# Sub-Voxel Micro-Architecture Assessment by Scattering of Mechanical Shear Waves

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**Introduction:** Magnetic Resonance Elastography (MRE) is now a well-known technique capable of noninvasively assessing the mechanical properties of tissues. Recently, it has been hypothesized that propagation of waves at a macroscopic scale might be influenced by the presence of micro-obstacles and hence lead to an apparent viscosity that can be revealed when exploring the tissue at different frequency [1]. Few papers describe *in vivo* experiments using Multifrequency MRE (MMRE) and show that MMRE can be more sensitive to specific pathologies such as fibrosis or steatosis [2-3]. It has been shown on calibrated phantoms that the dispersion of viscosity with frequency can provide direct insight into the underlying microstructures [4-5]. However, even if these papers argue a physical model mainly based on statistical models, they do not show any agreement between experiment and theory. Therefore - as pointed out in a recent paper [6] - if no theoretical model exists to justify the use of a power law to fit MMRE data and to explain the link between the microscopic and the macroscopic world, critical questions will remain and limit the potential benefits of this technology. Therefore, in this study we investigate in experiments, simulations, and a theoretical model of shear wave propagation in phantoms containing accurately controlled size distributions of scattering particles and demonstrate that shear waves are able to reveal at the macroscopic scale the hidden micro-architectural properties of the material.

**Material and Methods:** Gel phantoms were fabricated using an agarose solution at 15g/L (BRL, Type 5510UB). In order to create well defined scattering particle size distributions, colloidal suspensions of polystyrene microspheres with precisely known diameter (10µm diameter, Sigma–Aldrich) and concentrations (1.25-20%) were added to the gel before solidification. MRE was performed on a horizontal 7T imaging scanner (Pharmascan, Bruker, Erlangen, Germany) (Figure 1). The MRE sequence (spin echo,, field of view of 30×30 mm$^2$, , 300x300µm in-plane and 0.4 mm slice resolution, TE/TR (ms)= 13-35/270-505, 8 samples for time encoding, excitation frequencies: 600-1000 Hz) was acquired for the three spatial directions of motion in order to obtain volumetric images of the 3D mechanical wave propagating inside the phantom. Data were reconstructed with an isotropic reconstruction technique [7]. Wave propagation has been simulated in 2D using the Diffpack finite element code [8]. For both numerical and experimental approaches, a power law fit was used to study the influence of micro–particle size concentration on the real part $\beta$ of the complex-valued wave vector $k=\beta+i\alpha$ (with $\beta$ referring to the propagation and $\alpha$ to the attenuation) and to find a formula for its frequency-dependence. For simulations, the sample was assumed to be a homogeneous elastic medium (no viscosity) which was filled with very stiff particles of a fixed sized. Theoretically, the heterogeneous medium can be described by a probability density function which represents for a constant and isotropic material the lag time distribution steering the effect of multiple reflections: a characteristic length separates the fractal and the Euclidean regions of anomalous and normal scattering of waves. This length $\zeta$ must follow the simple geometric relationship $\zeta\sim\rho^{-1/d}$, with $\rho$ the density of particles submersed in the homogeneous background. As demonstrated in [9] the real part of the Fourier transform of the lag distribution function is equal to the wave propagation coefficient $\beta$.

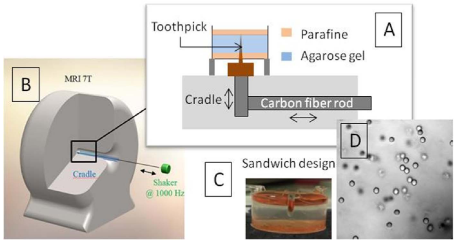


Figure 1: Phantom and experimental set-up. (A) A flexible carbon fiber rod transmits horizontal vibrations from a shaker to a toothpick mechanically coupled to the sandwich design phantoms (C) positioned in a 7T MRI scanner (B). (D) Confocal-microscopy image of the phantom with 1.25% in volume of 10 µm diameter microspheres.

**Results and Discussion:** Fig.2 compiles experiments, simulations, and theoretical results. Here, we present the slope of the frequency power-law fit $Y(\beta)$ as a function of particle density. At very low densities we observe slopes close to $Y(\beta)=1$ indicating a lossless material as expected for this type of background material. Interestingly, for increasing density of micro-particles a significant deviation from $Y(\beta)=1$ is observed with a minimum around 5%. Hence, scattering leads in this bandwidth of particle density to apparent viscosity dramatically changing the dispersion properties of the shear waves. When further increasing the density, the slope of $\beta$ approaches $Y(\beta)=1$, as expected. Quantitative differences between experiment and simulations are most likely due to the difference in dimensionality (2D vs 3D). It is however remarkable that our theoretical model based upon multiple reflections is capable to precisely predict the evolution of the dispersion as a function of particle density for the 3D experimental data.

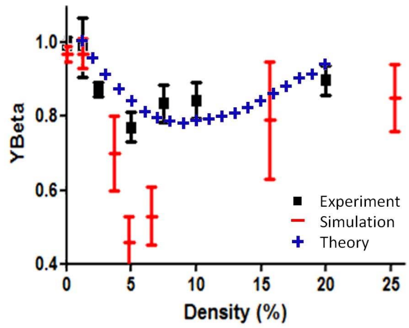


Figure 2: exponent of the power law fit for the wave propagation coefficient: good qualitative agreement between experiment, simulation and theory.

**Conclusion and Perspectives:** We demonstrated by simulation, experiment, and theory that the frequency-dependence of mechanical shear wave scattering can reveal the underlying micro-architecture even within one single voxel. We developed a theoretical framework based upon the geometrical description of the scattering particles in combination with multiple scattering of the shear waves. It actually predicts power law behavior for the frequency evolution of $\beta$ without any a-priori imposition of this property! As shown, the theory matches the data. Hence, we can thereby relate observed slopes for $\beta$ to underlying obstacle densities! We expect this technique to allow assessing fundamental information: for instance data measured at the macroscopic level providing information about micro vasculature of tumors, which is crucial for efficacy monitoring during cancer therapy.

**References:** [1] Lambert S.A., 2012,ESMRMB,Lisbon.[2] Asbach P. 2010, Radiology 257:80-86.[3] Garteiser P. 2012,ESMRMB,Lisbon. [4] Posnansky O., 2012, Phys. Med. Biol., 57, 4023–4040. [5] Guo J., 2012, Phys. Med. Biol., 57, 4041–4053. [6] Stumpf M.P.H, 2012, Science,335, 665-666.[7] Sinkus, R, 2005, MRI, 159–165[8] Langtangen, HP: LNCSE, Vol. 2, 1999. [9] O'Doherty, RF, Anstey, NA, Geophys. Prospect. 19:430 (1971)