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Structure-sensitive elastography: on the viscoelastic powerlaw behavior of *in vivo* human tissue in health and disease

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Elastography combines medical imaging with soft tissue mechanics and is used for the diagnosis of diseases associated with an altered stiffness of affected tissue. Beyond stiffness, dynamic elastography can measure viscoelastic constants sensitive to the network structure of polymers or biological materials. In this article current applications of *in vivo* multifrequency magnetic resonance elastography to healthy or diseased tissue are revisited in order to develop a unified framework for the interpretation of disease-related structural changes using viscoelastic powerlaw constants. The generalized view on different organs and processes such as liver fibrosis, neuronal tissue degradation, and muscle contraction reveals systematic signatures of the underlying microstructural changes to viscoelastic powerlaw constants. It is shown that *in vivo* powerlaw constants measured by elastography scale the mechanical properties of cellular networks into the macroscopic images obtained by magnetic resonance imaging (MRI) or ultrasound. This sensitivity to scales far below image resolution makes dynamic elastography an ideal diagnostic tool for the assessment of subtle alterations in living tissue occult to other medical imaging methods.

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Introduction

In terms of sensitivity, cost efficiency, side effects, and availability, manual palpation has outperformed all other diagnostic modalities for centuries. The high sensitivity of the palpating hand is related to the incredibly wide range of values of the shear modulus in the body, spanning over eight orders of magnitude: from fluids to bone.[1] This wide variation of values is unique in solid-state physics, in particular regarding living systems. Elastography was invented to exploit this high variability of constants by introducing the shear modulus into the image contrast of medical ultrasound[2,3] or magnetic resonance imaging (MRI).[4,5] From the heel fat pad to the brain, physicians are able to 'palpate' all kinds of body tissue using ultrasound elastography (USE) or magnetic resonance elastography (MRE). Today, both USE and MRE are in clinical use, predominantly for staging liver fibrosis or discriminating benign and malignant nodules in breast, liver, and prostate.[6–9]

Beyond classifying materials as being stiff or soft our haptic sensation can further distinguish between soft materials composed of densely cross-linked networks (as prevalent in biological tissue) or gel-like materials composed of relatively long but sparsely interlinked chains. This illustrates the sensitivity of our fingers to the scaling properties of viscoelastic constants: the effective (*i.e.*, global) elastic modulus tells us how much the strength and number of cross-links of the mechanical matrix of biological tissue is altered by diseases, while viscosity parameters are more related to geometrical aspects such as the shape of network elements, the peculiarity of branches, or their organization within the hierarchical lattice of mechanical building elements. For illustration, soft biological tissue and gel may present similar shear moduli, while they are haptically distinct due to differences in architecture on the level of cells or macromolecular chains.

Dynamic mechanical tests subsumed under 'rheometry' have been applied for decades for the mechanical-based analysis of microarchitectural properties of polymer samples. To this end, the sample is mechanically excited over a wide dynamic range for measuring the frequency dispersion of the complex shear modulus. Dynamic multifrequency elastography can acquire similar information in living soft tissue, leading us to hypothesize that elastography can be used to perform '*in vivo* rheometry' to unravel the microarchitecture of living tissue.

However, the global mechanical response to the microarchitecture of biological tissue is more complex and less understood than in polymers. The literature reports only a few elastography studies based on numerical simulations[10] and mouse models, which provide some insight into the relationship between the tissue's microstructure and the effectively measured viscoelastic constants.[11–14] In this article we examine

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