Time-dependent transverse relaxation reveals statistics of structural organization in microbead samples

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Purpose: To identify a novel kind of sensitivity to micrometer-level magnetic tissue structure in the transverse relaxation time course

Transverse relaxation in biological tissues is affected by diffusion of molecules across susceptibility-induced magnetic fields varying on the mesoscopic scale of paramagnetic cells, iron clusters, contrast doped extracellular space, etc. Recent theoretical analysis revealed an NMR signal metric that is exclusively sensitive to the statistics of the spatial organization of mesoscopic (cellular-level) tissue architecture.[1-3] In brief, both diffusion and transverse relaxation take their simplest form (Gaussian for diffusion and the monoexponential for relaxation) in the limit of long times when the diffusion distance covered by NMR-visible molecules is much greater than the characteristic length scale in the medium (e.g. the cell size). This asymptotic behavior is achieved with a slow power-law approach with a dynamical exponent taking half-integer values depending on the *type* of structural disorder in the medium (a proper definition is given below). In other words, *media can be random in a number of qualitatively distinct ways*.[1] Here we present the first direct experimental verification of such time-dependence of the transverse relaxation in disordered media of two distinct types. Specifically, we observe the theoretically expected behavior in a microbead phantom with two different types of structural disorder.

Theory

The characteristic power law approach of the transverse relaxation rate towards its long-time asymptote R_2^∞ can be visualized by computing the time derivative of the instantaneous time-dependent relaxation rate $\mathrm{d}R_2/\mathrm{d}t = -\mathrm{d}^2/\mathrm{d}t^2 \ln S(t) = \mathrm{const} \cdot t^{-\nu}$, where $S(t)$ is the free induction signal decay with time t. The *dynamical exponent* ν of the transverse relaxation has been shown to be connected to the type of structural organization, via $\nu = (p+d)/2$ in d dimensions.[3] Here p is the *structural exponent* determined in terms of how slowly the two-point correlation function $\Gamma_2 = \langle\chi(\mathbf{r})\chi(0)\rangle$ of magnetic susceptibility decreases at large point separation r.[2] Formally, p is defined via the asymptotic form $\Gamma_2 \sim k^p$ at $k \to 0$ of the Fourier-transformed $\Gamma_2(k)$ at small wave vectors k (corresponding to large r). **Fig. 1** shows $\Gamma_2(k)$ for microbead packings with the common short-range (Poissonian) disorder (structural exponent $p = 0$), and the maximally random jammed[4,5] (MRJ) packing ($p = 1$) associated with high volume fractions of ~65%. The predicted dynamical exponents for $\mathrm{d}R_2/\mathrm{d}t$ are $\nu = 3/2$ and $\nu = 2$, respectively.

Methods

Sample preparation: All samples were prepared in standard 5mm NMR tubes. We suspended polystyrene microbeads (Dynoseed TS10, Microbeads AS, Norway) in water doped with sodium chloride and Holmium(III) chloride hexahydrate ($HoCl_3 \cdot 6H_2O$) in various concentrations to adjust the solution density and magnetic susceptibility, respectively. Suspensions with 30% volume fraction of microbeads were prepared using a particle-density matched sodium chloride solution (c_{NaCl}=1.3M) to avoid sedimentation.[6] MRJ samples were prepared by particle sedimentation in c_{NaCl}=0.3M solution and careful removal of particle-free fluid from the top. **NMR measurements** were preformed on a Bruker DPX 200MHz using a standard zg30 sequence (AQT=4s, 16 aver., no spinning). The measurement acquisition parameters and shims were adjusted on pure D_2O sample. Heated and dried compressed air maintained the sample at T=309K during the measurement after an initial settling in period of about 5 minutes to ensure the preheated sample to reach thermal equilibrium. **Data Analysis:** The time derivative of $R_2(t)$ was calculated as the second derivative of -ln $S(t)$ using the Savitzky-Golay method with a linearly increasing kernel size[3] of $0.7 \cdot t$.

Results and Discussion

The experimental data from both sample types (**Fig. 2**) clearly follow the predicted power law exponents $\nu = 3/2$ and $\nu = 2$, thereby distinguishing short-range disorder from the MRJ packing. This provides the first experimental validation for the recently predicted way to distinguish different magnetic structural disorder types, and offers a new paradigm for characterizing and probing magnetic tissue structure.

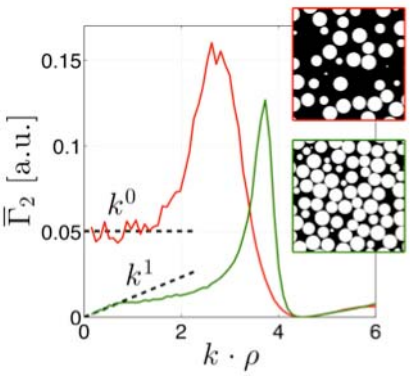

Fig. 1: Correlation functions of short-range disorder (red) and MRJ packing (green) for simulated media show the characteristic difference at low k, which translates into the measurable exponent ν.

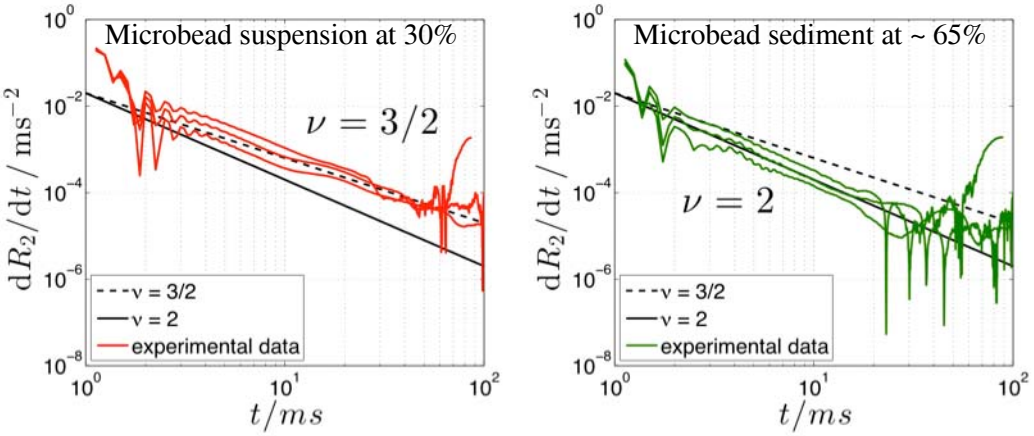

Fig. 2: Observed time derivative of the instantaneous transverse relaxation rate follows the theoretically predicted power law. The exponents $\nu = 3/2$ and $\nu = 2$ distinguish the random packing in the suspension and the dense, more ordered packing in the sediment (left and right, respectively). Shown are representative data sets with c_{Ho} = 1.5, 2.0 and 2.5 *m*M for the suspension (previously reported[6]) and c_{Ho} = 1.3, 1.8 and 2.3 *m*M for the sediment (new data). The exponent $\nu = 2$ is an evidence of the maximally random jammed state[4,5] in sediments.

Acknowledgement: This work was supported by DFG grant KI-1089/6-1. **References:** (1) D.S. Novikov et al. PNAS 111 (2014) 5088; (2) A. Ruh et al. Proc. ISMRM 20 (2012) 460; (3) A. Ruh et al. Proc. ISMRM 21 (2013) 3127; (4) S. Torquato et al. PRL 84 (2000) 2064; (5) A. Donev et al. PRL 95 (2005) 090604; (6) P. Emerich et al. Proc. ISMRM 22 (2014) 3124