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Multi-frequency Rayleigh damped elastography: *in silico* studies

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ABSTRACT

Rayleigh damping (RD) is commonly used to model energy attenuation for analyses of structures subjected to dynamic loads. In time-harmonic Magnetic Resonance Elastography (MRE), the RD model was shown to be non-identifiable at a single frequency data due to the ill-posed nature of the imaginary components describing energy dissipation arising from elastic and inertial forces. Thus, parametrisation or multi-frequency (MF) input data is required to overcome the fundamental identifiability issue of the model. While parametrisation allows improved accuracy of the identified parameters, simultaneous inversion using MF input data is a prerequisite for theoretical identifiably of the model. Furthermore, to establish good practical identifiability, frequencies should be separated over a wide range to produce different dynamic response. This research investigates the effects on practical identifiability of the RD model using MF data over different combinations of frequencies in noise-free heterogenous simulated geometry and compares the outcomes to reconstruction result based on single frequency input data. We tested eight frequencies *in silico* for a phantom type geometry comprises three independent material regions characterised by different mechanical properties. Combinations of two near or well separated frequencies are used to test the separation necessary to obtain accurate results, while the use of four or eight simultaneous frequencies is used to assess robustness. Results confirm expected non-identifiability of the RD model given single frequency input data. Practical identifiability of the RD parameters improved as more input frequencies were used for simultaneous inversion and when two frequencies were well separated. Best quality reconstruction results were achieved using full range data comprising eight available frequencies over a wide range. The main outcome is that high quality motion data over at least two frequencies over a wide range is required for establishing minimal practical identifiability of the model, while quality of the practical identifiability increases proportionally with more input frequencies used. Further simulation studies are required to determine acceptable signal-to-noise ratio (SNR) thresholds in motion data for accurate inversion of the RD parameters.

1. Introduction

Magnetic Resonance Elastography (MRE) quantitatively measures induced mechanical waves *via* phase-contrast MR imaging techniques [1,2]. Depending on the inverse problem methodology and constitutive model used, a number of parameters, describing mechanical properties of the material, can be estimated from the measured response data. Different models allow different parameters to be identified. For example, traditional linearly elastic [3–5] models can produce locally resolved maps of elasticity, also known as the stiffness or *storage modulus* (μ_R), while viscoelastic (VE) models [6–8] can provide additional information about viscosity or *loss modulus* (μ_I) of the material. However, more complex models, such as bi-phasic poroelastic [9] and Rayleigh damping (RD) models, incorporate additional parameters and, therefore, require higher quality motion data with adequate signal-to-noise ratio (SNR), as well as robust inversion methods for accurate parameter identification.

Model fit to the observed response is critical to accurate parameter identification. However, true parameter estimation cannot be assured only by data-model match condition. Structural model identifiability is another absolute prerequisite to ensure unique and correct parameter estimation [10,11]. While VE models can produce accurate estimation of the parameters given a single

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frequency of response data, RD models describe frequency dependent damping behaviour and rely on multi-frequency (MF) input data. Thus, accurate identification of the RD parameters is not possible given a single frequency of response data [12]. One way to overcome this limitation is to impose significant *a priori* information with a number of optimisation constraints and regularisation techniques under certain conditions and assumptions [13]. For example, parametrisation can be employed when only single frequency data is available [14]. However, this can only guarantee a limited trade off between data consistency and accuracy of estimated parameters. In fact, parametric approach is only recommended when a general qualitative profile of VE properties is sufficient.

Damping has long been recognised as an important property in characterisation of the tissue structure and composition. It is directly associated with the viscosity of the material and has been recently linked to various pathologies in different organs, such as the liver [15,16], the breast [17,18], muscle tissues [19,20], and the brain [8,21–25]. Depending on micro structural configuration tissue would undergo different behaviour under applied mechanical stress. For example, fluidic or tightly arranged cells will display different attenuation behaviour due to changes in physiological consistency and vasculature, such as may arise with cancerous tumours [26]. Thus, ability to accurately capture and quantify damping information within the tissue of interest might provide useful diagnostic merit and help in early disease detection and investigation of the pathological progression over time.

RD models are commonly used in structural dynamics, including automotive and civil structures [27]. They effectively extend the VE model, where damping is only defined by elastic forces, with the damping matrix represented as a scaled proportional combination of mass and stiffness terms. Thus, compared to the traditional VE model, the RD model incorporates an additional parameter to account for damping arising from viscous or *inertial* effects [28]. Previous phantom studies [29,30] showed sensitivity of the parameter to the material composition and ability to differentiate saturated porous tofu material from more tightly aligned course structure of the gelatine. Thus, it might provide valuable information for characterising tissue anatomy and might be particularly useful for imaging highly saturated structures, such as biological tissue. Since RD model renders two attenuation mechanisms governed by two different rheological effects, both elastic and inertial, it is hypothesised that the RD model can provide a more complete description of the intrinsic non-linear damping behaviour observed in the tissue *in vivo*.

RD models have been previously investigated *in silico* [29] and in phantom studies [31]. The latter only evaluated identification of elasticity and overall damping, while accurate identification of imaginary components was not assessed. Hence, it was structurally identifiable at that level. Further phantom experiments [30] demonstrated challenges of the MF approach and confirmed the necessity of the wide separation of the input frequencies, as well as selection of the appropriate frequency dependent model to account for the dispersion characteristics of the given materials. In this context, preliminary simulation studies demonstrated the potential to correctly identify RD parameters on simulated noise-free motions at a single frequency within a homogeneous geometry with a high level of damping present [29]. However, more complex heterogeneous geometries with varying spatial damping profile governed by different attenuation mechanisms have not been properly investigated. This research determines the requirements for the identifiability of the RD model in heterogeneous simulated geometry using single frequency and MF noise-free data for image reconstruction processing.

2. Materials and methods

2.1. RD model in time-harmonic MRE

The RD model is implemented through finite element (FE) based solution of a nearly incompressible linear isotropic Navier's equation, defined as

$$\nabla\cdot(\mu(\nabla\mathbf{u}+\nabla\mathbf{u}^T))-\nabla(\lambda\nabla\cdot\mathbf{u})-\nabla P=-\rho\frac{\partial^2\mathbf{u}}{\partial t^2}, \tag{1}$$

where $\mathbf{u}$ is the complex column displacement vector within the medium; λ is the first Lamé parameter ($\lambda = -1/3$ Pa for a nearly incompressible case), μ is the second Lamé parameter, also known as a shear stiffness; ρ is the density of the material, ∇P is a pressure term, related to volumetric changes through the bulk modulus, K, *via* the relationship: $\nabla P = K\nabla\cdot\mathbf{u}$.

It can be discretised and defined as

$$\mathbf{M}\ddot{\mathbf{u}}+\mathbf{C}\dot{\mathbf{u}}+\mathbf{K}\mathbf{u}=\mathbf{f} \tag{2}$$

for the mass, damping and stiffness matrices, $\mathbf{M}$, $\mathbf{C}$ and $\mathbf{K}$, respectively; displacement vector, $\mathbf{u}$, and known sinusoidal input forcing, $\mathbf{f}$. The RD assumption is facilitated through the RD definition:

$$\mathbf{C}=\alpha\mathbf{M}+\beta\mathbf{K}. \tag{3}$$

For a time-harmonic case, where input and resulting response are $\mathbf{f}(\mathbf{x},t)=\hat{\mathbf{f}}(\mathbf{x})e^{i\omega t}$ and $\mathbf{u}(\mathbf{x},t)=\hat{\mathbf{u}}(\mathbf{x})e^{i\omega t}$, Eq. (2) in the frequency domain is written as

$$\left[-\omega^2\left(1-\frac{i\alpha}{\omega}\right)\mathbf{M}+\left(1+i\omega\beta\right)\mathbf{K}\right]\hat{\mathbf{u}}=\hat{\mathbf{f}}. \tag{4}$$

By assuming stiffness and density to be complex, so that $\mu^*=\mu_R+i\mu_I$ and $\rho^*=\rho_R+i\rho_I$, Eq. (4) can be further simplified:

$$[-\omega^2\rho^*\mathbf{M}'+\mu^*\mathbf{K}']\hat{\mathbf{u}}=\hat{\mathbf{f}}, \tag{5}$$

where $\mathbf{M}' = 1/\rho(\mathbf{M})$ and $\mathbf{K}' = 1/\mu(\mathbf{K})$ are normalised mass and stiffness matrices, respectively. In particular, μ_R and ρ_R describe the real valued shear modulus and density in the undamped system. In contrast, μ_I and ρ_I represent two different damping components related to elastic and inertial effects, respectively. They both can be expressed in terms of the RD parameters:

$$\mu_I=\omega\beta\mu_R,\quad \rho_I=\frac{-\alpha\rho_R}{\omega}. \tag{6}$$

Rheologically, μ_R and μ_I represent storage and loss modulus of the material, while ρ_I is hypothesised to reflect fluid perfusion in a poroelastic media, such as biological tissue [12,30]. The resulting damping ratio, ξ_d, is defined as

$$\xi_d=\frac{1}{2}\left(\beta\omega+\frac{\alpha}{\omega}\right)\quad\Rightarrow\quad\xi_d=\frac{1}{2}\left(\frac{\mu_I}{\mu_R}-\frac{\rho_I}{\rho_R}\right), \tag{7}$$

where the stiffness proportional term ($\beta\omega$) contributes damping linearly proportional to the response frequency and the mass proportional term (α/ω) contributes damping inversely proportional to the response frequency. Therefore, the α and β coefficients govern the response to lower and higher input frequencies, ω, respectively.

Previous studies found correlation between biological tissue response to various excitation frequencies in a form of power-law (PL). More specifically, Fabry et al. [32] observed PL dependency of the complex shear modulus in variety of individual cell types subjected to number of excitation frequencies over a wide range (10–300 Hz). Similarly, Robert et al. [33] studied *ex vivo* liver specimens using MF based MRE in the range between 40 and 100 Hz and found PL trend in the dynamic response of the complex shear modulus.

A PL implies frequency dependant behaviour of the VE parameters, such as complex shear modulus, which can be derived from the fractional Zener and Kelvin VE models [34]. In this context, PL