Characterizing microstructure by a time-dependent transverse relaxation rate

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Introduction: Transverse relaxation in a uniform liquid, arising from dipole interactions on a molecular scale, is monoexponential. This follows by the virtue of the central limit theorem, from the many orders of magnitude difference between the correlation time of molecular motion (*ps*) and the typical time scale of MRI experiments (*ms*). Biological tissues possess structural complexity at the *mesoscopic* scale of micrometers [1], resulting in correlation times of *ms*, which is commensurate with the timing of MRI. The mesoscopic time scale is determined by diffusion of molecules across magnetic structure such as paramagnetic cells, iron clusters, contrast doped extracellular space, etc. The mesoscopic complexity induces the spatially-varying Larmor frequency offset $\Omega(\mathbf{r})$ and results in the *time-dependent relaxation rate* $R_2(t)$ that approaches a constant R_2^∞ only at long times. Here we relate the long-time dynamics of $R_2(t)$ to the statistics of large-scale organization of magnetic structure.

Results are presented in terms of the derivative $\mathrm{d}R_2/\mathrm{d}t$, which is zero for monoexponential relaxation. The difference in structural organization is depicted in the two-point Larmor frequency correlator $\bar{\Gamma}_2(k) = \langle \Omega(\mathbf{k})\,\Omega(-\mathbf{k})\rangle_{\mathbf{R}} / V$ and in particular characterized by the low-k behavior $\bar{\Gamma}_2(k\to 0) \sim k^p$, for example $p = 0$ for randomly positioned objects (Poissonian disorder) while for a perfectly ordered lattice $p = \infty$ [2,3]. Our main result for the approach of the asymptote, $R_2(t) = R_2^\infty - \mathrm{const}\cdot t^{-\nu+1}$, with the exponent ν in d dimensions, is given by Eq. (1).

$$\frac{\mathrm{d}}{\mathrm{d}t}R_2 = \mathrm{const}\cdot t^{-\nu} \quad \text{with} \quad \nu = \frac{d+p}{2} \qquad (1)$$

$$\frac{\mathrm{d}}{\mathrm{d}t}R_2(t) = \frac{1}{V}\int \frac{\mathrm{d}^d k}{(2\pi)^d}\,\Omega(-\mathbf{k})\,e^{-Dk^2 t}\,\Omega(\mathbf{k}) = \int \frac{\mathrm{d}^d k}{(2\pi)^d}\,\bar{\Gamma}_2(k)\,e^{-Dk^2 t} \qquad (2)$$

These expressions are obtained by finding the Green's function of the Bloch-Torrey equation using perturbation theory up to the second order in the Larmor frequency offset $\Omega(\mathbf{r})$. Here we present a physical picture behind the formal expressions in a way similar to that applied to heterogeneous diffusion [3]. Our analytical results are verified though numerical calculations and Monte Carlo simulations as described below.

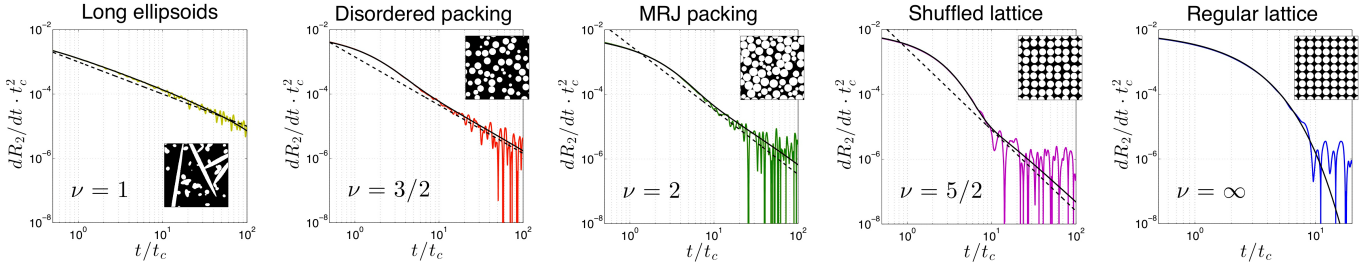
Discussion: It follows from the present result that $\mathrm{d}R_2/\mathrm{d}t$ equals the Fourier transformation of the self-energy part [2,4] that characterizes deviations from the Lorentzian line shape in the spectral domain. $\mathrm{d}R_2/\mathrm{d}t$ coincides with the temporal correlation function $K(t)$ introduced by Jensen and Chandra [5], who analyzed only Poissonian disorder. Here we consider a broad range of structural disorder classes as described below.

The origin of Eq. (1) and (2) can be understood in terms of well-known *diffusion narrowing*, as the effective self-averaging of the medium by diffusing molecules. The measure is the sample variance $(\delta\Omega)^2 \equiv \langle \Omega^2(\mathbf{r})\rangle$ of the Larmor frequency. The measured NMR signal from a macroscopically large sample is given by the average of the precession phase, $s(t) = \langle \exp(-i\varphi)\rangle \sim \exp(-\langle\varphi^2\rangle/2)$. Physically, each time a spin moves past the Larmor frequency correlation length l_c during the corresponding correlation time $t_c \sim l_c^2/D$, its phase acquires a random contribution $\sim \alpha = \delta\Omega\cdot t_c$. Over the long time $t \gg t_c$ the phase effectively acquires $N \sim t/t_c \gg 1$ such contributions, which results in the variance $\langle\varphi^2\rangle \sim N\,\alpha^2$ as the major effect according to the central limit theorem. This corresponds to the signal decay $s(t) \sim \exp(-R_2 t)$ with the rate $R_2 = -\mathrm{d}\ln s(t)/\mathrm{d}t \sim (\delta\Omega)^2\cdot t_c$. In what follows, we find it useful to consider its time derivative, representing this rate as $\mathrm{d}R_2/\mathrm{d}t_c \sim (\delta\Omega)^2$.

The deviation from the above monoexponential relaxation at long, but not infinitely long times, happens as a result of spatial *fluctuations* of $\Omega(\mathbf{r})$. Diffusion narrowing is in fact an averaging of medium properties over the diffusion length $L(t) \sim (Dt)^{1/2}$. This coarse-graining process can be described as a smoothing of the original Larmor frequency with a time-dependent Gaussian filter $\Omega(\mathbf{r}) \to \Omega_t(\mathbf{r}) \sim \exp(-r^2/[2\,L^2(t)]) \otimes \Omega(\mathbf{r})$. This results in a decreasing $\mathrm{d}R_2/\mathrm{d}t \sim (\delta\Omega_t)^2$ with the time dependence determined by the statistics of $\Omega(\mathbf{r})$, which we refer to as the disorder type. Using the identification $\Omega_t(\mathbf{k}) = \Omega(\mathbf{k})\cdot\exp(-Dk^2 t/2)$ in Eq. (2) yields exactly the same expression and validates these qualitative considerations.

Simulations: We illustrate our results using four types of structural organization of identical spherical susceptibility inclusions in three dimensions: a *disordered* packing with short-range (Poissonian) correlations ($p = 0$), a packing approximating a *maximally random jammed (MRJ)* state ($p = 1$), a *shuffled lattice* ($p = 2$), where the spheres are randomly displaced from their lattice positions, and for comparison a *regular lattice* ($p = \infty$) [2]. We also consider randomly placed long ellipsoids. With those objects effectively being one-dimensional $\bar{\Gamma}_2(k\to 0)$ is diverging with $p = -1$, cf. [3]. The Figures below show the exact exponents ν (dashed lines), which for long times are in good agreement with numerical integration in Eq. (2). For the regular lattice we observe an exponential decay, which agrees with the artificial exponent $\nu = \infty$. Colored lines show results of Monte Carlo simulations of freely diffusing spins with the dephasing strength $\alpha = \delta\Omega\cdot t_c = 0.10$. The second derivative of $\ln s(t)$ was obtained using a polynomial fitting with a linearly increasing kernel size (up to 20 t_c). The exponent $\nu = 1$ for long ellipsoids agrees with $\ln s(t) \sim t\ln t$ for blood vessels [6].

Conclusions: We have shown that the mesoscopic component of the transverse relaxation rate is sensitive to the spatial organization of magnetic structure causing this relaxation. The origin of this effect is the self-averaging, which is inherent to *diffusion narrowing*, when spins are exploring microstructure via diffusion. The present results enable an analysis scheme alternative to the previously proposed approach for the spectral domain [2], which broadens the possibilities to quantifying magnetic structure (e.g. iron, microvasculature) using measurements in the time domain.



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