$ and $m$ values decrease in softer phantoms. The increase in mass values with respect to the stiffness values increases the effectiveness of masses in determining the system response. This fact partly explains the decrease in error in mass values in softer phantoms.

- In Section 4.2, the effect of measurement noise caused by the ultrasound system and the correlation-based tracking is simulated. It is shown that the quality of the displacement data is of major importance in determining the mass and damping of the L-MSD chain. Even for low order systems, the obtained mass and damping results have considerably high errors, especially for layered L-MSD chain case of Section 4.2.4.2.

Figure 4.20: Comparison of transfer function method to the static elastography method proposed in [48]. The dashed line with dots shows the stiffness values obtained by the transfer function method. The solid line with ‘o’ symbols shows the stiffness values obtained by the static method.
• The transfer function approach produces stiffness plots with higher resolution and less error than the equations of motion method. The stiffness values are obtained from an average of the magnitude of the transfer function at low frequencies where it is approximately constant. Thus, a range of frequencies is used for stiffness estimations. This regularizes the data and might prove to be less sensitive to noise.

A comparison of the static method described in [48] and the transfer function method is given in Figure 4.20. For the simulation results, exactly the same synthetic tissue scatterer function and ultrasound system properties are used for both methods. The stiffness plots for the static method are obtained by compressing the simulated tissue by 1%. It is clearly seen in the overlaid plots that the deviation of the stiffness values from the true values are higher in the static case than the transfer function method results.
Chapter 5

Experiments

In this chapter, tissue mimicking materials are tested to validate the theory described in Chapter 3. The chapter starts with a description of the experimental setup. Then, the construction of the tissue mimicking materials is detailed. The experimental results are presented next, and remarks on the results conclude the chapter.

5.1 Experimental Setup

An overview of the setup is illustrated in Figure 5.1. The experimental setup is composed of an ultrasound machine, an excitation device for creating mechanical vibrations, a platform for analyzing tissue mimicking materials, and a PC for offline analysis.

A 5-12 MHz linear probe connected to a PC-based ultrasound machine (Ultrasonix RP500, Ultrasonix Medical Corporation, Burnaby, BC) is used for all scans. The probe is placed on one side of the rectangular tissue mimicking material, and a vibrator is placed on the opposite side. The vibrator is a voice coil as shown in Figure 5.2. The interface of the voice coil and the tissue mimicking material surface is established by an aluminum plate wider than the surface of the tissue mimicking material to meet the boundary conditions described in Section 3.1. The excitation of the vibrator is generated by a signal generator and amplifier. The amount of displacement on the tissue mimicking material surface is less than 2 mm. The vibrator is connected to a motion stage that controls the amount of pre-loading. A photograph of the test setup with a tissue mimicking
5.1 Experimental Setup

Material, the voice coil, the probe and the motion stage is given in Figure 5.3. The tissue mimicking material is lifted from the bottom surface during the experiments to prevent friction between the tissue mimicking material and the test platform. The tissue mimicking material is squeezed from both sides between the probe and the vibrator, so there is no lateral motion on the contact surfaces. The deformations are imaged by the ultrasound machine. Each RF-image is saved to be analyzed offline. All the algorithms described in Chapter 3 are implemented in MATLAB.

Figure 5.1: Overview of the experimental setup.

Figure 5.2: Voice coil attached to an aluminum plate.

The ultrasound system frequency is set to 5 MHz during the experiments. The RF signals are
5.1 Experimental Setup

Figure 5.3: Part of the experimental set-up includes a motion stage, a vibrator, an ultrasound probe, and a tissue mimicking material.

Sampled at 40 MHz. During the experiments two types of excitations are tracked by the ultrasound system: the step response, and the band-limited noise response. For analyzing the step response of the tissue mimics, the strong reflections from the boundary between the tissue mimic and the aluminum plate of the voice coil are tracked. This boundary is generally located around 60 mm away from the US probe since the axial size of the rectangular tissue mimics is around 60 mm.

The current imaging device is capable of accessing RF lines of length 45 mm. To be able to image the reflection, the location of the starting point of each RF signal is selected to be 20 mm away from the probe. This offset makes it possible to image up to 65 mm away from the transducer. The frame rate depends on the size of the RF line, the number of RF lines used to form the image, and the offset value. To increase the frame rate the number of RF lines in an image is set to 3. The frame rate for this configuration is 377 frames per second. For tracking band-limited noise response, the RF signals starting right after the probe to a distance of 45 mm is used. The frame rate is 494-499 frames per second for this configuration with offset value of zero.

5.1.1 Dynamics of the Voice Coil

The voice coil is modeled as a single mass-spring-damper system. The parameters of this system are calculated experimentally. A certain amount of displacement (controlled and measured by the motion stage) is applied to the springs of the voice coil. The exerted force by the springs is read
5.1 Experimental Setup

through a NANO 25 six-axis force-torque sensor (ATI industrial Automation). The stiffness is found to be 4780 N/m. The part of the voice coil that vibrates during the experiments has a mass of 0.163 kg. The damping of the voice coil is measured by analyzing the step response of the voice coil.

5.1.1.1 Step Response of the Voice Coil

The voice coil model is a 2nd order system with the force equation given as:

\[ F(t) = m_{\text{coil}} \ddot{x} + b_{\text{coil}} \dot{x} + k_{\text{coil}} x, \]  

(5.1)

where \( m_{\text{coil}} \) is the mass of the coil, \( k_{\text{coil}} \) and \( b_{\text{coil}} \) is the stiffness and the damping of the springs respectively. The step response of this system is written as follows, [16]

\[ y(t) = \frac{1}{k_{\text{coil}}} \cdot \left[ 1 - \exp(\sigma t) \cdot \left( \cos(\omega_d t) + \frac{\sigma}{\omega_d} \sin(\omega_d t) \right) \right], \]  

(5.2)

where \( \sigma = -\frac{b_{\text{coil}}}{2m_{\text{coil}}} \) and \( \omega_d = \sqrt{\frac{k_{\text{coil}}}{m_{\text{coil}}} - \left( \frac{b_{\text{coil}}}{2m_{\text{coil}}} \right)^2} \). It is clear from Equation (5.2) that the envelope of the step response is related only to the mass and the damping of the system. The step response of the voice coil is obtained experimentally by using the ultrasound system. The coil is excited by a step input via the signal generator. The current is assumed to create a step force onto the coil. The motion of the aluminum plate connected to the coil is tracked by the ultrasound system described above. Each RF image is composed of 3 RF lines with a length of 45 mm starting 20 mm away from the ultrasound probe. The frame rate of the ultrasound system is 377 frames per second. The separation between the ultrasound probe and the aluminum plate is filled with ultrasound gel. The amount of ultrasound gel is held as low as possible to minimize the viscous effect created by the gel. The step response of the coil is plotted in Figures 5.4.

By fitting an exponential decay function in the form of \( 1 - \exp(\sigma t) \) to the plot in Figures 5.4, the value for \( \sigma \) is obtained to be \(-16\). Since \( m_{\text{coil}} \) is measured to be 0.163 kg, \( b_{\text{coil}} \) is found to be 5.216 Ns/m by using the relationship given as \( \sigma = -\frac{b_{\text{coil}}}{2m_{\text{coil}}} \).

The 2nd order system parameters of the voice coil are used later to analyze the step responses of the tissue-mimicking materials. For the force equation method described in Chapter 3, these
5.2 Phantom Materials

A phantom is a tissue mimicking material. In the thesis, both acoustic and mechanical properties of tissue are considered in phantom construction. This includes the texture of the ultrasound image, the speed of sound, attenuation, stiffness, mass, and damping.

The phantoms used in this work are made from hydrogels, namely agar and gelatin. They are widely used in the field of ultrasound elastography because they are easy to produce, non toxic, and their acoustic and mechanical properties can be changed independently [26]. Hydrogels are water-based phantoms. They are produced by hydrating gel powder with deionized water, and adding glycerol to modify the speed of sound as desired. The mixture is heated above its gel point (35° to 40 °C for animal hide gelatins [26]) then it is cooled in a mould until it congeals (around 26 °C [26]). A realistic speckle pattern of the B-mode image is produced for agar and gelatin phantoms by adding 50-μm cellulose scattering particles (S-5504 Sigmacell, Sigma Chemical, St. Louis, MO) into the liquid gel solution before it congeals. The stiffness is controlled by adjusting the proportion of gel powder in the aqueous solution [26].
5.3 Motion Tracking in Ultrasound Signals

Correlation-based tracking is used to determine motion from ultrasound images. There are two parameters affecting the strain plots in correlation-based tracking algorithms: window size and window separations (defined in Chapter 4 as the distance between the centers of the two successive windows). In the field of elastography, the effects of these parameters on the quality and resolution of the elastograms are well studied [2,3]. In [3] a range of window sizes from 0.5 mm to 4 mm and window separations of 1/64 mm to 2 mm was tested for a 5 MHz simulated ultrasound probe.

The simulation study showed that window size and window separation both affect the resolution in a linear way, with the latter being more dominant. Window size, on the other hand, is mostly related to the quality of the motion estimate. As the window size gets smaller, the possibility of mismatching the window with different location increases [40]. On the other hand, increasing the window size not only decreases the resolution [3], but also the cross correlation of pre- and post-compression signal decreases [48]. The reason for that is the relative compression and the resultant progressive distortion of the data within a window pair [48].

For a fixed resolution, optimum window size depends on the medium, speckle pattern, ultrasound system, and amount of compression applied. In [2], it is advised to use the minimum window size possible for elastography studies. Shorter windows give more accurate results at low compression levels. However, at higher compression levels, the signal decorrelation increases. Therefore, the problem of mismatching the window with a different location also increases. In our experiments window sizes are set to around 2 mm as suggested in [2]. At shorter window sizes, we observed poor strain plots at compression levels of 1 %. Figure 5.5 shows typical RF signals and the window sizes used for tracking in our experiments.

The adaptive stretching algorithm proposed in Section 3.3.2 is compared with the standard correlation-based tracking algorithm with no stretching [48] and the adaptive stretching algorithm in [2]. The performance is checked at both 0.5 % and 1 % strain levels for a homogeneous gelatin phantom composed of 13 % gelatin powder (Gelatin from bovine skin, type B, G9382, Sigma Chemical, St. Louis, MO) and 3 % cellulose. All the experiments are done on the same homogeneous phantom. The window size is set to 2 mm with 50 % overlap. The performance is analyzed by checking two parameters: The correlation coefficients at different depths of the phantom, and the
5.3 Motion Tracking in Ultrasound Signals

Figure 5.5: The dashed rectangle shows the typical window size used in correlation-based tracking. The matching of a window in a pre-compressed RF-line in the post-compressed RF-line is given as an example. The signal is obtained from a homogeneous gelatin phantom.

variation in the strain values. Figure 5.6 shows the improvements in the correlation coefficients at each depth with the use of the adaptive stretching algorithms. It is also noted that the correlation coefficients are slightly higher for the adaptive stretching algorithm of [2] compared to the proposed adaptive stretching algorithm. Strain plots in Figures 5.7 clearly shows that adaptive stretching algorithms have better performance both for 0.5 % and 1 % strain levels. The ratio of the standard deviation (σ) and the mean value of the strains (μ) is used as a performance criterion for the strain plots in Figure 5.6. The quality factor σ/μ is given in Table 5.1 for two different compression levels for the three algorithms. Accordingly, the adaptive stretching algorithm proposed in [2] has a better performance than the proposed adaptive stretching algorithm.
5.4 Experimental Results for Homogeneous Gelatin Phantom with Markers

<table>
<thead>
<tr>
<th>Standard tracking algorithm [48]</th>
<th>σ/μ at 0.5 % strain</th>
<th>σ/μ at 1 % strain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adaptive stretching algorithm of [2]</td>
<td>0.1440</td>
<td>0.1273</td>
</tr>
<tr>
<td>The proposed adaptive stretching algorithm</td>
<td>0.1606</td>
<td>0.1470</td>
</tr>
</tbody>
</table>

Table 5.1: The standard deviations of the strain plots shown in Figure 5.7. The results are obtained from the same homogeneous phantom.

Figure 5.6: Effect of adaptive stretching of RF-lines on the correlation coefficients at different depths. All the experiments are done on the same homogeneous phantom. 0.5 % and 1 % compression cases are investigated in the left and right plots, respectively. In both plots the solid lines show the peak correlation coefficients obtained by the proposed adaptive stretching algorithm. The dotted lines show the peak correlation coefficients obtained from the standard correlation-based motion tracking algorithm without stretching. The dashed lines show the peak correlation coefficient obtained by the adaptive stretching algorithm proposed in [2].

5.4 Experimental Results for Homogeneous Gelatin Phantom with Markers

A phantom with markers is constructed for obtaining high accuracy tracking results. In the next sections, patterns are tracked in a media filled with speckles instead of tracking predefined markers.

A homogeneous gelatin phantom is constructed with dimensions 65 mm x 55 mm x 35 mm. The phantom is hydrated by 13 % (by mass) gelatin powder. The Young's modulus of the phantom is measured to be 16.63 kPa. During the construction four metal cylinders with 2.3 mm diameter
Figure 5.7: Effect of adaptive stretching of RF-lines on the strain plots. 0.5% and 1% compression cases are investigated in the left and right plots, respectively. In both plots the solid lines show the strain values obtained by the proposed adaptive stretching algorithm. The dotted lines show the strain values obtained from the standard correlation-based motion tracking algorithm without stretching. The dashed lines show the peak correlation coefficient obtained by the adaptive stretching algorithm proposed in [2]. The standard deviations of these plots are given Table 5.1.

are placed along the centerline of the rectangular mould with 1 cm displacement so that when the phantom is congealed four holes are obtained. Later the holes are filled with gelatin gel composed of 15% (by mass gelatin powder) and 3% (by mass) of cellulose particles. A scheme of the phantom is shown in Figures 5.8. An RF signal along the line where the markers are located is shown in Figure 5.9.

Figure 5.8: A scheme of the gelatin phantom with the markers.
5.4 Experimental Results for Homogeneous Gelatin Phantom with Markers

5.4.1 Step Response Analysis

An experiment is performed to obtain the overall damping constant of the gelatin phantom described above. In this experiment, the voice coil and the gelatin phantom are modeled as a single mass-spring-damper system. During the experiment the phantom is glued to the aluminum plate attached to the coil so that they can move as a unique body. Hence the combined voice coil and the phantom is modeled as a second order system as shown in Figure 5.10. The mass of the phantom is measured to be 0.13 kg. The step response of the combined system is obtained by the ultrasound system. Each RF image is composed of 11 RF lines with a length of 45 mm starting 20 mm away from the ultrasound probe. The frame rate of the ultrasound system is 119 frames per second. The step response is plotted in Figures 5.11.

Figure 5.9: RF line along the axis of the phantom where the gelatin markers are located.

Figure 5.10: Mass-spring-damper model of the phantom and the voice coil for the step test.
5.4 Experimental Results for Homogeneous Gelatin Phantom with Markers

The force equation of the combined system (the phantom with the coil) is written as follows:

\[ F(t) = (m_{\text{coil}} + m_{\text{phantom}}) \ddot{x}_1 + (b_{\text{coil}} + b_{\text{phantom}}) \dot{x}_1 + (k_{\text{coil}} + k_{\text{phantom}}) x_1. \]  

(5.3)

When a step force is applied to the system, the position of the mass element \( x(t) \) is given by

\[ x(t) = \frac{1}{k_{\text{coil}} + k_{\text{phantom}}} \left[ 1 - \exp(\sigma t) \cdot \left( \cos(\omega_d t) + \frac{\sigma}{\omega_d} \cdot \sin(\omega_d t) \right) \right] \]  

(5.4)

where, \( \sigma = \frac{b_{\text{coil}} + b_{\text{phantom}}}{2(m_{\text{coil}} + m_{\text{phantom}})} \) and \( \omega_d = \sqrt{\frac{k_{\text{phantom}} + k_{\text{coil}}}{(m_{\text{coil}} + m_{\text{phantom}})} - \left( \frac{b_{\text{phantom}} + b_{\text{coil}}}{2(m_{\text{coil}} + m_{\text{phantom}})} \right)^2} \).

An exponential decay function in the form of \( 1 - \exp(-\sigma t) \) are fitted to the step response as seen in Figure 5.11. The \( \sigma \) values used in the exponential functions is found to be \(-11.5\) by a trial and error procedure. \( b_{\text{gelatin}} \) is obtained to be \( 1.475 \text{ Ns/m} \) by Equation (5.5):

\[ b_{\text{gelatin}} = \sigma \cdot 2 \cdot (m_{\text{coil}} + m_{\text{gelatin}}) - b_{\text{coil}}, \]  

(5.5)

where \( m_{\text{coil}} + m_{\text{gelatin}} \) is measured to be \( 0.163 + 0.124 \text{ kg} \), and \( b_{\text{coil}} \) is found to be \( 5.216 \text{ Ns/m} \),

![Step response](image)  
Figure 5.11: Step response of the combined voice coil and the gelatin phantom with the markers.
5.4.2 Force Equation Method Results

The phantom is modeled as a four element mass-spring-damper system. The position information of each marker is considered as the motion of the mass elements in the model. The phantom is vibrated with a band-limited white noise with a band limit of 10 Hz for 4 seconds. The maximum applied compression is 1.3% with an approximate 7% pre-compression. Each RF image is composed of 3 RF lines with a length of 45 mm. The offset level of the RF signals is set to zero. The frame rate of the ultrasound system is 494 frames per second. The four markers are tracked by correlation-based algorithm with windows of 0.8 mm. No stretching was applied to the RF signals. The amplitude of the RF signal is low other than the places where the markers are located (Figure 5.9), hence the problem of mismatching windows with different locations does not occur during the tracking process. Figure 5.12 shows the marker motions as a response to the excitation. Acceleration and velocity estimates for each marker position is obtained as described in Chapter 3. For the four markers the acceleration and velocity estimates are shown in Figures 5.12 as well.

The stiffness, mass and damping values for the four node mass-spring-damper system is calculated by using Equation (3.31) and plotted in Figure 5.13. The identified parameter values are given with respect to the first spring element between the first and second marker. The value of this spring is set to 1, and all the other parameters are scaled according to this number. The expected mass and stiffness values are measured experimentally and compared to the obtained numbers in the same figures. The damping values are compared against the damping value obtained by the step response analysis.

The validity of these numbers is also checked by investigating the following matrix equation:

\[
\Phi x = U, \\
y(x) = \|Z^T U - Z^T \Phi x\|_2
\]  

(5.6)

where \( x \) refers to the unknown parameters, and \( \Phi, Z \) and \( U \) are matrices composed of element motions, velocities and accelerations at each time instant as defined in Equation (3.31). The least squares approximation gives \( x \) values such that \( y(x) \) is minimum. \( \frac{\partial y(x)}{\partial x_i} \) shows the effect of a small change of one parameter, \( x_i \), to the overall \( y(x) \) that is going to be minimized. If the derivative
5.4 Experimental Results for Homogeneous Gelatin Phantom with Markers

Position Estimates

Velocity Estimates

Acceleration Estimates

Figure 5.12: Position, velocity and acceleration estimates are given for each marker. 'x' and 'o' for the first and third marker, solid and the dashed lines for the second and forth markers respectively.

value is small it means the obtained parameter has minimum effect on the overall set of equations. This technique is used to relate the singular values of $Z^T \Phi$ to each unknown parameter. Table 5.2 shows the unknown parameters with the matched singular values of $Z^T \Phi$ by this technique.

The condition number of $Z^T \Phi$ of Equation (3.31) is $8.41 \cdot 10^7$. According to Table 5.2, the singular values belonging to the stiffness parameters are much higher than the singular values of the damping and mass parameters. It can be concluded that the stiffness estimates are the most reliable compared to mass and damping estimates. It is also noticed that singular values of mass parameters are around 1000 times greater than the singular values of the damping parameters. Thus, the damping values are the least sensitive to the overall minimization process in Equation (5.6).
Figure 5.13: The stiffness, the damping, and the mass values are shown as ‘.’ in the plots. The solid lines for the leftmost and the rightmost show the expected stiffness and mass values. The solid line in the middle plot shows the damping value obtained from the step response analysis.

<table>
<thead>
<tr>
<th>change in $y(x)$ with 20 % change in $x_i$</th>
<th>Singular values of $Z^T\Phi$</th>
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<tbody>
<tr>
<td>$k_2$</td>
<td>$4.80 \cdot 10^{-7}$</td>
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<td>$k_3$</td>
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<tr>
<td>$m_1$</td>
<td>$2.37 \cdot 10^{-9}$</td>
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<tr>
<td>$m_2$</td>
<td>$4.77 \cdot 10^{-10}$</td>
</tr>
<tr>
<td>$b_1$</td>
<td>$1.77 \cdot 10^{-11}$</td>
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<td>$b_2$</td>
<td>$2.87 \cdot 10^{-11}$</td>
</tr>
<tr>
<td>$b_3$</td>
<td>$1.14 \cdot 10^{-11}$</td>
</tr>
</tbody>
</table>

Table 5.2: Singular values of $Z^T\Phi$ corresponding to each model parameter. The homogeneous phantom model is a 4-element L-MSD system.

5.5 Homogeneous Gelatin Phantom with Uniform Scatterers

A homogeneous gelatin phantom is produced with dimensions 65 mm x 55 mm x 35 mm. The phantom is hydrated by 13% (by mass) gelatin. 3 % (by mass) of cellulose particles are added to form the speckle texture. The Young’s modulus of the phantom is measured to be 25 kPa. A typical RF signal obtained from the phantom is shown in Figures 5.14.
5.5.1 Step Response Analysis

An experiment is performed to obtain the overall damping constant of the phantom described above. The same type of analysis is done as described in Section 5.4.1. The reflection from the voice coil phantom boundary is tracked by the ultrasound system. Each RF image is composed of 3 RF lines with a length of 45 mm starting 20 mm away from the ultrasound probe. The frame rate of the ultrasound system for this configuration is 377 frames per second. The step response is plotted in Figures 5.15.

An exponential decay function in the form of $1 - \exp(-\sigma t)$ are fitted to the step response as seen in Figure 5.15. The $\sigma$ value of the exponential function is found to be 14 by trial and error procedure. Since $m_{coil} + m_{gelatin}$ is measured to be 0.163 + 0.133 kg, and $b_{coil}$ is found to be 5.216 Ns/m, $b_{gelatin}$ is obtained to be 3.1620 Ns/m by Equation (5.5).

5.5.2 Force Equation Method Results

The phantom is vibrated with a band-limited white noise with a band limit of 10 Hz for 4 seconds. The maximum applied compression is 0.9 % with an approximate 7 % pre-compression. Successive RF images are obtained. Each RF image is composed of 3 RF lines with a length of 45 mm. The offset level is set to zero. The frame rate of the ultrasound system is 494 frames per second. The RF signals are tracked with 40 windows of size 2 mm, with 50 % overlap. The proposed adaptive stretching algorithm (Section 3.3.2) is used for tracking. The first marker starts at a depth of 41
Figure 5.15: Step response of the combined voice coil and the gelatin phantom with scatterers.

mm and the last one is 2 mm away from the US probe.

The results obtained by using the force equation method of Equation (3.31) described in Section 3.1.6 are presented in Figures 5.16 and 5.17. In Figure 5.16, one of every eight markers is used for the analysis. Hence the tissue is modeled as a 5-element L-MSD system. In Figure 5.17, one of every four markers is used for the analysis. This refers to analysis of a 10-element L-MSD system. The obtained parameters are given with respect to the first spring element between the first and second marker. The value of this spring is set to 1, all the other parameters are scaled according to this number. The expected mass and stiffness values are measured experimentally and compared to the obtained numbers in the same figures. The damping values are compared against the damping value obtained by the step response analysis.

The quality of these numbers is also checked by investigating Equation (5.6). The amount of change in $y(t)$ as a result of changing each obtained parameter by 20% is given in Tables 5.3 and 5.4 with the singular values of $Z^T \Phi$.

According to Tables 5.3 and 5.4, the singular values belonging to the stiffness parameters are much higher than the singular values of the damping and mass parameters similar to the trend observed in Table 5.2. The condition number of $Z^T \Phi$ of Equation (3.18) is $3.68 \cdot 10^9$ when the
phantom is modeled as a 10-element L-MSD system, and it is $1.15 \cdot 10^8$ when the phantom is modeled as a 5-element L-MSD system. For lower order systems the condition number is smaller. It is expected to have a better parameter estimation with systems of lower order.

The damping values obtained by the step response analysis are 1.475 Ns/m and 3.1620 Ns/m, for the homogeneous phantom with the markers (first phantom) and the homogenous phantom with the scatterers (second phantom) respectively. The Young's modulus values for the first and second phantoms are 16.63 kPa and 25 kPa respectively. The mean values for $b/k_1$ ratios are $0.6 \cdot 10^{-3}$ and $1.8 \cdot 10^{-3}$ for the first and second phantom respectively. According to these measurements,
5.6 Layered Gelatin Phantom with Uniform Scatterers

A layered phantom is tested to see the performance of the proposed method for varying stiffness values. The dimensions of the phantom are 65 mm x 55 mm x 35 mm. The phantom is composed of three layers. The first and third layers are made of gelatin to make relatively soft layers compared to the middle layer. In particular, the two soft layers are hydrated by 13 % (by mass) gelatin powder. 3 % (by mass) of cellulose particles are added to form the speckle texture. No glycerol is used to modify the speed of sound in the gel. The middle layer is produced from a mixture of 4 % agar powder (High strength A-6924 Sigma Chemical, St. Louis, MO), 3 % cellulose particles to form the speckle texture, and 7 % of glycerol (by mass) to set the speed of sound close to the gelatin layer. The ultrasound image of the hybrid phantom is shown in the right image of Figure 5.23. The individual layers are barely seen in the conventional B-mode image.

The phantom is vibrated with a band-limited white noise with a band limit of 10 Hz for 4 seconds. The maximum applied compression is 1.7 % with an approximate 7 % pre-compression.

<table>
<thead>
<tr>
<th></th>
<th>change in $y(x)$ with 20 % change in $x_i$</th>
<th>Singular values of $Z^T \Phi$</th>
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<tbody>
<tr>
<td>$k_2$</td>
<td>$2.14 \cdot 10^{-8}$</td>
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<td>$k_3$</td>
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<td>$b_4$</td>
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<td>$m_3$</td>
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<td>$3.17 \cdot 10^{-4}$</td>
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<tr>
<td>$m_4$</td>
<td>$5.4 \cdot 10^{-13}$</td>
<td>$1.33 \cdot 10^{-7}$</td>
</tr>
</tbody>
</table>

Table 5.3: Singular values of $Z^T \Phi$ corresponding to each model parameter. The homogeneous phantom model is a 5-element L-MSD system.

$b_{\text{phantom1}}/b_{\text{phantom2}}$ ratio is found to be 5.4. The same ratio is 2.14 for the damping values obtained by the step response analysis. Both methods show an increase in the damping values from first to the second phantom.
5.6 Layered Gelatin Phantom with Uniform Scatterers

<table>
<thead>
<tr>
<th></th>
<th>change in ( y(x) ) with 20 % change in ( x_i )</th>
<th>Singular values of ( Z^T \Phi )</th>
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</tr>
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</tr>
<tr>
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<td>9.13 ( \cdot 10^{-5} )</td>
</tr>
<tr>
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<td>1.42 ( \cdot 10^{-4} )</td>
</tr>
<tr>
<td>( m_5 )</td>
<td>( 2.68 \cdot 10^{-11} )</td>
<td>1.21 ( \cdot 10^{-4} )</td>
</tr>
<tr>
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<td>( 1.13 \cdot 10^{-13} )</td>
<td>1.27 ( \cdot 10^{-7} )</td>
</tr>
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<td>( m_7 )</td>
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<td>( m_8 )</td>
<td>( 7.28 \cdot 10^{-13} )</td>
<td>4.75 ( \cdot 10^{-7} )</td>
</tr>
<tr>
<td>( m_9 )</td>
<td>( 4.21 \cdot 10^{-14} )</td>
<td>4.70 ( \cdot 10^{-8} )</td>
</tr>
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<td>6.47 ( \cdot 10^{-5} )</td>
</tr>
<tr>
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<td>( 2.53 \cdot 10^{-12} )</td>
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</tr>
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<td>( b_4 )</td>
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</tr>
<tr>
<td>( b_9 )</td>
<td>( 1.44 \cdot 10^{-13} )</td>
<td>2.35 ( \cdot 10^{-7} )</td>
</tr>
</tbody>
</table>

Table 5.4: Singular values of \( Z^T \Phi \) corresponding to each model parameter. The homogeneous phantom model is a 10-element L-MSD system.

Each RF image is composed of 3 RF lines with a length of 44 cm starting 0 cm away from the ultrasound probe. The frame rate of the ultrasound system is 499 frames per second. The RF signals are tracked with 40 windows of size 2 mm, with 50 % overlap. The proposed adaptive stretching algorithm (Section 3.3.2) is used for tracking. The first marker starts at a depth of 41 mm and the last one is 2 mm away from the US probe.
5.6 Layered Gelatin Phantom with Uniform Scatterers

5.6.1 Force Equation Method Results

The results obtained by using the force equation method of Equation (3.31) described in Section 3.1.6 are presented in Figures 5.18 and 5.19. In Figure 5.18, one of every eight markers is used for the analysis. Hence the tissue is modeled as a 5-element L-MSD system. In Figure 5.19, one of every four markers is used for the analysis. This refers to analysis of a 10-element L-MSD system. The true mass values are measured experimentally and compared to the obtained numbers in the same figures.

The quality of these numbers is also checked by investigating Equation (5.6). The amount of change in $y(t)$ as a result of changing each obtained parameter 20% is given in Tables 5.5 and 5.6 with the singular values of $Z^T \Phi$. 

![Figure 5.18](image1.png)

Figure 5.18: The $k$, $b$, and $m$ values obtained by using 5-element L-MSD model are shown as '.' in the plots. The solid line for the leftmost plot shows the expected mass values.

![Figure 5.19](image2.png)

Figure 5.19: The $k$, $b$, and $m$ values obtained by using 10-element L-MSD model are shown as '.' in the plots. The solid line for the leftmost plot shows the expected mass values.
change in \( y(x) \) with 20% change in \( x_i \) | Singular values of \( Z^T \Phi \) \\
--- | --- \\
\( k_2 \) | 1.43 \( \cdot 10^{-6} \) | 70.2 \\
\( k_3 \) | 9.84 \( \cdot 10^{-7} \) | 43.6 \\
\( k_4 \) | 3.96 \( \cdot 10^{-7} \) | 35.4 \\
\( b_1 \) | 1.08 \( \cdot 10^{-9} \) | 9.47 \( \cdot 10^{-7} \) \\
\( b_2 \) | 2.11 \( \cdot 10^{-9} \) | 2.41 \( \cdot 10^{-6} \) \\
\( b_3 \) | 3.61 \( \cdot 10^{-9} \) | 3.61 \( \cdot 10^{-3} \) \\
\( b_4 \) | 5.61 \( \cdot 10^{-10} \) | 5.24 \( \cdot 10^{-8} \) \\
\( m_2 \) | 2.59 \( \cdot 10^{-9} \) | 4.38 \( \cdot 10^{-4} \) \\
\( m_3 \) | 1.11 \( \cdot 10^{-9} \) | 1.42 \( \cdot 10^{-6} \) \\
\( m_4 \) | 2.26 \( \cdot 10^{-9} \) | 3.09 \( \cdot 10^{-4} \) \\

Table 5.5: Singular values of \( Z^T \Phi \) corresponding to each model parameter. The layered phantom model is a 5-element L-MSD system.

According to Tables 5.5 and 5.6, the singular values belonging to the stiffness parameters are much higher than the singular values of the damping and mass parameters similar to Tables 5.2, 5.3, and 5.4. The stiffness values are the dominant parameters affecting the system response.

The condition number of \( Z^T \Phi \) of Equation (3.18) is \( 4.52 \cdot 10^{10} \), when the phantom is modeled as a 10-element L-MSD system, and it is \( 1.34 \cdot 10^9 \), when the phantom is modeled as a 5-element L-MSD system. It is expected to have a better system identification at lower orders. When all 40 markers are used for the analysis, in other words, when the phantom is modeled as a 40-element L-MSD system, it is observed that even the estimated stiffness values have more than 50% error.

Another observation is that the condition number for the heterogeneous phantom is ten times higher than the homogeneous ones. The difference in the condition number results from the fact that the differences between the magnitudes of the parameters are higher in the heterogeneous phantom compared to the homogenous phantom. In the homogeneous phantoms if the phantom is modeled as a 5-element L-MSD system than \( k/m \) ratio is expected to be \( 3 \cdot 10^5 \), whereas for the layered phantom this ratio is expected to be 10 times higher since the phantom is 10 times stiffer although the density is the same. This may explain the poor results obtained for mass values compared to the homogeneous cases.

The damping value for the soft layer in the third phantom is found to be 0.0027 s, which is close to the damping values obtained for the second homogeneous phantom of 0.0020 s. Note that the
units of damping are given in seconds since they are with respect to the stiffness of the first spring element in each phantom. It should also be mentioned that although the soft layers of the layered phantom and the homogenous phantom are made according to the same recipe, their stiffness and damping might be slightly different.
Table 5.6: Singular values of $Z^T\Phi$ corresponding to each model parameter. The layered phantom model is a 10-element L-MSD system.

### 5.6.2 Transfer Function Method Results

The transfer function method described in Section 3.2 is applied to the same layered phantom described in Section 5.6. High resolution stiffness images are obtained. Two separate experimental data sets are analyzed. The first data set is the same data used in Section 5.6.1. The data is obtained by exciting the phantom by white noise band-limited to 10 Hz with a duration of 4 seconds and observing the phantom response at 499 frames per seconds.
5.6 Layered Gelatin Phantom with Uniform Scatterers

The power spectral and the cross-spectral densities are calculated by the pre-defined MATLAB functions `psd` and `csd`. The spectral information is used to obtain the transfer functions and the coherence functions by Equation (3.33) and Equation (3.34) in Chapter 3. Figure 5.20 shows typical transfer and coherence functions obtained from the first data set. The motions at a depth of 41 mm and 21 mm away from the ultrasound probe are considered as the input and the output of a linear system respectively. The transfer and coherence functions for this linear system are then obtained as described above and plotted as the solid and dashed lines in Figure 5.20 respectively.

In Figure 5.20, the coherence function is close to 0.9 even at 50 Hz. This suggests the presence of frequencies up to 50 Hz in the system output, whereas the input signal is band-limited to 10 Hz. One possible explanation for this fact is that the amplifier at the input side is turned on once the image acquisition starts. Therefore, high frequencies are introduced to the system input in the beginning of the excitation. The second reason is the presence of low amplitude high frequency signals in the input signal itself. During the experiments, the input noise is filtered by a sixth order Butterworth filter with a cutoff frequency of 10 Hz. So the higher frequencies are often attenuated but still present. For example, the signal at 20 Hz is 15 dB lower and 30 Hz is 19 dB lower than the signal amplitude at 10 Hz. Therefore, frequencies higher than 10 Hz are observed in the system output.

The transfer functions from the first marker (41 mm away from the US transducer) to all other
Figure 5.21: The left plot shows the low frequency values of the transfer functions for all the markers used in the transfer function analysis. The right plot shows the phases of the transfer functions from the 1\textsuperscript{st} marker to 10\textsuperscript{th} \( (H_{x1}^{10}) \), 1\textsuperscript{st} to 20\textsuperscript{th} \( (H_{x1}^{20}) \), 1\textsuperscript{st} to 30\textsuperscript{th} \( (H_{x1}^{30}) \), and 1\textsuperscript{st} to 40\textsuperscript{th} \( (H_{x1}^{40}) \).

39 markers are used for the transfer function analysis. The left plot in Figure 5.21 shows the low frequency values of the transfer functions for all the markers. In the same plot the shaded area indicates the frequencies used for averaging the stiffness data. Accordingly, frequencies up to 4 Hz are used to regularize the stiffness data. The stiff and soft regions can be visually identified by the density of the transfer functions at low frequencies from the left plot of Figure 5.21. The right plot in the same figure shows the phases of the transfer functions from the 1\textsuperscript{st} marker to 10\textsuperscript{th} \( (H_{x1}^{10}) \), 1\textsuperscript{st} to 20\textsuperscript{th} \( (H_{x1}^{20}) \), 1\textsuperscript{st} to 30\textsuperscript{th} \( (H_{x1}^{30}) \), and 1\textsuperscript{st} to 40\textsuperscript{th} \( (H_{x1}^{40}) \). The phase values are below 3 degrees even for \( H_{x1}^{40} \), the variations in phase of the transfer functions obtained from neighbouring locations are probably below noise level. Therefore, they may not infer any information related to tissue mechanics.

The stiffness variation along the phantom axis obtained by the transfer function method is given in the left plot of Figure 5.22. The right plot in the same figure shows the stiffness values obtained by the force equation method described in the previous section as a comparison.

The second experimental data set is obtained by exciting the phantom by white noise band-limited to 10 Hz with a duration of 4 seconds and observing the phantom response at 124 frames.
per seconds. Each RF-image is composed of 21 RF lines. 40 marker locations are tracked for each RF line; therefore a stiffness image of 21 x 40 is obtained. Similar to the first data set, the transfer functions and the coherence functions are calculated by the pre-defined MATLAB functions \textit{psd} and \textit{csd}. In Figure 5.23 the stiffness image and the B-mode image are given as a comparison.

Figure 5.22: The comparison of the results obtained by transfer function method and the force equation method. The left plot shows the stiffness values obtained by using the transfer function method. The right plot shows the stiffness values obtained by solving the force equation for a 10 element L-MSD chain.

Figure 5.23: On the right B-mode US image of the layered hydrogel phantom is seen, on the left, stiffness image obtained by using the transfer function method is seen.
5.7 Remarks on Experimental Results

- **Tissue Model**

The tissue is modeled as a one dimensional mass-spring-damper chain in the thesis. This model is used to explain the behavior of homogeneous and layered hydrogel phantoms in this chapter. The physical event during the experiments is wave creation and propagation in a three dimensional media. In our proposed method, tissue motion and wave propagation are in the same direction. These types of waves are called compressional waves in continuum mechanics. However, the compressional wave speed is a function of the compressibility of the tissue (Poisson’s ratio). The relation between the compressional wave speed ($C_t$) and the Poisson’s ratio ($\nu$) is given in [21] as:

$$C_t^2 = \frac{E}{2\rho(1+\nu)(1-2\nu)}$$  \hspace{1cm} (5.7)

where $\rho$ is the density and $E$ is the Young’s modulus (stiffness) of the media. In fact compressional waves propagate by changing the volume of the media (hence the name compressional waves). In other words, compressional waves can not be modeled and explained without the Poisson’s ratio, and the Poisson’s ratio can not be explained by 1D models. For the physical event to be explained by a 1D model, the tissue must be infinitely compressible ($\nu = 0$). In such a case all the particles in the 3D media would move in the direction of applied compression. However the tissue is known to be almost incompressible, (Poisson’s ratio is close to 0.5). Thus, the pressure applied only in the axial direction cause lateral and elevational expansions, which invokes the shear waves. In fact, it is stated in [9] that, as a result of a pulse excitation on a semi-infinite, isotropic, homogeneous solid, four kinds of waves are generated: A Rayleigh wave, a head wave, a compressional wave and a shear wave. Moreover it is also stated in [61] that when a tissue is modeled as a visco-elastic medium most part of the energy radiated from the surface propagates as a shear wave in the medium when the frequency of low frequency vibration is less than about 1 kHz. In their study on elastography by vibration analysis [61], the compressional wave component is neglected in the analysis. Another group working on vibration elastography [9], also did not mention compressional waves in their work. Shear waves only make sense at least for 2D, because the shear wave
5.7 Remarks on Experimental Results

Propagation and particle motion are perpendicular to each other. Hence it is also not possible to explain shear waves with 1D models.

It was mentioned in [46] that a 1D model approximation of 3D static tissue behaviour produces certain artifacts because of lateral and elevational tissue motion and variations in boundary conditions, but still stiffness values obtained in this way can be used in diagnostics, [33, 47]. The stiffness values obtained with the proposed force equation method for the layered phantom clearly differentiates the stiffer layer quantitatively. It is also known that tissue creep and relaxation is explained by 1D models such as Voigt, Maxwell, three-element models, [20]. Thus, using a 1D L-MSD chain to explain a variation in tissue damping also makes physical sense. However, solving for the mass by using Newton's second law, which states

\[
\text{Force} = \text{mass} \cdot \text{acceleration}
\]

is equivalent to solving the wave equations since the wave equations are derived from this law. As mentioned above, neither of the wave phenomenon can be explained by 1D models. A possible explanation of the poor mass estimates in the results section may be the fact that waves were analyzed by using a 1D model.

**Pressure Change Along the Axial Direction**

In a 3D media, an axial pressure applied to an elastic rectangular prism causes a variation in the pressure along the axial direction of the phantom. The pressure change is a function of the geometry, boundary conditions, Poisson's ratio, and the elasticity of the block. However, in the proposed force equation and transfer function methods the pressure is assumed to be constant along the tissue. The slight variation in strain towards the US probe (away from the pressure source) is related to variations in the stiffness along the axis of the phantom. The stiffness variation observed in Figures 5.13, 5.16, and 5.17 can be explained partly by this fact. A FEM simulation for a rectangular homogeneous material can show the real pressure distribution along the axial direction of the phantom. This information can then be used for correcting the stiffness values.

**Effect of Lower Strain Values in the Stiff Region in the Layered Phantom**

The stiffness estimates are expected to have a larger error in the stiffer region of the phantom, since the strain levels are lower. It is shown in the static experiment on the homogeneous phantom in Section 5.3 that the standard deviation of the strain values are lower for 0.5 % compression level than 1 % compression level (Table 5.1). Maximum applied compression is
Remarks on Experimental Results

1.3 % during the experiments with the layered phantom. The maximum strains in the stiffer middle layer are less than 0.3 %, since the middle layer is almost 10 times stiffer than the soft layers. Low strain levels in the stiffer region cause the higher deviations in the middle layer shown in left plot of Figures 5.22.

- **Effect of Speed of Sound on Motion Tracking**

The tissue motion at each depth is measured by successive ultrasound images. The major assumption in motion estimation is that each ultrasound image is a snapshot of the tissue motion at each time instant. However, the ultrasound images are formed by the reflection of traveling ultrasound waves at different depths of the tissue. Therefore, the time required to obtain a full RF line depends on the speed of sound, which is 1540 m/s in tissue and tissue mimicking gels. In other words, there is a time delay for the ultrasound wave to travel between two different depths, hence the deformation of these two locations cannot be observed at the same time instant. In our experiments, the deformation frequency of the tissue is up to 10 Hz, and the maximum tissue depth observed is less than 50 mm. Accordingly, the time delay between two locations with a separation of 50 mm is 65 μs, which is extremely small compared to 0.1 s (10 Hz) of tissue motion. Therefore, the effect of finite sound speed is neglected in our experiments.

- **Improvements in Motion Tracking**

The Poisson's ratio for most tissue and tissue-like materials is given as 0.5 [53], which refers to incompressibility. As a response of an axial pressure, the tissue bulges elevationally and laterally, which causes signal decorrelation in correlation-based tracking, [29–31]. In [30,31], this was partly compensated by tracking the tissue lateral motion as well. In our experiments the lateral and elevational tissue motion is ignored assuming that the beam width is wide enough to compensate the lateral and elevational motions of the scatterers. However, non-axial motion still degrades the quality of tissue strain values especially for the RF lines away from the centerline of the phantom, [2]. In our experiments, a lateral correction of tissue displacement information will improve the quality of the displacement data.
5.7 Remarks on Experimental Results

- Comments on Step Response

The voice coil is assumed to behave as a second order system in the step response analysis. According to this assumption, a damping value for the voice coil is obtained. The same type of analysis is applied to the phantoms as well. The comparison of Figures 5.4 and 5.15 shows that the step response of the voice coil can be more easily approximated by a second order system than the step responses of the phantoms. It should also be mentioned that according to Equation (5.5), for a 20% variation in $\alpha$, the resultant change in damping was 4 times. Therefore, this method is very sensitive to variations in $\alpha$ for obtaining an absolute value for damping. However, it should be noted that the aim of the step response analysis is not to obtain a gold standard for the tissue damping to be compared with the damping obtained by the proposed force equation method. The purpose is to get an idea of the order and the range of the damping values expected for the homogeneous phantoms.

- Force Equation Method Results

Discussion of the Sensitivity of Various Parameters:

In all the experiments the stiffness values are observed to be more dominant in determining the system response. Tables 5.2, 5.3, 5.4, 5.5, 5.6 show that the singular values belonging to the stiffness parameters are much higher than the singular values of the damping and the mass parameters. The condition number of $Z^T\Phi$ of Equation (3.18) is in the order of $10^9$ for all cases in the experiments. One reason for the high condition numbers is the low excitation frequencies (up to 10 Hz) used in the system identification. When the force equation is considered, the static component $K \cdot x$ is dominant in determining the total force than the dynamic components, which are $B \cdot \dot{x}$ and $M \cdot \ddot{x}$. Increasing the frequency of excitation increases the acceleration and velocity terms with respect to the displacements. Therefore, higher velocity and acceleration estimates in matrix $\Phi$ results in lower condition number at higher frequency excitations.

Comments on Lumping:

The condition numbers of the systems composed of fewer Voigt elements are lower. For example, the experiments conducted on the homogeneous gelatin phantom with scatterers have a condition number of $3.68 \cdot 10^9$ when the phantom is modeled as a 10-element L-MSD system, and $1.15 \cdot 10^8$ when the phantom is modeled as a 5-element L-MSD system. A similar
trend applies to the layered phantom. The condition number is $4.52 \cdot 10^{10}$ when the phantom is modeled as a 10-element L-MSD system, and it is $1.34 \cdot 10^9$ when the phantom is modeled as a 5-element L-MSD system. It is expected to have a better parameter estimation at lower orders. It is shown in Figure 4.8 that as the system order is halved, the $k/b$ ratio stays the same but the $m/k$ ratio increases by a factor of four. The increase in mass value with respect to the viscosity values increases the effectiveness of masses in determining the system response.

**Identification of Heterogeneous and Homogeneous Case:**

The condition number for layered phantom is ten times higher than the homogeneous ones. The same trend is also observed in the simulations of Section 4.1.5. The difference in the condition numbers results from the fact that the differences between the magnitudes of the parameters are higher in heterogeneous phantom compared to the homogenous phantom. In the homogeneous phantoms if the phantom is modeled as a 5-element L-MSD system than $k/m$ ratio is expected to be $3 \cdot 10^9$, whereas for the layered phantom this ratio is expected to be 10 times higher since the phantom is 10 times stiffer although the density is the same. This may explain the poor results obtained for mass values compared to the homogeneous cases.

**Relative Damping Values of the Three Phantoms Used in the Experiments:**

According to the damping values found for the homogeneous gelatin phantom with markers and with scatterers by using the force equation method, the overall damping value of the second homogeneous phantom is around 5 times larger than of the first phantom. A similar increase in the phantom damping is also observed in the step responses. The force equation method differentiated the relative damping change in the phantoms successfully. The damping values for the soft layer in the third phantom are found to be 0.0027 s, which is close to the damping values obtained for the second homogeneous phantom of 0.0020 s. Note that the units of damping are given in seconds since they are with respect to the stiffness of the first spring element in each phantom. Assuming the stiffness values for the first elements in the two phantoms are same, the damping values seem to be fairly close to each other. It should be mentioned that the phantom mechanical properties depends on many factors not only the amount of ingredients added but also the heating and cooling processes, so the same phantoms
may have slightly different mechanical properties.

*Damping Values of Homogeneous Gelatin with Scatterers Compared to the Viscosity of a Gel Phantoms Given in [34]:*

Shear modulus and shear viscosity values for a gel phantom was calculated in [34] by MRI elastography techniques. The damping values reported for the homogeneous gelatin phantom in Section 5.5 are very close to the findings for the gel phantom experimented in [34], which has an elasticity value close to the elasticity value of the phantom in Section 5.5. In [34], the shear modulus and shear viscosity of the gel block is given as 9 kPa and 15.3 Pa-s respectively. The shear modulus and shear viscosity is modeled as Voigt element, the same as in this thesis. There is a difference in convention to be noted. The elasticity values disclosed in the thesis are in terms of the Young’s modulus. Young’s modulus is a measure relating the axial pressure to the axial strain. Shear modulus \( (\mu) \) is related to the Young’s modulus \( (E) \) as \( E = \mu \cdot 3 \) for incompressible solids [14]. The Young’s modulus of the homogeneous gelatin phantom is calculated as 25 kPa in Section 5.5. The shear modulus is then one third of this value, hence 8.3 kPa. The means of the damping values given in Figures 5.16 and 5.17 are first calculated. The values are then scaled according to the shear modulus of the same phantom. The shear viscosity values are then found to be 16.7 Pa-s and 12.5 Pa-s, when the tissue is modeled as 5-element and 10-element L-MSD respectively. These values are close to 15.3 Pa-s which is reported in [34] for the gel with 9 kPa shear modulus value. Although the viscosity and the shear modulus values of the gels of both work are close to each other, the type of the gel and the construction details are not given in [34]. Type of the gel powder and the gelling process have a major effect to the mechanical properties of the gel. The only known similarity of both gels is the elasticity of the gels. Therefore, a direct comparison for the viscosity values can not be made. However, it can be concluded that the range of values proposed in this thesis for a 8.3 kPa gelatin phantom are similar.

- **Transfer Function Method**

  *Benefits of Averaging the Low Frequency Components of the Transfer Function:*

  The stiffness estimates by the transfer function method are obtained from an average of the magnitudes of the transfer functions at low frequencies where the magnitudes are approximately constant. Thus unlike in prior work, a range of frequencies is used for stiffness
estimation. This captures low-frequency tissue dynamics, not only static, and might prove to be less sensitive to noise.

- **Comparison of Transfer Function and Force Equation Methods**

In Figure 5.22, the stiffness variation for the layered phantom is plotted by using both the force equation and the transfer function methods. Both methods give the same amount of stiffness variation. The resolution is around 4 mm for the force equation method and 1 mm for the transfer function approach. The transfer function method has the advantage of being robust at high resolutions, whereas the stiffness values obtained by the force equation method have more than 50% error at 1 mm resolution.

- **Experimental Set-up**

The gap between the singular values corresponding to the mass parameters and the stiffness parameter decreases for softer phantoms with the same density (Simulation results of Table 4.5 in Section 4.1.4). This observation can be intuitively explained by considering the terms in the equation of motion. The inertial terms in the force equation will be as dominant as the static terms as the \( k/m \) ratio decreases. The softest phantom used in the experiments has an elasticity of 17 kPa with the current set-up. For elasticities lower than this value, it is not possible to keep the phantom lifted from the ground by holding it from the coil and probe sides due to the weight of the phantom. The weight causes the phantom to bend down in the middle. It would be possible to work with softer phantoms, in case the set-up is rotated vertically so that the phantom can stay standing and the vibration source is placed to the top surface. This will increase the quality of parameter identification.
Chapter 6

Summary and Future Work

6.1 Summary

This thesis presents an elastography system for extracting not only static but also dynamic properties of tissue. A computer-controlled vibrator induces motion over a range of frequencies simultaneously and the resulting displacement is recorded at multiple locations and time instants with a sequence of ultrasound images. The motion data is then used to extract the mechanical properties of tissue. Two methods are proposed for processing the motion data. In the first method, the tissue model is composed of a series of mass elements connected to each other by a spring and damper arranged in parallel. The mass elements represent the local density, the springs represent the elasticity and the dampers represent the damping of the tissue. The equation of motion for the developed 1D model is solved to extract the density, elasticity, and damping parameters.

A second method to identify the elasticity is developed on the principle of transfer functions. According to this method, the tissue dynamics between two axial locations is modeled as a linear dynamic system. The transfer functions between these locations are obtained by analyzing the spectrum of the recorded motion at these locations in the tissue. The low frequency portion of the transfer functions are then analyzed to obtain the relative elasticity distribution.

Accurate displacement measurements must be obtained for both methods. A new correlation-based tracking algorithm is developed for measuring tissue motion in successive ultrasound images. The algorithm is based on stretching the time domain ultrasound signals according to the local
compression applied along the axial direction. The accuracy of the new method is proved to be higher than the conventional time domain correlation-based algorithms. The algorithm is around two times slower than the standard correlation-based tracking; however the strain plots obtained by this technique were proven to have around four times less standard deviation for homogeneous regions than the standard correlation-based tracking. The proposed method is also compared against the adaptive stretching algorithm in [2]. The experiments performed on homogeneous gelatin phantoms show that the adaptive stretching algorithm of [2] has a slightly better performance than the proposed method; whereas the computation time is far higher than our method.

The methods are first tested and validated through computer simulations. A simulation environment for creating and exciting a 1D mass-spring-damper system is developed. Various systems with varying parameter values are simulated, and their motion is recorded. The motion data is analyzed by the proposed force equation methods in Chapter 3. The parameters are extracted within 1% error when the measurement noise level is set to 0%. The simulation environment is improved by adding a 1D ultrasound simulator to create successive ultrasound RF signals, instead of motions. The proposed adaptive stretching-based tracking is used to obtain measurements of motion from the simulated ultrasound RF signals. The motion data is then used to test the performances of both algorithms. The errors in damping and stiffness values are obtained to be within 5% at 4 mm resolution, and 12% at 6 mm for mass values, for a homogeneous phantom simulation. However, the errors in the stiffness and damping values are higher, and the mass estimates are poor for a layered phantom simulation. It is shown through the simulations that the increase in the frame rate at which the displacement data is sampled improves the estimated parameters for the force equation method. The simulation analysis on Section 4.1.3 shows that underestimating the number of elements in an L-MSD chain still gives reasonable results. The effect of underestimation is seen as a change in the ratios of mass versus stiffness and mass versus damping values. It is also observed in Figures 4.9 and 4.10 that the quality and reliability of the estimated parameters increases by the decrease in the system order. A simulation study is also done for performance analysis of the transfer function method. The transfer function method gives high resolution high quality elasticity values. A comparison of the static method described in [48] and the transfer function method is given in Figure 4.20. It is shown that the transfer function method gives more accurate results than the method in [48].
6.2 Future Work

The theory is then tested with physical phantoms. Three different hydrogel phantoms are produced. The first one is a homogeneous gelatin phantom with markers for accurate motion tracking. The Young's modulus of this phantom is measured to be 16.63 kPa. The damping, stiffness, and mass values are obtained at 10 mm resolution by the force equation method. The shear viscosity is calculated to be 3.3 Pa-s. The damping values are compared to the damping values obtained by analyzing the step response of the phantom. These values are found to be around 5 times higher than the force equation method findings. The mass estimates are 30 % lower than the expected values.

The second phantom is a homogeneous gelatin phantom with a Young's modulus of 25 kPa. Stiffness and damping values are obtained for the phantom at 4 mm and 8 mm resolution by using the force equation method. The resolution is determined by the number of elements used to model the phantom. The shear viscosity values are found to be 19.7 Pa-s and 12.5 Pa-s at 4 mm and 8 mm resolution respectively. In [34], the shear viscosity of the gel block having similar stiffness is given as 15.3 Pa-s. The damping values are compared to the damping values obtained by analyzing the step response of the homogeneous phantom. These values are found to be around 60 % higher than the force equation method findings.

The third phantom consists of three layers: one hard layer in between two soft layers. The elasticity and damping values are extracted. In Figure 5.22, the stiffness variation for the layered phantom is plotted by using both the force equation and the transfer function methods. Both methods give the same amount of stiffness variation. The transfer function method has the advantage of being robust at high resolutions, whereas the stiffness values obtained by the force equation method have more than 50 % error at 1 mm resolution. Although reasonable mass values are not obtained through phantom experiments, stiffness and damping values are substantial contribution to the art.

6.2 Future Work

A 1D tissue model is proposed for analyzing the tissue dynamic behaviour in this thesis. However, as mentioned in Chapter 5, 1D models are insufficient in explaining lateral tissue expansion, and shear wave phenomena. Reliable density maps and Poisson's ratio maps can be obtained by
rewriting the equations of motion at least for 2D continua. By this way, the expected artifacts in stiffness and damping maps as a result of using a 1D model may be diminished. Two different methods can be applied to formulate the 2D problem. The first method is constructing a 2D mass-spring-damper network. The second method is finite element modeling of shear wave propagation in a visco-elastic media. In the 2D case, the first challenge is accurate motion estimation in two directions, since the lateral resolution of ultrasound images is known to be less than the axial resolution. However, assumptions about tissue isotropy and incompressibility can be used for estimating the lateral tissue motion from axial motion [18].

The frame rate of the ultrasound system is kept as high as possible through the experiments by decreasing the number of RF lines obtained at each time instant. The performance of the system identification algorithms should be improved for lower frame rates so that images of damping and stiffness can be obtained to observe the variations of the dynamic tissue parameters in 2D. One possible way can be working on frequency domain especially with harmonic vibration. By this way, the time derivative operations can be replaced by amplitude and the phase information at each spatial location.

The simulation environment will be upgraded by using 2D and 3D FEM tools. A 2D or 3D FEM tool can be used to check the performance of the elastography method which uses a 1D mass-spring-damper model for modeling the tissue. The artifacts in stiffness values and damping values as a result of using a 1D model can be more easily analyzed. Additionally, the effect of ultrasonic noise can easily be implemented by using an ultrasound image generator software. The initial 2D or 3D scatterer locations can be rearranged according to an underlying FEM model so that at each time instant a 2D or 3D scatterer distribution can be obtained, which can then be used to obtain ultrasound images. This will be a valuable tool for the elastography community for checking the performances of any proposed dynamic elastography method.

Finally, clinical applications will be investigated. To do this, modifications to the experimental set-up are necessary to allow for more advanced in vitro and in vivo experiments. In vivo applications include breast imaging for cancer detection, and RF ablation for cancer treatment.
Bibliography


