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Dispersion in Tissue-mimicking Gels Measured with Shear Wave Elastography and Torsional Vibration Rheometry

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Abstract

Dispersion, or frequency-dependence of mechanical parameters, is a primary confounding factor in elastography comparisons. We present a study of dispersion in tissue-mimicking gels over a wide frequency band using a combination of ultrasound shear wave elastography (SWE) and a novel torsional vibration rheometry which allows independent mechanical measurement of SWE samples. Frequency-dependent complex shear modulus was measured in homogeneous gelatin hydrogels of two different bloom strengths while controlling for confounding factors such as temperature, water content, and material aging. Furthermore, both techniques measured the same physical samples, thereby eliminating possible variation due to batch-to-batch gel variation, sample geometry differences and boundary artifacts. The wideband measurement, from 1–1800 Hz, captured a 30–50% increase in the storage modulus and a nearly linear increase with frequency of the loss modulus. The magnitude of the variation suggests that accounting for dispersion is essential for meaningful comparisons between SWE implementations.

Keywords

shear wave elastography; rheometry; dispersion; tissue-mimicking gels; gelatin; shear modulus; storage modulus; loss modulus; viscoelastic; shear wave speed

Introduction

The goal in elastography is to quantify and/or visualize the mechanical properties of soft tissues. There is, however, a growing appreciation for the fact that the measured parameters are frequency dependent (Chen et al., 2009; Deffieux et al., 2009; Barry et al., 2014; Parker et al., 2015; Nightingale et al., 2015). Numerous dynamic elastography techniques have been proposed in the literature (Parker et al., 2011). Most of these use shear wave propagation as the basis for the estimation of mechanical parameters. They differ, however, in the shear wave excitation mechanism used, the imaging modality used to measure the deformation

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field, and in the data processing techniques used to estimate mechanical parameters (Doyley, 2012). A number of recent studies have reported that the parameters generated by different elastography techniques exhibit statistically significant variation in both clinical applications (Ferraioli et al., 2014) and phantom studies (Oudry et al., 2014; Mulabecirovic et al., 2016; Franchi-Abella et al., 2017). This variability confounds direct comparisons between techniques and systems, raises questions about the accuracy of the methodology, and hinders clinical adoption of these techniques (Ferraioli et al., 2014; Schmeltzer and Talwalkar, 2011). For example, Zhao et al. (2014), a study based on 50 patients, reported that shear modulus values of liver tissue as measured by ultrasound shear wave elastography (US-SWE) were approximately twice the values measured by magnetic resonance elastography (MRE). These discrepancies may be understood to result from viscoelastic effects in tissues, which results in the frequency dependence of elastic moduli. We show below that even gelatin exhibits significant frequency dependence in its shear mechanical properties.

Measurement discrepancies also exist between different implementations of the same elastography technique. An example is acoustic radiation force impulse based shear wave elastography (ARFI-SWE) which typically reports a shear wave speed (SWS). *The Ultrasound Shear Wave Speed Technical Committee organized by the Radiological Society of North America (RSNA)*, has been tasked with developing a protocol to allow direct comparison of shear wave speed measurements across systems. The committee performed an inter-laboratory study (Hall et al., 2013) comprising of both commercial and research systems across 15 sites and 11 pairs of homogeneous elastic phantoms. Although this first study reported an inter-system variability of under 5% in the SWS estimates obtained, a more recent Phase II study (Palmeri et al., 2015) using three viscoelastic phantoms reported inter-system variability over 17%. The higher variability reported for viscoelastic phantoms compared to elastic phantoms, once again, implicates the role of dispersion. We note that the frequency content of the ARFI generated shear wave pulse depends on a combination of system settings (Palmeri et al., 2014) and medium properties (as demonstrated in this study).

Moreover, there is growing interest in studying dispersion and reporting estimates of shear wave attenuation, or the shear loss modulus, in addition to shear wave speed (Barry et al., 2014; Parker et al., 2015; Nenadic et al., 2017; Rouze et al., 2017). The potential bias in ARFI-SWE derived attenuation estimates can be much bigger than the bias in shear wave speed estimates, 41% vs. 15% as estimated in Lipman et al. (2018).

The aim of the present work is to study the frequency dependence of shear viscoelastic moduli in gelatin that is responsible for dispersion. We use two methods that apply to complementary frequency ranges in order to obtain measurements of complex modulus over a large frequency range. Our study differs from the prior work discussed above in two important ways: (1) When elastography is compared to standard mechanical testing methods, a potentially important confounding factor is that the tests are typically performed on different physical samples. For example, a thin disk is typically for rheometry, while a larger bulk sample is typically needed for elastography. Even if both samples are manufactured with the same recipe and production method, differences can readily emerge due to shape-related inhomogeneities, differential rates of cooling, moisture loss, etc. Furthermore, as we show below, differential handling and storage of the samples can alter

the properties of one sample relative to another over time. Our study addressed this issue through a novel torsional vibration rheometry (TVR) technique which allowed both rheometry and elastography to be performed on the same physical samples. (2) Most commercially available ARFI-SWE systems do not account for dispersion and usually do not measure shear wave attenuation. Our study addresses both of these limitations.

The ARFI-SWE implementation used in this study is based on a forward model of shear wave propagation developed in Yengul et al. (2018). Our model-based inversion technique enables accurate estimation of the phase speed and shear wave attenuation at individual temporal frequencies. By combining this improved ARFI-SWE with TVR on the same physical samples, we report frequency dependent complex shear modulus, i.e. shear storage and loss moduli, measurements of homogeneous tissue-mimicking gels over a frequency range that spans three decades.

Theory

Rheometry is traditionally performed on thin discs of material as shown in Fig. 1a. More specifically, the user manual for the commercially available rheometer used in this study recommended using discs 3 mm or less in thickness. However, one of our main goals was to perform both rheometry and SWE measurements on the same physical sample and ARFI-SWE cannot be performed on such a thin disc. For this reason, we made the measurements on much taller samples than classical rheometry. The larger sample may experience torsional resonances in the operating frequency range of the rheometer measurement. The onboard rheometer software usually does not account for this vibrational dynamics and so could not readily provide credible shear modulus measurements. For this reason, the viscoelastic parameters of the sample material were estimated by fitting the raw torque and rotation measurement data recorded on the rheometer to a theoretical model of the torsional stiffness of the sample. We refer to this new technique as Torsional Vibration Rheometry. The underlying torsional dynamics model of the sample and the rheological material model used are described next.

Torsional Dynamics Model

To obtain the theoretical torsional stiffness of the gel sample, we model the gel material as a linear, homogenous, isotropic, viscoelastic solid. In such a medium, the strain response to an oscillatory stress will be an oscillation at the same frequency as the stress but lagging behind by a phase angle δ , which is called the *loss angle* and is a function of the internal friction of the material (Findley et al., 1989). Complex Lamé parameters can be used to represent this stress-strain relationship, and thereby a viscoelastic solid may be represented with the same type of constitutive equation as a corresponding elastic solid, simply by treating the Lamé coefficients, $\lambda(\omega)$ and $\mu(\omega)$, as complex rather than real. This is known as the elastic-viscoelastic analogy or the “correspondence principle” in viscoelasticity (Findley et al., 1989). A more detailed explanation of this principle is presented as an Appendix.

We can thus write Navier’s equation for time-harmonic, steady-state motion in a homogeneous isotropic viscoelastic solid with no excitation as

$$[\lambda(\omega) + 2\mu(\omega)] \nabla (\nabla \cdot U) - \mu(\omega) \nabla \times (\nabla \times U) + \rho\omega^2 U = 0. \quad (1)$$

Here $\lambda(\omega)$ and $\mu(\omega)$ are complex, frequency-dependent Lamé parameters, ρ is the mass density, ω is the angular frequency of the time-harmonic motion, and the displacement field $\mathbf{u}(\mathbf{x}, t)$ has been represented in the form

$$\mathbf{u}(\mathbf{x}, t) = \text{Re}\{\mathbf{U}(\mathbf{x})e^{-i\omega t}\}. \quad (2)$$

Using cylindrical coordinates, the motion of a cylindrical sample experiencing torsional deformation, $\Theta(z)$, about its axis of symmetry, can be described by a displacement field of the form

$$\mathbf{U}(r, \theta, z) = r\Theta(z)\hat{e}_\theta. \quad (3)$$

Navier's equation then reduces to the 1-dimensional torsional wave equation

$$\mu(\omega)\frac{d^2\Theta}{dz^2} + \rho\omega^2\Theta = 0. \quad (4)$$

The complex shear modulus may be written as

$$\mu(\omega) = \mu'(\omega) - i\mu''(\omega) \quad (5)$$

where μ' is called the shear storage modulus and μ'' is called the shear loss modulus. We note that the negative sign in eqn. (5) is due to the $e^{-i\omega t}$ time dependence chosen in eqn. (2) and with $\mu'' \geq 0$; this becomes apparent when a solution to the wave equation is written in terms of the complex shear wave number, which is inversely related to the shear modulus. Choosing the opposite convention for the time-dependence in eqn. (2) leads to the opposite sign in eqn. (5). If δ is the loss angle, or the phase lag between the shear stress and shear strain, then the ratio

$$\tan(\delta) = \frac{\mu''}{\mu'} \quad (6)$$

is widely used to quantify the damping capacity of viscoelastic materials (Findley et al., 1989). The complex shear wave number k_s is related to the shear modulus through the shear wave speed, c_s , as

$$k_s = \frac{\omega}{c_s}, c_s = \sqrt{\frac{\mu(\omega)}{\rho}}. \quad (7)$$

Eqn. (4) then becomes

$$\frac{d^2\Theta}{dz^2} + k_s^2\Theta = 0. \quad (8)$$

We now consider a cylindrical sample of radius r and length L , held fixed on the rheometer bottom plate ($z = 0$), while a harmonic torsional excitation is applied by the top plate ($z = L$). This situation is modeled through boundary conditions:

$$\begin{aligned} \Theta &= 0 \quad \text{at } z = 0, \\ \Theta &= \Theta_0 \quad \text{at } z = L. \end{aligned} \quad (9)$$

A general solution to eqn.(8) is of the form

$$\Theta(z) = Ae^{ik_s z} + Be^{-ik_s z}, \quad (10)$$

where A and B are constants that can be determined to satisfy the boundary conditions in eqn. (9). Doing so gives us the solution

$$\Theta(z) = \Theta_0 \frac{\sin(k_s z)}{\sin(k_s L)}. \quad (11)$$

The torque applied on the sample by the top plate, T_s , can be evaluated using the relation,

$$\begin{aligned} T_s(z = L) &= \mu(\omega)J \left. \frac{\partial \Theta}{\partial z} \right|_{z=L} \\ &= \mu(\omega)J \Theta_0 k_s \frac{\cos(k_s L)}{\sin(k_s L)}. \end{aligned} \quad (12)$$

Here $J = \frac{1}{2}\pi r^4$ is the polar moment of inertia of the sample's circular cross-section. We define the torsional stiffness as the ratio of the amplitudes of the applied torque (T_s) to the torsional displacement (Θ_0). Therefore, the torsional stiffness, Z , seen at the upper plate of the rheometer, can be written as

$$Z(k_s L) = \frac{T_s}{\Theta_0} = \frac{\mu(\omega)J}{L} k_s L \frac{\cos(k_s L)}{\sin(k_s L)}. \quad (13)$$

Equation (13) shows that the torsional stiffness, Z , depends on frequency through the shear wavenumber, $k_s = \omega/c_s$. As $\omega \rightarrow 0$, the torsional stiffness Z approaches $Z_0 = \mu J/L$. We note that even if the cylinder were made of a purely elastic material, so that both μ and c_s were constant with frequency, the torsional stiffness would still be frequency-dependent. In order to visualize this geometric frequency dependence, Fig. 2 shows the normalized torsional stiffness, Z/Z_0 , in eqn. (13), as a function of the non-dimensional frequency parameter, $Re(k_s L) = Re(\omega/c_s)L$, in a medium where the shear modulus, μ , is complex but constant with frequency.

Given a measurement of $Z(\omega)$, equation (13) can be used in principle to infer $\mu(\omega)$ at each individual frequency. The complicated frequency dependence of eqn. (13) and its near poles and zeros, however, make it ill-suited to solve for $\mu(\omega)$ frequency by frequency. Therefore, in order to infer $\mu(\omega)$ from TVR measurements of Z , we choose to parameterize $\mu(\omega)$ over the frequency range of the TVR measurements (1–100 Hz) through a rheological model.

Rheological Material Model

Most natural materials, and soft tissues in particular, exhibit viscoelastic behavior. As a result, their mechanical properties are functions of frequency. Rheological material models are used to parameterize this frequency dependence. The Maxwell and Kelvin-Voigt models are popular choices in SWE studies of both gels and soft-tissues. They are both two-parameter models and use one spring and one dashpot, either in series (Maxwell) or in parallel (Kelvin-Voigt) to characterize the frequency dependence of the storage and loss moduli, see Fig. 3(b,c). A different two parameter model, called the linear dispersion model, Fig. 3(d), was proposed in Nightingale et al. (2015) for characterizing dispersion in gels and tissue over a narrow frequency range. With only two parameters each, these models are limited in their ability to describe certain viscoelastic phenomena (Findley et al., 1989). For example, the Maxwell model does not describe time-dependent recovery while the Kelvin-Voigt model does not describe stress relaxation (time-dependent drop in stress under a constant strain). The three-parameter Standard Linear Solid (SLS) model is the simplest model that describes both these phenomena. It can be represented as a network of a spring in parallel with a series combination of another spring and a dashpot, Fig. 3(a). Both the Maxwell and Kelvin-Voigt models are a special case of the SLS model. We used the three-parameter SLS model for the TVR measurement, while SWE was performed in a rheological model-independent fashion.

The shear modulus μ can be expressed as a function of frequency, ω , and the three parameters in the SLS model (k_e , k_I , η). First, we define a time constant, τ , for the Maxwell arm as $\tau = \frac{\eta}{k_I}$, then

$$\mu(\omega, k_e, k_1, \tau) = k_e + \frac{\omega^2 \tau^2}{1 + \omega^2 \tau^2} k_1 - i \frac{\omega \tau}{1 + \omega^2 \tau^2} k_1. \quad (14)$$

See Findley et al. (1989) for a detailed derivation. (Equation (5.43) in Findley et al. (1989) gives the stress-strain relation. Fourier transforming that gives (14) with suitable notation changes.)

Materials and Methods

Study Design and Measurement Protocol

Samples of a soft gelatin hydrogel and a stiffer gelatin hydrogel were measured one week after manufacture using two measurement techniques: A novel torsional vibration rheometry (TVR) and ARFI-SWE. The particulars of gel manufacture and of both measurement techniques are described in later subsections. Samples were cylindrical in shape with a diameter of 41 mm and a height of 70 mm. A total of six samples, three samples each of the soft and stiff gelatin hydrogels, were used in the study. Samples were measured three times using SWE and two times using TVR yielding a total of 5 measurements of the shear storage and loss moduli for each sample. All measurements were performed on the same day in order to minimize the impact of material aging. Moreover, the measurements were interleaved as follows: SWE-1, TVR-1, SWE-2, TVR-2, SWE-3. Interleaving served as a check on the change in sample properties due to measurement related exposure to mechanical and environmental stresses. These included moisture loss, potential plastic strains or temperature fluctuations during measurement setup, handling and storage between measurements, etc. The mass and temperature of each sample was recorded at each of its 5 measurements. The measured dataset allowed for a check on the repeatability of the measurements by studying both intra-sample and inter-sample variability in the two types of gelatin. One of the stiffer gelatin samples was subjected to significant SWE imaging and related environmental exposure one day prior to the day of reported measurements. This allowed us to observe the effect of sample history, i.e., repeated imaging, mechanical handling and environmental exposure of the sample, on its mechanical properties.

Tissue-mimicking Gel Preparation

A 12% by weight gelatin recipe adapted from Hall et al. (1997) with the following ingredients was used: 90–110 g and 300 g Bloom strength, Type A gelatin from porcine skin (*Sigma-Aldrich* SKU G6144 & G2500, respectively), talc powder (*Sigma-Aldrich* SKU 18654), 1-Propanol (*Sigma-Aldrich* SKU 402893), 10% Buffered Formalin (*Fisher Scientific* Catalog No. SF100–20) and food color (*McCormick* food color and egg dye). Gelatin powder was hydrated with de-ionized and degassed water heated to and maintained at 45°C in a water bath. A suspension of talc powder was used as the ultrasound scattering agent in the gel instead of the graphite powder used in the original recipe. Talc powder is hydrophobic, so it was first stirred into 1-Propanol, and then added to the gelatin solution after the gelatin had dispersed and the solution had clarified. The mixture was degassed in a

vacuum chamber for 10 minutes to remove any trapped air bubbles. The degassed mixture was allowed to cool to 30°C before the Formalin solution was added and gently stirred in. For easy visual differentiation of samples made from the two kinds of gelatin, a few drops of food color were also added. The softer gel samples were colored red and the stiffer samples were colored blue. The cylinder shaped molds were previously cleaned, dried and coated with a thin layer of petroleum jelly (Vaseline® Jelly Original, Unilever US). The gelatin solution was poured slowly into the mold to avoid trapping any air bubbles. The opening was capped and the gel was allowed to cool at room temperature. To prevent the suspended talc particles from settling near the bottom, the cylinder molds were slowly turned at about 1 rpm for about 30 min, until the gel had sufficiently solidified. The molds were stored in a temperature controlled room at 4°C for exactly one week. After a week, the molds were disassembled and the formed gelatin cylinders were gently pushed out from one end. In order to prevent moisture loss via evaporation, the curved surfaces were coated with a thin layer of petroleum jelly. The flat surfaces of the cylinder were not coated with petroleum jelly to avoid slipping at these contact surfaces during rheometry. To further prevent drying, the samples were completely enclosed in plastic wrap and stored in a close fitting sealed container. A tissue moistened with de-ionised water was placed inside the container to stabilize the internal humidity.

Torsional Vibration Rheometry

The samples used in this study were cylindrical in shape: 41 mm in diameter and 70 mm in length. The increased size, from the recommended 3mm to 70mm, led to two key changes compared to classical rheometry: (a) the static torsional stiffness of the sample, which is inversely proportional to the cylinder length, was reduced by a factor of over 20 ($\approx 70/3$), and (b) the larger samples experienced torsional resonances in the 0.01–100 Hz operating frequency range of the rheometer measurement. The onboard rheometer software did not account for this geometry dependent dynamics. Therefore, the raw torque and rotation measurement data were recorded and the viscoelastic parameters of the gel material were estimated using the torsional dynamics model described in section b.

TVR Data Acquisition

Measurements were performed on a commercially available rheometer (Model AR-2000, TA Instruments, New Castle, DE, USA). A 40mm diameter flat plate rheometer accessory was used as the moving top plate in the measurement. Both the top plate and the fixed bottom plate were coated with a 1500 grit sandpaper to minimize slipping between the sample and the smooth metallic surfaces of the plates. The lower static torsional stiffness of the tall cylindrical sample as compared to the recommended thin disc, further reduces the possibility of slipping. We found that these two changes together made the static stiffness measurement more repeatable with our sample geometry than with the recommended thin discs. Preparatory measurements showed that drying of the sample leads to significant changes in the reported shear modulus. To minimize moisture loss the sample was placed inside a custom-designed acrylic environment chamber during the measurement, seen in Fig. 1b. Measurement consisted of a frequency sweep oscillation with a sinusoidal shear strain with peak amplitude of 1%. A frequency range of 1–100 Hz with 67 linearly spaced points, yielding a frequency resolution of 1.5 Hz, was used. The choice of 67 frequency points was

dictated by two competing requirements: the need for good resolution to adequately resolve resonance frequencies and modal damping, while minimizing the total measurement time. Long measurement times are undesirable because, in addition to the possibility of moisture loss, the sample can undergo creep due to the clamping normal force applied by the rheometer plates, causing a tiny but incremental change in the height and radius of the sample. The chosen frequency resolution resulted in a measurement time of about 10 minutes per sample. The normal clamping force used was 0.5 N for the soft samples and 1.5 N for the stiffer ones. Gravity and clamping force together lead to a maximum compressive strain of less than 10% in the sample, which is within the linear viscoelastic regime for gelatin (Hall et al., 1997). With this loading, creep strain was found to be well below 1%, and typically below 0.1%, during the 10 min. measurement interval.

At each individual excitation frequency, ω , the rheometer produced a sinusoidal rotational displacement of the form, $\Theta = \text{Re}\{\Theta_0 e^{-i\omega t}\}$, at the top plate and recorded the total torque needed, T_{total} , to produce the dynamic displacement. T_{total} is a complex quantity with both magnitude and phase. Since the inertia of the top plate and the motor shaft also contributed to T_{total} , a frequency dependent inertia correction term was applied to obtain the sample's contribution to the total torque, T_s , as

$$T_s = T_{total} - I\omega^2. \quad (15)$$

Here I is the effective rotational inertia of the moving parts of the rheometer. An estimate of I was provided by the rheometer during the initial calibration. This estimate was refined by a least squares fit described below. The frequency dependent rotational stiffness of the sample was then obtained as

$$Z_{means}(\omega) = \frac{T_s}{\Theta_0}. \quad (16)$$

TVR Data Processing

The shear modulus of the samples is estimated using a model-based inversion technique, see results in Fig. 5. Eqns. (13, 14) lead to a parametric model of the sample's torsional stiffness as $Z_{model}(\omega, r, L, k_e, k_1, \tau)$. In our experiment, the geometry parameters, r and L , and the frequency, ω , were known. Fitting this model to the measured data thus led to an overdetermined system for the three unknown model parameters. This was solved as a non-linear least squares minimization problem with the error functional

$$C(k_e, k_1, \tau, I) = \sum_{i=1}^N |Z_{means}(\omega_i, I) - Z_{model}(\omega_i, k_e, k_1, \tau)|^2. \quad (17)$$

Here, N is the total number of frequency points measured. Note, that the measured torsional stiffness in eqn. (17) is a function of the inertia correction parameter, I , from eqn. (15). A estimate for the SLS model parameters can be obtained by minimizing C :

$$[k_e, k_1, \tau, I] = \arg \min_{(k_e, k_1, \tau, I)} C(k_e, k_1, \tau, I) \quad (18)$$

This nonlinear minimization was performed using the routine *fminsearch* in the *Optimization Toolbox* in MATLAB® (MathWorks®, Natick, MA, USA). We included the inertia parameter, I , in the fitting optimization due to the uncertainty in the inertia correction applied by the rheometer software.

The novel TVR protocol was extensively validated before using it for the study. The optimization determined inertia I was validated using a blank measurement, i.e. a dynamic measurement with no sample present between the rheometer plates. In this measurement, the sample torque, T_s , in eqn. 15 is zero. Other validation steps included comparing results obtained using samples made of two different gel strengths and of different sizes. Repeatability of the results was studied while varying the normal contact force between plates, with and without a humidity control chamber, with and without sand-paper of two different grit-sizes, and studying linearity with the oscillating strain amplitude.

Shear Wave Elastography

The ARFI-SWE data acquisition and the data processing technique used for shear modulus estimation are described next.

SWE Data Acquisition

Acoustic Radiation Force Impulse (ARFI)-based ultrasound SWE was implemented on a Verasonics research ultrasound system (*Model V1, Verasonics, Inc., Kirkland, WA, USA*) at the *Brigham and Womens Hospital in Boston, MA*. The implementation was based on code from Nordenfur (2013). We used an *ATL L7-4* transducer, with 128 elements and an aperture of 38.4 mm, operated at its center frequency of 5 MHz. The sample and transducer setup is shown in Fig. 4(a). The cylindrical gel sample was placed on its side on a shape-conforming base of clear gelatin. The gelatin base preserved the cylindrical shape of the sample by minimizing stress concentration. It also reduced ultrasound reflection at the boundary. The ultrasound probe was held vertical and pointing down and it imaged a longitudinal section of the cylinder. A typical B-mode image is shown in Fig. 4(b). The SWE parameters are described in Fig. 4(c). A shear disturbance was excited using three ARFI pushes located along the center axis of the transducer aperture, at depths of 21.6, 20.2, and 18.8 mm, respectively. This corresponds to an F-number of approximately 0.5. The B-mode image in Fig. 4(b) shows the central ARFI push location. All three pushes were 100 μ s long with a wait time of 100 μ s between them. Three pushes were used mainly for the purpose of generating adequate signal. The distance between the three push locations is

small compared to the shear wavelength. The resulting shear wave was tracked for 10ms starting 1ms after the last push pulse, with an imaging pulse repetition frequency (PRF) of 10 kHz. Compounding was performed with 3 angles (-8° , 0° , 8°). During the 1ms before the first frame was measured, the P-waves had traveled about 1.5 meters, or well beyond the 38 mm wide ROI.

SWE Data Processing

We separated the shear wave pulse propagation measured in the time domain into its temporal frequency components via a Fourier transform to obtain shear wavefields at individual frequencies. ARFI excitation includes a range of excitation frequencies, and bandwidths from 50 Hz up to 1000 Hz have been reported in the literature (Hall et al., 2013). In our measurement, we obtained useful signal in wavefields in the frequency range 100–1000 Hz for the soft gelatin samples and 200–1800 Hz for the stiff gelatin samples, with a peak in the energy content of the shear waves in the 500–800 Hz range. The shear wavefield encodes the complex wavenumber of the shear wave, which is related to the shear modulus and the density of the medium.

Dispersion, i.e. frequency dependence of shear wave speed, can be characterized by estimating phase speed instead of group speed in ARFI-based SWE (Catheline et al., 2004), (Deffieux et al., 2009), (Chen et al., 2009). Measuring shear wave attenuation of the medium has proved much more challenging (Nenadic et al., 2017), (Rouze et al., 2015). Shear waves attenuate due to both material damping and geometric spreading. To estimate the attenuation caused by the medium, therefore, geometrical spreading must be taken into account. We adopted the approach in Yengul et al. (2018), in which a forward model of viscoelastic shear wave propagation suitable for ARFI-SWE was proposed. A key feature of this model is that it makes no assumption about the nature of geometric spreading of the wavefront, nor about the direction of shear wave propagation. Instead, it relies on the assumption that the source distribution is axisymmetric and confined to a small cylindrical region ($r < r_0$) near the axis of symmetry, and that the medium through which the wave propagates is homogeneous, linearly isotropic, and infinite. An inversion technique based on this forward model was used to obtain a robust estimate of the complex shear wavenumber, k_s , at individual temporal frequencies. The frequency dependent phase speed and shear wave attenuation can be calculated from the complex wavenumber, k_s .

To explain the application of this technique briefly, we represent the imaging plane in cylindrical coordinates (r, z) based on the assumption of axisymmetry about the excitation axis ($r=0$), and consider the measured time-domain shear wave propagation data, $u_z^M(r, z, t)$ (r, z, t). Here, the subscript z represents the axial, or depth, component of the particle displacement, u , and the superscript M indicates that it is a measured quantity. This spatio-temporal data is first separated into individual frequency components via a Fourier transform along the time dimension, to obtain $U_z^M(r, z, \omega)$. Then for each frequency, ω , the measured wavefield, U_z^M , is fitted to a predicted wavefield, $U_z(r, z, \omega, k_s)$, based on the forward model. The complex shear wavenumber, k_s , is found by minimizing the least squares difference

between the measured and predicted wavefields outside the source region, i.e. in the region $\Omega(r > r_0)$. This model-measurement mismatch was defined as

$$C(k_s, w) = \frac{\int_{\Omega} |U_z^M(r, z, w) - U_z(r, z, w; k_s)|^2 dr dz}{\int_{\Omega} |U_z^M(r, z, w)|^2 dr dz}. \quad (19)$$

The cost function (19) is minimized iteratively in three steps: (i) Choose a suitable radius r_0 and an initial guess $[Re(k_s), Im(k_s)]$. (ii) For the current guess, k_s , evaluate U_z based on the forward model, and finally (iii) Iteratively update k_s to minimize (19):

$$k_s^{opt}(w) = \arg \min_{k_s} [C(k_s, w)]. \quad (20)$$

The minimization was performed using the routine *fminsearch* in the *Optimization Toolbox* in MATLAB® (MathWorks®, Natick, MA, USA). The result was a set of two real positive numbers $[Re(k_s), Im(k_s)]$, that comprise the complex wavenumber, k_s . Based on an assumed value of mass density, ρ , the complex shear modulus can then be computed using the relations

$$c_s = w/k_s, \quad (21)$$

$$\mu = \rho c_s^2. \quad (22)$$

Choice of the initial guess for $Re(k_s)$, $Im(k_s)$

The initial values of $Re(k_s)$, $Im(k_s)$ in the optimization in eqn. (20) were obtained from fitting the phase and amplitude attenuation, respectively, of the measured wavefield in a narrow region near the source depth, located at $z \approx 19$ mm. This approach may be thought of as an application of shear wave spectroscopy (Deffieux et al., 2009). Estimating k_s by this method required assumptions about the direction of propagation (that the shear wave propagates laterally, or perpendicular to the excitation axis) and the geometric spreading of the wavefront. We arbitrarily chose spherical spreading for the initial guess, with the knowledge that any idealized assumption leads to an inaccurate estimate of the attenuation. The inaccuracy caused by these assumptions is mitigated by the optimization described in (eqns. 19,20).

Choice of Source Region ($r < r_0$)

In ARFI excitation, the force distribution is determined by the ultrasound transducer parameters, the excitation settings and the properties of the material medium, the latter of which are usually unknown. As a result it may be difficult to know a priori the source region ($r < r_0$) in the model. Indeed, due to the diffuse nature of the forcing, in the strictest sense of its definition, r_0 was larger than the aperture of the measuring transducer. However, since the radiation force was focused at a known location and its amplitude dropped rapidly away from the focus, a practical approximation was possible. We can define r_0 as the radius which when used with the forward model defined in Yengul et al. (2018), leads to the minimum deviation between the measured and fitted wavefields, eqn. (19). In other words, this approximation assumes that there is negligible contribution to the wavefield from the forcing that lies outside of the cylindrical region $r < r_0$ in comparison to measurement noise. An optimal r_0 was thus determined as the r_0 that gives the best match between the measurement and the forward model over all frequencies in the measurement bandwidth. The model mismatch over all frequencies was quantified as a residual, $\mathcal{R}$, defined as:

$$\mathcal{R}(r_0) = \frac{\sum_w \int_{\Omega(r_0)} |U_z^M(r, z, w) - U_z(r, z, w; k_s^{opt})|^2 dr dz}{\sum_w \int_{\Omega(r_0)} |U_z^M(r, z, w)|^2 dr dz}, \quad (23)$$

$$r_0 = \underset{r_0}{\operatorname{argmin}} \mathcal{R}(r_0) \quad (24)$$

The optimizations defined in (eqns. 20, 24) were performed in a nested fashion to arrive at one optimal r_0 and a corresponding frequency dependent shear wavenumber $k_s(\omega)$ for each SWE measurement.

In computing the measured wavefields, we truncated the time-domain data when the shear wave pulse reached the edge of the region of interest (ROI), which in this case was the width of the imaging transducer. The slower shear waves in the soft gelatin reached the boundary of the ROI in about 100 ms, while the faster waves in the stiff gelatin only needed about 50 ms to reach the boundary. With an imaging PRF of 10 kHz, the frequency resolution in the Fourier transform was therefore 100 Hz in the case of the soft gelatin and 200 Hz in the stiff gelatin. Using the procedure described above, frequency dependent storage and loss modulus estimates were obtained from the measured ARFI-SWE data: 3 measurements each in all six gelatin samples.

Results

Six samples of gelatin were measured twice with TVR and thrice with ARFI-SWE in an interleaved manner, leading to a total of $6 \times 5 = 30$ measurements of the shear storage and loss moduli as functions of frequency. As mentioned earlier, all measurements were performed on the same day to minimize the impact of material aging. The temperature of the samples over all 30 measurements varied between 21.5–22.9°C. The maximum T over the 5 measurements of any one sample was 1.2°C (for sample Soft-1), and the difference was typically well under 1°C for the other samples. Mass measurements of the samples during the course of all the measurements showed less than a 0.7% change overall and typically less than a 0.5% change. The data and results from a typical TVR measurement are presented in Fig. 5. Figs. 5(a) & (b) show the measured torsional stiffness and corresponding model-fit, (eqn. 13), for one soft and one stiff gelatin sample, respectively. Figs. 5(c) & (d) show the resulting frequency dependent storage and loss moduli for the corresponding samples as described by the optimally fit parameters, (eqn. 18). The optimally fit parameters of the SLS model for two measurements each on all six samples are presented in Table 1.

Data processing for the SWE measurements on one soft and one stiff gelatin sample is described in Figs. 6 & 7, respectively. The figures illustrate the model-based inversion technique for one wavefield at a temporal frequency of 400 Hz for both samples. The overall model mismatch, defined as the residual $\mathcal{R}$ in (23), was typically about 5%, and less than 7.5% for all 18 SWE measurements (6 samples $\times$ 3 SWE measurements each). Results from the interleaved measurements on the six samples were compared to study both intra-sample (Fig. 8) and inter-sample (Fig. 9) variation of the estimated shear storage and loss moduli. Fig. 8 shows the three SWE and two TVR measurements of one soft gelatin and one stiff gelatin sample. Fig. 9 shows the shear modulus estimates of the three soft and three stiff gelatin samples separately. The individual curves represent an average of the three SWE and the two TVR measurements for each of the three samples of both kinds of gelatin. For the samples that were stored and handled identically the inter-sample variation was found to be small, i.e. the three soft gelatin samples yield shear moduli estimates that showed good agreement, and so did two of the stiff gelatin samples. As mentioned earlier, the sixth sample (one of the stiffer gelatin samples) was subjected to significant SWE measurement and exposure to the environment a day prior to the main data collection. Figs. 9(c),(d) show that the differential handling of this sample resulted in a significant increase in the measured shear storage modulus, though not in its loss modulus. This observation is discussed below.

The low intra- and inter-sample variation observed in the TVR and SWE measurements allowed for studying the shear dispersion in the three soft and two stiff gelatin samples. Fig. 10 shows wide frequency-band characterization of the viscoelastic shear modulus of the two gelatin materials. The precision of these measurements at each frequency was quantified via the measurement variability as: $100 \times \|\delta\mu' - i\delta\mu''\|/\|\mu' - i\mu''\|$, where $\delta\mu$ is the largest measured excursion from the mean value at each frequency. For the SWE measurements, the maximum variability was lower than 4.7% at all measured frequencies, with a mean variability of 2.5%. The TVR measurements for the stiffer gels showed similarly low variability, with a maximum variability below 3.7% at all frequencies from 1 – 100 Hz. In

the softer gels, the TVR variability was higher, with an average of 7.4% and a peak of 16% at 100 Hz.

Discussion

The temperature and moisture controlled measurement strategy (e.g., see Fig. 1b) resulted in low variability between measurements. No trend was visible in the two TVR and three SWE derived shear moduli estimates and the progressively increasing timestamps of the successive measurements (see e.g. Fig. 8). This indicated that the confounding factors associated with gelatin variability were controlled successfully over this limited set of measurements. Results in Fig. 8, 9 also show that both TVR and SWE permit precise frequency dependent measurement of the complex shear modulus, i.e. of both the storage (μ') and loss (μ'') moduli.

The storage modulus measured using TVR showed an increasing trend with frequency in both soft and stiff gelatin samples. This trend was consistent with SWE measurements in a higher frequency range, leading to a change of roughly 30–50% from low to high frequency. The loss modulus also varied significantly, and approximately monotonically, within the frequency range measured.

We note that the complex modulus inferred from TVR measurements is obtained via parameter estimates in a standard-linear solid (SLS) model for the gelatin. Since this model has been validated only in the frequency range 1 – 100 Hz, i.e. the frequency range of the TVR measurements, it may not be assumed to apply outside this frequency range. In particular, this model may not predict the measured behavior at frequencies below 1 Hz, nor above 100Hz. We have not tested the validity of any model above 100 Hz.

For the softer samples, the loss modulus as measured by TVR was significantly higher at 100 Hz than the same quantity measured by SWE at 100 Hz. We attribute this to energy dissipation during the rheometer measurement caused by modes of vibration extraneous to the torsional vibration being measured and modeled in the data processing. Our visual observation of the experiment confirmed significant visible off-axis vibration of the soft samples during the higher frequency TVR measurements (between 50–100 Hz). Furthermore, we noted greatly diminished or no such extraneous vibrations in the stiffer samples, and in these samples, the loss modulus measurements by TVR and SWE are in closer agreement. Therefore, we believe the TVR measurement is overestimating the shear loss modulus, especially in the soft samples at higher frequencies. When these vibrations were present, TVR measurement variability was high; otherwise, precision (i.e. variability) was typically about 3 – 4%.

Comparison of SWE results between the soft and stiff gelatin samples indicated that the usable frequency range of ARFI-SWE depends on sample properties. The model based inversion scheme yielded precise shear modulus estimates in the frequency range 100–1000 Hz for soft gelatin samples, and in the range 200–1800 Hz in the stiffer gelatin samples. The shift to a higher usable frequency range in stiffer gelatin was partly due to the comparatively larger wavelengths in the stiffer gel. The lower frequency limit was determined by the fixed

38 mm imaging width of the L7–4 transducer which limited the number of wavelengths that could be observed in the wavefield; this problem was most acute in the stiffer gel at low frequency values, where wavelength was longest. The higher frequency limit was mostly determined by signal-to-noise considerations, a problem most acute at higher frequencies.

The impact of measurement noise was much greater on the estimation of shear wave amplitude attenuation than on the estimation of phase. Measurement noise therefore presented an additional challenge for shear loss modulus estimation. The inversion technique based on the model developed in Yengul et al. (2018) enabled the use of the entire measured wavefield for parameter estimation thereby benefiting from averaging. This mitigated the corrupting influence of noise and as demonstrated in Yengul et al. (2018), allowed precise measurements of μ'' over a wider frequency band than was possible with our implementation of shear wave spectroscopy (Deffieux et al., 2009). This coupled with the ability of the model to capture the exact geometric spreading and polarization of the excited shear waves enabled more accurate estimation of the complex shear modulus than is possible when these effects are neglected (Nenadic et al., 2017; Rouze et al., 2015).

The frequency ranges of the two measurement techniques in this study, TVR and ARFI-SWE, had no overlap. This is a limitation of our study, in that the independent methods cannot cross validate one another. Instead, the results can be seen as a wide-band characterization of the complex shear modulus (or dispersion) in gelatin hydrogels using two independent measurements of the same physical samples.

Given the wide frequency range of the measurements here, the frequency dependence of the shear storage and loss moduli were plotted on log-log plots. Linear scale plots of the same quantities give a very different impression of the frequency dependence, see Fig. 11, which plots exactly the same data as Fig. 10 (a, c) on a linear scale. In particular, we note that a linear extrapolation to zero frequency of the shear modulus as quantified by SWE disagrees with quasistatic measurement of shear modulus provided independently here.

These observations about the frequency dependence of mechanical properties may help explain variations reported in elastography validation studies. For example, Oudry et al. (2014) compared four techniques, namely, quasi-static compression, dynamic mechanical analysis, vibration controlled transient elastography and hyper frequency viscoelastic spectroscopy, and found significant variance and bias across the measurements, which they speculated was due to dispersion. Indeed, different techniques/vendors often correspond to mechanical excitations at different frequencies, possibly explaining in part the observed discrepancies. Both Mulabecirovic et al. (2016) and Franchi-Abella et al. (2017) assessed strain and shear wave elastography performance in calibrated gel phantoms with inclusions (CIRS®, Norfolk, VA, USA) and found high reproducibility within individual techniques but significant biases between them. Okamoto et al. (2011) compared magnetic resonance elastography (MRE) measurements in the 100–400 Hz frequency range to a novel dynamic shear test (20–200 Hz range) and found reasonable agreement in the shear storage modulus estimates (about 10% variation) but significant differences in the shear loss modulus estimates. Kishimoto et al. (2017) compared ultrasound-based point SWE and MRE to rheometry on 5 homogeneous phantoms and found a relative difference between –25% to

+25% in SWS estimates. In all of these cases, dispersion may be responsible for differences between values reported by different methods.

Gelatin Hydrogels for Elastography Comparison

Gelatin hydrogels have tissue-like acoustic properties, i.e. the speed of sound and P-wave attenuation are similar to those of biological tissues, and this similarity makes them a popular choice for ultrasound imaging and elastography. Moreover, gelatin is readily available, relatively cheap and is easy to manufacture. Gelatin hydrogels also exhibit linearly elastic mechanical properties up to relatively large strains of 10% or more (Hall et al., 1997). Furthermore, imaging contrast with ultrasound, MRI and elasticity imaging are independently tunable. Agar-based hydrogels were also considered for this study, but in our experience at least, the addition of ultrasound scattering agents like graphite or talc tended to make the material too brittle. In contrast, gelatin hydrogels were more tolerant to both of these scattering agents.

In spite of these desirable characteristics, gelatin hydrogels present significant challenges when used for the purpose of quantitative elastography comparisons. In particular, the elastic properties of these gels are highly sensitive to temperature, material aging (Hall et al., 1997), moisture loss and testing histories. These potentially confounding factors must be carefully controlled and accounted for before a meaningful comparison can be made. Strategies such as temperature controlled storage, same day measurements, identical handling, and an interleaved measurement protocol may prove necessary.

Identical vs. Similar Samples for Mechanical Testing

When making imaging phantoms, it is common practice to fill a mold of a desired shape with gel, and then to pour the same gel into a separate mold to create a test sample. Mechanical or other testing can be performed on the test sample thereby providing the properties of the gel used to make the imaging phantom. The inter-sample variability found in this study both partially justifies and partially invalidates this practice, however. The inter-sample variability on samples that were handled identically was found to be small. However, the mechanical properties of a sixth sample, that was subjected to significant SWE measurements a day prior to the main data collection, were found to change significantly due to the additional environmental exposure, see Fig.9(c). This shows that handling and use of an imaging phantom may alter its properties relative to those of a test sample, and vice versa, depending on how the two samples are stored, handled, and tested.

Conclusions

Torsional vibration rheometry (TVR) allowed independent mechanical testing of ARFI-SWE samples thereby eliminating two potential confounding factors in comparing or combining results: One being that mechanical test samples are different (typically much smaller in size) from elastography samples, and the other being that unequal handling of the samples can significantly alter their mechanical properties.

ARFI-SWE was shown to be capable of quantifying complex shear modulus in homogeneous gelatin hydrogels with an average precision better than 3% of the complex

modulus magnitude, and a worst-case precision of 4.7%, over about a decade of frequency. By contrast, the precision of TVR measurement was below 4% in the stiffer set of samples, but as high as 16% in the softer samples at higher frequencies where extraneous vibrations were visible. ARFI-SWE based complex shear modulus quantification in this study exhibits greater precision and is based on fewer assumptions than previous studies.

Gelatin is a material that is frequently claimed to be non-dispersive, yet our measurements demonstrate that even a relatively simple material like gelatin exhibits significant variation in its shear-elastic properties when measured over a wide frequency band. Therefore, in comparing measurements of elastic properties made by different elastography systems to one another, one must also somehow account for their frequency dependence.

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Appendix A.: Clarification of nomenclature for elastic parameters used here

A variety of different symbols and names are used to describe tissue mechanical properties in elastography literature. Here we attempt to clarify the different uses.

In MRE studies, the shear modulus is usually denoted by G and reported as a single real value, typically in units of Pa (pascals) or kPa (kilopascals = 1000 pascals). In the field of solid mechanics, both G and μ are used to denote shear modulus, with the latter symbol more prominent in mathematical treatments of the subject.

In viscoelastic materials, the shear modulus may be modeled as complex and frequency-dependent. That is:

$$G(w) \equiv \mu(w) = \mu' - i\mu'' \quad (\text{A.1})$$

This change to complex modulus is analogous to complex electrical impedance in electrical circuit analysis. The real component (μ') is called the shear storage modulus, and represents the elastic stiffness of the medium. The imaginary component (μ'') is called the shear loss modulus. The names “storage modulus” and “loss modulus” arise from their respective contributions to the storage/loss of strain energy during the shear deformation of the viscoelastic medium.

The shear loss modulus, μ'' , is directly related to viscosity, often denoted by η , and measured in units of Pa-sec, or stress per strain-rate. More precisely, if we denote by $\eta(\omega)$ the viscosity at a given frequency, then

$$\mu'' = \omega\eta. \quad (\text{A.2})$$

Young's modulus, E is related to $G \equiv \mu$. In an incompressible medium (i.e. one which is much easier to distort than to compress), the relationship is particularly simple,

$$E = 3G \equiv 3\mu. \quad (\text{A.3})$$

This is a reason why some elastography studies report Young's modulus estimates even though they actually measure the shear modulus. In those cases where μ is treated as complex, E as given in (A.3) would also naturally be complex.

The shear attenuation coefficient, denoted by α (Nenadic et al., 2017; Lipman et al., 2018), is related to the shear modulus through the complex shear wave number, k_s , which can be written as

$$k_s(w) = k(w) + i\alpha(w), \quad (\text{A.4})$$

where $k(\omega)$ is the real part of the complex wavenumber. If the density of the medium, ρ , is known, the shear modulus can be evaluated using the relation

$$\mu(w) = \rho c_s^2 = \rho \left(\frac{w}{k_s} \right)^2 \quad (\text{A.5})$$

$$= \frac{\rho w^2}{(k^2 + \alpha^2)} \left[1 - i \frac{2\alpha k}{(k^2 + \alpha^2)} \right]. \quad (\text{A.6})$$

In the special case when $\alpha \ll k$, this equation simplifies to

$$\mu(\omega) \approx \frac{\rho w^2}{k^2} \left[1 - i \frac{2\alpha}{k} \right]. \quad (\text{A.7})$$

Appendix B.: Elastic-Viscoelastic Correspondence Principle

The equation of motion in a solid with zero body force is given by (Mal and Singh, 1991)

$$\nabla \cdot \sigma = \rho \frac{\partial^2 u}{\partial t^2}. \quad (\text{B.1})$$

Here, σ is the stress, ρ is the mass density, and $u(x, t)$ is the displacement field. Under the assumption of small displacement gradients, the strain-displacement relationship can be written as (Mal and Singh, 1991)

$$2 \epsilon_{ij} = \frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i}. \quad (\text{B.2})$$

This linearized strain tensor is accurate for small deformations, for which the components of the displacement gradient tensor are small compared to unity (i.e., $\left| \frac{\partial u_i}{\partial x_j} \right| \ll 1$). Equations (B.

1) and (B.2) apply to either elastic or viscoelastic solids. Whether a solid is one or the other depends on the constitutive equation, or stress-strain equation.

For an isotropic elastic solid, the relation between stress, σ , and strain, ϵ , can be written as (Mal and Singh, 1991)

$$\sigma_{ij} = \lambda' \delta_{ij} \epsilon_{kk} + 2\mu' \epsilon_{ij}. \quad (\text{B.3})$$

Here, $[\lambda', \mu']$ are the classical Lamé parameters. The so-called correspondence principle allows us to use an equation similar in form to (B.3) to model a viscoelastic solid in the frequency domain as shown below.

Appendix B.1. Special Case: Kelvin-Voigt Viscoelastic Model

For a viscoelastic medium modeled using the Kelvin-Voigt viscoelasticity model, the stress-strain relation in eqn. (B.3) can be enhanced to include viscous effects as follows:

$$\begin{aligned} \sigma_{ij} = & \lambda' \delta_{ij} \epsilon_{kk} + 2\mu' \epsilon_{ij} \\ & + \eta_d \delta_{ij} \frac{\partial \epsilon_{kk}}{\partial t} + 2\eta \frac{\partial \epsilon_{ij}}{\partial t}, \end{aligned} \quad (\text{B.4})$$

such that, the two additional parameters, $[\eta, \eta_d]$, together model shear and bulk viscous effects. We now consider time harmonic response, where the displacement field can be written as

$$\mathbf{u}(\mathbf{x}, t) = \text{Re} \left\{ \mathbf{U}(\mathbf{x}) e^{-i\omega t} \right\}. \quad (\text{B.5})$$

Similar time dependence extends to the stress and strain variables, by substituting (B.5) in (B.4) and (B.2). Thus, the stress-strain relationship, in the frequency domain, becomes:

$$\sigma_{ij}(w) = \lambda' \delta_{ij} \epsilon_{kk}(w) + 2\mu' \epsilon_{ij}(w) - iw\eta_d \delta_{ij} \epsilon_{kk}(w) - iw2\eta \epsilon_{ij}(w) \quad (\text{B.6})$$

$$= \lambda(w) \delta_{ij} \epsilon_{kk}(w) + 2\mu(w) \epsilon_{ij}(w) \quad (\text{B.7})$$

Where

$$\lambda(w) = \lambda' - iw\eta_d \quad (\text{B.8})$$

$$\mu(w) = \mu' - iw\eta. \quad (\text{B.9})$$

Comparing eqns. (B.7) and (B.3) shows that this particular form of viscoelastic constitutive equation, i.e. the Kelvin-Voigt model, has the same form as the purely elastic constitutive equation (B.3), with complex-valued and frequency dependent $\lambda(\omega)$ and $\mu(\omega)$ in place of the classical real-valued Lamé parameters.

Appendix B.2. General Linear Viscoelasticity

Equations (B.7)–(B.9) show how, through the specific example of a Kelvin-Voigt model of viscoelasticity, a viscoelastic solid may be represented with the same type of constitutive equation as a corresponding elastic solid, simply by treating the Lamé coefficients, λ and μ , as complex rather than real. This is known as the elastic-viscoelastic analogy or the “correspondence principle” in viscoelasticity (Findley et al., 1989). Indeed, as described in Findley et al. (1989), all linear isotropic viscoelastic models may be written in the frequency domain in the form of equation (B.7), with appropriately chosen functions $\lambda(\omega)$ and $\mu(\omega)$. Therefore, the problem of characterizing the linear viscoelastic behavior of a medium may be reduced to that of determining the frequency-dependent functions, $\lambda(\omega)$ and $\mu(\omega)$.

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(a)

(b)

Figure 1: Rheometry vs. Torsional Vibration Rheometry:

(a) Rheometry is traditionally performed on a thin disc. Shown here is a 3mm thick gelatin disc (blue in color) sandwiched between the fixed bottom plate and the moving 40mm diameter top plate of a TA Instruments AR 2000 rheometer. (b) Modifications were done to both hardware and software to allow larger samples. The 70mm tall gelatin cylinder used in this study is shown mounted in the same rheometer. An acrylic environment chamber was custom designed to prevent moisture loss from the sample during the measurement by stabilizing the humidity level.

Figure 2: Torsional Dynamics Model:

The magnitude and phase of the normalized torsional stiffness of a cylinder of length L , fixed at one end, is plotted as a function of the normalized frequency parameter, $0.01 \leq \text{Real}\{k_s L\} \leq 20$. The magnitude of Z has been normalized by the low frequency asymptotic value, $Z_0 = \frac{\mu J}{L}$. In this plot, the cylinder material is modeled as a homogeneous, isotropic, and non dispersive viscoelastic medium with a damping factor $\tan(\delta) = 0.1$. Traditional rheometry using thin sample discs operates in the low frequency regime where the stiffness is real and constant. Torsional Vibration Rheometry, on the other hand, operates over a wider frequency band and exploits torsional resonances in the higher frequency regime.

Figure 3: Rheological Material Models:

The characteristic frequency dependence of the storage and loss moduli in four linear viscoelastic models is shown above. The Kelvin-Voigt model (b) and the Maxwell model (c) are both special cases of the standard linear solid model (a) which was used in processing the torsional vibration rheometry measurements in this study. The linear dispersion model (d) assumes a linear relationship between shear wave speed, c_s , and frequency, f , and the blue curve shown is the real shear storage modulus, $\mu = \rho c_s^2$. The parameter values used in these plots were: (a) $k_e = 10$; $k_i = 20$; $\eta = 0.1$; (b) $k = 10$; $\eta = 0.1$; (c) $k = 20$; $\eta = 0.1$; (d) $c_1 = 3.2\text{m/s}$ at 1Hz ; slope $m = 2.3\text{m/s/kHz}$. The spring stiffness values are in kPa, and the dashpot, η , is in kPa.s.

Figure 4: Shear Wave Elastography Setup:
(a) The cylindrical gelatin sample was placed on a shape conforming gelatin bed and the L7–4 transducer was setup to image a cross-section through the axis of the cylinder. (b) B-mode image showing the push location (red + symbol) and the region of interest (blue inset rectangle) used for data processing. (c) The parameters of the Verasonics based acoustic radiation force impulse (ARFI-)SWE implementation and transducer parameters.

Figure 5: Torsional Vibration Rheometry Results:

The red dots in plots (a) and (b) show the measured magnitude and phase of torsional stiffness of gelatin samples, Soft-1 in (a) and Stiff-1 in (b), at 67 individual frequencies spaced linearly in the range 1–100 Hz. The measurement is fitted to the torsional dynamics model in eqn. (13). The optimal fit, shown as the blue curve in (a) and (b), determines the SLS model parameters $[k_c, k_1, \eta]$ (center schematic). Plots (c) and (d) show the frequency dependent storage, μ' , and loss, μ'' , shear moduli for the corresponding samples. The optimally fit SLS model parameters for sample Soft-1 were [2.40 kPa, 1.79 kPa, 1.46 Pa·s] and for sample Stiff-1 were [12.4 kPa, 1.47 kPa, 3.07 Pa·s].

Figure 6: ARFI-SWE Result in Soft Gelatin:

Application of the forward model of shear wave propagation developed in Yengul et al. (2018) to an ARFI-SWE measured wavefield at 400Hz in a soft gelatin sample. (a) The real part of measured complex wavefield. (b) The propagated wavefield based on the axisymmetric propagation model. The model is valid outside the source region, or $r > r_0$, demarcated by the vertical lines. (c) The difference (a - b). The red solid and blue dotted lines in (a, b) show a cross section through the wavefields at the approximate push depth, i.e. at $z = 19\text{mm}$. The same color scheme is used to plot the phase angle, the normalized amplitude, and the normalized real part of the measured and propagated wavefields at this depth in (d,e,f) respectively, as functions of radial distance from the (assumed) axis of symmetry. The measured amplitude (e) is noisier than the phase (d) as expected. The source region which is not used in the data-fit is greyed out in (d-f).

Figure 7: ARFI-SWE Result in Stiffer Gelatin:

Application of the forward model of shear wave propagation developed in Yengul et al. (2018) to an ARFI-SWE measured wavefield at 400Hz in a stiffer gelatin sample. These plots are exactly analogous to the plots in Fig. 6. Of note is that the shear wavelength at 400Hz is about twice as large in the stiffer gelatin and so fewer wavelengths can be observed in the fixed imaging width of the linear L7-4 transducer. Also notable is that the optimally determined source region, $r - r_0$, (see eqn. 24), demarcated by the solid black lines in (a–c) and the greyed region in (d–f), is wider than the corresponding source region in softer gelatin. Furthermore, (d–f) are plotted on the same y-scale as (d–f) in Fig. 6 showing that with identical ARFI-push settings, the shear wave amplitude at 400Hz in the stiffer gelatin is significantly smaller.

Figure 8: Intra-sample Variation:

Results from the interleaved measurement protocol consisting of 2 TVR and 3 SWE measurements of shear storage and loss moduli in one soft gelatin sample figs. (a, b) and one stiff gelatin sample figs. (c, d) are shown here. TVR operates in the low frequency range from 1–100Hz while SWE results are in the range 100–1000Hz in soft gelatin, and 200–1800Hz in stiff gelatin.

Figure 9: Inter-sample Variation:

Plots showing the mean of two TVR and three SWE measurements of shear storage and loss moduli in 3 soft gelatin, figs. (a, b), and 3 stiff gelatin, figs. (c, d), samples. The three soft gelatin samples exhibit only small differences in their measured shear moduli and so do two of the 3 stiff gelatin samples. However, the third stiff gelatin sample which was subjected to a different handling protocol exhibited a significant increase in its shear storage modulus, though not in its shear loss modulus.

Figure 10: Summary of Shear Modulus Measurements in Gelatin:

The shear storage and loss moduli estimates for the soft gelatin samples are shown in plots (a,b) and those in the stiffer gelatin samples are shown in plots (c,d). The blue curves show the mean of the two TVR measurements each in 3 soft and 2 stiff gelatin samples. The grey region shows the min-max range of these TVR measurements. The red data points in the higher frequency range show the mean modulus estimates from 3 SWE measurements of each of the same samples at individual frequencies, i.e. 9 SWE measurements in soft gelatin and 6 SWE measurements in stiff gelatin. The error bars are the min-max range of these SWE measurements.

Figure 11: Shear storage modulus plotted on a linear frequency scale:

The same data plotted on a log-log scale in Figs. 10(a,c) are replotted here on a linear scale. These plots give a very different impression of the frequency dependence. In particular, the low-frequency linear extrapolation of the storage modulus is clearly inconsistent with the low frequency measurements in gelatin. This suggests that a linear extrapolation to zero frequency of shear storage modulus estimates as quantified by SWE is likely to disagree with quasi-static measurement of the shear modulus.

Table 1:

Torsional Vibration Rheometry results: The optimally fit parameters of the SLS rheological model obtained for two measurements each on the six samples is shown below. Recalling that the Kelvin-Voigt model is a special case of the SLS model used for the fit, we note that in 3 of the 12 measurements, the optimally fit parameters resulted in a nearly Kelvin-Voigt like frequency dependence of the shear storage and loss moduli, while the other 9 are best described by the SLS model over the frequency range 1–100 Hz.

Sample type-#	Meas. #	K_e [kPa]	k_1 [kPa]	η [Pa·s]
Soft-1	1	2.40	1.79	1.46
	2	2.41	1.84	1.54
Soft-2	1	2.46	9.5×10^3	2.16
	2	2.45	5.1×10^3	2.19
Soft-3	1	2.39	12.4×10^3	1.77
	2	2.42	1.55	1.62
Stiff-1	1	12.4	1.47	3.07
	2	12.0	1.96	3.37
Stiff-2	1	11.9	1.50	3.00
	2	11.4	1.93	3.48
Stiff-3	1	18.5	2.35	2.91
	2	18.0	2.65	3.02